

# REMOVAL OF AMOXICILLIN THROUGH DIFFERENT METHODS, EMPHASIZING REMOVAL BY BIOPOLYMERS AND ITS DERIVATIVES. AN OVERVIEW

FRANCISCA L. ARANDA AND BERNABÉ L. RIVAS\*

Polymers Department, Faculty of Chemistry, University of Concepcion, Casilla 3-C, Concepción, Chile.

## ABSTRACT

Although pharmaceutical compounds such as antibiotics have been of great help to animals and humans, the excessive use of them have become a global problem due to the resistance of pathogens to these drugs, for this reason a series of methods have been reported that we will see below that allow to remove efficiently, economically, and environmentally friendly compounds such as antibiotics.

The aim of this overview is the removal of amoxicillin via different methods, emphasizing removal by biopolymers and its derivatives.

**Keywords:** Antibiotics, Amoxicillin, Polymers, Removal, Bioadsorbents.

## 1. INTRODUCTION

A wide variety of organic compounds that we currently know are used in different areas of the work where pharmaceutical products are one of the most used compounds worldwide [1-3] and their effects have been studied extensively [4, 5], so that different authors [6-8] have established that these species are not biodegradable and it is estimated that more than 76% of the species that enter the different environmental matrices without presenting major changes. These compounds have physiological impacts on different organisms. Specifically, antibiotics are the pharmaceutical compounds with the greatest impact on different organisms, as well as on the environment. These are detected with high frequency in the aqueous medium due to their great use, both in the veterinary, human and aquaculture areas, where the elimination is of low or no efficiency in wastewater treatment plants [9], finding concentrations ranging from nanograms to milligrams per liter, in surface fresh waters they can reach up to 50 g L<sup>-1</sup> in the African continent, 10 g L<sup>-1</sup> in Europe, 15 g L<sup>-1</sup> in America and up to 450 g L<sup>-1</sup>, in Asian countries [10]. Although these concentrations do not have a major direct impact on humans, they do have an indirect impact, since microorganisms are seriously affected by antibiotics at concentrations below 10 µg L<sup>-1</sup> [11-13].

When antibiotics reach the environment, they can cause toxicity [14-16] in some organisms, added to this, is one of the biggest problems caused by antibiotics that is related to the development of resistant bacteria where every year about 33,000 people die [9, 17-19]. The presence of these compounds and their metabolites in water bodies are causing different types of human health problems due to these bacteria resistant and multidrug-resistant to different antibiotics, causing genotoxicity [20], mutagenicity, endocrine disruption, different types of cancer and even miscarriages.

It has been recorded that the consumption of antibiotics ranges between 100,000 and 200,000 tons per year, however, consumption in humans registered an increase of 36% between 2000 and 2010. There are 3 main pathways in which

antibiotics can enter freshwater bodies [10]: 1) Effluents from wastewater treatment plants, 2) chemical manufacturing plants, and 3) animal husbandry and aquaculture [21, 22]. With the information given, this article will review general aspects regarding antibiotics, resistance to them, effects and different methods of removal.

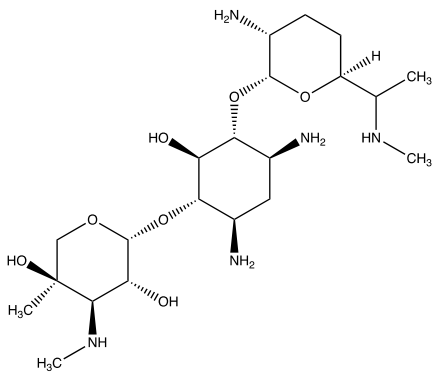
## 2. GENERAL ASPECTS ON ANTIBIOTICS

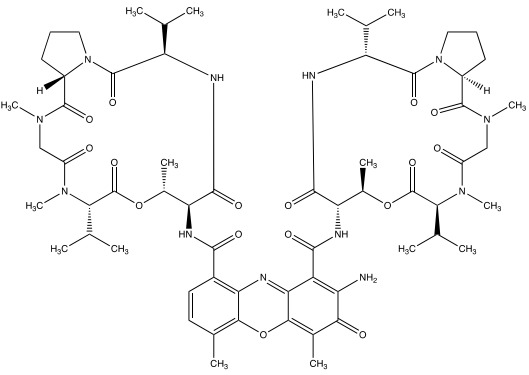
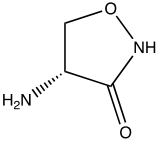
They are defined as natural, semi-synthetic and/or synthetic compounds with antimicrobial activity that can be applied parentally, orally or topically [23]. Used in different areas, such as medicine, agriculture and livestock, antibiotics are products that are widely used worldwide [24]. Since the discovery of penicillin in 1928, the development and discovery of antibiotics was what changed modern medicine, extending the half-life of people by 23 years [25]. However, since 1950 there has been a gradual decrease in terms of new antibiotics and with it the increase in their resistance, due to the wide use of them [26, 27]. It should be noted that, in the year 2000, more than 16,000 tons were produced in the United States alone, and more than 70% was used in livestock [28]; in 2015, countries such as India became the largest consumers of antibiotics [29]. While by 2050, it is estimated that the death of people will exceed 10 million a year from drug-resistant infections [30-32].

