

# Chitosan: an overview of its multiple advantages for creating sustainable development poles

Cristóbal Lárez-Velásquez<sup>1\*</sup> 

<sup>1</sup>*Grupo de Polímeros, Departamento de Química, Facultad de Ciencias, Universidad de Los Andes, Mérida, Venezuela*

\*[clarez@ula.ve](mailto:clarez@ula.ve)

## Abstract

An overview perspective of the potential of chitin and chitosan biopolymers to promote economically and environmentally sustainable development poles, which could be exploited especially in developing countries, is presented. Their following advantages have been considered and briefly outlined: (i) the natural sources of chitin have a wide distribution on the entire planet and are usually accessible as inexpensive waste materials; (ii) the great versatility of these materials, with applications in diverse fields such as agriculture, water treatments, food industry, environment, petroleum, healthcare, energy, technology, etc., with some trials conducted even off-planet; (iii) the production and use of these materials could promote advances in the endogenous capacity of some countries to create own technologies and generate products and applications, basic and advanced, in sensitive sectors, i.e., health services, food, water treatments, etc., in addition to promoting the necessary integration of the academic sector with other sectors such as industry and business.

**Keywords:** *sustainable growth poles, renewable sources, endogenous development, nanotechnology.*

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## 1. Introduction

It is difficult to find materials that offer such varied possibilities for the development of useful product lines, in so many fields of human activity, such as chitin and its main derivative, chitosan. But if this is not motivation enough, enthusiasm can be increased by the great diversity of easily accessible natural sources that allow them to be obtained sustainably, at relatively low costs from waste, as well as without the use of renewable resources traditionally employed to produce food for humans and animals. Other factors that can promote its use are related to the economic feasibility of its preparation<sup>[1]</sup> and the technological viability for the development of its applications in many industrial sectors<sup>[2]</sup>. As vivid examples of some of the fields of application in nanotechnology, the following can be briefly mentioned: the production of biodiesel using enzymes encapsulated in nanoparticles, which provide protection to bioactive species and extend the reusability of biocatalysts<sup>[3]</sup>; the use of nano-biocomposites for the preparation of active food packaging<sup>[4]</sup>; the use of chitosan nanoparticles as effective antimicrobial agents, especially due to the increasing resistance to traditional drugs developed by different pathogens<sup>[5]</sup>; the manufacture of nano-biocomposites with graphene and metal oxides, which have shown hopeful performances in hyperthermic magnetic therapy for cancer treatment<sup>[6]</sup>; etc.

On the other hand, there is little information on chitosan-based growth poles promoted by the public sector, although there are many private biotechnological companies specialized in the production and the commercial exploitation of diverse

products based on this biomaterial (see Table 1 with a brief list of them), which would point to the fact that this type of entrepreneurship can be economically sustainable.

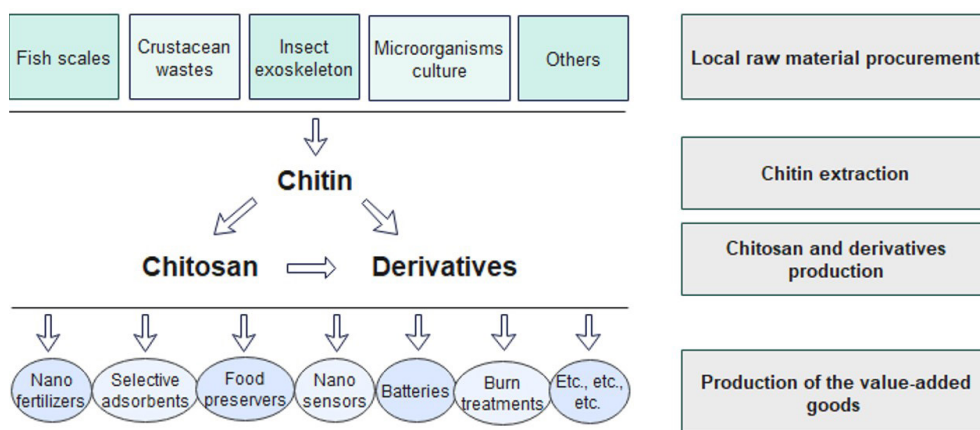
This article presents an overview of the potential applications of chitosan in sensitive areas for the development of a country, for instance, through the creation of local development poles (see Figure 1) capable of transforming local resources into value-added goods to be used to meet domestic and external demand. It is intended to stimulate research on them as well as their use for the generation of proprietary technologies that contribute to the growth of related industrial and technological sectors, particularly those able to launch sustainable growth pathways.

