ISSN: 2515-8260, Volume 09, Issue 07, 2022

ROLE OF CHITOSAN IN MAINTAINANCE OF GINGIVAL AND PERIODONTAL HEALTH

Dr. Priyanshu Kumari Ramuka, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha

Dr. Dhirendra Kumar Singh, Department of Periodontology and Oral Implantology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha

Tunisha Raha, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha

Diya Chakraborty, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha

Corresponding author: Dr. Dhirendra Kumar Singh, Department of Periodontology and Oral Implantology, Kalinga Institute of Dental Sciences, KIIT Deemed to be University, Bhubaneswar, Odisha. Email id: dr.dhirendra27@gmail.com

Abstract: Chitosan and its variations, have been used in a variety of scientific domains. Because of its unique physicochemical, biological, ecological, and physiological characteristics, such as biocompatibility, biodegradability, stability in the natural environment, non-toxicity, high biological activity, affordability, chelating of metal ions, and high sorption properties, chitosan is used in a variety of biomedical and industrial processes. The structure is more intriguing because of the reactivity of the amino and hydroxyl groups, which has a variety of uses in dentistry, biotechnology, biosensing, cosmetics, water treatment, and agriculture. Drug delivery, tissue engineering, wound healing, regenerative medicine, blood anticoagulation, and engineering of bone, tendon, or blood vessels are a few of these uses. The present article includes fresh research-based information about the role of chitosan in maintainance of gingival and periodontal health.

Keywords- Chitosan, Gingiva, Periodontium, Biocompatible material, Polysaccharides

Introduction: The potential of biomaterials developed 50 years ago to promote advancements in the biomedical profession which continues to draw a lot of interest. Numerous naturally occurring polysaccharides provide a wide range of resources that are useful in the biomedical industry. The most sought-after bio-polymer for use in therapeutic interventions these days is chitosan.[1]

In 1811, Braconnot discovered chitin which he extracted from mushrooms and named it fongine; Odier later changed the name to chitin. When Rouget introduced chitin in 1859, he founded the most primary chitin derivative, chitosan. Later Hoppe-Seyler gave it the name chitosan in 1894.[1,2]

Source of Chitosan: It is a linear amino polysaccharide.After cellusose, it is the second most widely used biopolymer. It is created by treating the chitin shells of crustaceans like shrimp with a basic substance like sodium hydroxide, D-glucosamine and N-acetyl-D-glucosamine. The exoskeletons of insects, crustaceans, and fungal cell walls contain it only as a structural element. Chitosan is only present in nature in small levels, whereas chitin is present in nature in huge amounts through a variety of sources. Typically, chitin is treated chemically or enzymatically to produce the chitosan that is employed in industrial or academic applications. Chitosan's cationic nature is fairly unusual because most polysaccharides in an acidic environment are normally neutral or negatively charged.[3]

Structure of Chitosan: Chitosan has hydroxyl groups in C-3 and C-6 as well as amino and amide groups in the C-2 position that are its active areas. Deacetylation causes enzymatic hydrolysis, which converts chitosan into an oligosaccharide with a low molecular weight that is water soluble. Chitosan creates a cationic polymer and is soluble in weak acids. Chitosan that has been chemically altered in the amino or hydroxyl groups yields derivatives that include cationic moieties. With its high viscosity and great capacity to bind water, this material is biocompatible and ideal for application in a variety of forms, including gels, chips, and membranes.[4-8]

Properties of Chitosan: Chitosan is a white odourless powder which is soluble in acetic, nitric, hydrochloric, perchloric, and phosphoric acids.It is insoluble in water and organic solvents.Aqueous acidic solutions with a pH lower than 6.5 can dissolve chitosan. [9-11] Its molecular weight and degree of deacetylation vary. The melting point is roughly 290 °C [27, 28]. The various properties are discussed below.

A. Bio-compatibility: Numerous toxicological studies have been conducted on the safety of chitosan to determine its bio-compatibility and implantation effects in medicinal products. Oral administration of daily doses of 4.5 g chitosan to human volunteers has been done without any negative outcomes being noted. [12,13] When utilised as a barrier membrane material in the regeneration of periodontal tissue, even higher oral doses of up to 6.75 g have been judged safe. Short-term human investigations

lasting up to 12 weeks reportedly found no significant clinical symptoms or indications of an allergic reaction. [14] In the process of in vitro breakdown, chitosan is primarily depolymerized using egg white and human lysozyme.[15-19]

