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Chitin, Chitinases and Chitin Derivatives in Biopharmaceutical, Agricultural and Environmental Perspective

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Abstract: Chitin is a major structural polysaccharide after cellulose and exists as the most abundant polymer in nature. Chitin is a nitrogen-containing homopolymer of β-(1,4) linked N-Acetylglucosamine. It is a key cell wall component of fungi, also found in a wide range of organisms, including viruses, plants, animals, insect exoskeletons, and crustacean shells. This review focused on the recent developments of applications of chitin, chitinases, and chitin derivatives in biomedicinal, agricultural and environmental perspectives for sustainable development. Chitinases are hydrolytic enzymes responsible for the degradation of chitin and are used in biocontrol against various fungal pathogens and insects to reduce the uses of synthetic fungicides and insecticides. These can serve as sustainable and eco-friendly alternatives to pesticides. Chitinases producing microorganisms are a potential alternative to these chemicals which are present in the soil as a part of the ecosystem. Chitin derivatives and chitinases have significant pharmacological values and are effective as an anti-inflammatory drug, ulcerative colitis, anticancer and gastrointestinal disorders. The significant medical roles of chitinases have also been observed to amplifying the functioning of antifungal drugs during the treatment of fungal diseases. These enzymes can be used for strengthened the human immune system and also employed antifungal creams and lotions as rightly expected. Chitin derivatives have a number of applications in the making of artificial medical articles, including contact lenses, artificial skin, and surgical stitches. These derivatives have been extensively used in making artificial medical products because of its non-toxic, non-allergic, biocompatible, and biodegradable properties. Chitin and its derivatives used for environmental applications comprise bioremediation of organic and inorganic contaminants from soil and water along with biological conversions of chitinous waste to the single-cell proteins, bioethanol, and biofertilizers as well.

Keywords: Chitin; Chitinases; Biomedicine; Biocontrol; Bioremediation; Biofertilizer.

1. Introduction

Chitin is an insoluble amino polysaccharide composed of β-1,4-N-acetylglucosamine [1]. It is a chief component of the cell wall among higher fungi belong to *Chytridiomycetes*,

Ascomycetes, *Basidiomycetes*, and *Deuteromycetes*, the exoskeleton of insects and crustacean external shells. Chitin present in a variety of microorganisms, which includes bacteria and fungi [2]. Bacteria are known for producing many secondary metabolites, which may have great potentials in the fields which are related to mankind [3]. Chitin was discovered by Henri Brancott in 1811, a professor of Natural History. It was first discovered by an English scientist, A. Hachette, who described it as a material that is predominantly resistant to the usual chemicals. In 1843 Lassaigne found that chitin contains nitrogen. Henri Brancott named it 'fungine'. It was found by the Oder in insects and plants in 1823, called it chitins. Chitin is found richly in nature and lies next to cellulose [4].

Chitinases are chemically hydrolytic enzymes liable to the degradation of chitin, a high molecular weight linear polymer of N-acetyl-D-glucosamine units. Chitinases can be found in a wide range of organisms' viz. plants, bacteria, fungi, and invertebrates [5-9]. Chitinase can be dividing into two types: i. endochitinases, and ii. exochitinases. The endochitinases can cleave chitin at internal sites to generate multimers of GlcNAc; however, the exochitinases facilitates the swift hydrolysis of chitin to produce GlcNAc, chitobiose, or chitotriose [10]. Chitinase-synthesizing bacteria are isolated from natural sources such as soil and other natural sources such as aquatic habitats [11-12]. Many bacteria, including *Serratia marcescens Aeromonas* sp., *Pseudomonas aeruginosa*, *Enterobacter*, and *S. griseus*, can synthesize several different chitinases [13-14]. Chitinases are the major factor of quite a lot of bacterial species, including *Aeromonas*, *Serratia*, *Vibrio*, *Streptomyces*, *Bacillus*, *Aeromonas hydrophila*, and *A. punctata* [10, 15]. Chitinolytic bacteria can also be isolated from the rhizosphere of a wide variety of plants [3, 16]. The fungal cell wall has a complex cross-linked structure composed of chitin, and the bacteria producing chitinase enzymes play an important role in lysing these cells by degrading the chitin [17].

In fungal chitinases play an important role in nutrition, morphogenesis, and biological roles like lysis of the cell wall, which helps in the screening of cells after division, hyphal autolysis, nutritional chuck, and morphogenetic formation, which helps in sporulation, spore germination, hyphal escalation and antagonistic dealings against additional microorganisms [17]. Chitinases can play a major role in many areas such as the production of single-cell protein, growth factors, mosquito control, ethanol and fertilizer, a biocontrol agent of fungal pathogens, isolation of fungal protoplasts, and antifungal drugs [18-25]. Thus, the need for microbial chitinase production has increased, and it fulfills two purposes: (i) trim down the environmental hazards and (ii) augmented production of industrially imperative value-added products [26]. The study was proposed to know the potential of different organisms for the production of chitinases and their sustainable role in human health, biocontrol, agriculture, and environment, etc.

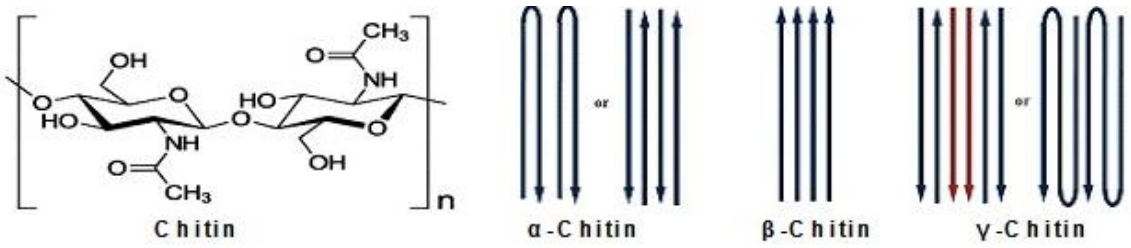

Figure 1. Molecular structure and different polymeric configurations of chitin.

