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Carbamazepine removal from contaminated water via different adsorption methods

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Abstract

Pharmaceuticals are bioactive substances with the ability to affect biological systems. Various pharmaceuticals reach the environment after being consumed or excreted through wastewater and sewage treatment systems. The complexities of these threats should not be underestimated. A common anti-epileptic medication resistant to degradation is Carbamazepine (CBZ). Because of this everyday ingestion and discharge in sewage systems, CBZ has been frequently discovered in aquatic ecology. One of the principal causes of CBZ in groundwater may be leaks from sewage systems and septic tanks. The existence and destiny of CBZ in the urban water cycle are addressed in this study, focusing on adsorption as a potential option for its removal. In this study, the ability of chitosan nanoparticles to eliminate the commonly used drug carbamazepine (CBZ) from aqueous solutions is investigated by focusing on the primary research topics related to the potential of Chitosan and its derivatives to remove Carbamazepine from wastewater, as well as how chitosan features are altered by physical and chemical interactions such as cross-linking and grafting. Further study that is correctly focused on discovering the underlying mechanism behind the properties of Chitosan will assist in developing this material to be a strong candidate for waste water treatment.

Keywords: crosslinking, Carbamazepine, adsorption, wastewater treatment, Chitosan.

1. Introduction

The increasing use of prescription drugs over the past few decades has led to an accumulation of pharmaceuticals in numerous water sources, including surface waterways, wastewater, groundwater, and drinking water, according to the World Health Organization (WHO) [1]. It has become a public health issue since many drugs have undertaken insufficient research on the effects of sustained low-level exposure and the absence of pharmaceutical waste management. Therefore More emphasis has lately been dedicated to developing new functional costly and unsustainable [2]. As a result, cost-effective pharmaceutical treatment methods are scarce. Long-term exposure to these low pharmaceutical levels in wastewater raises several potential health issues, particularly for young children, pregnant women, the elderly, and people with compromised immune systems. [3]. One of the drugs of interest detected in water sources is Carbamazepine. Due to the drug's materials for the environment and health waste treatment. Waste water treatment plants are considered the best place to establish barriers against pharmaceuticals before discharge, and several biological and chemical procedures are being investigated for their capacity to remove pharmaceuticals. Nevertheless, these procedures either fail to remove enough pharmaceuticals (pharmaceutical residues in low quantities ranging from ngL^{-1} to mg have been identified in the effluent of WWTPs, rivers, lakes, and potable water in a number of studies), or are too

widespread prevalence in municipal wastewater, Carbamazepine has recently attracted much attention [4]. Carbamazepine (CBZ) is a popular anti-epileptic medicine used to treat seizure disorders, neuropathic pain, and psychosocial difficulties[5]. it is resistant to degradation. Due to its regular use and drainage into sewage systems, CBZ has frequently been detected in the aquatic ecosystem. Consequently, several studies

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have been conducted to assess CBZ ecotoxicity, and the results show that CBZ is one of the most damaging substances in the aquatic environment (based on bioassays in microbes, algae, and micro-crustaceans). [6,7]. One of the primary sources of CBZ in groundwater may be leakages from sewage networks and septic tanks. When CBZ is not adequately removed by chemical, biological, and mechanical processes, high quantities of CBZ are formed, ranging from 6.60 ng/L to 11.50 g/L in surface water or wastewater [8,9] and 1.4-1250 ng/L in drinking water [10]. The elimination effectiveness of CBZ in WWTPs is frequently less than 10%, according to Zhang et al. [11]. This is because such chemically stable pollutants are not meant to be removed by WWTPs [12-14].To solve the issues mentioned above, numerous researchers have optimized the design of WWTPs. Wastewater treatment plants (WWTPs) employ a variety of processes. The first stage, primary treatment, may involve screening, coagulation, flocculation, and sedimentation. The second secondary treatment stage may include conventional activated sludge (CAS), trickling filters, and clarifying [15]. Adopting tertiary methods is thus feasible, including improved oxidation, membrane filtration, reverse osmosis, membrane bioreactors (MBRs), and/or adsorption [16–18]. (MBR) demonstrated remarkable removal of CBZ [19]. However, many improvement measures cannot be executed effectively due to the expense and complexity of the operation, non-selectivity, inefficiency at low concentrations, the production of undesired by-products, and technological feasibility. As a result, cost-effective CBZ removal from WWTP effluents is crucial. Adsorption can be an alternate method for removing numerous PhCs [20]. Highly selective, effective, and regenerable adsorbents would be the ideal solution to the problems with the technologies mentioned above [21]. Candidate adsorbents should be reasonably priced, flexible, regenerable, and environmentally friendly [22-23]. Activated carbon (AC), zeolites, ion exchange resins, silica gel, and activated alumina are commercially available adsorbents. [24]. Nevertheless, despite their ubiquitous availability and applicability for various contaminants, their usage is limited by their high cost and possible sustainability problems [25,26]. For instance, Snyder et al. [27] used powdered activated carbon to efficiently remove a variety of PhCs, including erythromycin (ERY), at ecologically relevant concentrations (>70%, 34-479 ng/L) (PAC). Contrarily, it has been shown that, with time, organic matter fouling decreases the bed life and efficiency of granular activated carbon (GAC) [28]. The adsorption of Carbamazepine (CBZ) provided evidence of this. Much focus has also been placed on the adsorption of PhCs using more novel substances, including inexpensive natural chemicals or those made from waste precursors. Considering both the economy and the ecology, these naturally generated, low-cost materials are appealing since current analytical equipment like LC-MS, HPLC, and GC-MS can only detect a small range of similar contaminants and lack rapid processing. Therefore it's crucial to monitor discharged waters with novel, affordable, and real-time methods due to changing components over time and place. This kind of Contaminant monitoring preserves the ecosystem and guarantees the ecological health of bodies of water. [29,30]. Monitoring options like biosensors have emerged as an alternative

to expensive instruments due to their ease of operation, elimination of pretreatment steps, faster response time, and higher sensitivity. They also allow for easy determination of pollutants without rigorous sample preparation and are more effective than other analytical equipment like GC-MS. They play a bigger role in drug development, food safety, environmental monitoring, and healthcare [31]. Chitosan seems to be Chitosan appears to be a promising substitute for synthetic polymers for use in biosensors due to its unique features and qualities. Chitosan, alone or in combination with other chemicals, can provide a robust and uniform substrate in various forms. Utilizing new smart materials in several fields, such as wastewater treatment and medical technology, is an important and fascinating area of research**.** Chitosan has demonstrated its superiority as a foundation for multiple objectives. Unfortunately, due to challenges with time and cost of in vivo creation with concurrent continual control of required features, smart materials are not currently being developed quickly enough. This review work proposes a simple strategy for predicting the stability and structure of newly found materials, such as chitosan nanocomposites. This strategy is based on techniques for molecular modeling, namely on a brand-new hybrid multiscale model of chitosan oligomers. This model has already demonstrated its efficacy for evaluating the mechanical properties of nanocomposites. This review attempts to identify PhCs **(**Carbamazepine (CBZ) in this case) that pose significant removal issues and non-commercial adsorbents that may have the capacity to do so.

2. Chitosan

Chitosan, one of the most economical and commonly accessible biopolymers, has various properties that make it an ideal absorbent for removing pollutants from wastewater. It has a high molecular weight and is non-toxic, cationic, linear, and biodegradable. Chitosan or poly-poly-(1→4) -2-amino-2-deoxy-b-d-glucose is a biopolymer formed by the alkaline de-acetylation (boiling in potassium hydroxide) of chitin, an acid-soluble material found in marine species such as crayfish, lobster, prawns, crab, and shrimp. Chitosan is one of the most abundant polysaccharides in the world.