## 2. Chitin and Chitosan Sources

The natural sources containing chitin are very varied, including the exoskeleton of insects as abundant as cockroaches<sup>[7]</sup> and crickets<sup>[8]</sup>, continuing with the cell walls of fungi such as *Mucor rouxii*<sup>[9]</sup> and finding in the shells of a variety of crustaceans the traditional source for its current production<sup>[10]</sup>. Furthermore, the scales of some fish have been recently added to the extensive list of potential sources of chitin<sup>[11]</sup>, which opens new horizons for using these resources. On the other hand, the controlled cultivation of microorganisms, such as microalgae<sup>[12]</sup> and fungi<sup>[13]</sup>, has also been explored, with increasing conviction, in search of materials whose physicochemical properties do not show

**Table 1.** Some specialized companies in the production and commercial exploitation of chitosan-based products.

Company	Products	Website
Alpha Chitin	Chitin and chitosan from <i>Hermetia illucens</i> larvae, fungi, or krill	<a href="http://alpha-chitin.com">http://alpha-chitin.com</a>
Chibio Biotech	Chitin-glucan, <i>Agaricus bisporus</i> chitosan, <i>Aspergillus niger</i> chitosan, Oyster mushroom chitosan, Carboxymethyl chitosan	<a href="https://www.chibiotech.com">https://www.chibiotech.com</a>
ChitoLytic	Crustacean chitosans, Mushroom chitosans, Chitosan lactate, Trimethyl chitosan, Chitin	<a href="https://chitolytic.com">https://chitolytic.com</a>
Polymar	Crustacean chitosan powder, Poly Flocc (flocculant), Poly Protec (fungicide)	<a href="https://www.polymar.com.br">https://www.polymar.com.br</a>
ISF Chitin & Marine Products LLP	Chitin and chitosan from marine product processing wastes, Carboxymethyl chitosan	<a href="https://www.isfchitin.com">https://www.isfchitin.com</a>
Chitosanlab	Chitosan from crustacean shells and squid pens, Micronized chitin and chitosan, Chitosan nanoparticles, Chitosan quaternary ammonium	<a href="https://chitosanlab.com">https://chitosanlab.com</a>

**Figure 1.** Tentative characteristics of prospective local development poles based on chitosan.

variations dependent on factors such as the stage of growth of the different species used for their traditional production, or the seasonality of their captures. Additionally, this type of material should have better qualities regarding allergen and metal contents<sup>[14]</sup>.

The origin of the chitin used in the production of chitosan is a key factor to consider in its applications. For instance,  $\beta$ -chitin (obtained from squid feathers and possessing fibrils made up of parallel-oriented polymer chains) is easier to hydrolyze than  $\alpha$ -chitin (obtained usually from crustacean shells, fibrils made up of polymer chains in anti-parallel orientation)<sup>[15]</sup>. Table 2 summarizes the main natural sources that have been assayed and used to obtain chitin.

### 3. Some Suggested Sectors for the Development of Chitosan-Based Applications

#### 3.1 Agriculture

Applications of chitinous materials in agriculture can cover each of the stages involved in the production of vegetables and even expand outside the planet, since NASA began in 1997 the development of aeroponic to produce food in space, achieving chitosan-based formulations for such purposes, such as BEYOND™ from AgriHouse<sup>[40]</sup>. A few examples of proven agricultural applications for these materials are shown below.

- *Soil conditioning and bioremediation*: chitin has been studied in the amendment and remediation of the soil where a certain crop will settle<sup>[41]</sup>. Similarly, chitosan has been investigated in the remediation of soils contaminated with metals<sup>[42]</sup>. Additionally, chitin has also shown nematocidal activity when applied by spraying/irrigation or added directly to the soil<sup>[43]</sup>.
- *Seed preservation and bio-stimulation*: chitosan-based coatings have notorious beneficial effects on seeds<sup>[44]</sup> which are not limited to protection due to their recognized fungicidal activity<sup>[15,45]</sup>, or as a germination stimulant<sup>[46,47]</sup>, but additionally these can serve as vehicles for the controlled release of other agrochemicals<sup>[48]</sup>. Another interesting application for these biopolymers could be the preparation of artificial or synthetic seeds (hydrated or dehydrated explants, naked or covered with a protective polymeric bead)<sup>[49]</sup>.
- *Inducer of resistance to diseases caused by phytopathogens*: chitosan is a potent stimulant of the acquired resistance system to pathogens in plants<sup>[50]</sup>, especially for the induction of defense mechanisms against fungi<sup>[51]</sup> such as suberization during the wound healing process in potato tubers<sup>[52]</sup>, stimulation of the production of secondary metabolites, including phytoalexins<sup>[53]</sup>, lignin<sup>[54]</sup>, phenolic compounds<sup>[55]</sup>, callose<sup>[56]</sup>, etc., whose deposition plays an important role in limiting the spread of pathogens<sup>[57]</sup> and seems to be controlled by the molecular weight and the