2. Chitin: structure, properties, sources, and extraction

2.1. Structure of chitin.

In nature, chitin can be found in three different polymeric forms: α, β, and γ [27]. The α form is universally found and is generally collected from crab and shrimp shells and has an antiparallel arrangement, and β form is mainly acquired from mollusks and has a parallel arrangement in contrast to the α form. The α and β forms of chitin are economic in nature, and both differ in the packaging and polarities of straight chains in the chitin sheets. While in the case of γ, chitin has two parallel strands and two antiparallel strands. The β form is not convertible into alpha form, but γ chitin is convertible into α chitin by treating it with lithium thiocyanate (Fig. 1).

2.2. Properties of chitin.

Chitin is not soluble in water due to the strong intermolecular hydrogen bonding [28]. But there are certain chitin-based derivatives which are soluble in water, such as chitosan or carboxymethyl, which can be obtained from chitin, and the most important advantages of these compounds in which they are really flexible so that they can be molded into various forms like fibers, hydrogels, beads, sponges, and membranes. Chitin is crystalline in nature, and the tensile strength is much higher than most of the manufactured materials [29]. The extensive hydrogen bonding within the chains of chitin is the reason for the high tensile strength of chitin. A significant amount of chitin is present in almost all fungi, which give the evidence that the polymer is widely distributed in the kingdom Fungi and phylum Arthropoda and Mollusca of kingdom Animalia [9, 30].

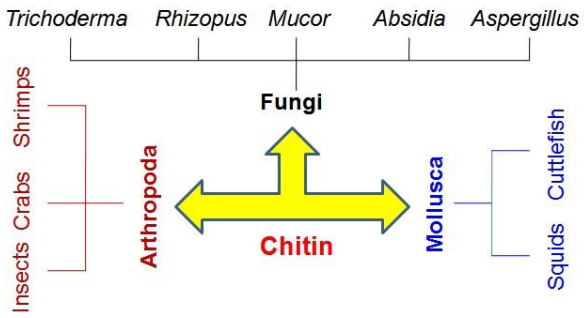

Figure 2. Potential natural sources of chitin.

2.3. Sources of chitin.

There are large numbers of complex intracellular processes are involved in the formation of chitin comprising the biotransformation of trouble-free metabolites and formation of the polymer, chitin [30]. The accumulation of catalytic units in the cell membrane allows polymerized GlcNAc molecules to be a force out into the extracellular environment. The raw materials which are widely available for the manufacturing of chitin are insects, crab shells, shrimps and lobsters, and fungi (Fig. 2) [31]. The main potential animal sources for chitin production and its harvestings are insects (e.g., Beetles, Moths *Bombyx mori*, Honey bees *Apis* sp., Mosquitoes *Aedes aegypti*, etc.); crabs (e.g., Golden king crab *Lithodes aequispinus,* Snow crab *Chionoecetes opilio,* Tanner crab *C. bairdi,* Korean hair crab *Erimacrus isenbeckii,* Blue king crab *Paralithodes platypus,* Red king crab *P. camtchaticus,* etc.); shrimps (e.g., *Penaeus*

carinatus, *P. monodon*, *Litopenaeus vannamei*, *Parapenaeopsis stylifera*, etc.); lobsters (e.g., *Homarus americanus*, *Jasus lalandii*, etc.); mollusks (e.g., Cuttlefish *Sepia offcinalis*, Squid *Loligo vulgaris*,etc.); fungi (e.g., *Absidia blakesleeana*, *A. coerulea*, *A. glauca*, *Aspergillus niger*, *Gongronella butleri*, *Lentinus edodes*, *Mucor rouxii*, *Phycomyces blakesleeanus*, *Rhizopus oryzae*, *Trichoderma reesei*, etc.) [32-53].

2.4. Extraction of chitin.

For the extraction, harsh treatments are required because chitin is found associated with other constituents. In the present chitin, production is hugely dependent on canning industries as they produce crab and shrimp shells as their waste products. Chitin is now commercially manufactured in India, Japan, Poland, Norway, and Australia. In India, the Central Institute of Fisheries Technology, Kerala, was the first to start research on chitin and reported that the dry waste of prawn had 23% chitin; however, dry *Squilla* had 15% chitin content [54]. The process of conversion of chitinous waste to commercial products is very useful in view of their great economic value and versatile biological and chemical applications, chiefly in medical and pharmaceutical areas (Fig. 3).

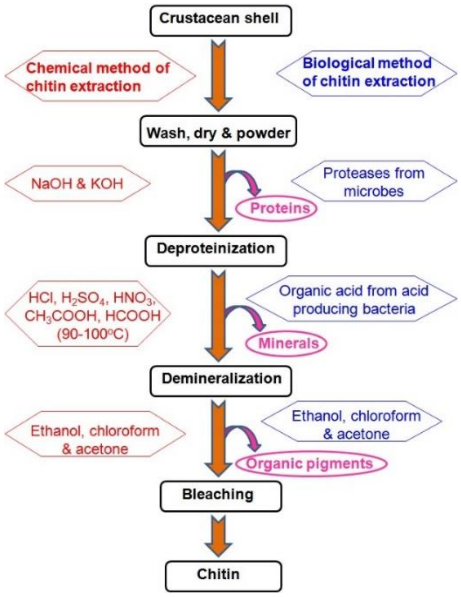

Figure 3. The extraction of chitin by chemical and biological methods.

3. Chitinase: structure, properties, and types

Chitinases are various groups of enzymes that show variations in the structure, substrate specificity, and acting mechanism [32]. The size range of these enzymes lies between 20kDa to about 90kDa [55].

