UNIVERSITÉ DU QUÉBEC À TROIS-RIVIÈRES

MODIFICATION CHIMIQUE DU CHITOSAN POUR L'ÉLECTROFILAGE DE NANOFIBRES POUR L'ÉLIMINATION DES RÉSIDUS PHARMACEUTIQUES DE L'EAU ET DES EAUX USÉES

CHEMICAL MODIFICATION OF CHITOSAN FOR ELECTROSPINNING OF NANOFIBERS FOR REMOVAL OF PHARMACEUTICAL RESIDUES FROM WATER AND WASTEWATER

THÈSE PRÉSENTÉE COMME EXIGENCE PARTIELLE DU DOCTORAT EN SCIENCES ET GÉNIE DES MATÉRIAUX LIGNOCELLULOSIQUES

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RÉSUMÉ

De nombreuses études indiquent la présence de contaminants émergents (CE) dans les eaux usées traitées et dans les autres sources d'eau. Ces contaminants menacent l'environnement même à très faibles concentrations et requièrent des technologies de traitement des eaux plus efficaces. La pollution des eaux de surface et souterraines provoquée par le déversement de produits pharmaceutiques a été reconnue mondialement comme un problème environnemental important. Ces contaminants sont résistants à la dégradation, très persistants dans le milieu aqueux et potentiellement capables de produire des effets néfastes sur les organismes aquatiques et d'avoir un impact négatif sur la santé humaine. Leur libération dans l'environnement entraîne des conséquences néfastes telles que la bioaccumulation dans les organismes aquatiques tels que les poissons qui finissent par atteindre la population humaine. La principale préoccupation est de savoir comment les éliminer de l'eau pour la durabilité des ressources en eau lorsque les systèmes traditionnels de traitement des eaux usées se sont avérés inefficaces pour les éliminer. Il est donc vital de développer des technologies de traitement plus avancées capables de les éliminer des eaux usées.

Des études récentes ont montré que le chitosane (CS) est l'un des matériaux les plus prometteurs dans les domaines pharmaceutique et biomédical en raison de sa structure chimique unique, il possède d'excellentes propriétés physicochimiques et des capacités de sorption sur les ions métalliques et les colorants. Les modifications chimiques du CS sont devenues de plus en plus étudiées pour le traitement de l'eau et des eaux usées en raison de leurs propriétés physico-chimiques uniques et de leur excellente sélectivité vis-à-vis des composés organiques. L'adsorption est reconnue comme l'une des techniques les plus efficaces et les plus pratiques pour éliminer les polluants de l'eau. De plus, l'électrofilage est largement considéré comme un excellent choix pour produire des membranes absorbantes en raison de sa capacité à produire des nanofibres dans une surface spécifique élevée. Ce projet était axé sur les modifications chimiques de la surface du chitosane par N-carboxyméthylation du

chitosane (NOCMCS), N-succinylation du chitosane (NSCS) et N-arylation du chitosane (N-ArCS) pour introduire des groupes chimiques appropriés pour l'élimination de contaminants pharmaceutiques présélectionnés. Ensuite, l'électrofilage du polymère a été réalisé, avec l'oxyde de polyéthylène (PEO) comme copolymère, pour fabriquer un matériau biosorbant à base de nanofibres qui pourrait être utilisées pour éliminer les contaminants des solutions aqueuses. Les propriétés chimiques de ces nouveaux substrats ont été caractérisées par spectroscopie FT-IR et analyse ^{1}H-NMR. Les propriétés géométriques et morphologiques des nanofibres ont été caractérisées par microscopie électronique à transmission (TEM) et microscopie électronique à balayage (SEM). Des tests de désorption ont été effectués en modifiant les conditions expérimentales, par exemple le pH, la concentration de fluoxétine, ibuprofène, venlafaxine, carbamazépine et la température. La composition des filtrats a été analysée par chromatographie liquide à haute performance avec un détecteur par réseau de diodes ultraviolettes (HPLC-UV-DAD). Des nanofibres de CS modifié et de PEO ont été développées et testées sur l'adsorption d'un contaminant pharmaceutique (fluoxétine) dans une solution aqueuse.

Les résultats ont démontré que le pH de la solution influence fortement les interactions électrostatiques, les attractions π-π et l'interaction hydrophobe entre la charge de surface nette de l'adsorbant et la charge électrique des molécules Fluoxétine (FLX). En comparaison avec d'autres adsorbants commerciaux et synthétisés, les nanofibres de NOCMCS /PEO ont obtenu les meilleurs résultats pour l'adsorption de FLX à pH 8,0 (capacité d'adsorption jusqu'à 79,7 ± 7,9 mg/g). L'efficacité d'élimination maximale (capacité d'adsorption) obtenue était respectivement de 72,22 % pour les nanofibres NPCS/PEO et de 81,16 % pour les nanofibres NSCS/PEO, ce qui a également démontré un bon candidat pour l'élimination du FLX des eaux usées.

En conclusion, l'applicabilité de l'approche proposée a été étudiée là où l'adsorption et l'élimination du polluant étaient efficacement accomplies, il a été vérifié que les dérivés CS modifiés adsorbants (NOCMCS), (NPCS) et (NSCS) ont montré la capacité pour adsorber FLX. Les résultats démontrent que les

membranes en nanofibres CS modifiées ont le potentiel d'atténuer l'encrassement dans les applications de traitement de l'eau. De plus, les nouvelles nanofibres super adsorbantes NSCS/PEO, NOCMCS/PEO et NPCS/PEO ont le potentiel d'être une nanofibre de biomatériau adsorbant viable qui est efficace, durable sur le plan environnemental et représente une meilleure stratégie pour éliminer les résidus pharmaceutiques de l'eau et des eaux usées. Cela pourrait profiter à la société autant économiquement que environnementalement.

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Mots clés : Traitement des eaux usées; Contaminant émergent; contaminants pharmaceutiques; modification du chitosane; électrofilage; nanofibres; adsorption / Désorption.

ABSTRACT

Many reports indicate the presence of emerging contaminants (ECs) in treated wastewater and other water sources. Environmental contaminants posing threats to the environment at very low concentrations have led to a need for more efficient treatment technologies as a result of their detection in the environment. The pollution of surface and ground waters triggered by the dumping of pharmaceutical products has been recognized globally as an environmental problem. These contaminants are resistant to degradation, very persistent in the aqueous medium and potentially capable of producing adverse effects in aquatic organisms and have a negative impact on human health. Their release into the environment causes detrimental consequences such as bioaccumulation in aquatic organisms such as fish that eventually reaches the human population. The main concern is how we eliminate them from water for the sustainability of water resources when traditional wastewater treatment systems have been found inefficient in removing them. Therefore, it is vital to develop more advanced treatment technologies capable of removing them from wastewater.

Recent studies have been shown, chitosan (CS) is one of the most promising materials in the pharmaceutical and biomedical fields based on its unique chemical structure, it has excellent physicochemical properties, and sorption capabilities on metal ions and dye. Chemical modifications of CS have become increasingly popular for water and wastewater treatment due to their unique physico-chemical properties and excellent selectivity towards organic compounds.

Adsorption is recognized as one of the most effective and practical techniques for the removal of pollutants from water. In addition, electrospinning is widely considered as an excellent choice to produce sorbent membranes because of its ability to produce nanofibers within high specific surface area. This project was focus on the chemical modifications of chitosan's surface by N,O-carboxymethylation of chitosan (NOCMCS), N-succinylation chitosan (NSCS), and N-arylation of chitosan (N-ArCS) to introduce suitable chemical groups for the

removal of preselected pharmaceutical contaminants. Then, electrospinning of the polymer was carried out to make nanofibers bio-sorbent material that could be used to remove contaminants from aqueous solutions. Efforts is required for the optimization of the electrospinning parameters for the creation of nanofibers. The chemical characterization of these new substrates was verified by using FT-IR spectroscopy and ^{1}H-NMR analysis. The geometric and morphological properties of nanofibers were characterized by transmission electron microscopy (TEM), and Scanning electron microscopy (SEM). With the use of high-performance liquid chromatography with ultraviolet diode array detection (HPLC-UV-DAD) system, sorption tests were performed by modifying experimental conditions, e.g., pH, the concentration of (Fluoxetine, Ibuprofen, Venlafaxine, and Carbamazepine) and temperature of the tested solutions. Nanofibers of modified Chitosan and a copolymer, polyethylene Oxide (PE), were developed and tested on the adsorption of a pharmaceutical contaminant (fluoxetine) in an aqueous solution.

The results revealed that the solution pH strongly influences the electrostatic interactions, π-π attractions, and hydrophobic interaction between the net surface charge of the adsorbent and the electric charge of Fluoxetine (FLX) molecules. In comparison with other commercial and synthesized adsorbents, N, O-CMCS/PEO nanofibers performed best in adsorption of FLX at pH 8.0 (adsorption capacity up to 79.7 ± 7.9 mg/g). The maximum removal efficiency (adsorption capacity) obtained were 72.22% for NPCS/PEO and 81.16% for NSCS/PEO nanofibers respectively, which also demonstrated a good candidate for removal FLX from wastewater. In conclusion, the applicability of the proposed approach was studied where the adsorption and the removal of the pollutant were efficiently accomplished it was verified that the adsorbent modified CS derivatives (NOCMCS), (NPCS) and (NSCS) showed the capacity to adsorb FLX.

The results demonstrate that modified CS nanofiber membranes have the potential to mitigate fouling in water treatment applications. The novel super adsorbent nanofibers NSCS/PEO, NOCMCS, and NPCS have the potential to be a viable adsorbent biomaterial nanofiber that is efficient, environmentally

sustainable, and a better strategy for removing pharmaceutical residues from water and wastewater. This could save money while also benefiting society and the environment.

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Keywords: Wastewater Treatment; Emerging contaminant; pharmaceutical contaminants; Chitosan modification; Electrospinning; Nanofibers; Adsorption / Desorption.

FOREWORD

The presence of pharmaceutical compounds in the environment and their potential effects constitute the focus of health organizations worldwide. However, pharmaceutical compounds continue to be released into the environment by medical facilities, private households and production effluents. Pharmaceuticals as emerging pollutants have become a major concern because of their low biodegradability, high persistence, and ease of bioaccumulation. These compounds include diverse types of pharmaceuticals, such as antibiotics, anti-inflammatory agents, blood lipid regulators, and steroidal hormones. Their release freely into the environment causes detrimental consequences such as bioaccumulation in aquatic organisms. The main concern is how we remove them from water for the sustainability of water resources when traditional wastewater treatment systems have been found inefficient in water remediation them. Therefore, it is vital to develop new advanced treatment technologies to remove them from wastewater.

Recent studies have been shown, chitosan (CS) is one of the most promising materials in the pharmaceutical and biomedical fields based on its unique chemical structure, it has excellent physicochemical properties. Chitosan derivatives by chemical reactions of the hydroxyl or amine groups have been shown to improve either water solubility or chemical properties. As part of the proposed doctoral project, various avenues being explored in order to develop, by electrospinning, effective, inexpensive nanofibers based on biomaterials (CS) to purify wastewater of various contaminants. Specifically, the research aims to reduce at source the residues of emerging products generated by the citizens and hospitals of large municipalities.

Develop a new low-cost and environmentally friendly adsorbent material with high adsorption capacity that may contribute to water sustainability and recognized as an excellent alternative to existing technologies for removal of emerging contaminants (pharmaceuticals) from wastewater. Thus, the development of new technologies and materials that can overcome this problem critical and essential

for water sustainability. In the near future, the new nanofibers prototypes will be tested on real water samples.

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$q_e = k_F C_e^{\frac{1}{n}}$	Equation2.8	36
$Inq_e = InK_F + \frac{1}{n} InC_e$	Equation2.9	36
$q_e = \frac{RT}{b} In(aC_e)$	Equation2.10	37
$q_e = a + bInC_e$	Equation2.11	37
$\Delta G^0 = -RTInK_c$	Equation2.12	37
$InK = \frac{\Delta S^0}{R} - \frac{\Delta H}{RT}$	Equation2.13	37
$\Delta G^0 = \Delta H^0 - T\Delta S^0$	Equation2.14	38
$DS = \frac{161A}{M_{CMCS-CS}} - 58A$	Equation5.15	67
$A = V_{NaOH} . C_{NaOH}$	Equation5.16	67
$Q_t = \frac{(C_0 - C_e)V}{m}$	Equation5.17	68
$Q_t = Q_e (1 - \exp^{-K_1 t})$	Equation5.18	69

$Q_t = \frac{K_2 Q_e^2 t}{1 + k_2 Q_e t}$	Equation5.19	69
$DS = \frac{161A}{M_{NSCS}} - 283A$	Equation6.20	95
$A = V_{NaOH} \cdot C_{NaOH}$	Equation6.21	95
$Q_e = \frac{(C_0 - C_e)}{W} V$	Equation6.22	99
$Q_t = Q_e\left(1 - \exp^{-k_1 t}\right)$	Equation6.23	100
$Q_t = \frac{K_2 Q_e^2 t}{1 + K_2 Q_e t}$	Equation6.24	100
$q = \frac{(C_0 - C_t)}{m} V$	Equation7.25	135
$q_t = q_e(1 - \exp^{-K_1 t})$	Equation7.26	136
$q_t = \frac{k_2 q_e^2 t}{1 + k_2 q_e^t}$	Equation7.27	136

ABBREVIATIONS

AA	Acetic acid
ACA	Acrylic acid
AC	Activated carbons
AOPs	Advanced oxidation processes
ArCS	N-arylation of chitosan
BET	Brunauer–Emmett–Teller
BOD	Biochemical oxygen demand
β-CD-CMC	β-Cyclodextrin carboxymethyl cellulose
CBZ	Carbamazepine
CMCS	Carboxymethyl-chitosan
COD	Chemical oxygen demand
COO	Carboxylate
CS	Chitosan
CSS	Chitosan succinate
CSP	Chitosan phthalate
CNTs	Carbon Nanotubes
CD	Cyclodextrin
DD	Deacetylation degree
DMSO	Dimethyl sulfoxane
DCA	Dichloroaceticacid
ECs	Emerging contaminants
EDCs	Endocrine disrupting compounds
EDTA	Ethylenediaminetetraacetic Acid
FA	Formic acid
FLX	Fluoxetine
FT-IR	Infrared spectroscopy
FRQNT	Fonds de recherche du Québec-Nature et Technologies
GAGs	Glycosaminoglycans
GC	Gas chromatography
HPLC-UV	High performance liquid chromatography-ultraviolet detector
HPLC-MS	High performance liquid chromatography-mass spectrometry
IUB	Ibuprofene
OH	Hydroxyl group
OSCS	O-Succinyl of chitosan
LNASP	Libyan-North American Scholarship Program (LNASP)
MBRs	Membrane bioreactors
MF	Microfiltration
MO	Morphine
MW	Molcular weight
NF	Nanofiltration
NCMCS	N-carboxymethylation of chitosan
NSERC	Natural Sciences and Engineering Research Council
NPCS	N-Phthalic chitosan
NSCS	N-succinylation chitosan
N-ArCS	N-arylation of chitosan
^{1}H-NMR	Proton nuclear magnetic resonance
PAA	Polyacrylic acid
PhACs	Pharmaceutical active compounds
PAHs	Polycyclic aromatic hydrocarbons
PCBs	Polychlorinated biphenyls
PCL	Polycaprolactone
PEO	Polyethylene oxide

PFO	Pseudo-first-order kinetic model
Pka	Acid dissociation constant
PLLA	Poly-L-lactide
PPCPs	Pharmaceutical and personal care products
PVC	Polyvinyl chloride
PH	Relative humidity
PSO	Pseudo-second-order kinetic model
R-P	Redlich–Peterson
RO	Reverse Osmosis
ROS	Reactive oxygen species
SEM	Scanning electronic microscopy
SS	Suspended solids
STPs	Sewage Treatment Plants
TEM	Transmission electronic microscopy
TFA	Trifluoroacetic acid
UF	Ultrafiltration
UK	United Kingdom
UV/H_2O_2	Advanced oxidation process
VEL	Venlafaxine
WWTPs	Wastewater treatment plants
ZP	Zeta potential

CHAPTER 1 – INTRODUCTION

1.1 Background

Contamination of water by pharmaceutical and personal care products (PPCPs) and other emerging contaminants is unavoidable as long as their uses remain indispensable components of a modern and healthy society (1). The occurrence and fate of pharmaceutically active compounds (PhACs) have become a major environmental issue for researchers in the 21st century (2). These compounds can find their way into the aquatic environment through several paths: excretion from human and animal systems, leaching from landfill, manure or biosolids applications, and improper disposal. Removal rates during wastewater and drinking water treatment are dependent on physical and chemical properties of molecules (3). There has always been a huge demand for water on earth, since time immemorial. Globally, billions of cubic meters are consumed each year. In order to preserve the quality of water, we need to develop innovative methods and materials (4). Both developed and developing countries are experiencing an increase in water pollution, undermining economic growth and human health (5). In developing countries, untreated sewage causes approximately 14,000 deaths per day due to water pollution (6). There is universal recognition that urban effluents pose health and environmental concern. As wastewater compositions become more complex, treatment processes become more expensive. In fact, they are crucial in light of the large amounts of waste produced both domestically and in industries. Therefore, cheap and simple methods of decontamination are essential (7). Surface and ground waters around the world are becoming increasingly contaminated and unsafe to drink. By 2050, the global population is expected to reach 9.8 billion (5). As shown in Figure 1.1, we may be facing greater freshwater shortages in the future. Additionally, most industrial countries will become more concerned about water pollution as regulations become stricter (8).

Figure 1.1 Water consumption by sector, 1995 and 2025 (5)

There has been considerable research into emerging organic contaminants such as pesticides (9), antibiotics, pharmaceuticals, drugs (illicit drugs), endocrine disrupting compounds (EDCs), steroids, hormones, personal health care products, disinfectants, disinfection by-products and those associated with oil and gas combustion (10). It is unclear how these chemicals behave in the environment, and there is no information on their fate (11). Various sources of organic contaminants in aquatic systems include wastewater treatment plants, on-site sanitation systems, livestock and crop production systems, animal and human health facilities, and waste dumps and landfills (10). Organic pollutants have many side effects and are carcinogenic, making them extremely harmful to human health and wildlife (12). Besides the parent compound, organic contaminants can be toxic if they have been biotransformed to electrophilic metabolites or free radicals, or if they are stimulated to produce reactive oxygen species (ROS) (13). Table1.1 summarizes the concentrations data of various pharmaceuticals present in effluents from Sewage Treatment Plants (STPs) or Wastewater Treatment Plants (WWTPs) and surface waters that published in literature between 2006-2009 (14). Therefore, in the current scenario, toxic organic pollutants must be removed from water.

Table 1.1 Occurrence and concentrations obtained from a literature survey of the various pharmaceuticals in effluents from Sewage Treatment Plants (STPs), Wastewater Treatment Plants (WWTPs) and surface waters (14).

Compounds	Range in concentration (ng/l)						Lowest PNEC (ng/l)	Percentage of parent compound excreted
	North America		Europe		Asia and Australia			
	Effluent, WWTP/ STP	Freshwater-rivers, canals	Effluent, WWTP/ STP	Freshwater-rivers, canals	Effluent, WWTP/ STP	Freshwater-rivers, canals		
Antibiotics								
Trimethoprim	<0.5-7900	2-212	99-1264	0-78.2	58-321	4-150	1000	≥70
Ciprofloxacin	110-1100	-	40-3553	-	42-720	23-1300	20	≥70
Sulfamethoxazole	5-2800	7-211	91-794	<0.5-4	3.8-1400	1.7-2000	20,000	6-39
Analgesics and anti-inflammatory								
Naproxen	<1-5100	0-135.2	450-1840	<0.3-146	128-548	11-181	37,000	-
Ibuprofen	220-3600	0-34.0	134-7100	14-44	65-1758	28-360	5000	≤5
Ketoprofen	12-110	-	225-954	<0.5-14	-	<0.4-79.6	15.6x106	-
Diclofenac	<0.5-177.1	11-82	460-3300	21-41	8.8-127	1.1-6.8	10,000	6-39
Salicylic acid	472-180	70-121	40-190	<0.3-302	9-2098	-	-	6-39
Mefenamic acid	-	-	1-554	<0.3-169	4.45-396	<0.1-65.1	-	-
Acetominophen	-	24.7-65.2	59-220	12-777	1.8-19	4.1-73	9200	5
Antiepilectic								
Carbamazepine	11.2-187	2.7-113.7	130-290	9-157	152-226	25-34.7	25,000	≤5
Beta-blockers								
Propanolol	-	-	30-44	20	00-50	-	500	<5
Atenolol	879	-	1720	214	-	-	10x106	50-90
Blood lipid regulators								
Clofibric acid	ND-33	3.2-26.7	27-120	0.1-14		22-248	12,000	-
Gemfibrozil	9-300	5.4-16	2-28.571	-	3.9-17	1.8-9.1	100,000	-
Bezafibrate	ND-260	-	233-340	16-363	-	-	100,000	40-69

Several studies have identified pharmaceutically active compounds (PhACs) as the leading cause of water pollution (15). According to research, about 90% of PhACs are excreted unmetabolized through urine or stool and enter domestic wastewater systems. As a result of ineffective water treatment, PhACs can be released into the environment via WWTP effluents (16). The pharmaceuticals and personal care products (PPCPs) class is a growing category of contaminants, including medicinal, cosmetic, and personal hygiene products. Surface, ground, coastal, and even drinking water have been detected with PPCPs. As a result of their potential adverse effects on human health and the ecological system, pharmaceutical residues in aquatic environments have raised concerns from many countries. PPCPs contain a wide range of organic compounds (17). Determination of pharmaceuticals and para-pharmaceuticals in environmental samples requires very sensitive and selective techniques of final analysis. At present chromatographic techniques, especially high-performance liquid chromatography (HPLC) and gas chromatography (GC), are mainly used (18).

The presence of pharmaceuticals in different compartments of the environment is a new challenge not only for technologists of water and wastewater treatment but also for analytical chemists involved in development of new analytical methods. Many drugs are not completely degraded in the human body. They are often excreted after only slight transformation or in unchanged form, mainly as polar molecules (11). Predicted paths of pharmaceuticals present in treated wastewater are shown in figure 1.2.

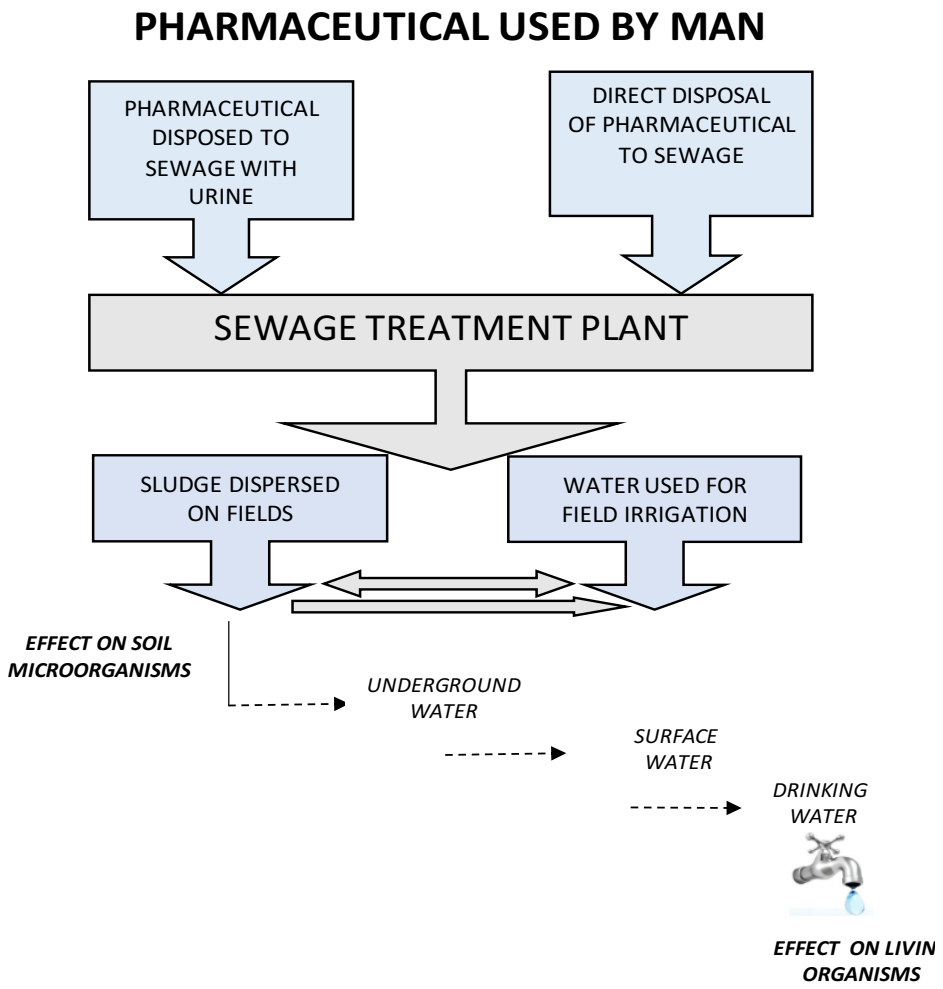

Figure 1.2 Pharmaceutical paths predicted in treated wastewater

Pharmaceutical wastewater treatment methodologies need to be introduced and applied in response to the ever-growing need for wastewater remediation techniques (19). It is desirable to establish environmentally benign and

economically cost-effective measures to keep such pollution under control. Significant efforts have already been made to improve wastewater treatment with different approaches, such as adsorption, coagulation, photocatalytic oxidation, and biodegradation (20). Unfortunately, their effectiveness in actual applications is frequently hampered by various factors (21), such as energy, efficiency, stability, and economy. Each approach has its own pros and cons, and none has the merits in all aspects. Nevertheless, scientists have never stopped looking for practices that can improve water treatment. The combination of biodegradation and nanotechnology is suggested as a potential efficient, low-cost, and environmental benign technique (22). Post-treatment techniques such as ozonation, membrane filtration (MF) and sorption on activated carbon (AC) are possible methods for removing most (PPCPs). Among these treatments, ozonation and AC are either too expensive or not effective enough. Few studies have been conducted on the use of AC as a sorbent to remove some pharmaceuticals. However, its high production costs and lack of environmental friendliness made it an unattractive and unsuitable adsorbent strategy against pharmaceutical traces (23). Studies involving the removal of pharmaceuticals with membrane bioreactors (MBRs) indicated that membrane technology would not completely eliminate micropollutant generation. Typically, WWTPs comprise a primary physicochemical treatment system and a secondary biological reactor formed from activated sludge (24).

In most cases, advanced physical techniques are the best option for treating the problem. It is now known that adsorption is one of the most effective ways to remove pharmaceuticals (ECs) from drinking water and wastewater (25). So far, AC and zeolites have been tested as effective adsorptive materials for wastewater treatment (26). While these adsorbents are highly efficient, they have several drawbacks, such as their lack of stability and inability to be recycled, which can lead to long and costly regeneration processes. For these limitations to be overcome, an impressive amount of effort has been directed toward developing low-cost, effective, and environmentally friendly polymeric adsorbents. Polysaccharides remain an interesting material due to their outstanding physical

and biological properties (27). It is important to consider and characterize the efficiency of processes for the removal of substances during wastewater and drinking water treatments (28). WWTPs have demonstrated varying removal rates, ranging from less than 20% to greater than 90% (29). Thus, the development of techniques and materials that can overcome this problem are essential and urgent. The use of biopolymer materials to produce electrospun nanofibers for the removal of PhACs from aqueous solutions by the adsorption process is promising and relevant.

Various domestic and industrial activities produce wastewater. There is a wide range of inorganic, organic and biological contaminants in it that are detrimental to the environment. Without proper oversight and treatment, these contaminants can pose health hazards. Among the sources of organic chemical pollutants are trace organic compounds, biodegradable materials, and floating substances. Among the sources of inorganic chemical pollutants are nutrients, trace metals, and inorganic gaseous pollutants. In addition to pathogenic bacteria, biological pollutants come from other sources. Finally, dissolved solids and suspended solids are sources of physical pollutants (30). Between 1999 and 2000, wastewater treatment and disposal problems have also increased (31).

Throughout this section, municipal wastewater purification, clarification, and disinfection techniques will be explored. Generally, the main types of treatments are preliminary (physical), primary (physical), secondary (biological), and tertiary. Evaluations will be conducted for every category in relation to their effectiveness in removing PPCPs. Figure 1.3 Shown the scheme of an activated sludge treatment plant.

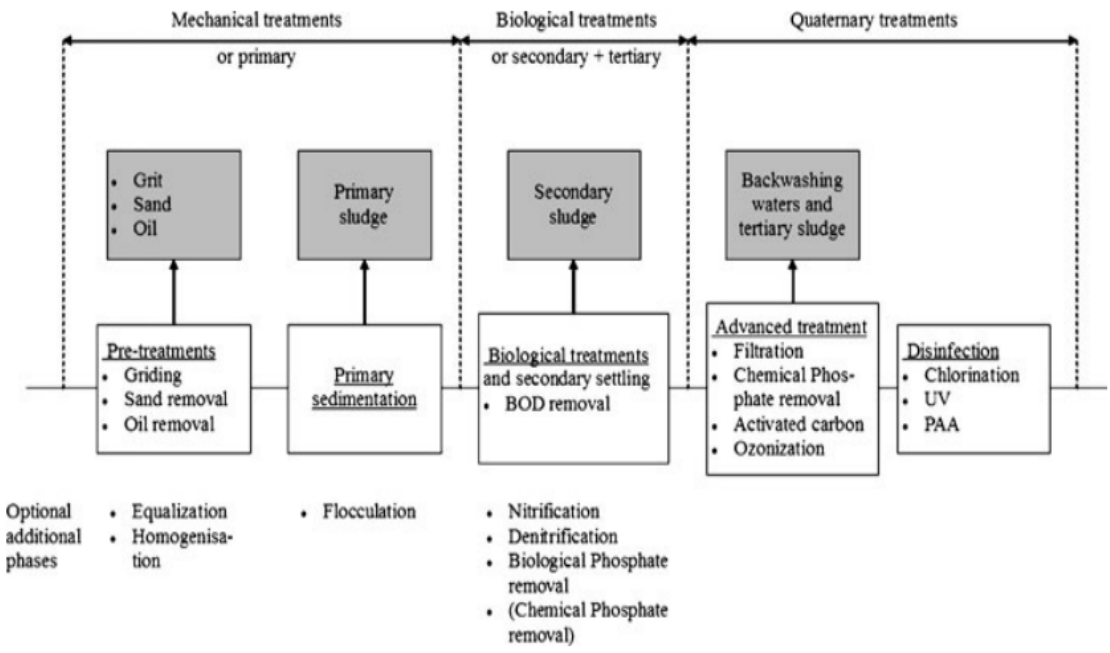

Figure 1.3 Scheme of an activated sludge treatment plant (32)

In adsorption applications, chitosan (CS) is one of the most promising and applicable materials. It has been shown that amino and hydroxyl groups on the molecules contribute to adsorption interactions between CS and pollutants (dyes, metals, ions, phenols, pharmaceuticals/drugs, pesticides, herbicides, etc.). Hence, these functional groups may assist in the establishment of modifications to the molecules (33). Furthermore, these functional groups are subjected to modifications (crosslinking and grafting) that could enhance their adsorption efficiency and specificity (34). In recent years, CS has been used in water and wastewater treatment industries as an adsorbent due to its high content of amino and hydroxyl functional groups (35). In some cases, CS is able to remove pollutants with high efficiency. In contrast to other polysaccharides (cellulose or starch), CS has a chemical structure that allows specific modifications to design polymers that are suitable for specific applications. Additionally, their reactive groups can be used to develop composites with other compounds that can adsorb wastewater pollutants and can withstand acidic environments (36).

The chemical modification of CS may open up new possibilities for obtaining materials with designed properties. Chemical and physical modifications of raw

CS led to the production of many derivatives of CS. Among them are cross-linking, grafting, and impregnation of the CS backbone (37). As a result of graft modification, many efforts were made to improve the solubility and physicochemical properties of CS (38). The basic structure of CS is not altered by chemical modification. It does, however, introduce new derivatives with improved properties for special applications (39). Thus, the adsorption properties of CS are improved in acidic media as well as their mechanical strength and chemical stability. Generally, cross-linking will reduce adsorption capacity since cross-link agents will bind with amino groups, making them unavailable (40). The reactive functional groups in the cross-linking agent structure can also enhance the adsorption capacity by cross-linking (41). Alternatively, hydroxyl and amine groups of chitosan can be directly covalently bound to different monomers to give new functional polymers. By increasing the density of functional groups in CS, grafting improves its sorption potential. It is also possible to increase the sorption properties of CS by grafting carboxylic functional groups on it. The synthesis of CMCS has been achieved by reaction of CS with chloroacetic acid in a suitable solvent (42). The NSCS exhibits remarkable biocompatibility as well as increased aqueous solubility without impairing its biological properties. Additionally, NSCS is excellent at absorbing moisture, has superior chelating abilities, significant apoptosis inhibitory activity, remarkable enzyme immobilization activity, strong antioxidant activity, and a higher bioactivity than its parent molecule CS. Consequently, researchers have extensively studied the biomedical applications of NSCS due to its intriguing properties (43). The scientific community has become increasingly interested in electrospinning over the last decade. Currently, ultrafine polymeric fibers are produced using this innovative and efficient technology. As a result of its versatility and low cost, electrospinning can potentially be used for a wide range of nanotechnology applications (44). Nanofibers can be produced with diameters ranging from a few nanometers to a few hundred nanometers using this process (45). A considerable amount of attention has been paid to nanofibrous composite materials such as CS nanofibres because of their remarkable properties and abundant availability.

Certain pollutants can be easily absorbed by them by adding specific functional groups (46). In addition, they offer an interesting solution to healthcare applications (47). In order to fabricate the required structures for the above-mentioned applications, chitosan-based electrospun nanofibers are a crucial step. With the aim of developing electrospun modified chitosan-based nanofibers with maximum chitosan content in stable electrospinning conditions, this thesis aims to develop fibers suitable for various applications, such as wound healing dressing membranes, heavy metal ion removal, and pharmacological residue removal.

Throughout this study, modified electrospun nanofibers will be examined for their potential use. In particular, chemically modified chitosan (CS) materials can easily be electrospun. It may be possible to remove pharmaceutical contaminants from wastewater by using such materials. While CS has been used in various research areas, their use as an absorbent for pharmaceutical removal has not been reported. For a better understanding of their effectiveness in water treatment, electrospinning solutions were evaluated based on their rheology, surface tension, electric conductivity, and charge demand while nanofiber membranes were examined based on their morphology, chemical composition, and thermal properties. Under controlled conditions, batch adsorption experiments were conducted to determine the effects of contact time, temperature, and pharmaceutical concentrations on adsorption capacity. In order to fit the kinetic adsorption data, pseudo-first order (PFO) and pseudo-second order (PSO) kinetic models were tested. Using HPLC-UV DAD method, the efficiency of the modified chitosan membrane was assessed. Using direct measurement of the effluent, contaminants were quantified in the chitosan adsorbent. As shown in figure 1.4, we outline the proposed project.

As compared to other commercially and synthetically produced adsorbents, the developed adsorbent had a greater adsorption capacity for removing FLX. It may prove to be an excellent alternative to existing technologies to develop low-cost bio adsorbents with high adsorption capacities. With this technology, people who already suffer from a lack of potable water can prevent diseases that can result from excessive consumption of contaminated water.

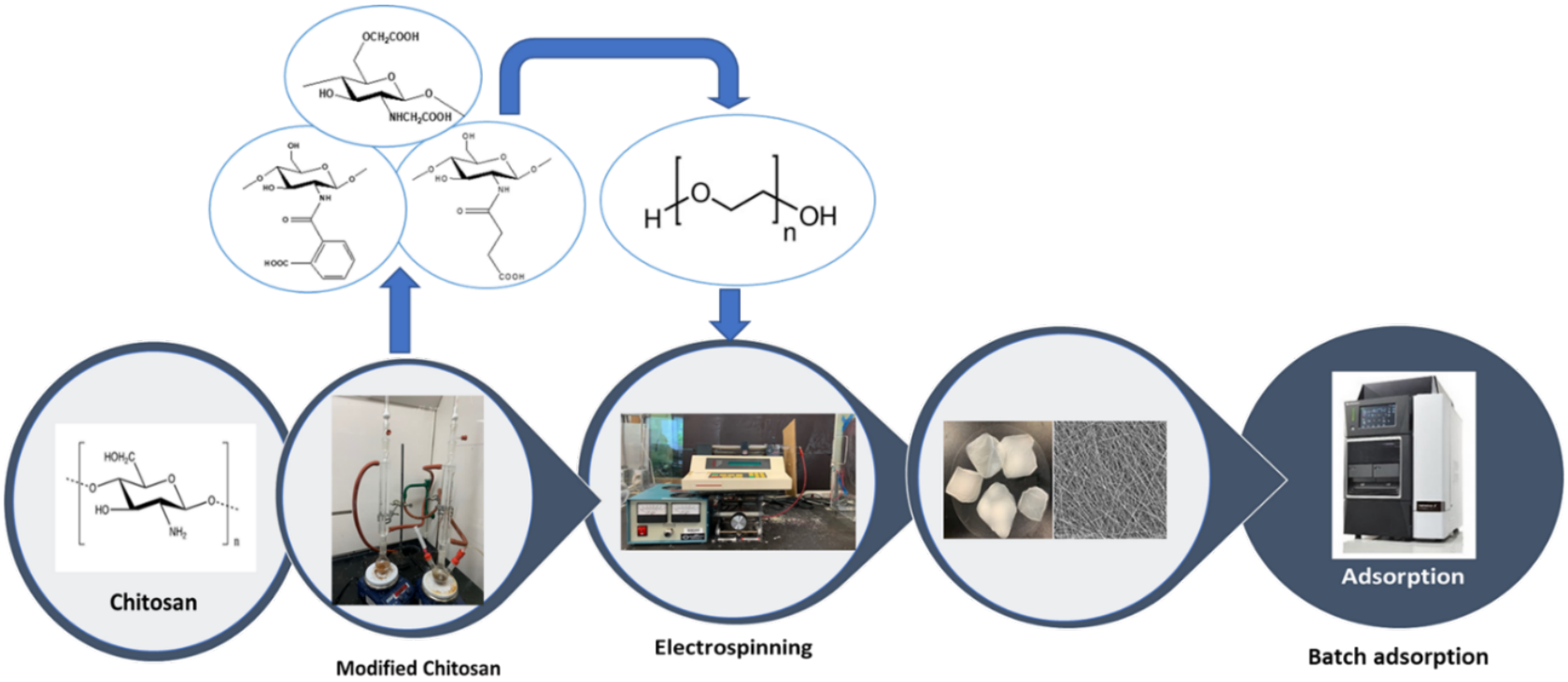

Figure 1.4 Schematic diagram of the proposed project

1.2 Research Objectives

1.2.1 Main objectives of this project are:

- Developing new materials and methods to make a novel adsorbent for the removal of ECs of interest that may bring a larger perspective for achieving the desired results and reduce the daily load of WWTPs;

- Improving the adsorption capacity of nanofibers to remove pollutants and bring interesting properties by chemically modifying CS using simple chemical reactions;

- Using electrospinning technology to generate nanofiber bio-sorbent materials which could be employed and reused in the adsorption of pharmaceuticals from aqueous solutions.

1.2.2 Specific objectives are:

- Synthesizing various chemical modification routes (alkylation, acylation, and arylation) of CS and evaluating the efficiency of the resulting chemical groups used to remove some preselected pharmaceutical contaminants such as flexitarian, ibuprofen, venlafaxine, and carbamazepine;

- Performing chemical characterization of the CS derivatives using Fourier Transformed Infrared Spectroscopy (FT-IR), and Nuclear Magnetic Resonance (^{1}H-NMR);
- Electrospinning parameters was optimized to create new nanofibers based on natural nanomaterials and synthetic polymers (i.e., polyethylene oxide (PEO));

- Evaluating sorption performance of modified chitosan by using kinetics, thermodynamics, and sorption isotherms;

- Studying the morphological properties of nanofibers characterized by scanning and electronic microscopy (SEM);

- Evaluating the efficiency of the chitosan modified membrane by HPLC-UV DAD coupled either with UV detector.

- Understand the nature and the theory behind chemical interactions (bonding) between pharmaceutical and nanofiber material

1.3 Organization of dissertation

There are seven chapters in this thesis. In **Chapter 1**, We have described and motivation was given for the work in this thesis. In the introductory chapter, the research question, problem statement, and research objectives are discussed.

An overview of the methodology used in the analysis is presented in **chapter 2**, this dissertation consists of a review of the relevant literature, followed by an analysis of its originality and main objectives, followed by an analysis of relevant literature concerning ECs, as well as treatments for ECs, including adsorption and electrospinning, which are considered green technologies. Furthermore, we will provide an overview of chitosan, as well as chemical modifications of chitosan, as well as applications of chitosan in removing various environmental pollutants. A batch adsorption experiment, electrospinning apparatus, and methodology for synthesizing materials and applications of modified chitosan are discussed in **chapter 3**, explaining and justifying the research methodology that was used.

Chapter 4 presents a general discussion of the main results, followed by three scientific articles in **chapter 5, 6 and 7**. The thesis presents the main contributions as scientific papers that have been published or submitted to scientific journals collection methods as well as the scope and parameters of the experiments. In general, **chapters 5,6, and 7** focuses on experimental conditions for synthesizing various adsorbents. These adsorbents have been synthesized by chemically altering chitosan, selecting the best adsorbent, optimizing electrospinner parameters, and adjusting adsorption conditions of pH to remove pharmaceutical contaminants. As part of this chapter, preliminary tests were conducted to evaluate the performance of the adsorbents with pharmaceutical contaminants, regeneration studies with various conditionals, and characterization techniques used to confirm and understand the mechanisms involved.

Chapter 8 concludes this thesis by summarizing the main findings and suggesting future research directions.

CHAPTER 2 - LITERATURE REVIEW

2.1 Emerging Contaminants (ECs)

Emerging contaminants (ECs) are chemical compounds that have various structures, are potentially harmful, and whose risk to the environment and to humans is not fully understood. They were either previously unknown or not detected and were consequently not monitored (48). Due to the relatively new introduction or detection of these pollutants, there exists a gap in the knowledge of their fate, behaviours and effects, as well as on treatment technologies for their efficient removal (49).

Various emerging contaminants (ECs) have been identified in treated wastewater and other water sources over the last few years (50). These ECs are ubiquitous in the aquatic environment, mainly derived from the discharge of municipal wastewater effluents. Their presence is of concern due to the possible ecological impact (e.g., endocrine disruption) to biota within the environment (51).

The presence of ECs in the environment is mainly attributed to the discharge of treated wastewater from WWTPs (52). Conventional secondary processes (activated sludge and trickling filters) represent the most extensively used and studied processes. However, these processes are not designed to remove ECs resulting in their discharge to receiving surface waters including rivers, lakes, and coastal waters (53).

