

Copper oxide/biopolymer nanocomposites: synthesis and applications, a comprehensive review

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Received: 25 May 2024; Accepted for publication: 30 August 2024

Abstract. Copper oxide (CuO) particles have a significant role in various fields due to their many properties like special shape, size, and high surface area. Thanks to their rarity and unique characteristics, such as their large surface area, paramagnetic nature, and ease of separation, CuO nanoparticles (NPs) have received the greatest attention. Chitosan, guar gum, tamarind, alginate, starch, cellulose, polysaccharide, etc. are examples of natural biopolymers that have proven to be excellent hosts for creating CuO nanoparticles. Long-established fabrication techniques for biopolymer-based CuO nanocomposites include co-precipitations, green synthesis, solvent casting method, Alco thermal method, and sol-gel method. Excellent biological characteristics of biopolymer/CuO nanocomposites include their potent antibacterial activity against a variety of diseases as well as bacteria that are resistant to antibiotics. These characteristics have sparked the creation of numerous strategies with direct biological applications, including customized surfaces with antimicrobial effects, wound dressings, and modified textiles. This study aims to provide a comprehensive overview of the very first biopolymer CuO NPs reported within the last ten years as well as its appealing methodology in diverse applications.

Keywords: copper oxide nanocomposites, biopolymers, carboxymethyl tamarind kernel gum, green synthesis.

Classification numbers: 2.9.3, 2.9.4, 2.7.2.

1. INTRODUCTION

Different types of microorganisms that microbially pollute the air, water, and soil cause problems for the living environment and are severe problems in the field of health care. Interesting alternative microbial agents, such as tiny antibiotics, cationic polymers, metal NPs, and antimicrobial peptides, have emerged due to the growth of antibiotic-resistant diseases [1]. CuO is a p-type, narrow bandgap transistor that belongs to the transition metal oxide group. It has a crystalline nature and numerous unique properties: Super thermal resistance, luminous characteristics, and great stability are all features of this material as well as antibacterial properties. CuO is widely employed in a variety of technical domains because of its unique features, including electro catalyst, biosensor, high efficiency, heat conductive materials, magnetic recording media with high selectivity, and photovoltaic applications [2]. When

compared to organic antimicrobial agents, the CuO NPs are more stable, stronger, and have a longer shelf life [3]. The discovery of new antimicrobial drugs has been triggered by the well-known concern of harmful bacteria becoming resistant to the multidrug population. In this regard, nano-Ag has undergone extensive research and is presently used in a variety of consumer and medical applications [4]. The CuO is more affordable than silver, simple to bind with polymer, and has generally stable physical and chemical characteristics due to its ability to be generated with exceptionally high surface areas and unique crystal morphologies. Highly nanoparticulate metal oxide such as CuO may be particularly useful antibacterial agents [5]. The potential application of CuO NPs in the medical field such as therapy for cancer [6], targeted drug carrier [7], wound dressing [8], and antibacterial activity [9] has recently attracted a lot of interest.

Biopolymers are naturally plentiful and environmentally acceptable polymer alternatives that are employed in medical, agriculture, environmental, and medical industries due to their particularly renewable, nontoxic, and sustainable features as compared to hydrocarbon polymer [10, 11]. In the last few years, researchers have been interested in biopolymer/CuO nanocomposite research areas such as guar gum, tamarind gum, starch, cellulose, alginate, pectin, polysaccharide, chitosan dextran, polyacrylic acid (PAA), gelatin, etc. [11 - 21].

The biopolymer/CuO nanocomposite has been created utilizing a variety of techniques including the solution casting method [22], thermal method [23], co-precipitation method [24], sol-gel method [25], microwave irradiation method [26], also green synthesis [27] and one-pot synthesis [28]. Natural biopolymer is mixed into NPs to enhance their application in areas like adsorbent activity [29], antifungal activity [30], anti-cancer activity [31], antioxidant activity [32], drug delivery carrier [33], and antibacterial activity [110].

This review is based on the preparation of CuO nanocomposite with different biopolymers such as chitosan, guar - gum, carboxymethyl cellulose, alginate, graphene oxide, carboxymethyl starch, etc. by traditional methods and their applications in various fields.

Table 1. Literature data of biopolymers/CuO nanocomposites.