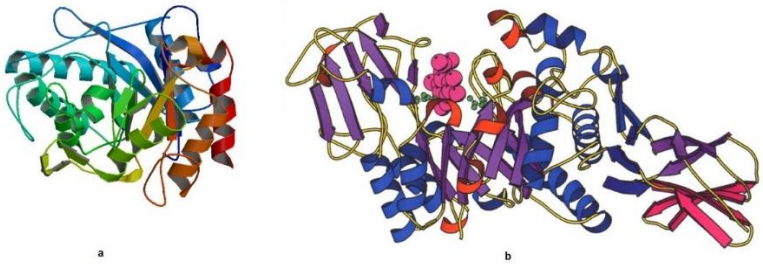

Figure 4. Structure of wild type chitinase (a) and bacterial chitinase-A, ChiA (b).

3.1. Structure of chitinases.

The structure of chitinase is modular, having one catalytic and single or many noncatalytic domains that could or couldn't play a task during substrate binding (Fig. 4). The bacterial chitinases showed no concern to the resemblance between the catalytic and chitin-binding domains in pairwise comparative accounts that implies to the fact that chitin-binding domains in bacterial chitinases are conserved evolutionarily (Fig. 4) [56]. As the chitinases of different families have no amino acid sequence similarity and have different three-dimensional structures, it is likely that they have evolved from different ancestors [57]. Family 18 contains repeats of amino acids, and their enzyme core consists of eight strands of parallel β sheets, which form a barrel, and alpha helices are present below this barrel, which is present in the form of a ring towards the outside (Fig. 5) [58]. The polydomain structure of family 19 included catalytic domains, a cysteine affluent chitin-binding domain, and a serine/ threonine rich glycosylated domain, which have been discovered as the structural characteristics of chitinases in various organisms (Fig. 5) [59]. The bacterial and fungal chitinases show a very close association in terms of their structure, strongly suggesting that the catalytic domains in all of these microorganisms are greatly similar.

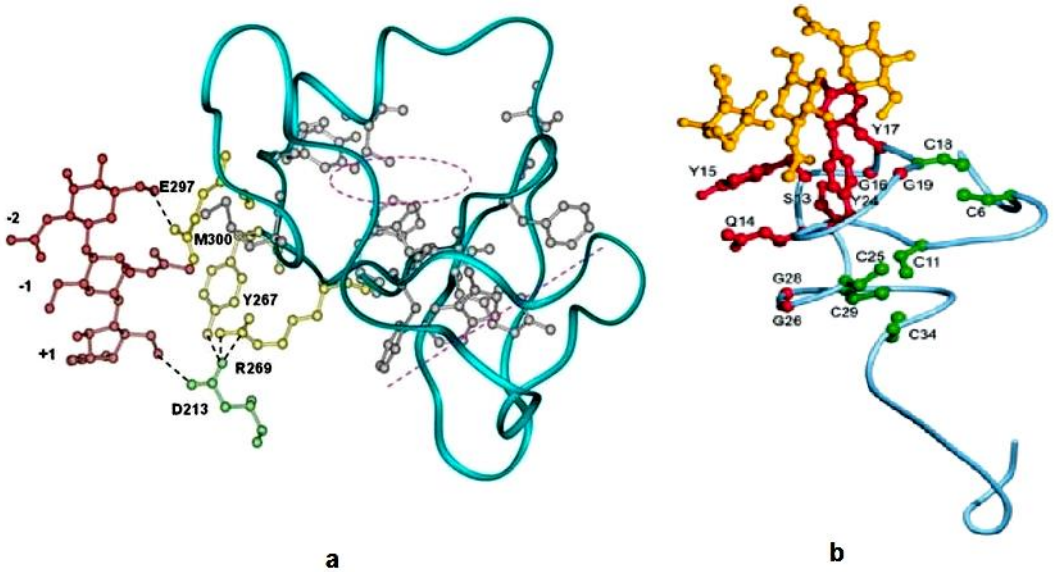

Figure 5. Structure of family 18 (a) and family 19 (b) chitinase.

3.2. Properties of chitinases.

The study substrate specificity is important for chitinases because it divulges the relationship between substrate specificity and physiological roles. Enzyme nomenclature has listed chitinolytic enzymes as chitinases and N-acetyl-β-glucosaminidase. The chitinase breaks chitin polymers, and the N-acetyl-β-glucosaminidase degrades terminal N-acetyl-β-glucosamine residues lying on the non-reducing end from chitobiose and higher analogs. Chitinases are hydrolytic enzymes that are capable of breakdown the β-(1,4)-glycoside bond of chitin, a main structural component in insect exoskeletons and fungal cell walls. Chitinases are created by higher plants, which utilize the catalysts to safeguard themselves against pathogenic assaults by corrupting chitin in the cell wall of microbes [6]. The chitin is degraded into chito-oligomers by chitinases, which serve a broad range of applications.

3.3. Types of chitinases.

Chitinases are broadly divided into two classes (endochitinases and exochitinases) on the basis of its synthesis and nomenclature [10]. The endochitinases split chitin and chitin microfibrils at random internal sites to produce soluble, low molecular mass products, e.g., chitotetraose, chitotriose, and diacetyl-chitobiose (Fig. 6). The exochitinases can catalyze the hydrolysis of chitin progressively to produce N-acetylglucosamine, GalNAc (Fig. 7). Exochitinases have been divided into two categories: chitobiosidases, and β-(1,4)-N-acetylglucosaminidases [8].