Parent chemicals are often excreted from the human body with a number of associated metabolites. As an example, ibuprofen is excreted as the unchanged drug (1%) and several metabolites: (β)-2-40-(2-Hydroxy-2-methylpropyl) phenyl propionic acid (25%), (β)-2-40-(2-carboxypropyl) phenyl propionic acid (37%) and conjugated ibuprofen (14%) (54). To date, a total of 15 illicit drugs and licit stimulants have been reported in UK wastewaters (51). As these contaminants are detected in the environment and are able to threaten the environment at very low concentrations, efficacious treatment technologies are needed. Researchers believe antibiotics represent the biggest concern among ECs since their

emissions can increase resistance to bacteria in the environment (55). In addition, other emerging compounds, particularly polar ones, such as acidic pharmaceuticals, acidic pesticides, and acidic metabolites of non-ionic surfactants, need to be taken into consideration and monitored. Since they have high solubility in water and poor degradability, they can potentially penetrate all natural filtration steps and treatments, posing a potential threat to drinking water (56). Researchers have gradually shifted their focus on water contaminants from conventional priority pollutants to emerging contaminants, including pharmaceuticals. Despite their high persistence and ease of bioamplification, pharmaceuticals still arouse considerable concern, both from researchers and the general public. Consequently, all efforts should be made to eliminate them from the water supply (57). Thus, PPCPs continue to enter the environment. In consequence, most PPCPs remain extremely harmful to human health and ecosystems (58).

2.1.1 Pharmaceuticals and Personal Care Products (PPCPs)

Our living environment is contaminated by synthetic compounds like PPCPs, since these compounds were first used (59). In addition to not being fully metabolized by the body, pharmaceutical compounds are excreted into wastewater. The discharge of treated water allows these micropollutants to reach the receiving environment unchanged (60). Researchers have found that over 3000 different substances are used as medicines, including analgesics, antibiotics, contraceptives, beta blockers, lipid regulators, tranquillizers, and impotence medications. Some of these chemical compounds can also be found in soaps and sunblock lotions, which are used for skin, hair, and teeth care. PPCPs are currently increasingly important in environmental issues (61). They are typically large and complex molecules. Chemically, they differ greatly between substances containing hydroxyl, carboxyl, ketone, and amine functional groups (62). Pharmaceutical wastewater is commonly treated with physical/chemical systems (63). These organic pollutants are considered a part of emerging contaminants (ECs), which enter water systems from various sources, such as human excretion (sewage), wrongful disposal, leeching from landfills, drain water,

or from industries. Even though it has been reported that these ECs are typically present at low environmental concentrations (ng/l to mg/l range), it is still unclear whether the levels of these compounds present in environmental waters can cause undesired physiological effects in wildlife and humans (64). In the environment, pharmaceuticals are released by humans or animals through urine or feces, through the sewage system, and through wastewater treatment plants as partially active metabolites (65). A recent study detected a total of 55 ECs in WWTP influent surface water, 41 ECs in effluent, and 40 ECs in environmental waters located upstream and downstream of the plant (64). It remains a complex issue how PPCPs behave in the environment for many reasons. As a starting point, PPCPs are manufactured with thousands of chemicals. Secondly, different types of chemicals react differently in wastewater treatment processes. Thirdly, wastewater treatment involves several processes that reduce nutrients, solids, and chemicals. Some PPCPs cannot be effectively removed from effluent by conventional wastewater treatment systems (66). With indirect potable reuse, figure 2.4 shows the sources and fate of contaminants. More than 80 compounds and several metabolites have been found in the aquatic environment and some in drinking water, which indicates that not all contaminants are removed during water treatment (59).

As wastewater and drinking water are treated by many factories, pharmaceuticals are disposed of and present in water. Scientists also consider these factors when assessing their risk to humans (67). There is no process that has been evaluated that removes 100% of all PPCPs. While some water remediation processes reduce pharmaceuticals to very low levels, others remain recalcitrant to conventional secondary or tertiary wastewater treatment (2).

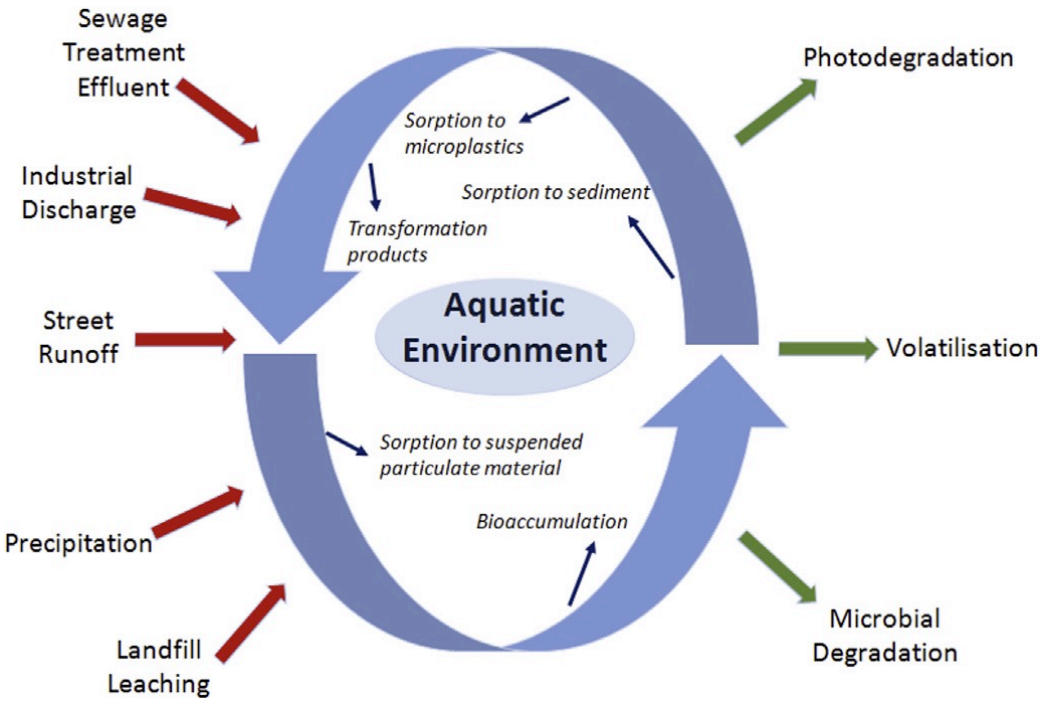

Figure 2.4 Sources and fate of PPCP and other ECs in the aquatic environment (59)

2.1.2 Conventional and Advanced Material for Emerging Contaminints (ECs)

As part of conventional WWTPs, primary settling are, activated sludge, biochemical filtration, and sand filtration is used, while advanced technologies include membrane filtration, adsorption on AC, and advanced oxidation processes (AOPs), which employ ozone, ultraviolet radiation, gamma radiation, electrooxidation, and reverse osmosis (RO) (68). In figure 2.5, a schematic diagram shows a conventional and advanced wastewater treatment processes.

Pharmaceuticals can reach the environment through several sources and routes. Nevertheless, wastewater treatment plants are the main point of collecting and releasing effluent wastewater and sludge into the environment. Activated sludge systems are still widely used for wastewater treatment because they produce effluents that meet required quality standards (suitable for disposal or recycling) while maintaining reasonable operating and maintenance costs. As a result, this

treatment can only remove a limited amount of pharmaceuticals from wastewater. (69).

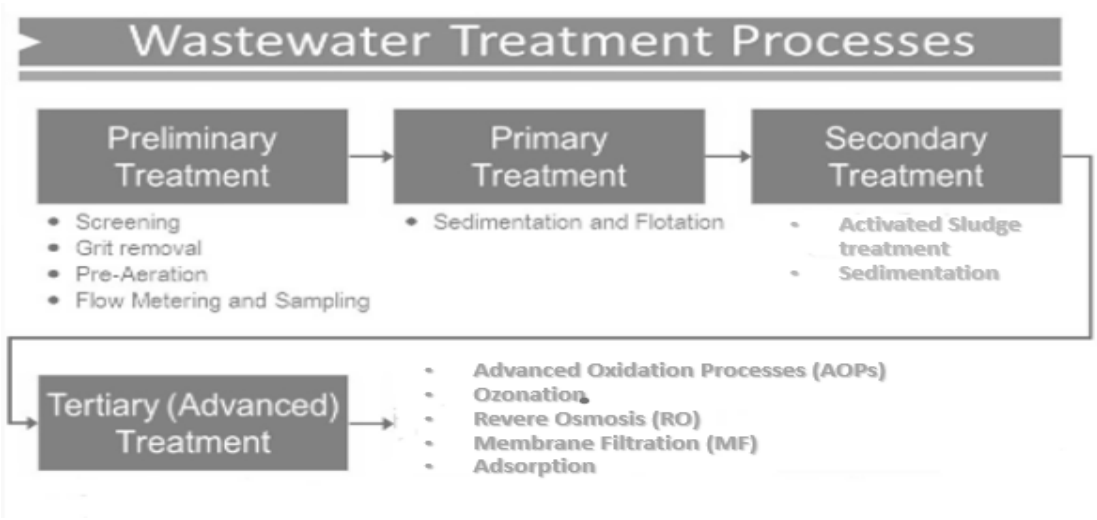

Figure 2.5 Processes for wastewater treatment

All design processes include preliminary treatment consisting of a bar screen, a grit chamber, and an oil and grease removal unit (70), usually followed by a primary gravity settling tank in all but a few smaller facilities. The primary-treated wastewater enters into a biological treatment process, usually, an aerobic suspended growth process where mixed liquor i.e., microorganisms responsible for the treatment) and biodegradable and nonbiodegradable suspended, colloidal, and soluble organic and inorganic matter is maintained in liquid suspension by appropriate mixing methods. During the aeration period, adsorption, flocculation, and oxidation of organic matter occur. After enough time for proper biochemical reactions, mixed liquor is transferred to a settling reactor (clarifier) to allow gravity separation of the suspended solids (in the form of floc particles) from the treated wastewater. Settled solids are then returned to the biological reactor (i.e., return activated sludge) to maintain concentrated biomass for wastewater treatment. Microorganisms are continuously synthesized; thus, some suspended solids must be removed to maintain a selected biomass concentration in the system. Removal

is performed by diverting a portion of the solids from the biological reactor to solid handling processes. The most common practice is to waste sludge from the return sludge line because return-activated sludge is more concentrated and requires smaller waste sludge pumps. The waste sludge can be discharged to the primary sedimentation tanks for co-thickening, to thickening tanks, or to other sludge-thickening facilities to increase the solid content of sludge by removing a portion of the liquid fraction. Through the subsequent processes, such as digestion, dewatering, drying, and combustion, the water and organic content are considerably reduced, and the processed solids are suitable for reuse or final disposal. To achieve better effluent water quality, tertiary treatment can be added to the above-outlined general process, e.g. activated carbon adsorption, additional nutrient removal etc. (69).

Most emerging compounds in water are treated with adsorption, which is a common physical process used to remove trace organic pollutants. It is also considered as one of the most efficient processes for the removal of many emerging compounds (71). Adsorption has the advantage of not generating byproducts that may be more toxic than the parent compound, which is one of the key benefits of adsorption. In fundamental terms, choosing a PPCPs removal technique needs to be based on its simplicity, rapidity, cost effectiveness, reusability, and environmental friendliness (72). Despite the need for further research, conventional WWTPs do not remove all pharmaceuticals from wastewater. The removal of pharmaceuticals from wastewater before they enter the environment must be done in an efficient and economically feasible manner (71). Table 1.2. Among the most effective technologies are RO, ion exchange, electrodialysis, electrolysis, and adsorption. In all cases except adsorption technology, the cost of water treatment ranges from 10-450 US$ per cubic meter. Adsorption is cheaper than other methods of water treatment (between 5.0 and 200 US dollars per cubic meter) (73).

Table 1.2 Comparison of the cost of water treatment of most effective technologies

Techology	Installation cost	Operation cost	Electricity concsumption	Range cost
Reverse Osmosis (RO) method	Low	Revatively low	High (High pressure pump is needed)	1,600 -3,200 $/ Cubic meter
Ion exchange method (Resin)	Low	Revatively low	High (Large pump capacity)	1,000 $/ Cubic meter
Electrodialysis (ED)method	High	Revatively low	Revatively low	10-450 $/ Cubic meter
Adsorption	Low	Low	Low	5.0-200 US $/Cubic meter

An Australian study found that some drugs become more dangerous during conventional treatment. It is possible for pharmaceuticals to change due to enzyme reactions or bacteria interactions. In the case of pharmaceuticals that contain an organic carbon base, chlorine disinfection could potentially produce dangerous byproducts (71). The most common adsorbents used in wastewater treatment are AC, clay, zeolites, and agricultural wastes. Adsorbents and industrial wastes include sludge, fly ash, and red mud, which are all low-cost adsorbents.

There are a number of traditional adsorbents used in wastewater treatment around the world (74) but AC is the most popular and widely used. So far, AC has been used to adsorb aromatic contaminants, including some pharmaceuticals. In addition to not generating toxic or pharmacologically active products, AC is an

efficient way to remove pharmaceuticals. In the meantime, AC generally has a high capacity to adsorb pharmaceuticals, depending on the AC type, pharmaceutical composition, and solution chemistry. There are major drawbacks to AC, despite its effectiveness. A lot of energy is needed to provide sufficient heat at such high temperatures during the activation stage. Consequently, high utility costs will lead to high production costs. Therefore, commercial AC is also expensive. In addition, AC is a non-ecofriendly product (71).

The adsorption by CS can be achieved using either cellulose bead. In addition to AC, CS is also commonly used in adsorption processes. As well as being biocompatible, biodegradable, and non-toxic, it is also environmentally friendly. In the present, it is used for the removal of dyes and heavy metals from aqueous solutions. However, it has only recently begun to be applied to pharmaceutical compound adsorption. CS adsorptions are influenced by the ionic charge of the adsorbent, the pH of the solution, and the chemistry of the pollutant. As a result of their low cost and high amino and hydroxyl content, chitin and CS derivatives have gained wide attention as effective biosorbents, as they have shown significant adsorption potential for the removal of various aquatic pollutants. It forms colloids in contact with water, dissolves in acids, form gels in aqueous solutions, has a low surface area, and is susceptible to biochemical and microbiological degradation in the presence of water. There have been some studies investigating carbon nanotubes' ability to remove PPCPs, including ketoprofen and carbamazepine (75). A natural zeolite is formed from silicate minerals, but they can also be synthesized at a commercial level. A recent study used biozeolite to remove pyridines and quinine (76). It is well known that AOPs are effective at oxidizing a variety of organic and inorganic compounds. However, these procedures often fail to degrade pollutants sufficiently. The performance of AOP and the safety requirements are not well understood, which is why it is not widely used. In addition to the by-products, ozonation can also have toxic properties (71). PhACs removal processes including nanofiltration (NF) and reverse osmosis (RO) show higher efficiency in removing organic and inorganic pollutants; they overcome the drawbacks of traditional methods. There are three

methods for removing micropollutants: size exclusion, electrostatic repulsion, and adsorption (77). It has been previously mentioned that conventional WWTPs are unable to fully remove PPCPs. To deal with wastewater containing in PPCPs, advanced chemical processes are required. For the degradation of toxic or recalcitrant organic pollutants in aqueous solutions, chemical oxidation processes such as ozonation, UV/H_2O_2, and gamma radiolysis are effective. In terms of PPCPs removal, ozone is the most widely used oxidation method (78).

2.2 Chitosan (CS)

2.2.1 Chemistry of Chitosan

CS is a material that is produced by N-deacetylation of chitin. A glycosaminoglycan (GAG) is a solid polymer that is colorless, odorless, and semicrystalline (79). Additionally, the deacetylation degree (DD), crystallinity, and polymer molecular weight (Mw) are used to characterize the polymer. Further, these parameters may affect its chemical and biological properties, as well as its conformation in solution. The most common methods of evaluating DD are IR and NMR spectroscopy (80). CS is insoluble in water or organic solvents, but at acidic pH (below pH 5), it becomes a soluble cationic polymer that is highly charged (81). A key advantage of CS over other polysaccharides (cellulose and starch) is the chemical structure that can be modified to design polymers with specific properties (82). Further, their reactive functional groups (amino group (-NH_2), primary and secondary hydroxyl (-OH)) can be used to create composites with different compounds that have proven to be more effective at absorbing wastewater pollutants and resistant in acidic environments (76). Most commercially available CS has a DD between 70 and 90% and a Mw between 100 and 1000 kDa (83).

CS contains a primary amino group (C2) as well as primary and secondary hydroxyl groups (C6, C3). Additionally, glycosidic bonds and acetamide groups can be considered functional groups (84) as shown in figure 2.6.

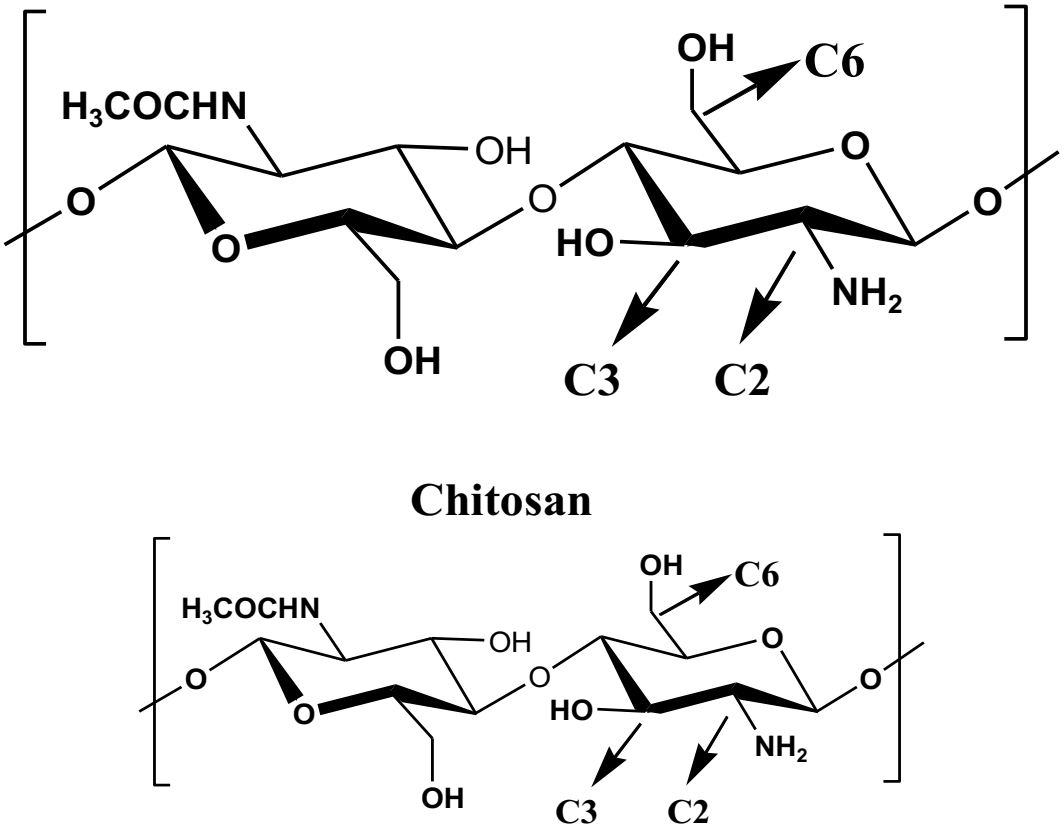

Figure 2.6 The chemical structure of chitosan (84)

In addition to its cationic properties, chitosan has an ionizable amino group, making it a cationic polyelectrolyte with a pKa of 6.5 and one of few naturally occurring materials that can form hydrogels when complexed with anionic polyelectrolytes. Because of it is pKa of approximately 6.5, CS is soluble in acid-aqueous media because of its large number of protonated -NH_2 groups. Chitosan becomes soluble when around 50% of all amino groups are protonated (84), (18), (85).

As CS is cationic at acidic pH (below pH 5), it can dissolve, swell, and exchange ions with anionic compounds in acidic media. Non-protonated amino groups in neutral media allow metal cations or organic chemicals to complex (86). In addition to its reactive amino(-NH_2) and hydroxyl(-Hydroxyl group) groups, CS

can also be covalently and ionically modified. A variety of groups can be added to modify specific properties such as biological and physical properties and be targeted at specific applications.

The presence of amino groups means that pH significantly affects the charged state and the properties of chitosan. As shown in (Figure 2.7), at pH between 6.0 and 6.5 in solution, the free amino groups of chitosan molecules become less protonated and hydrophobicity along the chitosan chain increases. Therefore, chitosan self-aggregates could be formed in acetate buffer solutions by intra- and inter-molecular hydrophobic interactions (87). At low pH (> 6.5) chitosan solutions exhibit phase separation, while at pH < 6.5 chitosan is soluble, carrying a positive charge because of the presence of protonated amino groups. Therefore, the amino group get protonated and become positively charged and that makes chitosan a water-soluble cationic polyelectrolyte. On the other hand, as the pH increases above 6, chitosan's amines become deprotonated and the polymer loses its charge and becomes insoluble. The soluble–insoluble transition occurs at its pKa value around pH between 6 and 6.5 (88), (89).

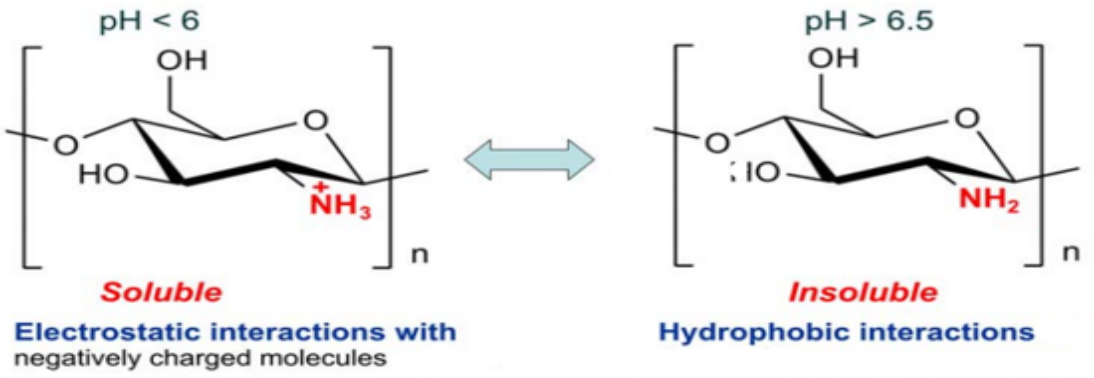

Figure 2.7 Scheme of chitosan in various pH conditions

2.2.2 Chemical Modification of Chitosan

In native CS polymers, hydroxyl and amino groups modify the pharmaceutical, physicochemical, and biological properties (90). This indicates that chitosan, which is a cationic polyelectrolyte, at low pH (less than about 6) chitosan can

electrostatically interact with negatively charged molecules or polymers, e.g., anionic glycosaminoglycans, proteoglycans, and other negatively charged molecules. At higher pH (above about 6.5) chitosan's amino groups are deprotonated and hydrophobic interactions with several substrates (e.g., fatty acids and cholesterol) (89), (91). Finally, as the pKa value is highly dependent on the degree of Ndeacetylation, the solubility of chitosan is dependent on the DD and the method of deacetylation used. Apart from the DD, the molecular weight is also an important parameter that significantly affects the solubility and other properties (88).

As a result of chemical modification, CS is capable of increasing its metal binding efficiency, such as with ethylene glycondiglycidyl ether, formaldehyde, glyoxal, epichlorohydrin, glutaraldehyde, and isocyanates. During crosslinking, not only is chitosan stabilized in acidic solution but it is also rendered insoluble in acidic medium, as well as enhanced mechanically (92). In addition to the free amine, CS contains hydroxyl groups, which can be modified to produce different derivatives. Since the amino group in CS is acid conjugated, its pKa value is about 6.5. Therefore, CS is positively charged and solubilized in acidic solutions with a charge density varying with pH and DD (93). Based on researches, By using chemical or physical processes, CS can enhance sorption kinetics, control the polymer's reactivity (94). By adding the polar groups able to form secondary interactions with CS, will improve its biodegradability and antibacterial activity as well as its hydrophilicity (95), (34). A major advantage of CS over AC and other biosorbents is its low price, high affinity for many contaminants (since it contains amino and hydroxyl groups), chemical stability, high reactivity, and selectivity. By adsorption, CS and its modified analogues have been successful in removing metal ions, dyes, phenols, various anions, pesticides, fungicides, and humic substances. In order to improve CS's sorption capacity, mechanical strength, and resistance to low pH values, several modifications have been applied (96).

The modification of CS in adsorption requires grafting or crosslinking with compounds, which allows it to interact more strongly with pharmaceuticals and immobilize chitosan at the same time (33), (97). Despite their inherent properties,

magnetic compounds remain an interesting alternative to sorbents due to the fact that they can be controlled by an external magnetic field, thus facilitating phase separation. Recently, magnetic adsorbent technology has received considerable attention as a means of solving environmental problems (98). As part of physical modification, CS can be blended and converted into different forms. It is common for polymer chains of CS to be expanded through physical modification, allowing easier access to internal sorption sites and reducing crystallinity (99). Additionally, blending with other materials can also be a good way to create composites with the desired structure (6).

Many potential applications of CS and its derivatives have been shown in medicine and pharmaceuticals, including drug delivery, gene therapy, hemostatic agents, wound healing, and antibacterial agents (100). In order to create derivatives with different viscosities, hydrophilic characteristics, affinity toward metals and dyes, and moisture content, CS can be chemically modified. There are two types of modifications: controlled degradation of CS chains or addition of chemical groups to CS chains (101). As a result of the addition of various chemicals to CS, its physical and chemical properties have been modified in the past. A variety of approaches can be used to synthesize these CS derivatives, including grafting approaches that add organic or inorganic esters and acyl derivatives to CS functional groups, as well as crosslinking approaches that crosslink copolymers to CS (101). In contrast, crosslinked polymers can be obtained in homogeneous or heterogeneous conditions by reticulation with bi- or poly-functional crosslinking agents, such as epichlorohydrin (chloromethyloxirane, C_3H_5ClO), ethylene glycol diglycidyl ether, glutaraldehyde, benzoquinone, maleic anhydride, or isocyanates. It is considered hazardous for the environment and can cause cancer and damage to cells (except for maleic anhydride) (102). In general, the crosslinking step may reduce metal ion uptake efficiency and sorption capacity, especially in chemical reactions involving amines (103). As far as chemical modifications of CS are concerned, this project will only focus on grafting approaches.

2.2.2.1 Alkylation of chitosan

A variety of chemical modifications can be applied to CS alkylation, including reductive alkylation using Schiff base reactions, acylation, carboxylation, and Michael addition (39).

It is possible to reduce hydrophilicity and crystallinity of CS by alkylating it. CS contains many amino and hydroxyl groups which, without alkylation, would normally form hydrogen bonds (100). A control of alkylation is necessary, and alkyl groups must be of the appropriate length to prevent insoluble CS derivatives (104). You can alkylate CS in one of two ways: either by reacting it with alkyl halides or by reacting the amino groups with compounds containing carbonyls. In order to create derivatives of CS with differing chemical and physical properties, alkyl halides are added to amino / hydroxyl functionalities on CS (Figure 2.8) (105).

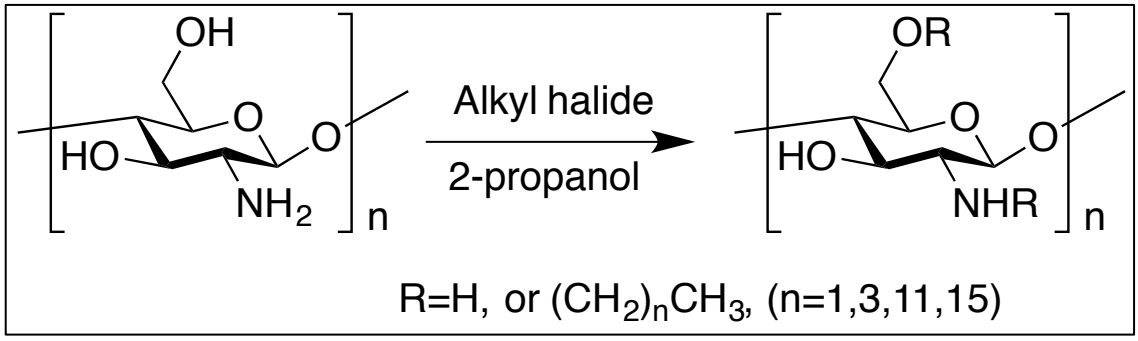

Figure 2.8 Alkylation of the amino and C6 hydroxyl moieties of chitosan

Additionally, amines on CS can be formed as imines by Schiff base reactions with carbonyls, followed by treatment with borohydride reagents (Figure 2.9) (106).

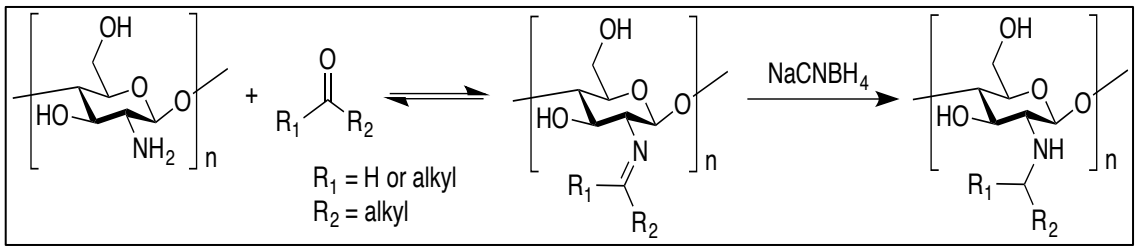

Figure 2.9 Alkylation of the amino group of chitosan via Schiff base formation and reduction

Alkylated chitosan derivatives with differing chemical and physical properties can be produced by tweaking the carbonyl R groups. In addition to being commonly used to produce N-alkyl CS, this method is also used to protect O-alkyl CS derivatives from oxidation(Figure 2.10) (101).

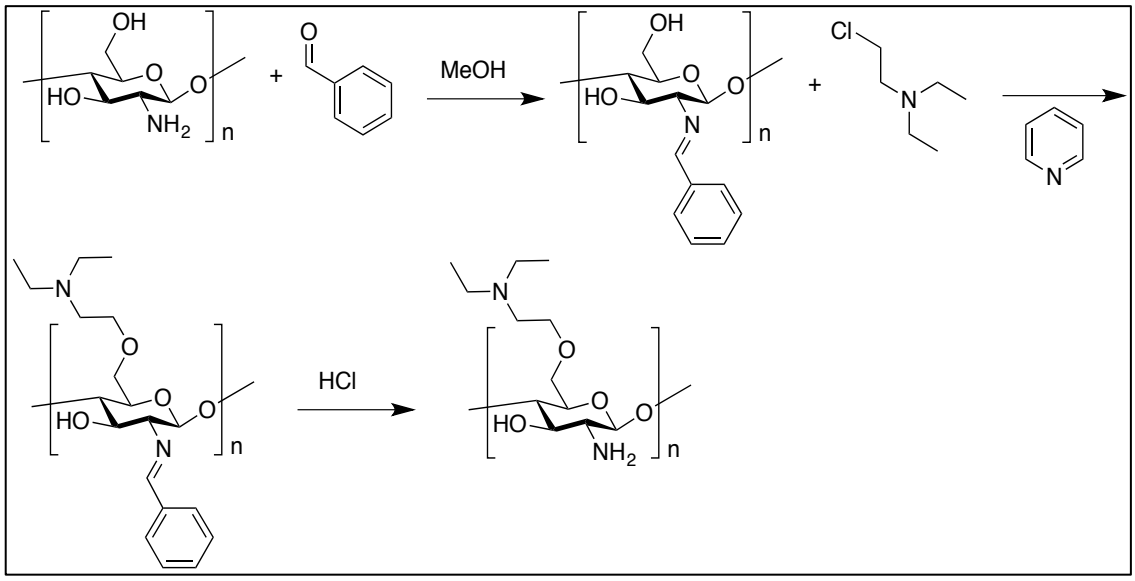

Figure 2.10 Synthetic scheme for the preparation of *O*-diethyl aminoethyl chitosan

- **Carboxyalkylation of chitosan**

In comparison to CS, carboxymethyl chitosan (CMCS) has enhanced biological and physicochemical properties, making it a promising biomedical material. Because carboxyalkylation is also an effective method of increasing the hydrophilicity of CS, many different carboxyalkylation methods have been explored in the past. Among these methods are carboxyalkylation with halo carboxylic acids, Schiff base reductive methods, and Michael addition methods.

Recently, N, O- carboxymethyl CS and its applications have received a great deal of attention. In contrast, Muzzarelli et al. have only reported a few methods for synthesizing N-carboxymethyl chitosan (N-CMCS). In 1982, the in-situ reduction of the imine generated by the reaction of the amino groups (NH_2) in CS with aldehydes (ACHO) in glyoxylic acid with $NaBH_4$ or $NaBH_3CN$ allowed the synthesis of N-CMCS (107). In this method, the starting material glyoxylic acid is relatively expensive, and there are two steps involved, resulting in decreased

yields. By using Na_2CO_3 as a binding acid agent, N-CMCS can be produced by reacting CS with chloroacetic acid at neutral aqueous solution. It is observed in neutral conditions that the amino site has exclusive reaction over the C6 hydroxyl group. Consequently, the carboxymethylation of CS can be achieved with improved yields in one step (108).

- **Carboxyalkylation with Halo Carboxylic Acids**

Many studies have been conducted using halocarboxylic acids to synthesize N-carboxyalkyl and O-carboxylalkyl CS. Due to its two steps, the reductive method is simpler, and it does not require expensive reactants, such as glyoxylic acid (109). Direct alkylation of mono chloroacetic acid, a mono halo carboxylic acid, at room temperature in an alkaline medium can produce carboxymethyl CS (Figure 2.11).

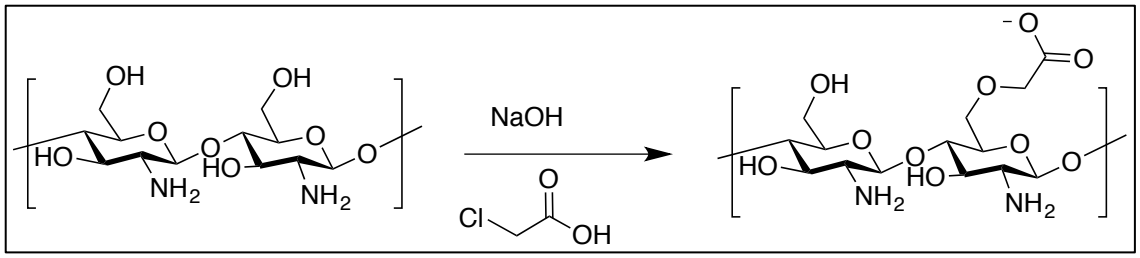

Figure 2.11 Carboxyalkylation of chitosan with monochloroacetic acid

- **Carboxyalkylation via a Schiff Base Reductive Process**

It has been possible to N-carboxyalkylate CS through reductive Schiff base reactions in the past. As early as 1982, Muzzarelli et al. reported this synthesis by using glyoxylic acid. As a result, these derivatives of N-CMCS have been widely explored for the preparation of insoluble polyampholytes after addition of transition metal ions to water at all pH values (110)

- **Michael Addition**

Michael addition allows many unsaturated carbonyl reagents to react with CS's amino groups, such as acrylic acid (AcA). Sashiwa et al. (2003) used AcA to react

with CS, where AcA performs the dual function of proton donor and Michael addition reagent (Fig. 2.12). After pH adjustment, NaOH was used to convert the carboxylic acid into its sodium salt, which was then dialyzed for two days to purify the mixture (72).

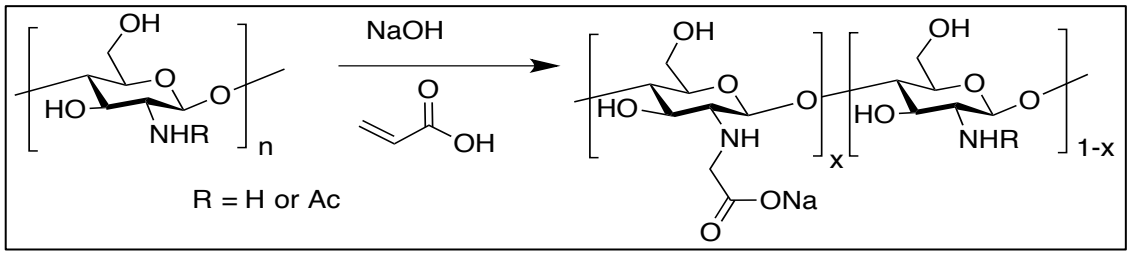

Figure 2.12 Synthesis of *N*-carboxyalkyl chitosan with acrylic acid

Previous reports have reported Michael additions of CS to methyl acrylate and ethyl acrylate. For the dissolution of AcA ester and CS, organic solvents such as methanol and acetic acid have been used. In these reports, water-soluble CS derivatives were also obtained by saponification. By reacting CS directly with acrylic acid via a Michael addition, saponification and organic solvents can be by passing CS straight through acrylic acid via a Michael reaction addition as shown above (111).

2.2.2.2 Acylation of chitosan

As another method of modifying CS, acylation with acyl halides or carboxylic anhydrides can also be used. In organic solvents, CS can be made more solubilized by tweaking the acyl groups' molecular weights (112). In the absence of modification, CS forms a crystalline structure that is normally insoluble in organic solvents due to its numerous intermolecular hydrogen bonds (113). As a result of acylation with aliphatic carboxylic acid chlorides such as hexanoyl, dodecanoyl, and tetradecanoyl chlorides, derivatives with a high degree of acylation are obtained. As shown in (Figure 2.13), CS is acylated with succinyl groups to prepare N-succinyl chitosan (NSCS). As an amphiprotic derivative, NSCS exhibits remarkable biocompatibility, significant increases in solubility in

basic and acidic media without compromising its biological properties (114). The NSCS molecule also has excellent moisture absorption and retention qualities, superior chelating capabilities, significant apoptosis inhibitory properties, remarkable enzyme immobilization properties, high antioxidant activity, and greater bioactivity than its parent molecule (72),(115).

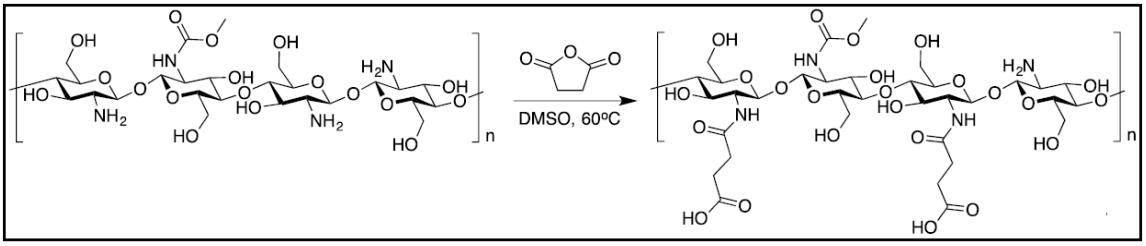

Figure 2. 13 Preparation of *N*-succinyl chitosan

- **Preparation of N-succinyl chitosan**

NSCS is highly soluble at pH levels below 4.5, and above 7, owing to its amphiprotic nature (contains both carboxylic acid, and amino groups). In basic solutions (pH > 7), NSCS exists as carboxylates ($-COO^-$), whereas in acidic solutions (pH 4.5), it consists of protonated amino groups ($-NH_3^+$). In aqueous solutions, both of these charged NSC species are more soluble. As NSCS exists in an isoelectric form, it is insoluble in solutions between pH 4.5 and 6.8; this fact is often exploited for precipitation purification. As NSCS contains multiple hydroxyl, amino, and carboxylate functional groups, it is also used as a chelating agent to absorb heavy metals, such as lead (116). Another derivative of CS, O-succinyl chitosan (OSCS), has properties similar to NSCS. When compared to NSC, OSCS shows similar absorption and chelating properties because it is equally amphiprotic. A similar synthesis is used to prepare OSCS (Figure 2.14). However, since the phthaloyl group is more nucleophilic than the C6 hydroxyl group, the amino groups are protected first with it. Using hydrazine, the phthaloyl group is removed after succinylation with a succinyl group (117).

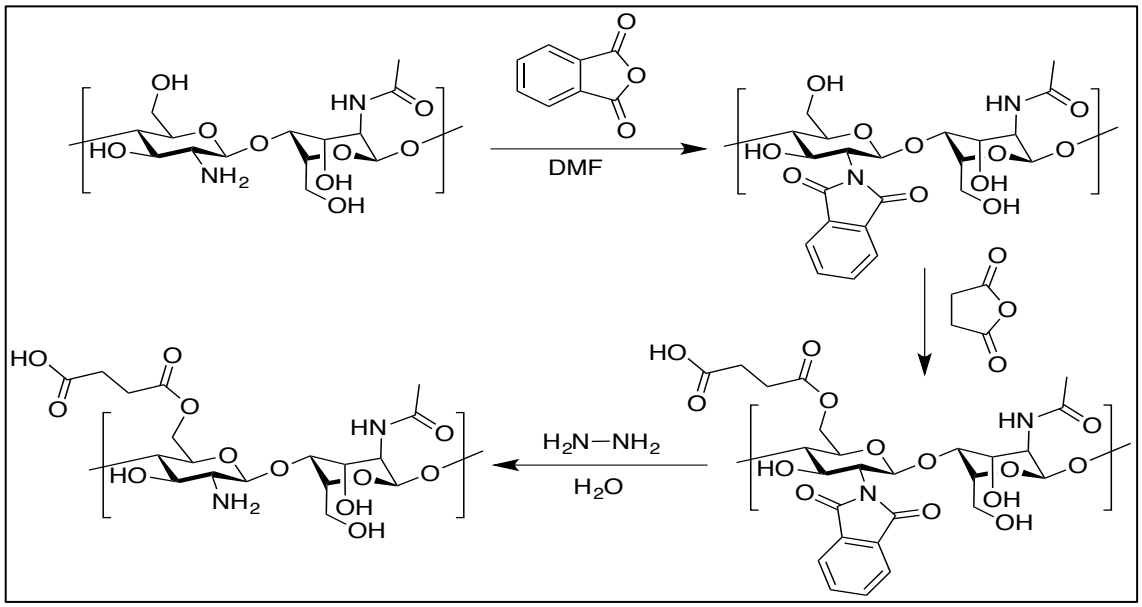

Figure 2.14 Synthesis of *O*-succinyl chitosan

2.2.2.3 Arylation of chitosan

N-Alkyl chitosan, one of the most important hydrophobic derivatives of chitosan, has been reported by several research groups. Much less attention has been paid on the synthesis of N-aryl chitosans. The reductive arylation of chitosan with salicylaldehyde has been reported along with its application in metal chelation (90).

2.3 Treatment as Green Technologies

2.3.1 Adsorption technology

In adsorption, one or more components (adsorbents) bond with a surface of a solid (adsorbent) in contact with them. Basically, adsorption is the accumulation of substances on surfaces or interfaces. During the treatment of water, the process occurs at the interface between the solid adsorbent and the contaminated water (103). Generally, there are two types of adsorption: physical adsorption involves weak intermolecular forces, and chemisorption involves chemical bonds between the adsorbents and contaminants (118). For a better understanding of adsorption kinetics and equilibrium isotherms, adsorption equipment must be

designed based on those concepts. They first determine adsorption capacity, and then they determine adsorption velocity (119).