**Table 2.** Main natural sources already explored to obtain chitin and chitosan.

Source	Specific examples
Arthropods	
- Insects	- Cockroaches <sup>[7]</sup> , crickets <sup>[8]</sup> , beetles <sup>[16]</sup> , flies <sup>[17]</sup> , bees <sup>[18]</sup> .
- Arachnids	- Spiders <sup>[19]</sup> , scorpions <sup>[20]</sup> .
- Crustaceans	- Crabs <sup>[21]</sup> , shrimps <sup>[22]</sup> , lobsters <sup>[23]</sup> , prawns <sup>[24]</sup> , krill <sup>[25]</sup> , spider crabs <sup>[26]</sup> .
- Myriapods	- Millipedes <sup>[27]</sup> and centipedes <sup>[28]</sup> .
Mollusks	- Squids <sup>[29]</sup> , cuttlefish <sup>[30]</sup> , clams <sup>[31]</sup> .
Fishes	- Tilapia <sup>[32]</sup> , rohu <sup>[11]</sup> , bocachico <sup>[33]</sup> .
Fungi	
- Basidiomycota	- <i>Lactarius vellereus</i> (yeast) <sup>[34]</sup> , <i>Agaricus bisporus</i> (common mushroom) <sup>[35]</sup> .
- Zygomycota	- <i>Mucor rouxii</i> <sup>[9]</sup> , <i>Rhizopus oryzae</i> <sup>[13]</sup>
- Ascomycota	- <i>Aspergillus niger</i> <sup>[36]</sup> , <i>Penicillium chrysogenum</i> <sup>[37]</sup> , <i>Penicillium camembertii</i> <sup>[38]</sup> .
Algae	
- Diatoms	<i>Thalassiosira fluviatilis</i> <sup>[39]</sup> , <i>Cyclotella</i> sp <sup>[12]</sup> .
- Green algae	<i>Pithophora oedogonia</i> , <i>Chlorella vulgaris</i> <sup>[39]</sup> .

degree of acetylation of the applied chitosan<sup>[58]</sup>. Among the numerous crops where elicitation by chitosan has been verified are tomato<sup>[59]</sup>, peach<sup>[60]</sup>, strawberry<sup>[61]</sup>, table grape<sup>[62]</sup>, etc.

- **Growth biostimulant:** chitosan is one of the most explored biostimulants in agriculture, with many successful applications<sup>[63]</sup>, i.e., its effect on root development in maize plants is notorious, especially in crop conditions under water deficiency<sup>[64]</sup>. Similarly, chitosan notably increases the production of some secondary metabolites in plants, as noted for the menthol production in mint crops<sup>[65]</sup>. Furthermore, the foliar treatment of tomato crops under salt stress with chitosan solutions prepared using citric or ascorbic acids increases the production of some metabolites, including osmolyte substances, which help to reactivate their development<sup>[66]</sup>.
- **Postharvest protection:** chitosan applications are profuse<sup>[67]</sup> because these biomaterials can simultaneously fulfill multiple functions such as an antimicrobial agent, elicitor, and physical isolation given their ability to form semi-permeable films<sup>[68]</sup>. Among the trends observed for these applications is the mixture with other natural materials to improve the effectiveness of these treatments, i.e., chitosan/*Aloe vera* gels to delay the post-harvest decay of mango fruits<sup>[69]</sup> and chitosan/carnauba wax/oregano oil to protect cucumber<sup>[70]</sup>. Likewise, research on the development of edible films by combining chitosan with other natural materials is copious and with striking results, highlighting the emblematic case of strawberries<sup>[71]</sup>.

### 3.2 Water treatments

The use of chitosan in processes related to water treatment is quite common today<sup>[72,73]</sup>, and a wide range of commercial products based on these biomaterials can be found on the market, such as Tidal-Clear, HaloKlear, Cesco FC-100, Crystal Lagoon, etc. The following is a summary of the applications of these biomaterials in related processes.

