Received: 30 April 2024 | Revised: 20 August 2024 | Accepted: 26 August 2024

DOI: 10.1002/app.56250

REVIEW

Applied Polymer SCIENCE WILEY

Advancements and potential of chitosan-genipin complex in biotechnological applications: A comprehensive review

Elí Emanuel Esparza-Flores[1,2] | Plinho F. Hertz[1] | Rafael C. Rodrigues[2]

[1]Enzymology Laboratory, Food Science and Technology Institute, Federal University of Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil

[2]Biocatalysis and Enzyme Technology Laboratory, Food Science and Technology Institute, Federal University of Rio Grande do Sul, Porto Alegre, Rio Grande do Sul, Brazil

Correspondence
Rafael C. Rodrigues, Biocatalysis and Enzyme Technology Laboratory, Food Science and Technology Institute, Federal University of Rio Grande do Sul, 9500 Bento Gonçalves Ave, P. O. Box 15090, ZC 91501-970, Porto Alegre, Rio Grande do Sul, Brazil.
Email: rafaelcrodrigues@ufrgs.br

Funding information
Conselho Nacional de Desenvolvimento Científico e Tecnológico, Grant/Award Number: 405418/2021-3; Fundação de Amparo à Pesquisa do Rio Grande do Sul, Grant/Award Numbers: 21/2551-0002270-1, 22/2551-0000397-4; Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) from Brazilian Government; Consejo Nacional de Humanidades; Ciencias y Tecnologías (CONAHCYT) from Mexican Government

Abstract

The chitosan-genipin complex has been extensively studied and applied in various fields, attracting increasing attention due to its unique characteristics and properties. This complex enables the development of novel materials for applications in biomedical engineering, biotechnology, and medicine. Chitosan is a natural biopolymer, and genipin is an extract obtained from some fruits, mainly from genipap and gardenia; both have demonstrated biodegradability, biocompatibility, and antimicrobial properties. Due to their versatile and reinforced structure, new materials have shown potential use in drug delivery, tissue engineering, scaffolds, curatives, food packaging, and enzyme immobilization. This review will discuss the chitosan and its modifications, the genipin and its reactivity, and finally, the complex chitosan-genipin, showing some recent developments and applications and some prospectives for other applications in new fields, especially as support for enzyme immobilization.

KEYWORDS

biomaterials, biomedical applications, biopolymers and renewable polymers, polysaccharides

1 | INTRODUCTION

Enzymes are highly efficient biocatalysts widely employed in industrial applications and biotechnological processes. However, their limitations include low stability, non-reusability, and susceptibility to harsh operating conditions. These drawbacks restrict their potential applications, particularly in continuous bioprocesses. As a result, enzyme immobilization has emerged as a promising approach to overcome these challenges and enhance enzyme performance.[1–3]

Immobilization involves making enzymes insoluble, enhancing their stability and reusability, and facilitating their separation from the reaction media, thereby enabling continuous operation.[4] Various materials have been studied and tested to support enzyme immobilization. These materials can be organic (such as alginate, gelatin, agarose, and chitosan) or inorganic (such as silica-based materials, magnetic particles, and ceramic materials), simple or hybrid, modified, or unmodified. Each support material has specific characteristics and properties that need to be compatible with the enzyme

and the intended bioprocess. Polysaccharides have emerged as desirable support materials. They are organic, biocompatible, and abundant, with some polysaccharides even derived from industrial waste, making them environmentally friendly alternatives to synthetic materials.[5–7]

Chitosan, derived from the deacetylation of chitin, is the second most abundant polysaccharide in nature, following cellulose. This versatile polymer finds extensive application across various fields, including biomedicine, agriculture, food technology, and bioprocesses.[5,8–10] Its desirable properties are related to its biocompatibility, non-toxicity, biodegradability, and demonstrated antimicrobial activity.[11–13] However, chitosan does have certain limitations. Its mechanical strength is relatively low and exhibits high solubility in acidic media. Crosslinking processes have emerged as the most effective alternative to overcome those drawbacks.

Various crosslinking agents have been extensively studied and applied to modify the polymeric structure of chitosan, thereby creating biomaterials suitable for a wide range of applications. These crosslinking agents are classified as inorganic, such as sodium tripolyphosphate[14–16] or 3-glycidoxypropyltrimethoxysilane,[17,18] or organic, such as polyglutamic acid,[19] gelatin,[20] glutaraldehyde,[21–23] or genipin.[24–26]

Among these agents, genipin deserves special attention. It is a natural compound derived from certain fruits; primarily *Gardenia jasminoides* Ellis and *Genipa americana*.[27,28] Genipin exhibits high reactivity with amine-containing species and can form self-polymerized aggregates.[29,30] Like chitosan, genipin has demonstrated biocompatibility and non-toxicity.[31] Genipin can crosslink and form stable polymeric complexes with chitosan polymer chains. Moreover, the resulting structure retains a significant amount of free functional groups that are available for enzyme attachment.

The unique characteristics and properties of chitosan and genipin make the crosslinked matrix suitable for diverse biomedical and biotechnological applications, particularly in enzyme immobilization. This review article aims to provide a comprehensive overview of the current state-of-the-art on chitosan, its characteristics, properties, primary applications, and some of the modifications of the polymer chain and structure. Afterward, the comprehensive overview will continue with the genipin, its characteristics, properties, and reactivity. Thus, advancements in the chitosan-genipin complex and the potential of this complex as a polymeric support for enzyme immobilization will be presented and discussed. Finally, this review will describe some challenges and perspectives of this versatile and promising biomaterial.

2 | CHITOSAN

Chitosan is an amino polysaccharide[32] obtained from the partial deacetylation of chitin in alkaline conditions by chemical, physical, and biotechnological methods.[33,34] Figure 1 illustrates the deacetylation reaction of chitin to produce chitosan. It is worth noting that chitin is the second most abundant polysaccharide in nature, surpassed only by cellulose. Chitin is part of the exoskeleton of crustaceous (lobster, krill, crab, shrimp), insects' cuticle, algae, corals, and cellular walls of some fungi and yeast.[33,35,36]

The chitosan chemical structure is $(C_6H_{11}NO_4)_n$. Is classified as a cationic and linear polysaccharide, built by N-acetyl-D-glucosamine and D-glucosamine chains, connected by glycosidic bonds β-(1, 4) in different proportions,[37] varying according to the deacetylation degree.[33] The N-acetyl-D-glucosamine subunits in chitosan can exist in two orientations: α- and β-. In β-chitosan, these subunits are oriented in a parallel manner, whereas in α-chitosan, the orientation is antiparallel. This distinction significantly impacts the interaction capacity of chitosan with other molecules. An example described in the literature is the higher binding capacity of β-chitosan with erythrocytes and its ability to promote faster and more efficient coagulation compared to α-chitosan.[38,39] The spatial disposition causes this difference, which allows for better interaction due to the parallel orientation in β-chitosan.

Chitosan has a pKa near 6.5[40] due to one primary amine and two hydroxyl groups on each subunit. Those groups are easily modified based on the required final application.[41] Moreover, it is an amphiphilic polyelectrolyte because of its capacity to stabilize emulsions.[42] In its solid state, chitosan appears as a white, fine powder and is insoluble at neutral pH.[34] However, it exhibits high solubility in acidic pH conditions, especially in the presence of certain organic acids such as acetic, formic, lactic, malic, tartaric, and trifluoroacetic, among others.[43,44] Due to the protonation of amine groups, chitosan exhibits the properties of a cationic polyelectrolyte ($—NH_3^+$).[32] This protonation leads to an increased capacity for water absorption, resulting in the formation of gels and films[45] with some plasticity and elasticity.[46] This capacity can be modified and modulated by ionotropic coagulation, macromolecule incorporation, covalent crosslinking, reverse microemulsions, and self-polymerization induction.[42] The cationic nature of chitosan facilitates its interaction with some anionic polysaccharides and teichoic acids found in cell walls, including bacterial cell walls, thus imparting antibacterial properties.[37]

Besides the traditional acid solubilization, the alkaline solubilization technique is also widely studied and

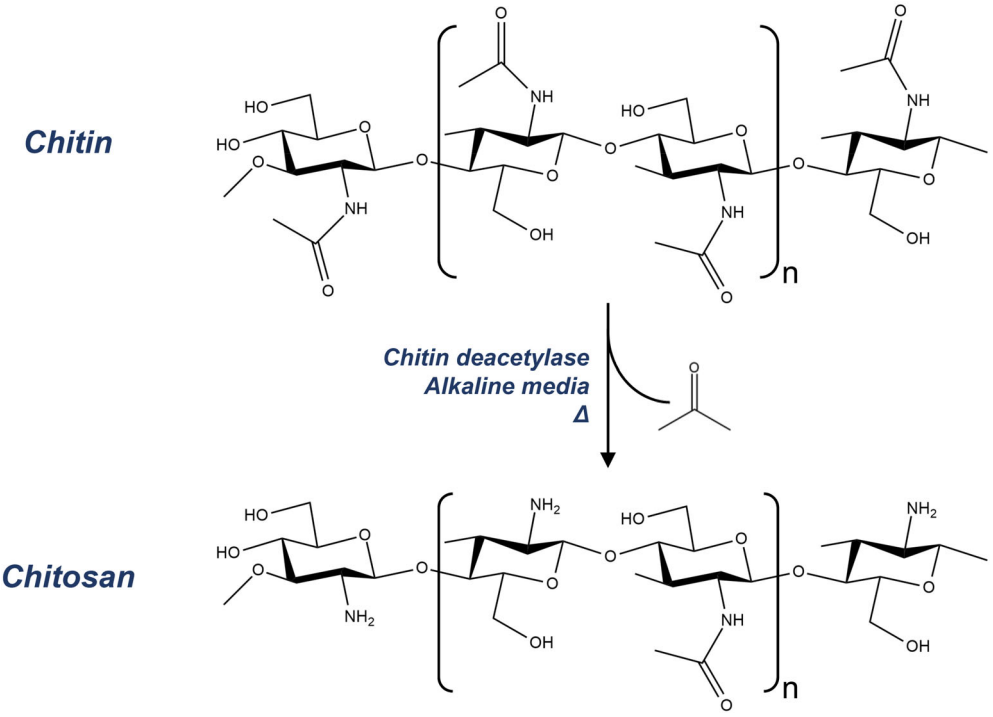

FIGURE 1 Deacetylation process of the chitin for the chitosan obtention. [Color figure can be viewed at wileyonlinelibrary.com]

well-documented. This technique used the freezing–thawing process to use epichlorohydrin, polyethylene glycol (PEG) substituted with four aldehyde groups, and LiOH/urea solution. This method breaks the hydrogen bonds between chitosan units and creates hydrogen bonds between alkali/urea and chitosan. The resulting hydrogel has demonstrated higher mechanical stability than the hydrogel obtained through acidic solubilization.[47,48]