In water pollution control, adsorption can remove/minimize a wide range of pollutants, including dye molecules, metal ions, and aromatic derivatives. Considering various types of contaminants can be removed with adsorption, it is the best method of removal (120). Among wastewater treatment methods, it is the best because of its universal nature, affordability, and ease of operation. In addition to soluble and insoluble organic pollutants, adsorption can also remove inorganic pollutants. By using this method, 99.9% of organic pollutants can be removed. A variety of organic pollutants have been removed from various contaminated water sources using adsorption as a result of these facts (8). For removing contaminants from wastewater, CS and its derivatives can be effective biosorbents (121). As a result of its simplicity (simple technique), efficiency, economic viability and social acceptability, adsorption technology was proven effective in removing pharmaceuticals from wastewater (122). A number of other adsorbents are used for eliminating pharmaceuticals, including activated carbon, resin, and zeolites. As a result, they exhibited a high adsorption capacity (123), Wastewater treatment surfaces that have been tested for their effectiveness as adsorptive surfaces. However, the use of these adsorbents caused several problems, such as stability and recycling, which required lengthy and costly regeneration procedures. Many efforts have been devoted to synthesizing novel, effective, and environmentally friendly adsorbents based on low-cost and natural polymeric materials. A wide range of harmful substances, including pesticides, heavy metals, dyes, petroleum derivatives, pharmaceutical drugs, etc., have been adsorption onto biopolymers due to human and industrial progressive growth (124).

There are three types of tests that can be carried out in order to provide more information about the mechanisms of adsorption processes, namely the kinetic, the isothermal, and the thermodynamic tests.

2.3.1.1 Adsorption equilibrium

When the amount of solute being adsorbed onto the adsorbent equals the amount being desorbed, adsorption equilibrium has been established. In order to depict the equilibrium adsorption isotherms, the solid phase concentration (C_o) as well as the liquid phase concentration (C_e) of the solute was plotted against one another. For adsorption process design, the adsorption isotherm explains interactions between adsorbate and adsorbent. For describing the experimental data of adsorption, the Langmuir, Freundlich, and Temkin isotherms are widely used (125). A value of q is obtained when the amount of adsorbate in the adsorbent equals the amount of adsorbate removed from the solution, as follows equation 2.1:

$$q = \frac{(C_o - C_e)}{m} V \qquad \text{Equation 2.1}$$

Where:

q = Adsorption capacity (mg/g);

C_o = Initial concentration of adsorbate (mg/L);

C_e = Concentration of adsorbate at equilibrium (mg/L);

V = Volume of the solution (L);

m = Adsorbent mass (g);

Information regarding adsorption equilibrium is essential for the proper analysis and design of adsorbate-adsorbent systems. Many empirical models have been developed over the years to analyze experimental data and describe adsorption equilibrium, including Langmuir, Freundlich, and Temkin two parameter isotherm models. As a result of these isotherm models, we are able to identify the distribution of available adsorption sites across the adsorbent surface, as well as the characteristics of adsorption (126).

2.3.1.2 Adsorption kinetics

It is crucial to study the kinetics of adsorption in wastewater because it provides insight into reaction pathways and mechanisms (127). Furthermore, we can use the adsorption Kinetic to understand the mechanism of adsorption and its potential rate-limiting steps. As a general rule, kinetic studies are conducted in batch

experiments by using linear or non-linear regression equations to determine the best-fitting kinetic model. This study identified three common kinetic models, namely the pseudo-first-order kinetic model (PFO), and the pseudo-second-order kinetic model (PSO). Using these models, we can learn more about parameters that may influence adsorption (128).

1. Pseudo-first-order kinetic model

In order to predict the adsorption kinetics of substances, pseudo first-order kinetic models are widely used. According to the pseudo first-order model, adsorption kinetics is as follows equation 2.2:

$$\frac{dq}{dt} = k_1(q_e - q_t) \qquad \text{Equation 2.2}$$

Where:

q_e = amount of the adsorbed contaminant at equilibrium (mg/g) in the first order model.

k_1 = first-order equilibrium constant (1/min).

q_t = quantity of contaminant adsorbed as a function of time (mg/g).

t = reaction time (min).

After definite integration by application of the condition's q_t =0 at t = 0 becomes (Equation 2.3):

$$\log(q_e - q_t) = \log - \left(\frac{k_t}{2.303}\right)t \qquad \text{Equation 2.3}$$

By plotting log ($q_e - q_t$) versus *t,* the adsorption rate can be calculated

2. Pseudo-second-order kinetic model

According to the pseudo-second order model, chemical adsorption dominates. Equations 2.4 and 2.5 that represent the model equation are as follows (129):

$$\frac{dq}{dt} = k_2(q_e - q_t)^2 \qquad \text{Equation 2.4}$$

$$\frac{t}{q_t} = \frac{1}{(k_2 q_e^2)} + \frac{t}{q_e} \qquad \text{Equation 2.5}$$

Where,

q_e = amount of contaminant adsorbed at equilibrium (mg/g).

k_2 = second-order equilibrium constant (1/min).

q_t = amount of contaminant adsorbed as a function of time (mg/g).

t = reaction time (min).

2.3.1.3 Adsorption isotherm

With more applications being developed, it becomes increasingly important to obtain the isotherm, because chitosan treatment systems require more accurate and detailed isotherm descriptions. It is therefore more important to describe and select isotherm systems with more accuracy the more complex the wastewater composition (130).

1. **Langmuir isotherm**

There are many sorption isotherms available, but the Langmuir adsorption model is perhaps the most widely known and applied. Several experimental data sets have been compared with the model, and they have shown good agreement (131), and in many adsorption processes, it is successfully applied. According to the Langmuir isotherm, the kinetic mechanism is the basis for the isotherm. Assumed are the following:

- There is no difference in energy between the surface and the inside molecule.
- There is no interaction between molecules adsorbing to each other.
- There is no migration of molecules across the surface because molecules adsorb at fixed sites.
- At maximum adsorption, a monolayer form.

The Langmuir equation is given by (Equation 2.6):

$$q_e = \frac{q_m k_L C_e}{1 + K_L C_e} \qquad \text{Equation 2.6}$$

The linearization of it gives the following form (Equation 2.7):

$$q_e = \frac{1}{q_m k_L} + \frac{C_e}{q_m} \qquad \text{Equation 2.7}$$

Where,

C_e=equilibrium metal concentration

q_m=Langmuir constants related to maximum adsorption capacity (mg/g)

K_L=relative energy of adsorption (1/mg)

2. Freundlich isotherm

Among the most popular mathematical models to explain experimental data over a wide range of concentrations is the Freundlich isotherm model. Based on a heterogeneous surface, active sites are distributed with their energies and enthalpies changing logarithmically. Freundlich's equation 2.8 is given by (132) :

$$q_e = k_F C_e^{\frac{1}{n}} \qquad \text{Equation 2.8}$$

The logarithmic form of equation:

$$\mathrm{In}q_e = \mathrm{In}K_F + \frac{1}{n}\mathrm{In}C_e \qquad \text{Equation 2.9}$$

Where n, is the heterogeneity factor (dimensionless)- adsorption intensity constant; k_F, is the Freundlich isotherm constant (mg/g); q_e, is the adsorption capacity at equilibrium (mg/g); C_e, is the concentration in solution at equilibrium (ppm).

All sites on an adsorbent surface are not considered equal in the Freundlich isotherm. Additionally, additional adsorbed species could still be accommodated once the surface has been covered (133).

3. Temkin isotherm

In the Temkin isotherm, the interaction between adsorbent and adsorbate is clearly taken into account. Despite the extremely low and large value of concentration, the model assumes that all molecules in the layer will decrease linearly rather than logarithmically with coverage. Temkin's isotherm can be expressed as follows (Equation 2.10 and 2.11):

$$q_e = \frac{RT}{b} \ln(aC_e) \qquad \text{Equation 2.10}$$

This model can be expressed linearly as follows:

$$q_e = a + bInC_e \qquad Equation\ 2.11$$

Where q_e is the amount of metal ion adsorbed per specific amount of adsorbent (mg/g), C_e is equilibrium concentration (mg/L), *a* is equilibrium binding constant (g^{-1}) and *b* is related to heat of adsorption (J/ mol) which are Temkin constants.

In the Freundlich equation, it is implicit that the fall in heat of sorption is linear rather than logarithmic, as in the Temkin isotherm (134).

2.3.1.4 Thermodynamic parameters

In order to determine whether an adsorption process is spontaneous, thermodynamic considerations must be taken into account. In chemical reactions, Gibb's free energy change, (ΔG^o) , is an indicator of spontaneity, thus serving as a criterion for spontaneity. In order to determine Gibb's free energy for a process, both enthalpy (ΔH^o) and entropy (ΔS^o) must be considered. In the presence of a negative (ΔG^o), reactions occur spontaneously at a given temperature. Adsorption free energy is related to equilibrium constant by the van't Hoff equation 2.12:

$$\Delta G^o = -RTInK_c \qquad \text{Equation 2.12}$$

Where,

K_c is the single point or linear sorption distribution coefficient.

T = absolute temperature (K)

R = universal gas constant (8.314 $Jmol^{-1}\ K^{-1}$)

After integration, the integrated form of Eq. 2.12 becomes (Eq. 2.13):

$$InK_c = \frac{\Delta S^o}{R} - \frac{\Delta H}{RT} \qquad \text{Equation 2.13}$$

ΔG^o can be expressed as the second thermodynamic law equation corresponds to (Eq. 2.14):

$$\Delta G^{o} = \Delta H^{o} - T\Delta S^{o} \qquad \text{Equation 2.14}$$

where ΔG° is the standard Gibbs's free energy (J mol^{-1}), ΔS° is the standard entropy (J mol^{-1} K^{-1}) and ΔH° is the standard enthalpy (J mol^{-1}) (135), (136).

When plotting Gibb's free energy change, ΔG^{o}, versus temperature, T, we obtain the slope and intercept as ΔH^{o} and ΔS^{o}. The thermodynamic relation between ΔG^{o}, ΔH^{o} and ΔS^{o} implies that either (1) (ΔH^{o}) or (ΔS^{o}) are positive and that the value of $T\Delta S^{o}$ is much larger than ΔH^{o}. (2) (ΔH^{o}) is negative and ΔS^{0} is positive or (3) (ΔH^{o}) or (ΔS^{o}) are negative and that the value of ΔH^{o} is more than $T\Delta S^{0}$. To be significant, Gibb's free energy change of adsorption must be negative.

2.3.2 Electrospinning technology

Electrospinning has gained increasing attention due to the rapid development of nanotechnology (137), as a versatile technique that can be applied to a range of organic and inorganic systems and for numerous applications (Figure 2.15) that can result in nanomaterials with tightly controlled size distributions.

In a variety of applications, such as health, energy, and environmental issues, polymeric nanofibers, specifically fabricated by electrospinning, offer viable useful means. During the past decade , desalination and water/wastewater treatment applications have been highlighted (138).

In comparison with other traditional methods of treatment, electrospinning nano-manufacturing is cost-effective. Electrospinning produces uniform, continuous nanofibers without the need for expensive purification (139). The use of electrospun membranes can improve membrane-based desalination and water/wastewater treatment systems. Through the electrospinning process, nanostructured / nanoengineered materials may be developed to address the current issues of meeting the demand for clean water (138).

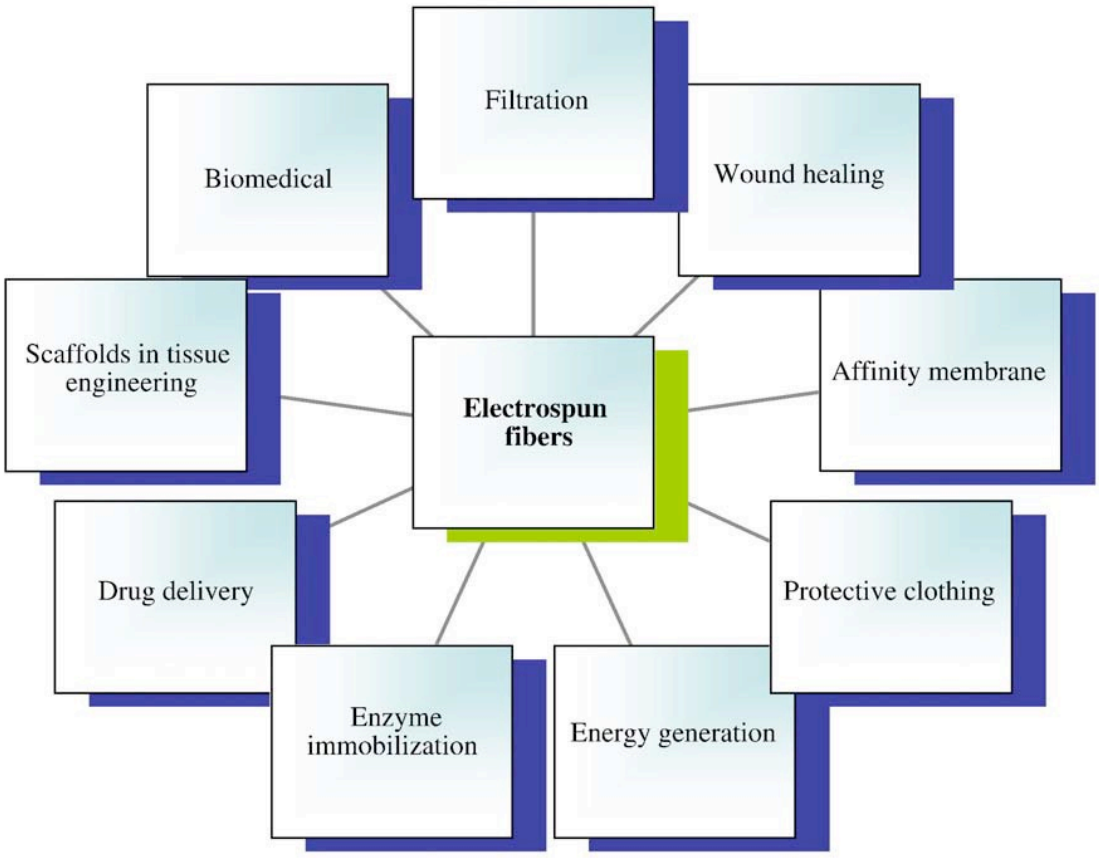

Figure 2.15 Some applications of electrospun nanofibers

2.3.2.1 Description of the electrospinning

Electrospinning is a relatively versatile method for fabricating nanofibrous porous membranes, including those used for filtration, desalination, and wastewater treatment (140). Furthermore, polymeric nanofibers can be produced using electrospinning or electrostatic spinning, which is a convenient and scalable method. Recently, this process has been scaled up for the production of nanofibers in the industrial environment (141). Nanofibers can be produced very easily with electrospinning because it is a very simple process. Electrospinning experiments typically require to obtain the desired nanofibers the following equipment (142):

(a). A syringe pump pushes the polymer solution or melt through a spinneret (a metallic needle) to the tip.

(b). A high-voltage power supply provides a charge to the solution in the syringe needle.
(c). A grounded collector on which the ejected fibers are captured.

Electrospinning usually involves injecting polymer solution into a syringe connected to a positive electrode. Initially, an electric field is applied to create an electrically charged jet of polymer solution or melt, which is emitted from the droplets on a pipette tip (140). In electrospinning, polymers are dissolved in a solvent, forming polymer solutions. Afterwards, the polymer fluid is fed into the capillary for electrospinning. At the end of a capillary, a polymer solution with low surface tension is introduced. With increasing intensity of the electric field, the hemispherical surface of the solution elongates to form a Taylor cone shape. Additionally, the polymer solution's electrified liquid jet develops a bending instability driven by electricity towards the collector, neutralizing the jet's charge. Lastly, the jet undergoes stretching before reaching the collector (143). After the solvent evaporates, the nonwoven fibrous membrane is deposited on the collector as a nanofiber (144). Electrospinning is similar to electrostatic spraying (electrospraying) in that both require high voltage to produce charged liquid jets. By breaking up the electrified jet in electrospraying, small droplets or particles are formed, whereas a solid fiber is formed by stretching the electrified jet in electrospinning. The electrospinning process takes place at room temperature under atmospheric conditions (145).

In top of that, electrospraying and electrospinning are based on the same fundamental principles. The main difference between these two processes is the stability of the jet. Due to capillary instability, the electrical jet in electrospraying breaks into droplets, but if there is enough entanglement in the fluid, it will be stabilized and form thin filaments as in electrospinning (146).

2.3.2.2 Electrospinning Processes and Parameters

The electrospinning process involves not only the polymer and the solution properties (e.g., molecular weight, viscosity, conductivity, surface tension), but also the electrospinning conditions themselves (e.g. applied electric voltage, tip-

to-collector distance, feeding rate, etc.) (146). As a result, it is important to understand how electrospinning parameters affect fiber morphologies. By controlling these parameters, fiber diameters and morphologies can be obtained much more easily. Ideally, a polymer should be electrospun into nanofibers under the following conditions:

A) Fiber diameters must be consistent and controlled.

B) Fiber surfaces must be defect-free or defect-controllable.

c) Nanofibers must be collectible in continuous form.

Electrospinning is largely dependent on fiber diameter. Additionally, the diameters of the fibers must be uniform. A major problem remains the occurrence of defects in the poly-L-lactide nanofibers (Figure 2.16) and NSCS/PEO nanofibers beads (Figure 2.17).

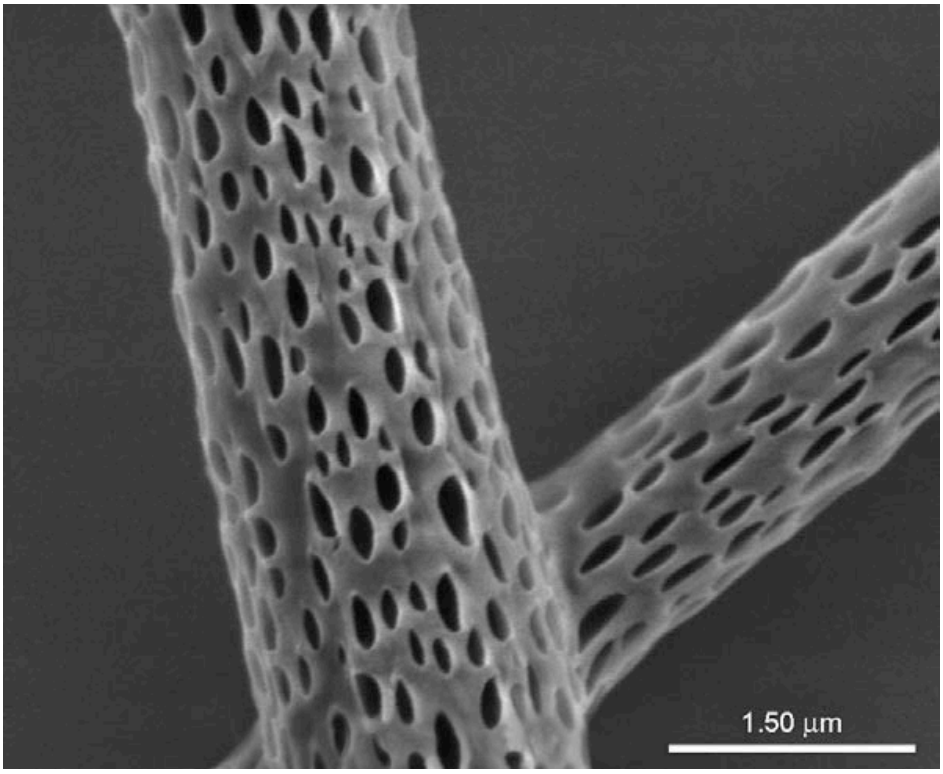

Figure2.16 SEM image of electrospun porous PLA nanofibers (147)

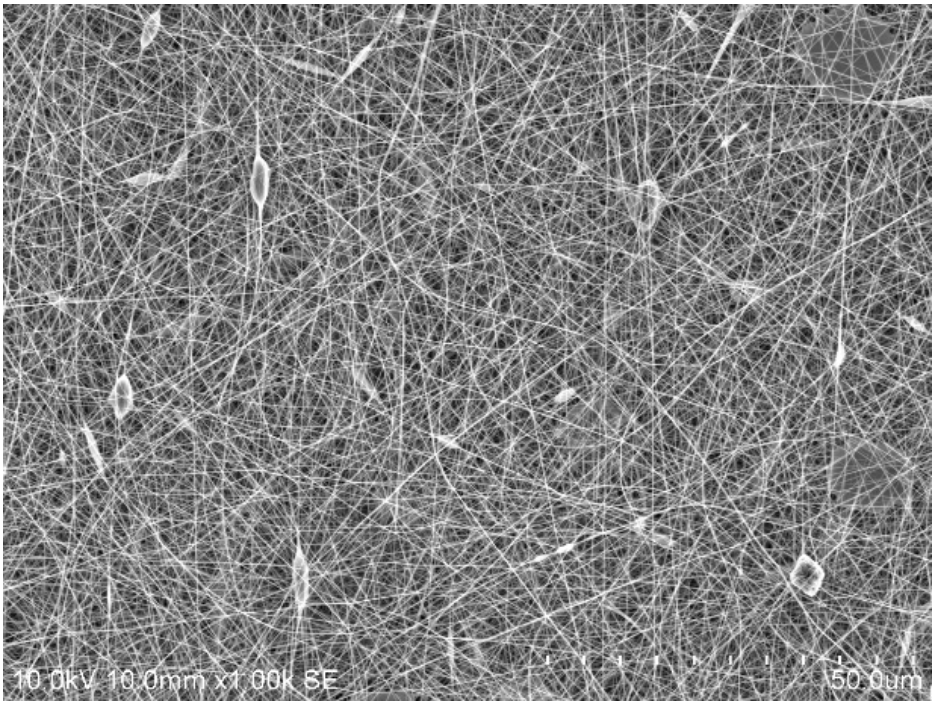

Figure 2.17 Electrospun NSCS/PEO nanofibers with beads obtained from electrospinning of 5 wt%/5 wt% and 6:4 mass ratio% (m/m)

There is no doubt that electrospinning is an efficient and flexible method for producing nanofibers; in many tests, the process parameters have been shown to affect fibre morphology and structure (148). While many studies have been conducted on the relationship between processing parameters and resulting microstructures, some effects remain unexplored (149). In this chapter, in more detail we explained how these parameters affect for electrospinning to produce nanofibers efficiently and effectively, many systemic, process and environmental parameters must be considered. So below are some of the most critical findings from previous studies. Researchers have extensively investigated electrospinning parameters to determine the characteristics of electrospun nanofibers. There are typically certain parameters that govern the electrospinning process, as shown in figure 2.18 including:

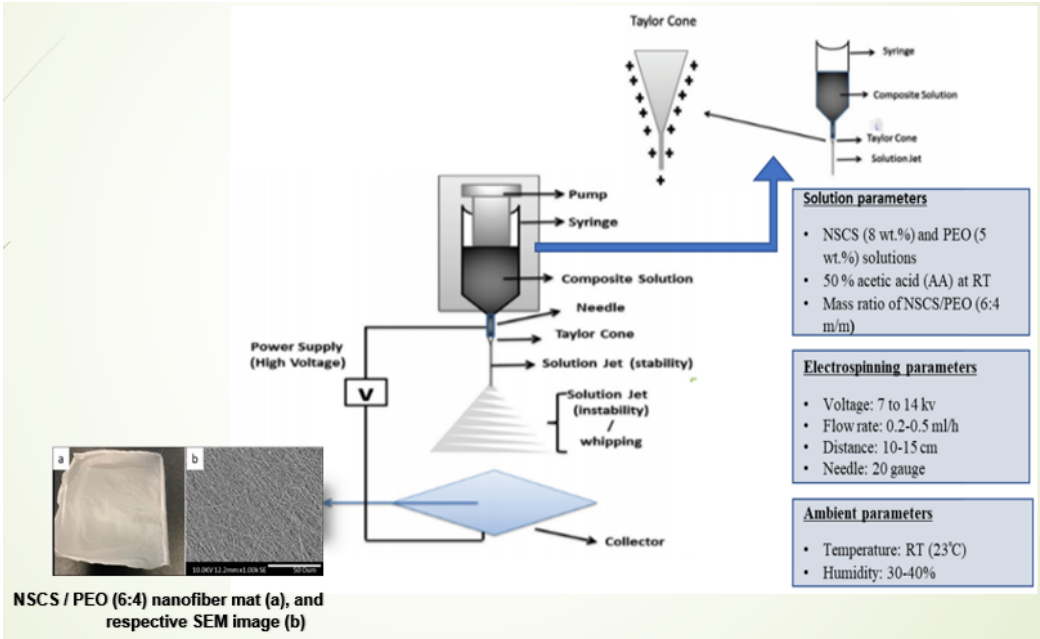

Figure 2.18 Schematic of production of the membrane (nanofibers)

(1) A solution's parameters include viscosity, conductivity, molecular weight, surface tension, polymer structure, and solution properties (conductivity / solution

charge density, surface tension, viscosity / concentration, molecular weight of polymers, dielectric constant and dipole moment).

One of the most commonly studied parameters is the concentration of the solution, which is closely related to its viscosity (148). A polymer solution with a higher molecular weight tends to be more viscous than one with a lower molecular weight when dissolved in a solvent. As polymer concentration increases in a solution, its viscosity increases as well. The viscosity of the solution and the entangled polymer chains are related (150). As the solution viscosity increases, the polymer chain entanglements also increase. Electrospun fibres containing beads are more likely to break into tiny droplets when polymer chains are entangled [67] (151).

(2) Parameters related to the process: applied electric field, distance between tip and collector, feeding or flow rate, capillary pressure, plate movement.

When sufficient voltage is applied, electrostatic forces prevail over solution surface tension, maintaining the drop's spherical shape at the needle tip. Taylor cones then form, followed by jets of polymer solution that reach the grounded collector, resulting in a Taylor cone and jet. All the parameters involved in the process must be precisely controlled so that the solvent evaporates from the tip and solid nanofibers are deposited on the collector (148).

Voltage is one of the important parameters that can be used to change the electric field between the needle and the collector plate. It is generally necessary for a positive or negative voltage of more than 6kV to initiate the jet from the Taylor cone (152). A higher voltage may be needed depending on the other processing conditions and solution parameters. With a higher voltage, the jet will accelerate more rapidly, resulting in more solutions emerging from the needle tip (150) Increasing the applied voltage leads to an increased electric field between the needle and the target, which in turn causes the solution to stretch more since the surface charges exert a more significant force on each other. Increasing the applied voltage decreases the diameter of electrospun nanofibres (153), (154),

(155). Literature suggests that polymer solution properties significantly affect electrospinning and fibre morphology (151).

(3) Ambient parameters: temperature and relative humidity (RH).

In general, all working parameters are crucial not only to understanding the nature and optimum conditions for electrospinning, but also, the conversion of polymeric solutions into nanofibers. In order to fabricate electrospun nanofibers with desired morphologies and diameters, it is crucial to control each of these parameters. Among these factors are humidity and temperature, which may affect the fibre diameter and morphology. Generally, the temperature is monitored since it impacts the solvent evaporation rate and solutions' viscosity (148). Increased temperature increases evaporation and decreases the viscosity of the solution (151). Also, by increasing the temperature, fibers with a smaller diameter are formed, while by decreasing humidity, the solvent is dried completely. There are very little data available about the influence of RH on electrospinning since it has been neglected and unexplored until recently. An electrospun product's morphology is affected by RH depending on its polymer composition. High RH values in electrospun hydrophobic polymers resulted in porous nanofibers. The formation of pores was explained by Medeiros et al. (156). In electrospinning, water acts as a nonsolvent when a hydrophobic polymer is used. The polymer film is formed around the liquid jet due to solvent evaporation. However, pores are formed to allow solvent molecules to evaporate and solidify nanofibers completely (148). In addition, increased humidity results in small pores appearing on the surface of fibers. Therefore, optimum conditions are required for improving fiber production (157).

2.3.2.2 Electrospinning of chitosan blends with synthetic polymers (PEO)

CS is difficult to form fibers from because of its limited solubility and polycationic nature. A wide range of solvent systems and concentrations have been used to electrospin CS (158). Even at concentrations where the CS chains were extensively dissolved in CS solution, no ultrafine fibers were obtained (139). In moderate concentrations, it becomes too viscous to overcome the electric field

and cannot be electrospun. Furthermore, CS is a cationic biopolymer that may affect the rheology of solutions (146). Nanofibers form successfully with electrospinning setups that maintain the solution's viscosity within a certain range (152). Since the electric field is not strong enough to overcome the viscosity of the solution above the upper threshold, fiber formation is hindered (159). Fiber formation is impossible below the lower limit because the polymer chains are not entangled, resulting in polymer beads (160). Thus, chitosan has been blended with materials that facilitate its processing and to improve electrospinability (161). For electrospinning to work, the co-spinning agent needs to be capable of producing entanglements and physical bonds with chitosan. Chitosan-based composite nanofibers can be produced using a wide range of synthetic polymers, including polyethylene oxide (PEO), polyvinyl alcohol (PVA), polylactic acid (PLA), and polycaprolactone (PCL) (162).

Earlier studies found that using chitosan grades with DDA of 54 (158), and 75-85%, a highly concentrated aqueous acetic acid solution (80-90%) worked well as another solvent for the fabrication of neat chitosan nanofibers. Increased acetic acid content of the solution has been found to reduce the surface tension of the solution, thereby improving chitosan's electrospinnability (163). However, TFA-based solvents are not ideal for electrospun chitosan nanofiber applications because the TFA/CS salt residues are very soluble in neutral and weak basic aqueous solvents. Moreover, the presence of toxic and harmful solvents in the final membranes raises serious concerns (164), (162).

Chitosan nonwoven fabrics have been prepared by electrospinning several times. While these attempts were not for pure CS systems, they blended CS with poly (ethylene glycol) or used derivatives of CS (165). As a result, electrospun nonwoven fabrics have not been prepared from pure CS yet (166). Blends of CS and PEO were electrospun to produce CS nanofibers (167). Electrospinning of highly deacetylated (97.5%) CS in 50% acetic acid (AA) in the presence of low-content polyethylene oxide (10 wt. %) produced beadless nanofibers of 60-80 nm in diameter (168). Additionally, CS is stable under film or fiber materials thanks to its H bond network in solid state (169). In order to explain how PEO improves the

electrospinnability of CS, the rheological properties of CS and PEO solutions were studied. Since surface tension and viscosity of the respective solutions were similar, positive charges on the CS molecule and its chain stiffness were considered the limiting factors for electrospinability of neat CS (170). Different blends of CS and PEO solutions were prepared with different component ratios (171). To increase the yield of CS, chitosan-based nanofibers were electrospun (172). The two techniques used for that purpose were: Firstly, PEO and CS solutions were mixed to produce nanofibers. A second step involved adding powdered PEO to CS solutions (167). Considering the toxicity of the used solvents, acetic acid was chosen at a concentration of 0.5 M, which corresponds to the maximum solubility of CS (167). As a result of its polycationic nature in solution, rigid chemical structure, and specific inter- and intramolecular interactions, CS is limited in its electrospinnability. A strong hydrogen bond prevents the free movement of polymeric chain segments exposed to the electrical field, resulting in jet break up (162). Also, the repulsive force between ionic groups on the polymer backbone prevents the formation of sufficient chain entanglements for continuous fiber formation during jet stretching, whipping, and bending: the process generally results in nanobeads instead of nanofibers (173). Furthermore, although high CS content CS-based nanofibers have been produced in the past years, several studies have used harmful solvents, such as trifluoro acetic acid (TFA) (174), and dimethyl sulfoxide (DMSO). Despite promising results, further research aimed at improving chitosan electrospinning was conducted (172).

CHAPTER 3 - EXPERIMENTAL DETAILS

3.1 Materials

Our general materials and methods for this project will be described in this chapiter. Chitosan (CS) of low MW (79-85% deacetylated, Sigma-Aldrich, powder) was used in this project as adsorbent material. Several acidic media, including dilute hydrochloric acid, glacial acetic acid (CH_3COOH) (AA) (99.7%, Fisher brand), were purchased from Fisher Science (Ottawa, Ontario, Canada), formic acid (FA), and dichloroacetic acid (DCA) was used. These acids were used as solvent in aqueous solution in order to prepare the CS solutions. Polyethylene oxide (PEO) with an average molecular weight of 900,000 g/mol (Sigma- Aldrich, St. Louis, MO, USA), was applied in this project as a copolymer agent to decrease CS viscosity and increase the electrospinning ability during the fiber's generation. The CS was mixed with another polymer (PEO), which can interfere with the rigid association of the CS molecules. Sodium Carbonate anhydrous (Na_2CO_3) (CAS 497-19-8 from Sigma- Aldrich), was employed for the membrane neutralization treatment. Fluoxetine hydrochloride (FLX) (CAS 56296-78-7), Carbamazepine (CBZ) (CAS 298-46-4), Ibuprofen (IUP) (CAS 15687-27-1), and Venlafaxine (VEN) (CAS 99300-78-4) all from Sigma-Aldrich (Oakville, ON, Canada) used as contaminants model for the adsorption studies. All chemicals were analytical grades and all solutions were prepared with distilled water. Chloroacetic acid ($ClCH_2COOH$) (CAS 79-11-8 from Sigma- Aldrich), sodium hydroxide (NaOH) (CAS 1310-73-2 from Sigma- Aldrich), pyridine (CAS 110-86-1 from Fisher Scientific), isopropanol (99.9%) and ethanol as solvent. Succinic anhydride, phthalic acid (CAS: 88-99-3 from Fisher Scientific, Ottawa, Ontario, Canada), dimethyl sulfoxide (CAS 67-68-5 from Sigma- Aldrich), and other reagents used in this experiment were of analytical grade. Sodium cyanoborohydride (CAS 25895-60-7 from Sigma- Aldrich), acetonitrile (HPLC grade), and O-phosphoric acid (HPLC grade; 85 wt.%) were purchased from Fisher Scientific (Ottawa, Ontario, Canada). (Siemens Super Transparent RO with 0.055 µS /cm

Conductivity). Deionized water was used for testing throughout all the studies (Siemens Ultra Clear RO).

The zeta potential in solution was determined using a ZetasizerNano (Malvern Instruments Ltd., model ZEN 3600).

3.2 Synthesis of Materials

3.2.1 Synthesis of N, O-Carboxymethylation of Chitosan (N, O-CMCS)

Chitosan (CS) (5.00 g) was added to a 20 Wt. % sodium hydroxide solution (50.00 mL) for 12 h at room temperature, and then separated by filtration. The treated CS was dip into 50 mL of 100% (v/v) anhydrous alcohol in a three-necked flask equipped with a stirring bar for 30 min at room temperature. Then, chloroacetic acid (3.58 g) was added into the reaction mixture and stirred for an additional 30 min. Then the mixture was heated to 60 ^{0}C and allowed to continue for the predetermined time (15, 30, 60, 90, 120 min). Finally, the resultant solution was filtered and the resulting cake dissolve in distilled water. The obtain solution was adjusted to pH 7.0 and precipitated by pouring into 100% (v/v) anhydrous alcohol. The white precipitate was filtered and washed three times with a 70% (v/v) ethanol solution and once with a 100% (v/v) anhydrous alcohol solution. The solution was then drying under vacuum at 80°C to obtain the products. The DS of N, O-CMCTS was determined using potentiometric titration (175). Characterization of carboxymethyl CS by FT-IR spectroscopy, and ^{1}H-NMR spectroscopy (176).

3.2.2 Synthesis of N-succinyl Chitosan (NSCS)

Two grams of CS, dipped into 20 mL of sodium hydroxide (20 wt.%) for 12h, filtered and added to 40 mL of dimethyl sulfoxide, and 2 g of succinic anhydride added at room temperature with stirring, and then placed in a 60°C oil bath and heated for a certain time. The contents of the flask poured into a 50 mL beaker followed by the addition of acetic acid solution with stirring until pH value of 7. Then, the precipitate filtered, and dissolved in distilled water and purified by

acetone. The product filtered and washed with ethanol (70%) for three times and anhydrous alcohol once, and then dried [**Erreur! Signet non défini.**].

3.2.3 Synthesis of N-aryl (N-Phthalic) Chitosan (NPCS)

CS dissolved in a solution of AA in methanol. Phthalic anhydride added to the solution and stirred at room temperature for 4Hrs. After standing the mixture for 3Hrs, $NaBH_4$ added and stirred at room temperature for 24Hrs. The solution then made alkaline by addition of sodium hydroxide. The precipitate formed after addition of sodium hydroxide was separated by filtration and oven-dried at 60°C for 24Hrs [**Erreur! Signet non défini.**].

3.3 Electrospinning Apparatus

The electrospinning experiments were performed at room temperature. A syringe pump device (KD Science, model 100), a high-voltage power supply (Gamma High Voltage Research USA), and a metallic wireframe as a collector were part of the electrospinning system. For the conservation and stabilization of the membranes, two laboratory ovens (Fisher Scientific IsotempOven, and Thermo Scientific HERAThermOven) were used. A schematic diagram of the electrospinning set-up used for the membrane preparation is depicted in Figure 3.19.

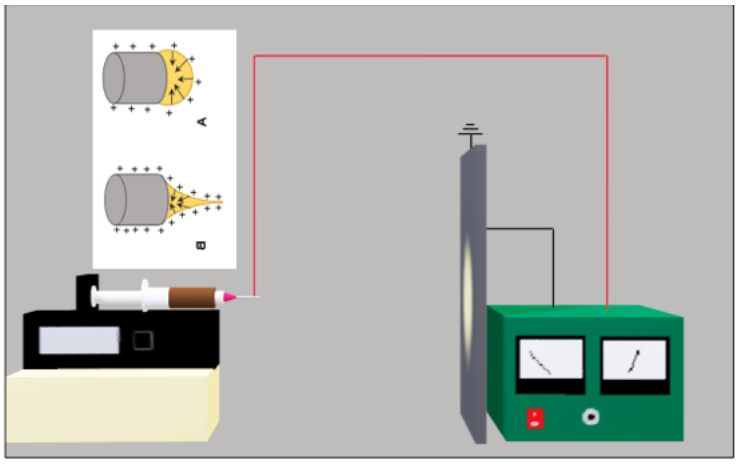

Figure 3.19 A schematic diagram of a typical electrospinning setup (177)

The polymer solution was placed into a 10 mL syringe with a capillary tip having an inner diameter of 0.6 mm. A copper wire connected to the positive electrode was inserted into the polymer solution. A copper plate wrapped with aluminum foil was used as collector and the latter was connected to the ground. A high-voltage power supply was employed to generate the electric field (0–30 kV). The applied voltage and the tip-to-collector distance were fixed at 15 kV and 150 mm, respectively.

3.3.1 Preparing the solution for electrospinning

The modified chitosan solution and PEO solution were dissolved separately at room temperature in acetic acid (AA) 50-90% solutions for 24 h until a complete dissolution was obtained. At room temperature, modified chitosan and PEO solutions were blended according to their different mass ratios for 24 hours until homogeneous. Following degassing, solutions were left to rest for 3 hours before electrospinning [**Erreur! Signet non défini.**].

3.3.2 Electrospinning Modified Chitosan

CS derivatives were electrospun with other water-soluble polymers such as PEO, PAA, and PVA in aqueous solutions containing chitosan derivatives (modified chitosan). Additionally, heat-induced esterification was optimized to render fibrous membranes insoluble in water (178). We examined the solubility of modified chitosan in a variety of solvents, including methanol, ethanol, acetone, acetonitrile, dimethyl acetamide, dimethyl sulfoxide, dimethyl formamide, water and acids, namely FA, AA, and TFA. An electrospinning set-up consisting of a dosing pump, a high-voltage source (0-30 kV) and a syringe with a needle tip of 0.7 mm was used to test the electrospinnability of the solutions. The collector consisted of an aluminum plate covered with aluminum foil and a metal frame. During electrospinning, the temperature was set at 22-25°C and the relative humidity was 30-35% [**Erreur! Signet non défini.**].

3.3.3 Nanofibers neutralization treatment

Stabilization will be performed by trying two different treatments including:

(1) Heating treatment at 110-180 °C for 30 min or (2) chemical treatment by immersing the nanofibers membrane in a (0.1 M) Na_2CO_3, or (acid, basic, acetic anhydride, methanol...etc) at RT (5,60, and 120 min), then Washing with distilled water until a neutral pH. finally, will be dried at room temperature for 24 h.

3.4 Batch Adsorption Experiments

The adsorption experiments will be performed in batch mode to investigate the adsorption of pollutants (Fluoxetine (FLX), Carbamazepine (CBZ), Ibuprofen (IBU), and Venlafaxine (VEL)) using electrospun membranes. For kinetic experiments, 25 mg of electrospun membranes and (50 ppm of pollutant initial concentration) will be added in 250 mL erlenmeyer flasks in order to evaluate the effect of adsorbent-adsorbate time contact on pollutants adsorption efficiency. The flasks will be shaken using an orbital shaker (Lab line Instrument) at room temperature, various pH and under a speed of 200 rpm. Agitation will be provided until the equilibrium. For equilibrium experiments, the same methodology will be adopted using different initial pharmaceutical concentrations (in the range of 50-100 ppm) at different temperatures (25°C, 50°C, 75°C). The adsorbed amount of pharmaceutical contaminate, q (mg/g) will be calculated using Equation 2.1 at various times ranging from 0 to 120 minutes.

3.4.1 Kinetic Models

Two types of kinetic modelling approaches have been considered in the adsorption literature to describe the transport of adsorbates inside adsorbent particles. The first type considers simple relationships between the adsorption performance and operating conditions. These models show how the mean adsorbent loading (q_t) changes with adsorption time. Models in this category include pseudo-first- and pseudo-second-order rate equations. The parameters obtained from these models will be used for adsorbent screening procedures. The second approach is the use of phenomenological models that attempt to describe the physics of the process. Information about the mechanism of adsorption can be obtained from the second type of models using the kinetic experimental results and the equilibrium adsorption data. Pseudo-first- and pseudo-second-order rate

equations and the intra-particle diffusion model will be used and applied to test the experimental data. The first-order rate equation, or the so-called Lagergren equation, can describe the initial phase in the adsorption process, although as adsorption progresses. The second-order rate equation suggests that chemisorption is the rate-controlling mechanism (179).

3.4.2 Equilibrium Study

The equilibrium adsorption isotherm is fundamental, and the equilibrium adsorption data will be analyzed using Freundlich, Langmuir and both isotherm equation models. Contaminant solutions with several concentrations were prepared to determine the equilibrium adsorption capacity of the chitosan derivatives. In equilibrium tests, 50 mg of adsorbent was added to glass tubes containing 10 cm^3 of the contaminant solution at a concentration ranging from 0 to 500 mg/dm^3. The pH was adjusted to 6.0, and the suspensions were agitated in the shaker for 2 h. The rest of the procedure was similar to the one previously described for kinetic tests.

3.4.3 Regeneration of Nanofiber Membranes

25 mg electrospun membranes were recovered by desorption of pharmaceutical contaminants in 50 mL contaminants solution (FLX) over 2.5 hours under stirring. The membranes were then dried at 70°C for 24 hours. We tested the membranes for reusability and contaminant recovery efficiency/adsorption capacity by performing five adsorption/desorption cycles.

CHAPTER 4 - SUMMARY OF ARTICLES

In the following three chapters, the key achievements of this research project are presented:

Chapter 5 describes the results of the first article: "Adsorption of Pharmaceutical Contaminants from Aqueous Solutions Using N, O-Carboxymethyl Chitosan/Polyethylene Oxide (PEO) Electrospun Nanofibers", that has been published in Journal of Materials Science and Chemical Engineering.

This paper presents an innovative treatment technology for water remediation based on electrospun nanofibers made of modified chitosan, a natural abundant biopolymer extracted from crabbing and shrimping industries' waste. Specifically, a nanofibrous nonwoven adsorbent is proposed to remove some fluoxetine (e.g. a common pharmaceutical residue largely discharged in urban effluents) from water. The following points are covered in the manuscript: a complete optimization of both the surface's modification of chitosan to caboxymethyl chitosan (N, O-CMCS) with easy chemical reactions and the electrospinning parameters, the fully characterization of nanofibers, some reported results of sorption tests conducted under different experimental conditions, and the determination of the best adsorption kinetic model. In addition, an interesting table comparing some adsorption capacities obtained from different existing adsorbents is provided to demonstrate the promising efficiency of the developed nanofibers. To our best knowledge, this study becomes the first one to report on the removal of pharmaceutical residues from water using N, O-CMCS electrospun nanofibers.

