REVIEW ON CHITOSAN/COPPER COMPOSITES AS POTENTIAL BIOCOMPOSITES FOR VARIOUS APPLICATIONS

Abstract

Chitosan copper composites are a novel class of materials created by combining copper nanoparticles with chitosan, a biodegradable polymer derived from chitin. This composite synergizes the remarkable properties of both constituents, offering a wide array of potential applications. Chitosan contributes its biocompatibility, biodegradability, and versatile binding capabilities, while copper nanoparticles add antimicrobial, electrical, and catalytic properties. This composite's synthesis methods, including solution blending and in-situ reduction, are detailed, highlighting their influence on final properties. As an innovative convergence of biopolymers and nanomaterials, chitosan copper composites present a promising avenue for developing advanced materials with diverse applications.

Keywords: Chitosan; biocomposite; copper coating; nano-materials.

Authors

Anjaly Gopinadhan
Department of Chemistry
Christ College (Autonomous)
Irinjalakuda, Kerala, India.
anjaly99gopinadhan@gmail.com

Meril Shelly
Department of Chemistry
Christ College (Autonomous) Irinjalakuda,
Kerala, India.
merils@christcollegeijk.edu.in

Tom Cherian
Department of Chemistry
Christ College (Autonomous) Irinjalakuda,
Kerala, India.
drtomcherian@gmail.com

I. INTRODUCTION

Nanotechnology is the study of materials whose dimensions ranges from 1 - 100 nm, which are designed for specialized applications [1]. A composite is a multiphase material that exhibits significant amount of each constituent phase's qualities, providing better combination of properties in such a way that better property combinations are created by the careful combining of two or more unique materials [2]. Composite materials containing nanoscale changes in one of the phases are called nano-composites (NCs). A wide variety of systems, including amorphous materials, one-dimensional, two-dimensional, and three-dimensional, made of distinctively different components that are combined at the nanoscale, are now included in the definition of nano-composite material, which has expanded significantly over the years. They were originally reported in 1950 followed by the studies of polyamide nanocomposites in 1976. However, they were not widely explored in both academic and industry facilities until Toyota researchers launched a systematic analysis of polymer/layered silicate clay material composites in the early 1980s and later became the most utilized material [3-4]. As per Azonano's findings in 2009, nanocomposites are materials characterized by a nanoscale structure, which enhances the overall properties of products. These nanocomposites are frequently composed of clay, polymers, carbon, or a combination thereof, using nanoparticle building blocks [5]. NC has grown in popularity recently as a result because of superior mechanical strength, solvent-resistant properties, better thermal stability as well as fire-retardant qualities [6]. The dispersion state, particle size and distribution, geometric shape, surface features, and the commercial accessibility of nano-particles have increased the production as well as applications of NC to a great extent [7].

1. **Classification:** Nanocomposites can be classified into various categories based on the materials incorporated, dimensions of the framework, types of reinforcement material, and synthetic approach. The commonly observed fillers used in nanocomposites are shown in Figure 1. They are a class of materials formed by integrating nanoparticles into a matrix, have emerged as a revolutionary area of research with diverse applications across scientific, industrial, and technological domains. The controlled manipulation of materials at the nanoscale imparts novel properties and functionalities, often surpassing those of their individual components. Among the intriguing array of nanocomposites, chitosan-copper nanocomposites stand out as a remarkable example of synergistic material engineering, combining the inherent strengths of chitosan and copper nanoparticles. This review delves into the synthesis methods, properties, and wide-ranging applications of chitosan-copper nanocomposites, underscoring their significance in various fields.