Chitosan is generally recognized as safe (GRAS) by the U.S. Food & Drug Administration (FDA), which facilitates its application in food. Additionally, the chitosan properties include antimicrobial activity (particularly against gram-positive bacteria),[46] biodegradability,[49] biocompatibility,[17] hemocompatibility,[50] anti-inflammatory properties,[51] antioxidant activity, non-toxicity,[36] inertness,[21] antifungal properties, efficient metal chelating,[43] high adsorption capacity,[52] and strong bioadhesives.[53,54] These characteristics make chitosan suitable for various bioprocess applications.[55] Beyond that, it has high bioavailability. It can be derived from the waste generated by the shrimp industry, making it an environmentally sustainable resource.[56]

This polymer is found in different purity, molecular weight, and deacetylation degrees, each contributing to its specific properties. The degree of purity directly affects the polymer's reactivity and physicochemical properties. Some impurities can make it challenging to access amine groups, which are crucial in chitosan and affect its adsorption capacity and metal chelation abilities.[43,52] Chitosan can be classified based on its molecular weight as low (<70 kDa), medium (190–310 kDa), or high (>500 kDa).[57,58] The molecular weight directly influences the viscosity of the formed hydrogel in acidic media. As the molecular weight increases, the viscosity and stability of derivatives also increase, providing better protection against enzymatic degradation. Conversely, low molecular weight reduces viscosity and enhances the potential for interactions with other charged species, such as when used as an adsorbent. On the other hand, the high molecular weight can cause solubility[52] and the controlled release of some encapsulated or associated compounds to the polymeric matrix.[41] The deacetylation degree of chitosan determines the extent of its positive charge on the subunits.[38,41] As mentioned, the amine groups in the D-glucosamine units have a pKa value of approximately 6.5. When the pH of the dispersion is lower than the pKa, the solubility of chitosan in aqueous solution increases, making it an effective emulsifier. When the pH of dispersion pH is lower than the pKa, the solubility of chitosan in aqueous solution increases, making it an effective emulsifier. However, when the pH is higher than pKa, the deprotonation of the amines reduces the number of charged groups, leading to internal interactions and increased hydrophobicity, resulting in self-aggregation of the polymer,[42,59] also leading to the formation of highly stable emulsions.[60]

The versatility of chitosan also lies in its ability to generate a wide range of configurations, sizes (from nano to macrostructures), geometries (2D and 3D), and

formulations such as hydrogels, films, membranes, and fibers.[52,61–63] The mechanisms attributed to its versatility include ionotropic coagulation,[22,64] crosslinking,[65] self-aggregation, desolvation, and coalescence.[66] Additionally, interactions such as ionic bonds between the protonated amine of chitosan and the oxygen of carboxylate anion, hydrogen bonds between the hydroxyl group from chitosan and some carbonyl group, and more complex interactions like the contact ion-ion-hydrogen contribute to this versatility.[32,47]

2.1 | Chitosan applications

Due to its multiple properties and characteristics, chitosan has been used in several areas, including agriculture, food technology, medicine, pharmacy, and the chemical industry. Some examples of these applications are described below:

2.1.1 | Agriculture and food technology

In agriculture, chitosan has been applied as a growth factor and protection against some fungi and other plagues[67] and used as a plant elicitor, vehicle, and adjuvant for biopesticides using essential garlic oil.[33] The food industry produces edible films for curated ham[68] and fruits like kiwi,[36] strawberry,[67] and minimally processed melon.[69] Chitosan is also employed as a wall material for the encapsulation of gelatin and carboxymethyl cellulose coacervates,[40] and it is used in the form of chitosan-gliadin nanoparticles for controlled release of curcumin, using sodium tripolyphosphate, phytic acid, and sodium phytate as crosslinking agents.[70] Additionally, it is utilized to encapsulate the green coffee bean extract in microparticles of chitosan crosslinked with xanthan gum.[71]

2.1.2 | Medicine and pharmaceutical area

Chitosan has numerous uses in the field of medicine and pharmaceuticals. It serves as a vehicle for the controlled release of growth factors, stem cells, peptides, and drugs,[17,34,37] such as rutin for stabilizing Pickering emulsions[53] and tamoxifen for breast cancer treatment.[34] Chitosan is employed in implants and tissue regeneration[37,72] and genic therapy.[41] It promotes curative effects by stimulating angiogenesis, fibroblast proliferation, collagen deposition, increasing hyaluronic acid synthesis, and preventing scar formation.[37] Crosslinked chitosan films with genipin are utilized as an anticorrosive of magnesium AZ31 sheets for internal mechanical prosthesis.[73] Injectable hydrogels made from chitosan photocrosslinked with 1,2-epoxy ethane and methacrylic anhydride showed potential application as drug delivery vehicles and in tissue engineering.[51] Chitosan scaffolds crosslinked with glutaraldehyde and reinforced with calcium phosphate granules and hydroxyapatite applied in bone tissue engineering.[62] Furthermore, nanofibers composed of chitosan/keratin/polyvinyl alcohol have biomedical applications as part of curatives.[63] Chitosan is also employed as an excipient in pills and tablets.[64]

2.1.3 | Chemical industry

Chitosan has various applications in the chemical industry. It is used as a wood adhesive when mixed with some phenolic compounds, low molecular weight aldehydes, or carbohydrates such as starch, glucose, and sucrose.[45] Chitosan also serves as a stabilizer for Pickering emulsions (oil–water)[42,74] and is stabilized by the association with silica nanoparticles[60] or hallosyte nanotubes applied for environmental remediation.[75] Chitosan aerogels crosslinked with 3-glycidoxypropyltrimetoxysilane and reinforced with graphene oxide to enhance its mechanical properties applied in chromium VI adsorption and removal.[18] In addition, chitosan aerogel crosslinked with glutaraldehyde and containing graphene oxide is used for cationic dye adsorption, specifically methyl blue.[65] Chitosan beads crosslinked with glutaraldehyde find application in gold III adsorption.[76] Further, chitosan has been applied as an antibacterial coating film to protect cultural heritage, including wood, stone surfaces, metal substrate, and paper.[77]

2.2 | Chitosan modifications

Chitosan is a polymer widely used and studied due to its characteristics, properties, and availability. However, it is a material described as having low mechanical resistance, high permeability to steam, and low porosity.[78] To improve these and other attributes that are considered harmful for specific applications, various physical and chemical modifications have been proposed.[52] Several methodologies have been published, such as crosslinking, involving the combination of chitosan with other organic and inorganic materials. In some cases, chitosan has been modified using physical methods without adding other materials. The main objectives of these modifications are to decrease its solubility in acidic media, increase its chemical and mechanical stability, and develop new materials for specific applications, particularly in food and biomedical sciences.

When chitosan interacts with some materials, it can exhibit new properties and open possibilities for various applications. In the biomedical field, for example, combining chitosan with alginate has improved cell interaction and adhesive properties in curatives.[37] Incorporating chitosan with bacterial nano-cellulose has enhanced mechanical properties and antibacterial activity.[79] Further, a supramolecular system based on modified chitosan and cellulose nanofibers demonstrated surface hydrophobization and improved fire resistance and mechanical strength, preventing paper combustion.[80] In those cases, the presence of chitosan plays a crucial role in achieving these improvements.

In food science, nanofibers made from chitosan/pullulan crosslinked with cinnamaldehyde presented improved stability in aqueous media and mechanical and thermic properties, with potential use in active packaging.[81] Also, chitosan films have been mixed with different polysaccharides (xanthan gum, propylene glycol, alginate propylene, and carrageen) and used to cover curated ham. These films have demonstrated the ability to maintain microbiological stability without causing sensorial modifications.[68]

Researchers employ physical and chemical modifications to enhance or introduce new properties to the chitosan polymer. The physical modifications include transforming the chitosan powder into membranes, fibers, films, or beads, which can be produced at macro, micro, or nano scales, as mentioned earlier. However, another physical modification technique described in some studies involves enhancing or reducing the porosity of the 3D structure of chitosan.

Some studies reported the formation of chitosan sponges to enhance the polymer porosity. The gel freezing–thawing process and posterior lyophilization typically obtain these sponges. For example, chitosan sponges have been crosslinked with epichlorohydrin and silver nanoparticles for curative application.[82] For the same application, chitosan sponges have been formed directly by lyophilization. In this case, the process involves forming a gel using chitosan, alginate, and hyaluronic acid. The gel is then crosslinked with genipin and lyophilized to create the sponge structure.[83] This process allows the production of porous materials with a matrix filled with interconnected macro and microporous. It offers the advantage of not using high temperatures, which can modify the polymer and compromise its native characteristics and properties.[84]

Chitosan structural modifications expand the possibilities of properties and applications. For instance, carboxylated chitosan can be a coating agent for mesoporous silica nanoparticles, enabling drug release to treat breast cancer.[17] On the other hand, for wound healing, the most common modifications have been *N*,*N*,*N*-trimethyl chitosan, and N-succinyl chitosan. This compound has shown high solubility in acidic and alkaline solutions and a high swallow capacity.[85] When combined with sodium alginate and micro cellulose, chitosan has demonstrated effectiveness as an antimicrobial agent against *Eschirichia coli* (*E. coli*) and *Staphylococcus aureus*. Furthermore, the 6-deoxy-6-amine chitosan has exhibited a higher antimicrobial capacity than chitosan itself against *S. aureus*, *E. coli*, *Pseudomonas aeruginosa* (*P. aeruginosa*), and *Aspergillus niger*.[86]

When the objective was to develop vehicles to release safranin O, N-carboxymethyl chitosan, and thiolated chitosan were utilized.[37] Additionally, spherical nanoparticles of chitosan-dicarboxylic acid derivatives (such as chitosan-succinyl amide, chitosan-glutaryl amide, chitosan-phthalyl amide, and chitosan-phenyl succinyl amide) crosslinked with 1-ethyl-3-(−3-dimethyl aminopropyl)-carbodiimide were employed.[64] Chitosan sulfonation, resulting in a compound characterized as anti-HIV-1, has shown additional benefits such as reducing protein absorption in the blood, exhibiting anticoagulant capacity, and possessing anti-thrombogenic properties compared to heparin.[50]

For solubility enhancement (hydrophilicity), chitosan has been combined with PEG, resulting in chitosan/PEG spherical nanoparticles and applied as carriers for indole-3-carbinol, a plant molecule active against several cancer types. The hydrophilicity of the novel nanoparticles may be due to the addition of a hydrophilic shell based on several polyoxyethylene groups.[87] Also, adding a deblock copolymer of ethylene oxide and propylene oxide has been tested for the therapeutic administration of molecules. Serum albumin was used as a model, and the system has demonstrated significant loading and release capacity.[88]