Second article in **Chapter 6** presents the " Nanofibrous Material of N-Succinyl Chitosan/Polyethylene Oxide for the removal of emerging pharmaceuticals from aqueous solutions" that ", that has been published in Journal of BioResources Journal.

It is not entirely different from first article that we have the objective of preparing defect-free nanofibers based on chitosan with high chitosan content in this work. As with article 1, we modified the chitosan surface as well as studied various properties, including surface tension, conductivity, viscosity, and acetic acid concentration. In this study, modified chitosan NSCS/PEO nanofibers were prepared by electrospinning, allowing for the formation of hydeophobic bonds in addition to electrostatic interactions bonds. By increasing the contact strength and interaction between bio-adsorbent (NSCS/PEO nanofibers) and contamination, the modified nanofiber membrane was able to increased adsorption capacity. A FTIR and NMR analysis confirmed the modification of the CS chemical structure.

"A comparison of the efficiency of different modified chitosan-based electrospun nanofibers for the removal of fluoxetine from wastewater" is presented in **Chapter 7**. It has been submitted in Arabian Journal of Chemistry.

Taking into account the distinctive findings of the first and second articles. In the third article, we compared fluoxenin adsorption on NSCS/PEO and a nanofibers material that contained the benzene ring (NPCS/PEO) to find a stronger adsorption. A study was conducted to investigate the effects of introducing benzene ring to chitosan surface, leading to the formation of π-π bonds alongside electrostatic interaction, hydrophobic interaction, and hydeogen interaction. According to our results, the hydrophobic interaction on chitosan surface decreased the polarity, thereby decreasing adsorption by decreasing contact between contaminant and bioadsorbent nanofibers (NPCS/PEO) in solution.

CHAPTER 5 - ARTICLE 1

Adsorption of Pharmaceutical Contaminants from Aqueous Solutions Using N, O-Carboxymethyl Chitosan/Polyethylene Oxide (PEO) Electrospun Nanofibers

Amna Hassan Issa Khierallah, Ilse Ileana Cardenas Bates, Bruno Chabot, André Lajeunesse

5.1 Foreword

This first article is entitled " Adsorption of Pharmaceutical Contaminants from Aqueous Solutions Using N, O-Carboxymethyl Chitosan/Polyethylene Oxide (PEO) Electrospun Nanofibers ". It has been published in Journal of Materials Science and Chemical Engineering, DOI: 10.4236/msce.2021.911003 Nov. 25, 2021.

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Amna Hassan Issa Khierallah is the main author of this article. She carried out all the scientific experiments and associated developments. Ms. **Ilse Ileana**

Cardenas Bates as a co-author, she contributed for this work to analysis the data for adsorption test. **André Lajeunesse** is the director of research and **Bruno Chabot** is the co-director of this research. All the authors participated in the revision and correction of the manuscript.

5.2 Résumé

Les résidus metabolite en decoulant quisont pharmaceutiques et les directs rejetés dans le milieu aquatique sont devenus un défi pour les stations d'épuration en raison de la hausse deleur concentration et de leurs propriétés physico-chimiques différentes. Ces contaminants émergents sont quotidiennement détectés dans les eaux de surface et les eaux usées rejetées par les municipalités. Pour assainir l'eau contaminée, diverses méthodes sont actuellement utilisées, notamment les méthodes primaires, secondaires et tertiairesavances. Cependant, certaines contraintes économiques et environnementales ont obligé la communauté scientifique à développer des procédés de désinfection alternatifs pour purifier les eaux usées. En tant que telle, la stratégie d'adsorption représente une solution "verte" peu coûteuse et efficace pour éliminer les polluants de l'eau. Dans cette étude, un nanomatériau composé de N, O-carboxyméthyl chitosan (N,O-CMCS) a été préparé à l'aide de chitosan (CS) et d'acide monochloroacétique dans diverses conditions. Le N, O-CMCS électrofilé a été synthétisé avec le copolymère polyéthylène oxyde (PEO) pour créer des membranes nanofibres présentant une meilleure spécificité vis-à-vis de contaminants diversifiés en fonction du pH du milieu. L'adsorbant développé a été utilisé pour éliminer la fluoxétine (FLX) des solutions aqueuses. Le nouveau nanomatériau a été caractérisé à l'aide de techniques FTIR, RMN et SEM. Des tests de sorption ont été effectués à l'aide d'une chromatographie liquide haute performance et d'un détecteur à barrette de diodes ultraviolettes (HPLC-UV DAD) dans des conditions expérimentales à pH contrôlé pour déterminer la capacité d'élimination des contaminants du nanomatériau. Les résultats d'adsorption prometteurs obtenus avec les nanofibres N, O-CMCS/PEO sont parmi les meilleurs à ce jour par rapport à d'autres adsorbants commerciaux et synthétisés

testés pour l'adsorption de FLX. Des expériences cinétiques ont été également effectuées pour étudier les effets des temps de contact sur l'adsorption FLX. Les résultats expérimentaux ont été ajustés aux deux modèles cinétiques courants de pseudo premier et second ordre. Ce dernier modèle cinétique décrit le mieux la sorption en surface. Elle a révélé un possible mécanisme de chimisorption avec liaison électrostatique pour les nanofibres N, O-CMCS/PEO.

Mots clés: N, O-Carboxymethyl Chitosan, Electrospinning, Nanofibers, Adsorption, Pharmaceuticals

5.3 Abstract

Residues of pharmaceutical and direct metabolites discharged into the aquatic environment have become a challenge for wastewater treatment facilities due to their increase in concentration and their different physicochemical properties. These emerging contaminants are daily detected in surface water and wastewater discharged by municipalities. To remediate the contaminated water, various methods are currently used including primary, secondary, and tertiary advanced treatments. However, some economic and environmental limitations have forced the scientific community to develop alternative disinfection processes to purify wastewater. As such, the adsorption strategy represents a “green” low-cost and effective solution to remove pollutants from water. In this study, a nanomaterial made of N, O-carboxymethyl chitosan (N, O-CMCS) was prepared using chitosan (CS) and monochloroacetic acid under various conditions. N, O-CMCS electrospun was synthetized with the copolymer polyethylene oxide (PEO) to create nanofiber membranes showing a better specificity toward diversified contaminants depending on the pH of medium. The developed adsorbent was used to remove fluoxetine (FLX) from aqueous solutions. The new nanomaterial was characterised using FTIR, NMR, and SEM techniques. Sorption batch tests were carried out using high-performance liquid chromatography and ultraviolet diode array detector (HPLC-UV DAD) under controlled pH experimental conditions to determine the contaminant removal capacity of the nanomaterial. The promising adsorption results obtained with N, O-CMCS/PEO nanofibers are

among the best ones obtained so far in comparison to other commercial and synthetized adsorbents tested for FLX's adsorption. Kinetic experiments were also performed to investigate effects of contact times on the FLX adsorption. Experimental results were fitted to both common kinetic models pseudo-first and second order. The latter kinetic model described the best the sorption on surface. It revealed a possible chemisorption mechanism with electrostatic bounding for N, O-CMCS/PEO nanofibers.

Keywords : N, O-Carboxymethyl Chitosan, Electrospinning, Nanofibers, Adsorption, Pharmaceuticals

5.4 Introduction

The contamination of natural resources such as water remains one of the most challenging issues of modern-day society. Worldwide water contamination by chemicals is especially of concern (180). Even though most of these contaminants are detected at very low concentrations (ng/L to µg/L), many molecules (and/or their treatment by-products) possess biological activity. They are daily discharged into water bodies and may cause severe environmental issues (e.g. detrimental effects to our natural water resources and aquatic organisms) if they are not properly removed (181), (182). Among listed contaminants, pharmaceutical products are now recognized as primary polluters retrieved in marine environments and ecosystems mainly after human or animal excretion (183), (184), (185)These pollutants are represented by a wide array of substances that include both non-prescription and prescription drugs (40). They are part of different classes (e.g. analgesics, antibiotics, β-blockers, lipid regulators, antidepressants, contraceptives, synthetic and natural hormones) (186), (187). In addition, industrial by-products, as well as some hospital effluents have been reported in literature as major contamination sources since they are released at higher concentrations in municipal effluents (188). Unfortunately, limited removal rates are frequently observed in wastewater treatment plants (WWTPs) for pharmaceuticals residues (189), (190).

Since traditional water and wastewater treatment systems are facing difficulties to provide an effective barrier against recalcitrant compounds, advanced treatment strategies need to be developed (191). As such, membrane filtration, advanced oxidation processes (AOPs), and UV irradiation are examples of processes that have the potential to improve the water remediation (192). Despite their effectiveness in removing pharmaceuticals residues, some of these may not be suitable due to “high-unit-volume” treatment costs. Additional efforts on the extraction methodologies are therefore required, especially with emerging nanotechnologies (193). In this way, adsorption of contaminants is now recognized as a promising and efficient separation technique for wastewater treatment (194). The adsorption phenomenon on surface’s materials can be described using different theoretical developed models of varied complexity. Thus, the uptake rate can be determined with pseudo-first-order (PFO) and pseudo-second-order (PSO) models, while mechanisms of sorption can be elucidated using well-known and recognized isotherms models (e.g. Langmuir, Freundlich, etc.) (195).

Among existing adsorbent materials, zeolites (196) and activated carbon (AC) (197), (198), (199), were largely studied for treating wastewater due to their high performance. However, a longer recycling time and expensive regeneration procedures have made them difficult to use on a regular basis. To overcome such drawbacks, a considerable work was spent in developing effective and environmentally friendly adsorbents based on available low-cost natural polymeric materials [10]. Accordingly, different biomaterials were found to be effective for the elimination of contaminants from aqueous effluent.

In the last decade, biomaterials have received a lot of attention because of their biodegradable and non-toxic composition (200). The naturally abundant polysaccharide chitosan (CS) produced from a deacetylation of chitin, has been used in several adsorption applications (201). However, its high viscosity, crystallinity, as well as its poor mechanical strength, limited solubility and instability in acidic medium have restricted its usefulness as adsorbent (202), (203). Hence, chemical modifications of CS are performed to improve some

properties (e.g. solubility, antimicrobial behavior, and ability to interfere with other compounds) (204), (205). A chemical modification may also be attempted in order to gain more specificity and a sorption versatility toward contaminants, depending on the grafted chemical functionalities on the surface of CS (206).

One well-known modified CS derivative is N, O-carboxymethyl chitosan (N,O-CMCS) (206), (207). This modified biopolymer is synthetized following an alkalization and a nucleophilic substitution (SN2) reaction using monochloroacetic acid ($ClCH_2COOH$) (207), (208). The medium temperature and reagents of the reaction (including their stoichiometry) influence both the substitution of the CMCS (N- and/or O-) and its ratio of substitution (178), (209). Aside from its high viscosity and hydrodynamic volume, CMCS has unique chemical, physical and biological properties (210). This modified biopolymer enables low toxicity, biodegradability, biocompatibility and high ability to form films, fibers, and hydrogels (211). Some chemical modifications achieved on CS's surface were exploited in order to increase its water solubility and broaden its range of applications (212), (213), (214). Other carboxymethyl derivatives having different properties were reported elsewhere (O-CMCS, N, O-CMCS, N-CMCS and N-succinyl chitosan (NSC)) (215).

Synthetized nanomaterials are of great interest for a variety of applications due to their sought characteristics, such as high specific surface area and porosity [26]. In this way, electrospinning has gained popularity because of its ability to produce polymer nanofibers with diameters varying from several micrometers to tens of nanometers (216), (217). During electrospinning, a high voltage is applied to generate an electrically charged jet of a polymer previously dissolved in solution. The elongated jet is then collected on a metallic surface (target electrode) upon the evaporation of the used solvent producing nanofibers as a nonwoven mat. The formation of electrospun nanofibers from polymer solutions has been extensively studied in terms of voltage, tip-to-collector distance, polymer solution extrusion rate, and polymer solution properties (217).

Until now, a wide range of harmful environmental contaminants such as heavy metals, dye materials, and a few pharmaceuticals residues have been adsorbed by CS nanofiber membranes (218), (219) , (220). Therefore, the use of membranes made of N, O-CMCS could represent an interesting alternative method to purify pharmaceutical residues from wastewater. To the best of our knowledge, there is no application reported yet on modified N, O-CMCS electrospun nanofibers used as adsorbent to extract pharmaceuticals residues from wastewater, especially the antidepressant fluoxetine (FLX) largely prescribed around the world by physicians to treat depression. This paper aims at the development of N, O-CMCS/PEO electrospun nanofibers, with a focus on the fundamentals of their manufacturing (e.g. chemical synthesis, characterization, electrospinning conditions). In addition, some batch tests are performed to determine the best adsorption conditions of FLX in aqueous solution. Finally, a kinetics study is also provided as complementary information to better understand the adsorption behavior of the synthetized membranes.

5.5 Materials and Methods

5.5.1 Materials

A low molecular weight chitosan (CS) (MW 50,000 - 190,000 g/mol, 75% - 85% deacetylated) was purchased from Sigma-Aldrich (Reykjavik, Iceland). Polyethylene oxide (PEO) with an average molecular weight of 900,000 g/mol (Sigma- Aldrich, St. Louis, MO, USA) was used as a co-spinning agent. Chloroacetic acid was purchased from Sigma-Aldrich, sodium hydroxide (NaOH), acetic acid (CH_3COOH), sodium carbonate (Na_2CO_3), isopropanol, and ethanol were also used for experimentations. All chemicals were analytical grades. Fluoxetine hydrochloride (FLX) (CAS 56296-78-7) from Sigma-Aldrich (Oakville, ON, Canada) was used for the adsorption batch test as a model contaminant. Methanol (HPLC grade), acetonitrile (HPLC grade), O-phosphoric acid (HPLC grade; 85 wt%), and glacial acetic acid ACS reagent (99.7%) were purchased from Fisher Scientific (Ottawa, Ontario, Canada).

5.5.2 Methods

5.5.2.1 Preparation of N, O-CMCS

An adapted methodology was used for the synthesis of N, O-CMCS by alkalization followed by carboxylation (6). CS (2.00 g) was mixed in 20 mL of a sodium hydroxide (20%) solution and stirred at room temperature (RT) for 12 h. The resulting CS of higher degree of deacetylation was separated by filtration. Next, 15 mL of isopropanol was added to the previously treated CS. Then, monochloroacetic acid (1.43 g) dissolved in isopropanol (10 mL) was slowly added dropwise into the treated CS isopropyl alcohol solution. The mixture was agitated for an additional 30 min. The flask was then put into a heated oil bath and stirred for 4 h. Then, the content was poured into a 50 mL beaker. Under continuous stirring condition, acetic acid (50%) was slowly added until the pH value reached 9. The product was in its salt-based form (N, O-CMCS-Na) due to the alkaline reaction medium. Finally, the reaction mixture was filtered, and the solid product was rinsed 3 times with a 200 mL ethanol solution, then once with absolute ethanol. The resulting solid was subsequently dried in an oven (50˚C) for three days. After, 1 g of N, O-CMCS-Na was suspended in 80% ethyl alcohol aqueous solution (100 mL), and then 10 mL of hydrochloric acid (37%) was added dropwise and stirred for 30 min to get the neutralized form. The resulting solid N, O-CMCS was filtered and rinsed using ethanol (70% - 90%) prior being dried out under vacuum overnight at RT (199).

5.5.2.2 Chracterization of N, O-CMCS

The Fourier transformed infrared (FT-IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy was used to confirm the addition of carboxymethyl groups on the CS amino and primary hydroxyl sites of the CS. Analyses were performed on an FT-IR spectrometer (FTIR Thermo iS10) at wavenumbers ranging from 600 to 4000 cm^{-1}. ^{1}H-NMR spectra of CS were obtained in D_2O, and N, O-CMCS in D_2O/HCl (100:1 v/v) using an NMR spectrometer (OXFORD NMR) under a static magnetic field of 200 MHz. To determine the zeta potential (ZP), a 1 M (10 mL) solution of N, O-CMCS was dissolved in distilled water for 1 h with moderate

shaking at room temperature. NaOH (0.01 M) was used to neutralize the pH of the solution. The zeta potential in solution was determined using a ZetasizerNano (Malvern Instruments Ltd., model ZEN 3600).

5.5.2.3 Electrospinning, Preparation of N, O-CMCS and PEO Solutions

Stock solutions of N, O-CMCS and PEO were prepared in distilled water at three specific concentrations: 2.5, 3.3 and 8.0 wt% for N, O-CMCS, and 1.5, 3.0 and 8.0 wt% for PEO. To ensure a full and homogeneous dissolution, both solutions were kept under agitation at RT (e.g. 2 h, N, O-CMCS; 20 h PEO). Then, appropriate amounts of N, O-CMCS and PEO were mixed at various ratios to prepare electrospinning solutions. Electrospinning solutions used in this study are summarized in Table 5.3 All electrospinning solutions were magnetically stirred for 2 h, then transferred in an ultrasonic bath for 15 min to remove air bubbles. Finally, the mixture was rested for 3 h before being used in the electrospinning setup. The N, O-CMCS/PEO solution was poured into an electrospinning plastic syringe or kept in a refrigerator at 4˚C.

Table 5.3 Electrospinning solutions prepared at various weight ratios for experimentations.

Electrospinning solution	Weight % ratio (CMCS: PEO)
1	2:1
2	1:3
3	3:1
4	3:4
5	1:4
6	4:3
7	4:1

5.5.2.4 Electrospinning Parameters

A syringe pump device (KD Science, model 100), a high-voltage power supply (Gamma High Voltage Research USA), and a metallic wireframe as a collector were part of the electrospinning system. For the conservation and stabilization of the membranes, two laboratory ovens (Fisher Scientific IsotempOven, Thermo Scientific HERAThermOven) were used. A schematic diagram of the electrospinning set-up used for the membrane preparation is depicted in Figure 5.20 Each electrospinning solution (Table 5.2) was poured into a 5 mL syringe

mounted with a 20-gauge needle and attached to a syringe pump providing a slow and steady flow rate of liquid (0.4 mL/h). A distance (6 - 8 cm) was set between the tip of the needle and the collector. A metallic frame was used for the collector. The voltage used ranged between 10 and 15 kV. Various electrospinning conditions were attempted to obtain an optimal jet as well (stable with minimal drop projections) and beadless nanofibers mats by varying the flow rate, distance, and electrical current. Electrospinning was carried out in a tailor-made enclosure, at RT and relative humidity ranging between 30% - 50%. The nanofibrous mat was removed from the frame at the end of the electrospinning process and dried for 24 h in an oven at 80˚C.

5.5.2.5 Stabilization of Nanofibers

N, O-CMCS/PEO nanofibers are soluble in water following the electrospinning process due to ionizable chemical functionalities of the material. After electrospinning, the nanofiber mat was dried overnight in an oven at 80˚C to remove residual solvent. A stabilization cycle was then completed by soaking resulting membranes in Na_2CO_3 (0.1 M) at RT for 3 h (219). Finally, to improve the nanofiber mat stability in aqueous media, a heat treatment at 140˚C for 30 min was applied. The material stability was determined by an immersion in water for up to 6 h. Effects of water on nanofiber structure and morphology were studied by SEM images.

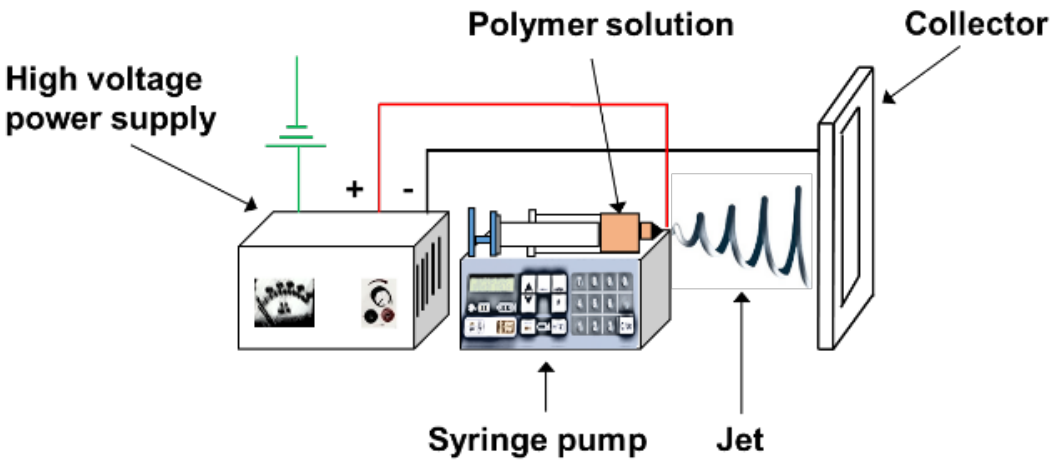


Figure 5.20. Schematic representation of the electrospinning setup

5.5.2.6 Characterization of Nanofibers

The degree of substitution (DS) of the sample was calculated using a potentiometric titration method (221). Briefly, dried N, O-CMC (0.20 g) was dissolved in 0.1 M hydrochloric acid solution (20 mL). Methyl orange was used as indicator for the end-point determination. A standard 0.1 M sodium hydroxide solution was used during titration (221), (178). The cumulative DS of the sample was determined using Equations 5.15 and 5.16:

$$\mathrm{DS} = \frac{161\mathrm{A}}{\mathrm{M}_{\mathrm{CMCS-CS}}} - 58\mathrm{A} \qquad \text{Equation 5.15}$$

$$A = V_{NaOH} \,.\, C_{NaOH} \qquad \text{Equation 5.16}$$

where M_{CMCS} is the mass of CMCS (g), V_{NaOH} and C_{NaOH} are representing respectively the volume and molar concentration (M) of NaOH, and finally 161 and 58 are associated to the molecular weights of the chitosan (glucosamine) and the CMCS group (178).

Morphologies of both nanofibers CS/PEO and N, O-CMCS/PEO were assessed using a scanning electron microscope (SEM) (Hitachi SU1510 Scanning Electron Microscope). The average diameter of electrospun nanofibers was estimated using SEM images and Image J software. In order to obtain an average value, the diameter of 50 nanofibers collected on three separate images was calculated (e.g. total of 150 nanofibers per sample).

Some infrared (FT-IR) spectra analyses of the electrospun nanofiber mats were performed using a Fourier transform infrared spectrometer (Nicolet iS10, Thermo Scientific) in the 400 to 4000 cm^{-1} wavenumbers range. In addition, ^{1}H-NMR spectra of CS and N, O-CMCS in D_2O/DCl were recorded using a 200 MHz NMR spectrometer (Varian).

5.5.2.7 Batch Adsorption Procedure

The adsorption of FLX by the electrospun nanofibrous mat was carried out in batch mode. A 25 mg sample of the membrane was inserted into one Erlenmeyer

flask containing 50 mL of an FLX solution (50 ppm) and 5% of methanol. The flask was then agitated on an orbital shaker (ORBIT Environ-shaker, Lab-Line) at RT. Before insertion of the membrane into the solution, an aliquot of 500 Ml was sampled to determine the initial FLX concentration. Batch tests were conducted over a period of 150 min to ensure that equilibrium was achieved prior to the collection of a 500 µL aliquot. The adsorption capacity at time t (Q_t) was determined using the following Equation 5.17:

$$Q_t = \frac{(C_0 - C_e)}{m} V \qquad \text{Equation 5.17}$$

Where C_e is the concentration of the contaminant (ppm) at time t (min), C_o is the initial concentration of contaminants (ppm), V is the volume of the solution (L), and m is the mass of adsorbents (g).

In order to determine the residual concentration of FLX in water samples during batch adsorption tests, a high-performance liquid chromatography (HPLC) system (Shimadzu Prominence I-series) coupled with a diode array detector (DAD) was used. The chromatographic separation was achieved using a C18 reverse-phase column (XB-C18, 100 Å, 150 × 3 mm, 2.6 µm particle size, Phenomenex, Kinetex®). The residual concentration of FLX in aqueous solution was determined by HPLC-UV DAD according to a method developed by Camiré et al. [44].

5.5.2.8 Kinetic Tests

Kinetic curves were obtained by collecting medium samples (500 µL) at predetermined periods (0, 5, 10, 15, 20, 25, 30, 40, 50, 60, 75, 90, 120, and 150 min). Tests were carried out at RT with an initial FLX concentration of 50 ppm. Concentrations of FLX in aqueous phase were determined using an HPLC-UV DAD system. All tests were performed in triplicate to provide mean and standard deviation values.

Adsorption kinetic models are used to characterize the adsorption process such as the movement of the adsorbate to the adsorbent's external surface, the internal diffusion of the adsorbate to the active sites, and the real sorption to the

adsorbent's external surface (222) , (122). Two models are mostly used in kinetics studies by researchers. Hence, it was decided to use nonlinear forms of pseudo-first order (PFO) (Equation 5.18) and pseudo-second order (PSO) (Equation 5.19) models in order to get the best-fit experimental data.

$$Q_t = Q_e\ (1 - exp^{-K_1 t}\ ) \qquad \text{Equation 5.18}$$

$$Q_t = \frac{K_2 Q_e^2 t}{1 + k_2 Q_e t} \qquad \text{Equation 5.19}$$

where Q_e is the amount adsorbed (mg/g) at equilibrium, Q_t is the amount adsorbed (mg/g) at time t (min), k_1 is the PFO adsorption rate constant (min^{-1}), and k2 is the PSO adsorption rate constant (g/g min).

Kinetic models are typically used to examine the mechanism involved during the adsorption process, as well as the location at the surface of adsorption, the chemical reaction involved, and/or the processes of diffusion. As the process of prevalence, the PFO model assumes a physical adsorption, while a chemical adsorption is inferred by the PSO model (223). Kinetic parameters (maximum adsorption potential and kinetic constant) were determined for both models using software: the kinetic equation solve feature for Microsoft Excel, and nonlinear regression analysis (MATLAB).

5.6 Results and Discussion

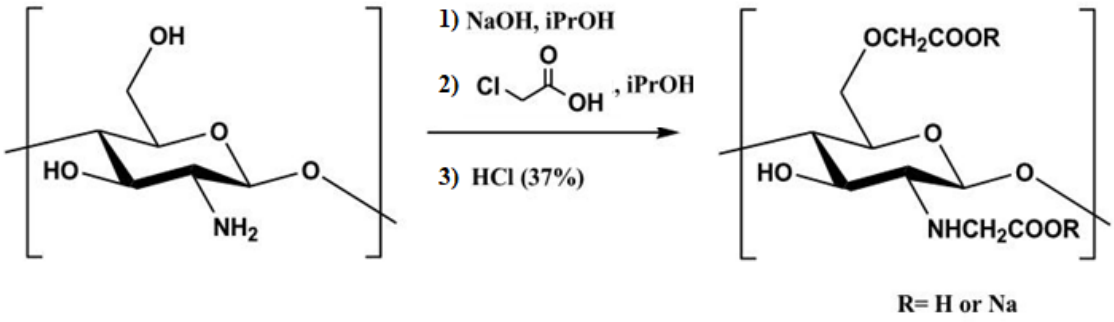
5.6.1 Characterization Techniques of CS and N, O-CMCS

N, O-CMCS was synthesized by alkalization followed by carboxylation as shown in Scheme 5.22 First, CS was treated with an alkaline solution of isopropanol using NaOH, which acted as a swelling agent. The latter enables the penetration of the relatively unreactive CS polymer. Then, the CS was treated with monochloroacetic acid to generate N, O-CMCS prior to its neutralization with HCl (37%) (224), (225). Infrared (IR) and ^{1}H-NMR spectroscopy provided evidence of the successful carboxymethylation and the presence on resulting spectra of distinctive CS and CMCS functional groups (225). As reported in the literature, this reaction does not go to completion and certain hydroxyl and amino moieties

remain unsubstituted (216). Furthermore, it must be taken into account that if CS is not fully deacetylated, certain units of glucosamine and acetylglucosamine from the partial deacetylation of the parent chitin may also interfere with the reaction (226), (227). According to Du and Hsieh (2008), the DS and yield of CMCS should be higher with longer reaction times of both alkalization (2-12 h) and carboxylation (2-5 h) (178). However, they only improved at higher temperature of alkalization (178). Based on these findings, we determined the best chemical reaction conditions and optimized the chemical synthesis of N, O-CMCS with DS value of 1.15. The carboxylation and alkalization were both conducted at 60˚C. During the carboxylation reaction (4 h), no additional gain was observed in terms of DS at extended time. However, increasing the reaction time of the alkalization from 2 h to 12 h had a tremendous impact on the DS. As expected, the resulting N, O-CMCS biomaterial is soluble in distilled water at 60˚C (228), (229),(108).

5.6.1.1 Infrared (FT-IR) Analysis

Infrared spectra of CS and N, O-CMCS are depicted in Figure 5.21. As shown, additional bands are well supporting the chemical structure of N, O-CMCS (DS 1.15). The broad band at 3301 cm^{-1} (axial stretching of the O-H and N-H bonds secondary amine) is present in FT-IR spectra (Figure 5.22(b)); this evidence suggests the formation of the modified compound at -NH position of the CS.



Scheme 5.21 Synthetic route of N, O-carboxymethyl chitosan

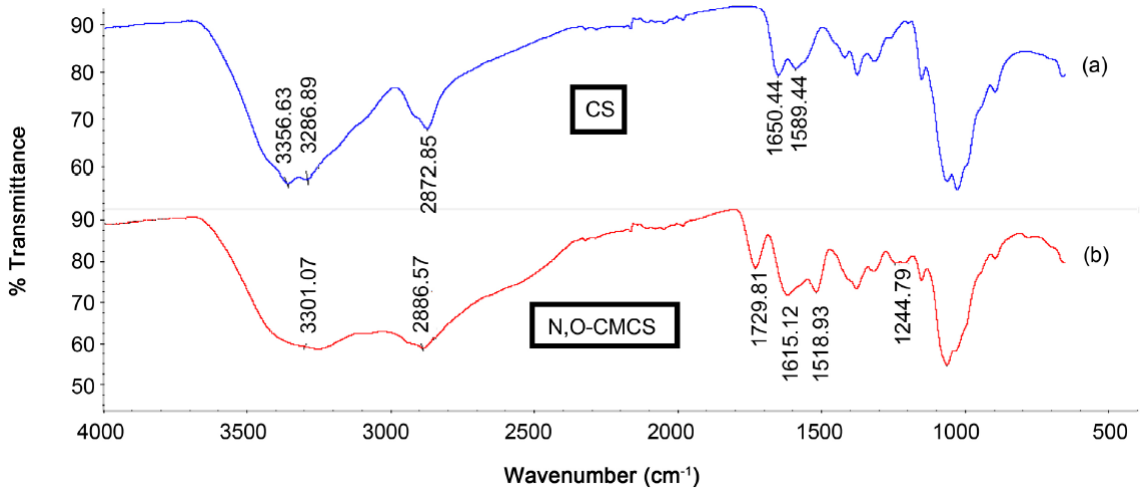


Figure 5.22 FT-IR spectra of CS (a), and N, O-CMCS (DS 1.15) (b)

In addition, the stretching vibration of C-O located in CH_2COOH group can be associated to peaks 1250 cm^{-1} and 1245 cm^{-1}. The peak at 2887 cm^{-1} corresponds to the axial stretching of the C-H bonds, and the peak 1730 cm^{-1} is related to the carbonyl group C=O from the newly formed COOH groups, which was not part of the initial CS spectrum. Bands at 1150 - 897 cm^{-1} of C-O and C-O-C appear in all spectra. Characteristic bands that belong to CS are also identified: 3357 cm^{-1} and 3287 cm^{-1} (O-H and N-H bonds), 1650 cm^{-1} and 1589 cm^{-1} (NH_2 primary amino group of CS prior to its chemical modification to a secondary amine). Reported FT-IR peaks and bands confirming the carboxymethylation conversion of CS to N, O-CMCS are consistent with other published studies (214) , (230).

5.6.1.2 ^{1}H-NMR Analysis

^{1}H-NMR spectra of CS and N, O-CMCS in D_2O/DCl are reported in Figure 5.23. Despite some similarities found within both spectra, the integration of peaks located at 3.95 and 4.66 ppm can be associated to respectively the -N-CH_2- and -O-CH_2- groups assigned to protons on C2 and C6 positions of the N, O-CMCS biomaterial. According to our expectations, a greater degree of N-carboxymethylation than O-carboxymethylation is observed. This result demonstrated the higher nucleophilicity of the nitrogen compared to oxygen. As

depicted in the ^{1}H-NMR spectrum of CS the multiple from 3.40 to 3.90 ppm is corresponding to H3, H4, H5, and H6 protons of the ring. Finally, the broad singlet at 2.90 ppm is owed to the H2 assigned to both CS and N, O-CMCS spectra (178),(108).

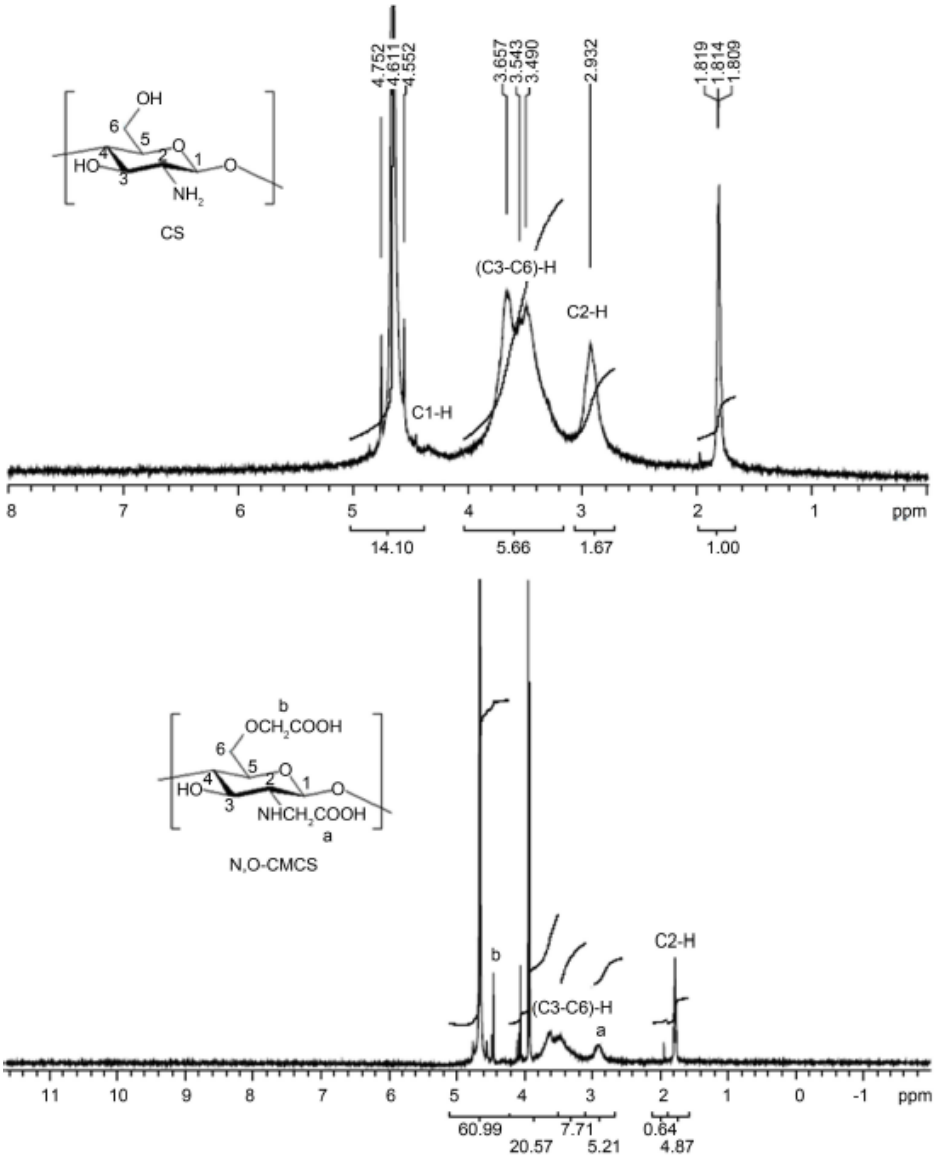


Figure 5.23 ^{1}H-NMR spectra of CS in D_2O and N, O-CMCS in D_2O/DCl

5.6.1.3 Zeta Potenial Results

The Zeta potential (ZP) is used to measure the effective electric charge on the membrane's surface; it can provide useful information on possible electrostatic

interactions between N, O-CMCS and FLX molecules. Based on the degree of substitution (DS) of the N, O-CMCS calculated using a potentiometric or acid-base titration method, this measure provides information about the ionization state of the grafted carboxylic acid moieties on the surface of the modified polymer. Figure 5.24 shows the ZP (mV) as a function of pH. As the pH increased, the ZP is decreasing to negative values. This indicates that N, O-CMCS becomes highly ionized with negative charges due to larger amount of deprotonated carboxyl groups ($-COO^-$). Under alkaline conditions, an electrostatic sorption mechanism is possible and favors the attraction of positive ions toward the negative surface of the modified biomaterial N, O-CMCS. However, at pH < 4.5 the - 3 RNH^+ group (from protonated secondary amine) is predominant along with positive ZP values. Around pH 4.5, an isoelectric point (pI) is generated by the presence of both charged species (e.g. - 3 RNH^+ /$-RCOO^-$) on the surface. Similar observations are reported in literature (230), (178), (222).

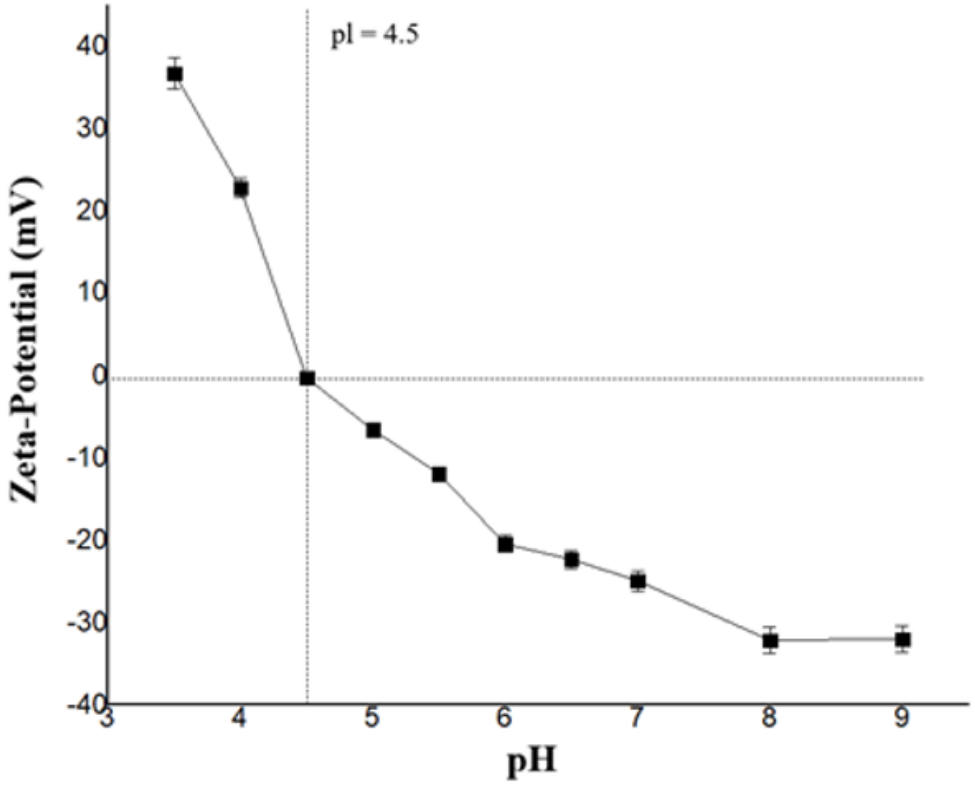


Figure 5.24 Zeta potential of N, O-CMCS as a function of pH

5.6.2 Electrospinning Parameters and Stabilization of Nanofiber Mats

Two of the most critical parameters affecting the electrospinning process are the concentration and the solution's mass ratio N, O-CMCS/PEO, since they play a key role in having defect-free nanofibers. Electrospun N, O-CMCS/PEO nanofiber mats were prepared from aqueous solutions at various N, O-CMCS concentrations and CMCS-PEO mass ratios. PEO was used as a co-polymer agent to facilitate the electrospinning process of CMCS. Electrospun N, O-CMCS/PEO mats were more stable with smaller nanofiber diameters than those obtained with CMCS dissolved in 1% acetic acid solution. They were also beads-free. In the present study, an optimization was conducted to find out as the best individual polymers concentrations and right mass ratios of N, O-CMCS/PEO that are offering suitable nanofibers web with expected diameters. Results of this optimization analysis is shown in Appendix (Table S1). Electrospinning of aqueous N, O-CMCS/PEO solutions at low concentrations (CMCS/PEO 2.5 wt%:1.5 wt%) brought droplets and unstable jet during certain experiments. By contrast, when both CMCS and PEO concentrations were prepared at higher concentrations (CMCS/PEO 8 wt%:8 wt%), nanofibers with beads and large diameters were obtained. Therefore, our findings proved that the aqueous mixture composition had an important effect on the morphology and diameter distributions of electrospun nanofibers.

A comparative study of cumulated results from manufactured nanofibers of unmodified CS and modified CS (N, O-CMCS) was also completed. Figure 5.25 shows SEM images of one CS/PEO electrospun membrane. The material was synthetized using mixed solutions made of CS 2.5% and PEO 1.5% (4:1). The CS polymer was dissolved in 90% acetic acid, and the experimental parameters were as follows: flow rate 0.2 mL/h, distance tip-collector 7 cm, and voltage 10 kV. Electrospinning was carried out at RT and relative humidity ranging between 16% - 20%. Thus, nanofibers of pure CS (140 ± 53 nm) were produced successfully with slight modifications of our previous developed protocol (219).

The optimal aqueous mixture (N, O-CMCS/PEO) was found to be the 4:3 ratio (Table S1). It is important to mention that the formation of nanofibers is greatly affected by humidity. Indeed, nanofibers were very thin and developed inconsistently at lower humidity levels. However, an electrospraying effect was found when the humidity was higher than 35%. During our optimization study, four N, O-CMCS/PEO mixtures have provided optimal nanofibers formation. Despite the fact we had similar adsorption results with two mass ratios (2.5 wt%/3 wt% (4:3); 2.5 wt%/3 wt% (3:1)), we selected the ratio 4:3 mainly because of a more stable jet obtained during winter and summer seasons (fluctuation of humidity observed). In addition, resulting nanofibers using a 4:3 ratios provided better adsorption capacity than other nanofibers synthetized with different N, O-CMCS/PEO mixtures.