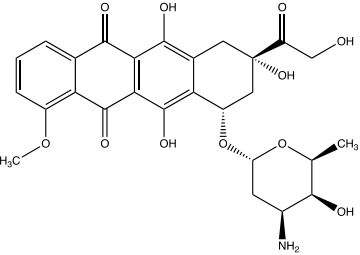
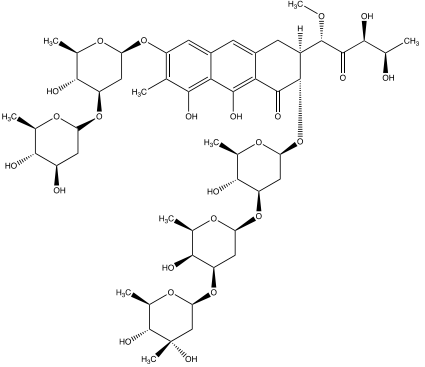
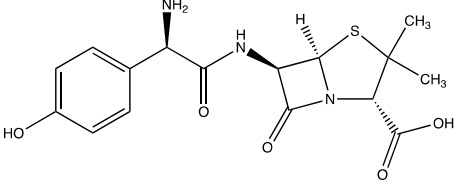
### 2.1 Classification of antibiotics

Antibiotics, organic compounds that have a series of classifications but where the most common is that based on their molecular structures, method of action and spectrum of activity [33] (see Table 1). Based on its mechanisms of action, inhibition of cell wall synthesis [34], alteration of the cell membrane [31], inhibition of protein synthesis [35], inhibition of nucleic acid synthesis, among others, [36].

**Table 1.** General classification of antibiotics.

Antibiotic	Molecular structure	Function	Active Ingredient	General use	Reference
Aminoglycosides		Inhibition of protein synthesis	Amikacin Apramycin Dihydrostreptomycin Gentamicin Kanamycin Neomycin Sisomicin Spectinomycin Streptomycin	Veterinary and human	[37-39]

<p>Actinomycines</p>		<p>Inhibition of the synthesis of nucleic acids</p>	<p>Actinomycin D</p>	<p>Human</p>	<p>[40, 41]</p>
<p>Amino-acid and peptide derivates</p>		<p>Inhibition of cell wall synthesis</p>	<p>b-peptides Magainins D-Cycloserine</p>	<p>Human</p>	<p>[42, 43]</p>

Antibiotic	Molecular structure	Function	Active Ingredient	Use	Reference
<p>Anthracyclines</p>		<p>Inhibition of DNA and RNA synthesis</p>	<p>Daunorubicin Doxorubicin Epirubicin Pirubicin Valrubicin</p>	<p>Human</p>	<p>[44-47]</p>
<p>Anthracenones</p>			<p>Mithramycin Streptozotocin Pentostatin</p>	<p>Human</p>	<p>[48-53]</p>
<p><math>\beta</math>-Lactams</p>		<p>Inhibition of cell wall synthesis</p>	<p>Amoxicillin Ampicillin Azlocillin Benzylpenicillin Carbenicillin Cloxacillin Cephalexin Cephalotin Cefazolin Ceftiofur Cefataxim Cefotiam Cefquinome Dicloxacillin Flucloxacillin Methicillin Mezlocillin Nafcillin Oxacillin Penicillin G Piperacillin</p>	<p>Veterinary and human</p>	<p>[54-60]</p>

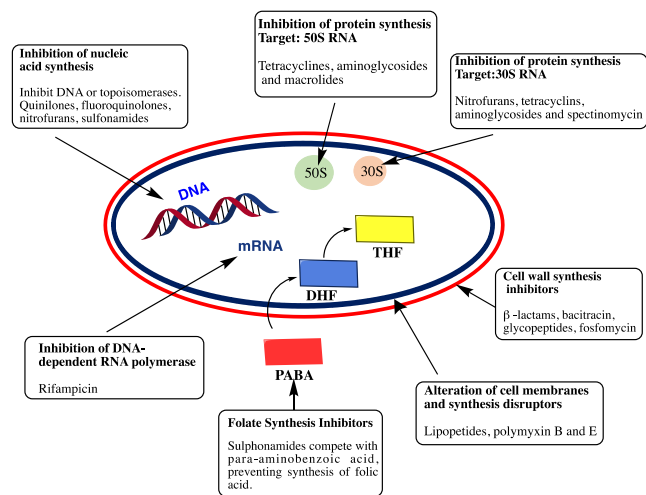
Diaminopyrimidine		Inhibition of purine and pyrimidine	Trimethoprim	Human	[61, 62]
Enediynes			Calicheamycin	Human	[63-65]
Epothilones		Inhibition of cell division	Epothilone A Epothilone B	Human	[66, 67]
Glycopeptides		Acting on the wall or membrane cell	Polymyxins (A & E) Teicoplanin Vancomycin Bleomycin	Veterinary and human	[68-70]
Lincosamides		Inhibition of protein synthesis by reversibly binding to the 50S ribosomal subunit	Clindamycin Lincomycin	Veterinary and human	[71, 72]
Macrolides		Inhibition of protein synthesis by reversibly binding to the 50S ribosomal subunit	Azithromycin Clarithromycin Erythromycin Natamycin Oleandomycin Roxythromycin Spiramycin Tilmicosin Tylosin	Veterinary, human and food additive	[71, 73-82]
Mitosanes		Inhibition of the synthesis of nucleic acids	Mitomycin C	Human	[83, 84]
Nitrofurans		Inhibition of the synthesis of nucleic acids	Furaltadone Furazolidone Nitrofurantoin Nitrofurazone	Veterinary and human	[85, 86]