- **Coagulation/flocculation:** chitosan has been proposed as a possible candidate to replace widely used coagulants such as aluminum sulfate and ferric chloride in a more environmentally friendly way<sup>[74]</sup>. Several mechanisms have been outlined to explain the coagulating/flocculant action of these biopolymers<sup>[75]</sup>: (a) neutralization of the negative surface charges of the suspended particles by electrostatic interaction; (b) the simultaneous formation of a bridge between the particles; (c) formation of charge neutralization patches. Reported studies include the separation of clay suspensions<sup>[76]</sup>, mill effluents treatment during oil palm processing<sup>[77]</sup>, the harvest of microalgae<sup>[78]</sup>, protein recovery from fishmeal manufacturing wastewater<sup>[79]</sup>, textile industry wastewater treatments<sup>[80]</sup>, etc.
- **Adsorption:** chitosan has been extensively studied as a bio-adsorbent in various water treatments<sup>[81]</sup>. In addition, its derivatives can be used in a variety of ways<sup>[82]</sup>: powder, hydrogel spheres, films, fibers, etc. The functional groups present in its structure, and those introduced through chemical modification reactions, allow it to act as an adsorbent both for organics (dyes<sup>[83,84]</sup>, drugs<sup>[85]</sup>, oils<sup>[86]</sup>, etc.) and inorganics (heavy metals<sup>[87]</sup>, anions such as phosphates and nitrates<sup>[88]</sup>, ammonium and other nitrogen-containing salts<sup>[81]</sup>, etc.). Various biocomposites based on chitosan and other natural materials have also been prepared and tested as adsorbents<sup>[89]</sup>.
- **Filtration:** chitosan-based membranes have also been extensively studied, with numerous reports on the removal of pollutants, e.g. pressure filtration of aqueous solutions for the removal of Cu(II)<sup>[90]</sup>; nanofiltration of effluents from the textile industry for the removal of dyes<sup>[91]</sup>; adsorptive filtration for the removal of anionic and cationic species<sup>[92]</sup>, etc.

### 3.3 Food sector

Chitosan has been approved some years ago for use as a food additive in different countries, such as Japan in 1983 and Korea in 1995<sup>[93]</sup>. Chitosan obtained from *A. niger* has been evaluated without objection by the Food and Drug Administration (FDA) of the United States in 2011 as a direct secondary ingredient in the production of alcoholic beverages<sup>[94]</sup> and approved by the Food Standards Agency of Australia and New Zealand in 2013 as a processing aid in the production of alcoholic beverages<sup>[95]</sup>. Also, chitosan from white button mushrooms (*A. bisporus*) was recently added by the FDA as a “generally recognized as safe” (GRAS) material for use in foods and beverages<sup>[96]</sup>. A summary of studies on its applications in this sector is presented below.

- **Preserver agent:** chitosan applications as a food preservation additive may take advantage of consumer preferences for natural products<sup>[97]</sup>. Proposals on this topic include its use in meat<sup>[98]</sup>, fish<sup>[99]</sup>, milk<sup>[100]</sup>, cheeses<sup>[101]</sup>, sauces<sup>[102]</sup>, freshly cut fruit coatings<sup>[103,104]</sup>, fruit juices<sup>[105]</sup>, etc. Furthermore, numerous studies have also been carried out on its applications in wine production<sup>[106]</sup> and to prevent its spoilage<sup>[107]</sup>.
- **Clarifying agent:** due to its cationic nature, chitosan can interact with anions through electrostatic interactions, as well as via hydrogen bonds and van der Waals forces,

with other types of molecules, such as proline-rich proteins, polyphenols, polysaccharides, metals, etc.<sup>[108]</sup>. Thus, chitosan has been studied as a clarifying agent for various beverages, such as fruit juices<sup>[109]</sup>, beers<sup>[110]</sup>, wines<sup>[111]</sup>, tea green<sup>[112]</sup>, etc.

- *Emulsion stabilizing agent:* chitosan has a stabilizing effect in classic emulsions<sup>[113]</sup>, which seems to be related to the increase of the continuous phase viscosity, auguring its potential applications in the food industry<sup>[114]</sup>. Emulsion stabilization with chitosan can be adjusted by varying parameters such as its concentration, molecular weight, degree of deacetylation<sup>[115]</sup>, etc. Additionally, chitosan-based systems have shown promising results for the stabilization of Pickering emulsions<sup>[116]</sup>, i.e., a fish oil-enriched mayonnaise<sup>[117]</sup>.
- *Films and packaging:* the use of chitosan films for food protection has expanded rapidly due to the ability of it to form blends with good antibacterial and barrier properties, which can be achieved by simple methods, i.e., evaporation of solvent from solutions, coating of products with biopolymer solutions by spraying or dipping, layer-by-layer assembly<sup>[118-120]</sup>, etc. Table 3 shows some agricultural commodities reported to be effectively protected by chitosan-containing films.

### 3.4 Environment

Due to its low cost, waste from seafood processing industries was the first chitinous materials to be evaluated as adsorbents<sup>[131]</sup>. These materials have been tested and commercialized as an alternative to chemical amendments to provide nitrogen and to control diseases associated with soil-borne pathogens<sup>[41]</sup> because their decomposition presumably generates a volatile fraction having fungistatic effects<sup>[51]</sup>. However, it is now possible to obtain chitosan-based materials with better control for specific applications such as the removal of nutrients<sup>[132]</sup> and soil contaminants such

as dyes (gentian violet, naphthol green and yellow 6)<sup>[133]</sup>, pesticides (Butachlor)<sup>[134]</sup>, heavy metal cations (Pb<sup>2+</sup>, Cu<sup>2+</sup>, Cd<sup>2+</sup>, Fe<sup>2+</sup>, Cr<sup>6+</sup>)<sup>[135]</sup>, etc. These materials can be also used as smart carriers, allowing a more rational dosage along with better environmental protection<sup>[136]</sup>.

