Chapter

New Perspectives on the Application of Chito-Oligosaccharides Derived from Chitin and Chitosan: A Review

Paul Edgardo Regalado-Infante,
Norma Gabriela Rojas-Avelizapa, Rosalía Núñez-Pastrana,
Daniel Tapia-Maruri, Andrea Margarita Rivas-Castillo,
Régulo Carlos Llarena-Hernández
and Luz Irene Rojas-Avelizapa

Abstract

The study of chitin and chitosan has stood out for many years due to their potential application in various areas such as the food industry, where they are either used as additives, prebiotics, or bio-conservatives; as to biomedical and pharmaceutical industries, where they function to treat diseases. Besides, in the agriculture field, it is known that they can cause a positive effect on the development of plants and optimize nitrogen fixation. In recent years, attention has been paid to their derivatives, chito-oligosaccharides which, unlike chitin and chitosan, they have different chemical characteristics, like their solubility, a characteristic that facilitates their use, contrary to chitin and chitosan. Moreover, the small size of chito-oligosaccharides can facilitate their entry into the cell. This review covers recent studies on the biological functions of chito-oligosaccharides and their impact on a priority area such as agriculture, where these compounds could be used to substitute the demand for chemical compounds that, until now, have generated serious health issues as well as environmental pollution.

Keywords: natural products, shrimp wastes, sustainable agriculture

1. Introduction

A world-class level concerning aspect is the accelerated population growth as well as an increased demand for goods and services. Against this background, it is important to define strategies that allow the supply of enough food for a population in continuous growth, through the implementation of efficient agricultural systems. Agriculture plays a key role in the development of any society; however, the various agrochemicals employed, such as biocides, growth stimulants, and fertilizers, among others, lead to several pollution issues that not only affect groundwater and soils, but also microbiota and surrounding wildlife, and of course, human health.

Therefore, it is essential to consider the implementation of products based on natural substances, whose characteristics may allow the substitution of chemical compounds in the agricultural sector. Biopolymers are one such possible solution to the problem because they are typically biodegradable materials obtained from renewable raw materials. Natural biopolymers include starch, cellulose, pectin, chitin, and chitosan, and have been part of humanity since its existence, being part of basic daily needs as fundamental as food and clothing, as well as medical materials, packaging, food additives, engineering plastics, chemicals for water treatment, among many others [1, 2]. The biopolymers known as chitin (poly-N-acetylglucosamine), and its derivative chitosan (obtained by deacetylation of chitin) have achieved a prominent place in the development of applications related to the treatment of water [3], soil moisture control [4], the intelligent release of fertilizers [5], growth stimulant [6], an inducer of defense mechanisms in plants [7], antimicrobial [8–10]. Their usefulness in this fight is such that their applications related to the control of population growth should also be considered due to the potential applications they have for the controlled release of contraceptives [11] and spermicides [12], including the expectations of creating a non-hormonal female contraceptive with no side effects [13]. One of the main biological applications of chitosan, which was recently discovered, is in the field of gene delivery, due to its ability to interact with anionic DNA [10, 14, 15].

Thus, the aim of this document is to present an exhaustive revision of the chito-oligosaccharides derived mainly from chitosan and their potential application in agriculture and other areas. In recent years, many studies have investigated the effects of chito-oligosacharides on human health, for example, as immunological modulators, [16, 17] anticancer [18, 19], antidiabetic [20, 21], and antimicrobial compounds [22, 23]. Some factors that potentiate the effect of chito-oligosacharides are their lower molecular weight and higher degree of deacetylation [24, 25]. The chito-oligosacharides can have antimicrobial properties, can induce plant resistance, and can stimulate plant growth as well, which makes them a promising alternative for the agricultural sector.

2. Shrimp species as a source of waste materials of industrial interest

Shrimp is one of the most important fishery resources worldwide, due to its nutritional value and high demand, especially in developed countries such as the United States of America, Japan, and the European Union [26].

Shrimp (*Penaeus* sp.) belongs to the animal kingdom, Phylum *Arthropoda,* class Crustacea, order Decapoda, and genus *Penaeus*. Like all arthropods, shrimp body is divided into three big main regions: cephalothorax, abdomen, and telson. It possesses various appendages such as antennules, antennae, mandibles, maxillae, maxillipeds, and pereiopods. This crustacean is essentially constituted by two parts: the crustacean muscular part, which corresponds to 50% of total mass, and the cephalothorax exoskeleton, including the tail, which is equivalent to the other 50% [27]. The cephalothorax is not fully exploited by man, so it is separated and broadly known as the shrimp waste. In Mexico, until recently, these residues were thrown back into the ocean or used as a source of proteins for fattening foods. However, in countries such as Japan, Thailand, and Korea, these shrimp wastes have acquired a very important commercial relevance [28].

Shrimp represented the 2.4% of the worldwide fishery production in 2018, with 3.75 million metric tons in live weight, and an establishedpotential of 4.0 million metric tons for the year 2021 [29]. China is the leading country in shrimp production, with about 1.5 million metric tons of the total fishing (**Figure 1**).

In Latin America, Ecuador is the leading country in shrimp production, and it was expected that the production in this country reached 700,000 metric tons in the year 2021, making Ecuador the third main worldwide shrimp producer, only after China and Vietnam (**Figure 2**). Although Mexico suffered severe losses in 2013, the Mexican industry was able to recover its production in 2015. Besides, it was expected a higher growth, where 180,000 metric tons were expected to be reached by 2021 [30]. In Mexico, in terms of catch volumes, the shrimp occupied second place in the national fishery production, with a live weight volume of 155,281 tons in 2018 (**Figure 3**).

In recent years there has occurred overexploitation in all the commercial fishing species, including shrimp, because of uncontrolled growth fishery activities, either artisanal or industrial. Due to this problem, preventive measures have been implemented, including a temporally closed season in 2003, in which it was prohibited any fishing of shrimp species; this closed season was extended until 2017. Besides, it was also implemented a specific fishing season under the Mexican Standard NOM-009-PESC-1993. The productions of aquaculture farms show an exponential growth tendency, while open sea mats and bay fishery have kept a constant behavior (**Figure 4**).