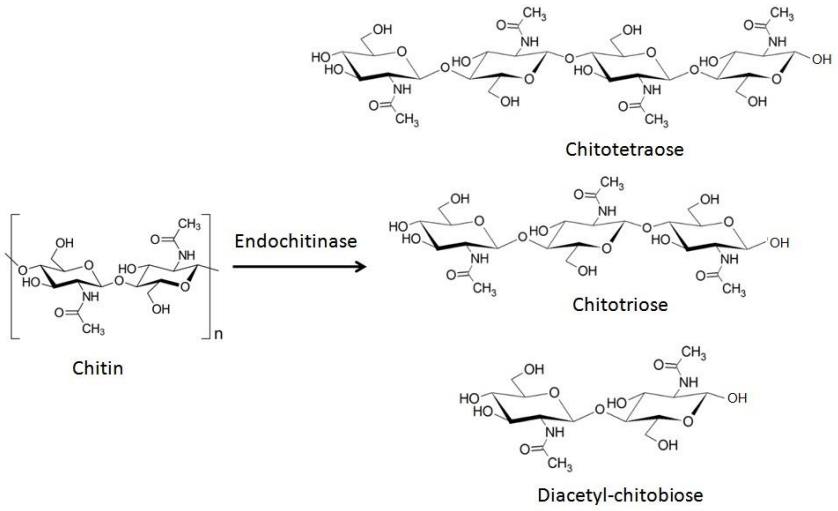

Figure 6. Chemical reaction for hydrolysis of chitin by endochitiases.

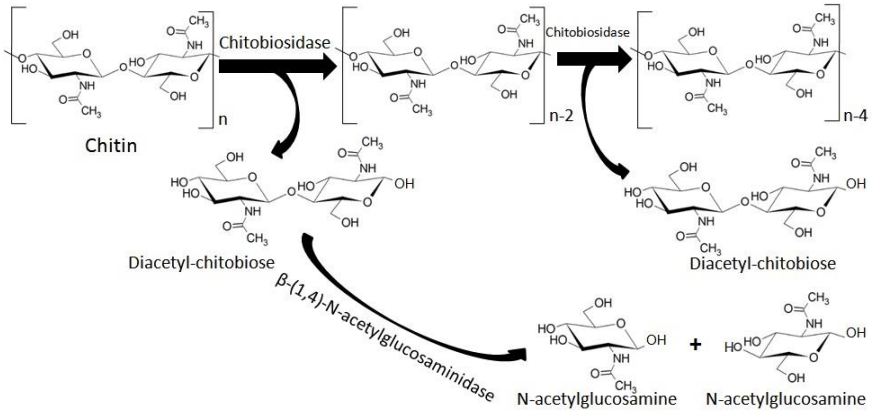

Figure 7. Chemical reaction for chitin hydrolysis by exochitiases.

The chitobiosidases act on a non-reducing terminal of chitin, and release di-acetylchitobiose dimer from the parent chitin chain. However, β-(1,4)-N-acetylglucosaminidases split the polymeric products (e.g., di-acetylchitobiose, chitotriose, and chitotetraose) into monomers of N-acetylglucosamine [30]. The gene sequences of the chitinases came to be known; these were further divided into six classes based on their sequences [60-62]. Class-I chitinases had a cysteine-rich N-terminal, leucine- or valine-rich signal peptide, and vacuolar localization. These chitinases are further subdivided on the basis of their acidic or basic nature into class-Ia and class-Ib, respectively. This group contains only plant chitinases, and most of these are endochitinases. Class-II chitinases had a similar sequence to class-I chitinases. These are found in plants, fungi, bacteria, and most of these are exochitinases. Class-III chitinases have no similar sequences to class-I or class-II. Class-IV chitinases had similar characteristics as class-I chitinases, but these chitinases were really

smaller in size than class-I chitinases. Class-V and class-VI chitinases are not clearly characterized so far.

3.4. Natural sources of chitinases.

The chitinases are derived from various natural resources, including bacteria, fungi, plants, and animals in variable quantities. Bacteria are major sources of chitinase and produce mainly to hydrolyze chitin and use it as a source of energy. Chitinase-synthesizing bacteria are isolated from natural sources such as soil and other natural sources such as aquatic habitats [11-12, 62]. Some chitinases produced from of chitinolytic bacteria, such as *Serratia marcescens*, *Enterobacter* sp. *Aeromonas hydrophila, A. punctata, Serratia, Vibrio, Streptomyces*, and *Bacillus* [10, 14, 15, 62]. Chitinolytic bacteria can also be isolated from the rhizosphere of a wide variety of plants [3, 16]. The fungal cell wall has a complex cross-linked structure composed of chitin, and the bacteria producing chitinase enzymes play an important role in lysing these cells by degrading the chitin [17].

The production of chitinase in the case of filamentous fungi can be observed throughout its life cycle [63]. In fungi, this enzyme plays an important role in releasing the spores and also in the hyphal branching [5]. In yeast, chitinase has a role in cell separation [64]. Chitinase also plays an essential role in nutrition by helping in the utilization of chitin for its carbon and nitrogen requirements [65]. In a few cases, it also plays a role in pathogenicity [66]. Many earlier scientists have been reported the purification and characterization of 3N-acetylglucosaminidase (GlcNAcases) from various isolates of *Trichoderma* spp. [67-69]. *Trichoderma spp*. have given the significant contemplation as biocontrol agents of soil-borne fungal pathogens. The chitinases and β-1,3-glucanases are isolated, purified, and characterized by *Talaromyces flavus* and *Trichoderma spp*. and their role in mycoparasitism against soil-borne fungi, *i.e., Sclerotium rolfsii, Rhizoctonia solani,* and *Fusarium sp*. has also been reported [70-72].