Other interesting applications of chitosan in this area involve the fabrication of electrochemical sensors<sup>[137]</sup>, including nanometer-sized systems<sup>[138]</sup> and nano biosensors<sup>[139]</sup>, which stand out for having great potential to determine organic<sup>[140]</sup> and inorganic<sup>[141]</sup> pollutants. Some applications for chitosan-based nanofibers have also been proposed in air pollution control, either for industrial processes or for personal protection<sup>[142,143]</sup>, and in clean energy production, such as so-called microbial fuel cells, where chitosan can be used as a material for the fabrication of proton exchange membranes and bioelectrodes<sup>[135]</sup>. Some of the reported applications for chitosan, including those related to environmental protection, are shown in Figure 2.

### 3.5 Energy

The search for biodegradable materials to replace synthetic polymers has driven the testing of a variety of biopolymers, such as cellulose derivatives, dextran, starch, etc., including chitosan, which has been mainly proven in the preparation of electrochemical double-layer capacitors or supercapacitors<sup>[144]</sup>, the fabrication of membranes and electrodes for fuel cells<sup>[61]</sup>, the manufacture of lithium batteries<sup>[145]</sup> and solar cells<sup>[146]</sup>, etc. The preparation of these materials takes advantage of the ability of chitosan to form films from its aqueous solutions, in which ionic compounds are also added to obtain the species responsible for the movement of electrical charges, such as MgCl<sub>2</sub><sup>[144]</sup>. Thus, the solvent evaporation technique yields chitosan films bearing the ionic elements.

### 3.6 Petroleum

Chitosan can potentially be used in the different phases of oil exploitation and research in this field has been growing

**Table 3.** Some agricultural commodities whose postharvest protection with chitosan-containing formulations has been reported.

Products	Assays
Avocado	Biocomposites of chitosan and pepper essential oil were applied on avocado fruits infected with <i>Colletotrichum gloeosporioides</i> with successful infection control <sup>[121]</sup> .
Apricot	Coatings based on <i>Alyssum homalocarpum</i> gum seed and chitosan produce beneficial effects during fruit storage <sup>[122]</sup> .
Banana	Coatings with different concentrations of chitosan were assayed on postharvest losses and the shelf life of bananas. The 1% chitosan showed the best performance <sup>[123]</sup> .
Pumpkin (slices)	A combined chitosan/vacuum packaging treatment maintained color, micro-biological load, and $\beta$ -carotene content during storage at low temperatures <sup>[103]</sup> .
Strawberry	The coating using a 61 kDa chitosan showed significant preservation of fruit qualities during storage at 4 °C <sup>[124]</sup> .
Guava	The effect of chitosan coatings added with lemongrass oil on guava quality during storage at 12 °C maintained the postharvest fruit quality for up to 10 days <sup>[125]</sup> .
Papaya	Immersion of fruits in hot water followed by coating with chitosan solutions delayed ripening symptoms without negative effects on sensory traits during storage <sup>[126]</sup> .
Mango (slices)	Slices were immersed for 30 min in water at 50 °C and then coated with chitosan; fruit firmness and color were maintained during storage for 9 days at 6 °C <sup>[127]</sup> .
Cucumber	Postharvest application of salicylic acid-grafted chitosan coatings reduced chilling injury and preserved cucumber quality during cold storage <sup>[128]</sup> .
Pineapple	Coatings based on <i>Aloe vera</i> , chitosan, and ZnO nanoparticles succeeded in reducing weight loss, delayed ripening, and oxidative spoilage of freshly harvested fruits <sup>[129]</sup> .
Tomato	Active packaging using chitosan films loaded with TiO <sub>2</sub> nanoparticles delayed the ripening process and quality changes of tomatoes <sup>[130]</sup> .