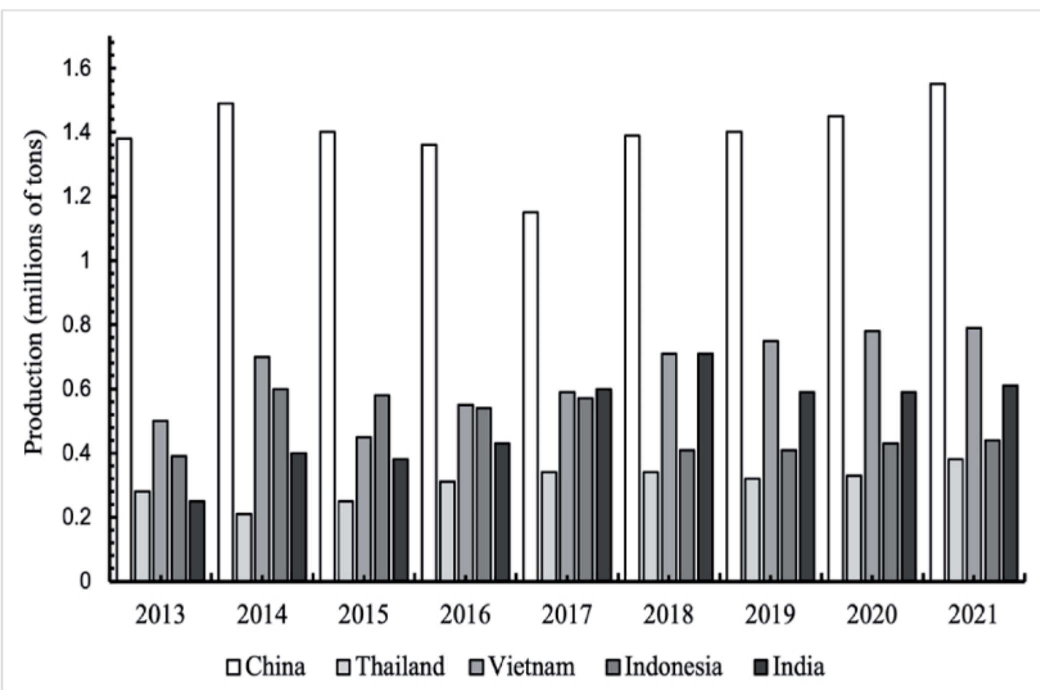

Figure 1.
Aquaculture shrimp production of the main producing countries. Sources: FAO (2020) [29] and Anderson et al., 2019 [30].

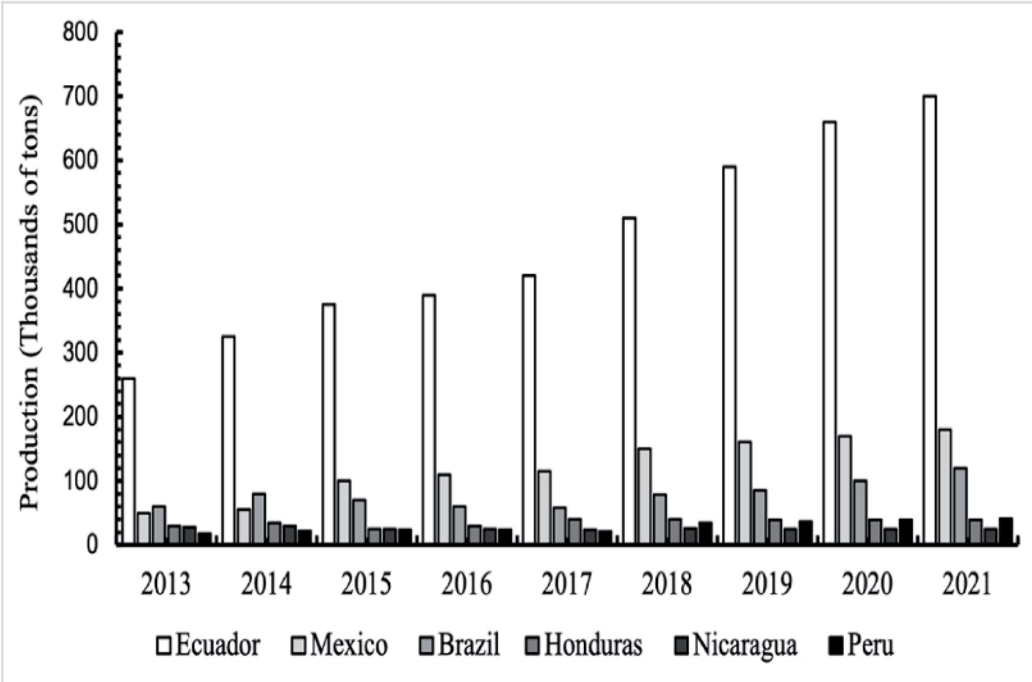

Figure 2.
Aquaculture shrimp production in the main producing countries of Latin America during 2013–2017 and projection for 2018–2021. Source: FAO (2020) [29] and Anderson et al., 2019 [30].

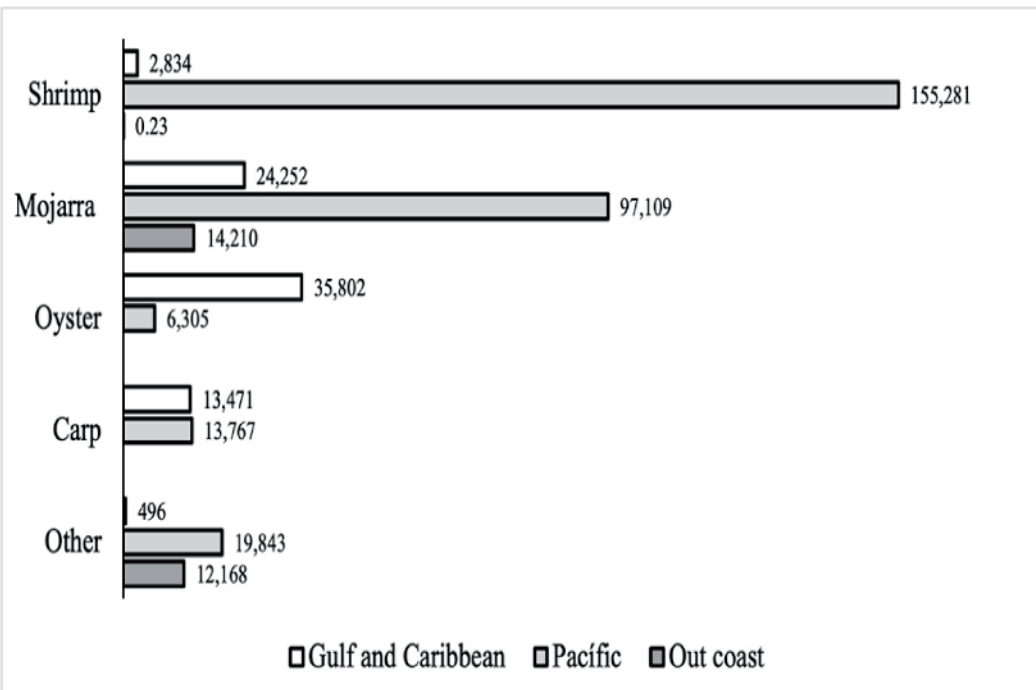

Figure 3.
Contribution of the main commercial species in the volume of national aquaculture production live weight in 2018. Adapted from the Mexican yearbook of aquaculture and fisheries, CONAPESCA (2018) [31].