Chitosan is a well-known amine-rich, biocompatible polymer with good film-forming properties [32, 33]. It is a D- and N-acetylglucosamine random copolymer that is created by completely or partially deacetylating chitin (Figure 1) [33, 34]. Unlike Chitosan, the bulk of chitin is made up of N-acetylglucosamine units. When the degree of de-acetylation surpasses 50%, protonation of the amino groups in an acidic pH leads in molecular solubilization [35]. Since amino groups are part of Chitosan's structure, it possesses special qualities [36]. The amino group protonates (converts to $NH3^+$) when the pH falls below 6.2, and Chitosan develops a positive charge on the D-glucosamine unit [35]. and this cationic nature allows Chitosan to interact with negatively charged compounds [36].Chitosan also has an easily modifiable hydroxyl group (primary at C6 and secondary at C3) in addition to the highly reactive amino group at C2 [36, 37]. Due to the tendency of these amino and hydroxyl groups to establish intra-molecular and intermolecular hydrogen bonds concurrently, linear aggregates with a high degree of crystallinity are produced [38].

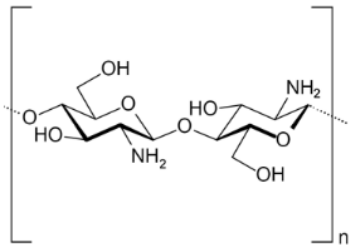


Fig 1: Chemical structure of Chitosan adapted with permission from [36] MDPI open access under a Creative Commons Attribution 4.0 International License. Copyright © 2015 by the authors; licensee MDPI, Basel, Switzerland.

Chitosan, a semi-crystalline polymer, is insoluble in water and most organic solvents but soluble in weakly acidic solutions [39]. Chitosan has also been solubilized using other dilute organic acids (formic acid, propionic acid, lactic acid) and inorganic acids (hydrochloric acid and nitric acid) [40]. Chitosan is classified as a base because it has a pKa value of 6.3[41] and contains the primary amino group of glucosamine. When Chitosan is dissolved in an acidic solution, protonation of the amino group occurs, and a cationic polyelectrolyte is formed. [42], as shown by equation 1.

$$\textbf{Chit-NH}_2\textbf{+H}_3\textbf{O}^+ \rightleftharpoons \textbf{Chit-NH}_3^+\textbf{+H}_2\textbf{O} \quad \textbf{(1)}$$

Chitosan is soluble in water as hydrochloride or acetate, creating acidity with a pKa of 6.0 [39]. Its unit cell has four glucosamine units and two chains arranged antiparallel. The primary hydrogen bonds are O3,,,O5 (intramolecular) and N2,,,O6 (intermolecular)[43]. Salts and derivatives, like Chitosan ascorbate and salicylate, also have crystal structures. Figure 2 depicts the structural unit with hydrogen bonds formed intera and inter molecularly.

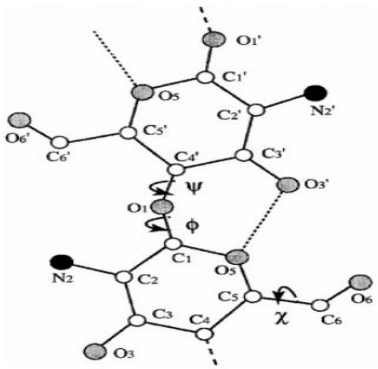


Fig 2: Chitosan chemical composition with position numbering in the disaccharide chain, displaying the psi and chi angles that define chain conformation and O6 orientation. O3-O5 hydrogen bonds are shown as dashed lines. Hydrogen bonds between neighboring chains are excluded. Adapted with permission from [44] Copyright © 2004, American Chemical Society

Given the properties above, it is probable that Chitosan has a high adsorption potential for pollutants such as heavy metals [45], dyes [46], and pharmaceuticals due to the various functional groups it contains. However, the adequacy of this substance within the adsorption handle is obliged by many drawbacks, counting its dissolvability in acid, restricted mechanical strength, and small surface area. This required several researchers to modify Chitosan for pharmaceutical removal, as explained in this review.

2.1. Molecular Weigh

The molecular weight of a macromolecule is one of the foremost fundamental components that characterize it. Understanding the molecular weight of polysaccharides is basic for understanding their uses and part in living frameworks. Utilizing strategies like chromatography [47], light scattering [48-49], and viscometry[50], it is conceivable to appraise the molecular weight of Chitosan, which is exceedingly subordinate on the de-acetylation conditions. Viscometry is the best and most broadly utilized strategy for calculating Chitosan's molecular weight. In any case, as the approach depends on the relationship between the intrinsic viscosity and molecular weight values, it has the downside of not being entirely exact. Chitosan with a molecular weight of between 10,000 and 1,000,000 Da is marketed commercially.

2.2. Viscosity

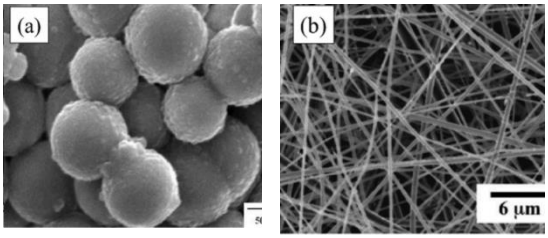


Figure 3:Chitosan-based materials with different shapes and sizes: (a) chitosan nanoparticles adapted with permission from [53] Copyright ©2012. Reproduced with permission from Elsevier Science Ltd; (b) chitosan nanofibers fabricated by electrostatic spinning technology adapted with permission from [54] Copyright © 2004.

Chitosan is a chitin N-deacetylation product Chitosan structure that is ideal is shown in figure 4 which delineates the receptive groups contained in Chitosan, that incorporate a primary amino group (C2) and primary and secondary hydroxyl groups (C6, C3). Glycosidic linkages and the acetamide groups are, moreover, Chitosan's viscosity increases with higher molecular weight and concentration [51]. Intensified de-acetylation also leads to higher viscosity due to distinct high and low deacetylated Chitosan conforming in an aqueous solution. Highly de-acetylated Chitosan adopts an expanded and flexible chain due to charge repulsion, while low levels of de-acetylation result in a rod-like or coiled shape with low charge density in the polymer chain.

3. Chemistry of Chitosan its preparation and its modification

Chitosan is available as a flake or powder and may be utilized directly or processed into nanofibers, spheres, membranes, and scaffolds. Its adaptability allows for a wide range of applications, such as forming Chitosan Nanofibers. Various processes like electrospinning, solvent spinning, and phase separation create chitosan nanofibers with benefits such as high surface area, scalable porosity, and strong durability. They have various applications like filters, controlled release carriers, sensors, and protective clothing.[52]. Nanoparticles, particularly chitosan ones, have gained interest due to their small size and high surface area, enabling the delivery of drugs to target sites through biological barriers. Various methods, including emulsion droplet coalescence, spray-drying, ionic gelation/polyelectrolyte complexation, emulsion solvent diffusion, and reverse micellization, have produced chitosan nanoparticles [53]. Figure 3 depicts the shape of chitosan nanofibers and nanoparticles.

functional groups. These functional groups empower many changes in polymers with novel characteristics and behaviors. Chitosan derivatives have been created to improve the qualities of Chitosan, such as solubility or biodegradability, or to present modern capacities or properties. De-acetylation, depolymerization, and quaternization, among other methods, have improved solvency in watery conditions [55].

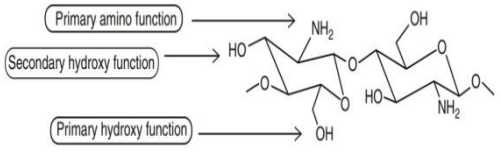


Fig 4: Functional groups in Chitosan that can be modified and adapted by permission from [55] with Copyright © 2015, Springer International Publishing Switzerland.

Raw Chitosan has benefits but may not suit all needs. Physical and chemical methods exist for modification, including quaternization, N-alkyl modification., N-acyl modification, C-6 oxidation for chemical modification, and blending and physical crosslinking for physical modification. These are highlighted in the next section.