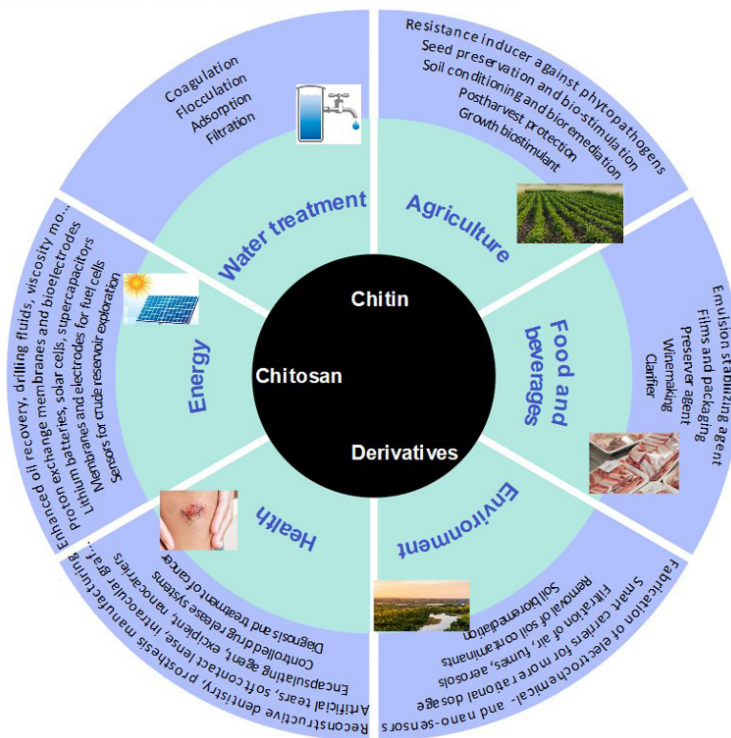


Figure 2. Several of the numerous applications of chitosan.

in recent years<sup>[147]</sup>. Some potential applications that have been initiated or could be initiated in the short term are mentioned below.

- *Reservoir exploration and characterization:* there is a lot of information on the fabrication of increasingly smaller and smarter sensors, such as the so-called nanorobots, which can allow the determination of the composition of the different strata and fluids of a reservoir, as well as monitoring its physicochemical conditions<sup>[148]</sup>. Many of the systems already investigated could be easily prepared using chitosan. Likewise, micro- and nano-motors prepared with chitosan and alginate have been proposed as active agents for environmental micro-cleaning and as sensors<sup>[149]</sup>, constituting interesting systems that could be modified for applications in crude oil reservoirs.
- *Drilling fluids:* selected chitosan derivatives have been proposed as additives in the preparation of aqueous drilling fluids<sup>[150]</sup>, some of which can simultaneously play multiple functions, such as reactive clay inhibitors, rheology modifiers, and filtrate loss reducers, with the added advantage of using a single biodegradable product to replace several additives<sup>[151]</sup>. The use of chitosan as a removal agent for metal ions such as Cr(II), Zn(II), Pb(II), and Cd(II) in drilling fluid waste has also been addressed<sup>[152]</sup>.
- *Enhanced oil recovery (EOR):* includes processes such as thermal and chemical injection<sup>[147]</sup>, with partially hydrolyzed polyacrylamide being one of the most widely used synthetic polymers to modulate the

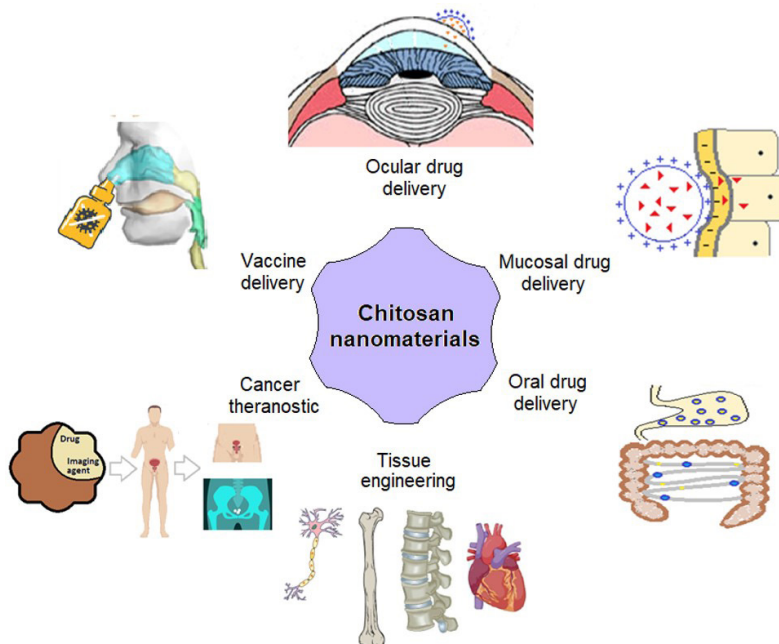
properties of injected fluids, despite its problematic<sup>[153]</sup> and environmentally unfriendly nature. Some chitosan derivatives that have been synthesized for testing in EOR have shown good performances, i.e., chitosan copolymers grafted with comonomers such as acrylamide, acrylates, acryl-amide-dodecyl-sulphonate<sup>[147,154]</sup>. Similarly, the interest in nano-materials in EOR has increased, perhaps due to the better performances observed during studies with Fe<sub>3</sub>O<sub>4</sub>/chitosan nanocomposites<sup>[155]</sup>.