Biopolymer	NP	Method	Size	Applications	Reference
Chitosan	CuO	Precipitation method	20 - 100 nm	Cytotoxic, antibacterial and antioxidant activity	[34]
Chitosan	CuO	Sodium tripolyphosphate as a cross linker	10 - 25 nm	Antibacterial activity	[35]
Chitosan	CuO	Co-precipitation method	35 - 40 nm	Drug delivery	[24]
Chitosan	CuO	Facile synthesis	40 nm	Antibacterial activity	[35]
Chitosan	CuO	Green synthesis	51 - 62 nm	Antibacterial activity	[27]
Alginate	CuO	Tugachi method	--	Antibacterial activity	[36]
Guar Gum	CuO	Sol-gel method	20 - 50 nm	Organic pollutant removal	[25]
Cellulose	CuO	<i>In situ</i> method	50 - 100 nm	Food packaging	[37]
Cellulose	CuO	Green synthesis	300 nm	--	[26]
Cellulose	CuO	<i>In situ</i> method	50 - 200 nm	Antibacterial activity	[38]

Starch	CuO	Solution casting method	30 - 50 nm	Antibacterial, antioxidants and wound healing activity	[32]
Starch	CuO	<i>In situ</i> method	30 - 40 nm	Antibacterial and colon-specific naproxen delivery	[39]
Starch and Polyurethane	CuO	Thermal degradation method	50 - 200 nm	Antibacterial activity	[40]
Starch	CuO	Solution casting method	--	Humidity sensor	[22]
Starch	CuO+ZnO	Solution casing method	--	Food-packaging applications	[41]
Carboxymethyl cellulose	CuO	<i>In situ</i> method	40 - 75 nm	Antibacterial activity	[28]
Graphene Oxide	CuO	Hydrothermal method	25 nm	Biosensors	[42]
PVA	CuO	Solution casting method	80 - 120 nm	Electric application	[43]
Dextran	CuO	Green synthesis	12 nm	--	[44]

Table 1 shows different biopolymers such as chitosan, alginate, guar gum, starch, dextran, carboxymethyl cellulose, etc. that have been mixed with CuO NPs using diverse synthetic techniques. Advanced techniques such as green synthesis, *in situ*, co-precipitation, microwave-assisted, aerothermal, solution casting, and thermal degradation methods have been used to develop the form and size of biopolymer/CuO-based nanocomposites. In this article, we go through the various synthetic approaches that can be utilized to create biopolymer/CuO using a variety of methods. Some synthetic methods of biopolymer/CuO nanocomposite are discussed in detail below.

The biopolymer/CuO nanocomposite exhibits significant quality due to its enhanced properties. Figure 1 demonstrates the thermal stability and mechanical strength of this composite material indicating its potential use in various industrial applications.

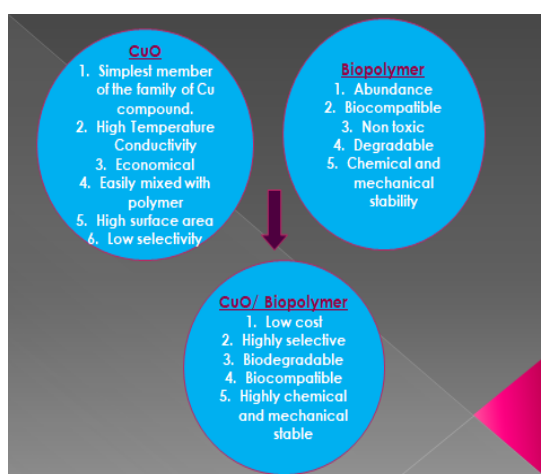
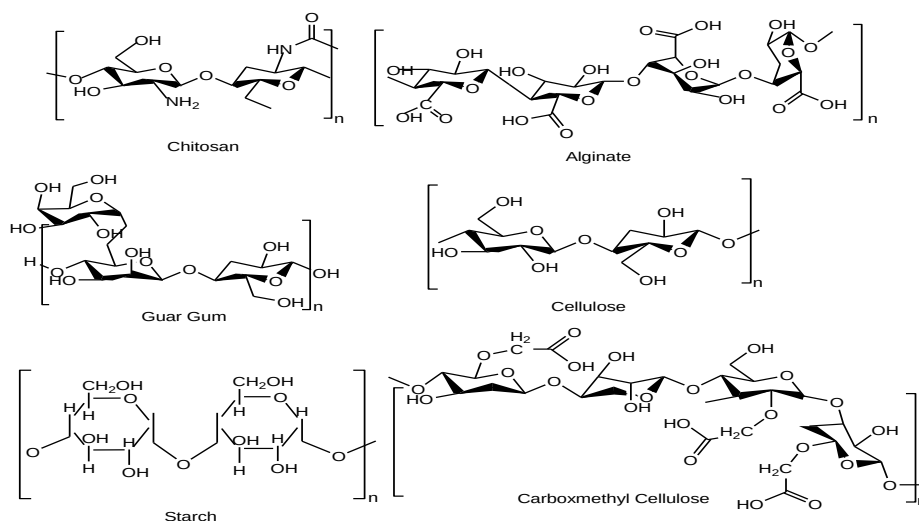