B. Biodegradability: In order to ensure the proper restoration of periodontal tissues, materials utilised as tissue regeneration barrier membranes in clinical practise often need to maintain a specific barrier function for 4-6 weeks.[20] Numerous research assessed the rate of chitosan membrane degradation produced using various ways . After 90 days of shaking in PBS at 40 rpm and 37C, pure chitosan membranes lost 15–40% of their initial weight. [21, 22] In vivo testing revealed that chitosan membranes retained their structure for six weeks. [23]

C. Tissue Regeneration: Chitosan also aids in tissue regeneration and repair, which is another benefit. In therapeutic settings, chitosan dressings for wound healing are frequently utilised and show promising curative results. [24] Chitosan's effects on the regeneration of periodontal tissue are starting to attract the attention of researchers. According to in vitro tests, chitosan can increase the proliferation of human periodontal ligament cells. Additionally, the submicroscopic structure of the chitosan-cultured cells was similar to that of normal cells. [25] An in vivo experiment revealed that the ligament cells in the chitosan scaffold not only multiplied but also attracted vascular tissue growth. It also revealed that proliferating periodontal ligament cells had alkaline phosphatase and osteopontin protein expression that had been increased. [26-48]

Recent advances

Recent advances are described in figure 1.Because of its antacid and antiulcer qualities, which reduce medication irritability, it is a nontoxic and adsorbable polymer mostly preferred in drug delivery [49,50]. They have cationic nature and capacity which creates porous networks. For bone repair and rebuilding, chitosan is combined with hydroxyapatite and bioactive glass ceramic. [51,52].

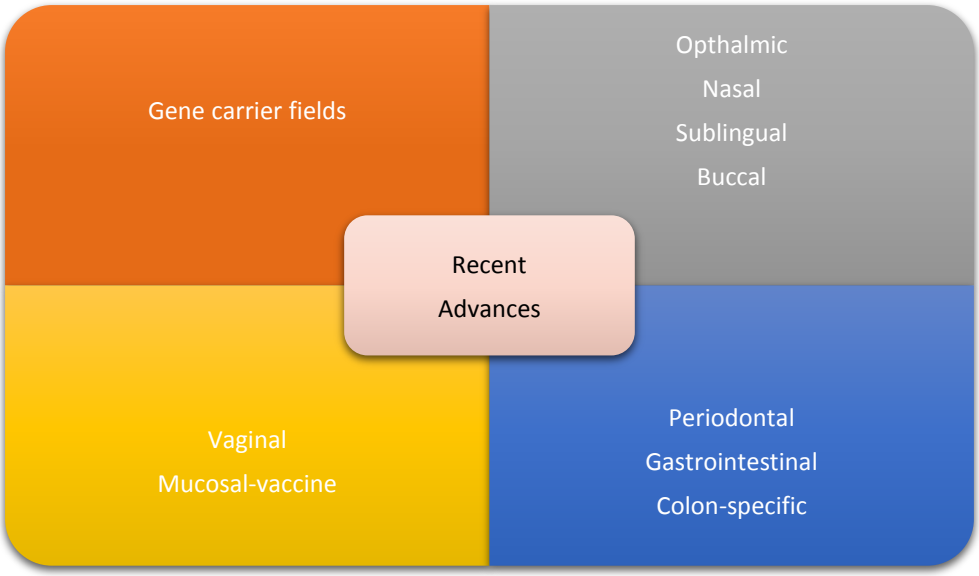

Figure -1 Recent Advances of Chitosan

Chitosan is an effective treatment for infectious disorders, according to studies done in this field. Different systems built on the foundation of chitosan have been presented [53]. These technologies have been demonstrated to decrease pharmacological adverse effects and improve therapeutic efficacy. In light of the COVID-19 and other viruses that are currently causing harm throughout the world, chitosan is also effective as a vaccine system.

Chitosan's effectiveness against bacteria has been confirmed as a medication for the removal of infected teeth's pulp [54]. Chitosan can serve as an effective agent in preventative dentistry. To avoid dental illnesses (caries, periodontitis), dental adhesives, toothpaste with an antibacterial ingredient, chewing gum with an antibacterial ingredient etc. [55]. The optical density method was used to study the hydrogels. It was discovered that the hydrogels have effective antibacterial properties. activities directed against E. coli. It is generally applicable in the field of pharmacy and biomedicine [56].