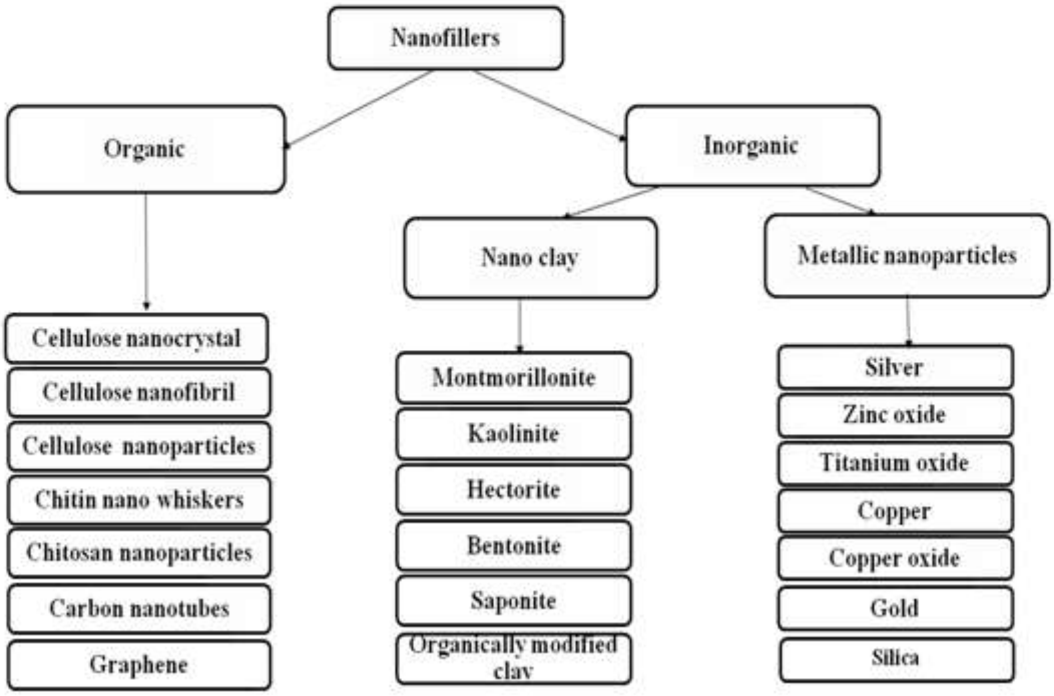

Figure 1: Fillers used for the preparation of nano-composites

2. **Properties of Copper and Chitosan as an Antimicrobial Agent:** The fusion of biopolymers and metals has emerged as a groundbreaking innovation with far-reaching implications across diverse industries. This convergence brings together the versatility of biopolymers, derived from renewable natural sources, and the unique properties of metal nanoparticles, often at the nanoscale, to create a new class of materials that transcends the capabilities of their individual components. The importance of biopolymer and metal composites spans numerous fields, from medicine to electronics, environmental remediation, and beyond. Biopolymers, such as chitosan, cellulose, and starch, embody sustainability. Sourced from renewable materials present a greener alternative to synthetic polymers. Chitosan is a natural, biodegradable, and cost-effective biopolymer. Chitosan possesses intriguing antimicrobial properties [8]. As a result, chitosan is commonly employed in antibacterial applications due to its antibacterial activities against gram-positive bacteria, gram-negative bacteria, and fungi [9]. Chitosan has piqued the interest of researchers as a nano-composite matrix due to its novel features for a variety of applications. Integrating them with metal nanoparticles, like silver, gold, copper enhances their functionalities, creating materials that are not only environmentally friendly but also biocompatible. Before the concept of germs which was first described in the eighteenth century, ancient societies made advantage of copper's antibacterial properties. Cu has the intrinsic ability to kill germs when it comes into touch with them [10-12]. In-depth research has been done on the molecular mechanisms behind copper's antibacterial effects. Additionally, researchers are demonstrating the inherent ability of copper alloy "touch surfaces" to eliminate a variety of germs that pose a concern to public health [13]. Victor Burq conducted considerable study to support his discovery that in 1852 that those who worked with copper experienced far fewer cholera mortality than anyone else. He submitted his research to the French Academies of Science and Medicine in 1867,

showing that applying copper to the skin could help prevent cholera [14]. An extensive variety of bacteria can be eliminated by copper alloy surfaces naturally. Over the past decade, numerous peer-reviewed studies have extensively examined copper's effectiveness in eradicating E. coli O157:H7, methicillin-resistant Staphylococcus aureus (MRSA), Staphylococcus, Clostridium difficile, influenza A virus, adenovirus, and fungi. The primary objective of these investigations is to safeguard public health, with a particular focus on healthcare environments serving vulnerable patient populations [15]. This field has witnessed a multitude of studies conducted in recent years.