3.1. Quaternized Chitosan Derivatives

Multiple studies[56-60] have shown that the positive charge of Chitosan can be altered to enable solubility in neutral, slightly alkaline, and various pH levels. One way to achieve this is through quaternization, which maintains a positive charge in Chitosan above pH 6.5. A common type of quaternized Chitosan is N,N, N-trimethyl chitosan chloride (TMC) [61] , produced through two reactions involving methyl iodide and Chitosan in the presence of N-methyl-2-pyrrolidinone (NMP) and an anionic exchange resin. Terayama, H. and Terayama, E created the first TMC called

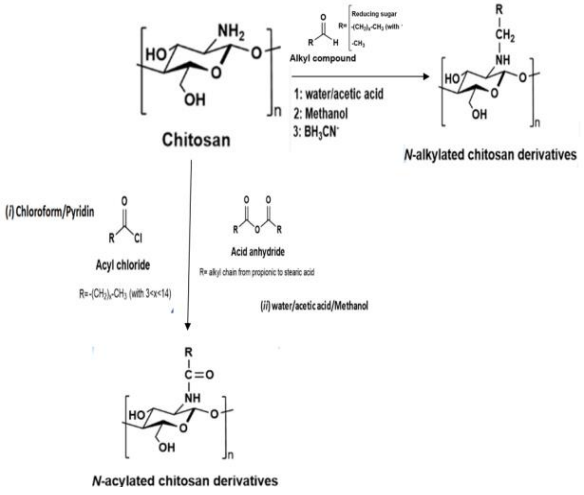


Fig 6: Production of chitosan derivatives by N-alkylation and N-acylation. Reaction adapted with permission from [56] MDI open access network Licensee MDPI, Copyright © 2019. Basel, Switzerland. Under the terms and conditions of the Creative Commons Attribution (CC BY) license.

3.3. Oxy-Chitosan Derivatives

Many academic studies [67–70] have examined the process of making water-soluble sodium chituronic acid (carboxylated chitin or Chitosan) utilizing TEMPO, an organic catalyst utilized to convert hydroxyl functional groups to aldehyde functional groups under the conditions of NaOCl and NaBr. The main use of TEMPO is the regioselective oxidation of primary hydroxyl groups in polysaccharides. It was created by Muzzareli et al.[71] to make oxy-chitosan macrame. Changing alkyl halides' carbon lengths can create various quaternized Chitosan. This performance is shown in figure 5 below.

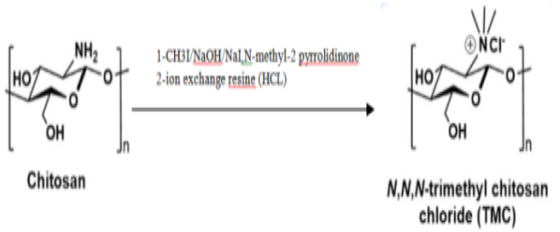


Fig 5 : . Production of chitosan derivatives by quaternized through two-step reaction adapted with permission from[56] MDI open access network Licensee MDPI, Copyright © 2019. Basel, Switzerland. Under the terms and conditions of the Creative Commons Attribution (CC BY) license.

3.2. N-acyl Chitosan Derivatives

Grafting fatty acids onto Chitosan via N-acylation creates hydrophobicity. This structure involves amidating -NH2 and -COOH groups utilizing acyl halides or acid anhydrides as reagents (Figure 6). The reaction is typically carried out in chloroform/pyridine, methanol/water/acetic acid, or pyridine/chloroform. Chitosan's -OH group. form O-alkyl chitosans. To prevent O-acylation, some suggest replacing the main hydroxyl group. With a trityl group. N-acylation can be accelerated [62] if chitosan chlorophylls are produced. The ability to create N-acyl Chitosan has been investigated with various acid anhydrides[63-66].

derivatives, specifically 6-oxyCS , one of the derivatives of oxychitoic acid. Chitin from fungus or shrimp cells pretreated (chemically or enzymatically) is the principal source of chronic sodium salt. Figure 7 depicts the oxy-chitosan formation.

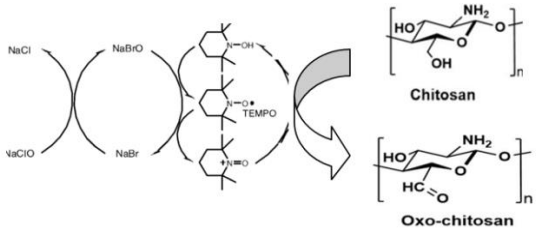


Fig 7 : oxidation of Chitosan via TEMPO The oxidation mediated by the TEMPO/NaClO/NaBr system adapted with permission from [72] under license Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. copyright © 2018 The Authors. Published by Elsevier Ltd.

3.4. Cross-Linked Chitosan Derivatives and blending modification.

Blending different polymers with Chitosan is an effective method for modification, especially through physical cross-linking and blending that creates new material. It is noteworthy that desired characteristics are not found in a single material. Chitosan hydrogel is encapsulated by mixing chitosan solutions and various blends, followed by a sol-gel transition. Additional modifications, such as adsorption, cross-linking, and covalent grafting, may also be utilized. They were blending Chitosan with polymer material. expands their uses, combining their best features and lowering costs. It's commonly used for heavy metal ion adsorption, pharmaceuticals, biomedical membranes, research, freshness, and the environment. In film production, the two oppositely charged polyelectrolytes, Chitosan and carboxymethyl glucomannan, may interact to create a cross-linked membrane with a network topology. By solution mixing, Sun et al. [73] produced a chitosan carboxymethyl glucomannan blend film, demonstrating the compatibility of the two materials is commonly used as a crosslinking agent due to its synthetic nature, accessibility, and affordability[74,76]. It undergoes a condensation reaction [77,76,78] with the primary amine groups from the CS chain, facilitated by labile hydrogen. Typically, the aldehyde groups.in GTA react with the amino groups of Chitosan through the Schiff base reaction. Epichlorohydrin, on the other hand, prefers hydroxyl groups. [79] While GTA can crosslink under mild aqueous conditions, it is also toxic. Therefore, natural alternatives like genipin [76], citric acid [80], and inorganic phosphate [81] are under study to produce CS hydrogels, as shown in figure 8. Lusiana et al. [80] used citric acid as a cross-linking agent for preparing a CS/PVA membrane. Cross-linking was used to stabilize biomaterial for hemodialysis membranes. Materials and Chitosan are firmly attached due to covalent cross-linking, preventing their separation from composites. For instance, it was anticipated that Cross-linking citric acid with CS would add COO- groups to the biomaterial, enhancing the CS membrane's bioactivity in transporting biomolecules like urea and creatinine. PVA improved the CS membrane's mechanical efficiency and hydrophobicity[78].

and the improvement of mechanical qualities with increasing carboxymethyl glucomannan concentration. Chemically cross-linked chitosan hydrogels are more resilient than physically cross-linked hydrogels in acidic environments. Covalent connections between the polymers provide chemically cross-linked Chitosan its high stability.