- *Other applications:* viscosity modifiers (surfactants that facilitate the extraction and transportation of heavy and extra-heavy crudes) obtained from o-carboxy-methyl-chitosan have been tested successfully<sup>[156]</sup>. Further applications to be developed include the preparation of biocorrosion inhibitors for steel pipes used in well acidizing, emulsifiers for bitumen, oil spill treatments, encapsulation of microorganisms for the degradation of hydrocarbons, treatment of wastewater contaminated with hydrocarbons, etc.

### 3.7 Health

Chitinous materials have recognized antitumor, antioxidant, and antimicrobial activities<sup>[157]</sup>. Some of its attractive properties, such as bioactivity, healing, and interaction with microorganisms, have recently been reviewed from the molecular structure point of view, considering the degree of deacetylation (GDA), molecular weight, and polymer chain configurations<sup>[158]</sup>. A few applications already tested or in the process of being developed for commercialization are listed below:

- **Pharmaceutical industry:** the use of chitosan as an excipient<sup>[159]</sup> as well as in the preparation of controlled drug release systems<sup>[160]</sup> has been explored, including the preparation of nanocarriers<sup>[161]</sup>. Moreover, chitosan has been studied in the encapsulation of various bioactive species, including live cells and microorganisms<sup>[162]</sup>, genes, vaccines, proteins, drugs, etc<sup>[163]</sup>. This strategy allows for the protection of the active agent during its transit through adverse environments and improves its residence time, thus increasing its performance<sup>[164]</sup>. In the case of COVID-19, for example, it could be inferred that the administration of chitosan-coated curcumin could favor the control of cytokine storm<sup>[165]</sup>.
- **Medicine:** the use of chitosan acetate dressings for the treatment of uncontrolled external bleeding is among the most developed applications of chitosan in the medical area, obtaining materials with better performance than traditional gauze dressings<sup>[166]</sup>. Among the systems that have shown greater effectiveness is the one used by North American soldiers (HemCon<sup>TM</sup>), whose high attributes were proven during military operations in Iraq and Afghanistan<sup>[167]</sup>. Likewise, a series of chitosan-based materials have been developed, including powder preparations, solutions, aerosols, hydrogels, films, etc., for the treatment of burns and the healing of wounds and lacerations<sup>[168]</sup>. On the other hand, the preparation of chitosan-based nanosystems has focused on the development of smart drug delivery systems for the diagnosis and treatment of cancer<sup>[169]</sup>. Regarding the COVID-19 pandemic, chitosan has played a key role in clarifying some mechanisms of the infective action of SARS-CoV-2. Moreover, some specific chitosan derivatives have shown remarkable antiviral activity, standing out the ones generically called N-[(2-hydroxy-3-trimethyl-ammonium)-propyl]-chitosan halides, which have demonstrated a high ability to block the SARS-CoV-2 spike proteins and prevent their interactions with the angiotensin II converting enzyme (ACE2) and other cellular receptors<sup>[170]</sup>. Likewise, some chitosan/glucan complexes obtained from the cell walls of the fungus *Gongronella butleri*<sup>[171]</sup> could be interesting candidates against SARS-CoV-2 due to the determinant role that glycoproteins seem to play in this fight<sup>[172]</sup>.
- **Dentistry:** the use of chitosan in this sector has been increasing in recent years, with applications in practically all its areas of action. Thus, it is possible to find applications in preventive and reconstructive dentistry, prosthesis manufacturing, endodontics, periodontics, etc.,<sup>[173]</sup> with many commercial products now available. Among the multiple studies reported, the following can be mentioned: the development of mouthwashes based entirely on biomaterials, i.e., combinations of bio-surfactants, chitosan, and peppermint essential oil to achieve products more environmentally friendly<sup>[174]</sup>; ionomeric dental adhesives with improved antibacterial properties for restorative dentistry<sup>[175]</sup>; improvement of root canal treatments, taking advantage of the bactericidal properties of chitosan, especially when its solutions in aqueous citric acid are used<sup>[176]</sup>.
- **Ophthalmology:** chitosan has been commonly used as a drug carrier and as a dosing system to maintain a controlled release of administered drugs. Its advantages in these applications are closely related to its muco-adhesivity and the different forms of application that can be used, i.e., films, hydrogels, solutions, etc. Additionally, chitosan has been employed to formulate artificial tears<sup>[177]</sup> and to prepare soft contact lenses<sup>[178]</sup> and intraocular grafts<sup>[179]</sup>. Figure 3 shows a few of the interesting biomedical applications of chitosan nanomaterials currently under study.