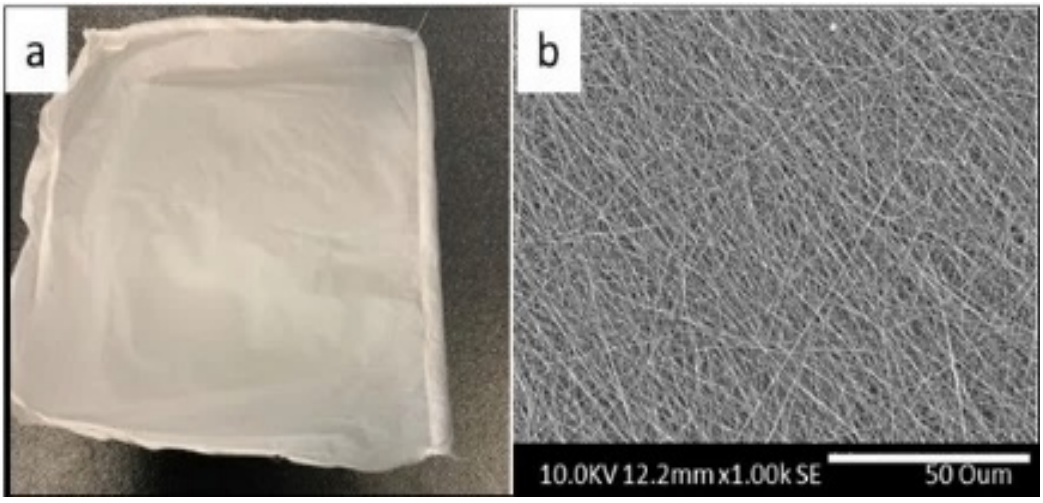


Figure 5.25 CS / PEO (4:1) nanofiber mat (a), and respective SEM image (b)

Optimal heating stabilization conditions of nanofibers were found to be 140˚C for 30 min. Under these conditions, membranes were stiffened, and fibers were strengthened without any surface modification. In addition, it was observed that the thermal stability was even higher, and the N, O-CMCS membrane was more water-resistant (178). Many attempts were made to get stable nanofibers in water via different chemical treatments Figure 5.26. In all cases, the tested chemical additive was not suitable; they destroyed or altered membranes rather than stabilize them. Therefore, thermal-cross-linking stabilization of membranes at

140˚C for 30 min was found the safer and optimal way to stabilize the N, O-CMCS/PEO nanofibers without any surface damage or modification Figure 5.27.

5.6.3 Adsorption Test and Kinetic Studies

As shown in Figure 5.28, FLX was quickly extracted from the solution by N, O-CMCS/PEO nanofibers. The adsorption of FLX reached an equilibrium state after approximately 40 min. The adsorption capacity (Q_t) of the targeted drug on the modified nanofibers increased sharply with the extended adsorption time, and then slightly decreased after 120 min. It was interesting to see that almost 75% of the adsorption capacity was reached in only 10 min. At the end of the adsorption test, close to 85% of the initial concentration of FLX was removed by the membrane.

To investigate the potential rate-controlling steps involved in the adsorption of FLX onto N, O-CMCS/PEO nanofibers, PFO and PSO kinetic models were used to fit the experimental data. Figure 5.29 shows the curves for both fitting models. Kinetic parameters are summarized in Table 5.4 for both models obtained by nonlinear curve fitting of experimental data with MATLAB software to reduce statistical discrimination bias (231).

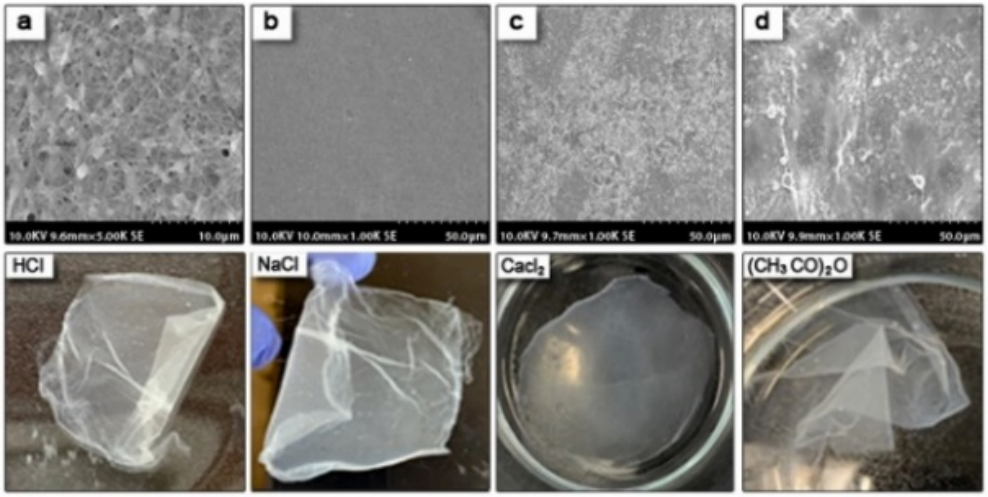


Figure 5.26 Chemical treatment of stabilization with HCl (1M) (a), NaCl (b), $CaCl_2$ (c), and acetic anhydride (d) for N, O-CMCS / PEO membrane made of 2.5 wt. % /3 wt. % (4:3)

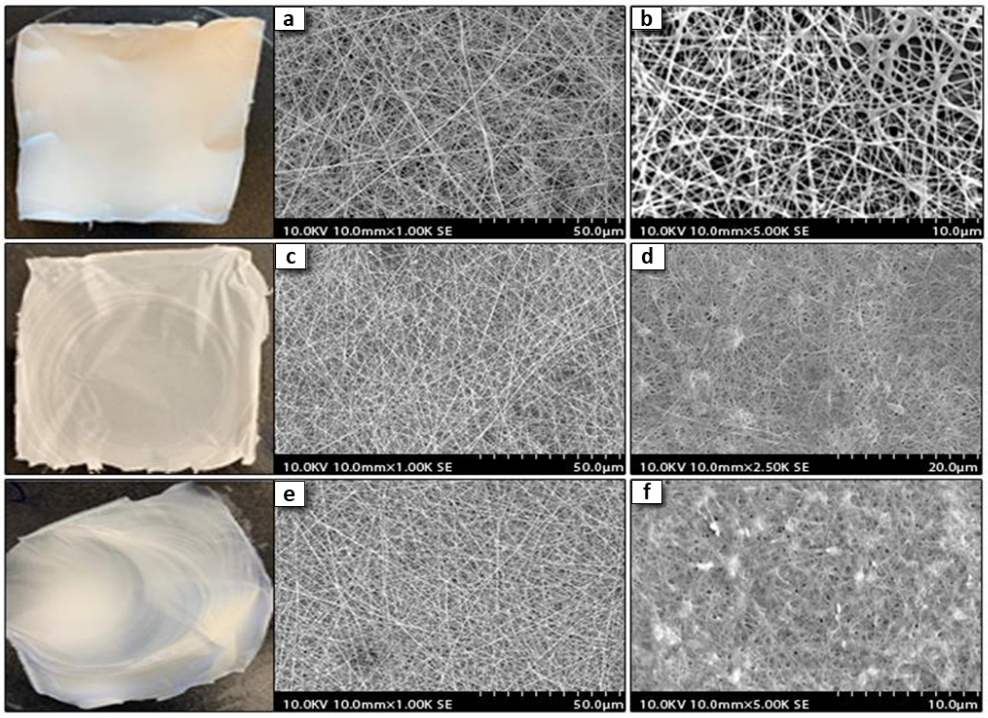


Figure 5.27 SEM before and after thermal-cross-linking stabilization at 140˚C for 30 min for N, O-CMCS/PEO: 2.5 wt%/3 wt% (3:1) ((a), (b)); (4:3) ((c), (d)); 8 wt%/1.5 wt% (3:1) ((e), (f))

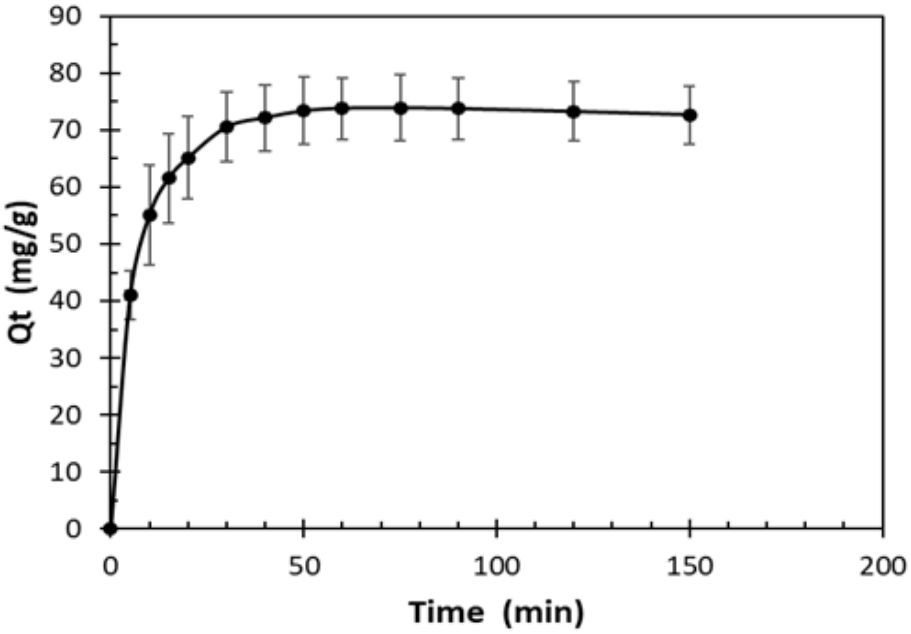


Figure 5.28 Adsorption capacity of FLX by N, O-CMCS / PEO 4:3 m/m at (pH = 8) electrospun nanofibers

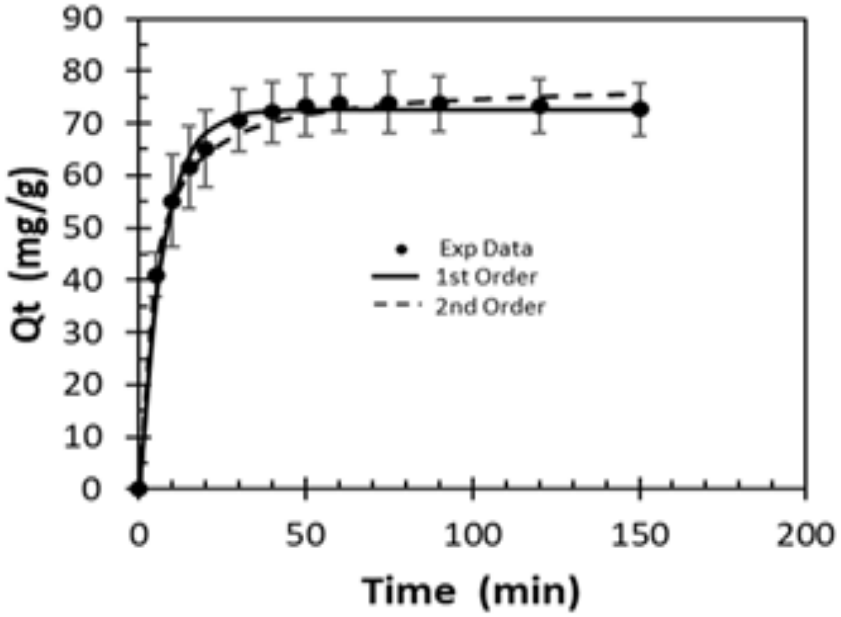


Figure 5.29 Kinetic models for adsorption of fluoxetine onto the N, O-CMCS/PEO 2.5 wt%/3 wt% (4:3) nanofibers

Table 5.4 Kinetic models parameters for the adsorption of FLX on N, O-CMCS / PEO 2.5 wt. % / 3 wt. % (4:3) nanofibers membrane: Initial concentration 50 mg/L, pH 8.0, adsorbent 25 mg, t = 150 min at 25°C

Experimental	**Pseudo first order model**			**Pseudo second order model**		
	k_1 (min^{-1})	Q_e (mg/g)	R^2	k_2 (min^{-1})	Q_e (mg/g)	R^2
pH 4.4	0.115	37.26	0.9987	0.0249	42.28	0.9863
pH 8.0	0.1434	72.63	0.9925	0.0031	77.72	0.9949

The correlation coefficients (R^2) of the pseudo-first order and pseudo- second-order curves at pH 4.4 were respectively 0.9987, 0.9863. However, at pH 8.0, calculated values of R^2 were 0.9925 and 0.9949. The higher rate of adsorption (Qt = 79.7 ± 7.9 mg/g) of FLX on N, O-CMCS nanofibers was obtained at pH 8.0. Based on R_2, kinetics curves at pH 8.0 followed a PSO rather than a PFO model. Therefore, a PSO kinetics might imply that the interaction between adsorbate and nanofibers is proceeding via chemisorption (e.g. electrostatic and ionic bonds). This type of interaction is in agreement with the experimental conditions carried out under a pH of 8.0. Precisely, N, O-CMCS nanofibers are presenting a negative ionized form (pKa COOH = 4.5), while FLX recognized as a weak base is protonated with a positive charge (pKa: 9.8). Interestingly, when the pH of the solution was 4.4, a PFO kinetic model was obtained revealing a process that could be much more governed by physical interactions (e.g. van der Waals and hydrogen bonds) at the surface of the modified biopolymer. The non-ionized form of the modified biopolymer is dominant along with its hydrophobic character (Figure 5.29). Accordingly, the removal yield of FLX under acidic condition is falling to 54%.

Table 5.5 Comparison of different existing adsorbents used for FLX removal

Adsorbents	Adsorption capacity ($mg\ g^{-1}$)	pH	References
N, O-CMCS / PEO nanofibers	79.7	8	---
Hydrochar, activated carbons	44.1	7	[56]
Biochar, rice bran pyrolysis	67.6	7	[57]
Biochar, Eucalyptus pyrolysis	6.4	7	[58]
Granular activated carbon and two synthetic zeolites (GAC) Synthetic zeolites (zeolite 13×) Synthetic zeolites (zeolite 4A)	234 32.1 21.9	9 7 9	[59]
β-Cyclodextrin carboxymethyl cellulose (β-CD-CMC) polymer	5.1	7	[60]
Lignin / PVA nanofibers	78.2	7	[43]
Paper mill sludge-based activated carbon with $ZnCl_2$	28.4	7	[61]

During batch adsorption tests, pH values ranged from 2 to 10. The maximum adsorption capacities of the adsorbent in acidic solution (pH = 4.4) were around 53.60 mg/g, in comparison to 79.7 mg/g when the pH was adjusted to a value of 8.0. The pH change of the medium had a direct impact on the rate of adsorption. Despite the good results obtained in this study, additional tests (e.g. temperature changes, weight of adsorbent, determination of isotherms and thermodynamics) are required: 1) to better understand the sorption mechanisms at the surface of the N, O-CMCS nanofibers, and 2) to improve its efficiency in terms of absorption rate. Finally, other tests will be carried out on the reusability of the new adsorbent with consecutive adsorption/desorption cycles. Serious challenges to meet increasing demands for clean water resources have been driving advances in technology including the use of low cost, abundant, and “green” adsorbent biomaterials. In the last decade, some articles were published on the removal of FLX in water by adsorption using different adsorbents manufactured from materials. A list of adsorbents along with their respective adsorption capacity is provided in Table 5.5. A comparison of the different adsorption capacities demonstrates the promising efficiency of N, O-CMCS/PEO nanofibers. Indeed, the developed nanometric membranes are offering large specific surface area and versatility in the choice of retention sought. Depending on the type of molecules

to be removed, a higher level of specificity can be achieved by simply adjusting the pH of the medium. This clearly open-up new interesting perspectives in terms of adsorption strategies (e.g. successive extractions of contaminants having different physicochemical properties).

5.7 Conclusion

The study presented an optimized methodology for the synthesis of N, O-CMCS/PEO electrospun nanofibers (176 ± 40 nm) used as adsorbent. The developed membranes exhibited an excellent ability for the removal of FLX from water at pH 8.0 (adsorption capacity up to 79.7 ± 7.9 mg/g). Kinetics tests performed on N, O-CMCS/PEO nanofibers under optimized conditions gave a better correlation with the PSO model. Data analysis is suggesting a possible chemisorption mechanism between FLX and the N, O-CMCS/PEO nanofibers. However, further tests (e.g. isotherms, thermodynamic) will be attempted in the near future to better understand the adsorption mechanism at the surface of the modified biomaterial. From promising results obtained so far during our experiments, and a comparison made with other existing sorbents, N, O-CMCS/PEO nanofibers are believed to be efficient and suitable to remove pharmaceutical residues such FLX in water.

CHAPTER 6 - ARTICLE 2

Nanofibrous Material of N- Succinyl Chitosan/Polyethylene Oxide in the Removal of Emerging Pharmaceuticals from Aqueous Solution by Adsorption/Desorption Method

Amna Hassan Issa Khierallah , Amel Hadj Bouazza , Daniel Montplaisir

6.1 Foreword

This second article is entitled " Application of Nanofibrous Material of N- Succinyl Chitosan/Polyethylene Oxide in the Removal of Emerging Pharmaceuticals from aqueous solution by Adsorption / Desorption method ". It has been published in Journal of BioResources 18 (1), 1971-1998 (2023)

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6.2 Résumé

Dans les écosystèmes aquatiques du monde entier, les métabolites et résidus pharmaceutiques ont été reconnus comme d'importants polluants environnementaux. Leur libération continue dans l'environnement à de graves répercussions, y compris la bioaccumulation chez les animaux aquatiques comme les poissons, qui peuvent éventuellement atteindre les gens et causer des problèmes de santé ainsi que des problèmes environnementaux à long terme. Ces polluants pharmaceutiques peuvent ou non être éliminés par les procédés des stations d'épuration (WWTP), en fonction de la nature du produit chimique et de l'architecture du système de traitement. En conséquence, de nouvelles techniques pour éliminer ces contaminants émergents des eaux usées sont nécessaires de toute urgence. L'un des biopolymères les plus prometteurs est le N-succinyl chitosan (NSCS), le NSCS, un chitosan chimiquement modifié, a été utilisé pour éliminer les résidus pharmaceutiques du milieu aqueux. L'avantage de la charge de surface négative du NSCS est qu'il est présélectionné pour la fluoxétine (FLX), la venlafaxine (VEL), l'ibuprofène (IBU) et la carbamazépine (CBZ). Pour confirmer les caractéristiques des NSCS ont été étudiées à l'aide de la spectroscopie infrarouge à transformée de Fourier (FTIR) et ^{1}H-RMN. Un microscope électronique à balayage (SEM) a été utilisé pour étudier la formation de nanofibres par électrofilage de ces membranes polymères biomatériaux verts NSCS/PEO. Les mécanismes d'adsorption de FLX, VEL, IBU et CAB, ainsi que les effets de la valeur du pH dans la solution d'origine sur les capacités d'adsorption ont été étudiés à l'aide de chromatographie liquide haute performance et de détecteurs à barrette de diodes ultraviolettes (HPLC-UV DAD) dans des conditions d'adsorption identiques. Nos résultats ont montré que les nanofibres NSCS/PEO d'un diamètre de 183 ± 38 nm étaient plus efficaces et peuvent être utilisés avec succès pour éliminer les résidus pharmaceutiques des milieux aqueux que d'autres adsorbants commerciaux et modifiés tels que le charbon actif (AC). L'adsorption FLX sur les nanofibres

NSCS/PEO a été favorisée à pH 8,0. Le modèle de pseudo-premier ordre était le plus adéquat pour représenter les données cinétiques, étant donné que les capacités d'adsorption maximales de FLX sur NSCS/PEO atteignaient jusqu'à 70 %. De plus, la désorption et la réutilisation de cet adsorbant ont également été démontrées à l'aide de quatre cycles de modules séquentiels d'adsorption et de désorption. En conclusion, les nouvelles nanofibres super-adsorbantes NSCS/PEO ont le potentiel d'être une nanofibre de biomatériau adsorbant viable, efficace, durable sur le plan environnemental et une meilleure stratégie pour éliminer les résidus pharmaceutiques de l'eau et des eaux usées. Cela pourrait économiser de l'argent tout en profitant à la société et à l'environnement.

Mot-clé: Traitement des eaux usées; N-succinyl chitosan ; résidus pharmaceutiques; Elect-trospinning ; nanofibres ; Adsorption/Désorption.

6.3 Abstract

Pharmaceutical metabolites and their residues have been identified as major environmental pollutants in aquatic ecosystems. N-succinyl chitosan (NSCS) was studied as a potential adsorbent for a pharmaceutical residue, fluoxetine, from aqueous media. NSCS was investigated using Fourier transform infrared (FTIR) and ^{1}H-nuclear magnetic residence (NMR) sperctroscopies. Scanning electron microscopy (SEM) was used to investigate the formation of nanofibers by electrospinning of these green biomaterial polymer membranes.The mechanism of FLX adsorption, as the effects of pH value in the original solution on adsorption capacities, were investigated using high-performance liquid chromatography (HPLC-UV-DAD) under identical adsorption conditions. It was found that NSCS/PEO nanofiberes with a diameter of 183 ± 38 nm were more effective to remove pharmaceutical residues from aqueous media than other commercial and modified adsorbents was favored at pH 8.0. Pseudo-first order model was the more adequate to

represent the kinetic data, being the maximum adsorption capacities of FLX on NSCS/PEO reached up to 70%. A study of the desorption potential and results, electrospun NSCS/PEO mats can be desorption and up to 4 times without significant loss adsorption capacility.

Keyword: Wastewater treatment; N-Succinyl Chitosan; pharmaceutical residues; Electrospinning; Nanofibers; Adsorption/Desorption.

6.4 Introduction

Water is an essential natural resource that is utilised at a global scale at rate of billions of cubic metres each year. A world without water would be a lifeless planet. It is critical to conduct research on its use and protection in order to create new ways and materials for maintaining water quality (4). Water contamination causes deaths and illnesses all over the globe, and roughly 14,000 people die as a result of it every day (232). Chemicals that are not routinely monitored or regulated in the environment are known as emerging contaminants (ECs) (233). There are various categories of chemical. Prescription and over-the-counter medications, fire retardants, insecticides, hormones, detergents, and personal care products are a few examples. Based on studies showing their presence in treated wastewater and in surface and drinking water, pharmaceuticals, and personal care products (PPCPs) have been identified as developing contaminants of concern (234). There are several problems identified with health and the environment that are caused by urban effluents and the ever-complicated drainage systems add to the complex disposal methods that are highly expensive (7). The vast volumes of waste generated by both residential and industrial use make impracticable to apply this method. Consequence, there is a need to find a low-cost and cleaning procedures to resolve these challenges (235). To solve some of the identified environmental challenges, less expensive adsorbents derived from electospun nanofibers could be developed, as this materials can be used to disinfect sewage treatment plants. Although biobased nanofibers have promising benefits when compared to the commercial filters, it is important to consider the manufacturing processes. Through this process, the electrospun nanofibers derived from natural biopolymers result in lower CO_2 emission when compared with others like synthetic membranes, activated carbons and carbon nanotube (236). Moreover, the world's ground and surface water are heavily contaminated and unsafe for human consumption. Therefore, water contamination will also become a major concern and focus for most wealthy countries as regulations become more rigorous (8). Pharmaceutically active compounds (PhACs) have been listed as the main issue in water quality research,

and up to 90% of PhACs supplies are excreted as unmetabolized products in urine or stools, where they enter household wastewater systems (237). These products are discharged into the atmosphere as parent chemicals or active metabolites via effluents from WWTPs due to poor water treatment. However, many countries have showed concern about the presence of pharmaceutical residues in the marine ecosystem due to their potential for negative effects on the natural environment and human health (238).

Thus, appropriate treatment procedures for pharmaceutical wastewater should be established and deployed in response to the growing demand for wastewater remediation strategies (182). Such post-treatment procedures includes ozonation, membrane filtration (MF), and adsorption onto activated carbon (AC) can remove the majority of PPCPs contaminants (239). However, there are some disadvantages, as therapeutic methods such as ozonation is either too expensive; it was inappropriate due to high production and maintenance expenses, as well as the fact that it was found to be unfriendly to the environment (240). Recently, novel membrane technologies have attracted interest in cleaning wastewater of pathogens, micropollutants, and salts using membrane filtration (MF) (241). The molecular weight cut-offs of membranes allow them to be classified into four groups: microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), and reverse osmosis (RO). Typically, micro-and ultrafiltration are installed as pretreatment devices in low-pressure contexts, whereas nanofiltration and reverse osmosis are typically used at high pressures to remove micropollutants. Physically, NF and RO membranes are the only membranes that would be suitable for PPCP removal purely on the basis of size exclusion. Since activated carbon has a large micropore volume and a high surface area, it is widely used as an adsorbent in water treatment for organic and non-polar substances (Zahng et al. 2015) (Cevallos-Mendoza et al. 2022). Indeed, AC and zeolites have been investigated as some of the most widely utilized and effective adsorbent materials for wastewater treatment. Despite their high efficiency, these adsorbents generate a host of issues, including stabilisation and recycling, necessitating time-consuming and expensive regeneration methods (242). WWTPs typically have a primary

physicochemical treatment solution and a secondary system made up of activated sludge produced by a biological reactor. Simply put, these traditional plants are ineffective in removing pharmaceuticals, and although they clean the wastewater, they are neither sustainable nor economical (Oulton et al. 2010) (239).

Pharmaceutical products have been treated in wastewater treatment facilities (WWTPs) and are not eliminated from the environment. Such pharmaceuticals include carbamazepine, atenolol, acetylsalicylic acid, diclofenac, and lincomycin have remediation efficiencies as low as 10% (243). In addition, pharmaceuticals cannot be entirely degraded in WWTPs since they are designed to handle organics in the mg/L range that are easily and partially degradable. However, pharmaceutical solubility, absorbability, volatility, biodegradability, polarity, and lifespan, on the other hand, are very variable and can be observed at extremely low concentrations (ng/L-g/L) (244). Most of the time, first and secondary WWTP treatments are insufficient to remove these contaminants, hence, allowing them to enter the drinking water system. As a result, as the population grows and per capita, opioid consumption rises, complex and effective tertiary treatment techniques will be required. Pharmaceuticals can be separated from water and wastewater using advanced oxidation processes (AOPs) and adsorption. AOPs and other therapies, on the other hand, generate a lot of oxidation and transformation products, some of which are toxic (182).

Adsorption is a prominent physical approach that is used to eliminating trace organic pollutants from water, and it is one of the key methods believed to be an effective treatment and low-cost process for removing most evolving chemicals from water (245). The main advantage of adsorption is that it does not products that can more harmful than the parent molecule. Processes for eliminating PPCPs ought to be quick, simple, cost-effective, reusable, and environmentally benign (246). Furthermore, unlike other approaches, adsorption does not necessitate the creation of materials. However, during usage, adsorption demands the regeneration or disposal of substantial volumes of adsorbent. Therefore, it is vital to destroy recoverable medicines and derivatives. To overcome these constraints,

a significant effort has been made to develop novel, efficient, and ecologically friendly adsorbents based on low-cost and natural polymeric materials (247).

In adsorption applications, chitosan (CS) has proven to be an effective versatile material. As a result of previous literature in the field, researchs have modified chitosan with a variety of functional groups. By the presence of amino and hydroxyl groups in with a variety of functional groups. Several adsorption interactions between chitosan (CS) and toxins (dyes, chemicals, electrons, phenols, pharmaceuticals/drugs, pesticides, herbicides, and so on) produce the existence of amino and hydroxyl groups on the molecules. These functional groups will assist in determining where modifications should be made (33). Additionally, these functional groups can be modified either by cross-linking and grafting to improve adsorption efficiency and specificity (34), (248). So because of its high abundance of amino and hydroxyl functional groups (249), the use of CS as an adsorbent has lately sparked the interest of researchers in the water and wastewater treatment sectors (35). CS has a chemical composition that enables the intricate polymer design alterations for specific purposes, unlike other polysaccharides (cellulose or starch). On the other hand, the primary hydroxyl and amine groups found on the backbone of CS are also responsible for the polymer's reactivity and serve as chemical modification sites. Moreover, composites made up of a variety of compounds have been shown to be more capable of adsorbing and avoiding wastewater pollutants in acidic environments (250). Despite the material's remarkable qualities, membranes totally made from it are frail and brittle, having low mechanical strength and flexibility. Cross-linked CS has been shown to have better mechanical qualities than individual CS among the ways utilised to improve CS mechanical properties (251).

There are various of derivatives generated from CS either by chemical or physical modification of the raw CS. However, chemically modified CS could result in some products or materials with qualities suited for the elimination of specific contaminants. The steps involved in CS modification includes cross-linking and grafting of the CS backbone impregnation (252). Several attempts have been undertaken to change CS after graft modification in order to increase its solubility

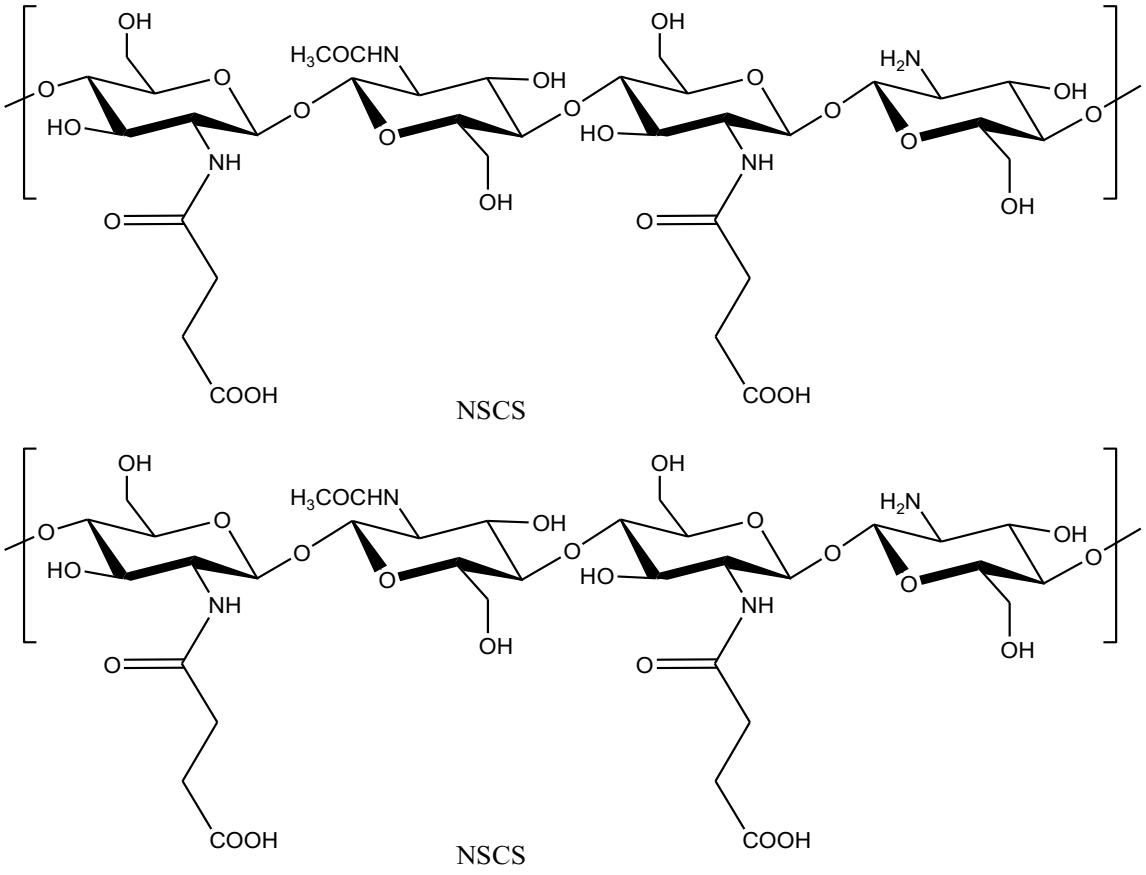
and physicochemical qualities (253). Although, the chemical change should not change the core structure of CS. However, this modification introduces new derivatives with improved features for specific applications in other domains of use. As a result of this approach, the adsorption properties of CS are strengthened, as well as the mechanical intensity and chemical stability of CS in acidic conditions (37), (35), (254). Various approaches such as chemical and physical modification of CS which depends on its application could be maximized to modulate the polymer reactivity and boost the adsorption kinetic (37). In addition to boosting biodegradability and antibacterial activity, the hydrophilicity generated by the introduction of polar groups capable of forming secondary contacts is a benefit of altering CS. In achieving an appropriate mechanical strength as an artificial medical device, dispersion of growth factors, and degradability are considered as important obstacles for potential alteration procedures (255). Furthermore, there are so many benefits of CS over the conventional AC and other bio-sorbents used including low prices, a high tolerance for some toxins (because to the addition of amino and hydroxyl groups), chemical stability, high reactivity, and emission selectivity. N-succinyl chitosan (NSCS) is created by adding succinyl groups to the N-terminal of chitosan's glucosamine units (see Scheme 6.30). Previous studies revealed that NSCS has physicochemical qualities, Therefore, the market price of NSCS may rise (256). This is due to its appealing and inherent features, such as facile solubility in a variety of pH levels without the need for an acidified media, high hydrophilicity, biocompatibility, and antibacterial activity, which are all present in pristine CS (257). To allow better interaction with water molecules, succinyl groups were added to the N-position of the glucosamine units of CS, which is a favourable material because of its solubility, biodegradability, low toxic (258), (259), and biocompatibility (260), (261). Many functional groups such as amine and hydroxyl could be found in the CS chain and despite its widespread application, the adsorption capacity of CS has yet to be fully realised (258), and no previous research on the adsorption capabilities of NSCS/PEO nanofiber has been published. Many reactive functional groups, amino groups, carboxyl groups, and

both primary and secondary hydroxyl groups at the C-3 and C-6 positions, respectively, are present in NSCS, a well-known CS derivative (258) Therefore, due to the fact that NSCS is made up of –NH and –COOH groups, it can easily react with a wide range of agents (261).

In order to compete with AC and obtain a satisfactory adsorption capacity for trace pharmaceutical pollutants, the surface area of the material must be increased (262). One of the strategies to achieve this step is by electrospinning. Electrospinning is a straightforward method for creating nanofibrous substrates with variable fibre sizes (262). Electrospun nanofibers have attracted a lot of attention because of their unusual properties, which include a large surface area, low weight, nano porous features, and design flexibility for specific physical and chemical functionalization. However, because of the entanglements and overlaps between polymer chains play a critical role in manufacturing bead-free and uniform nanofibers, high molecular weight polymers and high solution concentrations are commonly used in electrospinning. Although a study has shown that electrospinning low -molecular -weight compounds is a difficult task to achieve (263). The relevance of elasticity and relaxation time rather than molecular entanglements for electro-spinnability of solutions has also been established. Interestingly, over 30 polymers have been electrospun successfully so far (92), but no published work on the electrospinning of NSCS/PEO has been discovered by the authors. Herein, we are reporting for the first time the use of electrospinning fibres using electrospinning blended NSCS/PEO solutions in aqueous acetic acid.

This super structure of NSCS/PEO nanofiber with many reactive functional groups may allow for robust attachment to pharmaceutical contaminants in wastewater and improving adsorption capacity level. The possibility of developing a novel NSCS including nanofibers by electrospinning from NSCS/PEO mix solutions was demonstrated in this study. To our knowledge, there has been no research into the application of using modified NSCS/PEO nanofibers mats to remove the pharmaceutical residues (antidepressant fluoxetine) from wastewater. The effect of the pH value of the FLX solutions, the contact temperature, the adsorption

mechanism, and the contact time of single and various pharmaceuticals contaminate on the NSCS/PEO were studied. The adsorption capability of FLX and VEN (antidepressants), CBZ (anticonvulsant), and IUP (anti-inflammatory) on produced nanofibers from aqueous solutions were investigated. In additional, we performed the tests, carried out in batch systems, were studied in equilibrium condition to determine optimum adsorption conditions for NSCS/PEO to adsorb the FLX. Adsorption kinetic test was preformed. Furthermore, Desorption tests with various eluents will be also conducted out to assure the nanofibrous membrane's reusability and to quantify their possible environmental impact.



Scheme 6.30 The chemical structure of N- Succinyl Chitosan

6.5 Materials and Methods

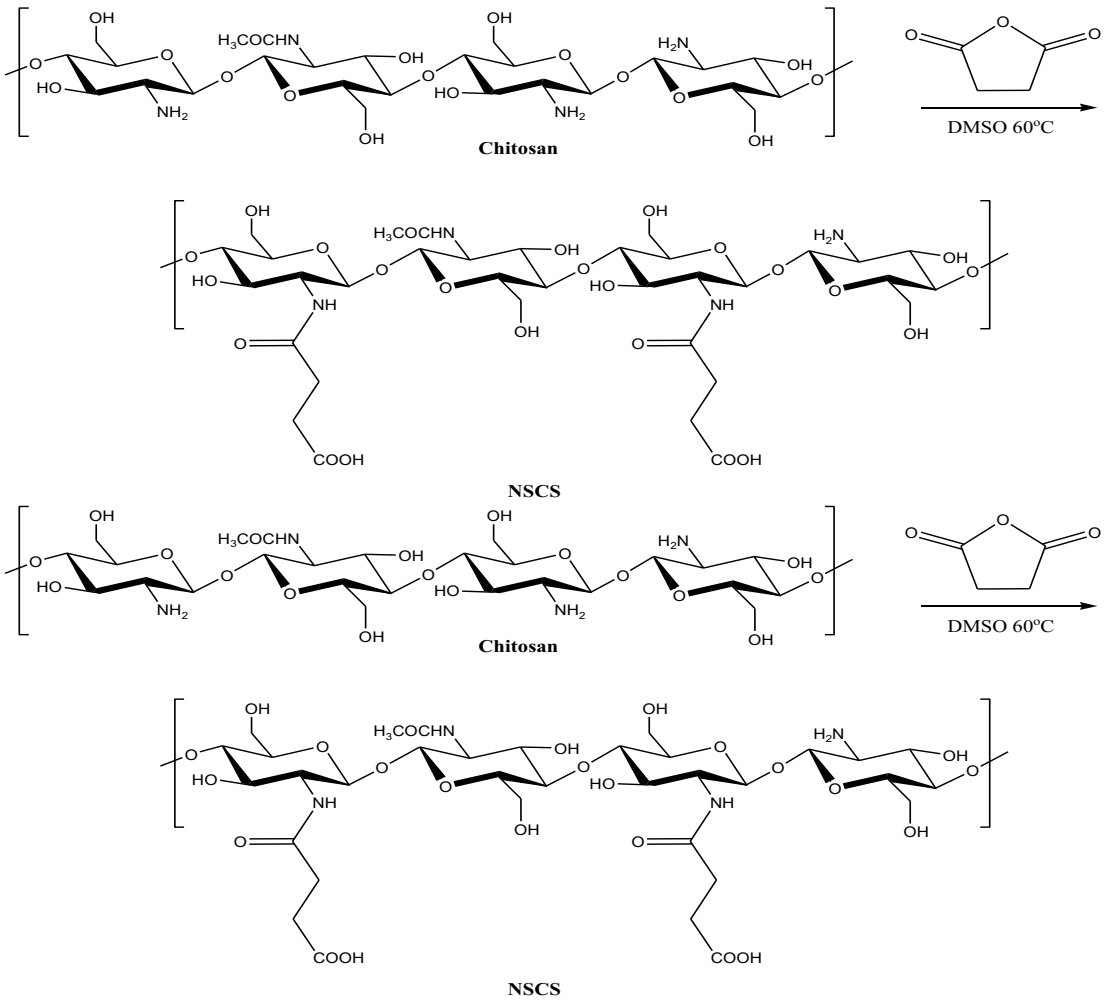
6.5.1 Materials

Low molecular weight chitosan (CS MW 50,000-190,000 g/mol, 75-85% deacetylated) was from Sigma-Aldrich (Reykjavik, Iceland). Polyethylene oxide (PEO) that was used as a co-spinning agent had a molecular weight of average was 900,000 g/mol was from Sigma-Aldrich (St. Louis, MO, USA). Succinic anhydride from Sigma-Aldrich (CAS 108-30-5), sodium hydroxide (NaOH), dimethyl sulfoxide DMSO, acetone and ethanol were analytically graded. As a model contaminant, the acquisition of Fluoxetine hydrochloride (FLX) (CAS 56296-78-7), venlafaxine hydrochloride (VEN) (CAS 99300-78-4), carbamazepine (CAB) (CAS 298-46-4) and ibuprofen (IBU) (CAS 15687-27-1) were provided by Sigma-Aldrich (Oakville, ON, Canada) for the adsorption test. Methanol (HPLC grade), acetonitrile (HPLC grade), O-phosphoric acid (HPLC grade; 85 wt./wt. %), and glacial acetic acid ACS reagent (99.7 %) were purchased from Fisher Science (Ottawa, Ontario, Canada). The water for the experiments was prepared with a reverse osmosis membrane, Siemens Super Transparent RO, to achive 0.055 µS /cm Conductivity. Deionized water was used for testing throughout all the studies (Siemens Ultra Clear RO).

6.5.2 Methods

6.5.2.1 Synthesis of N-succinyl Chitosan (NSCS) Polymer

Ring-opening reactions with succinic anhydride in a dimethyl sulfoxide (DMSO) framework yielded NSCS. NSCS was synthesised in the manner previously described (264), (265). First, 2 g of CS powder was applied to 40 mL DMSO and thoroughly mixed. Second, Succinic anhydride (4 g) was slowly applied to the CS solution and allowed to react for 6 hours at 65 ^{o}C.



Scheme 6.31. Preparation of N- Succinyl Chitosan

The sample was dissolved in ethanol at room temperature and reacted for 1 h after being filtered to eliminate the solvent. The pH of the solution was changed to 10 - 12 with NaOH (1 M) at the end of the reaction. Finally, the precipitate was dissolved in 90 mL distilled water, then 270 mL acetone was added, accompanied by washing and precipitation with ethanol and acetone, respectively, after the mixture was filtered. Ultimately, NSCS was dried in a vacuum oven at 50 °C. Scheme 6.31 shows the NSCS synthesis.

6.5.2.2 Characterization of N-succinyl Chitosan (NSCS)

Fourier Transform Infrared (FTIR) was utilized to examine and identify functional groups on CS and NSCS. At room temperature, the FT-IR spectrum of CS and NSCS

was recorded using a FT-IR spectrometer (Nicolet iS10, Thermo Scientific). The specimen was screened from 600 to 4000 cm^{-1}. The ^{1}H-NMR spectra were calculated using a (200 MHz Oxford NMR spectrometer) with CS dissolved in D_2O as the solvent and NSCS dissolved in D_2O/DH_3COOH as the solvent, with chemical shifts provided in ppm. Furthermore, the degree of succinylation in D_2O/CH_3COOH was determined using potentiometric titration, as well as ^{1}H-NMR.

6.5.2.2.1 Determination of Degree of Substitution (DS) of N-succinyl Chitosan (NSCS)

The degree of substitution (DS) of NSCS samples was calculated using a potentiometric titration method (266) (267). Briefly, dried NSCS (0.20 g) was dissolved in 0.1 mol/L hydrochloric acid solution (20 mL). Methyl orange was used as indicator for the endpoint determination. A standard 0.1 mol/L sodium hydroxide solution was used during titration (268). The cumulative DS of NSCS samples was determined using the Following equations 6.20 and 6.21:

$$\mathrm{DS} = \frac{161\mathrm{A}}{\mathrm{M_{NSCS}}} - 283\mathrm{A} \qquad \text{Equation 6.20}$$

$$\mathrm{A} = \mathrm{V_{NaOH}} \,.\, \mathrm{C_{NaOH}} \qquad \text{Equation 6.21}$$

where M_{NSCS} is the mass of NSCS (g), V_{NaOH} and C_{NaOH} represent,respectivily, the volume and molar concentration (M) of NaOH, and finally 161 and 283 are associated to the molecular weightsof the chitosan (glucosamine)and the NSCS group (269).