On the other hand, several compounds have been studied to enhance the hydrophobicity and stability of some chitosan derivatives and their affinity for cell walls (decreasing cellular toxicity and increasing the transfer rate in biological environments). These include EDC: 1-ethyl-3-(—dimethyl aminopropyl) carbodiimide, NHS: N-hydroxysuccinimide, DOCA-NHS: ester of deoxycholic acid NHS, and $ImCO_2H$: imidazo-4-ylacetic acid. These compounds have shown promising results in cellular transfection by forming micelles with the resulting amphipathic polymer.[41,89]

2.3 | The crosslinking process

Crosslinking is a reaction between chitosan and another molecule, generally called a crosslinking agent. At least

two functional groups of the crosslinking agent can react with the polymer, forming bridges between the polymeric chains. The process can also leave some free groups available for other potential bonds and interactions of interest.[9]

The chitosan crosslinking induces specific changes in the polymeric matrix, including particle size, superficial charge, porosity,[90] density, swallow capacity, and stability.[91] This process alters the microstructure by reorganizing the polymeric chains and their internal interactions. Chitosan also acquires new properties, such as increased mechanical resistance,[81] and swallow capacity,[31] as well as the addition of new functional groups that can interact with other molecules more effectively than unmodified chitosan. Crosslinking can occur through various mechanisms, including covalent and ionic bonds,[29,71,92] electrostatic interactions,[90] and other molecular interactions. The specific mechanism depends on the nature and structure of the reactive species and their functional groups, as well as the reaction conditions and the presence of catalysts (which can be other chemical species or external factors such as light and oxygen).[93] The crosslinking process between chitosan and the crosslinker agent is unique for each combination, so the reactivity of different species with the polymer produces products with specific characteristics, sometimes optimized when compared to the native polymer. The concentration of the crosslinking agent also plays a role in the properties of the resulting products.[90]

Some crosslinking agents described in the literature for chitosan are presented in Table 1. It is evident that these crosslinkers have different origins, being organic or inorganic, such as genipin and glutaraldehyde, respectively, and can be natural or synthetic, such as xanthan gum or GPTMS, respectively. However, they all share the same primary objective: to modify the polymer matrix to improve its characteristics and properties, making it suitable for specific applications. It is also noteworthy that most of the applications are in tissue engineering and drug release. Still, the knowledge gained from these studies can also be applied to agricultural and food technology, as mentioned earlier.

3 | GENIPIN

Genipin is a chemical compound that has recently gained relevance as a crosslinker agent for some protein and polysaccharides biopolymers, particularly those that contain primary amines, such as chitosan.[44] Chemically, the genipin is an aglycone glycosidic iridoid.[98] It is from plant sources through various physical, chemical, and enzymatic processes.[99,100] Researchers widely study genipap and gardenia for genipin extraction; genipap obtained from *G. americana*,[27,91] a fruit tree native to the region stretching from southeastern Mexico to northern Brazil,[101] and the gardenia fruit from *G. jasminoides* Ellis,[31,102] a plant native from Asia where its applications have been well-documented. Other secondary sources of this compound that have been studied and reported in the literature include *Bellardia trixago*, *Castilleja tenuiflora*, and *Eucommia ulmoides*.[28,103]

The main interest in genipin also stems from its well-known attributes. The medicinal use of genipap by some Native Americans has been documented. Additionally, its ability to produce dark blue dyes in the presence of light and oxygen from the air, which remains stable for several days, has led to its use as ink for tattoos due to its high reactivity with skin proteins.[91] Recently, more properties of genipin have been extensively studied and elucidated. These include its low cytotoxicity,[44] antimicrobial capacity,[101,102] high biocompatibility,[83] and antifungal capacity.[103] Furthermore, genipin has demonstrated therapeutical properties such as anti-inflammatory, antioxidant, and antitumoral effects,[104] anticancerogenic properties,[84] antidepressant effects,[98] and neuroprotective effects.[105,106] Additionally, genipin has been studied as an agent associated with the treatment of edema, hypertension, and jaundice.[107] It has also been investigated for its potential to address conditions related to inflammatory processes, including certain types of cancer such as colon, hepatocellular carcinoma, leukemia, breast and prostate cancer.[108,109] Due to all these characteristics, genipin can be used in live tissues and food, and it has been increasingly employed as a crosslinking agent for polymers like chitosan. This is because of its safety profile, which makes it a preferable alternative to other traditional substances such as glutaraldehyde and epoxy compounds.[31,92,110]

Genipin is found in gardenia and genipapo fruits in its glycosylated form known as geniposide. It can be separated from the aglycone group through enzymatic methods using β-glucosidase, as shown in Figure 2.[27] genipin exists as a colorless compound but can react with amine groups. The following factors, including the presence of light and oxygen, pH of the medium, reaction time, temperature, and the presence and concentration of specific amino acids,[24,28,111] strongly influence this reaction.

3.1 | Factors that influence genipin reactivity

Several factors influence the genipin reactivity. These factors can change the self-polymerization of genipin and

TABLE 1 Main crosslinker agents for chitosan and its derivatives.

Polymer composition	Configuration	Crosslinker agent	Practical application	Reference
Silica coated with chitosan	Nanoparticles	3-glycidoxypropyltrimethoxysilane (GPTMS)	Drug release for breast cancer therapy	17
Graphene oxide/ chitosan	Aerogel	GPTMS	Absorbent for Cr(VI)	18
Chitosan-gelatin-oxidized guar gum	Hydrogel	β-glycerophosphate	Study of the chemistry of hydrogels	94
Chitosan	Nanoparticles	Sodium tripolyphosphate (Na-TPPP)	Curatives designed for the removal of necrotic tissues and the acceleration of hemostasis	35
Chitosan	Nanoparticles	Na-TPPP	Peptide quantification	57
Chitosan	Nanoparticles	Na-TPPP	Study of crosslinking degree and antibacterial properties	66
Chitosan-alginate	Films	Ferulic acid	Films for fruit and vegetable packaging	95
Chitosan	Nanofiber	Poly(ethylene) oxide	Water-resistant membranes for biomedical, filtration, and food industries applications	61
Chitosan/ dicarboxylate conjugates	Nanoparticles	1-ethyl-3-(3-dimethyl aminopropyl)-carbodiimide	Nanocarrier for Safranin O	64
Chitosan	Hydrogel	Glycidyl methacrylate	Tissue engineering and delivery of therapeutic agents	96
Chitosan	Hydrogel	1,2-epoxy butane and methacrylic anhydride combined.	Tissue engineering and drug release	51
Chitosan	Nanoparticles	Sodium tripolyphosphate, phytic acid, sodium phytate.	Encapsulation and delivery of curcumin	70
Chitosan	Microparticles	Xanthan gum	Oral coffee extract delivery	71
Chitosan	Beads	Glutaraldehyde (GA)	Au(III) adsorption from electronic waste	76
Chitosan	Beads	GA	Immobilization of β-galactosidase from *B. circulans*	97
Chitosan	Beads	GA	Immobilization of catalase	21
Chitosan	Scaffolds	GA	Bone tissue engineering	62
Chitosan/ Pullulan	Nanofiber	Cinnamaldehyde	Active packaging	81
Chitosan/Ag	Nanocomposite sponge	Epichlorohydrin	Curatives with antibacterial activity against *S. aureus* and *E. coli*	82
Chitosan	Hydrogel	Genipin	Preparation, designing, and manipulation of crosslinked chitosan hydrogels	29
Chitosan	Films	Genipin	Coating of magnesium AZ31 sheets to avoid its corrosion	73

how genipin will crosslink with amine compounds. Among them are the presence of amino acids or amine compounds, the pH of the medium, reaction time and temperature, and genipin concentration.

Genipin can react with different amino acids and, in the presence of primary amines, form colored complexes (see Figure 3). When the reaction occurs with primary amines, the result is blue-purple colored compounds. The same color appears when the medium is rich in glycine and lysine amino acids. However, when genipin reacts with valine, methionine, or tyrosine, blue-green colored compounds are obtained. On the other hand, the

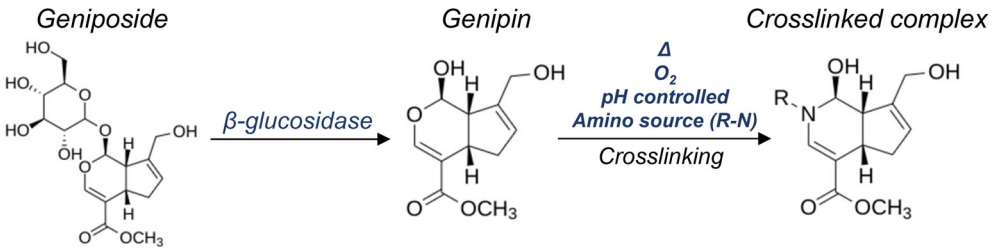

FIGURE 2 Enzymatic process of genipin extraction from geniposide and its subsequent crosslinking mechanism. [Color figure can be viewed at wileyonlinelibrary.com]

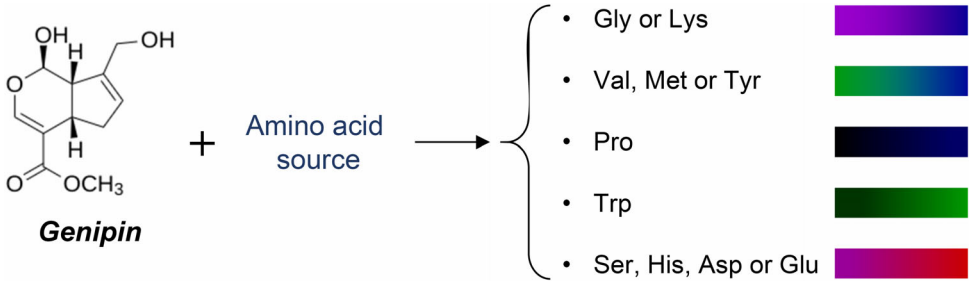

FIGURE 3 Colored complex formed from the reaction between genipin and specific amino acids. [Color figure can be viewed at wileyonlinelibrary.com]