Nitroimidazole		Inhibition of nucleic acid synthesis	Metronidazole Tinidazole	Human	[87-90]
Phenicol and amphenicols		Inhibition of protein synthesis	Chloramphenicol Thiamphenicol	Veterinary	[82, 91, 92]
Phosphonates		Inhibition of cell wall synthesis	Fosfomicin Phosphonothrixin	Human and herbicides	[93-95]
Polyetherionophores			Laidlomycin Lasalocidacid Maduramycin Monensin Narasin Salinomycin Semduramycin	Veterinary	[96-99]
Quinolones and Fluroquinolones		Inhibition of DNA replication	Ciprofloxacin Enrofloxacin Flumequine Marbofloxacin Nalidixic acid Ofloxacin Oxolinic acid	Veterinary and human	[100-104]
Rifamycins		Inhibition of nucleic acid synthesis	Rifampicin Rifapentine	Human	[105-107]
Sulfonamides		Inhibition of the folic acid synthesis	Mafenide Sulfachloropyridazine Sulfanilamide Sulfadimethoxine Sulphamethazine Sulfadimidine Sulfamethoxazole Sulfapyridine Sulfathiazole Sulfadiazine Sulfisoxazole	Veterinary and human	[108-111]
Tetracyclines		Inhibition of the protein synthesis	Chlortetracycline Doxycycline Oxytetracycline Tetracycline	Veterinary and human	[58, 112-116]

### 3. ANTIBIOTIC RESISTANCE

Although there is a large number of antibiotics with multiple functions, microorganisms have presented different mechanisms of action (see Fig. 1) that over time have allowed them to generate resistance to them, which can be of intrinsic or acquired origin that allows the microorganism the ability to survive these drugs [117]. Resistance can be a direct result of competitions between microorganisms in the environment but also due to spontaneous mutations that give them adaptation [118].

The wide range of antibiotics are difficult to fully absorb because the metabolic capacity is very limited. That is why the inappropriate use of antimicrobials in the area of human health, veterinary, agriculture and aquaculture [119, 120] are the main agents of release of this type of drugs to the environment and in particular to water. Once antibiotics come into contact with the environment, through discharges from hospital facilities, pharmaceutical industry, landfills [24, 121], groundwater, urine, feces, etc., they are maintained for a long time being very minimal their degradation, where it is established that between 20-90% [23, 113, 122, 123] of the antibiotics consumed are not metabolized and end up being excreted without presenting changes or in forms of derivatives or metabolites [124] reaching directly to the different aquatic systems. Thus, due to the (increasing) presence of this type of pollutants in the different aquatic systems, it is known as "emerging pollutants" [125].



**Figure 1.** Mechanisms of action of some antibiotics. Adapted and modified image [124, 126, 127].

Emerging pollutants are those that are not monitored on a regular basis or are simply not monitored [128] or regulated [129], so that the effects on the environment and health are not yet well known. It has been reported that between 2000 and 2015 the use of antibiotics increased by more than 65% and most have the ability to generate strains that are highly resistant in the environment [130-133]. This resistance occurs when bacteria change to the point that they can reduce or eliminate the effectiveness against the drug [134], and that their resistance can occur in several ways:

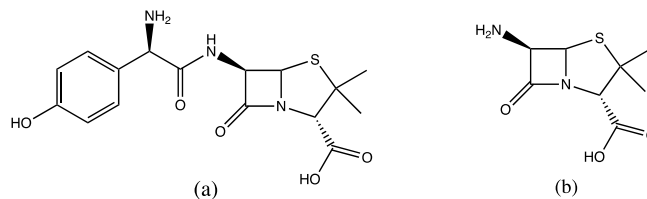
- Appearance of ( $\beta$ -lactamases that cleave the ring  $\beta$ -lactam of this type of antibiotics [135].
- The target can be altered so that it can reduce the affinity of the antibiotic [136-138].
- Mutations that upregulate the expression of transmembrane efflux pumps that can reduce the concentration of antibiotics in the bacterial cell. Thus, efflux pumps can pump out several different types of antibiotics causing a multidrug-resistant phenotype [139, 140].