Arun et al. examined the mechanical properties of the electrodeposited copper thin film on double zincated aluminum, specifically focusing on scratch resistance and microhardness. The size of the copper coating's crystallites was used to quantify the coating's scratch and microhardness and to correlate those values. With the decrease of crystallite size, it was discovered that both characteristic values increased. Utilizing the colony count technique, the antimicrobial efficacy of the coated sample was evaluated against Escherichia coli bacteria, and the results were compared to commercially available bulk copper. After six hours of contact with the copper-coated surface, a remarkable 94% reduction in E. coli viability was observed [17]. Liu et al. investigated the tensile strength of nanotwinned copper samples featuring various twin thicknesses. They achieved the production of a high-purity copper thin film with nanocrystalline characteristics on an aluminum touch surface through the electrodeposition process [18]. Neo et al. effectively achieved super hydrophilicity by subjecting aluminum (Al) to electrolytic plasma oxidation, followed by electroplating with copper (Cu) dots. This copper-plated and oxide-coated surface exhibited the capability to effectively eliminate E. coli ATCC 25922, methicillin-resistant Staphylococcus aureus (MRSA) ATCC 43300, and vancomycin-resistant Enterococcus faecium (VRE) ATCC 51299. The study revealed the exceptional antibacterial properties of the super hydrophilic Cu-dotted oxide coating provides an excellent technique for suppressing bacterial growth and survival on contact surfaces, lowering the danger of infection and disease spread, particularly in moist or wet conditions. [19]. Using the electrodeposition technique, a thin copper film was deposited onto aluminum that had undergone a double zincation process. The size of the crystalline structure directly influences the surface energy of the coating. Surface shape, in addition to surface energy, plays an important effect in surface wettability. The coating shape and crystallite size alter as the electrodeposition current density (j) changes [20].

By utilizing electrodeposition in a non-cyanide alkaline bath, Arun et al. successfully investigated the application of copper coating onto the aluminum surface. Before copper is got deposited, the substrate has been pre-zincated to ensure strong adherence and was confirmed by the Williamson-Hall method's strain energy calculation method. Furthermore, investigations are carried out to examine the wettability of double-distilled water concerning copper coatings electrodeposited at different current densities. The coating is more water-wettable at greater current densities because, under these circumstances, the coating's grain size is reduced, and its shape changes to a more advantageous dense nodularity [21]. They also studied the mechanism of action of copper ions on microorganisms in order to treat the E. coli ATCC 25922 culture using 99.99% pure copper thin film produced by the electrodeposition technique. Analysis has been done on the morphological alterations and the structural changes of the cell in E. coli cells. Studies using electron microscopy showed that copper-treated E. coli cells had more wrinkling and damage than untreated ones. This is because the lesions that the copper ions cause a large number of ions and amino acids to inflow and efflux [22]. This biocompatibility is paramount in medical applications, where the potential for reduced toxicity and adverse effects makes biopolymer-metal composites ideal candidates for implants, drug delivery, wound healing, and potential materials for touch surfaces. Table 1 displays the chitosan/copper composites synthesized by various methods

Table 1: Applications of chitosan/copper nanocomposites

Sl no	System	Method of preparation	Applications
1	chitosan-copper nanocomposite(CS-Cu)	Produced without the use of any outside chemical reducers.	Photocatalyst Antimicrobial agent Anticancer agent [23]
2	chitosan-based copper nanocomposite (CCNC),	Combining copper nanoparticles with chitosan.	Wound healing [24]
3	Chitosan/cuprous oxide nanocomposites	electrochemical deposition	Photocatalyst for Brilliant Red X-3B degradation [25]
4	CuO/chitosan nanospheres	straightforward wet chemical procedure	Photocatalyst for destruction of organic pollutants [26]
5	Chitosan (ChdSb)/copper oxide (CuO) nanoparticles		Photocatalyst [27]
6	Cu_2O/cross linked-chitosan nanocomposites (Cu_2O/CS NCs)	straightforward liquid phase precipitation-reduction	Photocatalyst for decolorization of dye X-3B [28]
7	Chitosan (CS) attached copper oxide (CuO)	chemical precipitation process	Photocatalyst for Methylene blue (MB) dye degradation, Antibacterial agent [29]
8	Chitosan base copper oxide (CH-CuO) nanoparticles	environmentally friendly production	Photocatalyst, Antibacterial agent [30]
10	Copper oxide nanoparticles (CS-CuO nanocomposite)	Eco-friendly production	Antibacterial agent [31]
11	Chitosan nanoparticles soluble in water that are loaded with mixed valence copper	hydrothermal approach	Antibacterial agent [32]
12	Copper nanoparticles (NpCu) with chitosan matrix	Green synthesis	Antibacterial agent [33]
13	Copper-chitosan nano composites	Metal-vapor synthesis (MVS)	Antifungal agent [34]