The plant chitinases have been reported in both monocotyledonous and dicotyledonous species and have been found in different types of structures like embryos and cotyledons, seeds, leaves, and stems, roots and flowers, and protoplasts [7, 73-75]. Chitinases have also been reported in crops (e.g., barley, rice, onion, wheat, etc.) and non-crop species like *Arabidopsis*, poplar, and rubber [8]. Their production is influenced by a variety of factors, such as infection, stress conditions, and phytohormones [76]. The plant chitinases are delivered as proteins in plant self-preservation because of the assault of phytopathogens [77]. The chitinases take part in vital physiological processes of plants, like embryogenesis and ethylene synthesis [56]. Garg and Gupta isolate and purify the chitinase from moth beans attacked by the fungus *Macrophomina Phaseolina* strain 2165 [78].

3.5. Production of chitinases.

Microbial chitinases have been fashioned by liquid batch fermentation, incessant fermentation, and fed-batch fermentation (Fig. 8) [1]. Additionally, solid-state fermentation and biphasic cell systems have also been used for the mass scale production of chitinases. The chitinases produced by microbes are usually inducible categories. Components of media, carbon sources, nitrogen sources, and agricultural residues *viz*., rice bran, wheat bran, etc. also affect extracellular chitinase production [13, 79]. An alluring impact of glucose on chitinase creation was accounted for when glucose was utilized with chitin in the creation medium [79].

On the other hand, Miyashita *et al*. reported a suppressing effect of glucose on chitinase production [80]. The temperature, pH, and aeration, also influence chitinase production. Production of chitinase from *Bacillus* sp. BG-1, also increases when the growth medium is added with amino acids such as tryptophan, tyrosine, glutamine, and arginine (0.1mM) [79]. The extracellular chitinase production by *Serratia marcescens* in an aqueous two-phase system (ATP) of PEG and dextran was reported by Chen and Lee [81].

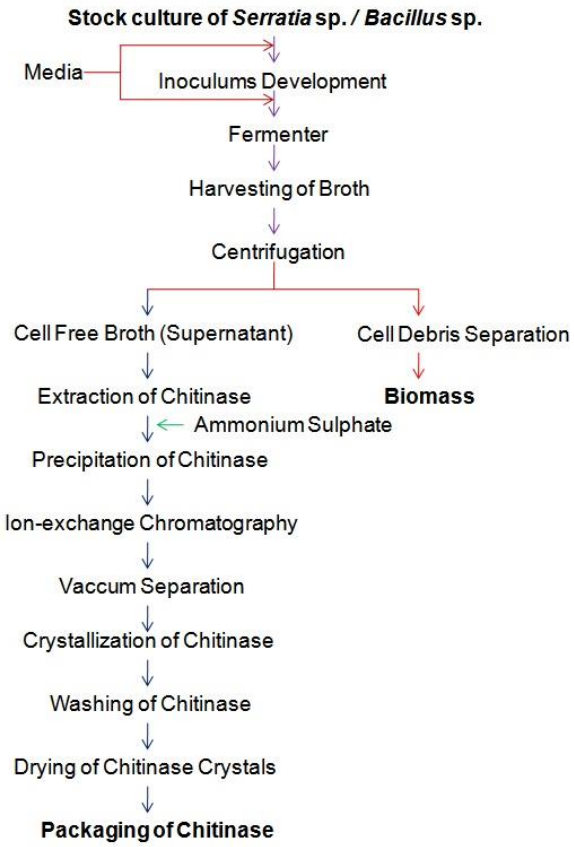

Figure 8. Flow chart showing batch fermentation, production, purification, and packaging of chitinases.

3.6. Application of chitinases.

Chitinases can play a major role in many areas such as the production of single-cell protein, growth factors, mosquito control, bioethanol and biofertilizers, a biocontrol agent of fungal pathogens, isolation of fungal protoplasts, and antifungal drugs (Fig. 9) [1, 18-25].

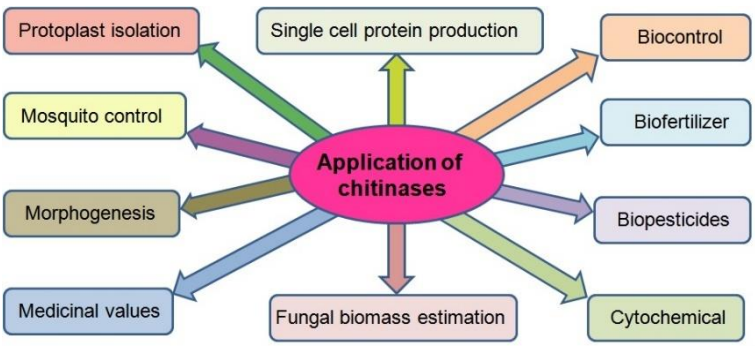

Figure 9. Potential diversification in applications of chitinases.

Thus, the need for microbial chitinase production has increased and solved two purposes: (i) shrink the environmental hazards and (ii) augments manufacture of industrially

important value-added products [26]. Chitinases are useful for the production of ophthalmic products by the use of chitinases and micro biocides [82]. An important medical use of chitinases has also been observed in amplifying the functioning of antifungal drugs in the treatment of fungal diseases [21]. Due to their applications, their use in antifungal creams and lotions is rightly expected. Several pieces of evidence have explained the importance of chitinases in the defensive immune system of mammals [22]. The presence of bacterial chitinases in humans can play an important role as a component of defense mechanisms against fungal attack [83].

4. Chitin derivatives and its applications

GlcNAc (a polymer of chitin) itself acts as an anti-inflammatory drug. It is synthesized in the human body from glucose, and after being synthesized, it is then incorporated into glycoprotein and glycosaminoglycans. The GlcNAc, which is administered in the human body, has been found to be effective in the treatment of ulcerative colitis, gastrointestinal disorders, and inflammation [84]. The uses of chitin might be limited because of its helpless dissolvability, low porosity, and surface zone [85]. Henceforth to conquer the impediments and control the properties of chitin, different noteworthy subsidiaries are created (Table 1). Chitosan is one of the most significant subordinates of chitin as far as appropriateness [86]. Chitin derivatives have a number of applications in the making of artificial medical articles such as contact lenses, artificial skin, and surgical stitches. These derivatives have been extensively used in making artificial medical products because these chitin derivatives have been found to be non-toxic, non-allergic, biocompatible, and biodegradable [87]. Rameshthangam *et al*. discuss the different biomedical applications of chitin and its derivatives (Fig. 10) [30].