The increased contacts also result in higher mechanical resistance. In order to join the chains and create a three-dimensional molecule network, cross-linked CS must be prepared using certain chemical reagents[74,75,76] since Chitosan's network structure can be modified by adjusting reaction conditions. Increased cross-linker concentration and extended reaction time result in higher density, greater consumption of Chitosan's functional groups, and stronger mechanical properties. To create CS-based hydrogels, CS is often covalently cross-linked in acidic or basic environments in the presence of aldehyde derivatives such as glyoxal, formalin, or glutaraldehyde [76]. Typically, the creation of Schiff base results from the cross-linking interaction with CS (imine) [75,61,76]. Glutaraldehyde (GTA)

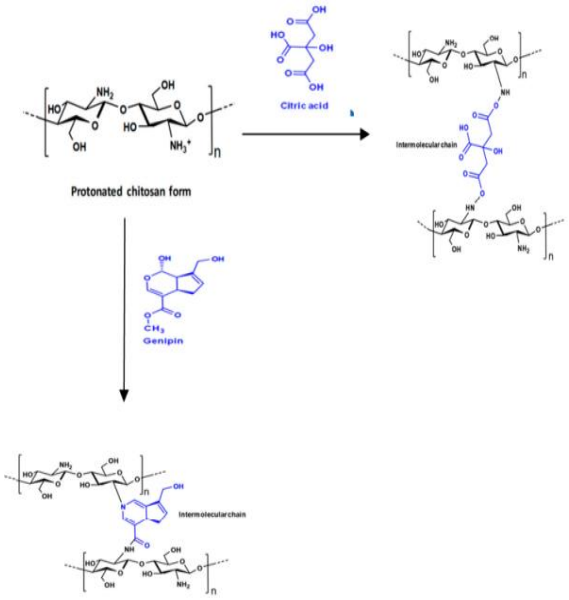


Fig 8: The main cross-linking reactions using Chitosan Adapted with permission from [56] MDI open access network Licensee MDPI, Copyright © 2019. Basel, Switzerland. under the terms and conditions of the Creative Commons Attribution (CC BY) license.

4- Application of chitosan nanoparticles

Chitosan nanoparticles (ChNP) possess the qualities of Chitosan alongside the traits of nanoparticles, including surface and interface effect, negligible dimensions, and quantum size effects [82]. When in contact with anions, Chitosan can create a gel and generate beads. The capability of this property permits its utilization In drug delivery. Despite various techniques employed for synthesizing ChNP, their application remains limited due to the beads' large size ranging from 1-2 mm. Currently, five available techniques are accessible for use: ionotropic gelation, macroemulsion, emulsification solvent diffusion, polyelectrolyte complex and reverse micellar method [83], According to Ma et al. In 2010, chitosan nanoparticles were acquired through the degradation of Chitosan utilizing hydrogen peroxide. The inclusion of pulp, impregnation, dispersion coating on hand sheets, and insufflations was employed to integrate it into the antimicrobial paper. The insufflated paper exhibited the highest potency in fighting off both Escherichia coli and Staphylococcus aureus bacteria Using an atomic force Microscope (AFM), the However, in regards to S. aureus at a concentration of 1mg/ml, only a 2.0 mm diameter was detected when the concentration was 10mg/ml, and the diameter zone of inhibition was recorded to be 7.5 mm. Figures 9 and 10 depict the area of suppression attributed to CSNP about E.coli and S. aureus bacterial strains, respectively in a counterclockwise direction. The concentration of CSNP (1, 2, 5, and 10 mg/mL) increased progressively. The control was applied on the central aperture yielding an inhibition zone with no

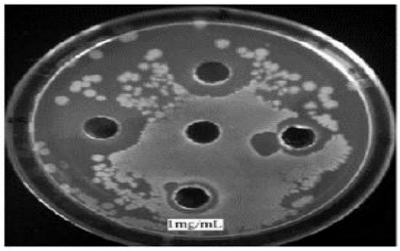


Figure 10:. The inhibition zone around the holes for S. aureus adapted with permission from [86] Copyright © Taylor & Francis Group, LLC

diameter. Also, in another study, Qi et al. [85] conducted an assessment to determine the antibacterial effectiveness of chitosan nanoparticles ((ChNP)) and (ChNP) containing copper when used In vitro against E. coli, Staphylococcus choleraesuis, Salmonella Typhimurium, and S.aureus. According to the findings, the growth of all bacteria under examination was impeded by chitosan nanoparticles and those infused with copper. The microbial inhibitory concentration ((MIC)) was below 0.25 lg/ml, while the structure and dimensions of the particles were assessed and discovered to possess a sleek appearance and a nearly 36 nm measurement. Studies have demonstrated that H2O2 can decompose CSNP, while a high-frequency ultrasonic cleaning device can facilitate its dispersion. The techniques with the highest usage rates are ionotropic gelation and polyelectrolyte complex [84]. These techniques are easy to implement and do not employ organic solvents or exert excessive shear force.

4.1. Antibacterial Activity of CSNP

The inhibition zone approach was used to assess CSNP's antibacterial activity. The hole-plate test was used to conduct a qualitative analysis. In the vertical holes, five 7mm diameter holes were filled with 80 µL of CSNP-0.5% HAc solutions (1, 2, 5, and 10 mg/mL). If the sample had antibacterial activity, an inhibition zone developed. The greater the inhibitory zone, the more influential the antibacterial action. At a concentration of 1mg/ml, the diameter of the zone of inhibition for E.coli was 5.0 mm, and the inhibitory area expanded to 9.0mm when the concentration reached 10mg/ml.

minimum bactericidal concentration ((MBC)) of the nanoparticles was 1 lg/ml.

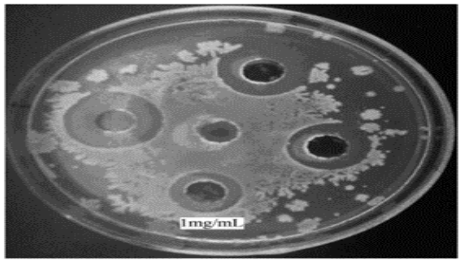


Fig 9: The inhibition zone around the holes for E. coli adapted with permission from [86] Copyright © Taylor & Francis Group, LLC

4.1.1.AFM Analysis

AFM was utilized to analyze the morphology of E.coli and S.areus that had undergone CSNP treatment.The AFM image in figure 11 displays evenly sized spherical particles with a smooth surface, characterized by surface heights that span between 26 to 48mm. This demonstrates that the use of a high frequency ultrasonic cleaner makes it possible to evenly disseminate these particles, as discussed in previously described techniques for nanoparticle preparation, while degrading them through the use of hydrogen peroxide. Additionally, the morphology of S. choleraesuis that received CSNP treatment was altered. AFM examined The application of CSNP to the bacteria for varying periods up to 3 hours as shown in figure 12 resulted in noticeable disruption of the

cell, causing the release of cytolytic elements as well as fragmentation. Various suggestions have been made regarding how Chitosan operates as an antimicrobial agent. The following can be listed as:

1- Cheating Chitosan with important nutrients or trace elements makes it possible to impede bacterial growth[87].

2- Chitosan has the potential to combine with negatively charged groups on the cell exterior and create polyelectrolyte complexes with surface compounds [88] of bacteria, resulting in a barrier surrounding the cell that restricts the entrance of crucial solutes into the cell[89].

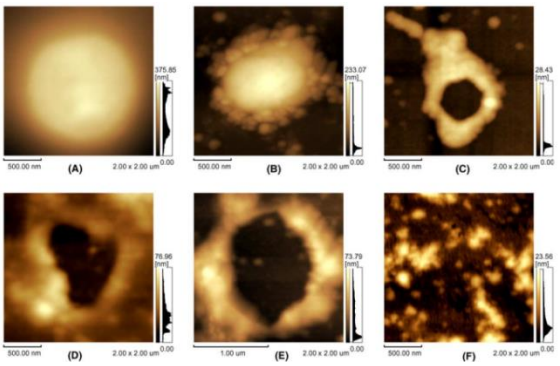


Figure 12. Atomic force micrographs (AFMs) of S. choleraesuis cells after treatment with chitosan nanoparticles suspension for different times. Nontreated cells (A); treated cells for 30min (B), treated cells for 1 h (C), treated cells for 1.5 h (D), treated cells for 2 h (E), and treated cells for 3 h (F) adapted by permission [90] copyright Ó 2004 Elsevier Ltd.

Some writers say that CS can kill certain types of bacteria by sticking to their cell walls and changing their texture until The CS can get inside The cell. This works for both kinds of bacteria called Gram-negative and Gram-positive. It works by electrical charges interacting between CS and parts of The cell Wall made of molecules called teichoic and lipoteichoic acids, as well as lipopolysaccharides [91].