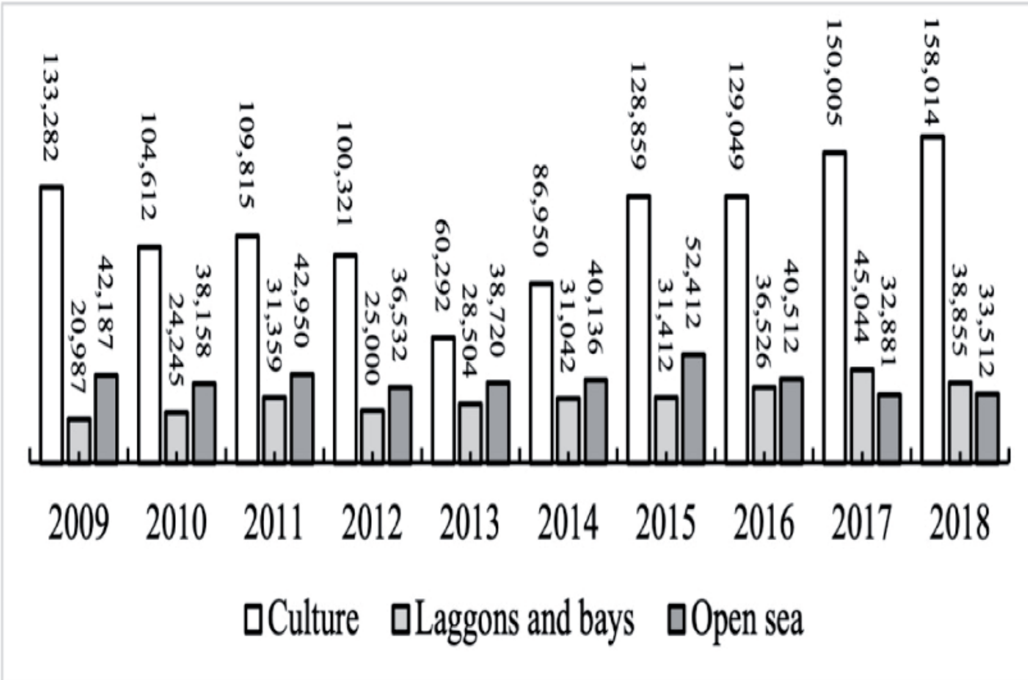

Figure 4.
Mexican live weight shrimp production by origin 2009–2018. Adapted from the Mexican yearbook of aquaculture and fisheries, CONAPESCA 2018 [31].

2.1 Current situation: the birth of Mexican industries based on the harnessing of shrimp wastes

Chitin and its derivates have commercial use in different countries, mainly Japan, China, and the USA. All these countries already have a consolidated industry around this polymer, being China the main producer and exporter of chitin. As to Chile and Spain, both countries are in an early stage, like the rest of Latin America. In Mexico, the interest in the chitin sector, as well as in chitosan, and their derivatives, is relatively new; therefore, both academic institutions and industries have manifested their interest in this topic. For example, scientists from Centro de Investigación en Alimentación y Desarrollo AC (CIAD) in Sonora, México [32], have informed that the head and exoskeleton of shrimp should be consider not as a waste but as source for chitin and chitosan production. Additionally, there are enterprises such as "Neptuno", where researchers and businessmen collaborate to produce these polysaccharides and their derivates. Until now, they have actively participated in conferences and presentations aiming to awaken the interest in this field. Another enterprise called "Polímeros acuícolas", from Guasave, Sinaloa, pretends to exploit shrimp wastes to produce substances of interest to satisfy the global need. Furthermore, some well-known Mexican enterprises, like Resistol and Comex, have already created links with the former company.

2.2 Chemical composition of shrimp wastes

Shrimp obtained from fishery is destined for direct human consumption; it can be found in different presentations that require diverse industrial processes, or also can

Author	[35]	[36]
% Water	7.87	4
% Dry matter	92.13	96
% Crude fiber	26.89	N/D
% Crude protein	34.5	46.3
& Fat	5.14	9.04
% Ashes	25.60	17.04
% Calcium	16.69	7.0
% Phosphates	0.85	3.03
Chitin energetic content	938*	2500
Chitin	18.7	9.82

**Calculated by the method of Schaibel (1980).*

Table 1.
Proximal analysis of the shrimp waste showing its content of chitin and energy (kcal/kg).

be consumed fresh or frozen. Considering that almost 50% of the crustacean weight is thrown before their consumption, it was calculated that the production of shrimp wastes in México will reach 79,138 tons in 2018 [31].

The crustacean exoskeletons are formed by successive protein-chitinous layers, with a high calcium carbonate content. Depending on the species, the chitin content can vary from 0.01 to 40% on a dry base, while protein content can fluctuate between 50 and 80%. Through X-ray diffraction studies, it has been determined that the polysaccharide chains of chitin in crustaceans, specifically in shrimp species, are tied in an antiparallel way, given a crystalline structure called type β [33]. Protein molecules adopt an antiparallel conformation of folded chains, while chitin molecules are arranged in a perpendicular way with respect to the protein chains, resulting in a tridimensional reticular structure, organized in layers with high mechanic strength. Therefore, such different protein-chitinous layers can adopt a "sandwich" structure, in whose center would be a nucleus made by chitin molecules, surrounded by layers of fibrous proteins arranged transversally [34]. In addition, it is important to emphasize that there are factors that can produce significant changes in the percentual composition of shrimp wastes, such as the crustacean species, season and geographical region of capture, and the storage of samplesas well. In general, there can be considered that such wastes contain an average of 34.5% protein, 26.89% crude fiber, and 25.60% ashes. More detailed data is shown in **Table 1**, where can also be seen that they possess a high calcium carbonate content and various phosphates. Therefore, these kinds of wastes mayrepresent one of the possible non-conventional protein sources for animals, with a good nutritional potential, because such proteins are especially rich in lysine, which could equilibrate diets based on cereals [37].

3. Chemical structure of chitin, chitosan, and their derivative chito-oligosaccharides

3.1 Chemical structure and properties

Chitin is a non-linear polymer constituted by units of N-acetyl-2-amino-2-deoxy-D-glucose (N-acetyl-glucosamine or NAG), joined by glycosidic bonds β (1 → 4) [38, 39].

The conformation of such glycosidic bonds produces an alternative spatial location of the N-acetyl groups along the polymer chain, where the N-acetyl-glucosamine dimer chitobiose can be considered as the minimal structural repeating unit of chitin (**Figure 5**) [34]. On the other hand, chitin is one of the most abundant natural polymers, like cellulose and hemicellulose [40]. In nature, chitin is forming cover structures of arthropods, insects, arachnids, mussels, fungi, and some algae [41].

Concerning chitosan, this is also a lineal polysaccharide that could be obtained after the extensive deacetylation of chitin and, therefore, it is composed of two different aminated monosaccharides, which are randomly placed along the polymeric chain. Such monosaccharides are amino sugars NAG and D-glucosamine (GA), which are linked, likewise, by glycosidic bonds β (1 → 4), (**Figure 6**). It is important to point out that the total deacetylation of chitin is a quite complicated process, and therefore is possible to generally obtain mixtures of chitosans with different degrees of deacetylation (generally higher than 45%); thus, the criteria used to differentiate them is mainly their solubility in aqueous diluted acidic solutions [38].

3.2 Chitosan depolymerization to produce chito-oligosaccharides

Due to the very high molecular weight of chitosan, and its high viscosity as well, the use of this polymer becomes difficult for some applications. Therefore, this problem was solved by using the resulting products of its hydrolysis. However, such substances could be harder to obtain in the amounts required for large-scale industrial processes. In this regard, it has been reported that the hydrolysis or depolymerization of chitosan can be done through different methods: physical (ultrasound), chemical (hydrolytic reactions), or biological (using hydrolases). Among them, chemical hydrolysis is the most used at an industrial scale.

3.2.1 Chemical obtention of chito-oligosaccharides from chitosan

Chitosan can be hydrolyzed chemically either through acidic depolymerization or by an oxidative-reductive treatment. The acidic depolymerization is carried out by using a variety of chemicals such as hydrochloric, hydrofluoric, nitrous, sulfuric, and acetic acids. However, the use of such chemicals brings disadvantages, as their low yields obtained. Although they are relatively fast and cheap processes, they are inconvenient for their commercialization due to the production of toxic compounds and their considerable risk for the environment, since the materials used are highly residual [38]. There are multiple reports of chitosan oligomers obtained in this way and used alternatively in agriculture [43–46].