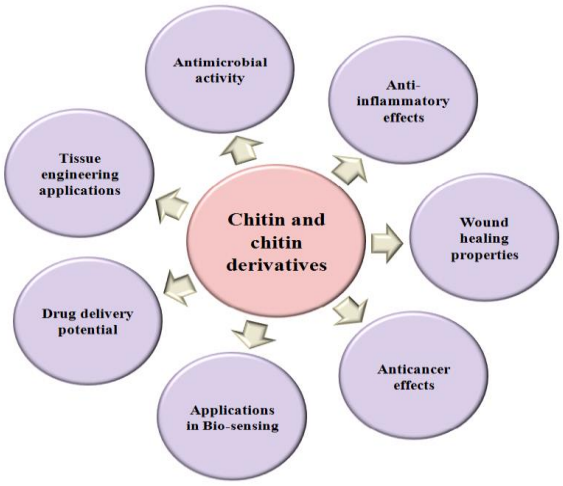

Figure 10. The biomedical applications of chitin and its derivatives.

4.1. Application in nanomedicine and biomedical engineering.

Chitosan is one of the most extravagant biopolymers got from characteristic chitin that normally exists in the exoskeletons of arthropods, shellfish shells, creepy crawlies, and parasitic cell dividers [88]. Chitosan is a natural and cationic polysaccharide, has been considered as a promising nanomaterial with broad clinical applications [89-90]. It has remarkable properties, for example, nontoxicity, biocompatibility, biodegradability, bioactivity, and mucoadhesion [91-92]. It very well may be corrupted by interior proteins, for example, lysozymes and chitosanases, to procure oligosaccharides and monosaccharides,

which are in this manner consumed by the body [93]. Be that as it may, different methodologies for adjusting chitin and chitosan have been created to address these issues [94-95]. Free amino and hydroxyl bunches have been used to create a wide scope of subsidiaries with improved solvency dependent on its high proclivity with useful proteins and the ability to self-collect [96-97]. It tends to be handily prepared in differing structures, for example, films, strings, tablets, layers, and microparticles/ nanoparticles, permitting the plan of an assortment of clinical and pharmacological gadgets versatile to end purposes. Specifically, in medication, chitosan might be valuable in swathes to decrease draining, and as an antibacterial operator can likewise be utilized to help convey drugs through the skin (Fig. 11). It is additionally utilized in the improvement of chitosan medicate control discharging frameworks, including chitosan wipes, chitosan film, chitosan dabs, chitosan microbeads (microspheres), and chitosan nanoparticles. In other words, nano-magnetic is the center and chitosan polymer covering the magnetic centers. The procedure is called a coating. These magnetic nanoparticles can be utilized as incredible transporters for chemical immobilization, and chitosan nanoparticles have an antitumor job through improving the ” body’s safe capacity or immune system [98]. In spite of the notable points of interest of exploiting chitosan in these fields, extra work should be done to streamline ” chitosan’s details and upgrade its physicochemical properties for various employments.

Table 1. Biomedical and industrial application of various chitin derivatives.

S.No.	Chitin derivatives	Process of synthesis	Applications	References
1.	Chitosan	Deacetylation	Anticancer, antibacterial agent, enzyme immobilization,	[85-86, 99-100]
2.	Alkyl chitin	Deacetylation of chitosan	Antimicrobial agents	[101]
3.	N and O sulfated chitin	Sulfation	Anticoagulant agent, heparin	[102]
4.	Dibutyryl chitin	Reaction of the chitin with butyric anhydride	Intermediates for further chemical modifications	[103-104]
5.	Carboxymethyl chitin (CMCH)	Carboxymethylation	Excipients for oral drug delivery	[105-106]
6.	Chito-oligosaccharides (COS)	Acid hydrolysis and oxidative, reductive depolymerization	Nutraceutical additive	[107-108]
7.	Chitin nanofibers (CNF)	Loosening of tightly bonded fibrils bundles by removal of minerals, proteins, pigments, and lipids with the treatment of HCl, NaOH, and ethanol	Tissue engineering wound dressing, cosmetic, skin health, stem cell, anticancer therapy, drug delivery, obesity treatment, anti-inflammatory	[109-111]
8.	Chitin nano-whiskers (CNW)	Treatment of chitin with 3N HCl at 100°C or 3M H_2SO_4 solution	Nanotechnology and nanocomposite material for drug/gene delivery or nanoscaffolds in tissue engineering	[112-113]
9.	Chitin nanoparticles (CNP)	Treatment of chitin in 3M HCl for 1.5 h at 90°C	Biocompatible, biodegradable, and non-toxic	[114-116]
10	Chitin nanocomposites (CNC)	By chitin whisker and tannic acid,cross-link chitosan, or chitin nanofibers or adding metal nanoparticles into chitin matrix	Drug encapsulation, improving the drug load, and controlled release action	[76, 117]
11.	Chitin hydrogels (CHG)	NaOH treatment of chitin	Bone tissue regeneration, cell scaffolds and drug delivery vehicles	[118-120]