Recent advances of chitosan in drug delivery methods for periodontal diseases

A. Fibers: Fibers are reservoir-type systems .For the sustained release of the medication that has been trapped there, they are inserted in the periodontal pockets and fixed with cyanoacrylate adhesive. Tetracycline is rapidly released from cellulose acetate fibres through the diffusion process. When put into periodontal pockets, fibres containing 20% of chlorhexidine showed a quick and noticeable reduction in periodontal disease signs and symptoms compared to the less effective tetracycline delivery using hollow fibres. As matrices for the delivery of medication to the periodontal pocket, a number of

polymers, including poly (e-caprolactone), polyurethane, polypropylene, cellulose acetate propionate, and ethyl vinyl acetate (EVA), have been studied. In this regard, monolithic EVA fibres were discovered to be successful in regulating the release of encapsulated medication, as shown by several in vitro and in vivo investigations.[57]

B. Films: Film, produced either by direct milling or solvent casting, has proven a much more popular type of intra-pocket delivery method. Larger films might be put into the site of action by being cut or punched into the proper sizes, or they could be applied inside the cavity to the gingival or cheek mucosa surface. Drugs are dispersed throughout the polymer in films, which are matrix delivery systems, and are released through drug diffusion, matrix breakdown, or matrix erosion.A taurine-enriched film made of the innovative natural polymer chitosan also uses it as a polymeric matrix (antioxidant agent).[58]

Chitosan's ability to heal wounds is enhanced by taurine, which may be helpful for tissue repair in degenerative illnesses like periodontitis. Additionally, Perugini et al. used a novel chitosan/PLGA film delivery system to transport ipriflavone to the periodontium. Comparing monolayer films made of PLGA micromatrices filled with ipriflavone to multilayer films made of chitosan/PLGA/chitosan (three layers). In vitro tests showed that the composite micromatricial films are an appropriate dosage form to extend the release of ipriflavone for 20 days. In a different investigation, a two-layered film made of biodegradable PCL and mucoadhesive chitosan was created.

C. **Injectable System:** Particularly appealing are injectable methods for the antibiotics are delivered into the periodontal tissue pocket. The application is quick and simple to use taken done using a syringe and without discomfort. Thus, the cost of the treatment is significantly decreased compared to gadgets that require more time to install and secured. An injectable delivery device is also included. These platforms enable simple therapeutic agent administration employing a syringe. They also reduce costs.

D. Gels: On the basis of hydroxyethyl cellulose, corbopol 974 and polycarbophil, mucoadhesive, MTZ-containing gel systems have been created. Using a blunt cannula and syringe, gel is injected sublingually. The gel has a negligible impact on the number of anaerobic microorganisms. This can be because there aren't many bacteria that are MTZ-susceptible or because there are bacterial biofilms present.

ISSN: 2515-8260, Volume 09, Issue 07, 2022

Controlled release DOX gel administered locally may partially offset smoking's detrimental effects on periodontal repair after nonsurgical treatment [59]. The first involved loading tetracycline base into the halloysite, a microtubular excepient covered with chitosan to further slow drug release. To make sure that distribution to the periodontal pocket was simple, the syringeability of this formulation at various temperatures was assessed.The first involved loading tetracycline base into the halloysite, a microtubular excepient covered with chitosan to further slow drug release. To guarantee simple administration to the periodontal pocket, the syringeability of this formulation at various temperatures was assessed. To investigate how the thermoresponsivity changed over time, a stability study was conducted [60].

E. Injectable Gels: Gel or semisolid formulations can indeed have some benefits. Gels can be made and delivered more readily, despite the included drug's substantially rapid release. Chitosan has demonstrated potential in the treatment of chronic periodontitis in a gel form with or without 15% metronidazole. The ability of a bioadhesive semisolid, polymeric system to easily flow through a cannula into a periodontal pocket, where it hardens in place to supply the therapeutic substance for an extended period, makes it a useful intra-pocket delivery vehicle. These systems display a pseudoplastic flow and thermoresponsive behavior, transitioning from a liquid to a gel between 34 and 37 degrees Celsius.

F. Strips and Compacts: The evaluation of acrylic strips loaded with amoxycillin-clavulanic acid is published in a later study.[60] The first 24 hours saw the release of the most potent antibacterial agent, and the following 9 days saw the release of therapeutic levels of medicines. Even three weeks following the acrylic strip removal, the effect was maintained. N-butyl-2-cyanoacrylate was employed to create tissue adhesive implants because it can trap drugs and release them gradually when added to the design of a biodegradable local drug delivery device.