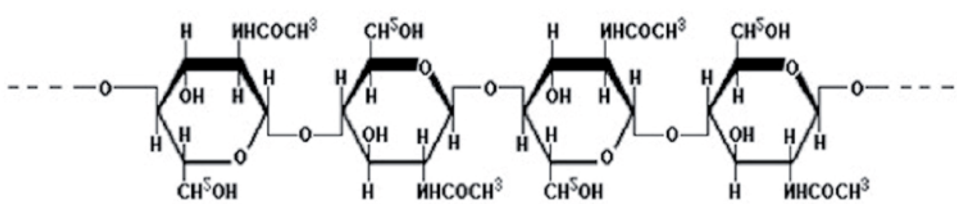

Figure 5.
Chemical structure of chitin.

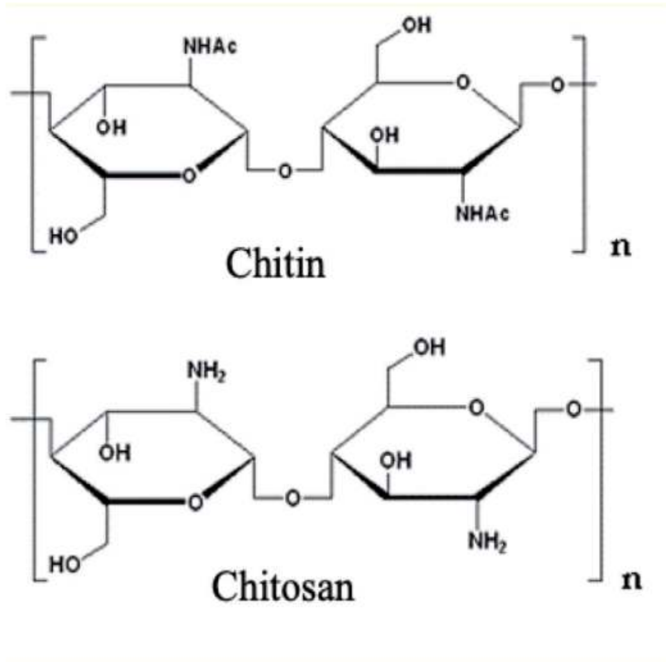

Figure 6.
Comparative chemical structures of chitin and chitosan [42].

3.2.2 Enzymatic obtention of chitosan oligosaccharides

Such enzymatic processes are carried out generally in discontinuous reactors and are preferred over the chemical methods, due to the reduction of adverse factors. These processes require specific enzymes like chitosanases or some less specific ones like cellulases, lipases, hemicellulases, and pectinases [47]. Chitosanases are enzymes broadly distributed in nature, which are capable of degrading chitosan into low molecular weight oligomers. These enzymes have been found in bacteria, viruses, fungi, and plants [48, 49]. However, there is a limitation in the use of these specific enzymes, because of their high cost and low availability in high amounts [50]. Due to this, some researchers have explored the use of non-specific commercial enzymes, which showed to be able to degrade chitosan, almost with the same efficiency than chitosanases, but cheaper [51]. As occurred with specific chitosanases, hydrolases are also able to catalyze the breakdown of β- (1,4)-glycosidic bonds present in chitosan. These enzymes have been found in microorganisms like viruses, bacteria, and fungi. During a recent research performed by Olicón-Hernández *et al.* (2017) [52], the extracellular chitosanase from *Bacillus thuringiensis*, grown in a chitosan containing medium, was used as a crude enzyme previously sterilized by filtration to produce a mixture of mono-, di-, tri-, and tetra-saccharides using colloidized chitosan as the substrate. These results are encouraging because they show that it is possible to transform chitosan obtained from shrimp wastes, through a microbial process, into products with biotechnological importance, avoiding the traditional use of chemical substances, as different acids.

4. Chitin and chitosan uses

Chitin can be used in a variety of fields. For instance, it was studied as a wound healing and blood thinner for medical purposes. It was also used as stationary support for the enzyme immobilization in column chromatography, due to its gelling and adhesive properties. In pharmacy is used as an excipient and dispenser of drugs. Besides, chitin has applications as an adhesive in textile and paper industries, and in agriculture for soil improvement. Due to its chelating properties, chitosan is used in water treatment and also for the decontamination of effluents. On the other hand, chitosan possesses physicochemical, functional, and biological properties, being useful in different fields such as medicine, pharmacy, agriculture, and food industry, among others. Chitosan has a high capacity for the sequestration of metallic ions, which is useful for the decontamination of industrial wastewater. Its polycationic nature grants a flocculant action, being also a good support for enzyme and cell immobilization, both in biotechnology and food industry [53].

Chitosan is also an excellent former of fibers, films, and membranes [54], and can be used to prepare microspheres or microcapsules; these capabilities, along with its biocompatibility and biodegradability, allow its use in both biomedical and pharmaceutic industries [55]. Also, it has been studied the use of chitosan as an excipient, to propitiate the controlled release of drugs and to reduce the cholesterol levels [56] and as a boost for the immune system and for the elaboration of the gels used in cosmetology [57]. Likewise, it has been described its antimicrobial action against pathogens and microorganisms that damage fruits and vegetables; this activity has been explained by supposing changes in the permeability of cells, due to the interactions between chitosan (a polycation) with the electronegative charges placed on the cell surface. Other therapeutical use concerns weight, high cholesterol, and burns controls [58]. Other applications, based on the polar capability of the hydroxyl and carboxyl groups of chitosan, have been proposed to make bio-electro sensors able to detect cancerogenic cells and at the same time being useful to administer antitumor agents to specific cells [59].

5. Some uses of chito-oligosaccharides

As indicated above, it is possible to obtain low-molecular-weight derivates of the above-cited polymers, by chemical or enzymatic treatments, which are known as chito-oligosaccharides, whose structure main contain scarcely 3 to 10 monosaccharide units. However, some authors consider that such chito-oligosaccharides may contain until 20 monosaccharide units in their chains. These compounds, particularly those derived from chitosan hydrolysis, can be used in a variety of biotechnological areas, standing out in medicine and pharmacy, due to their beneficial effects on human health, as is described hereafter [52].

5.1 Medical uses

Chito-oligosaccharides from chitosan confer an immunological modular effect, because theyit boost the immune system through cellular proliferation, besides possessing other stimulative immunological effects [57, 60–63]. In this particular instance, it is known that chito-oligosaccharides accelerate theformation of antibodies and also induce the cellular differentiation of leukocytes. Oligosaccharides from chitosan also possess an accelerating effect on intestinal transit since they help the proliferation of *Bifidobacterium* and *Lactobacillus* cells present in the intestinal flora [64].

Another important finding refers to their anti-tumoral activity, as it is believed that they can suppress and prevent cancer [65]. As metabolic emulators chito-oligosaccharides have anti-cholesterolemic effects, because they are able to reduce cholesterol, triglycerides and glucose levels in the blood; besides they reduce blood pressure and have anti-obesity effects.

As food additives, chito-oligosaccharides are used as dietary fiber, and dietary supplement for poultry species and livestock [63]. Other relevant applications for these compounds involve their use in arthritis control and as an antidiabetic; also in the treatment of gastric ulcers, as antimutages, anti-inflammatories and as low caloric sweeteners [66, 67].

On the other hand, it is important to point out that there are two factors that should be considered among the most relevant, related to the biological activity of chito-oligosaccharides; one is the length of their chains and the other is their deacetylation degree [68]. In general, the longer chito-oligosaccharides are, the stronger effects they may have. However, this does not imply that the shortest oligosaccharides do not possess similar (or other different) biological effects. For example, it has been observed that penta-, hexa- and hepta-glucosamines present the strongest and more varied biological effects [69].