In this particular case, we will detail in a particular antibiotic, reviewing both general aspects, such as removal via classic treatments and new methods of removal.

#### 3.1 Amoxicillin (AMX)

It is a  $\beta$ -lactam antibiotic that belongs to the group of penicillins [141, 142]. The basic structure of penicillins, 6-aminopenicillanic acid (see Fig. 2b) consists

of a ring of thiazolidine fused with a ring of  $\beta$ -lactam with a side chain. Amoxicillin (Mw: 365.4 g mol<sup>-1</sup>) presents in the side chain an amino group (see Fig. 2a) that improves stability towards acids, however, it can be part of consecutive reactions in neutral or alkaline conditions.

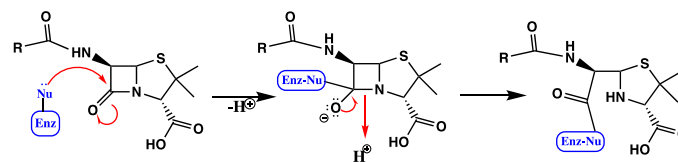


**Figure 2.** Molecular structure of AMX (a) and 6-aminopenicillanic acid. Design of molecules via ChemDraw. Adapted figures [113, 143].

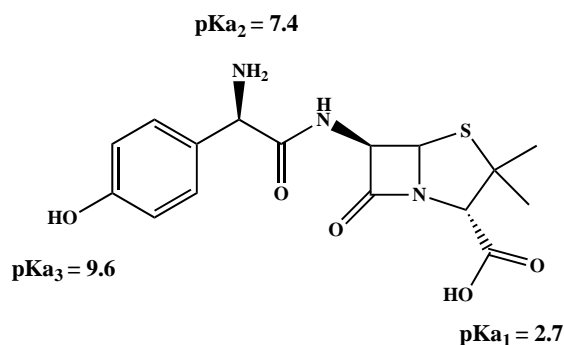
In human medicine, penicillins are the most commonly consumed antibiotics in the European Union, where amoxicillin is consumed in 22 of 30 countries. Also in other countries such as India [144] or Brazil [145]. Amoxicillin is very active against both Gram positive (Gram+) and Gram-negative (Gram-) organisms, including several enteric pathogenic organisms. Amoxicillin is widely used in veterinary practice for the treatment of systemic gastrointestinal infections. Amoxicillin is a known penicillin that is added to medicated foods at a level of 250 to 500 mg kg<sup>-1</sup>, due to its resistance to gastric juice. In the case of humans, after oral intake of amoxicillin, 43 - 75% is excreted and not metabolized [142, 146, 147]. Considering that there is a high rate of excretion and that its half-life is 9 days, this antibiotic has been found in wastewater [148, 149] and effluents from wastewater treatment plants and even in surface water [150].

##### 3.1.1 Mechanism of action of amoxicillin

This antibiotic is commonly used due to the broad spectrums in terms of its mechanism of action (see Fig. 3) as it stops the proliferation of different bacteria [151, 152]. In general, penicillins inhibit a bacterial enzyme called the transpeptidase enzyme that is involved in the synthesis of the bacterial cell wall [153]. The  $\beta$ -lactam rings are involved in the inhibition mechanism. Penicillin covalently binds to the active site of the enzyme, leading to irreversible inhibition. In addition to the above, it is important to mention that amoxicillin has amphoteric properties [154], a property conferred by its three main functional groups, COOH (pK<sub>a1</sub> = 2.7), NH<sub>2</sub> (pK<sub>a2</sub> = 7.4) and OH (pK<sub>a</sub> = 9.6) as shown in Figure 4 [155-157].



**Figure 3.** Mechanism of action of amoxicillin.



**Figure 4.** pK<sub>a</sub> values of the main groups of amoxicillin. Adapted image [155].

In this way, the molecular structure is affected by the pH changes to which it may be subjected. In this way, at pH 10 amoxicillin degradation is recorded in time of 24 h at pH 5 there is no further degradation and at pH 1 degradation is recorded transforming amoxicillin into amoxicillin acid (see Fig. 5) [158-160].

Thus, at pH values close to neutral, amoxicillin is more stable and has less degradation than at acidic or basic pH. However, it should be considered that at high temperatures (55°C) approximately amoxicillin, even if it is in a solution at neutral pH, it decomposes [161].