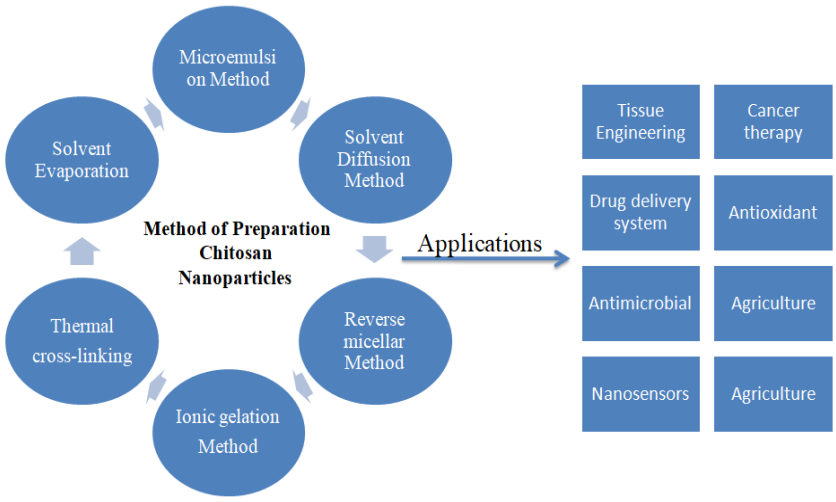

Figure 11. Strategies for production and application of chitosan nanoparticles.

4.2. Application in sustainable agriculture management.

4.2.1. Antifungal activity.

A highly limiting factor in the production of the crops is the diseases that are caused by the phytopathogenic fungi [23, 25]. These diseases affect the seeds right from germination and throughout development, consequently reducing the yield by 30% [121]. Therefore plant disease control has become highly dependent upon the fungicides to control these fungal diseases. The investigation has reported potentially unfavorable environmental side effects. Increased awareness and the concern regarding the accumulation of the residues of these chemical fungicides in the biosphere and also the development of the resistance against conventional antibiotics have done the search for new antimicrobial agents, a field of utmost importance in disease management. Organisms producing chitinase can be exploited as biocontrol agents in both direct and indirect manner by using their purified proteins or via gene manipulation [122]. According to estimation, the crop loss because of disease-causing pathogens is around 25% of the total yield in the developed countries, and in the developing countries, it is around 50% [123]. Fungal infections alone cause a threat f these diseases. Nonspecific toxicity and adverse effects of commercial fungicides on the environment have led our thinking on other options of pest control like the use of chitinases/ chitinolytic enzymes as antifungal agents to control pathogens [19]. The characteristic of chitinases to hydrolyze chitin can be exploited, suggested a greener approach that can be exploited to control plant and fungal pathogens.

Biological control is the most accepted alternative because it is environment friendly. These specific microorganisms are used, which interfere with the plant pathogens and pests and doing so to overcome the problems caused by the chemical methods. Among the microorganisms, the bacteria are considered as the most suitable as they are able to produce a variety of antimicrobial products. The bacterial species of *Streptomyces*, *Bacillus*, and *Pseudomonas* are commonly used as biocontrol agents [124]. There has been a lot of information reported on the antagonism between the bacteria and fungi and about its potential role in biocontrol [125-126]. Some bacterial secretions have the ability to kill the phytopathogenic fungi. These secretions contain many enzymes that lyse the structural component of the fungal cell wall. One of the enzymes in these secretions is chitinase. Chitinase plays an important function in biocontrol of fungal plant diseases by hydrolyzing chitin

polymer of fungal pathogen's cell walls so that altered fungal growth, hyphal tips, and germ tubes [24, 71, 127].

The rectified chitinases of *Streptomyces rimosus* exhibited *in vitro* antifungal properties against *Fusarium solani* and *Alternaria alternata* [128]. Correspondingly, the chitinolytic potential of *Streptomyces viridificans, in vitro* was observed against *Curvularia, Pythium, Colletotrichum, Fusarium Aspergillus, Sclerotinia,* and *Rhizoctonia* [28]. Amongst *Streptomyces* spp. Recovered from rhizosphere soils, the *S. hygroscopicus* was effective antagonistic against *Colletotrichum gloeosporioides* and *Sclerotium rolfsii* [16]. The damping-off disease of sugar beet, caused by *Rhizoctonia solani*, can be controlled *in vitro* with streptomycetes [129]. It was observed that GH19 chitinases show antifungal properties against fungi: *Rhizoctonia solani, Colletotrichum gossypii, Pythium aristosporum,* and *Fusarium oxysporum*. *Streptomyces viridodiasticus* isolates caused extensive cell wall lysis of *Sclerotinia minor* when grown in a carbon-free salt solution [27]. These isolates, individually or in combination, decrease disease incidence in greenhouse conditions [130]. The combined effect of chitinolytic enzymes and an antifungal compound, 2-furancarboxaldehyde of *Streptomyces cavourensis* was found to be a potential biocontrol agent of anthracnose in pepper [131]. An earlier report showed that *Bacillus thuringiensis* isolates exhibited antifungal activity against *Verticillium* spp. *in-vitro* [132]. The isolates of *Bacillus cereus* reduced the severity of *Verticillium* wilt on eggplant up to 70% in 14 days [133]. The endochitinase and chitobiose from *Serratia marescens* inhibited *Botrytis cinerea in vitro*. The red pigment Prodigiosin, produced by *S. marescens*, enhanced the rate of inhibition [134]. The damping-off disease of cucumber, which is caused by *Phytophthora capsici*, also controls by Prodigiosin. The *in vitro* chitinase activity of *Enterobacter* spp. was assessed in opposition to the common cocoa leaf pathogen, *Colletotrichum gloeosporioides*. The in vitro outcomes demonstrated that the contagious hyphae developed in deviant shapes and were broken or lysed, which was probably brought about by *in vivo* assays, established a decreased severity of the disease [135]. Many chitinolytic bacteria also possess plant-growth-promoting properties, e.g., a *Pseudomonas* sp. enhances nodulation in chickpea [136].