5.2 Agricultural applications

It is known that chitin, and its derivates, have a broad range of biological activities which include antioxidant and, antimicrobial effects, and other properties that can be used on an industrial scale as well. Chitosan has been used for seed coverings, with the objective of controlling plagues and improving plant defense system against microorganisms [70]. It has been demonstrated that chito-oligosaccharides have diverse effects on plant cultivation and, on the enhancement of plant growth and development, besides improving both the quality and yield of the vegetable products [71]. In a study made by Mahdavi & Rahimi (2013) [70], it was tested the effect of chito-oligosaccharides in stimulation, specifically for germination and growth, of *Trachyspermum ammi*, observing that its growth was accompanied by a decrease in the damaging impact caused by abiotic stress like high salinity. Likewise, a study using three fractions of chito-oligosaccharides of different molecular weights, obtained from the same initial chitosan sample, clearly demonstrated that the fraction with the lowest molecular weight produced a higher acceleration in the germination of zucchini seeds covered with these compounds. In another study reported by Zou *et al*., (2017) [72], it was observed the significant benefits for soy yields, seed germination, and plant growth. Other uses of chito-oligosaccharides in the agricultural sector are as agents to conserve seeds [73], as plant defense enhancers and for the protection against plagues and diseases [74].

5.2.1 Effects on plant resistance to diseases

Jia *et al*., (2016) [75] used *Arabidopsis* plants which were pre-treated with 50 mg/L of chito-oligosaccharides per day, before their inoculation with the tobacco mosaic virus (TMV); it was found that the expression of defenses, associated with genes related to pathogenicity, resulted strengthened.

In another study, the efficiency of chito-oligosaccharides to prevent and control the southern rice striped black dwarf virus was demonstrated, evidencing that these compounds regulate the increase of proteins related to plant defenses. Also, a field test has been carried out after treatment with chito-oligosaccharides as an antifungal agent in grape plantations, where results showed that the mortality and infection rates were reduced significatively on inoculated plants with pathogens such as *Diplodiaseriata* y *Phaeomoniella chlamydospora* [76].

5.2.2 Effects on growth and plant development

The use of oligosaccharides can help to improve plant growth, seed germination, chlorophyll content, nitrogen fixation, and nutrient absorption. Oligomers from chitosan not only have the property of inducing resistance, but they can promote plant growth and development. During their interaction with tobacco cells, these compounds regulate concentrations of indole-3-acetic acid (IAA) and their related peroxidases, which indicates a growth accelerator effect. Also, field tests have been done to evaluate oregano growth using different oligosaccharide doses (50–1000 ppm),

Species	Properties of QOS*	Concentration used	Mode of use	Effects/ observations	Reference
Tomato	—	25, 50, 75, 100 mg/L	Foliar	Plants height, leaves number, fruit yield	[77]
Wheat	93% GD	15 mg/L	Foliar	Chlorophyll, activity PEPC, saccharose content, TCA cycle	[78]
Mint	90% GD	40, 60, 120, 160 mg/L	Foliar spray	Longer root length	[79]
Lemmon grass	90% GD	40, 60, 80, 100 mg/L	Foliar spray	Root length	[80]
Chili	91.4% GD; PM 8 kDa	50 mg/L	Foliar	Increase on chlorophyll content	[81]
Wheat	95% GD	0.01%	Foliar	Sprout length, root length, chlorophyll content, sugar content	[72]
Bean	85% GD	100 mg/L	Foliar	Plant height, more vanilla pods, seeds yield	[82]
Barley	Different PM	—	Plant tissue culture	Higher growth and seed yield	[83]
Lavender	80% GD; PM 16 kDa	30, 40, 100 mg/L	Plant tissue culture	Higher plant length, multiplication, and sprout weight.	[84]
Curly kale	—	10, 50, 100 mg/L	Hydroponic cultivation	Enhance of growth and reduction for harvesting time	[84]
Soy, wheat and rice	—	10–100 mg/L	Hydroponic cultivation	They promote growth under stress	[85]

**GD = degree of deacetylation, PM = molecular weight.*

Table 2.
Some reports of the effects of oligosaccharides on the physiological attributes of plants.

where results indicated that, from 200 to 500 ppm chito-oligosaccharides, there was an increase in plant height, while doses from 50 to 200 ppm significantly regulated the concentration of polyphenols.

5.2.3 Effects on the quality of vegetable products

Studies carried out in this regard showed that treatment with chito-oligosaccharides can significantly improve the quality of strawberry plants; in such research a treatment with 50 mg/L of these chito-oligosaccharides, applied to the fruits prior to harvest them, increased their pulp viscosity, lignin content, sugar, protein, and titratable acidity; besides, they strengthen the strawberry antioxidant capability due to a higher production of components such as anthocyanins, total phenols, flavonoids, and vitamin C. **Table 2** shows some works concerning the effects of chito-oligosaccharides on diverse physiological attributes of plants.

6. Conclusions

Sustainable agriculture is a relevant topic considering the growing population worldwide and the severe damage that chemicals have caused to the environment due to their use for agricultural purposes. Many agrochemicals used nowadays are costly in the global market; however, they promote agricultural production. There is well known that many of these compounds used to protect crops against diseases and to increase yields, are considered pollutants of soil, crops, biological diversity, microbiota and, in addition, may cause diseases in animals and humans. Thus, there is currently an enormous need to promote healthier ecosystems and support sustainable soil management to minimize the use of these harmful synthetic agrochemicals, while promoting the development of methods and products for the control of pests and diseases, that could be more respectful to the environment. The utilization of protein-chitinous residues, which are abundant in our country (and without the correct management, may also generate pollution to the environment), for the obtention of derivates like chitin, chitosan, and chito-oligosaccharides from chitosan, among others, are considered valuable in many fields, due to their properties like biocompatibility, biodegradability, and null toxicity. Therefore, they are an alternative to conventional agriculture, being a feasible alternative to enhance productivity and crop protection. To that effect, chito-oligosaccharides may fulfill environmental and health requirements to help meet the needs of a constantly growing population, which involve the production of high-quality food along with low environmental impact. Unlike chitin and chitosan, chito-oligosaccharides are soluble in water, and due to their low molecular weight, they can enter the cell and have a higher biological effectivity, not to mention their relevant capability to stimulate seed germination, plant growth, to activate resistance mechanisms in crops, antimicrobial activity, and more important, they can be obtained by microbial methods that are harmless to the environment and at a low cost.

Acknowledgements

We are deeply grateful for the editor of Chitin-Chitosan Isolation, Properties, and Applications. We are also grateful to IntechOpen and Universidad Veracruzana which supported our research in various ways.

Conflict of interest

The authors declare no conflict of interest.