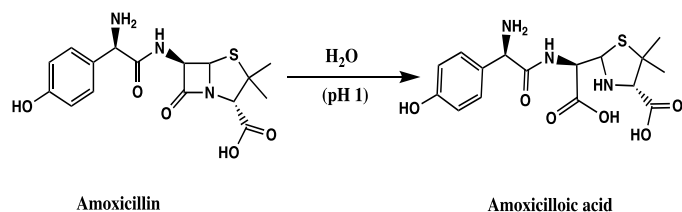


Figure 5. Passage from amoxicillin to amoxicilloic acid at acidic pH.

#### 4. REMOVAL OF ANTIBIOTICS

Antibiotics are known to fight the presence of diseases caused by bacteria around the world. However, these have become a global problem in recent years, due to the presence in aqueous systems, being considered as emerging pollutants like many other organic pollutants. Because of this, many organic compounds have been considered highly dangerous because they can cause serious problems in both humans and different ecosystems [162, 163]. To reduce the problem of the presence of antibiotics in environmental systems, a wide variety of techniques have been reported that can range from biological to chemical [164, 165] that allow to obtain very good results in terms of the removal of these contaminants. Among these techniques that are considered of great importance due to the removal of antibiotics are the physicochemical processes such as advanced oxidation (AOPs) and ozonation [166] which has two mechanisms for the effective degradation of antibiotics based on ozone, which corresponds to indirect oxidation through the generation of free radicals, which function as alternatives or complementary in traditional wastewater treatment [167-169].

It is important to mention that advanced oxidation processes are processes that have technologies to degrade and mineralize the recalcitrant organic matter found in different bodies of water when reacting with hydroxyl radicals [170, 171] responsible for decreasing the levels of Chemical Oxygen Demand (COD) / Biological Oxygen Demand (BOD) by separating the oxidizing organic and inorganic components, therefore, it is considered an alternative to traditional methods and that make it possible to increase the degradability of pollutants in wastewater and also, the inactivation of pathogenic organisms [172, 173] so that concentrations can be eliminated or reduced in ranges that do not affect environmental systems, there is also the removal of antibiotics in wastewater through the use of cellulose membranes [174], granular activated carbon [175], powdered activated carbon [176], clays [177], polymers [178], among others adsorption techniques. To effectively perform this removal of compounds, the latter are used (adsorption) because they are the most economical, easy to obtain, with high percentages of reuse and environmentally friendly [162, 179, 180].

This overview will look at the removal of amoxicillin via different methods, emphasizing removal by biopolymers and its derivatives.

##### 4.1 Removal of Amoxicillin (AMX)

###### 4.1.1 AOPs for amoxicillin removal

The different advanced oxidation processes have been used effectively for the removal of different types of contaminants, whether for metals [181, 182], pesticides [183, 184], pharmaceutical compounds [185, 186], among others. In this way we find that there are advanced oxidation processes based on sulfate radicals (SR-AOP) since their high oxidizing power allow a high capacity to degrade organic compounds, so when detailing in factors such as temperature, pH, amount of catalyst [187] and concentration of the oxidant it was determined that they affect the elimination rate of AMX so this study allows to demonstrate that SR-AOP have the ability to degrade organic pollutants such as amoxicillin [188].

Other studies are based on the treatment of AMX by irradiation and/or ultrasonic ozonation of medium - high frequency. They considered that the presence of alkaline species and humic acid presented a negative effect on elimination, decreasing by about 50%, thus, the application of ozonation allowed a rate of elimination 50 times faster than the mere use of ultrasound, so the use of the hybrid oxidation system was the best option in terms of the elimination of

amoxicillin [189]. In this study they relied on the oxidative degradation of amoxicillin, suggesting 3 possible mechanisms based on hydroxylation (addition of  $\text{OH}\cdot$  to the original compound), opening of the ring  $\beta$ -lactam of four members and decarboxylation of free carboxylic acid and reorganization of the five-membered thiazole ring [190-194].

The study considers the different ionized forms of amoxicillin (see Fig. 6) in order to demonstrate that degradation is greater when the amine is deprotonated (pH 10), there is a pair of free electrons for electrophilic attack, in addition there is a greater solubility of AMX crystals at that pH [195].