4.1.2. Bionanocomposites for food industry

The preservation of food quality and safety greatly relies on the use of appropriate materials for packaging, which effectively blocks the intrusion of moisture, chemicals, light, carbon dioxide, oxygen, and microorganisms. Numerous endeavors have been

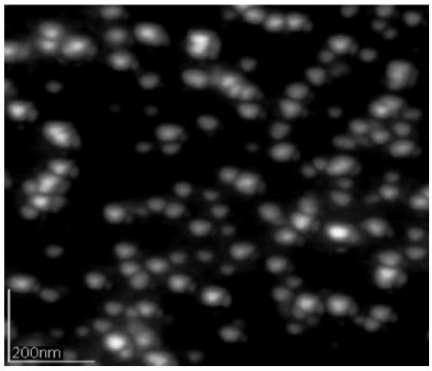


Fig 11. AFM image of high concentration CSNP adapted with permission from [86] Copyright © Taylor & Francis Group, LLC

to substitute petroleum-based plastic food packaging, known for its inability to decompose, with biopolymer-based materials. Using Chitosan, a biopolymer, can effectively hinder the growth of bacteria, fungi, and viruses. Nanofillers are integrated into them to create nanocomposites to boost the strength of biodegradable, renewable, and water-absorbing biopolymers [92]. For packaging purposes, which shows much promise. Additionally, CS has been recognized as a substitute for reducing microbial growth and enhancing shelf life in post-harvest food preservation. Because of its ability to form films[93], CS has become a viable option for application, as it enables customization in creating edible films and coatings[94].

Maintaining food quality and delaying spoilage using physical harm, chemical processes, and metabolic responses [95] are major challenges for edible films and coatings. Edible films and coatings grounded on CS have efficiently accomplished these objectives using chitosan nanoparticles as a natural, eco-friendly fungicide. Studies indicated that applying chitosan nanoparticles was highly effective in controlling the growth of Botrytis cinerea, the main fungus responsible for strawberry gray mold. This alternative method of protecting strawberries could potentially eliminate the need for harmful chemical fungicides Apriyanti et al. [96] used a functional CS film with green tea extract and packed strawberries with CS coatings containing lemon essential oil Perdones et al. [97] showed no notable change in strawberry properties. In short, lemon essential oil prolonged the shelf-life of strawberries and is effective in preserving cheese according to Brown et al. [98] who Used CS, hydrogen peroxide, lauricarginate, and calcium sulfate

to cover fresh cheese. Thus far, there is abundant proof that CS is proficient in prolonging the durability of food products and mitigating the prevalence of harmful pathogens. The durability of food products and mitigating the prevalence of harmful pathogens.

Although Chitosan has exceptional film-forming capabilities, its limited water resistance prevents it from being used in some situations. The natural material can be chemically altered to increase its water resistance. For instance, the interaction of hydrophobic chitosan films with perfluorinated acid derivatives has been previously reported [99]. The need for alternatives has arisen due to perfluorinated application in food flavoring, have propelled it to become a noteworthy ionic cross-linker. . According to studies, the amalgamation of Chitosan and citric acid produces an amide linkage shown in Figure 13. Citric acid, a vital element in human metabolism, can be produced sustainably through a feasible alternative method. One can develop this resource through the process of fermentation using sucrose or glucose, which can be obtained from sources such as sweet potatoes[101,102] or the black liquor that is a byproduct of wood pulping.

Adding glycerol to the chitosan-citric acid films enhances their flexibility by functioning as a plasticizer and expanding the intermolecular gaps. The cross-linking of citric acid with chitosan results in a more condensed network, and hence, glycerol is introduced to optimize the film's flexibility for food packaging usage. Glycerol, commonly utilized as a plasticizer, has also been employed in creating bio-decomposable polyesters made from citric acid [103].

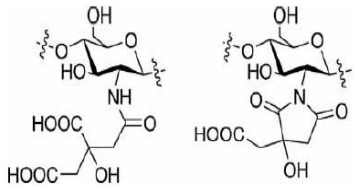


Fig 13: potential amide structures formed by citric acid and chitosan reaction.(cyclic and acyclic amides) adapted with permission [103]Open access created by Taylor & Francis Group, LLC Under liscence Creative Commons Attribution 3.0 Unported License Copyright © Taylor & Francis Group, LLC

use of infrared spectroscopy demonstrated the impact of glycerol addition on chitosan-citric acid films and aided in the characterization of the resulting films. This is significant because citric acid can create cyclic and acyclic amides. However, based on Figure 14, it can be inferred that Chitosan only produces acyclic amides, proven through IR analysis. The 2500-3500 cm-1 peak range was widened due to the presence of OH groups in citric acid. Equally, the C=O absorption of Chitosan at 1182 cm-1 encountered a corresponding change. The wider extent results from compounds' persistence, bioaccumulation, and probable endocrine disruption [100].

4.1.3. Modifying chitosan films for better water resistance using green reagents.

Packaging membrane's water and oxygen barrier properties are affected by structure, morphology, additives, and cross-linking factors. Using covalent and salt bonds can boost chitosan film's water resistance. Popular cross-linkers include glutaraldehyde, genipin, and tripolyphosphate. Citric acid's biocompatibility, antimicrobial and antioxidant attributes, as well as its extensive

the involvement of C=O bonds in the production of citric acid. The residual alterations in the spectra can be credited to creating an amide linkage between the amine group of Chitosan and citric acid. Theoretically, amides that are both acyclic and cyclic can exist. An occurrence of absorption involved the stretching of a C=O bond. The reading is 1708 wavenumbers per centimeter. As per the literature, the unadulterated citric acid displays two C=O peaks which are situated at approximately 1750 cm-1 and 1700 cm-1, respectively. These peaks signify the existence of unbound and bonded carboxylic acid groups. The disappearance of the 1750 cm-1 peak and the absence of new peaks in the 1730 cm-1 range post the chitosan reaction clearly suggest a lack of esterification. The results of a literary review on citric acid amides indicated that a non-cyclic amide exhibited a distinctive C=O absorption at approximately 1625 cm^{-1}, whereas the cyclic amide counterpart was observed at approximately 1770 cm^{-1} [104]. The lack of spikes observed in the 1770 cm^{-1} region of the chitosan-citric acid spectrum eliminates the possibility of a cyclic structure. Chitosan exhibits NH2 bending oscillations, which can be observed at 1648 cm-1 and 1581 cm-1. As the amount of citric acid increases, the peaks shift towards lower wavenumbers and a broadening effect occurs. Mima et al. have indicated that the peaks are most distinct for Chitosan with 99% de-acetylation, and they slowly vanish as acetylation increases[105], creating amide bonds. Hence, it can be deduced that an acyclic amide was generated through the interaction between Chitosan and citric acid in the given experimental circumstances. Additional proof of Chitosan's structural disruption can be observed through the expanded peaks within the range of 560-670cm^{-1}.

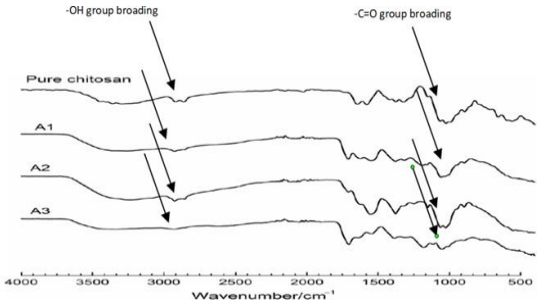


fig 14 : IR spectra of chitosan-citric acid films (%T). adapted with permission [103]Open access created by Taylor & Francis Group, LLC Under license Creative Commons Attribution 3.0 Unported License Copyright © Taylor & Francis Group, LLC

Adding glycerol to the process of forming the film did not have a noteworthy effect on the infrared spectroscopy results. The absence of additional peaks within the ester C=O absorption area signifies that esters were not created between glycerol and citric acid using the specified conditions. The measure of water absorption was ascertained by weighing pure Chitosan and film D1 prior to and post-immersion in water, as depicted in Figure 15. The initial three minutes of exposure saw the highest water absorption rate in both films. The moisture level of the altered film remained constant after that. Pure Chitosan showed a relatively higher water absorption rate of 96% after six hours compared to film D1, which had a lower % absorption rate of 44%. Comparable outcomes were observed in thickness evaluations. The thickness of the chitosan film in its pure form experienced a 42% increase, while film D1 experienced an uptick of merely 11%.