Author details

Paul Edgardo Regalado-Infante[1], Norma Gabriela Rojas-Avelizapa[2], Rosalía Núñez-Pastrana[1], Daniel Tapia-Maruri[3], Andrea Margarita Rivas-Castillo[4], Régulo Carlos Llarena-Hernández[1] and Luz Irene Rojas-Avelizapa[1*]

1 Faculty of Biological and Agricultural Sciences, Universidad Veracruzana, Veracruz, Mexico

2 Research Center in Applied Science and Advanced Technology, CICATA-Instituto Poitécnico Nacional, Qro, Querétaro, México

3 Biotic Product Development Center, CEPROBI-Instituto Politécnico Nacional, Yautepec, Morelos, México

4 Technological University of the Metropolitan Zone of the Valley of Mexico UTVAM Tizayuca, Hidalgo, México

*Address all correspondence to: luzrojas@uv.mx

References

[1] Hill JW, Kolb DK. Chemistry for Changing Time. 14th (ed) ed. Vol. 816. Malaysia: Prentice Hall; 2015

[2] Marsh K, Bugusu B. Food packaging-roles, materials, and environmental issues. Journal of Food Science. 2007;**72**:39-55

[3] Lárez-Velásquez C, Millán-Barrios E. Chitosan for pesticide control on environmental protection and water purification. In: Gertsen N, Sonderby L, editors. Series: Air, Water and Soil Pollution Science and Technology. Chapter 4 ed. New York, United States of America: Nova Publisher; 2009. ISBN: 978-1-60741-599-2

[4] Sabadini R, Martins V, Pawlicka A. Synthesis and characterization of gellan gum: Chitosan biohydrogels for soil humidity control and fertilizer release. Cellulose. 2015;**22**(3):2045

[5] Pereira A, Martins A, Paulino A, Fajardo A, Guilherme M, Iecher-Faria M, et al. Recent advances in designing hydrogels from chitin and chitin–derivatives and their impact on environment and agriculture: A review. Revista Virtual de Química. 2017;**9**:17

[6] Malerba M, Cerana R. Recent advances of chitosan applications in plants. Polymers. 2018;**10**(2):118. DOI: 10.3390/polym10020118

[7] Xing K, Zhu X, Peng X, Qin S. Chitosan antimicrobial and eliciting properties for pest control in agriculture: A review. Agronomy for Sustainable Development. 2015;**35**(2):569-588. DOI: 10.1007/s13593-014-0252-3

[8] Kong M, Chen X, Xing K, Park H. Antimicrobial properties of chitosan and mode of action: A state of theart review. International Journal of Food Microbiology. 2010;**144**(1):51-63. DOI: 10.1016/j.ijfoodmicro.2010.09.012

[9] Guzmán K, Kumar B, Vallejo M, Grijalva M, Devut A, Cumbal L. Ultrasound- assisted syntesis and antibacterial activity of gallic acid-chitosan modified silver nanoparticles. Progress in Organic Coatings. 2019:1-8. DOI: 10.1016/j.porgcoat.2019.01.009

[10] Kumar S, Deepak V, Kumari M, Dutta PK. Antibacterial activity of diisocyanate- modified chitosan for biomedical applications. International Journal of Biological Macromolecules. 2016;**84**:349-353. DOI: doi.org/10.1016/j.ijbiomac.2015.12.027

[11] Agrawal S, Pruthi J. Development and evaluation of matrix type transdermal patch of ethinyl–estradiol and medroxyprogesterone acetate for anti–implantation activity in female Wistar rats. Contraception. 2011;**84**(5):533. DOI: 10.1016/j.contraception.2011.03.005

[12] Smith R. Chitosan as a Contraceptive. Patent No.: US 4,474,769 A. 1984

[13] Kootala S, Filho L, Srivastava V, Linderberg V, Moussa A, Trombotto H, et al. Reinforcing mucus barrier properties with low molar mass chitosans. Biomacromolecules. 2018;**19**(3):872. DOI: 10.1021/acs.biomac.7b01670

[14] Kumar S, Koh J. Physiochemical and optical study of chitosan-terephthaldehyde derivative for biomedical applications. International Journal of Biological Macromolecules. 2012;**51**:1167-1172. DOI: 10.1016/j.ijbiomac.2012.09.001

[15] Kumar S, Garg P, Pandey S, Kumari M, Hoon S, Jang K, et al. Enhanced chitosan–DNA interaction by 2-acrylamido-2-methylpropane coupling for an efficient transfection in cancer cells. Journal of Materials Chemistry B. 2015;**3**:3465-3475. DOI: doi.org/10.1039/C4TB02070G

[16] Bahar B, O'Doherty JV, Maher S, McMorrow J, Sweeney T. Chitooligosaccharide elicits acute inflammatory cytokine response through AP-1 pathway in human intestinal Epitheliallike (Caco-2). Cellular & Molecular Immunology. 2009;**51**(3):283-291. DOI: 10.1016/j.molimm.2012.03.027

[17] Walsh AM, Sweeney T, Bahar B, Flynn B, O'Doherty JV. The effect of Chitooligosaccharide supplementation on intestinal morphology, selected microbial populations, volatile fatty acid concentrations and immune gene expression in the weaned pig. Animal. 2012;**6**(10):1620-1626. DOI: 10.1017/S1751731112000481

[18] Shen KT, Chen MH, Chan HY, Jeng JH, Wang YJ. Inhibitory effects of Chitooligosaccharides on tumor growth and metastasis. Food and Chemical Toxicology. 2009;**47**(8):1864-1871. DOI: 10.1016/j.fct.2009.04.044

[19] Kim EK, Je JY, Lee SJ, Kim YS, Hwang JW, Sung SH, et al. Chitooligosaccharides induce apoptosis in human myeloid leukemia HL-60 cells. Bioorganic & Medicinal Chemistry Letters. 2012;**22**(19):6136-6138

[20] Ju C, Yue W, Yang Z, Zhang Q, Yang X, Liu Z, et al. Antidiabetic effect and mechanism of Chitooligosaccharides. Biological and Pharmaceutical Bulletin. 2010;**33**(9):1511-1516. DOI: 10.1248/bpb.33.1511

[21] Karadeniz F, Artan M, Hong C, Kim S. Chitooligosaccharides protect pancreatic b-cells from hydrogen peroxide-induced deterioration. Carbohydrate Polymers. 2010;**82**(1):143-147

[22] Quintero-Villegas M, Aam B, Rupnow J, Sorlie M, Eijsink V, Hutkins R. Adherence inhibition of Enteropathogenic *Escherichia coli* by Chitooligosaccharides with specific degrees of acetylation and polymerization. Journal of Agricultural and Food Chemistry. 2013;**61**(11):2748-2754. DOI: 10.1021/jf400103g

[23] Xia W, Liu P, Zhang J, Chen J. Biological activities of chitosan and Chitooligosaccharides. Food Hydrocolloids. 2011;**25**(2):170-179

[24] Benhabiles M, Salah R, Lounici H, Drouiche N, Goosen M, Mameri N. Antibacterial activity of chitin, chitosan and its oligomers prepared from shrimp Shell waste. Food Hydrocolloids. 2012;**29**(1):48-56

[25] Fernandes J, Eaton P, Nascimento H, Giao M, Ramos O, Belo L, et al. Antioxidant activity of chitooligosaccharides upon two biological systems: Erythrocytes and bacteriophages. Carbohydrate Polymers. 2010;**79**:1101-1106. DOI: org/10.1016/j.carbpol.2009.10.050

[26] Caso M, Pisanty I, Ezcurra E. Diagnostico ambiental del golfo de México. In: Ecosur, editor. Secretaría del Medio Ambiente y Recursos Naturales. Vol. 2. México: Instituto Nacional de Ecología; 2009. pp. 899-936

[27] Carranco M, Calvo C, Arellano L, Pérez-Gil L, Ávila E. Inclusión de la harina de cabezas de camarón *Penaeus* sp. en raciones para gallinas ponedoras. Efecto sobre la concentración de pigmento rojo de yema y calidad de huevo. Interciencia. 2003;**28**:328-333. ISSN 0378-1844

[28] Rojas-Avelizapa L, Cruz-Camarillo R, Guerrero M, Rodríguez-Vázquez R, Ibarra J. Selection and characterization of a proteo-chitinolytic strain of *bacillus thuringiensis*, able to grow in shrimp waste media. World Journal of Microbiology and Biotechnology. 1999;**15**:261

[29] FAO. El Estado Mundial de la Pesca y la Acuacultura 2020. La sostenibilidad en acción Roma; 2020. DOI: 10.4060/ca9229es

[30] Anderson J, Valderrama D, Darryl EGOAL. Revisión de la producción mundial de camarones. Global Aquaculture Alliance. 2019;**2019**:1-5

[31] Anuario de acuacultura y pesca 2018 [internet]. 2018. Available from: https://www.conapesca.gob.mx/work/sites/cona/dgppe/2018/ANUARIO_2018.pdf

[32] Centro de Investigación en Alimentación y Desarrollo A.C. 2008 [internet]. 2008. Available from: http://www.ciad.mx/content/view/173/1.