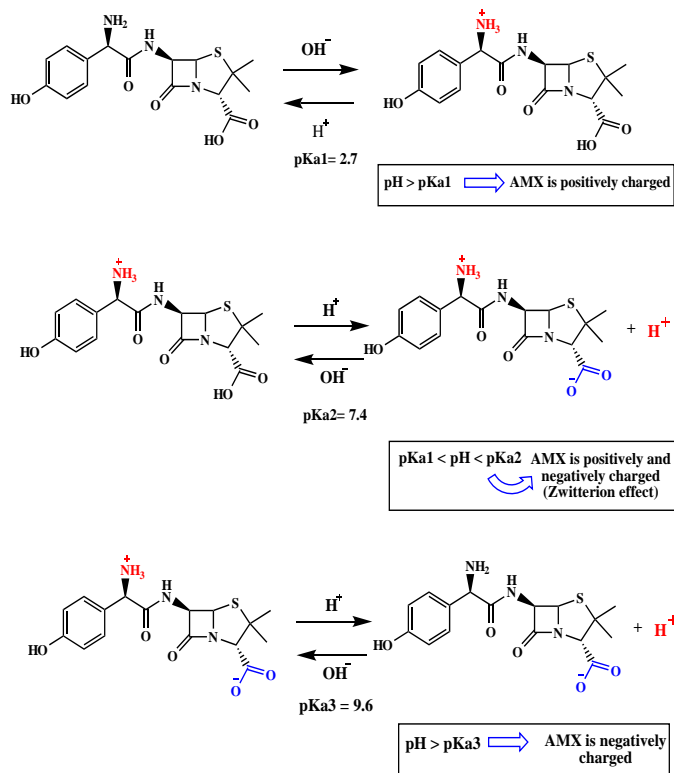


Figure 6. Ionized forms of amoxicillin in its different pKa values.

However, despite the fact that oxidative degradation is observed, the authors mention that many of the existing AOPs do not lead to complete degradation, so a large number of intermediates are generated in the reaction. In this way, it is important to study these intermediates because, more toxic compounds may be generated than the initial one, so it is recommended that no type of treatment be carried out [189].

In addition to these, there are electrochemical processes [196], bioelectrochemical [197], Fenton and photo-fenton [198], AOPs based on UV rays [199], among others.

###### 4.1.2 Biochar for amoxicillin removal

The use of biomass for the preparation of new materials is a good avenue for the removal of contaminants at low cost and friendly to the environment. This is why many authors have worked by using biochar for the removal of different types of antibiotics such as AMX.

There are studies based on the manufacture of biochar derived from sludge from domestic wastewater treatment plants [200]; Biochar compatible with Ag/Fe nanoparticles for effective removal of antibiotics, with 86% effectiveness [201]; biochar from banana pseudostem fibers impunged with  $\text{CoFe}_2\text{O}_4$  nanoparticles determining that it is a good AMX adsorbent over a wide pH range [202]; another type is one that is prepared with microsphere catalysts consisting of magnetic Cu-Fe-FeC3 in biochar doped with nitrogen, using chitosan as a carrier material. This catalyst allowed its application in a wide pH range, in addition to having very good stability and low leaching of metal ions allowing a high degradation of organic pollutants. So the synthesis and use of efficient catalysts based on biochar in electro - Fenton heterogeneous systems highly beneficial, obtaining removals of 99.3% and even in the tenth cycle a elimination rate of 93% was recorded demonstrating a good stability of the material [203];

there is also biochar derived from poultry waste feathers, so it is considered an ecological, cheap and practical method. Based specifically on the keratin of the pen, a 99.97% was obtained in terms of elimination efficiency [204].

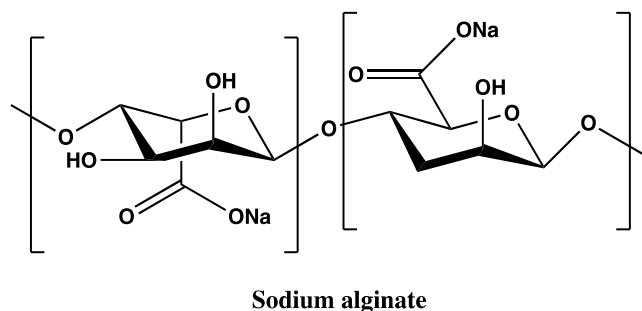
#### 4.1.3 Biopolymers for amoxicillin removal

As is well known, the release of pharmaceutical compounds, such as antibiotics, have been of growing concern globally due to the effects they have on the environment and the general population. Over time, a wide variety of methods have been studied to make the removal of these compounds possible. However, most of these methods have important disadvantages such as the associated economic [205] and energy costs [206], which are not friendly to the environment, the complex assembly and even the formation of toxic intermediate compounds [189]. Therefore, it is necessary to develop economical, environmentally friendly, efficient and easy-to-use materials [207, 208]. Among them, biopolymers have these characteristics in addition to their easy modification and biocompatibility [209, 210] make them ideal for application in different methods of elimination.

A very wide variety of antibiotic removal has been reported using different types of polymers and biopolymers [114, 211-218], among which we find removal of tetracyclines [112, 113, 219] and oxytetracyclines [114], ciprofloxacin [220], sulfamethoxazole [221], metronidazole [222], chloramphenicol [223], penicillin [224], amikacin [225], amoxicillin [59, 125], among other antibiotics.

##### 4.1.3.1 Removal of amoxicillin by alginate

Alginate is an anionic polysaccharide (see Fig. 7) that has non-toxic characteristics, is stable, biocompatible and has the ability to form cross-links with different types of cations such as calcium carbonate, it is also a cost-effective material that allows its use in different areas such as tissue engineering, biomedical, environmental, etc. [226, 227].