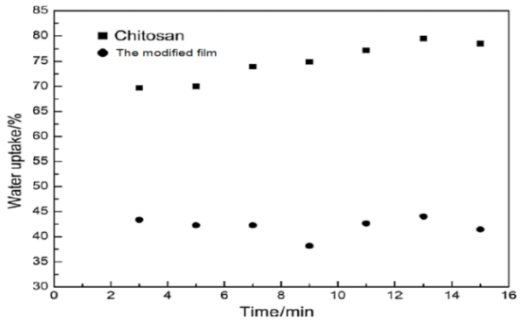


Figure15: Water uptake over time by pure Chitosan and modified chitosan film**.** adapted with permission [103]Open access created by Taylor & Francis Group, LLC Under liscence Creative Commons Attribution 3.0 Unported License Copyright © Taylor & Francis Group, LLC

Using carbon nanotubes as filters is a viable solution to address Chitosan's hydrophobic nature, figure 16 as suggested by a theoretical study employing molecular modeling techniques. By performing ab initio DFT calculations, an optimized structure for Chitosan was obtained before assessing the binding energy between Chitosan and CNT through classic molecular dynamics. CNTs exhibit hydrophobicity, and such phenomenon intensifies at higher temperatures, which therefore attracts the polymer molecule towards the nanotube. A research study discovered that as the temperature drops, the chitosan molecule is more inclined to remain in the aqueous environment rather than on the nanotube's surface. Researchers investigated water filling in nanopores of different lengths and widths at specific temperatures, discovering that water molecules must overcome energy barriers and break hydrogen bond networks to enter narrow CNTs. This entrance resistance can be overcome by changing the diameter or increasing the temperature. Interestingly, the number of water molecules entering the CNT increases linearly with time until the CNT is entirely filled.

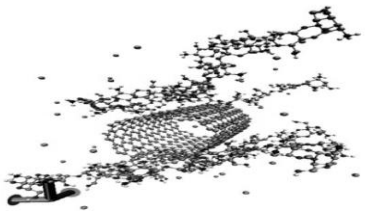


Figure 16: Complex of CNT and Chitosan adapted by permission from [106] Copyright © 2012, Pleiades Publishing, Ltd.

The radial distribution functions of the O atom belonging to the CH2OH (a) group and the N atom of the chitosan amino group (b) with CNT are illustrated in Figure 17. According to the findings, CNT predominantly interacts with a pair of chitosan groups, namely the oxygen of the CH2OH group and the nitrogen of the amino group. As the temperature reduces, the permittivity rises. Regarding physical changes, when the temperature drops, the dipoles in the surroundings become arranged in order, reducing entropy for the dipole system. When the temperature decreases, the permittivity rises, and this reduces the bond strength between Chitosan and CNT since the computed binding energy between the chitosan monomer and CNT was determined to be 0.83 eV after a sequential removal of individual components from the overall system, based on the findings of the radial distribution's relationship with temperature. The attraction

with the ion-induced dipole aspect is consistently inversely proportional to the relative permittivity of the medium. In addition, it has been stated earlier that chitosan flakes can undergo physical alteration by transforming them into gel beads [107]. These beads can effectively boost the material's porosity, stretch its polymer chains, boost its surface area, decrease its crystallinity, and enhance accessibility to internal absorption locations.

5- Chitosan based sensor

Sensors are instruments capable of identifying and responding to signals or stimuli. The apparatus often comprises delicate elements which transform the signal into an electric current [108]. In their work, Setter and colleagues have provided a concise description of a sensor, essentially a compact tool capable of transforming chemical or biochemical data into a signal that can be effectively analyzed [109]. Sensors may be categorized based on the signal variety they identify, specifically chemical, biochemical, or electrical signals. For instance, biosensors can sense both biochemicals and bioreactions [110].
In comparison, transducers translate one type of energy into another form, while sensors convert any energy type into an electrical signal. Occasionally, chemical sensors are grouped with biochemical sensors such as biosensors, enzyme sensors, and multi-array sensors [108,111]. An example of a biosensor includes a transducer, which may be electrochemical or optical, coupled with biological material or molecules like enzymes, microorganisms, or tissues, and supported by electronic or signal processing capabilities to display the output. Hulanicki et al.

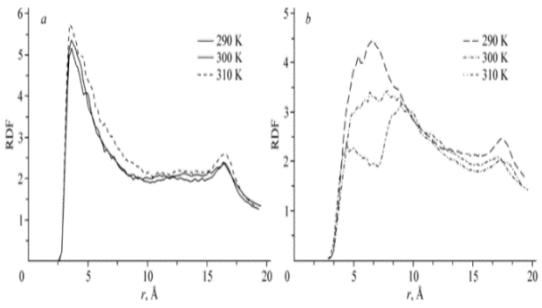


Fig. 17. Radial distribution functions of the O atom from the CH2OH group (a) and the N atom of Chitosan (b) in the interaction with CNT. By permission from [106] Copyright © 2012, Pleiades Publishing, Ltd.

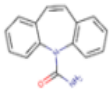
Classified chemical sensors by transducer principle[112].
Four sensor types: optical, electrochemical, electrical, mass-sensitive. Chitosan's structure allows for dispersion and modification, making it useful in creating selective sensors and intelligent materials via electrostatic interactions with amino groups. When protonated, these groups attract anions. Chitosan acts as a reducing and protective agent for metal nanoparticles due to its hydroxyl and amino groups, which provide electrons to metal ions.
Since -CH3OH group can also be reduced to -CHO or -COOH [113-117]. Due to its ability to form robust hydrogel clusters [118] and its potential for electrodeposition as a thin layer, Chitosan holds promise for developing miniature biosensors. and as a medium for immobilizing various biosensors. Incorporating Chitosan into many layers of polymer film results in a more porous structure, increasing surface area and electrical conductivity. The chitosan-based sensor was effectively utilized for quantifying real samples in both biological and authentic fluids, producing satisfactory results that demonstrate its practicality. Moreover, it has been discovered that sensors infused with Chitosan exhibit an extensive linear dynamic range and exceptional sensitivity at a low limit of quantification. Therefore, we can deduce that this sensor has the potential to be utilized in various applications and for the instantaneous detection of specific molecules in biological fluids, as well as for identifying low concentrations of pharmaceutical waste Due to its exceptional ability to form films, lack of toxicity, compatibility with living organisms, and ability to decompose naturally. They exhibit considerable advancements in The field of sensor technology. The cationic nature of Chitosan enables it to interact with different molecules and exhibit strong adsorption capacity, making it suitable for use as a sensor to detect Carbamazepine in wastewater and for its removal. Numerous studies have delved into The mechanism by which CBZ binds to certain substances and have linked this behavior to The physical and chemical characteristics of CBZ, which will be further elucidated in The forthcoming sections.