3. **Chitosan- Copper Nanocomposites:** Copper-based nanocomposites have harnessed their antibacterial properties to improve wound healing and infection control [35]. Animals treated with copper nanoparticles displayed a marked increase in wound contraction. The study revealed that a chitosan-based copper nanocomposite significantly facilitated cutaneous wound healing through the modulation of various cells, cytokines, and growth factors at different stages of the healing process [36]. It has been known that, adding copper to wound dressings would improve wound healing when compared to dressings without copper or commercially available wound dressings containing silver. This demonstrates the ability of copper based materials to promote wound healing and gives information on the molecular mechanisms by which copper oxide-impregnated dressings promote wound healing [37]. Due to these advantages they have been used in biological applications such as the production of drug-resistant antimicrobials and anticancer medicines [23]. To enhance the antibacterial capabilities and corrosion resistance of the substrate, the coating of chitosan-copper nanocomposite on stainless steel 316L using electrophoretic deposition was conducted by varying concentrations of Cu nanoparticles after the in-situ synthesis of Cu nanoparticles modified by chitosan. Several microorganisms were used to examine the antibacterial effects of nanocomposite coatings. Results showed that the antibacterial activity and corrosion resistance of 316L stainless steel substrates were significantly improved [25]. The first environmentally-friendly bio-inspired chitosan/copper oxide (CS-CuO) nanocomposite utilising rutin was developed and has been developed as a potential anticancer drug [38]. The assessment of the antibacterial effectiveness of chitosan/copper nanocomposites (CS/Cu-NCs) and chitosan/polyacrylic acid/copper hydrogel nanocomposites (CS/PAA/Cu-HNCs) against bacteria, fungi, and yeast revealed that CS/PAA/Cu-HNCs exhibited greater swelling capacity and copper release when compared to CS/Cu-NCs. [39].

Sun et al. prepared chitosan-copper-gallic acid nanocomposites (CS-Cu-GA NCs) using microwave-assisted techniques. Chitosan, Cu NPs, and Cu^{2+} all have built-in antibacterial capabilities that are combined in CS-Cu-GA NCs. The prepared systems promoted the wound healing infected with *S. aureus* while causing no harm to healthy tissues [40]. The eco-friendly synthesis method presented an environmentally friendly approach for producing biologically active copper oxide nanoparticles using an extract derived from Ficus carica leaves. When comparing the antibacterial efficacy of copper nanoparticles and chitosan individually, it was observed to be inferior to the antibacterial activity of the Cu-chitosan nanoparticle composite, signifying a substantial enhancement in the antibacterial properties of CuO NPs with the addition of chitosan stabilizer [41]. The coating material's effectiveness, as indicated by the degree of improvement in % RBC against both Gram-positive and Gram-negative bacteria, follows the descending order: fabric coated with CuO/chitosan nanocomposite > fabric coated with chitosan nanoparticles > uncoated fabric. The notably higher % RBC results correspond to the enhanced antibacterial activity of the treated fabric samples [42].

Miao et al. developed L-ascorbic acid-stabilized Cu-CTS nanocomposites by employing an in situ reduction method for immobilizing copper nanoparticles on the amino-enriched surface of chitosan (CTS). These copper nanoparticles had an average size of 2.6 ± 0.5 nm. The Cu-CTS nanocomposites exhibited broad-spectrum antibacterial capabilities and displayed high antimicrobial efficacy against Monilia albican and S. aureus [43].In a separate study, Umoren and team produced chitosan-copper oxide (CHT-

CuO) nanocomposites using CuSO4 .5H2O as a precursor and olive leaf extract (OLE) as a reducing agent. The antibacterial activity of the synthesized nanocomposites was assessed through cup plating and disc diffusion methods. The as-synthesized CHT-CuO nanocomposite demonstrated promising antimicrobial properties and holds potential for use as an antibacterial agent in both packaging and medical applications [44].