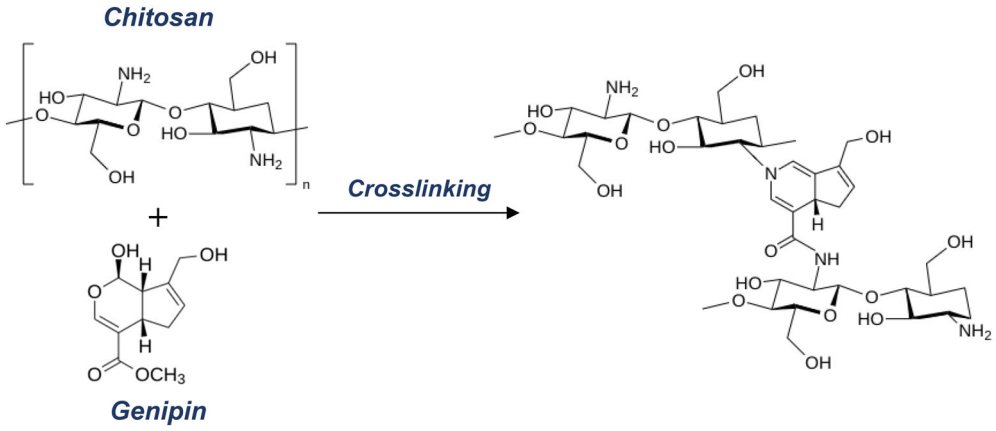

FIGURE 4 Crosslinking process between chitosan and genipin performed under a robust acidic environment. [Color figure can be viewed at wileyonlinelibrary.com]

derivative color is black when genipin reacts with proline and green when it reacts with tryptophan.[28] Additionally, when the medium is rich in serine, histidine, asparagine, and glutamine, the resulting colors are red-purple.[112] These colorations become more intense and darker as the concentration of amine groups available to react with genipin increases[101]

Moreover, two main routes conduct the reaction of genipin with other compounds rich in amine groups: in an acidic and alkaline medium. In the case of a strongly acidic medium, the presence of protons induces the formation of $-NH_3^+$, which is highly reactive, leading to accelerated nucleophilic attack on the C3 position of the genipin ring. Subsequently, a slower nucleophilic substitution occurs, replacing the ester group with the chitosan amine group. This results in a crosslinked network with short distances between the polymer chains (see Figure 4).[113,114]

Figure 5 presents the reaction of genipin when the pH of the medium is close to neutral. As mentioned earlier, the genipin ring opens, leading to the formation of a heterocyclic amine. In this scenario, the crosslinked intermediate can react with other intermediates, forming crosslinked networks with short chains of crosslinked bridges (dimers, trimers, tetramers, etc.). In this case, the nucleophilic substitution of the genipin ester does not occur.[30]

On the other hand, when the reactional media is highly alkaline (see Figure 6), the presence of OH^- ions promotes the opening of the genipin ring almost spontaneously, facilitating the covalent bonding with the available amine groups from the other reacting species. Additionally, the alkaline environment can promote the internal polymerization of genipin, resulting in self-polymerized genipin intermediates that can react with other intermediates or external amine groups. These

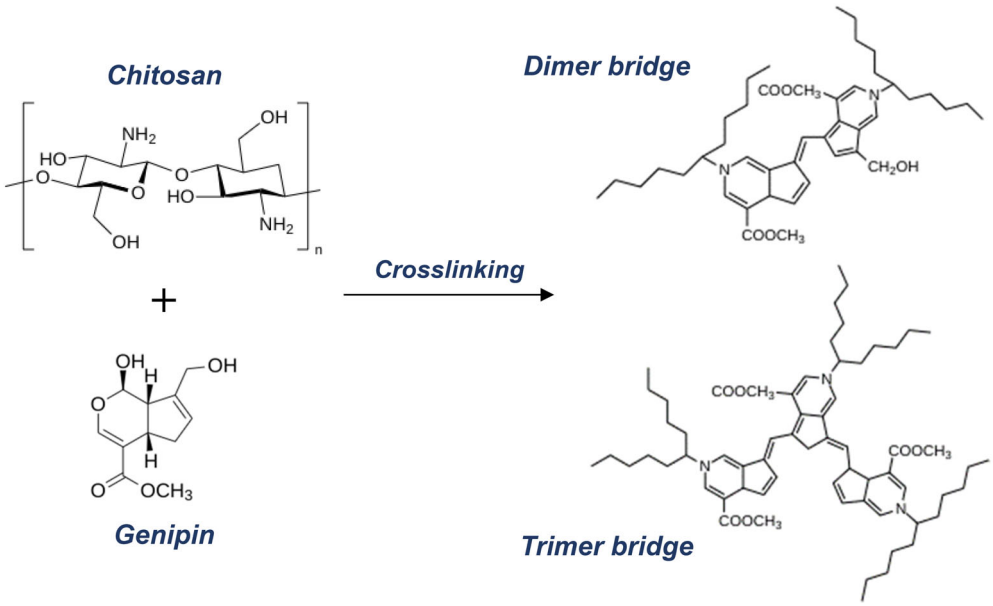

FIGURE 5 Crosslinking process between chitosan and genipin at near-to-neutral pH conditions. [Color figure can be viewed at wileyonlinelibrary.com]

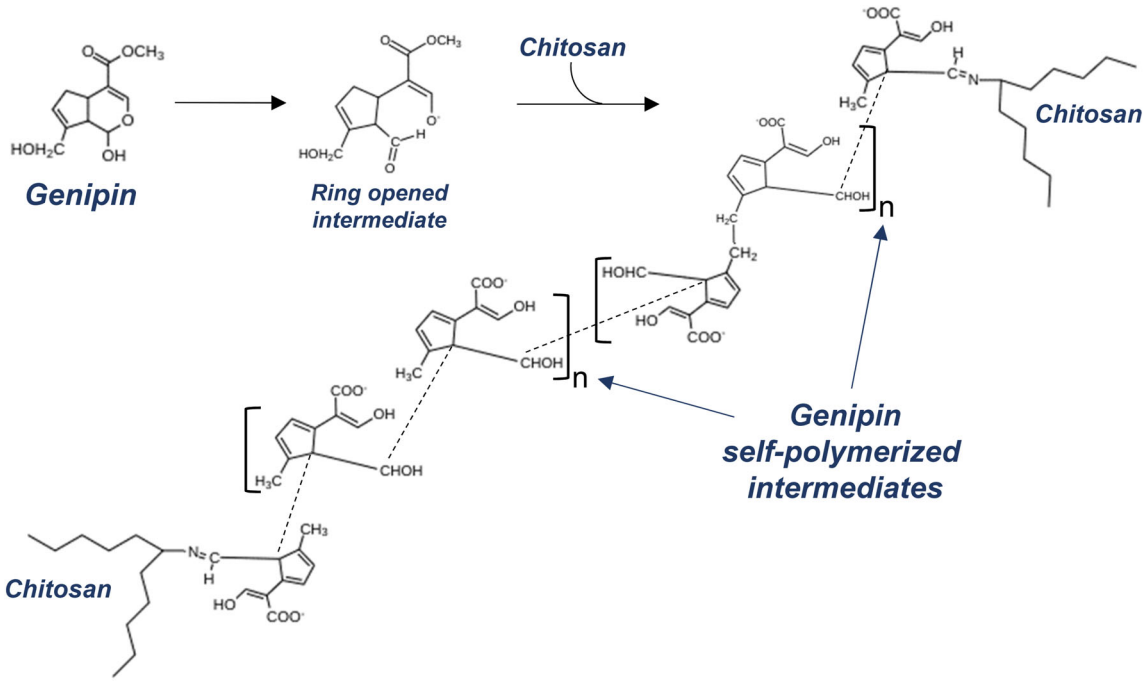

FIGURE 6 Crosslinking process between chitosan and genipin performed under a robust alkaline environment. [Color figure can be viewed at wileyonlinelibrary.com]

processes enable the formation of long and flexible genipin chains that can also respond with chitosan, leading to a greater separation between the polymer chains. One advantage of this reaction is that it does not require high temperatures or harsh chemicals to occur.[24,29,30]

Reaction time and temperature form a crucial binomial that significantly impacts the reaction rate and how genipin reacts with chitosan. Genipin can react with species-rich amine groups and undergo self-polymerization. Self-polymerization is favored in crosslinking when longer reaction times and higher temperatures are employed.[24,100]

Also, its concentration influences the genipin reactivity. As the genipin concentration increases, the possibility of internal genipin self-polymerization also increases. These modifications can positively impact the mechanical stability of chitosan 29,100 by affecting the crosslinking between genipin and chitosan and directly

influencing the density of the resulting crosslinked network formed with the polymer.

All these factors have already been studied for the β-galactosidase from *A. oryzae* immobilization for polymeric support production, finding that increasing the genipin concentration led to an increase in the density of available groups for enzyme attachment, resulting in higher immobilization yields. However, there was a point where the immobilization efficiency started to decline, possibly due to internal genipin self-polymerization and the formation of multipoint enzyme attachments. This could cause distortions in the protein structure, particularly in the tertiary and quaternary configurations, leading to a loss in catalytic capacity.[29,115] Flores et al.[24] examined the effects of time and temperature. Even with prolonged reaction times, low temperatures resulted in a weak crosslinked network, making the chitosan susceptible to dissolution in acidic media.

On the other hand, high temperatures, even with short reaction times, produced supports with limited capacity to attach the enzyme, possibly due to extensive internal genipin self-polymerization. Also, the authors evaluated the pH of the reaction and observed that as the pH value increased, the blue coloration became darker and more intense. pH nine was the optimal condition for enzyme immobilization in terms of yield, efficiency, and recovery activity. These parameters are crucial in any enzymatic immobilization process.[24]

4 | THE COMPLEX CHITOSAN-GENIPIN

Genipin can react with the amino groups of chitosan to form the complex chitosan-genipin. Several authors have described the crosslinking reaction between chitosan and genipin. Genipin forms covalent bonds with chitosan during the crosslinking process and can promote its self-polymerization. In the previous section, we discussed how reaction parameters affect crosslinking. They modify the characteristics and properties of the polymer. Besides chitosan, genipin can crosslink other polymers such as gelatin, collagen, and alginate, among others.[83,91,116]

Due to its characteristics and properties, the complex chitosan-genipin has been applied in various areas, including biomedical, environmental, and biotechnology. Some applications described in the literature include the preparation of chitosan-hydroxyapatite hydrogel crosslinked with genipin to form 3D scaffolds for bone tissue engineering applications.[102] Chitosan and genipin were also applied, associated with cellulose, for adsorption of anionic dyes (methyl orange and reactive red 195), which showed antibacterial capacity against *E. coli* and *S. aureus*.[117] Additionally, chitosan films crosslinked with genipin have been used in biosensors to detect aflatoxin B1 using acetylcholinesterase from *Electrophorus electricus*. The biosensor showed improved results when using high molecular weight chitosan and high deacetylation degree.[118] More information and discussion about using chitosan-genipin complex in different areas can be found in recent review papers.[119–126] Next, we will review using the chitosan-genipin complex as a matrix for enzyme immobilization.