5.1 Chemical properties of Carbamazepine and its metabolites and there occurrence in waste water.

CBZ or Carbamazepine is a tricyclic compound that belongs to the dibenzoazepine class, specifically the 5H-dibenzo[b,f]azepine type, and has a carbamoyl substituent located on the nitrogen atom of the azepine. It is chemically similar to tricyclic antidepressants (TCA) and it possesses properties that make it useful in treating pain and preventing seizures. A moderate hydrophobicity characterizes CBZ as it exhibits a value of the octanol-water partitioning coefficient log Kow below 3, shown in Table 1, which renders it a non-volatile compound. Moreover, considering the

available solubility values, it is deemed soluble in water. Additionally, within the context of water surroundings, CBZ appears in an uncharged state in most water and wastewater treatment procedures as its pKa greatly differs from neutrality, which is the typical pH condition utilized in these treatments[119]. Several drugs with hydrophobic properties, like CBZ, can be conveniently adsorbed onto the organic element of granular materials, enhancing their resistance to degradation and leading to noteworthy accumulation on the substrate. However, Compound hydrophobicity alone cannot assess CBZ adsorption and distribution behavior. Adsorption is affected by solubility, structure, and acidity. Yan et al. observed that the potent van der Waals attractions between CBZ and the substrates stem from its elevated polarizability. CBZ's water solubility is also fairly limited[120], making it easier to transport into the substrates. Table 1 provides an overview of the formula, structure, and identification number (CAS), along with the primary physical and chemical attributes of CBZ.

Table 1: Main CBZ physiochemical characteristics

Cas no	Formula	Structure	Molecular Weight	PKa	Log Kow
298-46-4	$C_{15}H_{12}N_2O$		236.274 g/mol	2.3 [121] 13.9 [122]	2.45[123]

CASn: chemical Abstracts Service number, Formula : Chemical formula; pka : log of acid dissociation constant; log kow: log of octanol-water partition coefficient

About 72% of orally ingested Carbamazepine is assimilated. In their research, Miao and Metcalfe [124] and Miao et al. [125] examined the presence of Carbamazepine metabolites in both surface water and wastewater treatment plant effluent. They discovered that one of the major urinary metabolites, CBZ diol trans-10,11-dihydro-10,11 dihydroxy Carbamazepine, was present in high concentrations. This metabolite can also be produced as a byproduct of oxcarbazepine [126]. Interestingly, the concentration of CBZ-diol was almost three times higher than that of Carbamazepine since the drug's metabolites go through enterohepatic circulation before urination. As a result, it is expected that water sources would have a greater level of CBZ-diol concentration. Therefore, further investigation is required regarding the environmental destiny of carbamazepine by-products. About 28% of orally ingested Carbamazepine remains unchanged and is excreted in feces. The liver's extensive metabolism of Carbamazepine means that only approximately 1% of the dosage is eliminated from the body without any alteration. The duration it takes for Carbamazepine to be eliminated from the body is influenced by the dosage and typically falls between 25 to 65 hours after intake [127].

Another important metabolite found in urine is 10,11-expoxycarbamazepine (CBZ-epoxide),[128]. Crucially, it exhibits the same level of pharmaceutical activity as its original drug (carbsamazepine). Fig. 18 depicts the metabolic mass balance of Carbamazepine , About 30% of the oral dose consists of CBZ-diol, equivalent to the quantity of unmodified Carbamazepine.

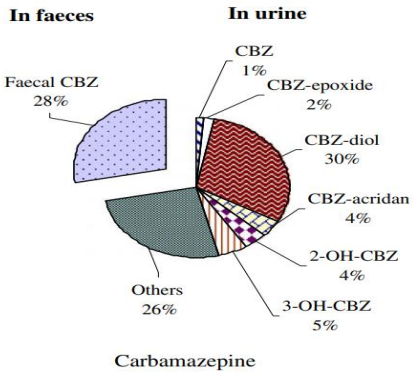


Fig 18: Identified metabolites of Carbamazepine and its percentages of oral dosage. Adapted by permission from [129] Copyright © 2008 Elsevier .

6. Review of proposed mechanisms of Carbamazepine adsorption on different modified chitosan films

As previously noted, Carbamazepine is not highly soluble in water because it possesses an aromatic

group, a double bond, and a long hydrocarbon chain that repels water. However, the utilization of nanoparticle technology shows the potential to enhance its solubility. Decreasing the size of particles to nanometers leads to a wider contact area between the compound's surface and the medium, which in turn boosts solubility, dissolution rate, and drug permeability. This is attributable to the heightened ability of chitosan nanoparticles, which possess a cationic feature owing to the presence of the amino group, to penetrate cells effectively. This cationic characteristic also encourages a robust electrostatic interaction between Chitosan and anionic drugs. Hence, its application is highly beneficial in the transportation mechanism of medications.

6.1. Formation of carbamazepine –chitosan nanoparticle

Chitosan nanoparticles can be synthesized via ionic gelation, as previously stated. This approach relies on the electrostatic attraction between Chitosan's positively charged amino group (-NH2) and the negatively charged group of the polyanion, Na-TPP [130]. In addition, Additionally, Na-TPP boasts advantages due to its cross-linking properties that are non-toxic, cost-effective, and stable. Furthermore, its high concentration of negative charges results in more robust interactions compared to other polyanions, [131]. One reason why the ionic gelation method is widely used is due to its straightforwardness, accessibility, and lack of requirement for heat in its execution [132]. The literature review indicates that carbamazepine nanoparticle formation is achievable, as evidenced by the successful binding of azithromycin and Chitosan to create azithromycin chitosan nanoparticles due to the similarity of the carbonyl group in azithromycin with that in Carbamazepine.

With a pKa of 6.5, low-viscosity chitosan can be considered a feeble base. Consequently, it easily dissolves in acidic solutions with a pH of under 6 [39]. Under low pH conditions, Chitosan's amino group (-NH2) gains a proton and becomes a polycationic (-NH3+) molecule. This enables it to dissolve in water and form ionic bonds with the anionic drug. Nevertheless, Chitosan's amino group was incapable of crosslinking with other counter ions when the pH exceeded 6 [130] due to its deprotonation. Moreover, Aquadest demonstrated good solubility of Na-TPP due to its ionization into polyphosphoric ion (P3O105-) and sodium ion (Na+) in a neutral pH environment that surpasses pKa value. As a result, the cationic group of Chitosan (NH3+) is engaged in a chemical interaction with the polyphosphoric ions (P3O105-) present in TPP [133]. Figure 19 shows the interaction of Carbamazepine, Chitosan, and Na-TPP to form a nanoparticle.

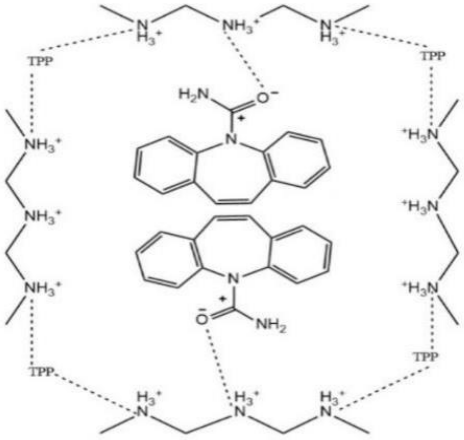


Fig 19 : Illustration of chemical interactions formed between Carbamazepine, Chitosan, and TPP adapted with permission from [131] open access under liscence Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License. Copyright (c) 2022 JURNAL FARMASI DAN ILMU KEFARMASIAN INDONESIA

Chitosan trapped Carbamazepine through an interaction between their carbonyl and NH3+ groups. O has a higher electronegativity than C in the carbonyl group. This causes resonance in the C-O bond, shifting electrons to O and creating a negatively charged intermediate on C-O. [134] Chitosan cation binds to carbamazepine carbonyl O- via ionic interaction. Nanoparticle formation is completed through cross-linkage. Between chitosan and Na-TPP molecules, entrapping Carbamazepine within the particle.