4. **Chitosan-Copper Nanocomposite Hydrogel:** Copper nanoparticles were prepared through a precipitation process and a pseudo-natural cationic chitosan biopolymer was employed as a stabilizing agent in the formulation of a chitosan-copper nanocomposite hydrogel. Solution casting was used to create the nanocomposite hydrogels from the produced nanoparticles in a 1:1 blend of chitosan and pluronic F127 polymer solution. Through an inhibition zone method, the created nanocomposite hydrogels were evaluated for their antibacterial efficacy. The findings demonstrated that the copper-embedded chitosan-pluronic F127 nanocomposite hydrogels may be utilized successfully for both wound care and antibacterial applications [45]. Studies on copper-chitosan nanocomposite-based chitosan hydrogels (Cu-Chit/NCs hydrogel) show that these hydrogels have antifungal activity against aflatoxigenic strains of A. flavus and that the antifungal activity of nanocomposites in vitro can be successful depending on the type of fungal strain and concentration of the nanocomposite. It was also observed that Cu-Chit/NCs hydrogel reduces the impact of G6DP isozyme without changing the activity of peroxidase isozymes [46]. By adding the Cu^{2+} ions to a hydrogel made of chitosan, Vanashi et al. created a copper-containing hydrogel (Cu/CH). For the formation of the hydroxyl radical, a catalytic mechanism was suggested. The research on reusability revealed that Cu/CH can be recycled multiple times without losing its catalytic activity. The performance of various metal ions injected into the hydrogel in the generation of hydroxyl radical was also examined [47]. Paul *et al.* concentrate on creating a topical administration system for a greenly synthesized copper oxide nanocomposite gel. In order to treat human diseases, the healthcare sector is under a lot of strain and requires unique, multifunctional materials. The most innovative materials now used in the medical field are biopolymers covered with nanocomposites. The CS-CuO nanocomposite gel that was created possesses antibacterial qualities and works well when applied topically [48].

5. **Chitosan-Copper Beads:** The possibility of chitosan – copper beads in drug delivery applications were studied by Sana *et.al.* Using sodium tripolyphosphate as the cross-linker, they created CuO nanoparticles in situ as the mechanically cross-linked chitosan hydrogel beads developed. They demonstrated effective antibacterial qualities against S. Aureus and E. Coli [49]. Copper chitosan composites represent a promising and innovative class of materials with lots of future applications. Through the synergistic combination of chitosan's biocompatibility and copper's antimicrobial properties, these composites offer unique advantages in various fields such as biomedicine, environmental remediation, and food preservation. The incorporation of copper into chitosan matrices enhances their antimicrobial efficacy, making them effective agents against a broad spectrum of pathogens. This is particularly valuable in medical applications where reducing the risk of infections is critical.

II. CONCLUSIONS

The versatile nature of copper chitosan composites allows for their adaptation into different forms, such as films, membranes, coatings, and nanoparticles, thereby enabling their use in diverse scenarios. Their biodegradability and reduced environmental impact compared to traditional antimicrobial agents also contribute to their attractiveness from a sustainability standpoint. However, challenges still remain in terms of optimizing the composite's properties, ensuring consistent performance, and addressing potential cytotoxicity concerns. Further study is required to fully comprehend the stability over the long run, release kinetics, and interactions of these composites with various environments. In the coming years, as research and development in the field of materials science progress, copper chitosan composites are likely to play a pivotal role in revolutionizing multiple industries, offering innovative solutions to address microbial contamination, infection control, and environmental preservation. Continued efforts in advancing their formulation, synthesis techniques, and application methods will unlock their full potential, leading to a safer and healthier future.

III. ACKNOWLEDGEMENT

The authors would like to acknowledge Christ College Research SEED Fund (CCRSF) (2023-2024) provided by Christ College (Autonomous), Irinjalakuda, Thrissur, Kerala, India for providing the research and funding facilities.