4.1 | Complex chitosan-genipin as support for enzymatic immobilization

Chitosan can support enzyme immobilization, primarily through the entrapment method. However, when it is crosslinked with genipin, additional advantages are gained, and existing ones are enhanced. The chitosan-genipin complex has a high affinity for proteins, excellent mechanical stability, resistance against chemical degradation, and antimicrobial capacity. Furthermore, it offers the possibility to obtain different forms in terms of geometries and sizes, the addition of functional groups, and the combination with other organic or inorganic species. Additionally, its porosity can also be modified. In summary, the possibilities for generating different types of support are significantly increased.[100,127]

In enzymatic immobilization, the selection of the support material is essential. This is not only because it constitutes the insoluble part of the biocatalyst but also because it provides a compatible surface that is both physically and chemically suitable for the enzyme. The relationship between the support and the enhanced catalytic capacity and stability (both under storage and operational conditions) has been reported in some cases. Furthermore, the support enhances the enzyme's stability by creating a microenvironment on its surface that protects the enzyme against changes in the reaction media. This factor defines the functionality and feasibility of the biocatalyst.[1,128–130] Also, in some cases, the support can diminish the possibility of allergenic responses to the protein and even increase the range of applications for the immobilized enzyme.[4,131,132]

Enzyme immobilization can be performed by attachment to the support, entrapment (or encapsulation), and crosslinking.[3,133] Each method has advantages and drawbacks; some are ideal for some enzymes or bioprocesses. The stability of the enzyme is directly related to the type of bond formed with the support. Sometimes, multipoint attachment can modify the enzyme structure and flexibility, diminishing its catalytic capacity. The degree of confinement in entrapment immobilization can cause

diffusion-related issues. Also, enzyme orientation is another factor to consider, as bonding the enzyme to the support surface may result in the catalytic site being oriented away from the substrate. The microenvironment created between the enzyme and the support can protect against significant changes in the reaction media. Lastly, the immobilization conditions can confer robustness to the enzyme, enabling better performance throughout the bioprocess.[1,4,130,134-137]

The bonds between the enzyme and the support are essential to biocatalyst properties. They can be chemical, such as covalent bonds, which are solid and stable, or physical, such as Van der Waals forces, hydrogen bonds, and ionic and hydrophobic interactions. These physical interactions form weaker bonds, facilitating enzyme leaching from the support when applied.[129,130,138] As mentioned before, the bonds' nature, orientation, and density directly affect the enzyme activity. Therefore, conducting a detailed study of the immobilization conditions for each enzyme and the material support to be used is crucial.

Some strategies have been used to immobilize different proteins in the chitosan-genipin complex, each with different objectives and applications (see Table 2). The β-galactosidase from *Aspergillus oryzae* was immobilized on chitosan-genipin beads mainly for lactose hydrolysis and galactooligosaccharides (GOS) production. These studies also focused on investigating the effects of crosslinking conditions (pH, temperature, and time) on the immobilization parameters such as yield, efficiency, and recovery activity.[24] Additionally, the impact of chitosan deacetylation degree on the crosslinking process with genipin was explored, and structural analysis was conducted using scanning electron microscopy (SEM). At the same time, thermic and mechanical properties were determined.[58] More recently, the same enzyme was immobilized on chitosan beads with modified porosity, using Na_2CO_3 as a porogen agent and crosslinked with genipin. An in-depth structural characterization using conventional and unconventional techniques was performed to better understand the modifications and reactivity of the complex during the crosslinking and immobilization processes; also, the resultant biocatalyst was applied for GOS production.[139] Also, the same porous chitosan-genipin-based support was used for the immobilization of the β-galactosidase from *A. oryzae* and the resultant biocatalyst, differently from the previous study, was analyzed from the point of view of the immobilization parameters, performing several stabilities (pH, thermal, storage, and continuous and batch lactose hydrolysis), and including pH modifications on the immobilization process, to elucidate more about the support and enzyme structural modifications and its interactions.[140]

Other investigations focused on comparing genipin and glutaraldehyde as crosslinking agents. Bellé et al.[27] examined their use for lactose hydrolysis application and determined the crosslinked polymer's genipin concentration and rheological properties.[27] GOS production in a discontinuous bioprocess was also studied. The obtained beads were characterized using Fourier transform infrared (FTIR) spectroscopy and thermogravimetric analysis, and thermal and operational stabilities were also assessed.[132] Similarly, in the immobilization of a keratinase from *Purpureocillium lilacinum*, the genipin concentration, crosslinking time, and temperature were studied, along with the thermal, pH, and operational stabilities of the biocatalyst obtained.[100] A similar comparison was made during the immobilization of β-glucosidase from almonds, where the genipin concentration was evaluated, and the resulting biocatalyst was subjected to pH, temperature, and operational stability analyses.[141]

The immobilization of β-galactosidase from *Kluyveromyces lactis* on chitosan-genipin beads was applied for lactose hydrolysis, specifically using diluted UHT milk. The thermal stability of the biocatalyst was evaluated, and the structure of the beads was examined using SEM.[142] In another investigation, laccase from *Trametes pubescens* was entrapped in chitosan beads crosslinked with genipin. The genipin concentration and contact time during crosslinking were evaluated to determine the optimal immobilization parameters. Subsequently, the stability of the immobilized laccase was assessed in a discontinuous process for the decolorization of synthetic dyes.[93]

Scaffolds of chitosan-genipin were already synthesized for drug release, like the bone morphogenetic protein-2 (BMP-2). Different concentrations of the crosslinker agent were tested, and the crosslinking degree and effects in vitro regarding swelling, degradation, and cytocompatibility were determined.[143] The same structure was used as a carrier for nerve growth factor (NGF), and its subsequent release, in this case, was determined by its mechanical properties and permeability.[144]

Chitosan macroparticles modified with Na_2CO_3 as porogen were fabricated for papain immobilization. Afterward, crosslinking with genipin was conducted. These macroparticles were explicitly designed for controlled hydrolysis of egg white. The thermal stability of the resulting biocatalyst was determined.[145] In another study, chitosan microspheres crosslinked with genipin were used for lysozyme immobilization. The obtained biocatalyst was analyzed using SEM and attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR).

Additionally, the pH stability and swelling capacity were determined. In a different approach, $CaCO_3$

TABLE 2 Complex chitosan-genipin as support for protein immobilization.

Polymer composition	Configuration	Protein immobilized	Practical application	Reference
Chitosan	Beads	β-galactosidase from *A. oryzae*	Study of the crosslinking process and immobilization process for lactose hydrolysis in batch process	24
Chitosan	Beads	β-galactosidase from *A. oryzae*	Characterization of the hydrogels and effect of the chitosan deacetylation degree on the immobilized enzyme	58
Chitosan	Beads	β-galactosidase from *A. oryzae*	Structural characterization of the chitosan-genipin complex and application for GOS continuous production	139
Chitosan	Beads	β-galactosidase from *A. oryzae*	Study of the immobilization process under different pH conditions, characterization of the resultant biocatalysts through its stabilities (pH, thermal, storage, and continuous and batch lactose hydrolysis)	140
Chitosan	Beads	β-galactosidase from *K. lactis* and from *A. oryzae*	Study of the immobilization process and application for lactose hydrolysis	27
Chitosan	Beads	β-galactosidase from *A. oryzae*	Lactose hydrolysis and galactooligosaccharides production	132
Chitosan	Beads	β-galactosidase from *K. lactis*	Batch lactose hydrolysis from diluted UHT milk	142
Chitosan	Beads	Laccase from *T. pubescens*	Decolorization of synthetic dyes	93
Chitosan	Beads	Keratinase from *P. lilacinum* LPSC #876	Study of the immobilization process and stability of the biocatalyst	100
Chitosan	Beads	β-glucosidase from almonds	One-step genipin-mediated immobilization for production of bioactive genistein	141
Chitosan	Beads	Pectinase	Study the immobilization process and practical application of orange and grape juice clarification	148
Chitosan-hyaluronic acid	Scaffolds	Bone morphogenetic protein-2 (BMP2)	Controlled BMP2 delivery for bone tissue engineering	143
Chitosan	Scaffolds	Nerve growth factor (NGF)	Peripheral nerve regeneration	144
Chitosan-sodium alginate-$CaCO_3$	Nanoparticles	β-glucosidase from *A. aegirit*	Study of the immobilization process, stability of the biocatalyst obtained, and effects of the $CaCO_3$ nanoparticles	147
Chitosan	Microspheres	Lysozyme	Antimicrobial properties against *S. aureus* and *P. aeruginosa*	146
Chitosan-nanosilica	Macroparticles	Papain	Hydrolysis of egg white for foamability enhancement	145

nanoparticles were coated with sodium alginate and adsorbed with chitosan.[146] Posteriorly, crosslinking with genipin was conducted to immobilize β-glucosidase from *Agrocybe aergirit*, and the immobilization parameters were determined. The biocatalyst stability was also analyzed in terms of pH, temperature, reusability, and storage stability.[147]

These studies highlight the versatility of the chitosan-genipin complex for immobilizing different enzymes and proteins. Researchers have demonstrated high interest in this complex by modifying the formulations and using different crosslinking techniques, and the resulting biocatalysts have assessed its properties and characteristics.

Indeed, the chitosan-genipin complex has excellent potential as a support for immobilizing various proteins in various formats, including beads, nanoparticles, and scaffolds. The versatility of this complex enables the immobilization of a wide range of enzymes and proteins, offering numerous possibilities for biocatalysis in different fields. Table 2 summarizes the leading and most recent

applications, revealing that most of these applications focus on enzyme immobilization, particularly for β-galactosidases and β-glucosidases, opening possibilities for developing new biocatalysts using other enzymes and proteins for applications in bioprocessing and the biomedical field, where the immobilized enzymes can offer enhanced stability, reusability, and improved performance. The chitosan-genipin complex promises new opportunities for advancing bioprocessing techniques and applications.

5 | CHALLENGES AND LIMITATIONS

As previously discussed, the chitosan-genipin complex has several practical applications, many of which are promising. However, these applications still face significant challenges and limitations that must be addressed to realize their full potential.

The mechanical properties and long-term stability of the chitosan-genipin complex require further research and enhancement. Although the complex exhibits improved mechanical strength compared to pure chitosan, it still needs to be improved for specific demanding applications, such as bone tissue engineering and biomedical implants. Strategies to address these limitations include incorporating hybrid materials with inorganic compounds and physical and chemical modifications. However, the biocompatibility of these modified composites requires further clarification. Additionally, while advancements improve long-term stability—especially in applications like enzyme immobilization in continuous reactors—further refinements are necessary for physiological environments where conditions fluctuate. Striking an optimal balance between rigidity and flexibility in such dynamic environments is essential, particularly for applications that demand controlled biodegradability and biocompatibility. For instance, wound healing materials require rapid degradation, whereas tissue scaffolds must maintain structural integrity over extended periods.