6.5.2.2.2 Zeta Potential (ZP) Measurement

The zeta potential (ZP) of the NSCS were measured at room temperature (23°C). The zeta potential can be defined as the electrical potential at a hydrodynamic slip plane adjacent to the NSCS. To calculate the ZP, a 1 M (10 mL) solution of NSCS was dissolved in distilled water for 1 h with gentle shaking at room temperature, and the pH values ranged from 2.0 to 11. NaOH (0.01 M) was used to neutralize the pH

solution. The ZP in solution was determined using a Zetasizer Nano (Malvern Instruments Ltd., model ZEN 3600).

6.5.2.3 Preparation of Solutions and Operating Procedures for Electrospinning of NSCS/PEO Nanofibers

The electrospinning unit was set up as shown in Figure 6.32. NSCS (8 wt.%) and PEO (5 wt.%) solutions were prepared separately by dissolving in 50 % acetic acid (AA) at room temperature (23°C) until a homogeneous viscous solution was obtained after (1 h, NSCS; 20 h PEO) after agitation at 200 rpm. The mass ratio of NSCS/PEO was set to (3:2, 5:5 and 6:4 m/m), and the resulting solution was stirred for 2 h at 200 rpm. To remove bubbles, the mixture was placed in an ultrasonic bath for 15 min. Finally, the mixture was allowed to rest for 3 h before being used in the electrospinning process. The electrospinning fluid (NSCS/PEO) was pushed into a 5 mL syringe with a 20-gauge needle and attached to a syringe pump device (KD Science, model 100) that provides a steady and slow liquid flow. For the electrospinning phase, the flow rate was 0.2-0.5 mL / h. The distance between the nozzle tip and the collector was measured with a syringe pump positioned at a horizontal gap (10 to 15 cm). Throughout the electrospinning, the height of the syringe pump was kept constant. During the electrospinning process, a metallic wireframe was used as a collector, and the needle and collector were both connected to a power supply (Gamma High Voltage Research USA) that produced a high voltage output. The voltage ranged from 7 to 14 kV. Different electrospinning conditions were tried for each NSCS/PEO ratio by changing the flow rate, current, and distance between the needle and collector (wireframe) to obtain the optimal jet (steady jet with limited drop projections) and narrow beadle nanofibers. Both experiments were carried out at room temperature (23 °C) in a handcrafted electrospinning enclosure. Between the two layers, relative moisture was preserved (30 to 40 %). The nanofibrous mat was removed from the frame at the end of the electrospinning process and dried in an oven (Fisher Scientific Isotemp Oven, Thermo Scientific HERATherm Oven) at 80 °C for 24 h.

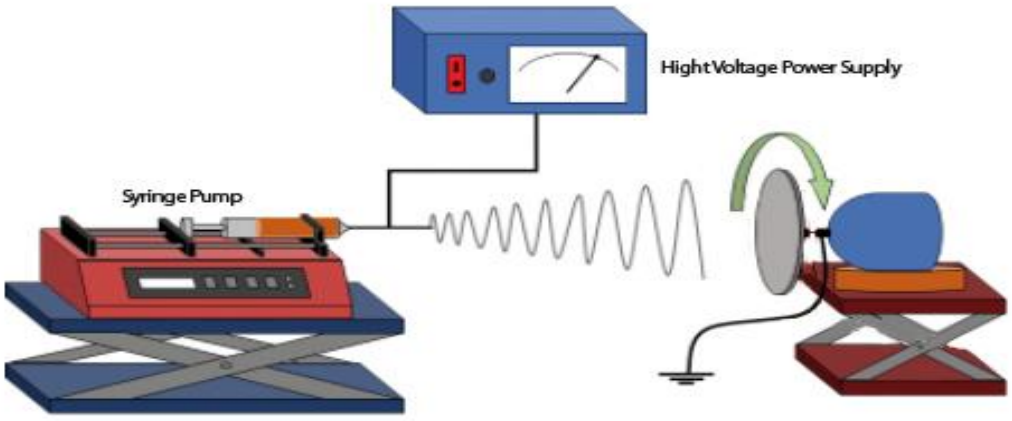


Figure 6.32 Schematic representation of the setup for electrospinning

6.5.3 Nanofibers Characterization

The morphology of the nanofiber membrane was assessed before and after adsorption test using an SEM (A Hitachi SU1510 Scanning Electron Microscope). This was used to image the morphologies and diameters of nanofibers. Furthermore, the diameter was calculated using Image J tools (Rasband, W.S., ImageJ, US National Institutes of Health, Bethesda, MD, USA, https://imagej.nih.gov/ij/,1997-2018). The diameter of 50 nanofibers obtained on 3 different photos (a total of 150 nanofibers per sample) was measured in order to achieve an average value. And the data are presented as the average ± standard error.

6.5.4 Batch Adsorption Procedure

A stock solution of FLX was prepared using deionized water. The pH of the solutions was adjusted as needed with HCl (0.01 M) or NaOH (0.01 M). By employing a pH meter, the initial pH (natural pH solution of FLX 5.5) value were 5.5 during the batch experiments so pH adjustment was made throughout the

study to reach pH values of 3 to 10. Therefore, the effects of pH FLX on Q_t values at room temperature (RT) for varying contact duration were investigated in this study. Individual (FLX) and multiple pharmaceutical contaminants (FLX, IBU, VEN, and CAR) batch adsorption on NSCS/PEO membranes was investigated. By dissolving the corresponding stock solutions in a 5% methanol solution, separate 2500 ppm standard solutions of FLX, VEN, CAR, and IBU were prepared. These solutions were then diluted in preparation for adsorption tests. Stock solutions (2500 ppm) of FLX, IBU, VEN, and CAR were made by weighing and dissolving the required amount of the corresponding substance in 5 % methanol. The homogeneity of the solution, as well as the temperature and pH of the medium, were all checked ahead to the start of the sorption tests. A 50 ppm FLX solution was used as a model contaminated water in tests using one contaminant on NSCS/PEO membranes. For tests with multiple contaminants, 12.5 ppm of FLX, IBU, VEN, and CAR were added to simulate contaminant water. The tests were carried out over a 150 min period to ensure that equilibrium was reached. Sorption tests were carried out with a 25 mg sample of the membrane inserted into conical flasks (250 ml) containing 50 mL of a FLX solution as single contaminant model (50 ppm) and 5 % of methanol. The agitation speed was adjusted at 200 rpm for all adsorption–desorption tests using (ORBIT Environ-shaker, Lab-Line) under controlled temperature. Before insertion of the membrane into the solution, an aliquot of 500 µL was sampled to determine the initial FLX concentration. Batch tests were conducted over a period of 150 min to ensure that equilibrium was achieved prior the collection of a 500 µL aliquot. The adsorption capacity at time t (Q_e) was determined using Eq. 6.22,

$$Q_e = \frac{(C_0 - C_e)}{W} V \qquad \text{Equation 6.22}$$

where C_e is the final concentration of the contaminant (ppm) at time t (min), C_o is the initial concentration of contaminants (ppm), V is the volume of the solution (L), and W is the mass of adsorbents (g).

In order to determine the residual concentration of FLX in water samples during our batch adsorption tests, a high-performance liquid chromatography (HPLC) system (Shimadzu Prominence I - series) coupled with a diode array detector (DAD) was used. The chromatographic separation was achieved using a C18 reverse - phase column (XB-C18, 100 Å, 150 x 3 mm, 2.6 µm particle size, Phenomenex, Kinetex®). The residual concentration of FLX in aqueous solution was determined by HPLC-UV DAD, Camiré et al. (220).

6.5.5 Kinetic Test

Pipetting (500 µL) samples at room temperature with an initial concentration of (50 ppm) of FLX yielded kinetic curves, and the concentration of FLX was measured by HPLC-UV DAD. During the adsorption, such determinations were carried out at brief intervals until an equilibrium was attained. Samples of FLX solution were taken at 5, 10, 15, 20, 30, 40, 50, 60, 75, 90, 120, and 150 min after the adsorbent was added. To determine the equilibrium time at 150 min, a kinetic adsorption test was done first. The injected samples' adsorption capacity were calculated, and a curve showing adsorption capacity over time was created. The tests were repeated triplicate, and a mean curve was calculated. To examine kinetics adsorption data, the pseudo-first order and pseudo-second-order rate equations are commonly used (270). Adsorption can be characterised using a variety of adsorption kinetics models. For characterising the adsorption mechanism in this study, pseudo-first-order (PFO) and pseudo-second-order (PSO) kinetic models were utilized. Nonlinear pseudo-first-order (Eq. 6.23) and nonlinear pseudo-second-order (Eq. 6.24) models were used to fit experimental data (271).

$$Q_t = Q_e\left(1 - \exp^{-k_1 t}\right) \qquad \text{Equation 6.23}$$

$$Q_t = \frac{K_2 Q_e^2 t}{1 + K_2 Q_e t} \qquad \text{Equation 6.24}$$

where Q_e, is the amount adsorbed (mg/g) at equilibrium; Q_t, is the amount adsorbed (mg/g) at time t (min); k_1, pseudo-first order (PFO) adsorption rate

constant (g/g min^{-1}); k_2, pseudo second order (PSO) adsorption rate constant (g/g min^{-1}).

The kinetic parameters (maximum adsorption capacity and kinetic constant) for all models were determined using the kinetic equation, the solution function in Microsoft Excel, nonlinear regression analysis, and MATLAB software. The obtained parameters were used to plot pseudo-first order and pseudo-second-order curves, which were then compared to experimental data.

The adsorption kinetics data were fitted using different models in order to gain a better understanding of the mechanism of NSCS/PEO membrane adsorption. The pseudo-first order and pseudo - second - order rate equations were used (271).

6.5.6 Desorption Experimental

Desorption is the reversal of adsorption, and it is particularly important since it determines the adsorbent 's capacity to be reused (272). The NSCS/PEO mats were rinsed with deionized water after adsorption and dried overnight at room temperature. At low pH, desorption studies on the recyclability of the NSCS/PEO nanofibers were done utilizing several circumstances, including a 1M HCl and 5% acetic acid solution. In addition, heating of the solution in an ultrasound bath (sonication) by using hot water was used to realize the effect of temperature and sonication on the adsorption and desorption of FLX. Methanolic solutions (100%) were used to assess the environment in which the contaminant is strongly soluble. In all cases, the membranes were soaked in a solution (50ml) for 3 hours. To assess the recovered FLX concentration, original and final tests were loaded into HPLC-UV DAD. For numerous adsorption/desorption cycles, the desorption technique with the best desorption performance was chosen to assess reusability. Between each measurement, the membranes were removed and dried in a vacuum desiccator.

Results and Discussion

6.5.7 Synthesis of N-Succinyl Chitosan (NSCS)

CS with high DS can not be soluble in water for the strong intermolecular hydrogen bonding (H-bond), nevertheless, various modification can occur on the –OH and $–NH_2$ positions of CS to increase its water solubility (273), so for this reason, the amino group of CS was replaced by a succinyl group in this study, and CS was modified through N-acylation using succinic anhydride. The addition of -COOH through the succinyl group improves hydrophilicity (274), (275). Hydrophilicity also improves its attractive properties by forming electrostatic interaction and hydrophobic interaction as well hydrogen bonds with the target molecular. In contrast to CS, since the intermolecular hydrogen bonding interactions of NSCS were weakened as compared with CS, the water solubility of NSCS was improved dramatically (248), (249), (276). The succinylation reaction involves a condensation reaction between the polysaccharide amine group and the anhydride's electrophilic carbonyl group, followed by the formation of an amidic bond with the anhydride ring opening. The reaction is primarily catalysed by the nucleophilic attack of primary amine from CS's glucosamine component on succinic anhydride's carbonyl carbon. The O-substituted derivative can be formed because oxygen from hydroxyl groups has a nucleophilic character. Despite this, the N-substituted derivative is preferred because nitrogen electrons are more readily available than those from oxygen (277). Scheme 6. 31 shows the chemical structure of NSCS, which has a strong water-soluble property at various pH (278), (265). After the reaction, the pH was changed to precipitate NSCS, which was obtained in a salt shape ($COO^- Na^+$) with a stronger water interaction. The succinyl group was grafted onto CS and used as a hydrophilic group, but not all the intermediate products (NSCS) were water soluble. The succinyl groups were grafted onto the amine group of CS, as provided evidence by infrared (IR) and ^{1}H-NMR spectroscopy of CS and NSCS functional groups (261). Given that the succinylation reaction occurs primarily at the N-position of CS, the number of amino groups, which serve as the key adsorption sites in CS,

decreases as the degree of N-succinylation increases, resulting in a decrease in adsorption ability. However, as compared to pure CS, the adsorption potential of NSCS with different DS improves noticeably and increases marginally with increasing DS (115). According to previous study (279), homogeneous and heterogeneous conditions are the most critical synthesis parameters that can affect the reaction between the CS and succinic anhydride which impact the DS of NSCS, in our work no experiments have been conducted to confirm the effectiveness of these parameters on the reaction.

6.5.7.1 Structural Characterization

Figure 6.33 Based on IR and ^{1}H-NMR spectra, the succinyl groups were grafted onto the amino group of CS in this study. Since succinylation occurs of CS, and NSCS. The most compelling evidence of the successful transformation of CS to NSCS comes from the transformation the amine (NH_2) adsorption observed in the spectra of CS at 3358 cm^{-1}. The disappearance of this adsorption coupled with the appearance of a carbonyl peak representing the new amide functionalities at 1648 cm^{-1} prove that the amide has been formed (-NHC=O) Further evidence for the generation of NSCS comes from the (-NH) adsorption peak at 1559 cm^{-1} and a new peak appeared at 1728 cm^{-1}, which was assigned to (-COOH) which is characteristic of NSCS (43), (280), (276).

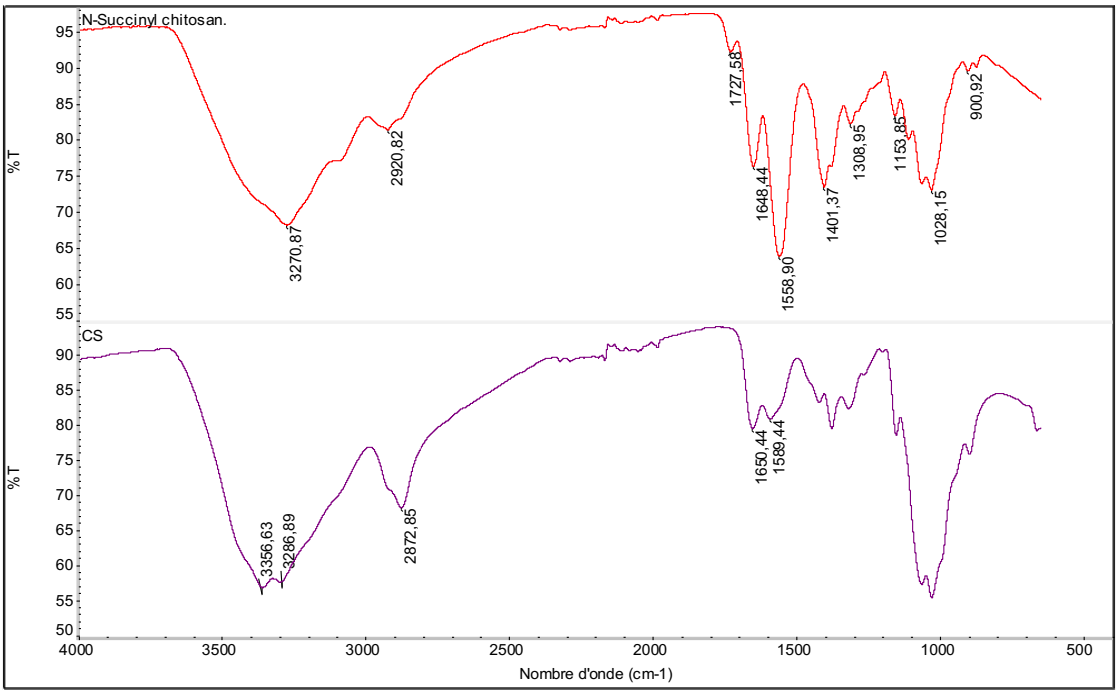


Figure 6.33 FTIR spectra of CS and NSCS

The ^{1}H-NMR further supports the transformation of CS to NSCS. A triplet observed at 1.0 ppm in the spectrum of NSCS is characteristic of the CH_2CH_2 moiety belonging to the succinyl group ($NHCOCH_2CH_2COOH$). Peaks at 3.4-3.6 ppm are characteristic of CS and belong to the CS backbone hydrogen (261). As such, these peaks are present in the ^{1}H of both CS and NSCS was given in Figure 6.34. Similar observations are reported in literature (276), (280).

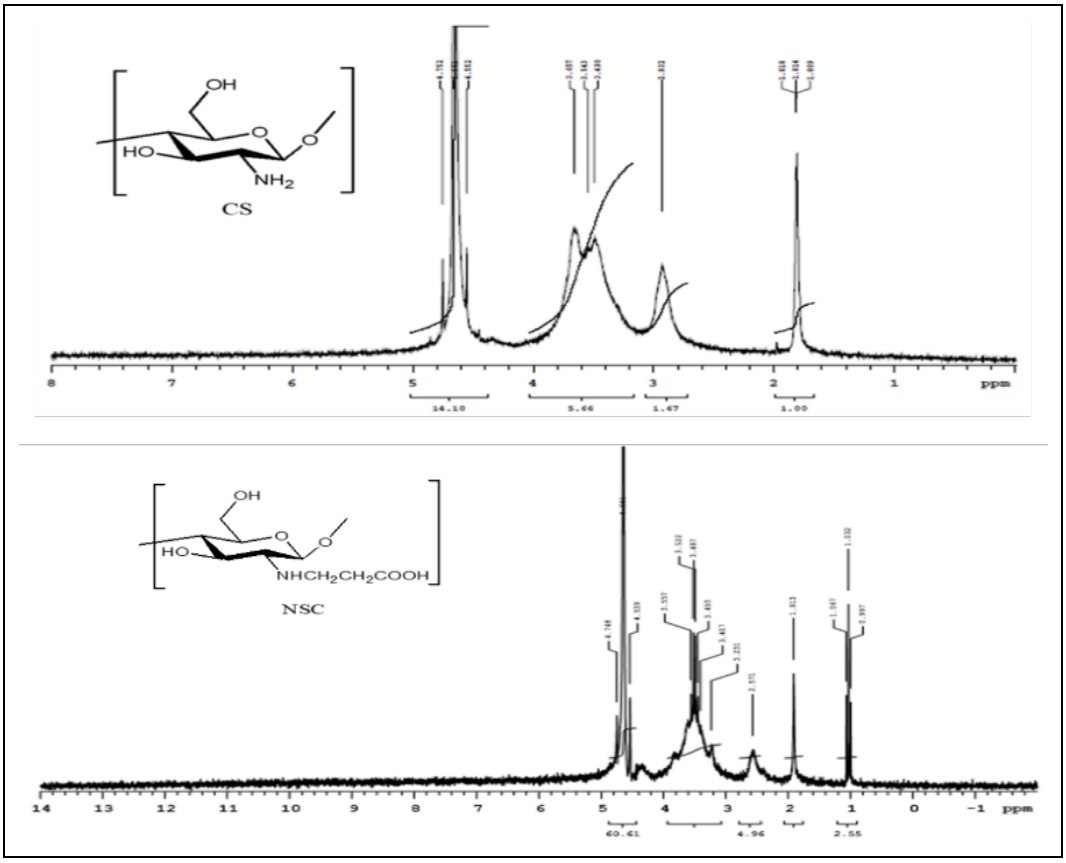


Figure 6.34 ^{1}H NMR spectrum of CS in D_2O and NSCS in D_2O / CH_3COOH

6.5.7.2 Measurement of Zeta-Potential (ZP) and Potentiometric Titration

One of the primary parameters determining their grafted carboxylic acid moieties on the surface of the modified polymer, which leads to probable electrostatic interactions between NSCS and FLX molecules, is the surface charge of the modified polymer. Figure 6.36 depicts the modified polymer's ZP at various pH levels. A potentiometric titration method and ^{1}H-NMR in D_2O/CH_3COOH revealed a succinylation degree of 35%. The pH-dependent ZP of NSCS varied from + 26 mV at pH 3.0 to – 41.5 mV at pH 10.0. As shown in Fig. 6.35, the isoelectric point at pH 6.3, and the ZP NSCS had a positive value at acidic pH that rose from 15 to 26 mV as the pH was decreased. At basic pH, the ZP decreases to negative values as the pH rises. This indicates that NSCS becomes highly ionized with negative charges due to larger amount of deprotonated carboxyl groups ($-COO^{-}$). Which completely agreed and supported with published studies (281), (282).

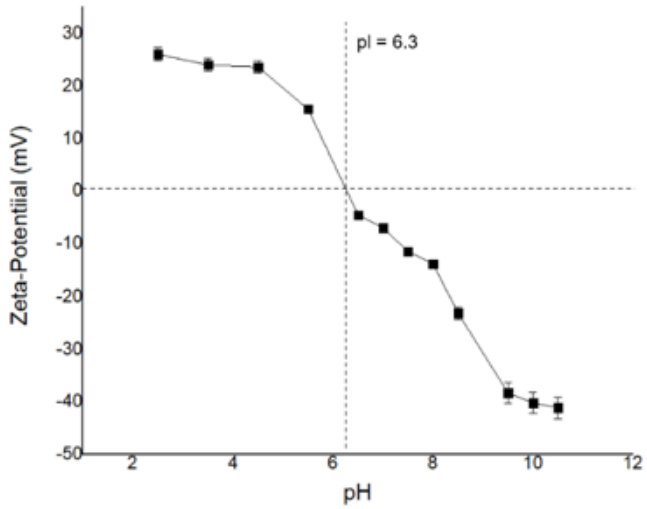


Figure 6.35 Zeta potential of NSCS as a function of pH

6.5.8 Characterization of NSCS/PEO Nanofibers

Electrospinning is a flexible and effective nanofiber-making process. Beads abound in the electrospun materials used in this study. The primary cause of beads is lower surface tension. As the surface tension of electrospun materials increases, the size and number of beads decreases (282). Electrospinning parameters, which are important to comprehend, affect the diameter and morphologies of electrospun fibres. To achieve the desired fibre morphologies and diameters, these parameters can be easily adjusted. The three main categories that affect electrospun fibre parameters such as morphology and diameter are (a) intrinsic properties of the solution, (b) manufacturing conditions, and (c) atmospheric parameters (283). Electrospun NSCS/PEO nanofibers with the best diameters were around (183 ± 38 nm). Even though the fibre diameters were high in comparison to the diameter of pure CS/PEO ratio 4:1 (140 ± 53 nm) as reported in our previous work (284), the solvent evaporation rate during electrospinning was slow. However, we attempted 50% acetic acid as solvent that easier to evaporate than water, but we were not successful to control other defects such as the droplet production, unstable jet, formation of high particles with

nanofiber, and very large diameter nanofibers also it resulted low adsorption capacity for FLX. One basic parameter, such as NSCS solution concentration/viscosity, was used to monitor fibre diameter, with increased viscosity resulting in thicker fibres. The concentration of polymer solution has a huge impact on electrospun nanofiber formation. The viscosity of a solution is considered to be proportional to the viscosity of a polymer solution (285). The greater the nanofiber diameter, the higher the viscosity of the sample. As a result, fibre production in electrospinning requires a minimum concentration. This was the most difficult part during electrospinning, so we tried different conditions to form the continue nanofiber with small diameters. Furthermore, electrospray forms in its position when very low amounts of electricity are electrospun. This is due to the solution's high surface pressures and low viscosity.

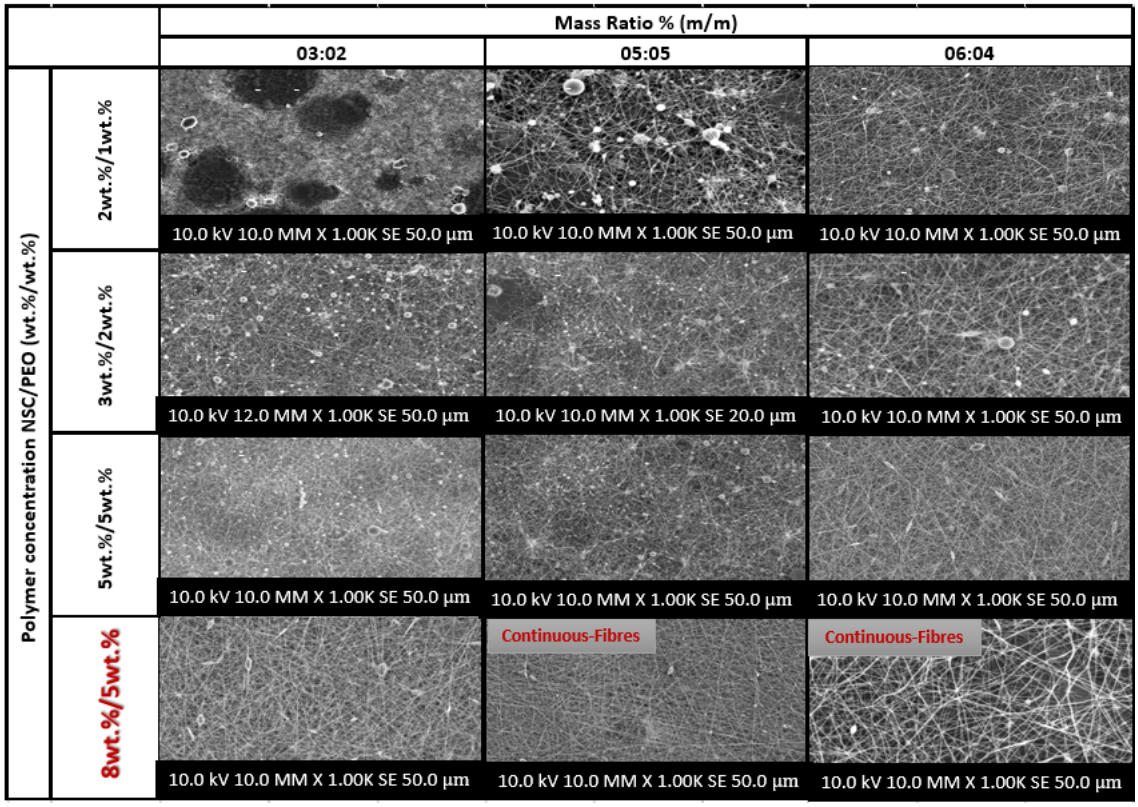
The concentration and mass ratio NSCS/PEO of the solution are two of the most important parameters affecting the electrospinning process, and they play a crucial role in creating defect-free nanofiber mats, as shown in **(**Table 6.5). The copolymer, on the other hand, was the most important factor influencing the electrospinning operation. As a result, increasing the amount of PEO (Co-polymer) in the solution aided in the manufacture of the best NSCS/PEO nanofiber (6:4 mass ratio). Moreover, when the viscosity was low, and the distance between the needle and the collector was longer, a higher voltage was needed. In fact, CS solutions containing 100% were not tested. We attempted to compare the three mass ratios (2:1, 3:2, and 6:4) when the NSCS concentration was increased from 3% to 8%, respectively, in this analysis. In order to find the optimum electrospinning parameters and the highest adsorption potential, the viscosity of the solutions was increased by increasing the concentration of the solution. The following parameters were optimized: a distance of 10-15 cm between the needle and the collector was configured, with a flow rate of 0.01-0.5 mL/h. The optimum voltage, which ranged from 7 to 14 kV, was calculated by observing the jet behaviour. 2:1 (0.01 mL/h, 8kV, 15cm), 3:2 (0.3 mL/h, 12kV, 12cm), and 6:4 (0.5 mL/h, 14kV, 10cm) were the three sets of parameters. Despite this, due to its low viscosity, a pure NSCS aqueous solution is not electrospinnable. As a result, PEO

is often applied to the NSCS solution to improve its electrospinnability. The hydrogen-bonding interactions between the hydroxyl groups of PEO and NSCS make them completely compatible and miscible. NSCS has a low viscosity than pure CS. Since mild viscosity is needed for electrospinning processes, raising the voltage beyond a certain point resulted in much more liquid droplet projection on the collector surface, as well as destabilization of the jet. To solve this problem, increase the concentration of the solution while carefully lowering the flow rates and distance.

According to previous work (6), due to the larger amount of fibers in the corners of the frame during an electrospinning operation, a nanofiber web begins to form, resulting in the build-up of surface charges. As a "spider's web," the deposition process will begin until a mesh fully covers the space inside the frame. Furthermore, using a frame as a collector allowed for easier nanofiber removal, allowing researchers to quickly determine whether an electrospraying /electrospinning process is taking place, because even if some nanofibers are deposited, the particles will split them, preventing, or reducing mat formation. As a result, using a farm as a collector device has many advantages over using regular aluminum foil in an electrospinning setup. Reusability, a smoother mat recovery method using a simple cutter, and a quicker way to assess the morphology of the collected material are the most significant benefits (285). Scanning electron microscope (SEM) images of uniform nanofibers, particles, and beaded electrospun NSCS/PEO nanofibers prepared in our research lab are shown in Table 6.6. The following graphs show the effects of different electrospinning parameters. The concentration and mass ratio were compared in this table. It was discovered that, even with low viscosity, most parameters created nanofibers with particles or beads, and that most electrospinning parameters produced liquid droplets in the collector's field. We got nanofibers with a lot of particles and beads at low concentrations. Since the electrospinning method was quicker, simpler, and free of particles and beads than the others, the solution with an NSCS: PEO (ratio 6:4) with 8wt.%/5wt.% concentration was the

best solution for processes. It also resulted in FLX having a higher adsorption capacity as shown in (Figure 6.36).

Table 6.6 SEM images of NSCS/PEO nanofiber membranes with different condition adjustments of the electrospinning parameters



NSCS/PEO nanofiber membranes were treated with heat treatment temperatures at 100-150 ° C (Figure 6.36B**)** and chemical methods with 2% dilute acetic acid (Figure 6.37C). It was discovered that chemical stabilization with 2 % dilute acetic acid at pH below 4.4 resulted in low weight losses of the nanofiber membranes compared to using 0.01 HCl. The diameters of nanofiber mats treated chemically with dilute acetic acid, on the other hand, were smaller than those treated chemically with HCl. Therefore, the diameter of the nanofibers was changed during the stabilization test. The diameter of the nanofiber before stabilization test was (183 ± 38 nm), then it increased on each stabilization processes, so at heat-treatment was (188 ± 45 nm); and in chemical treatment with acetic acid was (196 ± 40 nm) as show in figure 6.36 (D), (E) and (F) respectively. Ultimately, due to

high humidity, we were unable to electrospun NSCS / PEO under the same conditions of parameters.

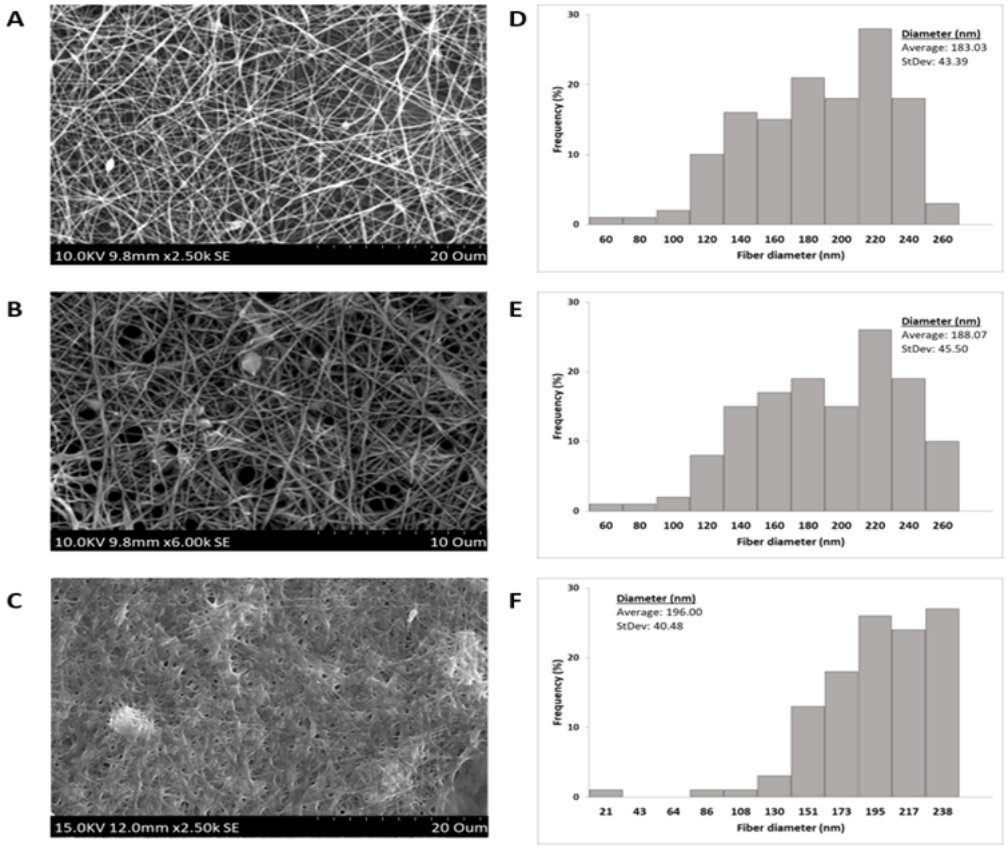


Figure 6.36 SEM images of NSCS/PEO electrospun nanofibers and diameter at concentration (8wt.%/5wt.%) (6:4 mass ratio) (A); After heat treatment of nanofibers membrane (100-150 ^{o}C) (B); after Chemical stabilization in 2% dilute acetic acid (C)

6.5.9 Adsorption Kinetic Studies

The experimental adsorption results clearly show that FLX is adsorbed by NSCS / PEO, with agreement that this biomaterial can adsorb FLX up to 80%. Given that adsorption is preferred at pH 8, kinetic and equilibrium studies were carried out at various pH values with additional adjustments. As previously stated, FLX adsorption on NSCS/PEO nanofibers is preferred at high pH levels. The pH of the solution has a significant impact on both the medicinal charge and the functional groups present on the NSCS surface. These findings indicate that the appropriate

adsorption of FLX into NSCS/PEO transforms this inexpensive and ecologically acceptable material into a tool with promising applications in the removal of pharmaceuticals from wastewater.

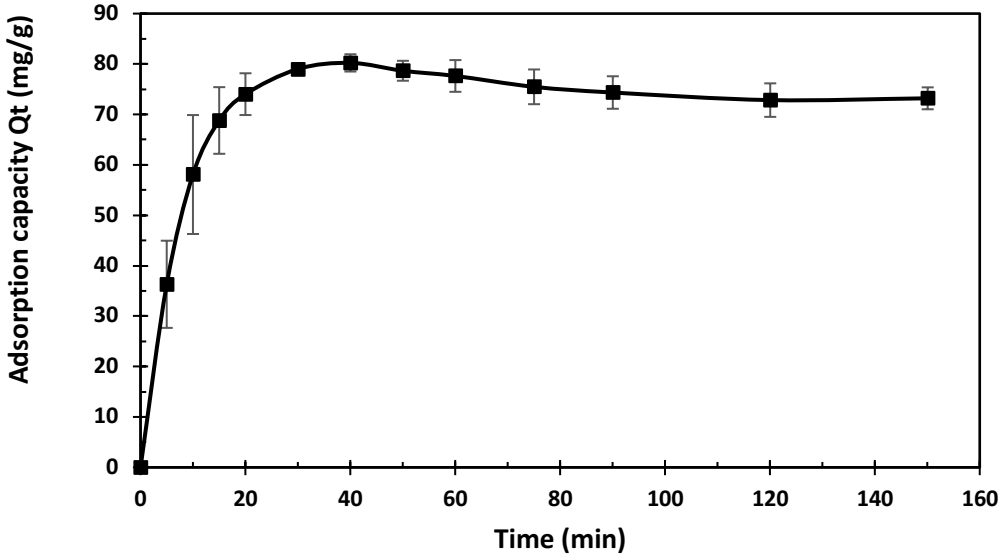


Figure 6.37 Sorption capacity of FLX on NSCS/PEO nanofibers 8wt%/5wt% (6:4) at (pH 8)

The FLX adsorption potential on NSCS/PEO nanofibers mass ratio (6:4) improved significantly as the adsorption time increased. In bout 30 minutes, the maximum FLX adsorption on NSCS nanofibers were observed. Due to that, we chose a 30-minute adsorption cycle to ensure that equilibrium was reached under our test conditions. Pseudo - first order and pseudo-second-order kinetic models were used to examine the potential rate-controlling steps involved in the adsorption of FLX onto NSCS/PEO nanofibers in order to match the experimental results. Figure 6.37 shows the curve for kinetic models. The experimental data map was used to measure the rate constants k_1 and k_2. Table 6.7 displays the kinetic models' rate constants, coefficient of correlation, and calculated Q_e. The correlation coefficients (R^2) for pseudo-first order and pseudo-second order at pH 7.0 are (0.9908-0.9613), at pH 8.0 are (0.9979-0.9969), and at pH 9.0 are (0.9971-

0.9713) respectively. The surface of the modified CS after FLX adsorption, indicating that FLX was adsorbed NSCS/PEO nanofibers. The findings also revealed that the adsorption of FLX was dependent on hydrogen-bond and hydrophobic interactions, as well as a mild electrostatic interaction between opposite charges (286).

Table 6.7 Kinetic Parameter values in the pseudo-first, and pseudo-second-order models for adsorption of FLX on NSCS/PEO 8wt%/5wt% (6:4) nanofibers: Original concentration 50 mg/L, pH (7.0, 8.0, and 9.0), adsorbent 25 mg, t = 150 min at RT.

Experimental	**Pseudo first order model**			**Pseudo second order model**		
pH	$k_1(min^{-1})$	$Q_e(mg/g)$	R^2	$K_2\ (min^{-1})$	$Q_e(mg/g)$	R^2
pH 7.0	0.06424	64.79	0.9908	0.00106	74.51	0.9613
pH 8.0	0.06764	66.29	0.9979	0.001013	81.16	0.9769
PH 9.0	0.07205	71.89	0.9971	0.001178	78.75	0.9713

A proposed mechanism for FLX adsorption on NSCS/PEO. Electrostatic interaction, hydrophobic interaction, and the H-bond all affect the solubility of CS derivatives in aqueous systems dependent on CS. According to previous study, since the amino groups are converted to –NH–CO– groups in the current method, only a few groups can be protonated or dissociated in distilled water (287). Theoretically, electrostatic interaction is not the most important factor in NSCS/PEO adsorption into FLX. The decrease in the intermolecular H-bond facilitates NSCS dispersion into solution, in addition to acetyl groups and glycosidic rings, the remaining intermolecular H-bond, and new hydrophobic moieties in NSCS prevent from dissolving in water and forming a true solution. The poor intermolecular H-bonding caused by the –NH–CO– and –OH groups along the NSCS macromolecular chains, as well as hydrophobic interaction among the hydrophobic moieties in NSCS, such as $–CH_2CH_2$, acetyl groups, and

glycosidic rings, are the driving forces for NSCS/PEO nanofiber adsorption in water (288).

The pH of the media was modified and optimised because high adsorption capacity for NSCS/PEO nanofibers at standard value (5.3) are difficult to achieve. As a result, experiments were conducted at pH levels ranging from 7 to 10, and it was discovered that pH 9.00 was the most effective for adsorption (best Q_t). The adsorbent had overall adsorption efficiencies of about 71.89 mg/g at the pH of the solution (9.0). On the other hand, the optimum pH is 8.0 because going further then pH 8.5 the membrane becomes soluble in medium and more degraded. The relationship between FLX adsorption time and NSCS/PEO adsorption capacities is depicted in figure 6.38. Within 2.5 hours at 25°C, the adsorption potential increases rapidly in the early stages of the reaction. The pseudo-first order and pseudo-second order models were used to analyse the experimental data and determine the adsorption kinetics mechanism. The best-fitting kinetic model for FLX sorption on NSCS/PEO nanofibers was found using the pseudo-first-order rate (correlation factor $R^2 = 0.9979$) expression. According to the mechanism, the rate of FLX adsorption is influenced by the pH of ions at the adsorbent surface which supported by the fact of the ZP value that resulted high negative charge surface in basic media. The calculated rate constant k_1 is 0.06764 g/mmol/h. In 30-minute, FLX adsorption achieves equilibrium. The effect of time on the adsorption behaviour of FLX by NSCS/PEO nanofibers followed the pseudo-first-order model.

As a result, second order kinetics could indicate that the chemosorption is involved in the interaction between adsorbate and nanofibers. Based on finding of a ZP measurement of the surface charge of NSCS, the surface charge of NSCS showed a negative charge in the alkaline media, confirming the validity that the adsorption capacity (Q_e) increases gradually as pH level is increase from 6.5 to 9 in the alkaline media. In order to understand how NSCS/PEO nanofibers interact with target drugs (FLX), it's important to understand that FLX is normally pka = 9.8, which means running NSCS/PEO nanofibers in basic medium at pH > 9.0 will cause no protonation of nitrogen. Therefore, adjust the pH at 7 and 8 are the

optimum pH conditions to have attractive side ionic exchange to give stronger bonding. NSCS/PEO nanofibers are presenting a negative ionized form (pKa_{-COOH} = 4.5), whereas FLX, which is a week base, has appositive charge protonated on it (pKa = 9.8). According, to ZP the NSCS/PEO nanofiber mats the found pi around (6.3) so which mean at pH higher then (6.3) should bring high ionize surface so getting more or higher negative charge at basic medium this leads to get more soluble and degrading at pH higher than 9.0 as showed in Figure 6.38.

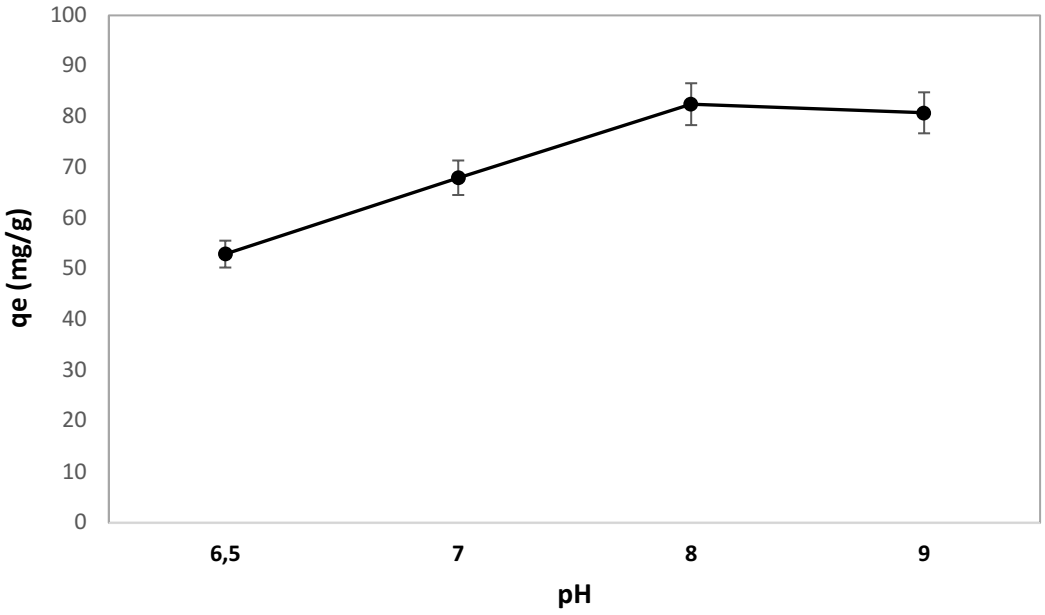


Figure 6.38 Effect of pH on the adsorption of FLX onto NSCS/PEO (6:4) nanofibers

Currently, the physical contact is mastering the processes at the surface of the modified biopolymer in low pH solution (acidic medium). The kinetic experiment will follow the pseudo first order because the described adsorption capacity of FLX is around (Q_e=71.89 mg/g). Many studies have looked at using continuous adsorption to treat drug contaminants because of its benefits, such as high adsorption performance, flexibility, and adsorbent renewal capacity. Furthermore, pharmaceutical residues have a significant environmental impact, thus their management has been the subject of numerous studies (289). Batch adsorption can handle enormous amounts of drug solution while still achieving excellent

removal efficiency. It may also be easily scaled up from a laboratory to an industrial setting (Lemus et al., 2017).