REFERENCES

[1] R. ed., Waser, *Nanotechnology: volume 4: information technology II*. John Wiley & Sons,2008.
[2] W.D., JrCallister,. *Materials science and engineering an introduction*,2007.
[3] C.C. Okpala, Nanocomposites–an overview. *International Journal of Engineering Research and Development*, *8*(11), pp.17-23, 2013.
[4] B.Briell, Nanoclays-counting on consistency. *Southern Clay Products, Inc*.,2000.
[5] C.C.Okpala, The benefits and applications of nanocomposites. *Int. J. Adv. Eng. Tech*, *12*, p.18.,2014
[6] I. ed.Manas-Zloczower, *Mixing and compounding of polymers: theory and practice*. Carl Hanser Verlag GmbH Co KG.,2012.
[7] T.V. Kosmidou, A.S.Vatalis, C.G.Delides, E. Logakis, P. Pissis, and G.C. Papanicolaou, Structural, mechanical and electrical characterization of epoxy-amine/carbon black nanocomposites. *Express Polymer Letters*, *2*(5), pp.364-372,2008.
[8] K.Wang, S. Pan, Z. Qi, P. Xia, H. Xu, W. Kong, H. Li, P. Xue, X. Yang, and C. Fu, Recent advances in chitosan-based metal nanocomposites for wound healing applications. *Advances in materials science and engineering*, *2020*, pp.1-13, 2020.
[9] [9]A. Mohandas, S. Deepthi, R. Biswas, and R.Jayakumar, Chitosan based metallic nanocomposite scaffolds as antimicrobial wound dressings. *Bioactive materials*, *3*(3), pp.267-277, 2018.
[10] D. HHA, Historic uses of copper compounds in medicine. *Trace Elements Med*, *2*, pp.80-87, 2001.
[11] G. Borkow, and J. Gabbay, Copper, an ancient remedy returning to fight microbial, fungal and viral infections. *Current Chemical Biology*, *3*(3), pp.272-278, 2009.
[12] S.S. Siwal, Q.Zhang, A.K. Saini, and V.KThakur,Antimicrobial materials: new strategies to tackle various pandemics. *Journal of Renewable Materials*, *8*(12), pp.1543-1563, 2020
[13] W.H. English, Copper, 29 Cu. *History*, *7440*, pp.50-8.
[14] S. Love, Copper Destroys Viruses and Bacteria. Why Isn't It Everywhere. *VICE, March*, *18*, 2020
[15] Z.A. Avakian, and I.L.Rabotnova,On determination of copper concentrations toxic to microorganisms. *Mikrobiologiia*, *35*(5), pp.805-811, 1966.
[16] Z.A. Avakian, and I.L.Rabotnova, On determination of copper concentrations toxic to microorganisms. *Mikrobiologiia*, *35*(5), pp.805-811, 1966.

[17] A.Augustin, P.Huilgol, K.R. Udupa, and U.Bhat,Effect of current density during electrodeposition on microstructure and hardness of textured Cu coating in the application of antimicrobial Al touch surface. *Journal of the mechanical behavior of Biomedical materials*, *63*, pp.352-360., 2016.

[18] L. Lu, X. Chen, X. Huang, &K. Lu, Revealing the maximum strength in nanotwinned copper. *Science*, *323*(5914), 607-610, (2009).

[19] Y.Nie, C. Kalapos, X. Nie, M. Murphy, R. Hussein, and J.Zhang, Superhydrophilicity and antibacterial property of a Cu-dotted oxide coating surface. *Annals of Clinical Microbiology and Antimicrobials*, *9*(1), pp.1-10, 2010.

[20] A. Augustin, K.U.Bhat, K.R. Udupa, and A.C.Hegde, October. Electron microscopic study of nodules formed during electrodeposition of copper on aluminium. In *Materials Science Forum* (Vol. 830, pp. 371-374). Trans Tech Publications Ltd., 2015.

[21] A. Augustin, K.R. Udupa, and K.U.Bhat, Effect of coating current density on the wettability of electrodeposited copper thin film on aluminum substrate. *Perspectives in Science*, *8*, pp.472-474, 2016.

[22] A. Augustin, H. Thaira, K. Udaya Bhat, and K.R.Udupa, Effect of Electrodeposited Copper Thin Film on the Morphology and Cell Death of E. Coli; an Electron Microscopic Study. *Biotechnology and Biochemical Engineering: Select Proceedings of ICACE 2015*, pp.227-232, 2016.