Scalability and reproducibility present challenges for industrial-scale production due to the variability in the sources of chitosan and genipin. These variations can affect the interaction between chitosan and genipin, mechanical strength, crosslinking degree, and, consequently, the properties of the final product. This issue is essential for enzyme immobilization and especially critical for biomedical applications, where the purity and reproducibility of the derivatives are paramount. Moreover, the high purity required for chitosan and genipin in biomedical applications can increase production costs, necessitating the optimization of processes and the integration of green chemistry principles.

The crosslinking process also requires greater control and understanding, as it is sensitive to even minimal changes in conditions such as temperature, pH, and reactant concentration, causing the formation of intermediates and residues not wholly elucidated, characterized, and evaluated its toxicity. Literature has shown the hepatoxicity, cardiotoxicity, and nephrotoxicity in zebrafish larvae exposed to genipin by the induced oxidative stress.[149] By refining this knowledge, it will be possible to produce materials with desirable and reproducible properties, which is essential for scalability, particularly in biomedical applications like drug delivery and tissue scaffolds.

Even though chitosan and genipin are derived from natural sources and are subject to inherent variations, such as the degree of chitosan deacetylation and the purity of genipin, they must undergo rigorous regulatory scrutiny. The chitosan-genipin complex must demonstrate safety and biocompatibility to be commercialized, which includes compliance with regulatory laws and extensive toxicological studies, especially for food and biomedical applications.

Although the chitosan-genipin complex shows significant promise as a multifunctional biomaterial, researchers must overcome several challenges to transition from research to customized products for specific applications. Collaboration across different research disciplines is essential to optimize and improve derivatives of the complex, ensuring the development of safe, reproducible, biocompatible, and cost-effective products.

6 | FINAL REMARKS AND FUTURE PERSPECTIVES

Chitosan and genipin-based materials have demonstrated massive potential as biomaterials in various fields, including biomedical, food technology, biotechnology, and the chemical industry. Researchers utilize these materials to develop innovative approaches in tissue engineering, enzyme immobilization, therapeutics, food packaging, and drug delivery. Different material configurations, such as nanoparticles, nanofibers, coatings, beads, hydrogels, and films, have been extensively explored.

However, specific mechanical strength and stability challenges still need to be addressed. Future research should focus on overcoming these drawbacks and finding new solutions to broaden the range of applications for these biomaterials in diverse bioprocesses. Although the crosslinking process conditions have been widely studied and described, the derivatives characterized, and the applications well identified, the thermodynamics of

the reaction needs to be addressed to have more in-depth knowledge about the chitosan-genipin formation. Additionally, comprehensive testing and regulatory approval are essential to ensure their safety and effectiveness, particularly for chitosan-genipin materials intended for biomedical applications.

In the field of enzyme immobilization using the chitosan-genipin complex, current research primarily focuses on enzyme performance, biocatalyst stability, and commonly used characterization techniques. However, there is a need for more in-depth investigations into the influence of the crosslinking process on the resulting structure and its impact on enzyme attachment, stability, and applicability across various bioprocesses. Several factors strongly influence the crosslinking reaction, and the formed matrix may undergo structural modifications during the bioprocess. These modifications can affect the enzyme's performance and the support material's stability and functionality.

Therefore, future research should explore the relationship between the crosslinking process, the resulting matrix structure, and its behavior during different bioprocess conditions. Understanding these factors will provide valuable insights into optimizing enzyme immobilization techniques and improving the performance of the chitosan-genipin complex as a support material for various bioprocess applications.

Despite the existing challenges, current research demonstrates significant interest in chitosan and genipin-based materials. As further investigations and developments continue, more practical applications will emerge soon.

AUTHOR CONTRIBUTIONS

Elí Emanuel Esparza-Flores: Conceptualization (equal); data curation (lead); investigation (lead); writing – original draft (lead). **Plinho F. Hertz:** Conceptualization (equal); project administration (equal); writing – review and editing (equal). **Rafael C. Rodrigues:** Conceptualization (equal); funding acquisition (equal); project administration (equal); writing – review and editing (equal).

ACKNOWLEDGMENTS

This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq–process 405418/2021-3), Fundação de Amparo à Pesquisa do Rio Grande do Sul (FAPERGS–processes 21/2551-0002270-1 and 22/2551-0000397-4), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) from Brazilian Government, and Consejo Nacional de Humanidades, Ciencias y Tecnologías (CONAHCYT) from Mexican Government.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Rafael C. Rodrigues https://orcid.org/0000-0001-8592-850X

REFERENCES

[1] C. Garcia-Galan, Á. Berenguer-Murcia, R. Fernandez-Lafuente, R. C. Rodrigues, *Adv. Synth. Catal.* **2011**, *353*, 2885.
[2] O. Barbosa, C. Ortiz, Á. Berenguer-Murcia, R. Torres, R. C. Rodrigues, R. Fernandez-Lafuente, *Biotechnol. Adv.* **2015**, *33*, 435.
[3] L. Cao, **2005**, 217.
[4] R. A. Sheldon, S. van Pelt, *Chem. Soc. Rev.* **2013**, *42*, 6223.
[5] B. Krajewska, *Enzyme Microb. Technol.* **2004**, *35*, 126.
[6] F. Rafiee, M. Rezaee, *Int. J. Biol. Macromol.* **2021**, *179*, 170.
[7] D. M. Liu, J. Chen, Y. P. Shi, *Trends. Analyt. Chem.* **2018**, *102*, 332.
[8] B. Qu, Y. Luo, *Int. J. Biol. Macromol.* **2020**, *152*, 437.
[9] A. C. Sadiq, A. Olasupo, W. S. W. Ngah, N. Y. Rahim, F. B. M. Suah, *Int. J. Biol. Macromol.* **2021**, *191*, 1151.
[10] A. O. Silva, R. S. Cunha, D. Hotza, R. A. F. Machado, *Carbohydr. Polym.* **2021**, *272*, 118472.
[11] F. S. Rezaei, F. Sharifianjazi, A. Esmaeilkhanian, E. Salehi, *Carbohydr. Polym.* **2021**, *273*, 118631.
[12] Y. Qin, P. Li, Z. Guo, *Carbohydr. Polym.* **2020**, *236*, 116002.
[13] P. S. Bakshi, D. Selvakumar, K. Kadirvelu, N. S. Kumar, *Int. J. Biol. Macromol.* **2020**, *150*, 1072.
[14] T. Kadri, A. Cuprys, T. Rouissi, S. Kaur, R. Daghrir, J. Lauzon, *Biochem. Eng. J.* **2018**, *137*, 1.
[15] Z. Sang, J. Qian, J. Han, X. Deng, J. Shen, G. Li, Y. Xie, *Carbohydr. Polym.* **2020**, *230*, 230.
[16] C. Y. Yang, C. H. Hsu, M. L. Tsai, *Carbohydr. Polym.* **2011**, *86*, 659.
[17] G. Lohiya, D. S. Katti, *Carbohydr. Polym.* **2022**, *277*, 118822.
[18] D. Kong, L. He, H. Li, F. Zhang, Z. Song, *Colloids. Surf A. Physicochem. Eng. Asp.* **2021**, *625*, 625.
[19] G. Nie, K. Hong, E. Zhang, N. Liu, M. Wang, L. Wang, Y. Zang, *Int. J. Biol. Macromol.* **2020**, *159*, 986.
[20] J. Y. Shin, S. J. Jeong, W. K. Lee, *J. Ind. Eng. Chem.* **2019**, *80*, 862.
[21] J. Kaushal, G. Singh, S. K. Arya, *Biotech. Rep.* **2018**, *18*, e00258.
[22] M. P. Klein, M. R. Nunes, R. C. Rodrigues, E. V. Benvenutti, T. M. H. Costa, P. F. Hertz, J. L. Ninow, *Biomacromolecules* **2012**, *13*, 2456.
[23] S. Bhandari, V. K. Gupta, H. Singh, *Biocatal. Biotransform.* **2009**, *27*, 71.
[24] E. E. E. Flores, F. D. Cardoso, L. B. Siqueira, N. C. Ricardi, T. H. Costa, R. C. Rodrigues, M. P. Klein, P. F. Hertz, *Process Biochem.* **2019**, *84*, 73.
[25] C. R. Hackenhaar, C. F. Rosa, E. E. E. Flores, P. R. Santagapita, M. P. Klein, P. F. Hertz, *Carbohydr. Polym.* **2022**, *291*, 119483.
[26] R. A. A. Muzzarelli, M. El Mehtedi, C. Bottegoni, A. Aquili, A. Gigante, *Mar. Drugs.* **2015**, *13*, 7314.