6.2. Adsorption of Carbamazepine on polypyrrole – Chitosan magnetic nanocomposite.

Magnetic nanoparticles (MNP) exhibit great potential for effective removal and adsorption due to their high surface area-to-volume ratio. MNPs have the added advantage of being easily customizable on their surface, which allows for the specific sorting of substances [135-137]. The traits possessed by MNPs render them suitable as an absorbent material in eliminating trace organic pollutants and hazardous metals from wastewater, with a faster, more efficient, and more accurate approach than current methods. The alliance of MNPs and the intended substance can be swiftly extracted using an external magnet situated on the exterior of the receptacle without any need for extra filtering or spinning of the specimen. Thus, magnetic separation is a cost-effective, expedient, and fast method for isolating tiny particles that is simpler than a complex filtration procedure. MNPs and Fe3O4

nanoparticles are commonly used due to their ability to degrade and interact well with living systems in the physiological environment [138].
To guarantee steadiness and hinder clumping, the surface must be coated to generate either electrostatic or steric repulsion[139]. The surface enhancement can lead to improved suspension stability by spreading magnetic particles throughout the matrix. Additionally, this modification generates a dynamic surface that can selectively interact with specific molecules for analytical purposes. One illustration is the use of a biologically active medication compound coupled with a ligand to form a specialized outer layer designed for the targeted removal of certain metallic elements [140-141]. MNPs are coated with both inorganic and polymeric substances (organic) for surface modification. Several non-organic materials such as silicon dioxide, metal oxide, graphite, and pieces of semiconductor have been utilized [142-144]. The present times have led to a great interest in the polymerization process aimed at stabilizing MNPs. As a result of their ability to perform multiple functions. Developed over time. Many types of polymers have been created. The MNPs' surface was typically functionalized in previous studies [145-146]. By making certain alterations, it is possible to create magnetic nanoparticles (MNPs) with qualities such as resilience, compatibility with living
organisms, and the ability to bond with specific molecules. Polymeric coatings have been developed through both artificial and organic means.

MNPs coating is achieved through the utilization of different types of polymers, both natural and synthetic. Some examples of synthetic polymers include polyethylene glycol (PEG), polyvinyl alcohol (PVA), polylactic acid (PLA), polyvinyl pyrrolidone, alginate, and polyacrylic acid (PAA). On the other hand, Chitosan (CS), starch, gelatin, dextran, and modified cellulose are considered natural polymers according to their classification [147].
Extensively, conductive polymers with electrical and magnetic characteristics such as Poly pyrrole and its variations are used as surface coatings in extraction scenarios [148]. Due to its versatile characteristics, PPy holds great potential for performing separation and sample preparation procedures [146]. The features of π-interaction, hydrogen bonding, polar functional groups, ion exchange tendencies, acid-base character, environmental stability, and ease of synthesis are associated with hydrophobicity. Despite possessing noteworthy characteristics, PPy also encounters certain limitations, such as its inadequate mechanical properties, relatively inferior thermal stability in oxygen, and non-degradable composition, which have constrained its utilization. Incorporating natural biodegradable polymers into the PPy matrix is a highly challenging task. The amalgamation of CS and PPy is anticipated to enhance their characteristics, particularly in adsorption and mechanical properties.
Magnetic nanoparticles consisting of CS and Fe3O4 were synthesized by coprecipitating iron salts with Chitosan. Subsequently, PPy-CS-Fe3O4 MNCs were created via chemical oxidative polymerization of pyrrole on magnetic chitosan MNCs to serve as a competent, cost-effective, and repeatable sorbent employed in the elimination of CBZ from pharmaceutical wastewater.

By subtracting the final concentration of the drug in the solution from its initial concentration, the amount of CBZ connected to the synthesized PPy-CS-Fe3O4 MNC was determined. The measure for the ability of MNC to absorb substances,
was determined using the mass equilibrium equation 2 [149].

$$q_e = \frac{(C_0 - C_e)V}{m} \qquad (2)$$

here, V (L) and m (mg) are the solution volume and the sorbent mass used in the process and C0 and Ce are the CBZ concentration in the solution at primary and equilibrium states (mg L− 1), respectively.
The MNC exhibited a certain degree of effectiveness in removing CBZ, as indicated by the percentage of removal efficiency observed.
Assessed through equation 3 :

$$RE\% = \frac{(C_0 - C_e)}{C_0} \times 100 \qquad (3)$$

Where C0 and Ce refer to the quantity of CBZ present in the solution at the beginning and end of the experiment, respectively. The state of equilibrium is expressed in milligrams per liter (mg/L).

Figure 20 Illustrates the structure of PPy-CS-Fe3O4 MNCs and proposes the potential interplays between the Fe3O4 and polymeric coatings. The literature states that both amine and hydroxyl groups are implicated in the intricate combination of iron and Chitosan [150]. The amino and hydroxyl groups found in the same or distinct polymers of chitosan function as coordinated sites for iron ions. In an aqueous environment with high acidity, the amino groups present in CS become protonated, leading to a positive charge. As a result, CS molecules have an affinity for

molecules with negative charges, as the hydroxyl (Fe-OH) groups present on the surface of MNPs [151]. As anticipated, the CS-Fe3O4 particles have a strong affinity for pyrrole molecules and can efficiently adsorb them by forming hydrogen bonds between the –NH group in pyrrole monomers and CS's –OH and –NH2 groups on its surface. Consequently, the pyrrole molecules can adhere to the CS-MNPs' surface by creating a compound in the solution. PPy-CS-Fe3O4 MNCs were generated through chemical oxidative polymerization of polypyrrole under the influence of CS-Fe_3O_4.

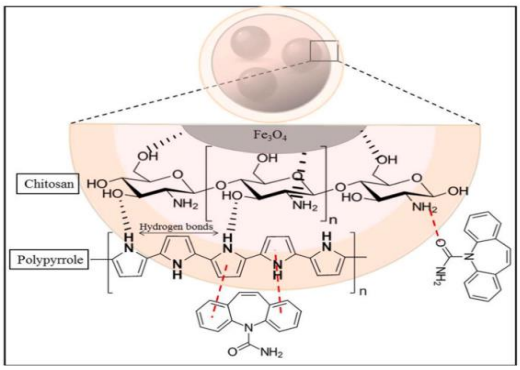


Fig 20 : . Diagrammatic representation of the PPy-CS-Fe3O4 MNCs structure and the different possible interactions.adapted by permission of [152] copyright© 2021 Published by Elsevier Ltd.

7. Conclusion

employing and recycling Chitosan and its alterations in wastewater treatment, particularly toevaluate their durability and repeated use, as it may prove instrumental in reducing Carbamazepine medication, its by-products, and corresponding derivatives.

Chitosan, an abundant biopolymer, is commonly employed in wastewater treatment to eradicate various pollutants. Various approaches are being considered. Adsorption has experienced significant progress in recent years, enabling the potential for future industrial progress, and providing a reliable supply and characterization of chitosan samples. Chitosan exhibits great potential as an adsorbing agent and can be modified in diverse ways, such as grafting, cross-linking, and functionalization to generate composites. Chitosan has noteworthy potential and is derived from chitin, a plentiful substance in marine environments, specifically the exoskeleton of crustaceans, mollusk cartilages, insect cuticles, and microorganism cell walls. The initial part of this review focused on the discussion of the existence of CBZ in both the inflow and outflow of the plants responsible for treating wastewater and potable water. Based on our research analysis, the elimination of CBZ in wastewater treatment plants is below 50% when only secondary treatments are employed, but the utilization of primary or tertiary treatments results in improved CBZ elimination.

Moreover, the harmful elimination of CBZ often occurs due to conjugated chemical recombination within the plant or through solid release. Chitosan displayed hopeful outcomes for sensing and eliminating CBZ from wastewater. As a result, it is crucial to explore effective methods for further

Ecotoxicological impact of pharmaceuticals found in treated wastewaters: Study of Carbamazepine, clofibric acid, and diclofenac. Ecotoxicol. Environ. Saf. 2003, 55, 359–370. [CrossRef].

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