Figure 1. Properties of copper oxide/biopolymer nanocomposites.

The biopolymer structure used in this review is detailed in Scheme 1. This schematic representation helps to understand the molecular configuration and functional groups available for interaction.



Scheme 1. Structure of biopolymers used in this literature review.

2. SYNTHESIS OF BIOPOLYMERS/CuO NANOCOMPOSITES

For the production and stability of biopolymers/CuO composites, researchers have used friendly, non-toxic synthetic materials.

Figure 2 shows some common methods for the synthesis of biopolymer/CuO nanocomposites including *in-situ*, co-precipitation, sonochemical method, etc.

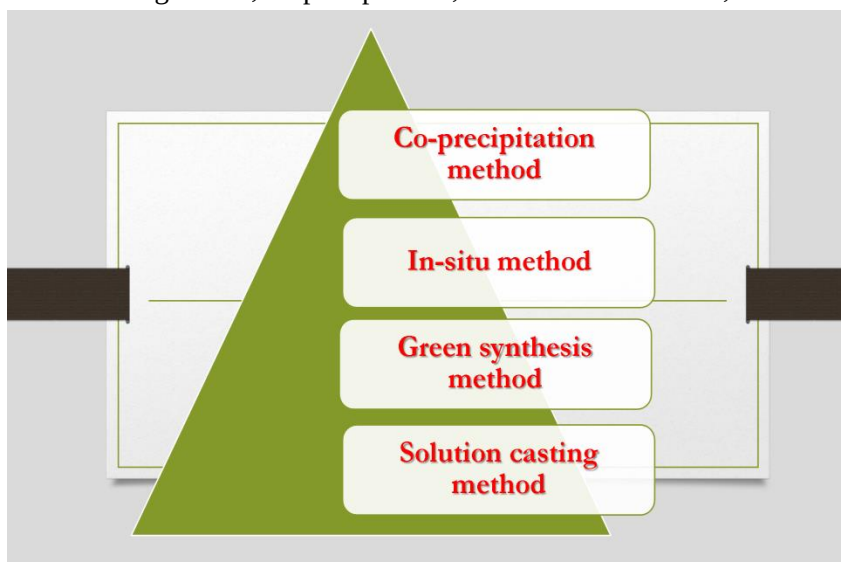


Figure 2. Some common methods for the synthesis of biopolymer/CuO nanocomposites.

2.1. Co-precipitation method

Co-precipitation is a very useful method for synthesizing biopolymer/CuO nanocomposites [102]. Copper acetate monohydrate (0.2 M, 600 mL) and sodium hydroxide (6 M, 30 mL) solutions were prepared separately in distilled water for the synthesis of CuO nanoparticles. At 100 °C with constant stirring, glacial acetic acid (2 mL) was dissolved in copper acetate monohydrate solution. At 100 °C, sodium hydroxide solution was then gradually added to the previously created solution in a dropwise fashion until a clear black colour was obtained. The precipitate was gathered, washed three times with ethanol and distilled water, dried in an oven at 100 °C, then ground into a fine powder. CuO NPs were obtained by calcining the powder at 500 °C for 4 hours. NPs of different sizes have been prepared with a notable speed employing organic compounds as stabilizing and reducing agents. These organic compounds include polyvinyl alcohol (PVA), polyethylene glycol, and citric acid which effectively control the growth and prevent agglomeration of NPs. Other biopolymers that have stabilized CuO NPs include chitosan, starch, guar gum, alginate, etc. demonstrating the versatility and effectiveness of these organic compounds in nanoparticle synthesis [1, 34, 45].