Indeed, real-world wastewater contains many toxins that are not separated in nature. To put it another way, they exist in groups and in combination with other pollutants. As a result, there is mounting evidence that the toxicity of medicinal combinations is greater than the toxicity of individual drugs. The adsorption of FLX, VER, CBZ, and IUP to NSCS/PEO nanofibers was studied to learn more about the adsorption mechanism of those pollutants on NSCS/PEO in aqueous solutions. In comparison to the experimental data, our understanding of the adsorption behaviour of numerous pharmaceuticals revealed that the adsorption capacity reduces as expected for neutral and acidic drugs (e.g. CBZ and IUP) and increases in the case of a basic drug (e.g. FLX and VEX) (290). Furthermore, drug adsorption is greatly influenced by pH.

Table. 6.8 and Figure 6.39 illustrates the results of the experiment for various medications and individuals. Different adsorption experiments were carried out using a mixture of four pharmaceuticals (FLX, VEX, CBZ, IUP) in 50 ppm concentration for each single pharmaceutical, and multiple pharmaceuticals 12.5 ppm for each drug to test the influence of the presence of other drugs in solution on the single adsorption process. As a result, the adsorption capacity of each medication in both systems did not match. As can be seen, single pharmaceuticals have a higher adsorption capacity than multiple pharmaceuticals, implying that in batch adsorption of single pharmaceuticals, the chemical interaction between the adsorbent (NSCS/PEO) and the one pharmaceutical (FLX) as an alkaline drug is more direct, with no side effects. As a result, in the case of one pharmaceutical, the interaction will be strong, whereas in the case of multiple pharmaceuticals, the adsorbent will be unable to bond with the various pharmaceuticals because the four pharmaceuticals have different behaviours and functional groups, making it difficult to form interactions between them. As a result, the chance for the NSCS/PEO to adsorb the pharmaceutical will be reduced.

Table 6.8 Experimental for Individual and Parallel Pharmaceuticals Adsorption capacity.

Contaminant	Individual adsorption capacity mg /g	Individual adsorption capacity mg /g
Fluoxetine (FLX)	82.11 ± 3.77	33.10 ± 0.15
Venlafaxine (VEN)	54.02 ± 0.31	17.62 ± 1.50
Carbamazepine (CAB)	47.51 ± 2.16	10.24 ± 0.81
Ibuprofen (IBU)	25.98 ± 1.27	4.89 ± 1.99

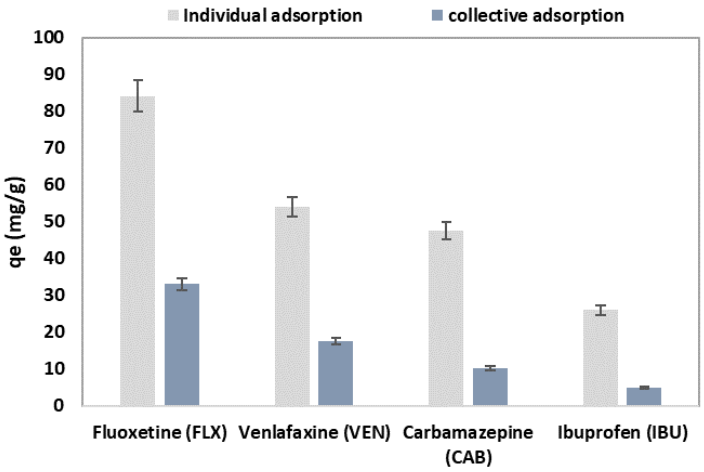


Figure 6.39 The adsorption of various medications in single/multiple pharmaceuticals in solution at pH 7 and 25 °C was compared

The NSCS/PEO nanofibers' pharmaceutical adsorption capacities were compared to those of other adsorbents in earlier research, and it was shown that their adsorption capacities were substantially higher than those of other adsorbents (Table. 6.9).

Table 6.9 The adsorption capacity values for the adsorption of FLX on different adsorbents

Adsorbents	Adsorption capacity (mg/g)	References
Mesoporous ferrite nanoparticles of ruthenium ($RuFeO_3$) and cerium ($CeFeO_3$)	729.6 (>99%)	(291)
NSCS/PEO nanofibers	82.3	---
N, O-CMCS/PEO nanofibers	79.7	(284)
Lignin/PVA nanofibers	78.2	(177)
Biochar, rice bran pyrolysis	67.6	(292)
Hydrochar, activated carbons	44.1	(231)
Biochar, Eucalyptus pyrolysis	6.4	(293)
β-Cyclodextrin carboxymethyl cellulose (β-CD-CMC) polymer	5.1	(294)

6.5.10 Desorption Studies

The desorption process and mechanisms of the adsorbed FLX on the NSCS/PEO nanofibers are critical to understand. Reusing used adsorbents is seen as a key economic factor in cutting down on material prices. For the NSCS/PEO nanofiber, we investigated a range of desorption conditionals, including altering the pH (acidic pH) with different concentration (0.1, 0.01, and 0.001M) of HCl and acetic acid (5, 10 and 50%), 100% methanolic solutions, and heating the solution in an ultrasound bath. The desorption procedure took more than two months to complete, making it the most time consuming part of the study. There were numerous attempts to produce the safest and most optimal desorption conditions. It was determined that low concentration of HCl boosted the desorption removal capacity in acidic media at pH 3, and that increasing the concentration of HCl, and acetic acid led to increase the adsorption capacity, but the nanofiber membrane lost too much weight and disintegrated.The NSCS/PEO has total desorption removal capabilities of 71% at pH 2.0 (1% HCl) and 78 % in 10% acetic acid.

However, even after numerous cycles, the adsorbent was found to successfully retain FLX.

First, even at low concentrations of methanolic solution, the amount of desorption of NSCS/PEO nanofibers was too low in addition to deteriorating, causing the membrane to lose weight too quickly. The solution was then heated in an ultrasonic bath. It helped to desorb the membrane by elevating the temperature, as opposed to the first scenario discussed above. Supporting the heating with ultrasound, on the other hand, resulted in a small increase in desorption. Damaged, degraded, and losing the weight of the adsorbent (NSCS/PEO) mat were the outcomes in both cases. As the pH of the solution was elevated, the proportion of NSCS/PEO desorption reduced drastically, indicating the preferred desorption condition. At pH 5.0, desorption was minimal, while at pH 2.0, the most desorption was recorded. Because substantial desorption was seen at pH 2.0, it was concluded that FLX adsorption on NSCS/PEO is predominantly owing to electrostatic attraction, validating the pH influence on adsorption. To clarify, the principal adsorption interactions of NSCS/PEO nanofibers were electrostatically preferred in many other works, thus when the pH was less than 5, the chemical interaction became weak and the electrostatic connection broke, resulting in FLX desorption. In view of that, the desorption of nanofibers NSCS/PEO has not been widely investigated, so more experimental conditions and mechanisms study is needed.

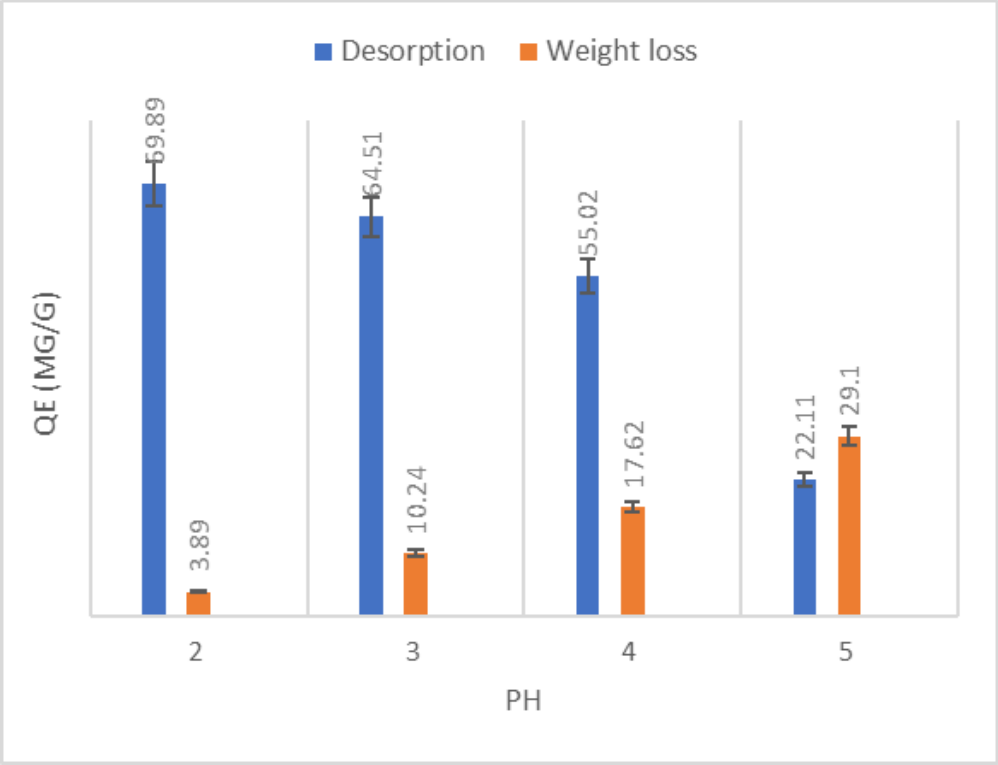


Figure 6.40 Various pH experimental conditions on NSCS/PEO (6:4) for desorption solution, and weight loss of the nanofiber membrane

Figure 6.40 indicates that in a basic media, not only poor desorption, but the nanofibers are also broken (degraded), resulting in large weight losses in the nanofibrous. Acid pH can produce high desorption without significant weight loss. Desorption efficiency rises with pH 2.0 so because the electrostatic connections between the NSCS/PEO mat and FLX are decreased in an acidic environment, FLX desorption from the membrane is improved.

Furthermore, for the economic feasibility of adsorbent for water filtration, it is critical to regenerate wasted adsorbent. The regeneration of NSCS/PEO nanofibers was investigated using four adsorption/desorption cycles as shown in Figure 6.41. Desorption studies can aid in the understanding of an adsorption process' mechanism. If water can desorb the FLX adsorbed on the adsorbent, it is thought that the FLX is attached to the adsorbent by weak bonds; if strong acids (such as H_2SO_4 and HCl) can desorb the FLX, it is thought that the FLX is attached

to the adsorbent via ion exchange or electrostatic attraction (295). As a result, the influence of pH on FLX desorption capacity onto NSCS/PEO nanofibers were tested using distilled water with various pH values. The desorption capacity fell significantly as the pH increased; the lowest desorption capacity was at high pH up to 7.0 (basic pH), while the highest desorption capacity was at pH 2. It is obvious that electrostatic attraction had a substantial role in the adsorption of FLX onto the NSCS/PEO nanofibers (295). The adsorbed FLX on NSCS/PEO can be desorbed into the solution at varied concentrations of HCl (1, 0.1,0.01, and 0.001 M, respectively). The desorption of FLX increases for HCl, as the regenerant concentration is increased to 1 M. When acids are utilised as regenerants, the amine functional groups on the sorbents are protonated, causing a repulsive force between the adsorbed FLX and the $-NH_3^+$ groups, resulting in FLX being released into the solution (296).

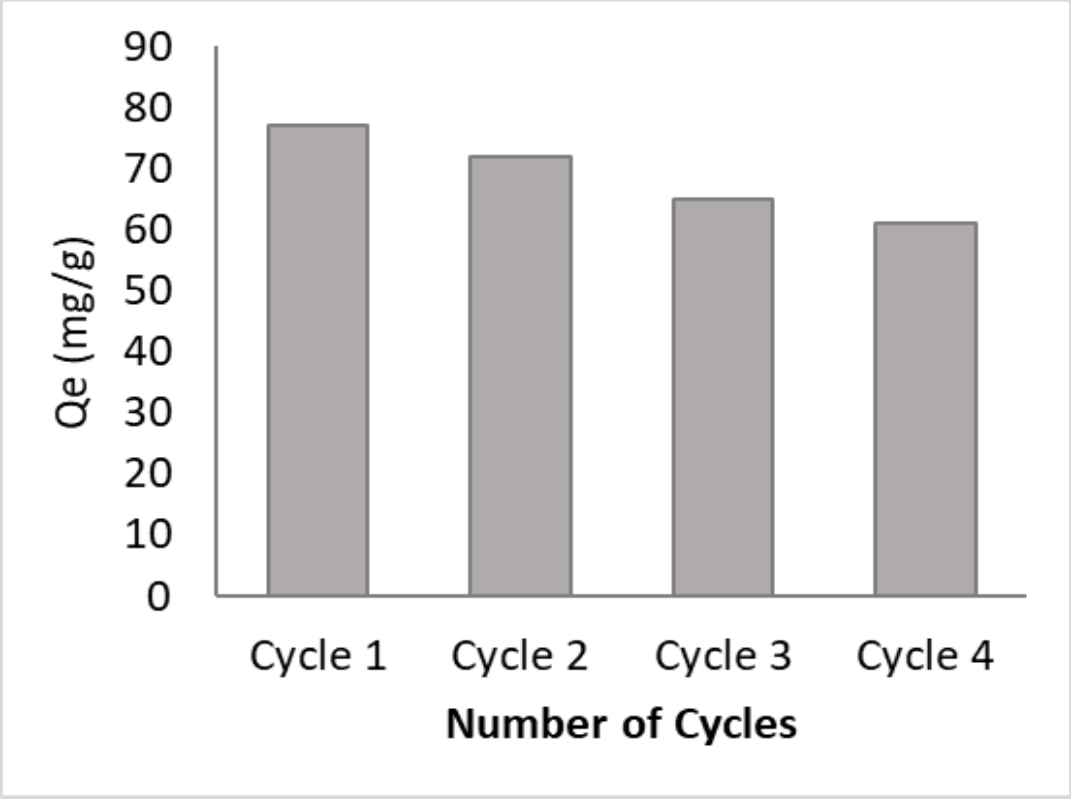


Figure 6.41 Desorption cycles of NSCS/PEO (6:4) for fluoxetine using 1M HCl (pH 2)

6.6 Conclusion

The overall goal of this research is to develop new adsorbent biomaterial nanofibers that can be combined with, or used instead of, traditional wastewater treatment approaches to become "ecologically sustainable" technological solutions that can reduce costs while benefiting the community and the environment. NSCS has been successfully synthesised, a novel biocompatible CS derivative with a well-designed structure. The NSCS/PEO nanofiber is a promising adsorbent for FLX elimination. FTIR and ^{1}H–NMR were used to successfully manufacture and verify NSCS. Due to its adsorption capabilities and the availability of waste materials used to create it, this eco-friendly material with an average diameter of 183 ± 38 nm is a promising adsorbent to replace activated Carbone (AC). Repeated adsorption-desorption cycles proved this sorbent material's remarkable reusability potential, making it appropriate for water purification. For electrospinning, different ratios of NSCS and PEO were tried to find the optimal nanofiber for adsorption of FLX as a model of pollutants in aqueous solution. To develop ideal NSCS/PEO nanofibers, the effects of pH on the FLX adsorption system were examined. Batch adsorption investigations revealed that the NSCS/PEO adsorption capability for FLX elimination is highly dependent on the starting pH. The pseudo-second-order model accurately represented the FLX adsorption equilibrium on NSCS/PEO mats, according to the kinetics studies. NSCS/PEO has achieved the highest percentage removals at a pH value of 8.0, a maximum adsorption capacity up to 82.3 ± 3.4 mg/g for FLX. Because of the study's good findings, the adsorbents could be employed in large-scale wastewater treatment plants, ensuring reduced detrimental environmental consequences and long-term sustainability. Future research will concentrate on real-world wastewater samples and advancements in adsorbents that may effectively remove many pollutants at once.

CHAPTER 7 - ARTICLE 3

Comparative Study on the Efficiency of Novel Modified Chitosan-Based Electrospun Nanofibers for Removal of Fluoxetine from Wastewater Treatment

Amna Hassan Issa Khierallah, Amel Hadj Bouazza, Daniel Montplaisir

7.1 Foreword

This first article is entitled " Comparative Study on the Efficiency of Novel Modified Chitosan-Based Electrospun Nanofibers for Removal of Fluoxetine from Wastewater Treatment ". It has been submittied to Journal Arabian Journal of Chemistry.

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7.2 Résumé

Les résidus pharmaceutiques, ainsi que leurs métabolites et conjugués, sont excrétés par l'urine et les fèces pendant et après le traitement médical. L'élimination de ce type de contaminants des eaux usées fait donc l'objet d'une attention intense. Dans cette étude, le médicament antidépresseur fluoxétine a été retiré de la solution à l'aide d'une nouvelle technique basée sur des nanofibres électrofilées constituées de chitosan N-phtalique (NPCS) et de N-succinyl chitosan (NSCS) combinés avec du PEO comme copolymère pour l'électrofilabilité. Afin d'obtenir la meilleure morphologie des nanofibres déterminée par microscopie électronique à balayage. L'ajout des bons groupes chimiques à la surface du chitosane par modification chimique permet l'élimination des contaminants pharmaceutiques. En utilisant la spectroscopie FTIR et ^{1}H-NMR, les propriétés du chitosane modifié ont été étudiées. Des expériences sur la solution FLX ont été utilisées pour caractériser le processus d'adsorption à l'aide d'une chromatographie liquide à haute performance. Les processus ont été bien décrits par adsorption cinétique, le FLX a été éliminé en modifiant le pH des paramètres expérimentaux pour rechercher l'impact du pH de la solution. Le pH du média doit être ajusté afin d'améliorer l'élimination des polluants et d'avoir une capacité d'adsorption élevée. Les capacités d'adsorption maximales pour les nanofibres NPCS/PEO et NSCS/PEO, respectivement, étaient de 72,22 % et 81,16 %.

Mot clé : Chitosane Modifié ; Phtalate de Chitosane ; Chitosane Succinyle; Fluoxétine; Electrofilage; Nanofibres ; Adsorption.

7.3 Abstract

Pharmaceutical residues, along with their metabolites and conjugates, are excreted through urine and faeces both during and after medical therapy. The elimination of those contaminants from wastewater is therefore the subject of intense attention. In this study, the antidepressant medication fluoxetine was removed from the solution using a new technique based on electrospun nanofibers made of N-phthalic chitosan (NPCS) and N-succinyl chitosan (NSCS) combined with PEO as a copolymer for electrospinnability. In order to achieve the best nanofiber morphology as determined by scanning electron microscopy. Adding the right chemical groups to the surface of chitosan through chemical modification allows for the elimination of pharmaceutical contaminants. Using FTIR and ^{1}H-NMR spectroscopy, the properties of modified chitosan were studied. Experiments on the FLX solution were used to characterize the adsorption process using a high-performance liquid chromatography. The processes were well described by kinetic adsorption, the FLX was removed by changing the pH of the experimental settings to research the impact of the solution's pH. The media's pH needs to be adjusted in order to improve pollutant removal and have a high adsorption capacity. The maximum adsorption capacities for NPCS/PEO and NSCS/PEO nanofibers, respectively, were 72.22% and 81.16%.

Keyword: Modified chitosan; Chitosan phthalate; Succinyl chitosan; Fluoxetine; Electrospinning; Nanofibers; Adsorption.

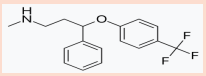
7.4 Introduction

Water is an essential solvent for maintaining life. Water must therefore be free from contaminants and readily available in sufficient amounts. But water contamination is growing in importance worldwide (297) , (298). Worldwide reports have indicated the presence of new pollutants, such as pharmaceuticals, in the aquatic environment (299) , (300). One of the most studied issues throughout the years is the topic of pharmaceuticals and their presence in wastewater or the environment. Despite the years that have passed since the first mention of drug emissions polluting the aquatic environment, treatment technologies that can resolve the problem are still not in use (301). Due to this, aquatic organisms may be affected physiologically and behaviorally by the presence of antidepressants in municipal wastewater (189) , (6). The challenge is caused by the variable impurity characteristics and composition of the wastewater delivered to the treatment plant, including the low absorbability and biodegradability of cytostatic medicines. However, inadequate removal and degradation of pharmaceutical contaminants during wastewater treatment increases the likelihood that these compounds may be released into the aquatic environment (301).

Antidepressants like fluoxetine (FLX) and venlafaxine (VLF), which are among the most often consumed pharmaceutical pollutants, have seen increased use as a result of the stressful lives that the majority of the world's population now leads (300). With a concentration of VLF (196 ng/L) the River St. Lawrence, Canada, was one of the highest values so far reported in an aquatic environment (302). Additionally, FLX at values of a few ng/L have been found in surface waters (302). The presence of FLX in the aquatic environment, even at low concentrations (few ng/L), may adversely affect aquatic organisms, such as fish, algae, and crustaceans (303). High FLX concentrations in aquatic environments, according to certain research, have led to the bioaccumulation of FLX and its demethylated metabolites in wild-caught fish, particularly in their brain, liver, and muscle tissues (304). A common anti-depressant drug used to treat depression is FLX (305). As seen in table 7.10. The FLX's chemical composition (306). Both large and tiny

levels of FLX rejection are found in the urine up to 0.101 µg/L were detected (305), (307).

Table 7.10 Chemical properties of fluoxetine

Chemical Name	Fluoxtine (FLX)
Chemical Structure	
Molecular Formula	$C_{17}H_{18}F_3NO.H$
Molecular Weight (g/mol)	345.79
pKb	9.5
Log Kow	1.22

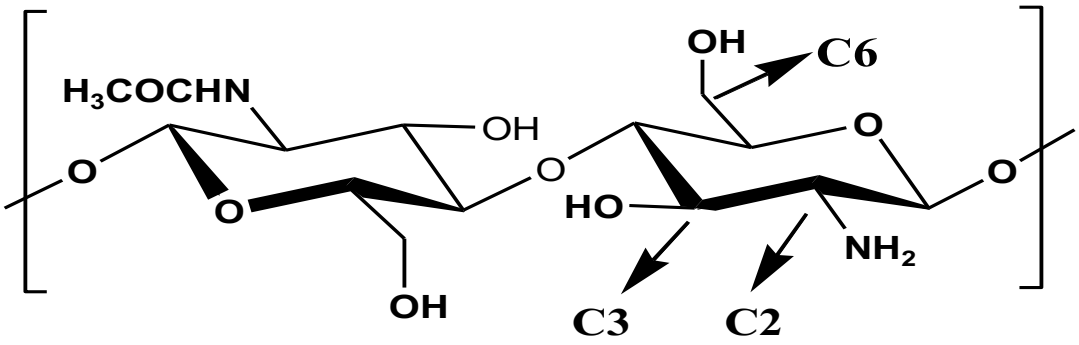
An earlier investigation found that the ability of a primary treatment method to remove and/or degrade antidepressant residues in wastewater is limited (6), (308). In the literature, other findings from the use of analytical techniques for pharmaceutical and personal care products (PPCPs) have previously been reported. The Montreal WWTPs used a physicochemical technique, which involves adding ferric chloride or alum as a coagulant and anionic polymer as a coagulant aid, to produce the results that were reported in 2006. The direct discharge of treated effluent into the St. Lawrence River has demonstrated that the amount of PPCPs removed by the physical and chemical methods used today is quite low. However, physicochemical treatment does not eliminate these molecules (6). Adsorption is a successful tertiary way to dispose of medicines (309). Due to their low cost and excellent adsorption efficiency, biochar materials have recently been demonstrated to be viable remedies (305). Unquestionably, activated carbon (AC) is a strong adsorbent with a high adsorption capacity that may be employed in a variety of liquid and gas phase applications, including the

treatment of wastewater (298). However, due to the adsorbent material's potential for high operational costs for wastewater treatment systems, its use has been restricted. Therefore, it's necessary to look for less expensive options. The invention of innovative methods for FLX's adsorption and removal from wastewater is of major interest because it can be extremely hazardous to the environment and aquatic life (304). Most medications cannot be effectively removed by conventional water treatment techniques because WWTPs are not equipped to degrade or remove these new emergent pollutants(298). For the elimination of medicines, it is consequently vital to use a cost-effective treatment technique.

Due to its adaptability, low energy consumption, simplicity, and great efficacy in removing pollutants, the removal of pharmaceuticals by adsorption is one of the most alluring strategies for the treatment of wastewater (298). Although recent studies have shown that commercial adsorbents like activated carbon, carbon nanotubes, and synthetic zeolites are effective and offer excellent removal rates, their high cost prevents their use in large-scale systems (310). Therefore, there is a pressing demand for alternative, affordable, and biodegradable adsorbents. Due to their abundance in nature, low cost, strong mechanical and chemical resilience, and biodegradability, wastes originating from agriculture or forestry have recently drawn the interest of the scientific community (294). The circular economy idea and increasingly strict environmental regulations that prevent disposal methods like landfilling and incineration are both in line with the utilization of waste materials as adsorbents (294). Many efforts have been made to create efficient and environmentally friendly adsorbents based on affordable and natural polymeric materials in order to get beyond these limitations.

The use of CS as a potential site-specific biopolymer among natural biopolymers has received widespread acceptance (311). According to figure 7.42, CS is a heteropolysaccharide made composed of amino groups, a linear polyamine, and reactive hydroxyl groups at the C2, C3, and C6 locations. In order for the structure of CS to change, these groupings are crucial. While CS with a lower degree of deacetylation is semi-crystalline, CS that is 100% deacetylated is crystalline. CS

dissolves well in organic and inorganic acids but is insoluble in neutral and basic solutions. It is also soluble in mixes of water with methanol, ethanol, and acetone. The free amino and N-acetyl groups that are present in CS's structure play a role in its solubility (304). CS is a bioproduct that is produced by treating chitin with alkali. The quality of the CS that is produced relies on the extraction conditions, such as alkali concentrations and acid-sample reaction times (312). The amine group (-NH_2) and hydroxyl (-OH) on the CS's active side give it the properties of ion exchangers (312). Because it contains reactive amine groups, CS is easily altered. Due to their vastly different physicochemical qualities from the unmodified CS, its derivatives might offer certain advantages over it (313). In recent years, a number of CS derivatives have been created in an effort to acquire various advantageous features over CS, which has water solubility over a wider pH range (314), (313). CS change is required to solve this issue. CS is readily chemically altered due to the presence of amine groups (NH_2) and hydroxyl (OH) from the compound. Both intra- and intermolecular hydrogen bridges can be provided by the hydroxyl and amine groups. Chitosan becomes insoluble in water as a result of the formation of a robust hydrogen network. Numerous research has been conducted to determine the effectiveness and use of CS in various applications. By introducing multiple functional groups into CS structures, CS modification was done to tie CS quality (312).



Chitosan

Scheme 7.42 Chemical structure of chitosan (carbon number)

Phthalic anhydride modification of CS will enhance load density, can form chitosan phthalate (CSP) compounds that are not easily dissolved by high-level substitution, and has the potential to produce ion transmitters due to the end-chain chain CO-COOH ease of ionization. Given that NPCS is a crucial intermediary that enables carefully regulated modifications to CS(6). High affinity for organic solvents was shown by the NPCS, however it was slightly less than that of the product with additional O-phthaloyl groups (315). The formation of N, O-phthaloylation from the reaction of CS with phthalic anhydride in N, N-dimethylformamide (DMF) required the removal of the O-phthaloyl groups through tritylation-detritylation, hydrolysis, or alcoholysis in order to produce NPCS. However, flawless functional group discrimination was made possible, and NPCS could be produced in a straightforward one-step process both selectively and quantitatively. Tritylation indicated that the resulting N-phthaloyl chitosan (NPCS) was more reactive than N, O-phthaloyl chitosan (N, O-PCS) and shows promise as a C-6 substitution precursor (315). Anhydrous phthalates have been added to CS to diminish its crystallinity, which has increased the membrane's hydrophilic properties(312).

One of the main areas of interest in the innovative wastewater treatment techniques is nanotechnology. It is acknowledged as the upcoming technology. Researchers and scientists working in the field of nanotechnology must alter materials at the atomic and molecular levels (316). Nanofibers can be made from a variety of substances, including natural polymers like cellulose and CS as well as synthetic polymers like polycaprolactone and polyurethane. One of its key qualities is thought to be the synthetic polymers' increased flexibility in their synthesis and modification (317). One of the most well-known and often applied methods for creating nanofibers is electrospinning (146). The major difficulty with this method is manufacturing nanofibers on a wide scale (318). Numerous applications for the nanofibers produced by the electrospinning technique include filtration, tissue engineering, scaffold fabrication, wound dressings, and drug delivery (319). Many electrospun mixtures of CS and synthetic polymers,

including polyvinyl alcohol (PVA), polyethylene oxide (PEO), polyethylene terephthalate (PET), polycaprolactone (PCL), poly lactic acid (PLA), polyamide, and others, have been developed recently (320), (321). These polymers are added to improve the mechanical, biocompatible, and antibacterial qualities of CS (304). Synthetic polymers alone or in combinations with natural and synthetic polymers can be used to create nanofibers. Due to the instability and toxicity of synthetic polymers after decomposition, which could harm cells, it is preferable to combine natural and synthetic polymers to create nanofibers with improved mechanical and biological properties (322). Water soluble polymers poly (vinyl alcohol) (PVA) and poly (ethylene oxide) (PEO) are frequently combined to create nanofiber mats because of their superior spinnability (323).

This comparative study on the preparation and examination of chitosan succinate (CSS) and chitosan phthalate (CSP) are the main topics of this work. We changed CS to produce CSS and CSP through a substitution reaction involving succinic acid and phthalic acid. The removal of pharmaceutical pollutants from wastewater is a potential use for these novel biomaterials. The mechanism of FLX adsorption will be examined using HPLC-UV-DAD and other kinetic parameters. Batch adsorption studies will be carried out under controlled settings to determine the impact of experimental variables, such as pH, on adsorption capabilities. In order to apply nanotechnology to remove FLX from wastewater, it is necessary to evaluate the sorption capacity of CSS/PEO and CSP/PEO nanofibers as well as the impact of the pH of the solution on these new CS derivatives.

7.5 Materials and Methods

7.5.1 Materials

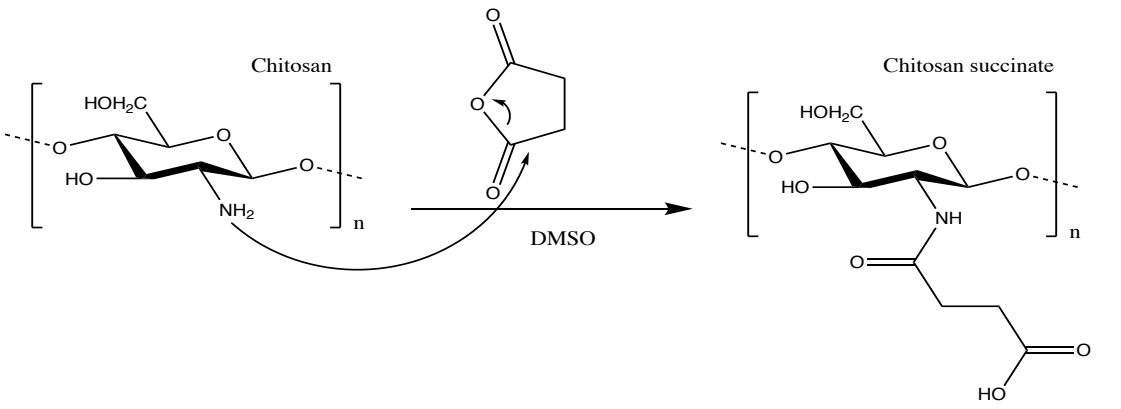
Sigma-Aldrich (Reykjavik, Iceland) provided the low molecular weight chitosan (CS MW 50,000-190,000 g/mol, 75-85% deacetylated). Polyethylene oxide (PEO) was employed as a co-spinning agent; the molecular weight average was 900,000 g/mol, Sigma Aldrich (St. Louis, MO, USA). Analytically graded

substances included sodium hydroxide (NaOH), sodium chloride (NaCl) pyridine, acetone, and ethanol. Phthalic anhydride from Sigma-Aldrich (CAS 85-44-9), Succinic anhydride from Sigma-Aldrich (CAS 108-30-5) were also used. To be used as a model contaminant in the adsorption test, fluoxetine (CAS 56296-78-7) was purchased from Sigma-Aldrich (Oakville, ON, Canada). The following items were purchased from Fisher Science: methanol (HPLC grade), acetonitrile (HPLC grade), O-phosphoric acid (HPLC grade; 85 wt. / wt.%), and glacial acetic acid ACS reagent (99.7%). (Ottawa, Ontario, Canada). 0.055 μS/cm conductivity (Siemens Super Transparent RO) Deionized water was used throughout all of the trials. Everything was used exactly as it had been.

7.5.2 Methods

7.5.2.1 Preparation N-succinyl Chitosan (NSCS)

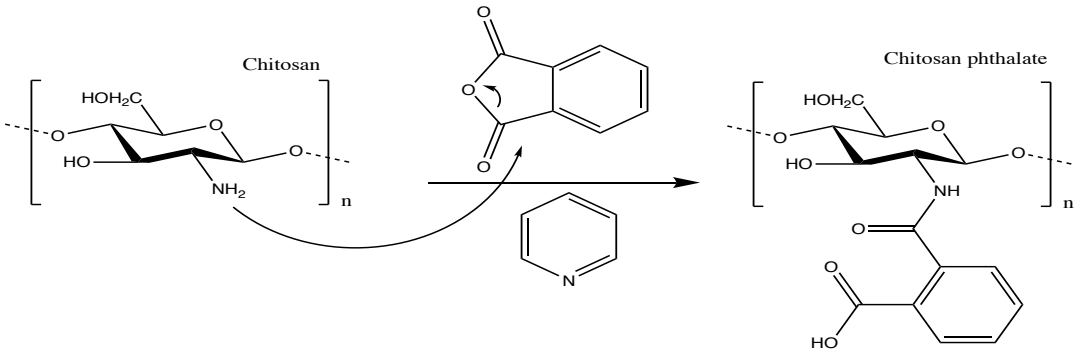
Chitosan was succinylated using the procedure described by (324), (280), and had a low molecular weight (MW) of 50,000–190,000 g/mol and was 75–85% deacetylated. Scheme 7.43 depicts the creation of N-succinyl chitosan (NSCS). NSCS was produced through ring-opening processes with succinic anhydride in a dimethyl sulfoxide (DMSO) framework. First, 40 mL of DMSO and 2 g of CS powder were combined thoroughly. The CS solution was then slowly added (4 g of succinic anhydride), and the reaction was allowed to run for 6 hours at 65 °C. After being filtered to remove the solvent, the sample was then dissolved in ethanol at room temperature and allowed to react for an hour. At the conclusion of the process, NaOH (1 M) was added to the solution to adjust its pH to 10–12. The precipitate was then dissolved in 90 mL of distilled water, followed by the addition of 270 mL of acetone, followed by washing with ethanol and precipitation with acetone, respectively, after the mixture had been filtered. Finally, NSCS was dried at 50 °C in a vacuum oven.



Scheme 7.43 Synthetic of N-succinyl chitosan (NSCS)

7.5.2.2 Preparation of N-phthaloyl Chitosan (NPCS)

By substituting main amino groups using substituent techniques, NPCS was synthesized. According to (Aiedeh and Taha 1999) (325), the synthesis reaction of NPCS was carried out (325). In a nutshell, CS (5.00 g, or 31 mmol glucosamine) was dissolved in 300 ml of HCl aqueous solution (0.37%) at room temperature. The polymeric solution was then vigorously stirred while phthalic anhydride solution (31.25 mmol; 4.6 g) in pyridine was added dropwise. Dropwise addition of NaOH solution was used to keep the reaction's pH at 7.0. (1.0 M). After 40 minutes, the reaction was stopped by adding 500 ml of NaCl aqueous solution (20%). After filtering, washing with acetone and diethyl ether, and drying in a vacuum oven at 50 °C, the precipitate produced NPCS (313) , (311). Scheme 7.44 demonstrates the creation of N-phthalic Chitosan (NPCS).



Scheme 7.44 Synthetic of N-phthalic chitosan (NPCS)

The Fourier transform infrared (FT-IR) spectrum of CS and CSP was captured using an FTIR Thermo iS10 spectrometer. The material was screened between 600 and 4000 cm $^{-1}$. With chemical shifts given in ppm, the ^{1}H-NMR spectra were generated using a 200 MHz Oxford NMR spectrometer with CS dissolved in water, NSCS dissolved in water/DH_3COOH, and NPCS dissolved in DMSO-d_6.

7.5.2.3 Electrospinning

It was possible to create NPCS/PEO and NSCS/PEO nanofibers by electrospinning. Figure 7.45 shows a schematic of the experimental equipment used to create modified electrospun nanofibers based on CS. A mixture of NSCS with PEO and NPCS with PEO were used to create the electrospinning solutions, respectively. Each polymer concentration was dissolved in acetic acid (50–90% v/v), and the results are given as w/v % (g/ml). An 8% NSCS with 5% PEO polymer solution and a 2.5% NPCS with 3% PEO polymer solution at the ratios of (6:4 NSCS) and (3:2 m/m NPCS) were prepared by dissolving the polymers in 50% acetic acid for NSCS and 90% for NPCS as the electrospinning solution at room temperature until a homogeneous viscous solution was obtained after (1 h, NSCS; 20 h PEO) The solutions were then mixed for 2 hours with constant stirring. The mixtures were then immersed in an ultrasonic bath for 15 minutes to eliminate bubbles. For the mixes to reach the necessary polymer concentrations and be prepared for electrospinning processes, they were given a final rest period of 3 hours before being utilized in the electrospinning procedure. The produced solutions were transferred to a 5 mL plastic syringe fitted with a 20-gauge needle and connected to a syringe pump that produces a continuous, slow liquid flow in order to create nanofibers. The tip of the needle and the collecting plate were placed in an electric field created by a high-voltage generator. The syringe needle's tip served as the generator's positive terminal, and a titanium frame

served as the negative terminal. The syringe injection flow rate of (0.2-0.5 mL/h), a distance of (10-15 cm) between a metallic frame and the tip of the needle, and a voltage varied between (10-14 kV) at room temperature were the optimal electrospinning parameters used to create the nanofibers for NPCS/PEO and NSCS/PEO. Finally, to get rid of moisture and the last of the solvent, the electrospun NPCS/PEO and NSCS/PEO nanofibers were dried in an oven (Fisher Scientific Isotemp Oven, Thermo Scientific HERATherm Oven) at 80°C for 24 h.

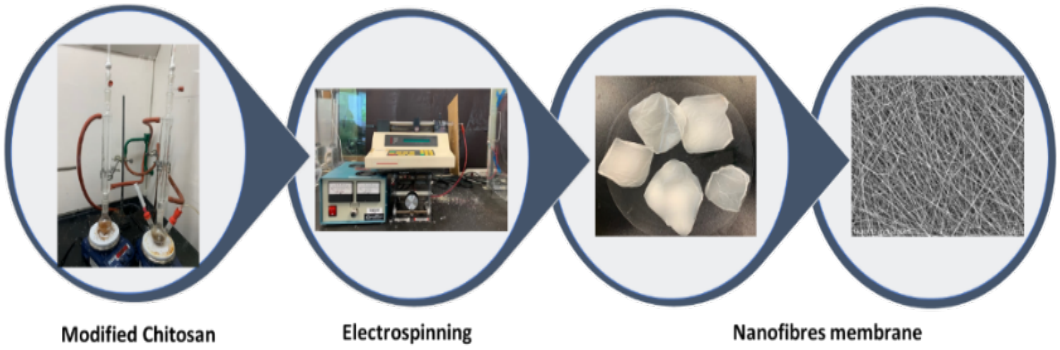


Figure 7.45 Schematic experimental setup for synthesizing modified chitosan based Electrospun Nanofibers

7.5.2.4 Fiber characterization

The resulting fibre morphologies were analysed using scanning electron microscope (SEM) (JEOL JSM 5500). The obtained SEM images were further examined using the ImageJ software to measure the fiber diameters using over 100 measurements for each formulation in order to obtain an average and standard deviation (Rasband, W.S., ImageJ, US National Institutes of Health, Bethesda, MD, USA, https://imagej.nih.gov/ij/,1997-2018). In comparison to any other known form of the material, the polymeric fiber exhibits many advantages when its diameter is decreased to micrometers or nanometers, including a higher surface area to volume ratio, elasticity, and improved mechanical properties

(stiffness and resistance to traction). Polymer nanofibers are the best candidates for numerous crucial applications due to these characteristics (326).

7.5.2.5 Batch Adsorption Experiments

In each batch experiment, 25 mg of adsorbent (NSCS/PEO and NPCS/PEO nanofiber mats) was combined with 50 mL of FLX solution and shaken at 200 rpm. Either HCl or NaOH was used, depending on the situation, to change the pH of the starting solutions. By altering the pH between 2.0 and 9.0, the impact of pH was examined. There were three duplicates of each experiment. Periodically, samples were collected, and the remaining concentration of FLX in solution was determined by HPLC analysis. (Equation 7.25) was used to determine the amount of FLX that was adsorbed at time t, qt (mg/g).

$$q = \frac{(C_0 - C_t)}{m} V \qquad \text{Equation 7.25}$$

where V (L) is the volume of the FLX solution, m (g) is the mass of adsorbents, C_o (mg/L) is the initial concentration of FLX, C_t (mg/L) is the concentration of FLX in solution at time t, and (NSCS and NPCS nanofibers). Between pH 2 and pH 9, the impact of the solution pH on FLX adsorption by modification CS was examined (298). In order to conduct kinetic studies, 50 mL of FLX aqueous solution was shaken with a chosen mass of CSS and CSP nanofiber mats (25 mg) until equilibrium was established over time intervals of 0, 5, 10, 15, 20, 30, 40, 50, 60, 75, 90, 120, and 150 min. The injection volume was fixed at 50 µL, and the column's temperature was set at 25 °C. The composition of the mobile phase solution, 60:40:0.1 v% acetonitrile, water, and phosphoric acid.

To calculate adsorption capacity and comprehend the underlying adsorption mechanism, the adsorption kinetic model is frequently utilized. The pseudo-first order (PFO) and the pseudo-second order (PSO) kinetic models were used to analyses the experimental data in order to evaluate the kinetics of the adsorption of FLX among the several kinetic models that are currently in use. Pseudo-first

order and pseudo-second order models were used to simulate the adsorption data for FLX at various time intervals. Non-linear pseudo-first order (Equation 7.26) and non-linear pseudo-second order (Equation 7.27) models were used to match experimental data reported as follows in order to clarify the adsorption mechanism involved (327).

$$q_t = q_e(1 - \exp^{-K_1 t}) \qquad \text{Equation 7.26}$$

$$q_t = \frac{k_2 q_e^2 t}{1 + k_2 q_e^t} \qquad \text{Equation 7.27}$$

q_t is the adsorption capacity of FLX at time t (mg/g); q_e is the adsorption capacity at equilibrium (mg/g); k_1 is the pseudo-first order adsorption rate constant (g mg^{-1} min^{-1}); and k_2 is the pseudo-second order adsorption rate constant (g mg^{-1} min^{-1}).