Conclusion: Chitosan is currently being studied and used widely in a variety of fields related to biotechnology, medicine, pharmacy, and industry because of its accessibility, renewability as a raw material, and special qualities..Better performing polymer-based biomaterials will undoubtedly be in great demand in the upcoming years. Large-scale

distribution of chitosan-based biomaterials could serve as a sustainable and renewable resource for future scientific advancements.

References

1. Periayah MH, Halim AS, Saad AZ. Chitosan: A Promising Marine Polysaccharide for Biomedical Research. Pharmacogn Rev. 2016 Jan-Jun;10(19):39-42.

2. Kmiec M, Pighinelli L, Tedesco MF, Silva MM, Reis V. Chitosan-properties and applications in dentistry. *Adv Tissue Eng Regen Med Open Access.* 2017;2:205–11.

3. Singh G, Jamwal U. Chitosan hydrogel: Its applications in medicine and dentistry. *Int J Prev Clin Dent Res.* 2018;5:71–6.

4. Wieckiewicz M, Boening KW, Grychowska N, Paradowska-Stolarz A. Clinical application of chitosan in dental specialities. *Mini Rev Med Chem.* 2017;17:401–9.

5. Rinaudo M. Chitin and chitosan: Properties and applications. Prog Polym. 2006;31:603–32.

6. Tanikonda R, Ravi R, Kantheti S, Divella S. Chitosan: Applications in dentistry. Trends Biomater Artif Organs. 2014;28:74–8.

7. Seda Tiğli R, Karakeçili A, Gümüşderelioğlu M. In vitro characterization of chitosan scaffolds: Influence of composition and deacetylation degree. J Mater Sci Mater Med. 2007;18:1665–74.

8. Biagini B, Muzzarelli RA, Giardino R, Castaldini C. Biological materials for wound healing. In: Brine CJ, Sandford PA, Zikakis JP, editors. Advances in Chitin and Chitosan. London, New York: Elsevier; 1992. pp. 16–24.

9. Zhang J, Xia W, Liu P, Cheng Q, Tahirou T, Gu W, et al. Chitosan modification and pharmaceutical/biomedical applications. Mar Drugs. 2010;8:1962–87.

10. Sankararamakrishnan N, Sanghi R. Preparation and characterization of a novel xanthated chitosan. Carbohydr Polym. 2006;66:160–7.

11. Kurita K. Chitin and chitosan: Functional biopolymers from marine crustaceans. Mar Biotechnol (NY) 2006;8:203–26.

12. Baldrick P. The safety of chitosan as a pharmaceutical excipient.Regul Toxicol Pharm 2010;56:290–299.

13. Gades MD, Stern JS. Chitosan supplementation and fecal facal fatexcretion in men. Obes Res 2003;11:683–688.

14. Tapola NS, Lyyra ML, Kolehmainen RM, Sarkkinen ES, SchaussAG. Safety aspects and cholesterol-lowering efficacy of chitosantablets. J Am Coll Nutr 2008;27:22–30.

15. Ylitalo R, Lehtinen S, Wuolijoki E, Ylitalo P, Lehtimaki T. Cholesterol-lowering properties and safety of chitosan. Arzneimittelforschung 2002;52:1–7.

16. Varum KM, Myhr MM, Hjerde RJ, Smidsrod O. In vitro degradation rates of partially N-acetylated chitosans in human serum.Carbohydr Res 1997;299:99–101.

17. Hayami JW, Surrao DC, Waldman SD, Amsden BG. Design and characterization of a biodegradable composite scaffold for ligament tissue engineering. J Biomed Mater Res A 2009;92:1407–1420.

18. Zhuang ZX, Lin ZY, Cao JF. Biocompatibility of chitosan-carboxymethylchitosan as membrane for periodontal guided tissue regeneration. Shanghai Kou Qiang Yi Xue 2003;12:362–365.

19. Shin SY, Park HN, Kim KH, Lee MH, Choi YS, Park YJ, Lee YM, Ku Y, Rhyu IC, Han SB, Lee SJ, Chung CP. Biological evaluation of chitosan nanofifiber membrane for guided bone regeneration. J Periodontol 2005;76:1778–1784.

20. Park YJ, Nam KH, Ha SJ, Pai CM, Chung CP, Lee SJ. Porous poly (L-lactide) membranes for guided tissue regeneration and controlled drug delivery: Membrane fabrication and characterization. J Control Release 1997;43:151–160.

21. Kuo SM, Chang SJ, Chen TW, Kuan TC. Guided tissue regeneration for using a chitosan membrane: An experimental study in rats. J Biomed Mater Res A 2006;76:408–415.