[27] A. S. Bellé, C. R. Hackenhaar, L. S. Spolidoro, E. Rodrigues, M. P. Klein, P. F. Hertz, *Food Chem.* **2018**, *246*, 266.
[28] I. A. Neri-Numa, M. G. Pessoa, B. N. Paulino, G. M. Pastore, *Trends. Food. Sci. Technol.* **2017**, *67*, 271.
[29] K. Delmar, H. Bianco-Peled, *Carbohydr. Polym.* **2015**, *127*, 28.
[30] F. L. Mi, S. S. Shyu, C. K. Peng, *J. Polym. Sci., Part A: Polym. Chem.* **1985**, *2005*, 43.
[31] R. A. A. Muzzarelli, M. El Mehtedi, C. Bottegoni, A. Gigante, *Int. J. Biol. Macromol.* **2016**, *93*, 1366.
[32] T. N. Lugovitskaya, A. B. Shipovskaya, S. L. Shmakov, X. M. Shipenok, *Carbohydr. Polym.* **2022**, *277*, 118773.
[33] J. Ma, Y. Faqir, C. Tan, G. Khaliq, *Food Chem.* **2022**, *373*, 131407.
[34] R. Vivek, V. Nipun Babu, R. Thangam, K. S. Subramanian, S. Kannan, *Colloids Surf., B* **2013**, *111*, 117.
[35] S. S. Biranje, P. V. Madiwale, K. C. Patankar, R. Chhabra, P. Dandekar-Jain, R. V. Adivarekar, *Int. J. Biol. Macromol.* **2019**, *121*, 936.
[36] H. M. P. C. Kumarihami, Y. H. Kim, Y. B. Kwack, J. Kim, J. G. Kim, *Sci. Hortic.* **2022**, *292*, 110647.
[37] H. Liu, C. Wang, C. Li, Y. Qin, Z. Wang, F. Yang, Z. Li, J. Wang, *RSC Adv.* **2018**, *8*, 7533.
[38] A. Sabab, S. Vreugde, A. Jukes, P.-J. Wormald, *J. Clin. Neurosci.* **2021**, *94*, 128.
[39] T. H. Fischer, A. P. Bode, M. Demcheva, J. N. Vournakis, *J. Biomed. Mater. Res A.* **2007**, *80*, 167.
[40] D. Li, H. Cui, K. Hayat, X. Zhang, C.-T. Ho, *Food. Hydrocolloids.* **2022**, *124*, 107341.
[41] Y. Cao, Y. F. Tan, Y. S. Wong, M. W. J. Liew, S. Venkatraman, *Mar. Drugs.* **2019**, *17*, 381.
[42] M. Yue, M. Huang, Z. Zhu, T. Huang, M. Huang, *LWT* **2022**, *154*, 112595.
[43] M. Flórez, E. Guerra-Rodríguez, P. Cazón, M. Vázquez, *Food Hydrocolloids* **2022**, *124*, 107328.
[44] Q. Li, X. Wang, X. Lou, H. Yuan, H. Tu, B. Li, Y. Zhang, *Carbohydr. Polym.* **2015**, *130*, 166.
[45] X. Xi, A. Pizzi, H. Lei, B. Zhang, X. Chen, G. Du, *Int. J. Adhes. Adhes.* **2022**, *112*, 103027.
[46] J. Lu, Y. Chen, M. Ding, X. Fan, J. Hu, Y. Chen, J. Li, Z. Li, W. Liu, *Carbohydr. Polym.* **2022**, *277*, 118871.
[47] Y. Sun, Y. Li, J. Nie, Z. Wang, Q. Hu, *Chem. Lett.* **2013**, *42*, 838.
[48] E. Susilowati, A. Maryani, *J. Phys. Conf. Series* **2019**, *1153*, 012135.
[49] A. Zubareva, B. Shagdarova, V. Varlamov, E. Kashirina, E. Svirshchevskaya, *Eur. Polym. J.* **2017**, *93*, 743.
[50] S. Ouerghemmi, S. Dimassi, N. Tabary, L. Leclercq, S. Degoutin, F. Chai, C. Pierlot, F. Cazaux, A. Ung, J. Staelens, N. Blanchemain, B. Martel, *Carbohydr. Polym.* **2018**, *196*, 8.
[51] J. W. Seo, S. R. Shin, M. Y. Lee, J. M. Cha, K. H. Min, S. C. Lee, S. Y. Shin, H. Bae, *Carbohydr. Polym.* **2021**, *251*, 117036.
[52] M. Keshvardoostchokami, M. Majidi, A. Zamani, B. Liu, *Carbohydr. Polym.* **2021**, *273*, 118625.
[53] M. H. Asfour, H. Elmotasem, D. M. Mostafa, A. A. A. Salama, *Int. J. Pharm.* **2017**, *534*, 325.
[54] Y. Xiong, X. Li, M. Xiong, S. Vikash, P. Liu, M. Wang, Y. Zhu, W. Yuan, Q. Zhang, B. Fu, C. Qin, *Int. J. Biol. Macromol.* **2018**, *118*, 2092.
[55] K. Meller, M. Szumski, B. Buszewski, *Sens. Actuators. B. Chem.* **2017**, *244*, 84.
[56] B. A. Omar, R. Elmasry, A. Eita, M. M. Soliman, A. M. El-Tahan, M. Sitohy, *Saudi J. Biol. Sci*. **2022**, *29*, 911.
[57] M. Carvalho, V. Lopes, R. Corrêa, F. Kelley, J. Raimundo, D. O. Neto, A. Amorim, L. Borges, D. Menezes, *A. Corrêa* **2018**, *119*, 32.
[58] L. Tavares, E. E. Esparza Flores, R. C. Rodrigues, P. F. Hertz, C. P. Z. Noreña, *Food. Hydrocoll.* **2020**, *106*, 105876.
[59] W. W. Mwangi, K. W. Ho, B. T. Tey, E. S. Chan, *Food. Hydrocoll.* **2016**, *60*, 543.
[60] L. Alison, A. F. Demirörs, E. Tervoort, A. Teleki, J. Vermant, A. R. Studart, *Langmuir* **2018**, *34*, 6147.
[61] P. Kianfar, A. Vitale, S. Dalle Vacche, R. Bongiovanni, *Carbohydr. Polym.* **2019**, *217*, 144.
[62] R. V. Pinto, P. S. Gomes, M. H. Fernandes, M. E. V. Costa, M. M. Almeida, *Mater. Sci. Eng., C* **2020**, *109*, 110557.
[63] M. T. Islam, R. M. Laing, C. A. Wilson, M. McConnell, M. A. Ali, *Carbohydr. Polym.* **2022**, *275*, 118682.
[64] I. Dmour, M. O. Taha, *Int. J. Pharm.* **2017**, *529*, 15.
[65] M. Salzano de Luna, C. Ascione, C. Santillo, L. Verdolotti, M. Lavorgna, G. G. Buonocore, R. Castaldo, G. Filippone, H. Xia, L. Ambrosio, *Carbohydr. Polym.* **2019**, *211*, 195.
[66] C. Pan, J. Qian, C. Zhao, H. Yang, X. Zhao, H. Guo, *Carbohydr. Polym.* **2020**, *241*, 116349.
[67] M. Kumar, A. Brar, M. Yadav, A. Chawade, V. Vivekanand, N. Pareek, *Agriculture (Switzerland)* **2018**, *8*, 8.
[68] W. Shao, Y. L. Campbell, T. W. Phillips, C. Freeman, S. Kundu, C. A. Crist, J. B. Williams, M. W. Schilling, *J. Stored. Prod. Res.* **2021**, *94*, 101899.
[69] G. Ortiz-Duarte, L. E. Pérez-Cabrera, F. Artés-Hernández, G. B. Martínez-Hernández, *Postharvest. Biol. Technol.* **2019**, *147*, 174.
[70] S. Yang, L. Liu, H. Chen, Y. Wei, L. Dai, J. Liu, F. Yuan, L. Mao, Z. Li, F. Chen, Y. Gao, *Food. Hydrocoll.* **2021**, *112*, 112.
[71] A. F. L. W. Cerqueira, G. P. Neiva, M. F. Fernandes, J. L. M. Conegundes, R. Stephani, L. F. C. de Oliveira, Z. M. D. C. Ludwig, V. D. C. dos Anjos, F. M. P. Vilela, E. Scio, G. D. Tavares, M. P. Rodarte, *Biocatal Agric Biotechnol* **2020**, *29*, 29.
[72] E. Khor, L. Y. Lim, *Biomaterials* **2003**, *24*, 2339.
[73] L. D. Y. Pozzo, T. F. Da Conceição, A. Spinelli, N. Scharnagl, A. T. N. Pires, *Carbohydr. Polym.* **2018**, *181*, 71.
[74] B. Wu, Y. Li, Y. Li, H. Li, S. Ji, Q. Xia, *React. Funct. Polym.* **2021**, *169*, 105074.
[75] M. R. Caruso, G. D'Agostino, J. Wasserbauer, P. Šiler, G. Cavallaro, S. Milioto, G. Lazzara, *Adv. Sustain. Syst.* **2024**, *8*, 1.
[76] T. H. Bui, W. Lee, S. B. Jeon, K. W. Kim, Y. Lee, *Sep. Purif. Technol.* **2020**, *248*, 116989.
[77] M. R. Caruso, G. D'Agostino, S. Milioto, G. Cavallaro, G. Lazzara, *J. Mater. Sci.* **2023**, *58*, 12954.
[78] S. Sady, A. Błaszczyk, W. Kozak, P. Boryło, M. Szindler, *Food. Packag. Shelf. Life.* **2021**, *30*, 100756.
[79] P. Zhang, L. Chen, Q. Zhang, F. F. Hong, *Front. Microbiol.* **2016**, *7*, 260.
[80] L. Lisuzzo, G. Cavallaro, G. Lazzara, S. Milioto, *Carbohydr. Polym. Tech.* **2023**, *6*, 100380.
[81] Z. Qin, X. Jia, Q. Liu, B. Kong, H. Wang, *Carbohydr. Polym.* **2020**, *247*, 116734.

[82] P. Zhou, Z. Xia, C. Qi, M. He, T. Yu, L. Shi, *Int. J. Biol. Macromol.* **2021**, *192*, 272.

[83] X. Meng, Y. Lu, Y. Gao, S. Cheng, F. Tian, Y. Xiao, F. Li, *Int. J. Biol. Macromol.* **2021**, *182*, 512.

[84] V. Perez-Puyana, J. F. Rubio-Valle, M. Jiménez-Rosado, A. Guerrero, A. Romero, *React. Funct. Polym.* **2020**, *146*, 104414.

[85] R. V. Rios, R. Garzón, S. C. S. Lannes, C. M. Rosell, *LWT—Food Sci. Technol.* **2018**, *96*, 260.

[86] S. Sayed, T. Millard, A. Jardine, *Carbohydr. Polym.* **2018**, *196*, 187.

[87] M. N. Melo, F. M. Pereira, M. A. Rocha, J. G. Ribeiro, A. Junges, W. F. Monteiro, F. M. Diz, R. A. Ligabue, F. B. Morrone, P. Severino, A. T. Fricks, *Mater. Sci. Eng., C.* **2021**, *124*, 112089.

[88] P. Calvo, C. Remuñán-López, J. L. Vila-Jato, M. J. Alonso, *J. Appl. Polym. Sci.* **1997**, *63*, 125.

[89] A. S. Kritchenkov, S. Andranovitš, Y. A. Skorik, *Russ. Chem. Rev.* **2017**, *86*, 231.

[90] J. Yang, G. Liang, T. Xiang, W. Situ, *Food Chem.* **2021**, *354*, 129476.

[91] J. Miras, C. Liu, E. Blomberg, E. Thormann, S. Vílchez, J. Esquena, *Colloids. Surf A. Physicochem. Eng. Asp.* **2021**, *616*, 126229.

[92] R. A. A. Muzzarelli, *Carbohydr. Polym.* **2009**, *77*, 1.

[93] H. F. Ma, G. Meng, B. K. Cui, J. Si, Y. C. Dai, *Chem. Eng. Res. Des.* **2018**, *132*, 664.

[94] S. Maiti, P. S. Khillar, D. Mishra, N. A. Nambiraj, A. K. Jaiswal, *Polym. Test.* **2021**, *97*, 107155.

[95] K. Li, J. Zhu, G. Guan, H. Wu, *Int. J. Biol. Macromol.* **2019**, *122*, 485.

[96] J. Ahn, J. Ryu, G. Song, M. Whang, J. Kim, *Carbohydr. Polym.* **2019**, *217*, 160.

[97] C. R. Hackenhaar, L. S. Spolidoro, E. E. E. Flores, M. P. Klein, P. F. Hertz, *Biocatal. Agric. Biotechnol.* **2021**, *36*, 102136.