2.2. Green synthesis method

The green synthesis method is an economical, environmentally beneficial, and energy-efficient way to create nanoparticles. The term green synthesis of nanomaterials refers to the formation of NPs using natural sources such as microorganisms, plant residue, crop residue, etc. Researchers are looking at using microbes, plant extracts, and other biomaterials as synthesis processes for metal NPs since there is an increasing demand to create "green" and cost-effective processes. The probability of pollutants is significantly reduced when natural bioactive substances are used to create metal nanoparticles. Different sizes of NPs were obtained when different biopolymers were mixed with CuO. Sysame *et al.* [27] prepared CuO/chitosan with an average size of 51 - 62 nm by green synthesis method. Crystals of CuO/biopolymers of different sizes and forms can be produced depending on the process parameters and the materials utilized [46 - 47].

2.3. *in situ* method

The enormous variety of functionalized biopolymers currently available and the various categories of NPs that may be created have combined to enhance the number of biopolymers that can now be made. Functional polymers, origins, interactions, the reaction that creates nanoparticles, and the structure of CuO NPs are the variables that influence how biopolymers behave. Biopolymers operate as a nonreactor in the process and offer a constrained intermediate for the synthesis of nanocomposite. They also isolate and stabilize the generated NPs to prevent their accumulation. Numerous biopolymer and CuO NPs have been synthesized and stabilized using *in situ* techniques such as the usage of chitosan, starch, and sodium tripolyphosphate as cross-linking agents [37, 39, 48].

2.4 Solution casting method

The most common process for creating composites remains solution casting, especially in small-scale lab settings. In the solvent casting method, prepolymer and polymer are combined and dissolved in an appropriate solution. The NPs dispersed in the same solution or a separate solution, but the polymer, which was the matrix phase, is completely soluble in the solution. NPs of variable size have been synthesized using different polymers. Starch-based CuO (20 - 30 nm),

and carboxymethyl CuO (30 - 50 nm) sized NPs were obtained using solution casting method [32, 41].

3. COPPER OXIDE/BIOPOLYMER NANOCOMPOSITE APPLICATIONS

Generally, CuO is used in the medical field due to its antimicrobial, antifungal, and anticancer activity. Because of their remarkable chemical, physical and biological properties, biopolymer-based CuO NPs have been extensively applied in several technical fields instead of other ions. On combining CuO nanoparticles with biopolymer, biopolymer/CuO composite offers a distinct advantage over simple CuO nanoparticles. These polymer matrices not only enhance the dispersion of CuO nanoparticles but also contribute to their biocompatibility and biodegradability which makes the composite suitable for biomedical applications such as drug delivery systems and biosensors where control of release and toxicity is crucial. Many biopolymers such as chitosan/CuO, starch/CuO, alginate/CuO, etc. are widely used in various applications such as antibacterial agents [103], antimicrobial agents [104 - 105], food packaging [106], metal removal from wastewater [107], etc. Figure 3 differentiates the applications of biopolymer/CuO nanocomposites.



Figure 3. Various applications of copper oxide/biopolymer nanocomposites.

3.1. Applications of biopolymer/CuO nanocomposite to remove heavy metals from wastewater

Human depends on water resources for their health, cleanliness, food, energy, and economies among other necessities. Water resources are also essential for the survival and existence of the human population. Chemicals, detergents, fertilizers, pesticides, heavy metals, textile dyes, etc. are constantly released into the environment, contaminating the water. The popularity of biopolymer-based composites has increased, and they offer numerous benefits over conventional adsorbents due to their affordability, environmental-friendliness, and ease of availability [49 - 52]. Generally, for the adsorption and removal of metals, a large number of biopolymers such as chitosan, alginate, cellulose, etc. play a significant role [53, 57, 61]. Table 2 shows the removal of metals by different biopolymers/CuO nanocomposites with different adsorption capacities.

Table 2. Literature data on removing metal from wastewater by biopolymer/CuO nanocomposites.