22. Lee EJ, Shin DS, Kim HE, Kim HW, Koh YH, Jang JH. Membrane of hybrid chitosan-silica xerogel for guided bone regeneration. Biomaterials 2009;30:743–750.

23. Ku Y, Shim IK, Lee JY, Park YJ, Rhee SH, Nam SH, Park JB, Chung CP, Lee SJ. Chitosan/poly(L-lactic acid) multilayered membrane for guided tissue regeneration. J Biomed Mater Res A 2009;90:766–772.

24. Boateng JS, Matthews KH, Stevens HN, Eccleston GM. Wound healing dressings and drug delivery systems: A review. J Pharm Sci 2008;97:2892–2923.

25. Ji QX, Zhong de Y, Lu R, Zhang WQ, Deng J, Chen XG. In vitro evaluation of the biomedical properties of chitosan and quaternized chitosan for dental applications. Carbohydr Res 2009;344:1297–1302.

26. Liao F, Chen Y, Li Z, Wang Y, Shi B, Gong Z, Cheng X. A novel bioactive three-dimensional beta-tricalcium phosphate/chitosan scaffold for periodontal tissue engineering. J Mater Sci Mater Med 2010;21:489–496.

27. Sivaramakrishna D, Bhuvanachandra B, Mallakuntla MK, Das SN, Ramakrishna B, Podile AR (2020) Pretreatment with KOH and KOH-urea enhanced hydrolysis of α-

chitin by an endochitinase from Enterobacter cloacae subsp. cloacae. Carbohydr Polym 235:115952.

28. Goy RC, Britto DD, Assis OB (2009) A review of the antimicrobial activity of chitosan. Polimeros 19:241–247.

29. Zargar V, Asghari M, DashtiA (2015) A review on chitin and chitosan polymers: structure, chemistry, solubility, derivatives, and applications. ChemBioEng Rev 2(3):204–226.

30. Mourya VK, Inamdar N (2012) Details on chitosan, its chemistry, physiochemical properties and chitosan derivatives with their applications. Chapter 1: Chitosan and Chemically Engineered Chitosan, in: Comprehensive Chemistry and Biomedical Applications of Chitosan and Chemically Engineered Chitosan. Career Publishers, India, 1st ed. 1–24

31. Wang W, Xue C, Mao X (2020) Chitosan: structural modifcation, biological activity and application. Int J Biol Macromol 164:4532–4546.

32. Perinelli DR, Fagioli L, Campana R, Lam JKW, Bafone W, Palmieri GF, Casettari L, Bonacucina G (2018) Chitosan-based nanosystems and their exploited antimicrobial activity. Eur J Pharm Sci 117:8–20.

33. Kurek D (2013) Sovremennoye sostoyaniye fziko-khimicheskix metodov opredeleniya osnovnix kharakteristik khitozana i ego proizvodnix. Khitozan/ pod red. K.Q. Skryabina. M.: Sentr «Bioingeneriya» RAN (in Russian) 61–70

34. Richter T, Gulich M, Richter K (2012) Quality control and good manufacturing practice (GMP) for chitosan-based biopharmaceutical products, Chitosan-based biopharmaceutical delivery, targeting and polymer therapeutics / Eds. B. Sarmento, J. Neves, John Wiley & Sons 503–542

35. Chung YC, Chen CY (2008) Antibacterial characteristics and activity of acid-soluble chitosan. Bioresour Technol 99(8):2806– 2814.

36. Jain N, Gaurav K., Javed S, Iqbal Z, Talegaokar S. Ahmad FJ, Khar RK. Recent approaches for the treatment of periodontitis. Drug. Discov. Today 2008; 1 (21-22): 932-943.

37. Miyazaki S, Ishii K, Nadai T (1981) The use of chitin and chitosan as drug carriers. Chem Pharm Bull 29:3067–3069. https:// doi.org/10.1248/cpb.29.3067 115.

38. Humbatova SF, Zeynalov NA, Taghiyev DB, Tapdiqov SZ, Mammedova SM (2016) Chitosan polymer composite material containing of silver nanoparticle. Dig J Nanomater Biostruct 11(1):39–44 116.

39. Kim I-Y, Seo S-J, Moon H-S, Yoo M-K, Park I-Y, Kim A-C et al (2008) Chitosan and its derivatives for tissue engineering applications. Biotechnol Adv 26:1–21.