[33] Kurita K. Chitin and chitosan: Functional biopolymers from marine crustaceans. Marine Biotechnology. 2006;**8**:203-226. DOI: 10.1007/s10126-005-0097-5

[34] Cruz-Camarillo R, Rojas-Avelizapa L. Las quitinasas bacterianas y sus posibles aplicaciones biotecnológicas. In: Avances en purificación y aplicaciones de enzimas en biotecnología. México: UAM-Iztapalapa; 1999. pp. 238-324

[35] Mahata M, Dharma A, Rianto I, Rizal Y. Effect of substituting waste hydrolysate of *Penaeus merguensis* for fish meal in broiler performance. Pakistan Journal of Nutrition. 2008;**7**:806-810 ISSN 1680-5194

[36] Faniamo A, Oduguwa B, Oduguwa O, Ajasa O, Jegede O. Feeding value of shrimp meal for growing pigs. Archivos de zootecnia. 2004;**53**:77-85

[37] Okoye F, Ojewola G, Njoku-Onu K. Evaluation of shrimp waste meal as a probable animal protein source for broiler chicken. International Journal of Poultry Science. 2005;**4**:458-461. DOI: 10.3923/ijps.2005.458.461

[38] Castañeda R, Fuente S, Pacheco R, Ortiz-Rodríguez T, Barboza J. Potencial de los quito-oligosacáridos generados de quitina y quitosana. Acta Universitaria. 2014;**21**:14-23. DOI: 10.15174/au.2011.16

[39] Zhu X, Zhou Y, Feng J. Analysis of both chitinase and chitosanase produced by *Sphingomonas* sp. CJ-5. Journal of Zhejiang University Science B. 2017;**8**:831-838. DOI: 10.1631/jzus.2007.B0831

[40] Roberts G. Truth or myth Euchis. Newsletter. 2006;**21**:5-6

[41] Mukhtar K, Khan M, Siddiqui H, Jahan A. Chitosan and its oligosaccharides, a promising option for sustainable crop production- a review. Carbohydrate Polymers. 2019;**115**:1-64. DOI: 10.1016/j.carbpol.2019.115331

[42] Ghanbarzadeh B, Almasi H. Biodegradable Polymers. Chapter 6: Life of Science. IntechOpen Science; 2013. pp. 141-185. DOI: 10.5772/56230

[43] Dzung N. Enhancing crop production with chitosan and its derivatives. In: Kim S-K editor. Chitin, Chitosan, Oligosaccharides and their Derivatives. Vol. 14. Department of Physics, Korea Advanced Institute of Science and Technology: CRC Press; 2010. pp. 619-631. DOI: 10.1201/EBK1439816035-c42

[44] Katiyar D, Hemantaranjan A, Singh B, Bhanu N. Future perspective in crop protection: Chitosan and its oligosaccharides. Advances in Plants &

Agriculture Research. 2014;**1**:2-8. DOI: 10.15406/apar.2014.01.00006

[45] Ahmed K, Khan M, Siddiqui H, Jahan A. Chitosan and its oligosaccharides, a promising option for sustainable crop production - a review. Carbohydrate Polymers. 2020;**227**:115-331. DOI: 10.1016/j.carbpol.2019.115331

[46] Jia X, Rajib M, Yin H. Recognition pattern, functional mechanism and application of chitin and chitosan oligosaccharides in sustainable agriculture. Current Pharmaceutical Design. 2020;**26**:3508-3521. DOI: 10.2174/1381612826666200617165915

[47] Abdel-Aziz S, Kahil T, Keera A. Kinetic behavior of free and in situ immobilized chitosanases produced by the fungus *Mucor rouxii*. World Applied Sciences Journal. 2014;**30**:01-09. DOI: 10.5829/idosi.wasj.2014.30.01.13980

[48] Zhang P, Zhou W, Wang P, Wang L, Tang M. Enhancement of chitosanase production by cell immobilization of *Gongronella* sp. JG. Brazilian Journal of Microbiology. 2013;**44**:189-195. DOI: 10.1590/S1517-83822013005000017

[49] Sinha S, Tripathi P, Chand S. New bifunctional chitosanase enzyme from *Streptomyces* sp. and its application in production of antioxidant chito-oligosaccharides. Applied Biochemistry and Biotechnology. 2012;**167**:1029-1039. DOI: 10.1007/s12010-012-9546-6

[50] Rodriguez-Herrera R, Contreras-EsquivelJ,Mauricio-BenavidesJ, Garza-Garcia Y, Charles-Rodriguez A. Chitosanase production by a new bacterial source. Research Journal of Biological Sciences. 2008;**3**:957-963

[51] Struszczyk K, Szczęsna-Antczak M, Walczak M, Pomianowska E, Wojciechowska J. Enzymatic preparations from *Mucor moulds* and their application in oligoaminosaccharides production. Progress on Chemistry and Application of Chitin and its Derivatives. 2009;**14**:89-100. DOI: 10.15259/PCACD.21.09

[52] Olicón-Hernández D, Vázquez-Landaverde P, Cruz-Camarillo R, Rojas-Avelizapa L. Comparison of chito-oligosaccharides production from three different colloidal chitosans using the endochitonsanolytic system of *bacillus thuringiensis*. Preparative Biochemistry and Biotechnology. 2017;**47**:116-122. DOI: 10.1080/10826068.2016.1181086

[53] Lathouder K, van-Benthem T, Wallin S, Moulijn J. Polyethyleneimine (PEI) functionalized ceramic monoliths as enzyme carriers: Preparation and performance. Journal of Molecular Catalysis B Enzymatic. 2008;**50**:20-27. DOI: 10.1016/j.molcatb.2007.09.016

[54] Wittaya-areekul S, Prahsarn C, Sungthongjeen S. Development and *in vitro* evaluation of chitosan- Eudgragit RS 30D composite wound dressings. AAPS PharmSciTech. 2006;**13**(3): 123-128. DOI: 10.1016/j.ijpharm.2006. 01.027

[55] Sezer A, Cevher E, Hatipoglu F, Ogurtan Z, Bas A. Preparation of fucoidan-chitosan hydrogel and its application as burn healing accelerator on rabbits. Biological and Pharmaceutical Bulletin. 2008;**31**:2326-2333. DOI: 10.1248/bpb.31.2326

[56] Zhao W, Yin Y, Liang Q. Controlled released of salidroside from chitosan-alginate microcapsules. Food Fermentation Industries. 2004;**30**:66-69. DOI: 10.1002/jps.2600830213

[57] Li X, Piao X, Kim S, Liu P, Wang L. Effects of chito-oligosaccharides

supplementation on performance nutrient Digestibilly, and serum composition in broiler chickens. Poultry Science. 2007;**86**:1107-1114. DOI: 10.1093/ps/86.6.1107