**Figure 7.** Molecular structure of sodium alginate. Adapted image [228].

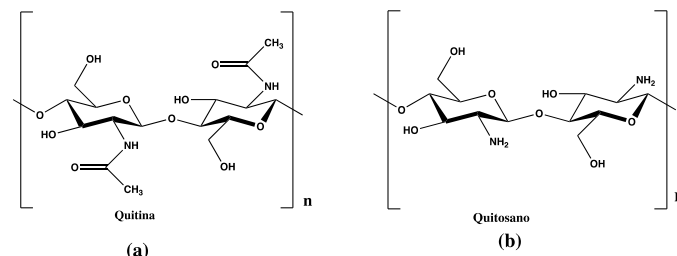
Based on this material, a series of investigations have been reported in which the removal of amoxicillin is quite efficient. For this purpose, magnetic beads of alginate/glycodendrimer have been designed for the elimination of tetracycline and amoxicillin, these beads were prepared by encapsulating triazine dendrimer functionalized with  $\text{Fe}_3\text{O}_4$ /maltose in alginate. The authors mention that the adsorption of antibiotics was strongly affected by temperature, pH, contact time, adsorbent dose, ionic strength and initial antibiotic concentration. However, the maximum adsorption capacity was  $475.19 \text{ mg g}^{-1}$  for tetracycline and  $416.67 \text{ mg g}^{-1}$ , and its adsorption was possible through electrostatic interactions, hydrogen bonds and  $\pi$ - $\pi$  interactions, so the removal of antibiotics turned out to be quite effective with this type of alginate-based polymers [229]. Other materials based on alginate correspond to graphene oxide/calcium alginate biocomposites for the elimination of amoxicillin [230], giving very good results since on the surfaces of graphene oxide we can find epoxy, hydroxy, carbonyl, carboxylic acid groups, and where alginate provides hydroxyl groups and functional carboxylic acid groups. Where the mechanism of amoxicillin adsorption is explained, as in other cases, by ionic interaction, hydrogen bonds and  $\pi$ - $\pi$  interactions [229].

There are also nanocomposites based on limestone, activated carbon, and sodium alginate in order to remove antibiotics and different types of drugs from aqueous solutions. This compound showed advantages such as the speed of removal, the simplicity of its preparation, multifunctionality and high efficiency. Therefore, the results show an amoxicillin removal of 99.6% in a contact time of 40 min [231]. In this way, there are other investigations in which they refer to

the removal of amoxicillin and other antibiotics such as: cephalixin, through the use of *Saccharomyces cerevisiae* (corresponds to a fungus, type of yeast used in the manufacture of bread, beer and wine) immobilized in calcium alginate as a biosorbent [232], sulfamethoxazole, using sodium alginate/magnetic hydrogel microspheres [226], among others.

##### 4.1.3.2 Removal of amoxicillin by chitosan

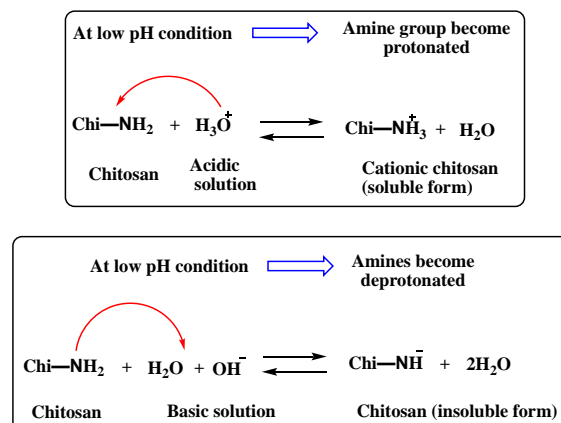
Chitosan, derived from chitin [233] (see Fig. 8) is one of the substances with the greatest abundance and distribution after cellulose [234]. Chitosan, (1,4)-2-amino-2-deoxy-D-glucan, is a linear polyamnosaccharide obtained after N-deacetylation of chitin [235-237]. Chitin is the structural component of the exoskeleton of shrimp, lobsters and crabs [234] it is also present in the cell walls of fungi and yeasts [237, 238], green algae and cuticles of insects and arachnids. Chitosan has gained great momentum due to its biological properties, non-toxicity [239] and its applications in the medical, food, etc. Sectors [233, 235, 240]. The recovery of chitosan from seashell waste and seafood debris generated by the food processing industries makes this polymer one of the most important renewable assets. Now, due to the extensive properties of chitosan [241], several investigations have been reported regarding the removal of antibiotics through the use of it. Thus, the literature indicates the adsorption of antibiotics such as ciprofloxacin [113], erythromycin, amoxicillin [242], amikacin [243], tylosin, norfloxacin [244], among others, in which adsorption was established as high capacity.