40. Chow KS, Khor E (2000) Novel fabrication of open-pore chitin matrixes. Biomacromolecules 1:61–67.

41. Kokubo T (1991) Bioactive glass ceramics: properties and applications. Biomaterials 12:155–163.

42. Huang Y, Onyeri S, Siewe M, Moshfeghian A, Madihally SV (2005) In vitro characterization of chitosangelatin scafolds for tissue engineering. Biomaterials 26:7616–7627.

43. Sarasam A, Madihally SV (2005) Characterization of chitosan_ polycaprolactone blends for tissue engineering applications. Biomaterials 26:5500–5508.

44. Goodson JM et al. Monolithic tetracyclinecontaining fibres for controlled delivery to periodontal pockets. J. Periodontol. 1983;(54): 575–579.

45. Tonetti MS, Piniprato G, Corelli. P. Principles and clinical application of periodontal controlled drug delivery with tetracycline fibers . Int. J. Periodontics and Restorative Dent. 1994 ;14(5): 421- 435.

46. Vyas SP, Sihorkar V, Mishra V. Controlled and targeted drug delivery strategies towards Intraperiodontal pocket disease. J.Clin Pharm Ther. 2000 :25 (1): 21-42.

47. Collins AEM. Evaluation of a controlledrelease compact containing tetracycline hydrochloride bonded to tooth for the treatment of periodontal. Int. J. Pharm 1989; (51): 103- 114. 15.

48. Kelly HM, Deasy PB, Ziaka E, Cleffey N. Formulation and preliminary in vivo dog studies of a novel drug delivery for the treatment of periodontitis. Int. J. Pharm. 2004; 15 (1): 167 – 183.

49. Esposito E, Carrota V, Scabbia A, Trombelli L, Antena PD, Menegatti E. Comparative analysis of tetracycline containing dental gels: poloxamer and monoglyceride based formulations. Int. J. Pharm. 1996; (142): 9-23.

50. Jones SD, Woolfson DA, Brown FA, Michael J, Neill O. Mucoadhesive, syringeable drug delivery systems for controlled application of metronidazole to periodontal pocket. In vitro release kinetics, syringeability, mechanical and and mucoadhesive properties J. Contr. Rel. 2002;49(1): 71-79.

51. Eskanderi MM, Ozturk OG, Eskandari HG, Balli E and Yilmaz C. Cyanoacrylate adhesive provides efficient local drug delivery. Clin. Orthop Releat Res 2006; (12): 45-55.

52. Mastiholimath VS, Dandagi PM, Gadad AP, Patil MB and Manvi FV. Formulation and evaluation of ornidazole dental implants for periodontitis . Indian J. Pham Sci. 2006 ;68(1): 68-71

53. Dasagrandhi CH, Park S, Jung W, KimY (2018) Antibacterial and bioflm modulating potential of ferulic acid-grafted chitosan against human pathogenic bacteria. Int J Mol Sci 19:2157.

54. Asghar MA, Yousuf RI, Shoaib MH, Asghar MA (2020) Antibacterial, anticoagulant and cytotoxic evaluation of biocompatible nanocomposite of chitosan loaded green synthesized bioinspired silver nanoparticles. Int J Biol Macromol 160:934–943.

55. Emamy FH, Bumajdad A, Lukaszewicz JP (2021) Adsorption of hexavalent chromium and divalent lead ions on the nitrogen-enriched chitosan-based activated carbon. Nanomaterials 11(8):1907.

56. Vilela PB, Dalalibera A, Duminelli E, Becegato VA, Paulino A (2019) Adsorption and removal of chromium (VI) contained in aqueous solutions using a chitosan-based hydrogel. Environ Sci Pollut Res 26:28481–28489.

57. Yuan D, Zhang W, Cui J, He L, Wang J, Yan C, Kou Y, Li J (2020) Facile fabrication of magnetic phosphorylated chitosan for the removal of Co(II) in water treatment: separation properties and adsorption mechanisms. Environ Sci Pollut Res 27:2588–2598.

58. Sheth Y, Dharaskar S, Khalid M, Sonawane S (2021) An environment friendly approach for heavy metal removal from industrial wastewater using chitosan based biosorbent: A review. Sustainable Energy Technol Assess 43:100951.

59. Cunha BS, Bataglioli RA, Taketa TB, Lopes LM, Beppu MM (2019) Ionic liquid functionalization of chitosan beads for improving thermal stability and copper ions uptake from aqueous solution. J Environ Chem Eng 7(3):103181.

60. Cheraghipour E, Pakshir M (2020) Process optimization and modeling of Pb(II) ions adsorption on chitosan-conjugated magnetite nano-biocomposite using response surface methodology. Chemosphere 260:127560.