[23] N. Arjunan, C.M. Singaravelu, J. Kulanthaivel, and J.Kandasamy, A potential photocatalytic, antimicrobial and anticancer activity of chitosan-copper nanocomposite. *International journal of biological macromolecules*, *104*, pp.1774-1782, 2017

[24] A. Gopal, V.Kant, A.Gopalakrishnan, S.K. Tandan, and D. Kumar, Chitosan-based copper nanocomposite accelerates healing in excision wound model in rats. *European journal of pharmacology*, *731*, pp.8-19, 2014.

[25] E.S.H.R. Tabesh, H.R.Salimijazi, M. Kharaziha, M. Mahmoudi, and M.Hejazi, Development of an in-situ chitosan-copper nanoparticle coating by electrophoretic deposition. *Surface and Coatings Technology*, *364*, pp.239-247, 2019.

[26] J.Y. Chen, P.J. Zhou, J.L.Li, and Y. Wang, Studies on the photocatalytic performance of cuprous oxide/chitosan nanocomposites activated by visible light. *Carbohydrate Polymers*, *72*(1), pp.128-132, 2008.

[27] V.S. Narayanan, P.V. Prasath, K. Ravichandran, D. Easwaramoorthy, Z.Shahnavaz, F. Mohammad, H.A.Al-Lohedan, S. Paiman, W.C. Oh, and S.Sagadevan, Schiff-base derived chitosan impregnated copper oxide nanoparticles: An effective photocatalyst in direct sunlight. *Materials Science in Semiconductor Processing*, *119*, p.105238, 2020.

[28] C.Cao, L.Xiao, L. Liu, H. Zhu, C. Chen, and L. Gao, Visible-light photocatalytic decolorization of reactive brilliant red X-3B on Cu_2O/crosslinked-chitosan nanocomposites prepared via one step process. *Applied Surface Science*, *271*, pp.105-112, 2013.

[29] Y. Haldorai, and J.J.Shim, Multifunctional chitosan-copper oxide hybrid material: photocatalytic and antibacterial activities. *International Journal of Photoenergy*, *2013*

[30] M.H. Sarfraz, S. Muzammil, S.Hayat, M. Khurshid, and A.H. Sayyid, Fabrication of chitosan and Trianthemaportulacastrum mediated copper oxide nanoparticles: Antimicrobial potential against MDR bacteria and biological efficacy for antioxidant, antidiabetic and photocatalytic activities. *International Journal of Biological Macromolecules*, *242*, p.124954, 2023.

[31] S. Sathiyavimal, S. Vasantharaj, T. Kaliannan, and A. Pugazhendhi, Eco-biocompatibility of chitosan coated biosynthesized copper oxide nanocomposite for enhanced industrial (Azo) dye removal from aqueous solution and antibacterial properties. *Carbohydrate polymers*, *241*, p.116243, 2020.

[32] S. Basumallick, P.Rajasekaran, L. Tetard, and S. Santra, Hydrothermally derived water-dispersible mixed valence copper-chitosan nanocomposite as exceptionally potent antimicrobial agent. *Journal of nanoparticle research*, *16*, pp.1-11, 2014.

[33] D.A. Marin-Silva, N.Romano, L.Damonte, L. Giannuzzi, and A. Pinotti, Hybrid materials based on chitosan functionalized with green synthesized copper nanoparticles: Physico-chemical and antimicrobial analysis. *International Journal of Biological Macromolecules*, *242*, p.124898, 2023.

[34] M.S. Rubina, A.Y.Vasil'kov, A.V.Naumkin, E.V.Shtykova, S.S.Abramchuk, M.A. Alghuthaymi, and K.A. Abd-Elsalam, Synthesis and characterization of chitosan–copper nanocomposites and their fungicidal activity against two sclerotia-forming plant pathogenic fungi. *Journal of Nanostructure in Chemistry*, *7*, pp.249-258, 2017.

[35] M. Shi, H.S. Kwon, Z. Peng, A. Elder, and H.Yang, Effects of surface chemistry on the generation of reactive oxygen species by copper nanoparticles. *ACS nano*, *6*(3), pp.2157-2164, 2012.