**Figure 8.** Structures of chitin (a) and chitosan (b).

Chitosan, being a polysaccharide that has different characteristics such as being biocompatible, presenting biodegradability and antibacterial activity [245, 246] it has been shown that its use exhibits better properties than other commercial pearls or microbeads [247] and can adsorb potentially toxic compounds [248]. The literature mentions that the use of chitosan either in the form of chitosan beads [249], chitosan-carbon pearls [250] chitosan resin pearls [251] etc. for the removal of antibiotics such as amoxicillin is quite effective.

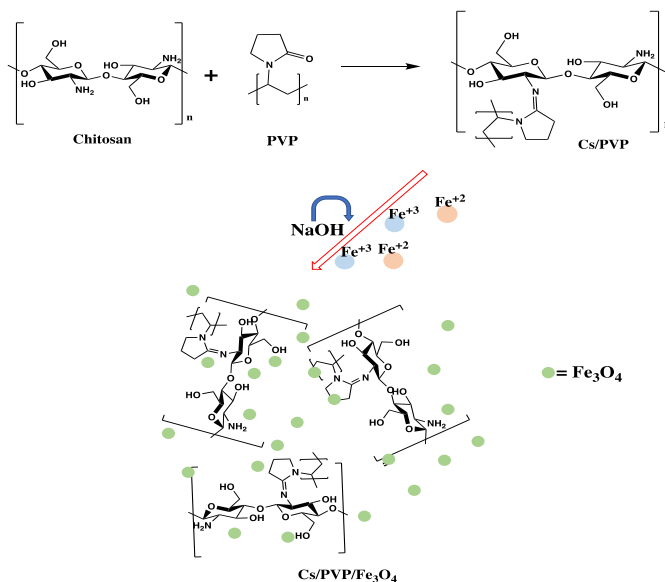
Chitosan, like many molecules has different behaviors depending on the pH at which they are faced, figure 9 details the behavior of chitosan against basic and acidic solutions. In general, chitosan molecules are ionized approximately up to pH 6 and ionization increases as the pH moves towards lower values. Thus, the amino groups of the chains, at a certain pH, capture the  $\text{H}^+$  ions in solution [252, 253]



**Figure 9.** Outline of the behavior of chitosan against acidic and basic solutions. Adapted image [254].

For the removal of amoxicillin,  $\text{Fe}_3\text{O}_4$ /activated carbon/chitosan adsorbents prepared by co-precipitation methods have been used, which turns out to be a fairly simple technique; this method yielded good results in terms of the removal of 3 antibiotics under study among which is AMX. The authors mention that the absorption value decreases almost linearly as the amount adsorbed increases. Finally, an approximate elimination of 72% of amoxicillin was achieved [255]. Chitosan has also been used to remove mixed contaminants such as pharmaceutical compounds and heavy metals. Specifically, the design of Fe/Ni bimetallic nanoparticles that have been stabilized with chitosan were quite effective for the removal of AMX and Cd(II) from aqueous solutions with results of 68.9% and 81.3% elimination of AMX and Cd(II) respectively [256]. With a series of results obtained via SEM, EDS, XDR, and FTIR, they were able to verify that the formation of iron oxides allowed the adsorption of Cd(II) on the oxide [257], at the same time, the nanoparticles designed showed functions of catalytic reduction of contaminants. Regarding the reuse of the material, results of decrease in disposal efficiency ranging from 68.9% to 2.2% for AMX and 81.3% to 22.8% for Cd(II) after the third cycle were obtained. This behavior is explained due to the formation of oxides, adsorption of Cd(II) and corrosion on the surface of the nanoparticle which leads to a leaching of the Fe/Ni system, so it is determined that the nanoparticle loses its reactivity [258].

Another quite attractive compound for the removal of AMX consists of the synthesis of a magnetic compound of chitosan / PVP (CPF) by means of a co-precipitation [259] to finally form the compound chitosan / PVP /  $\text{Fe}_3\text{O}_4$  (see fig. 10) taking into account different proportions (CPF37, CPF55, CPF73), where they report that the best adsorbent corresponds to CPF37 reaching 93% efficiency at pH 8. The use of different spectroscopic techniques such as FTIR, SEM-EDX, TEM, VSM, XDR, TG-DTA, DSC allowed them to have an excellent characterization of the material.



**Figure 10.** Chitosan/polyvinylpyrrolidone/ $\text{Fe}_3\text{O}_4$  compound design for the removal of AMX and Cd(II). Adapted image [259].

### CONCLUSIONS

Organic pollutants, particularly antibiotics, are compounds of high environmental concern globally due to the serious problems they generate. So over the years, a series of environmentally friendly methods have been sought and at the same time economical and efficient to allow an effective removal of this type of contaminants. In this way, bio-based materials have greater and better characteristics than conventional treatments. In general, chitosan-based materials are highly effective in terms of the removal of different types of contaminants, in addition to their non-toxic, biocompatible, economic, natural origin, economic, easy-to-use nature, among other characteristics, making it an ideal material for use in environmental remediation issues.

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