**Figure 3.** Some of the interesting biomedical applications of chitosan nanomaterials currently under study.

**Table 4.** A few examples of feasible development using chitinous materials by application area.

Area	Products
Agriculture	Crustacean shells or chitin-based soil amendments; solutions for seed preservation and/or fungicide treatments; sprays for foliar antifungal treatments.
Water	Filtration membranes; selective adsorbents, i.e., molecularly imprinted adsorbents; recovery of proteins during the manufacture of fishmeal.
Foods	Clarifying agents for juices and wines; emulsion stabilizers (Pickering) used in sauces and mayonnaise; post-harvest fruit preservers.
Environment	Hydrogels for the removal of pollutants; nano-biosensors for the determination of contaminants; air filtration systems for industrial and personal protection.
Energy	Preparation of elements for solar cells; preparation of ionic polyelectrolytes for batteries; supercapacitors.
Petroleum	Nanobots for crude well exploration; preparation of viscosity modifiers; bio-corrosion inhibitors for pipes used in crude well acidification.
Health	Hydrogels for wound healing and burn treatment; formulation of mouthwashes using only biomaterials; films for the treatment of burns and wound healing.
Technology	Solvent purification; microorganisms' encapsulation for crude oil degradation; nanosystems for carrying active molecules in cancer treatment/diagnosis.

#### 4. Limitations Overcome by Chitosan

There are a few practical limitations to the more widespread use of chitin and chitosan. Regarding chitin, the main limitation has to do with its insolubility in the usual aqueous media and most organic solvents; however, its dissolution has been achieved in some aqueous systems (solutions of mineral acids, inorganic salts, and alkaline species) as well as in non-aqueous systems (the dimethylformamide-LiCl mixture, methanol saturated with  $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ , ionic liquids, deep eutectic solvents, protic organic solvents, etc.)<sup>[180]</sup> Furthermore, some salts of lithium halides acidified with HCl effectively convert chitin into N-acetylglucosamine and other water-soluble oligomeric species<sup>[181]</sup>, opening new routes to produce water-soluble chitin oligomers.

On the other hand, chitosan shows a greater versatility due to its easy dissolution in acidic aqueous media, although it is unable to dissolve in alkaline aqueous solutions. However, chitosan solutions prepared in acidic aqueous media could cause certain toxic effects, for example in plants, which have been usually attributed to the acid component<sup>[182]</sup>; these negative effects could be avoided by using water-soluble oligo-chitosans. Besides, chitosan chemical modifications have become increasingly specific and routine, yielding derivatives that dissolve over a wide pH range, such as their classic quaternary ammonium salts<sup>[183]</sup> and carboxy-methyl-chitosans<sup>[184]</sup>. In addition to solubility, other interesting properties of chitosan may be favored by some derivatization processes, such as antimicrobial activity<sup>[185]</sup> and muco-adhesiveness<sup>[164]</sup>. Thus, in the current fight against coronaviruses, some of these derivatives have shown antiviral activities that can be optimized by varying the physicochemical properties of the starting chitosan<sup>[170]</sup>.

It is important to note the need to eliminate, for pharmaceutical and biomedical applications, the allergens that may be present in chitosan obtained from marine sources, which could cause intoxication in sensitive individuals; this limitation has been overcome by obtaining fungal chitosans, with further benefits of avoiding dependence on the seasonality and variability of traditional sources<sup>[186]</sup>.

#### 5. Concluding Remarks

Chitin and chitosan may play a prominent role in the care of the planet due to the diversity of biochemical activities they possess and the variety of inexpensive sources from which can be sustainably obtained. As it can be inferred from this very summarized overview, some of the developments are in the initial studies phase, but many others are in advanced stages, especially those related to clinical studies for biomedical applications<sup>[187]</sup>. However, for some applications, urgent progress must be made in long-term studies of the resistance mechanisms of microorganisms to these biomolecules, i.e., as biocidal agents. Similarly, nanosystems could be considered as a coin with two very different sides: the good one for their beneficial effects, i.e., as antimicrobial treatment, and the bad one for the cytotoxic effects that could hypothetically be generated during its application<sup>[188]</sup>.

Finally, and within the context of this work, it is important to appreciate that many of the products and applications that can be developed by using these biomaterials could lead to the satisfaction of a significant part of the basic needs of a population (see Table 4 for a few examples). Thus, the use of these materials could contribute to the development of own technologies for the generation of products and applications, both basic and advanced, in sensitive areas, as briefly discussed above. An additional benefit of the exploitation of these materials is that the necessary integration between the academic sector and other sectors such as industry, business, etc., could be effectively achieved, a situation that is not very usual in developing countries.

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