At pH 2, pH 7, and pH 9, the impact of solution pH on FLX adsorption by inexpensive bio-sorbents was examined. Using HCl and/or NaOH solutions, the FLX solution's original pH was changed to the desired levels. 50 ppm of FLX solutions with starting pH values of 2, 7, and 9 were applied to the adsorbents. Samples were collected after the equilibrium period had passed, and the remaining FLX-HCl concentration was determined by HPLC analysis (294).

Shimadzu Prominence I-series high performance liquid chromatography with diode array detection was used to conduct the FLX adsorption test (HPLC-UV-DAD). Using a Shimadzu with a reverse-phase column XB-C18 column, 100 Å, 150 X 3 mm, 2.6 µm particle size (Phenomenex, Kinetex®), and a flow rate of 0.3 mL/min, (328). developed a method for this. The kinetic equation, Excel's solution function, nonlinear regression analysis, and MATLAB software would be used to obtain the kinetic parameters (maximum adsorption capacity and kinetic constant) for all models used in the adsorption test. With the help of the derived parameters, curves representing pseudo-first order and pseudo-second order were plotted and compared to the experimental data.

7.6 Results and Discussion

67.6.1 Synthesis and Characterization of NPCS and NSCS Polymers

Since CS has three different types of reactive groups in its repeating units and is not soluble in common organic solvents, regulated chemical modification reactions are challenging. However, in addition to the N-substitution, CS is typically somewhat O-phthaloylated after being treated with phthalic anhydride. Both phthalic and succinic anhydrides are powerful electrophiles and rapidly react with the nucleophilic amine groups of CS when present with DMF/pyridine (325), (313). In order to facilitate acylation, pyridine was added. The amino groups were likely selectively acylated because they had a stronger nucleophilic nature than the nearby hydroxyl groups (Scheme 7.43). As shown in this study, CS and phthalic anhydride were combined to create N-phthaloyl chitosan (NPCS) (Scheme 7.44). By substituting main amino groups using substituent methods, NPCS was synthesized. Since NPCS is soluble in several organic solvents in addition to a weak acid, it is particularly advantageous to produce the composite membranes using PEO (329). By adding a succinyl group to the amine group of CS, N-succinyl-chitosan (NSCS) is created, improving CS's solubility in water (329), (330). Chitosan's application and basic research have been constrained by its low solubility in water and insolubility in common organic solvents. Numerous efforts have been made to produce functional derivatives by chemical changes in order to solve these issues (331). New chitosan-functional nanofiber materials like NPCS/PEO and NSCS/PEO are being developed thanks to grafting modifications with synthetic polymers like PEO or PVA. It is likely that the ionization of the carboxylic acid moieties under alkaline circumstances, which results in the carboxylate anions, is what causes both semisynthetic polymers to have the maximum solubilities in alkaline environments. The remaining amine groups in the NPCS and NSCS chitosan derivatives have been protonated, which contributes to NPCS and NSCS's partial solubility in acidic environments. The better hydrophilic nature of the succinic moieties makes it clear that NSCS is more soluble than NPCS in aqueous media, regardless of the pH levels, as the

hydrophobic aromatic rings within the phthalate moieties are expected to prevent water from penetrating them(313). The FTIR spectra of CS, NSCS, and NPCS are displayed in Figure 7.46. For the CS, the -NH_2 bending vibration is responsible for the absorption peak at 1650 cm^{-1}. The -OH stretching vibration is attributed to the absorption peak at 3356 cm^{-1}, while the -NH_2 stretching vibration is attributed to the absorption peaks at 3030–3330 cm^{-1}. Due to intramolecular and intermolecular hydrogen bonding, the infrared spectra of CS do not show an absorption peak around 3080 cm^{-1} (329). The -NH_2 of CS has been largely substituted by succinyl groups (-NH(CO)-CH_2-CH_2-COOH), turning the primary amines (-NH_2) into secondary amides.

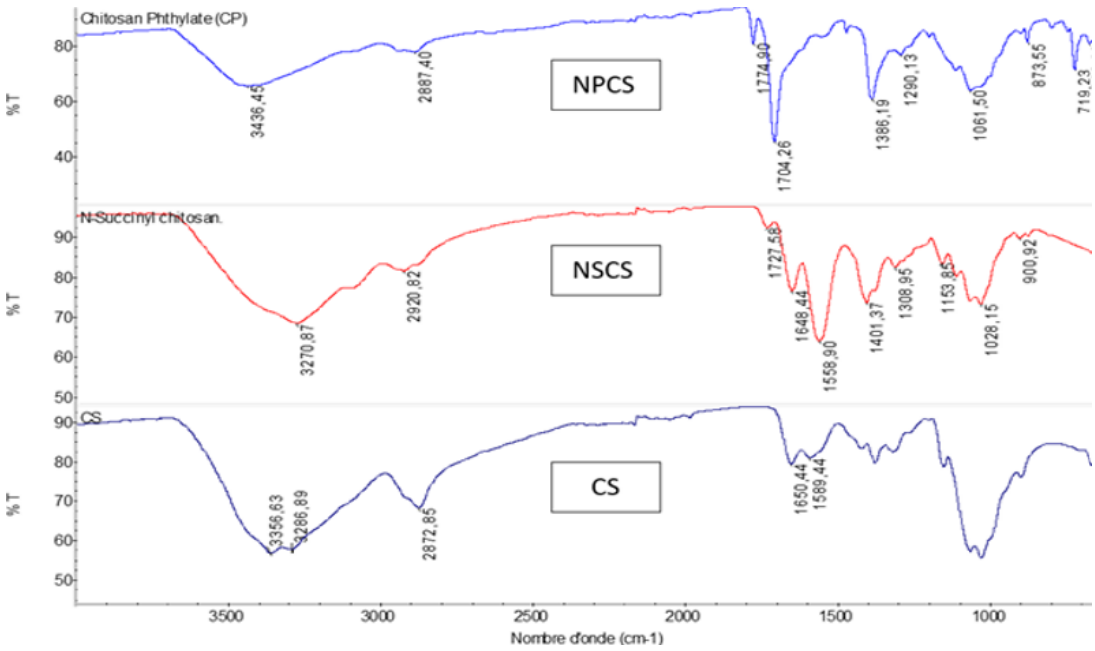


Figure 7.46 Schematic graph of synthesis FTIR spectrum of CS, NSCS and NPCS

For the NSCS, two additional distinctive absorption peaks at 1648 cm^{-1} and 1401 cm^{-1} correspond to the synthesis of -CO-NH-. The N-H absorption is responsible for the absorption peak at 1558 cm^{-1} in the NSCS spectra, according to research (332) , (43). Figure 7.46. shows the peaks at 3436 $cm^{-1}$for the OH group, 2887 $cm^{-1}$for the sp3 CH group, 1774 cm^{-1} for the imide C=O, and 1386 $cm^{-1}$for the C-

N group in the FT-IR spectra of the NPCS that were measured for product confirmation. Additionally, the aromatic C-C group is represented by the peak at 719 cm^{-1} and the C-OH group by the peak at 1061 cm^{-1} (329).

Further evidence for the conversion of CS to NSCS comes from ^{1}H-NMR. The CH_2CH_2 moiety of the succinyl group is characterized by a triplet in the spectra of NSCS at 1.0 ppm ($NHCOCH_2CH_2COOH$). Peaks between 3.4 and 3.6 ppm are typical of CS and belong to the hydrogen in the CS backbone [38]. As a result, Figure 7.47 showed that these peaks may be found in the ^{1}H of both CS and NSCS. Similar findings have been documented in the literature [54, 60]. Figure 7.47. shows the NPCS's ^{1}H-NMR. demonstrates important NPCS-specific signals. The aromatic region's peaks at 7.07 and 7.10 correspond to the aromatic rings from phthalate functionalities, while the peaks between 4.7 and 3.0 denote the CH of the sugar rings in NPCS (325). Phthalate and succinate chitosan (NPCS, NSCS) were successfully produced, according to the spectra data.

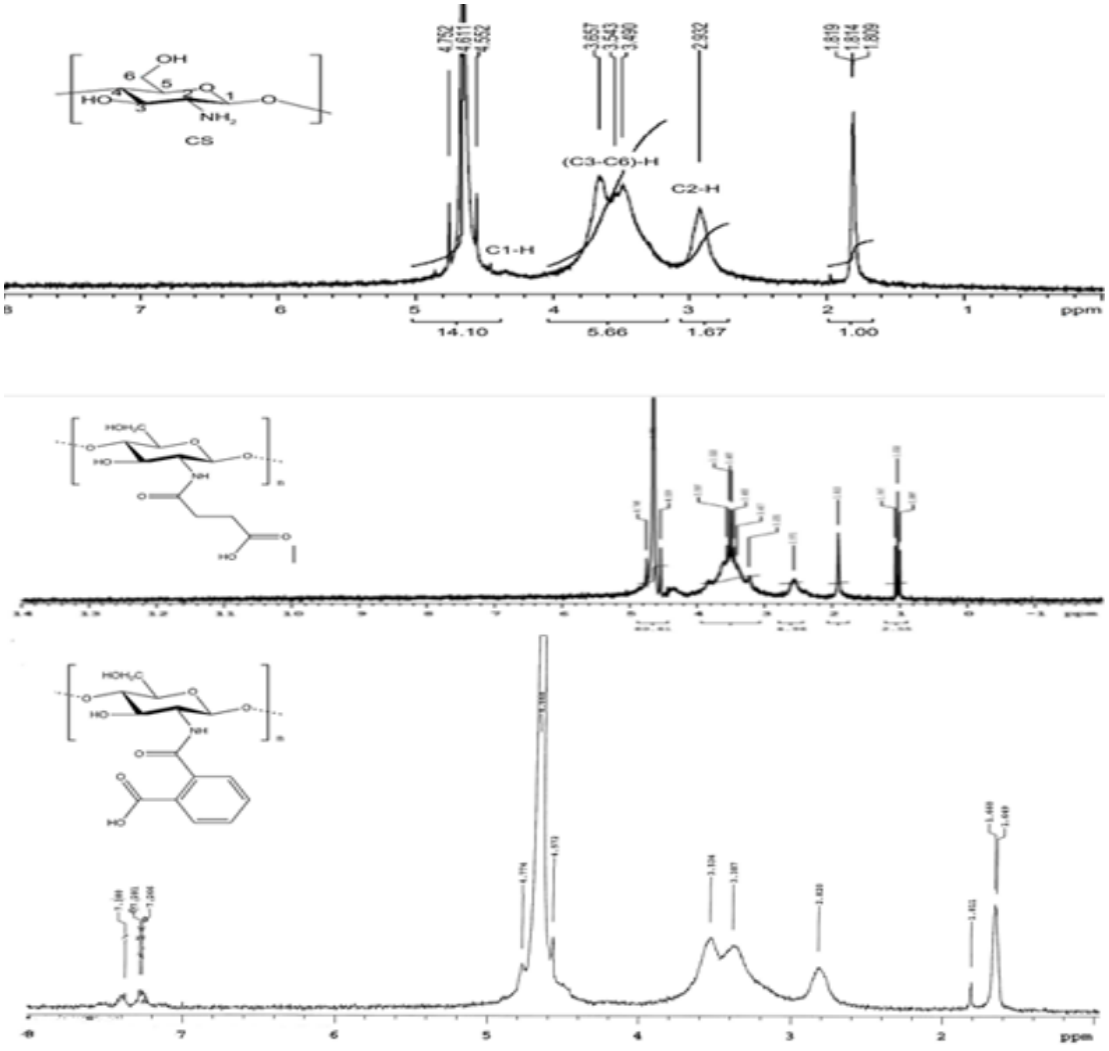


Figure 7.47 ^{1}H-NMR spectrum of CS, NSCS and NPCS

7.6.2 Electrospinning and Optimization (Morphology)

The optimum diameters for electrospun NSCS/PEO nanofibers were around (183±38 nm). The solvent evaporation rate during electrospinning was slow, despite the fact that the fiber diameters were large compared to the diameter of pure CS/PEO ratio 4:1 (140 ± 53 nm) as reported in our earlier work (284). However, despite using 50% acetic acid as a solvent because it evaporates more quickly than water, we were unable to control other flaws such the generation of droplets, an unstable jet, the formation of big particles with nanofibers, and low

fluoxetine adsorption capability. Fiber diameter was tracked using a single fundamental parameter, such as the concentration/viscosity of the NSCS solution, with thicker fibers being produced as viscosity increases. The production of electrospun nanofibers is significantly influenced by the polymer solution concentration. A polymer solution's viscosity is inversely correlated with that of a solution (280). The sample's viscosity increases with increasing nanofiber diameter. As a result, a minimal concentration is needed for fiber formation in electrospinning. We experimented with various settings to generate the continuous nanofiber with small diameters because this was the most challenging component of the electrospinning process. Additionally, when extremely little amounts of electricity are electrospun, electrospray occurs in that location. This is caused by the solution's low viscosity and high surface pressures. As shown in figure 7.48 (A), the electrospinning process is greatly influenced by the concentration and mass ratio of the solution, which are both essential for producing defect-free nanofiber mats.

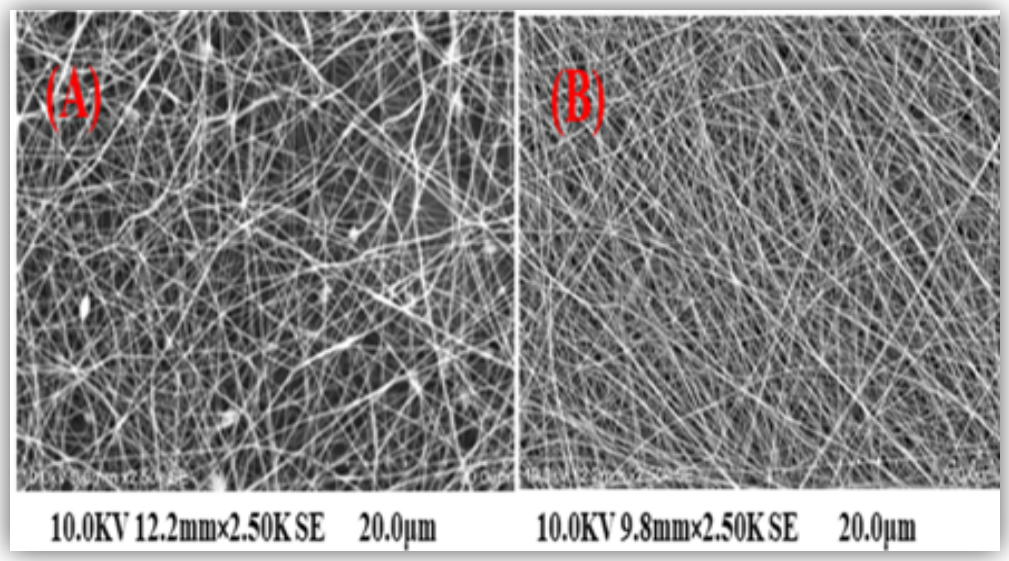


Figure 7.48 Respective SEM images of NSCS/PEO (ratio 6:4) (A), and NPCS/PEO (ratio 3:2) (B) nanofibers mat

On the other side, the copolymer had the greatest impact on the electrospinning process. The best NSCS/PEO nanofiber (6:4 mass ratio%) was produced as a result of increasing the amount of PEO (Co-polymer) in the solution. Additionally, a larger voltage was required when the viscosity was low and the distance between the needle and the collector was longer. In actuality, 100% CS solutions were not evaluated. In this analysis, we tried to compare the three mass ratios (2:1, 3:2, and 6:4) when the concentration of NSCS was raised from 3% to 8%, respectively. The viscosity of the solutions was enhanced by raising the concentration of the solution in order to discover the best electrospinning settings and the greatest adsorption potential. The following settings were optimized: a flow rate of 0.01–0.5 mL/h and a configuration of 10-15 cm between the needle and the collection. The optimal voltage was determined by watching the behavior of the jet and varied from 7 to 14 kV. The three sets of parameters were 2:1 (0.01 mL/h, 8 kV, 15 cm), 3:2 (0.3 mL/h, 12 kV, 12 cm), and 6:4 (0.5 mL/h, 14 kV, 10 cm). Despite this, a pure NSCS aqueous solution cannot be electrospun because to its low viscosity. In order to increase the NSC solution's electrospinnability, PEO is frequently added to it. They are totally compatible and miscible because to the hydrogen-bonding interactions between the hydroxyl groups of PEO and NSCS. NSC is less viscous than pure CS. Raising the voltage past a certain point led to substantially more liquid droplet projection on the collector surface as well as the destabilization of the jet since electrospinning procedures require light viscosity. Increase the solution's concentration while gradually reducing the flow rates and distance to find a solution to this issue. During an electrospinning process, a nanofiber web starts to form because the frame's corners have more surface area than the rest of the frame, which causes surface charges to accumulate. The deposition procedure will start as a "spider's web" and continue until a mesh completely encloses the interior of the frame. In addition, the use of a frame as a collector made it simpler to remove nanofibers, which made it easier for researchers to determine whether an electrospraying or electrospinning process was occurring. Even if some nanofibers were deposited, the particles would split them and prevent or reduce mat formation. As a result, employing a

farm as a collector device in an electrospinning system offers many benefits over using conventional aluminum foil. The most important advantages are reusability, a smoother mat recovery process utilizing a simple cutter, and a speedier approach to evaluate the morphology of the collected material (271). We obtained nanofibers that included modest concentrations of beads and a lot of particles. The solution with an NSCS: PEO (ratio 6:4) with 8wt.%/5wt.% concentration was the optimum solution for electrospinning procedures because it was quicker, easier, and freer of particles and beads than the other methods. Additionally, it led to fluoxetine having a greater potential for adsorption. When compared to the chemical approaches used in this work, heat treatment of NSCS/PEO nanofiber membranes at temperatures between 100 and 150 o C was one of the successful methods to stabilise the membrane. Figure 7.48 (B). shows NPCS/PEO electrospun nanofiber SEM pictures. NPCS 2.5% and PEO 3% mixed solutions were used to create the material. The ratio of 3:2 was discovered to be the ideal aqueous mixture (NPCS/PEO). The testing conditions were as follows: flow rate 0.3 mL/h, distance tip-collector 14 cm, voltage 12 kV, and the NPCS polymer was dissolved in 90% acetic acid. At room temperature and relative humidity levels between 30% and 40%, electrospinning was performed. As a result of our previously developed methodology. (265). Then, the ideal temperature for stabilizing nanofibers during heating was discovered to be 140 ˚C for 30 min. Without changing the surface of the fibres, membranes became stiffer under these circumstances. It is our understanding that there is no formal literature on the production of nanofiber membranes by electrospinning NPCS PEO (333).

7.6.3 General Adsorption of NPCS/PEO, and NSCS/PEO Nanofibers

Figure 7.49 shows the link between the FLX adsorption time of NSCS/PEO (mass ratio 6:4) and NPCS/PEO (mass ratio 6:4) adsorption capacities. The adsorption potential of NSCS/PEO and NPCS/PEO increases significantly in the initial phases of the reaction within 2.5 hours at 25 °C. The experimental data were examined using the pseudo-first order and pseudo-second order models to ascertain the adsorption kinetics process. The pseudo-first-order rate expression

with a correlation factor of R^2 of 0.9926 was found to be the most accurate kinetic model for FLX sorption on NSCS/PEO nanofibers. The mechanism states that the pH of the ions at the adsorbent surface affects the rate of FLX adsorption. The rate constant (k_1) is calculated to be 0.130 g/mmol/h. FLX adsorption reaches equilibrium in 30 minutes. Figure 7.50 depicts the impact of time on the FLX adsorption behavior by NSCS/PEO nanofibers.

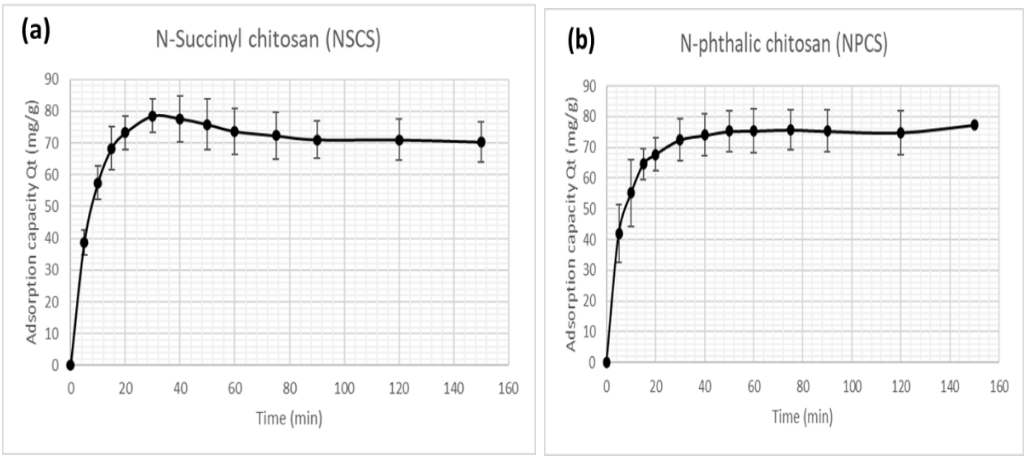


Figure 7.49 Adsorption capacity of FLX by NSCS/PEO (a), and NPCS/PEO (b) electrospun nanofibers

FLX adsorption on NPCS/PEO followed the pseudo-first-order model rather than the pseudo-second-order model. The optimum kinetic model for FLX sorption on NPCS/PEO nanofibers, on the other hand, was determined to be a pseudo-second-order rate equation (correlation factor R^2 = 0.9926). According to the mechanism, FLX adsorption is influenced by the pH of the ions on the adsorbent surface. The computed value for K_1 is 0.130 g/mmol/h. In 30 minutes, FLX adsorption achieves equilibrium. Figure 7.50 shows how the adsorption of FLX by NSCS/PEO nanofibers is impacted by time. At various solution pH levels, kinetic tests were conducted to ascertain the adsorption of FLX onto modified CS (NSCS) and (NPCS). The curves of kinetic energy shown in Figure 7.51 demonstrate that it takes roughly 2.5 hours for FLX to adsorb onto NSCS and reach equilibrium.

The highest absorption, 78.5 mg/g, was attained at pH 9, among the several solution pH levels examined. The electrostatic interaction between the adsorbent and the electric charge of FLX molecules is responsible for the discrepancies between the kinetic curves produced at various pH values. For all pH values studied ($pH < pK_a$), the molecules were primarily protonated with positive charge once the pK_a of FLX hydrochloride is 9.5 [3]. The adsorbent is positively charged (+Ve) at pH values between 2 and 5, which promotes electrostatic repulsion between the adsorbent and the adsorbate. The removal of FLX molecules by electrostatic attraction is enhanced at pH 8.8 because the adsorbent is negatively charged (-Ve), in contrast (250).

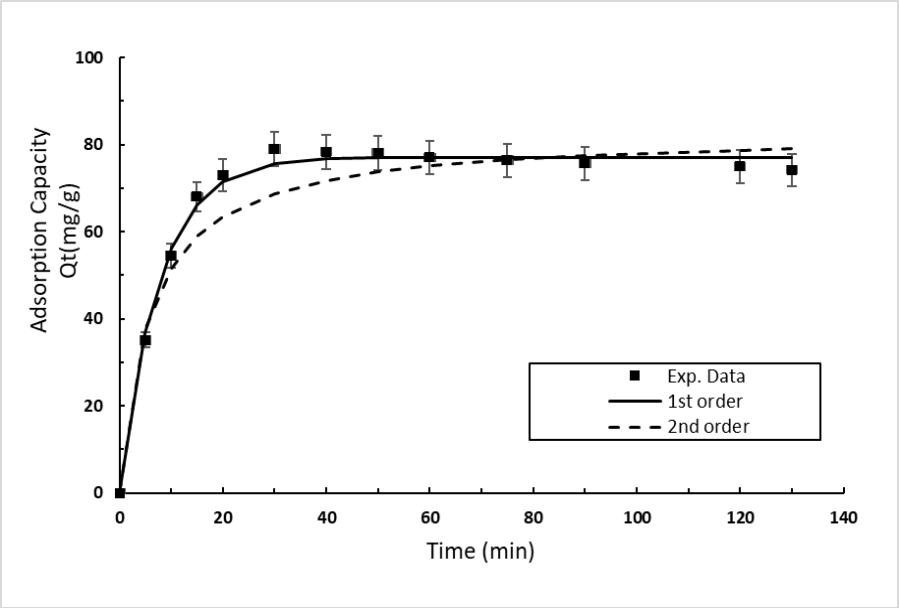


Figure 7.50 Kinetic models for adsorption of fluoxetine onto: NPCS/PEO (3:1 m/m) nanofibers at room temperature

In reality, it was anticipated that FLX would have a stronger affinity for adsorption and, as a result, a higher adsorption capacity given that the Known value of its adsorption capacity into was higher NSCS than NPCS. In kinetic studies, variations in each adsorbent's behavior might be linked to the chemical makeup of the drugs. On one side of FLX, there is a highly polarized trifluoromethyl group,

next to it is a highly hydrophobic benzyl group, there is an ether group in between, and on the other side of the molecule is a highly polarized secondary amine group. Given that FLX can interact more strongly with the adsorbent's surface and that the molecule's adsorption sites are clearly defined, it may firmly bind to the surface.

Table 7. 11 Parameter values in the pseudo-first- and pseudo-second-order models for NSCS/PEO (6:4 m/m) and NPCS/PEO (3:1 m/m) nanofibers original concentration 50 mg/L, pH 8, adsorbent 25 mg, t = 150 min at room temperature.

Experimental	Pseudo first order model			Pseudo second order model		
Adsorbent	k_1(min $^{-1}$)	Q_e(mg/g)	R^2	K_2 (min $^{-1}$)	Q_e(mg/g)	R^2
NSCS/PEO	0.01300	76.15	0.9932	0.00265	82.70	0.9654
NPCS/PEO	0.00526	73. 80	0.9926	0.00448	78.40	0.9579

The results displayed in Figure 7.49 show that the adsorption of FLX onto the NPCS biopolymer grows extremely quickly within the first 30 to 40 minutes and achieves a saturation adsorption capacity of 74 mg/g after 150 minutes. According to FTIR data and earlier research (334), the high adsorption capacity of (NPCS) may be caused by interactions of the -bond (associated) between the aromatic ring in NPCS and the FLX aromatic ring. However, there are strong interactions between the FLX and NPCS, such as hydrogen bonds and van der Waals interactions. As Figure 7.51 proposed mechanism of fluoxetine adsorption onto NPCS and NSCS polymers showing all the chemical and physical interaction.

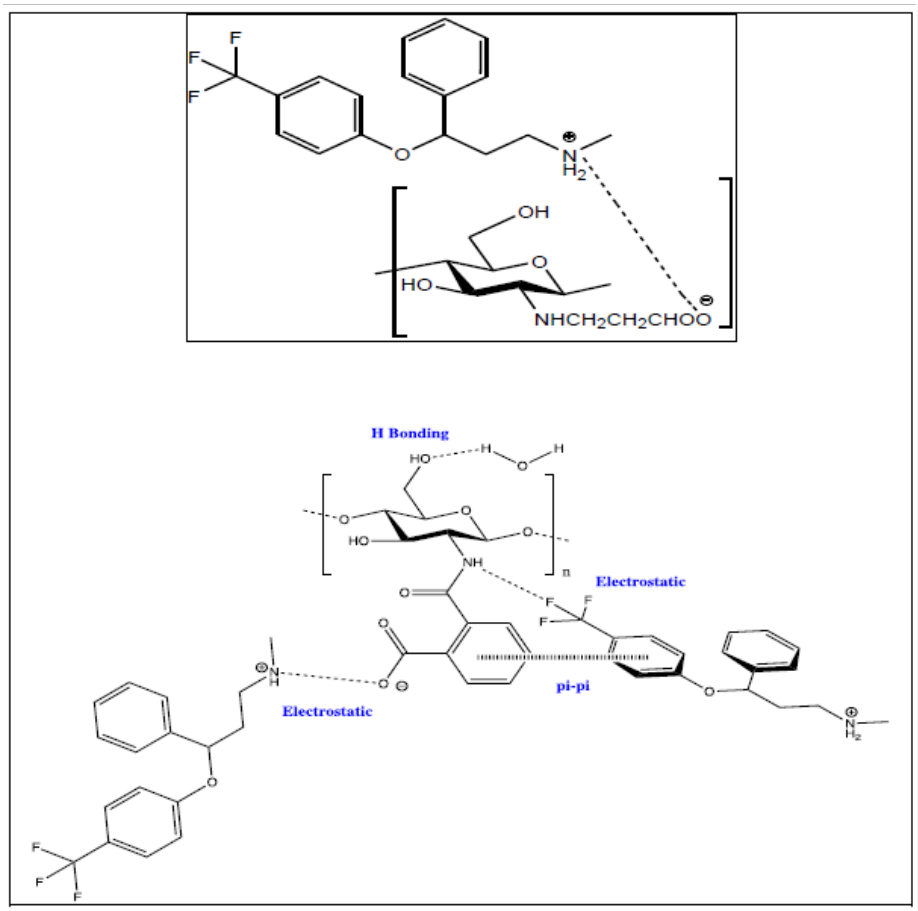


Figure 7.51 The proposed mechanism of fluoxetine adsorption onto NPCS and NSCS polymers

Additionally, the FLX molecules and NPCS polymer can interact more frequently thanks to both physical and chemical adsorption into the biopolymer network. as shown in table 7.11. The FLX adsorption process onto the NPCS polymer can be explained by the pseudo-second-order kinetic model, according to research by (Liu et al.). that showed a correlation (R^2) of N-Phathalic chitosan (NPCS). This behavior is consistent with the theory that a polymer matrix with a higher proportion of polymers has an inner network of hydrogen bonds and other dipolar interactions that is denser and tighter. Since the carboxylic acid residues inside the polymer will exist mostly as the less hydrophilic unionized form, such

interactions are predicted to limit water penetration through the matrix, especially under acidic circumstances. It should be noted that unaltered CS matrices totally disintegrated in the acidic medium (0.1 M HCl for 2 h), which is not surprising given that the amino groups within the CS structure are predicted to primarily exist as the very hydrophilic quaternary ammonium cations under acidic conditions. As a result, the polymer matrix can be soaked up water without resistance, leading to the polymer's final disintegration. It is clear from Table 7.9 that chitosan succinate matrices (NSCS) absorbed more fluid than chitosan phthalate (NPCS). The higher hydrophilic nature of the succinate moieties is consistent with this behavior. It is anticipated that the hydrophobic aromatic rings of phthalate moieties will prevent water from penetrating (325).

7.6.4 Effect of pH Solution

The pH of the solution is among the most significant variables that influence the adsorption process (335). The solution is influenced by pH and the electrostatic interactions between the target molecules (FLX) and the adsorbent surface (NSCS/PEO and NPCS/PEO nanofiber mats). corresponds to the pH level where the adsorbent's surface charge turns electrically neutral. The adsorbent surface gets positively charged at low pH while becoming negatively charged at high pH. (14). Lower pH results in more adsorption because all processes are more vigorous and because the functional groups on the adsorbate may become protonated, which adds to the adsorption's driving power. Additionally, molecules may be rejected by the solution in addition to being adsorbed by the forces of attraction with solids (336). Therefore, less hydrophilic substances, like FLX, may be adsorbed more readily when the ionic strength of the solution is increased by the addition of protons. According to the pKa values of carboxylic and amino functional groups, the adsorption process in the pH range under investigation may be implicated. The FLX exhibit a predominance of the species with positive charge at pH values below their pK_b (9) and will reach a maximum positive overall charge at pH values 2, therefore maximizing the attraction of adsorbent/adsorbate (300). As pH increases, functional groups become deprotonated (become negatively

charged), which favours adsorption of the FLX (10). 2019 (Silva et al.). At pH 2, 7, and 9, the impact of solution pH on FLX adsorption by bio-sorbents (NSCS/PEO and NPCS/PEO nanofibers) was examined. The protonation/deprotonation of adsorbates and/or changes in the surface charges of adsorbents with varied pH values make the pH of a solution an especially important element in the adsorption process. The pH effect can be explained by comparing the solution pH, the pK_b of the target molecule (FLX), and the adsorbent's (NSCS/PEO and NPCS/PEO nanofibers). The results shown in Figures 7.49 and 7.50 demonstrate that higher pH values, 7 and 9, were required to achieve the highest FLX uptake for all adsorbents. The electrostatic interaction between the adsorbent's surface charge and the electric charge of FLX molecules is the cause of the variations in uptake values found at various pH levels. Once FLX - HCl has a pK_b of 9.8, the molecule adopts an ionized state (positive charge) at pH levels below pK_b, and the ionized and nonionized forms are both present in the same proportion at pH levels equal to pK_b. FLX molecules are protonated with a positive charge for each of the three pH levels considered (pH 2, 7 and 9). ($pH < pK_b$). Because all bio-sorbents have positively charged surfaces at pH 2, this causes electrostatic attraction between the adsorbent and the adsorbate, which accounts for the decreased adsorption capacity at this pH level. Low-cost bio-sorbents are negatively charged at pH 7 and pH 9 (and higher), which improves the removal of positively charged FLX molecules through electrostatic attraction (294).

7.7 Conclusions

Several medicines and their byproducts, primarily from WWTP effluents, have been introduced in aquatic environments. The release of these contaminants into the aquatic environment has the potential to cause chronic toxicity, which can affect reproduction, as well as the emergence of microorganism strains that are resistant to antibiotics. Therefore, it is vital to consider fresh approaches to lessening their impact on the environment. The current study intends to examine the efficacy of FLX adsorption capacity by a unique nanofiber material made from chitosan succinate and chitosan phthalate, which are chemical modifications of

chitosan. As far as the authors are aware, there haven't been any papers or studies published that cover their use for producing modified CS nanofibers (NSCS) and (NPCS) and then using those fibers to remove FLX from aqueous solutions. The electrospinning settings as well as the solvent concentration have a significant impact on the optimal parameters electrospinning procedures for modified CS (NSCS), (NPCS), nanofibers with diameters of (150 ± 25 nm), and (183 ± 38 nm), respectively. Adsorption technology using biopolymers, like modified CS, provides significant environmental advantages, including the reduction of pollutants and the value-adding of residues that would otherwise be challenging to handle and dispose of. Alternative bio-sorbent nanofibers that can compete with commercially available adsorbents are being used, however this is still a new area of study that has to be explored further. The novel biomaterials polymer has a high affinity for FLX and an adsorption capacity of 80 mg/g, according to the findings of the current study. The creation of a variety of contacts, including electrostatic interactions, aromatic ring interactions (-bonds), hydrophobic interactions, and strong interactions like H-bonds, may be linked to the adsorption of FLX onto the nanofiber's polymer (NSCS) and (NPCS). Additionally, the pseudo-first-order and pseudo-second-order kinetic models can explain the adsorption process. According to the findings of the current investigation, electrostatic interactions between the net surface charge of the sorbent and the electric charge of the fluoxetine molecules result in a considerable influence of pH on the adsorption capacity. Since the surface of the adsorbents is primarily negatively charged at these pH values, which improve the electrostatic interactions with the positively charged FLX molecules, the greatest absorption capacities were achieved at higher pH values, ranging between (7 and 9). Real wastewater samples and the development of adsorbents that can successfully remove numerous contaminants at once will be the main topics of future study. The influence of numerous experimental parameters, such as temperature and beginning FLX concentration, will then be determined in the adsorption method. Following that, isothermal and thermodynamic adsorption data will be collected in the near future. The possibility of desorption and adsorbent reuse will be

discussed in the following section. This comparative investigation shows that, in contrast to pH 2, where the matrices resisted dissolving, maximal adsorption capacity release was found under pH 8. More effectively than chitosan phthalate (NPCS/PEO nanofibers), chitosan succinate (NSCS/PEO nanofibers) may eliminate pharmaceutical pollutants from aqueous systems.

CHAPTER 8 – CONCLUSIONS

The objective of this Ph.D. project was to develop an electrospun nanomaterial low cost, envornomental friendly and high adsorption capacity for the adsorption of pharmaceutical residues in water and wastewater from modified chitosan.

The new nanofiber materials developed make it possible to remove up to 70-80% of pharmaceutical contaminants in the experimental conditions, Therefore, the eco-friendly nanofiber materials are promising biosorbents to replace activated carbon (AC), which removes 90-98 % of pharmaceutical

Batch adsorption investigations revealed the adsorption capacity for FLX elimination was highly dependent on the starting pH based on zeta–potential. In general, mostly the devolopment materials were excellent canidad to adsorb FLX and the hight adsorption capicaty was nanofubers materials of NSCS/PEO (86±4 mg/g) which was so closed to nanofibers materials of N,O-CMCS/PEO (84±2mg/g) and then NPCS/PEO (70±3 mg/g).

Consequently, promising adsorption results obtained with the kinetic adsorption revealed a possible chemisorption mechanism with electrostatic bonding between the contaminants and modified nanofiber materials.

Several cycles of adsorption and desorption are possible without loss of adsorption efficiency.

Comparison made with other existing sorbents, modified nanofiber materials are believed to be efficient and suitable to remove pharmaceutical residues such as FLX in water.

Overall, the Ph.D. project aimed to highlight, develop, and demonstrate methods and materials based on modified chitosan nanofibers that may contribute to achieving the desired results to adsorb pharmaceuticals residues and reducing the daily load of WWTPs.

In future work, determine whether satisfactory results can be obtained in real wastewater from typical industries, such as mining and pharmaceuticals.

Develop a hybrid composite of modified chitosan and cellulose using the electrospinning technique in order to devolope altranitive nanofibers materials.

Further tests of (isotherm, and thermodynamics) will be attempted in the near future for a better understanding of the adsorption mechanism, in additional, characterize the nanofiber materials (porosity, mechanical properties and permeability).

Finally, we are not strong enough to fight against contaminations but if we cut it at the source before reaching the wastewater treatment plants the chance will significantly increase to remove them

Table 7.12 Summarize all results of this project

Nanofiber Materials	Electrospinning NOCMCS/PEO		Contamanents Model	Adsorption			Kinetic Model	Desorption Cycles
				Capacity mg/g	Effeciency %	pH		
N,O CMCS/PEO	4:1	2.5/3	FLX	84 ± 2.0	79.7	8	PS1,PS2	4
NSCS/PEO	**6:4**	**8/5**	**FLX**	**86± 3.77**	**81.1**	**8**	**PS1**	**5**
NPCS/PEO	3:2	2.5/3	FLX	70 ± 3.1	74.8	8	PS1	4

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ANNEXE A

- List of publications (Articles)

1- Khierallah, A.H.I ; Bates,I.I.C ; Chabot,B ; Lajeunesse,A. Adsorption of Pharmaceutical Contaminants from Aqueous Solutions Using N, O-Carboxymethyl Chitosan/Polyethylene Oxide (PEO) Electrospun Nanofibers, published on Journal of Materials Science and Chemical Engineering, DOI: 10.4236/msce.2021.911003 Nov. 25, 2021.

2- Khierallah, A.H.I; Bouazza, A.H; Montplaisir,D. Nanofibrous Material of N- Succinyl Chitosan/Polyethylene Oxide in the Removal of Emerging Pharmaceuticals from Aqueous Solution by Adsorption/Desorption Method, published on Journal of BioResources, 18(1) February (2023), 1971-1998.

3- Khierallah, A.H.I; Bouazza, A.H; Montplaisir,D. Comparative Study on the Efficiency of Novel Modified Chitosan-Based Electrospun Nanofibers for Removal of Fluoxetine from Wastewater Treatment, published on Journal of Hydrology: Current Research, Volume 14:01, 23 January, 2023, DOI: 10.37421.2157-7587.2023.14.448

- List of publications (Posters)

1- Khierallah, A.H.I ; Chabot,B ; Lajeunesse,A. Nanofibrous Material of N- Succinyl Chitosan/Polyethylene Oxide in the Removal of Emerging Pharmaceuticals from Aqueous Solution by Adsorption/Desorption Method, 29e édition du Concours d'affiches scientifiques (2022), Trois Rivieres, Canada.

2- Khierallah, A.H.I; Bouazza, A.H; Montplaisir,D. Adsorption of Pharmaceutical Contaminants from Aqueous Solutions Using N, O-Carboxymethyl Chitosan/Polyethylene Oxide (PEO) Electrospun Nanofibers, posted in Forum Québécois Matériaux avancés, (13,14 April, 2023), ExpoCité - Centre de foires, 250A Boulevard Wilfrid-Hamel Québec, QC G1L 5A7.

ANNEXE B

- Table S1. Effect of CMCS/PEO ratio on electrospinning using different CMCS and PEO solution concentrations

Table S1. Effect of CMCS/PEO ratio on electrospinning using different CMCS and PEO solution concentrations.

CMCS Conc. wt.%	PEO Conc. wt.%	CMCS/PEO Ratio% (wt./wt.)	Flow rate (mL/h)	Optimal voltage (kV)	Distance (cm)	Relative Humidity %	Jet stability	Nanofibers	Drops	Beads
2.5	1.5	2:1	0.001	8	12	32	–	+	–	±
2.5	1.5	1:3	0.01	10	10	35	–	±	+	–
2.5	1.5	3:1	0.01	8	10	35	–	±	±	–
2.5	1.5	3:4	0.01	12	12	41	±	±	+	±
2.5	1.5	1:4	0.3	12	12	35	–	+	+	–
2.5	1.5	4:3	0.01	10	13	36	–	–	+	–
2.5	1.5	4:1	0.3	13	12	36	–	–	+	–
2.5	3	2:1	0.002	6	10	48	±	+	–	±
2.5	3	1:3	0.001	7	12	35	–	±	+	±
2.5	**3**	**3:1**	**0.2**	**6**	**11**	**53**	**+**	**+***	**–**	**–**
2.5	3	3:4	0.001	7	12	36	–	±	–	±
2.5	3	1:4	0.002	8	11	35	–	±	–	±
2.5	**3**	**4:3**	**0.1**	**7**	**10**	**44**	**+**	**+***	**–**	**–**
2.5	**3**	**4:1**	**0.03**	**6**	**10**	**35**	**–**	**+***	**–**	**–**
3.3	3	2:1	0.01	13	12	42	–	±	–	+
3.3	3	1:3	0.3	10	15	40	+	–	–	+
3.3	3	3:1	0.001	11	11	41	–	–	+	–
3.3	3	3:4	0.002	11	11	33	–	–	–	+
3.3	3	1:4	0.03	10	11	36	±	–	–	+
3.3	3	4:3	0.001	11	11	41	+	–	–	–
3.3	3	4:1	0.001	13	12	42	–	±	–	–
8	**1.5**	**2:1**	**0.03**	**8**	**11**	**45**	**+**	**+***	**+**	**+**
8	1.5	1:3	0.001	11	13	40	–	±	–	–
8	1.5	3:1	0.002	10	10	44	+	±	–	–
8	1.5	3:4	0.01	8	11	41	±	–	+	+
8	1.5	1:4	0.005	14	11	42	+	–	–	+
8	1.5	4:3	0.001	10	10	44	+	±	–	±
8	1.5	4:1	0.02	11	12	40	+	±	±	±
3.3	8	2:1	0.002	11	10	40	+	–	–	+
3.3	8	1:3	0.001	12	11	33	+	±	–	±
3.3	8	3:1	0.02	11	11	34	+	±	–	+
3.3	8	3:4	0.003	10	10	41	+	±	–	–
3.3	8	1:4	0.008	12	11	41	+	±	–	±
3.3	8	4:3	0.001	12	12	43	+	±	–	+
3.3	8	4:1	0.007	6	10	41	+	±	–	–

Legend: (+) Positive result, (–) Negative result, (±) Moderate result, (*) Optimal conditions and parameters for nanofiber formation.