4.3.1. Insecticide activity.

The well-known biocontrol agent of insects in agriculture is *Bacillus thuringiensis.* Chitinases have also been demonstrated to affect insect growth, which ultimately leads to death [24]. The chitinases were weakening the peritrophic membrane that lines the gut epithelium of the larvae [137]. Brandt *et al*. found that the *Orgyia pseudotsugata* peritrophic membrane was besmirched by chitinases, and an equivalent effect was also observed *in vivo* with *Spodoptera littoralis* and *E. coli* that expressed the endochitinase ChiAII from *Serratia marescens* [138-139]. The *B. thuringiensis* blends two chitinases that improved the insecticidal action of Bt crystal protein against hatchlings of *Spodoptera exigua* and *Helicoverpa armigera* [119, 140]. *Bacillus pumilus* inhibited the growth of *Scirpophaga incertulas*, a rice pest [141]. *Paenibacillus illinoisensis* deformed and destroyed the eggshell of the root-knot nematode (*Meloidogyne incognita*) [101]. Singh *et al*. found that *Paenibacillus* sp. D1, could be used to control *Helicoverpa armigera*. *Stenotrophomonas* and *Chromobacterium were* observed to inhibit egg hatch of the potato cyst nematode (*Globodera rostochiensis*) *in vitro* [142-143]. A GH18 chitinase isolated from *Pseudomonas* sp., had amino acid sequence identity with chitinases of *Serratia marescens*, showed little insecticidal activity towards *Spodoptera litura* larvae [144].

4.4. Application in environmental management.

The biggest source of chitinous waste is the seafood industry. In order to maintain the ecosystem's carbon-nitrogen balance, its recycling is highly essential. The insoluble nature of chitin and its inactivity towards most chemical agents makes it mandatory for the utilization of more feasible biological processes. Keeping the above facts in view, enzyme chitinase can be adequately used for the biological conversion of industrial seafood waste [18]. It executes two functions at the same time in a manner that makes use of chitinous wastes and reduces the production cost of the microbial chitinases [20]. Soil and water pollution by organic and inorganic contaminants affect human health and the environment. Environmental protection is very important nowadays, and industries try to develop new technologies that resolve the contaminants problem [145-147]. Recently chitin and its derivatives were used for remediation of organic and inorganic contaminants from soil and water (Fig. 12). The biocompatible nature of chitins and its derivatives are used for the immobilization of chitinases for sensing the environment hazardous chemicals [148]. Chitin and chitosan help for the removal of dyes, organic and contaminants, and remediation of heavy metals [149-153]. After some modifications like functionalization of chitin is using irradiated grafting of acrylonitrile on chitin, polypyrrole, acetophenone derivatives of nanochitosan, cross-linking chitosan into nanohydrogel, poly, chitin nanofibers having better heavy metal adsorption potential (154-156]. Chitinous waste of marine organisms can be converted into simpler useful depolymerized components by chitinases, which reducing water pollution (2, 157-158]. Chito-oligomers obtained by the action of chitinases have a wide range of biotechnological applications in biochemical, food, and various chemical industries (Fig. 12). Chitinase can also be used in the conversion of chitinous waste into biofertilizer, insecticides, and fungicides so that these can be more potent and ecofriendly as compared to chemically synthesized active agents (Fig. 12).

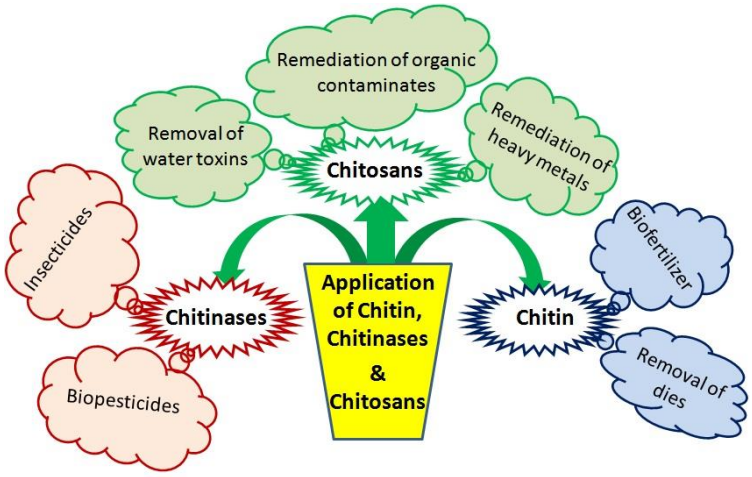

Figure 12. Application of chitin, chitinases, and chitosans for sustainable management of the environment.

5. Conclusions

The chitin is naturally available in insects, fungi, and some algae; these are widely used for the manufacturing of chitin; chitinases play a significant role in biocontrol against various fungal pathogens and insects. These can serve as sustainable and eco-friendly alternatives to chemical pesticides. Chitinase producing microorganisms are a potential alternative to these chemicals because they are present in the soil and part of the ecosystem. For the industrial applications, the production of chitinase is carried out in the liquid batch fermentation,

continuous fermentation, and fed-batch fermentation by chitinolytic microorganisms. Chitin derivatives and chitinases have significant pharmacological values, as an anti-inflammatory drug, antifungal drugs, anticancer, immunity booster, antifungal creams, wound healing, contact lenses, artificial skin, surgical stitches, and used in making artificial medical products because these chitin derivatives have been found to be non-toxic, non-allergic, biocompatible, and biodegradable. In the environmental remediation process, using chitin and its derivatives may lead to the development of futuristic methods to reduce the environmental toxins because these are eco-friendly biodegradable material. Other applications of chitinases include the biological conversions of chitinous waste to the single-cell proteins and ethanol and fertilizers. We hoped that this review would encourage the use of chitin, chitinases, and chitin derivatives for the sustainable development of pharmaceutical, agricultural, and environmental perspectives for the benefit of society and nature.

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Conflicts of Interest

The authors declare no conflict of interest.

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