Biopolymer/CuO	Removing metal	Maximum adsorption capacity (Q _{max}) mg/g	Reference
Chitosan/PVA/CuO	Pb (II)	6.8 mg/g	[53]
Hydroxyethyl cellulose/CuO	Cr (VI)	--	[54]
Chitosan/Cu(OH) ₂	As (V)	39.0 mg/g	[55]
Chitosan /Cu(OH) ₂	Cr (VI)	1.42 m mol/g	[56]
Hydroxyethyl cellulose/CuO	Pb (II)	--	[54]
Chitosan/CuO	As (V)	28.1 mg/g	[55]
Chitosan/CuO	Cr (VI)	2.62 mg/g	[54]
Alginate/CuO	Pb (II)	118.40 mg/g	[57]
Calcium alginate/CuO	Cr (VI)	--	[58]
Sodium alginate/CuO	Zr (IV)	28.73 mg/g	[59]
Sodium alginate/CuO	Co (II)	3.70 mg/g	[59]
Sodium alginate/CuO	Pb (II)	55.24 mg/g	[59]
Sodium alginate/CuO	U (VI)	24.44 mg/g	[59]
FeOOH/Water bamboo cellulose (WBC)/CuO	As (III)	76.1 mg/g	[60]
Cellulose/CuO	Pb (II)	150.14 mg/g	[61]

Chitosan-based CuO and Cu(OH)₂ sorbents were prepared by co-precipitation method in an alkaline solution of copper chloride (CuCl₂). The alkalization regulates the kind of CuO deposited in the polymer particle framework. These sorbents were effective for the adsorption of As(V). The effective adsorption of As(V) was calculated at equilibrium at pH around 6. Anions and the anionic charge of the sorbents are involved in the sorption mechanism, which is related to an anion transfer mechanism (which is confirmed by pH_{pzc} of the chitosan-based CuO biocomposite). At 20 °C and an equilibrium pH between 5 and 6, the highest capacities for chitosan/Cu(OH)₂ and chitosan/CuO were obtained at 39.0 and 28.1 mg g⁻¹, respectively. The process of sorption was endothermic [55]. An easy and efficient approach for the creation of a highly porous adsorbent is to encapsulate CuO NPs in the sodium alginate matrix and then perform high-temperature thermal oxidation. The conclusion of the experiment shows that nanostructured CuO granules may be utilized for water and wastewater treatment because they are a powerful adsorbent for the removal of Pb(II), Zr(IV), U(VI), and Co(II) from aqueous solutions [59]. The synthetic FeOOH/CuO @WBC exhibited strong As(III) removal capabilities, and the highest adsorption capacity was achieved when the pH was raised to 3.5 at room temperature. The utility of the materials in the experimental application is improved by the renewability of FeOOH/CuO @WBC for the adsorption of As(III) and the percentage removal can still be as high as 50 % after the recycling [60].

3.2. Biopolymer/CuO nanocomposites for organic impurities/dye removal

In today's material removal industries and technologies, organic impurities and dyes have received substantial consideration and utilization. As a result of the development of robust, poisonous, cancer-causing, non-biodegradable, and mutagenic species, they contribute to several environmental issues. Because of their complicated aromatic structures, organic dyes are highly stable and can appear cationic, anionic, or non-ionic. Recently, developed economical, non-

toxic, cost-effective, and productive tiny materials have attracted interest in many scientific fields including water treatment. Pollutants in wastewater can be removed very effectively using adsorbent-based nano-scale materials. Due to their special properties such as increased adsorption efficiency, biocompatibility, cost-effectiveness and promising outcomes in wastewater treatment, eco-friendly polymeric materials have been developed quickly for various applications [62 - 65].

Table 3 displays the applications of CuO-incorporated biopolymer nanocomposite with maximum adsorption capacity ($Q_{\max}$) in mg g^{-1} .

Table 3. Applications of biopolymer/CuO nanocomposites for organic impurity removal.

Biopolymer/ Metal	Organic impurity/dye removal	Maximum adsorption capacity ($Q_{\max}$) mg g^{-1}	Reference
Chitosan/carboxymethyl cellulose/CuO	Methyl orange dye	--	[64]
Carboxymethyl cellulose/guar gum/CuO	Malachite green	18.5 mg/g	[29]
Chitosan/CMC/CuO	Eosin yellowish dye	--	[64]
Chitosan/CuO	Congo red	119.70 mg/g	[66]
Chitosan/CuO	Erichrome black t	235.70 mg/g	[66]
Chitosan/PVA/CuO	Acid blue 25	171.4 mg/g	[67]
Chitosan/CuO	Indigo carmine	--	[68]
Chitosan/CuO	Congo red	--	[68]
Chitosan/CuO	Methyl orange	--	[68]
Poly AMPA/chitosan/CuO	Doxycycline	203.94 mg/g	[69]
Alginate/ Fe_3O_4 /CuO	Oxytetracycline	--	[70]
CMC/ NiO_2 /CuO	Eosin yellowish	--	[71]
Cellulose/CuO	4- Nitro phenol	--	[72]

CMC - Carboxy methylcellulose; PVA - Polyvinyl alcohol; Poly AMPA - Poly(2-acrylamide-2-methyl-1-propane sulfonic acid).