[36] A. Gopal, V. Kant, A. Gopalakrishnan, S.K. Tandan, and D.Kumar, Chitosan-based copper nanocomposite accelerates healing in excision wound model in rats. *European journal of pharmacology*, *731*, pp.8-19, 2014.
[37] G. Borkow, J.Gabbay, R. Dardik, A.I.Eidelman, Y.Lavie, Y.Grunfeld, S. Ikher, M. Huszar, R.C. Zatcoff, and M.Marikovsky, Molecular mechanisms of enhanced wound healing by copper oxide- impregnated dressings. *Wound repair and regeneration*, *18*(2), pp.266-275, 2010.
[38] D. Bharathi, R.Ranjithkumar, B. Chandarshekar, and V.Bhuvaneshwari, Bio-inspired synthesis of chitosan/copper oxide nanocomposite using rutin and their anti-proliferative activity in human lung cancer cells. *International Journal of Biological Macromolecules*, *141*, pp.476-483, 2019.
[39] M.E. Abd El-Aziz, S.M.M. Morsi, D.M. Salama, M.S.Abdel-Aziz, M.S. Abd Elwahed, E.A.Shaaban, and A.M. Youssef, Preparation and characterization of chitosan/polyacrylic acid/copper nanocomposites and their impact on onion production. *International journal of biological macromolecules*, *123*, pp.856-865, 2019.
[40] X. Sun, M. Dong, Z. Guo, H. Zhang, J. Wang, P. Jia, T.Bu, Y.Liu, LLi,. and L. Wang, Multifunctional chitosan-copper-gallic acid based antibacterial nanocomposite wound dressing. *International Journal of Biological Macromolecules*, *167*, pp.10-22, 2021.
[41] S.M.Syame, W.S.Mohamed, R.K. Mahmoud, and S.T. Omara,Synthesis of copper-chitosan nanocomposites and their applications in treatment of local pathogenic isolates bacteria. *Orient J Chem*, *33*(6), pp.2959-2969, 2017.
[42] M. Gouda, and A.Hebeish, Preparation and evaluation of CuO/chitosan nanocomposite for antibacterial finishing cotton fabric. *Journal of Industrial Textiles*, *39*(3), pp.203-214, 2010.
[43] [43] M. He, L. Lu, J. Zhang, and D.Li, Facile preparation of L-ascorbic acid-stabilized copper-chitosan nanocomposites with high stability and antimicrobial properties. *Science Bulletin*, *60*(2), pp.227-234, 2015.
[44] P.S.Umoren, D. Kavaz, A.Nzila, S.S. Sankaran, and S.A.Umoren, Biogenic synthesis and characterization of chitosan-cuo nanocomposite and evaluation of antibacterial activity against gram-positive and-negative bacteria. *Polymers*, *14*(9), p.1832, 2022.
[45] T.Jayaramudu, K. Varaprasad, K.K. Reddy, R.D.Pyarasani, A. Akbari-Fakhrabadi, and J. Amalraj, Chitosan-pluronic based Cu nanocomposite hydrogels for prototype antimicrobial applications. *International journal of biological macromolecules*, *143*, pp.825-832, 2020.
[46] K.A. Abd-Elsalam, M.A.Alghuthaymi, A.Shami, M.S.Rubina, S.S.Abramchuk, E.V. Shtykova, and A.Yu. Vasil'kov, Copper-chitosan nanocomposite hydrogels against aflatoxigenic Aspergillus flavus from dairy cattle feed. *Journal of Fungi*, *6*(3), p.112, 2020.
[47] A.K. Vanashi, and H. Ghasemzadeh, Copper (II) containing chitosan hydrogel as a heterogeneous Fenton-like catalyst for production of hydroxyl radical: A quantitative study. *International Journal of Biological Macromolecules*, *199*, pp.348-357, 2022.
[48] S.Paul, D. MK, and S.Peter, Development of green synthesized chitosan-coated copper oxide Nanocomposite gel for topical delivery. *Journal of Pharmaceutical Innovation*, pp.1-10, 2022.
[49] S. Farhoudian, M. Yadollahi, and H. Namazi, Facile synthesis of antibacterial chitosan/CuO bio-nanocomposite hydrogel beads. *International journal of biological macromolecules, 82,* pp.837-843, 2016.