[98] C. A. Hobbs, M. Koyanagi, C. Swartz, R. Maronpot, L. Recio, S. Hayashi, **2018**, *118*, 695.

[99] J. C. Monta, M. De, L. Reyes-vega, A. M. Ramos-de-la-pe, M. E. Hendrickx, *J. C. Contreras-Esquivel.* **2015**, *63*, 1347.

[100] I. A. Cavello, J. C. Contreras-Esquivel, S. F. Cavalitto, *Process Biochem.* **2014**, *49*, 1332.

[101] J. E. Brauch, S. P. Zapata-Porras, M. Buchweitz, J. K. Aschoff, R. Carle, *Food. Res. Int.* **2016**, *89*, 365.

[102] K. Zafeiris, D. Brasinika, A. Karatza, E. Koumoulos, I. K. Karoussis, K. Kyriakidou, C. A. Charitidis, *Mater. Sci. Eng., C* **2021**, *119*, 111639.

[103] J. Ko, N. Shin, S. Park, Y. Cho, J. Kim, C. Seo, I. Shin, *Int. Immunopharmacol.* **2017**, *53*, 49.

[104] Y. S. Sun, C. Y. Huang, C. S. Chen, J. H. Chang, W. T. Hou, S. J. Li, Y. L. Hao, H. Pan, H. H. Huang, *Surf. Coat. Technol.* **2018**, *350*, 918.

[105] W. Cui, A. Wang, J. Zhao, J. Li, *Adv. Colloid Interface Sci.* **2016**, *237*, 43.

[106] Y. H. Lin, S. C. Tsai, C. H. Lai, C. H. Lee, Z. S. He, G. C. Tseng, *Biomaterials* **2013**, *34*, 4466.

[107] J. Shin, S. Lee, *Toxicol. Appl. Pharmacol.* **2017**, *328*, 25.

[108] M. K. Shanmugam, H. Shen, F. R. Tang, F. Arfuso, M. Rajesh, L. Wang, A. Prem, J. Bian, B. Cher, A. Bishayee, *Pharmacol. Res.* **2018**, *133*, 195.

[109] S. Lee, H. Jun, S. Cheul, D. Lee, *Food Chem. Toxicol.* **2018**, *116*, 70.

[110] M. C. G. Pellá, M. K. Lima-Tenório, E. T. Tenório-Neto, M. R. Guilherme, E. C. Muniz, A. F. Rubira, *Carbohydr. Polym.* **2018**, *196*, 233.

[111] M. C. Chen, C. T. Liu, H. W. Tsai, W. Y. Lai, Y. Chang, H. W. Sung, *Biomaterials* **2009**, *30*, 5560.

[112] S. Hao, J. Wang, S. Li, F. Shang, Y. Qin, T. Wu, X. Bao, Q. Cao, C. Wang, B. Sun, *Food. Biosci.* **2020**, *35*, 100582.

[113] S. C. Chen, Y. C. Wu, F. L. Mi, Y. H. Lin, L. C. Yu, H. W. Sung, *J. Controlled. Release.* **2004**, *96*, 285.

[114] S. H. Yu, S. J. Wu, J. Y. Wu, D. Y. Wen, F. L. Mi, *Carbohydr. Polym.* **2015**, *126*, 97.

[115] H. W. Sung, Y. Chang, I. L. Liang, W. H. Chang, Y. C. Chen, *J. Biomed. Mater. Res.* **2000**, *52*, 77.

[116] V. Perez-Puyana, M. Jiménez-Rosado, A. Romero, A. Guerrero, *Int. J. Biol. Macromol.* **2019**, *139*, 262.

[117] Q. Liu, N. Xia, W. Wan, Y. Gao, S. Zhu, *Int. J. Biol. Macromol.* **2021**, *189*, 722.

[118] V. A. Mirón-Mérida, M. Wu, Y. Y. Gong, Y. Guo, M. Holmes, R. Ettelaie, F. M. Goycoolea, *Sens. Biosensing. Res.* **2020**, *29*, 100339.

[119] J. Fourie, F. Taute, L. du Preez, D. de Beer, *Regen. Eng. Transl. Med.* **2022**, *8*, 1.

[120] Y. Yu, S. Xu, S. Li, H. Pan, *Biomater. Sci.* **2021**, *9*, 1583.

[121] M. M. Islam, M. Shahruzzaman, S. Biswas, M. Nurus Sakib, T. U. Rashid, *Bioact. Mater.* **2020**, *5*, 164.

[122] Y. L. Nunes, F. L. de Menezes, I. G. de Sousa, A. L. G. Cavalcante, F. T. T. Cavalcante, K. da Silva Moreira, A. L. B. de Oliveira, G. F. Mota, J. E. da Silva Souza, I. R. de Aguiar Falcão, T. G. Rocha, R. B. R. Valério, P. B. A. Fechine, M. C. M. de Souza, J. C. S. dos Santos, *Int. J. Biol. Macromol.* **2021**, *181*, 1124.

[123] V. G. Tacias-Pascacio, E. García-Parra, G. Vela-Gutiérrez, J. J. Virgen-Ortiz, Á. Berenguer-Murcia, A. R. Alcántara, R. Fernandez-Lafuente, *Catalysts* **2019**, *9*, 1.

[124] S. Mallakpour, M. Tukhani, C. M. Hussain, *Adv. Colloid Interface Sci.* **2021**, *292*, 102415.

[125] A. C. Alavarse, E. C. G. Frachini, R. L. C. G. da Silva, V. H. Lima, A. Shavandi, D. F. S. Petri, *Int. J. Biol. Macromol.* **2022**, *202*, 558.

[126] M. Saeedi, O. Vahidi, M. Moghbeli, S. Ahmadi, M. Asadnia, O. Akhavan, F. Seidi, M. Rabiee, M. R. Saeb, T. J. Webster, R. S. Varma, E. Sharifi, A. Zarrabi, N. Rabiee, *J. Controlled. Release.* **2022**, *350*, 175.

[127] C. Coscolín, A. Beloqui, M. Martínez-Martínez, R. Bargiela, G. Santiago, R. M. Blanco, G. Delaittre, C. Márquez-Álvarez, M. Ferrer, *Appl. Catal A. Gen.* **2018**, *565*, 59.

[128] C. Bernal, K. Rodríguez, R. Martínez, *Biotechnol. Adv.* **2018**, *36*, 1470.

[129] K. Hernandez, R. Fernandez-Lafuente, *Enzyme Microb. Technol.* **2011**, *48*, 107.

[130] R. C. Rodrigues, C. Ortiz, Á. Berenguer-Murcia, R. Torres, R. Fernández-Lafuente, *Chem. Soc. Rev.* **2013**, *42*, 6290.

[131] A. Rempel, T. Machado, H. Treichel, E. Colla, A. C. Margarites, L. M. Colla, *Bioresour. Technol.* **2018**, *263*, 163.

[132] M. P. Klein, C. R. Hackenhaar, A. S. G. G. Lorenzoni, R. C. Rodrigues, T. M. H. H. Costa, J. L. Ninow, P. F. Hertz, *Carbohydr. Polym.* **2016**, *137*, 184.

[133] M. Chen, T. Runge, L. Wang, R. Li, J. Feng, X. Shu, *Carbohydr. Polym.* **2018**, *200*, 115.
[134] V. Sol, M. Vr, **2018**, *202*, 694.
[135] E. Poorakbar, A. Shafiee, A. A. Saboury, B. L. Rad, K. Khoshnevisan, L. Ma'mani, H. Derakhshankhah, M. R. Ganjali, M. Hosseini, *Process Biochem.* **2018**, *71*, 92.
[136] L. S. Duarte, J. D. N. Schöffer, A. S. G. Lorenzoni, R. C. Rodrigues, E. Rodrigues, P. F. Hertz, *Process Biochem.* **2017**, *55*, 96.
[137] L. Betancor, F. López-Gallego, A. Hidalgo, N. Alonso-Morales, G. Dellamora-Ortiz, C. Mateo, R. Fernández-Lafuente, J. M. Guisán, *Enzyme Microb. Technol.* **2006**, *39*, 877.
[138] A. Tanriseven, Y. Aslan, **2005**, *36*, 550.
[139] E. E. Esparza-Flores, L. B. Siquiera, F. D. Cardoso, T. H. Costa, E. V. Benvenutti, I. E. Medina-Ramírez, M. Perullini, P. R. Santagapita, R. C. Rodrigues, P. F. Hertz, *Food Hydrocolloids* **2023**, *144*, 109034.
[140] E. E. Esparza-Flores, F. D. Cardoso, L. B. Siquiera, P. R. Santagapita, P. F. Hertz, R. C. Rodrigues, *Int. J. Biol. Macromol.* **2023**, *250*, 126234.
[141] N. Phadungcharoen, W. Winotapun, A. Khomniyawanit, F. Krataichan, T. Rojanarata, *Sustain. Chem. Pharm.* **2019**, *14*, 14.
[142] P. C. Lima, I. Gazoni, A. M. G. de Carvalho, D. Bresolin, D. Cavalheiro, D. de Oliveira, E. Rigo, *Food Chem.* **2021**, *349*, 349.
[143] S. D. E. Nath, C. Abueva, B. Kim, B. T. A. Lee, *Carbohydr. Polym.* **2015**, *115*, 160.
[144] Y. Yang, W. Zhao, J. He, Y. Zhao, F. Ding, X. Gu, *Eur. J. Pharm. Biopharm.* **2011**, *79*, 519.
[145] Y. Liu, K. Wang, H. Zheng, M. Ma, S. Li, L. Ma, *Food. Hydrocoll.* **2023**, *139*, 108551.
[146] A. Cerón, S. Costa, R. Imbernon, R. de Queiroz, J. de Castro, H. Ferraz, R. Oliveira, S. Costa, *Process Biochem.* **2023**, *128*, 116.
[147] M. Iqbal, Y. Deng, Q. Chen, C. Yang, Y. Zhu, Z. Chen, J. Wang, K. Hu, G. He, D. Li, *Green. Synth. Catalysis.* **2022**, *3*, 265.
[148] V. Zimmermann, E. E. Esparza-Flores, C. P. Partichelli, E. F. C. da Silva, R. C. Rodrigues, *Process Biochem.* **2024**, *139*, 1.
[149] Z. S. Xia, E. W. Hao, Y. Ting Wei, X. T. Hou, Z. M. Chen, M. Wei, Z. C. Du, J. G. Deng, *Comp. Biochem. Physiol. C Toxicol. Pharmacol.* **2021**, *241*, 108951.

How to cite this article: E. E. Esparza-Flores, P. F. Hertz, R. C. Rodrigues, *J. Appl. Polym. Sci.* **2024**, *141*(46), e56250. https://doi.org/10.1002/app.56250