[58] Sugano M. A novel use of chitosan as a hypocholesterolemic agent in rats. The American Journal of Clinical Nutrition. 1980;**33**:787-793

[59] Wu J, Tsai G. Cellulase degradation of shrimp chitosan for the preparation of a water-soluble hydrolysate with immunoactivity. Fisheries Science. 2004;**70**:1113-1120. DOI: 10.1111/j. 1444-2906.2004.00912.x

[60] Suzuki K, Mikami T, Okawa Y, Tokoro A, Suzuki S. Antitumor effect of hexa-N-acetylchitohexaose and chitohexaose. Carbohydrate Research. 1986;**151**:403-408

[61] Shibata Y, Foster L, Metzger W, His-Myrvik Q. Alveolar macrophage priming by intravenous administration of chitin particles, polymers of N-acetyl-D-glucosamine, in mice. Infection and Immunity. 1997;**65**:1734-1741. DOI: 10.1128/iai.65.5.1734-1741.1997

[62] Hsiao Y, Lin Y, Su C, Chiang B. High degree polymerized chito-oligosaccharides synthesis by chitosanase in the bulk aqueous system and reversed micellar microreactors. Process Biochemistry. 2008;**43**:76-82. DOI: 10.1016/j.procbio.2007.10.017

[63] Dalian Haixin Chemical Industry Co. [internet]. Available from: http://www.ec21.com/offer_details/sell_chitosan_oligosaccharide--8054608.html

[64] Hyean-Hoo L, Yoon-Sun P, Jong- SJ, Woon-Seob S. Chitosan oligosaccharides, dp 2-8, have prebiotic effect on the *Bifidobacterium bifidum* and *lactobacillus* sp. Anaerobe. 2002;**1**:319-324. DOI: 10.1016/S1075-9964(03)00030-1

[65] Fernandes J, Sereno J, Garrido P, Parada B, Cunha M. Inhibition of bladder tumor growth by Chito-oligosaccharides in an experimental carcinogenesis model. Marine Drugs. 2012;**10**:661-1675. DOI: 10.3390/md10122661

[66] Liu B, Wan-Shun L, Bao-Qin H, Yu-Yin S. Antidiabetic effects of chito-oligosaccharides on pancreatic islet cells in streptozotocin-induced diabetic rats. World Journal of Gastroenterology. 2007;**13**:725-731. DOI: 10.3748/wjg.v13.i5.725

[67] Nam K, Kim M, Shon YH. Chemopreventive effect of chitosan oligosaccharide against colon carcinogenesis. Journal of Microbiology and Biotechnology. 2007;**17**:1546-1549

[68] Choi Y, Kim E, Piao Z, Yun Y, Shin Y. Purification and characterization of chitosanase from bacillus sp. strain KCTC 0377BP and its application for the production of chitosan oligosaccharides. Applied Environmental Microbiology. 2004;**70**:4522-4531. DOI: 10.1128/AEM.70.8.4522-4531.2004

[69] Zhang N, Andresen B, Zhang C. Inflammation, and reactive oxygen species in cardiovascular disease. World Journal of Cardiology. 2010;**2**:408-410. DOI: 10.4330/wjc.v2.i12.408

[70] Mahdavi B, Rahimi A. Seed priming with chitosan improves the germination and growth performance of ajowan (*Carum copticum*) under salt stress. Eurasian Journal of Biosciences. 2013;**7**:69-76

[71] Larez-Velasquez C, Chirinos A, Tacoronte M, Mora A. Chitosan oligomers as bio–stimulants to zucchini (*Cucurbita pepo*) seeds germination. Agricultures (Poľnohospodárstvo). 2012;**58**:113-119

[72] Zou P, Tian X, Dong B, Zhang C. Size effects of chitooligomers with certain degrees of polymerization on the chilling tolerance of wheat seedlings. Carbohydrate polymers. 2017;**160**:194-202. DOI: 10.1016/j.carbpol.2016.12.058

[73] Abu-Hassan M, Pei-Li T, Noor Z. Coagulation and flocculation treatment of wastewater in textile industry using chitosan. Journal of Chemical and Natural Resources Engineering. 2009;**4**:43-53

[74] Dutta P, Dutta J, Tripathi V. Chitin and chitosan: Chemistry, properties, and applications. Journal of Scientific & Industrial Research. 2004;**63**:20-31

[75] Jia X, Meng Q, Zeng H, Wang W, Yin H. Chitosan oligosaccharide induces resistance to *tobacco* mosaic virus in Arabidopsis via the salicylic acid-mediated signalling pathway. Nature. 2016;**6**:26144. DOI: 10.1038/srep26144

[76] Cobos R, Mateos R, Alvarez JM, Olego M, Sevillano S. Effectiveness of natural antifungal compounds in controlling infection by grapevine trunk disease pathogens through pruning wounds. Applied Environmental Microbiology. 2015;**81**:18. DOI: 10.1128/AEM.01818-15

[77] Monirul I, Humayun K, Mamun A, Pronabananda D. Studies on yield and yield attributes in tomato and chilli using foliar application of oligo-chitosan. GSC Biological and Pharmaceutical Sciences. 2018;**3**:20-28. DOI: 10.30574/gscbps.2018.3.3.0038

[78] Zhang X, Li K, Xing R, Liu S, Chen X. miRNA and mRNA expression profiles reveal insight into chitosan-mediated regulation of plant growth. Journal of Agricultural and Food Chemistry. 2018;**66**:3810-3822. DOI: 10.1021/acs.jafc.7b06081

[79] Ahmad B, Khan M, Jaleel H, Sadiq Y, Shabbir A. Exogenously sourced γ-irradiated chitosan-mediated regulation of growth, physiology, quality attributes and yield in *Mentha piperita* L. Turkish Journal of Biology. 2017;**41**:388-401. DOI: 10.3906/biy-1608-64

[80] Jaleel H, Khan M, Ahmad B, Shabbir A, Sadiq Y. Essential oil and Citral production in field-grown lemongrass in response to gamma-irradiated chitosan. Journal of Herbs, Spices & Medicinal Plants. 2017;**23**:378-392. DOI: 10.1080/10496475.2017.1349702

[81] Dzung P, Phu D, Du B, Ngoc L, Duy N. Effect of foliar application of oligochitosan with different molecular weight on growth promotion and fruit yield enhancement of chili plant. Plant Production Science. 2017;**20**:389-395. DOI: 10.1080/1343943X.2017.1399803

[82] El-Sawy N, El-Rehim H, Elbarbary A, Hegazy S. Radiation-induced degradation of chitosan for possible use as a growth promoter in agricultural purposes. Carbohydrate Polymers. 2010;**79**:555-562. DOI: 10.1016/j.carbpol.2009.09.002

[83] Luan L, Nagasawa N, Tamada M, Nakanishi T. Enhancement of plant growth activity of irradiated chitosan by molecular weight fractionation. Radioisotopes. 2006;**55**:21. DOI: 10.3769/radioisotopes.55.21

[84] Hafiz M, Muhamad O, Muhammad S, Ahmad M. Irradiated chitosan as plant promoter. Proceedings. Symposium Biological Gunaan. 2003; **3-4**:1-7. DOI: 10.1063/1.4940072

[85] Tham L, Nagasawa N, Matsuhashi S, Ishioka N, Ito T. Effect of radiation-degraded chitosan on plants stressed with vanadium. Radiation Physics and Chemistry. 2001;**61**:171-175. DOI: 10.1016/j.jrras.2015.03.008