For the effective removal of acid blue 25 (AB 25) from the aqueous system an easy, economical, and safe chitosan-PVA@CuO composite was created. In the synthesized chitosan-PVA@CuO composite, the CuO nanocomposite was significantly dispersed throughout the organic matrix. With a high adsorption capacity of 171.4 mg/g , the chitosan-PVA@CuO has proven to be a successful adsorbent for the quick removal of AB 25. The elimination capacity of the chitosan-PVA@CuO composite also shows a significant temperature-dependent and spontaneous rise, according to the thermodynamic constants ΔG° , ΔH° , and ΔS° [67]. CuO@poly(AMPA)/chitosan, a novel adsorbent, was created to remove doxycycline (DXN) from an aqueous solution. The optimal conditions (at 203 K) for DXN removal utilizing CuO@poly(AMPA)/chitosan were evaluated via response surface methodology (RSM). The maximum removal efficiency and maximum adsorption capacity for DXN were determined to be 98.89 % and 203.94 gm/g , respectively. The kinetic and isotherm studies showed that the adsorption of DXN from aqueous solution was best characterized by the pseudo-second-order kinetic model with $R^2 > 0.9875$ and the Langmuir adsorption isotherm model with $R^2 > 0.99$ [69]. Alginate beads often contain Ba^{2+} or Ca^{2+} ions as cross-linkers to provide structural

stability. Over repeated use, these cross-linking ions can be released into the solution, leading to an increase in the pore size within the alginate matrix. After employing the alginate beads multiple times and releasing Ba^{2+} into the solution, CuO-Fe₃O₄-Fe⁰/alginate reactivity was improved. The addition of Fe⁰ to the alginate, which was then coated with CuO-Fe₃O₄, improved the cycling performance. After the third recycling, the deterioration efficiency reached nearly 100 %. The efficiency of the degrading process was significantly increased by the use of photo-fenton [70].

3.3. Antibacterial, antioxidant, and anticancer applications of biopolymer/CuO nanocomposites

Public health worldwide is seriously threatened by the spread of infectious illnesses in general, particularly by the rise of bacterial strains that are resistant to antibiotics. In general, it is believed that both Gram-positive and Gram-negative bacterial strains pose a serious threat to public health [73]. It is commonly known that copper is very cytotoxic to bacteria (*P. aeruginosa*, *E.coli*, and *S. aureus*) making it a useful antibacterial agent that can be utilized in water treatment and food packaging [27]. CuO shows great antibacterial and antimicrobial properties against both gram-negative and gram-positive bacterial strains. When CuO NPs were incorporated with a biopolymer matrix, both their antibacterial and antimicrobial activities against gram-negative and gram-positive bacteria were enhanced.

Table 4 shows the antibacterial and antimicrobial applications of CuO incorporated with different biopolymers.

Table 4. Antibacterial, antimicrobial, and anti-cancerous applications of biopolymer/CuO nanocomposites.

Biopolymer/metal	Function of activity	Reference
Chitosan/carboxy methyl/CuO	Antibacterial activity against <i>S. aureus</i> and <i>E. coli</i>	[74]
Chitosan/CuO	Antibacterial activity against Gram-positive: (i) <i>streptococcus pneumonia</i> (ii) <i>staphylococcus epidermidis</i> Gram-negative: (i) <i>E. coli</i> (ii) <i>proteus mirabilis</i>	[75]
Alginate/CuO	Antibacterial activity against (i) <i>pseudomonas auriginosa</i> (ii) <i>staphylococcus aureus</i> (iii) <i>streptococcus pyogenes</i> (iv) <i>staphylococcus epidermidis</i>	[76]
Polyethyleneterephthalate/alginate/CuO	Antibacterial activity against Gram-positive: (i) <i>S. aureus</i> (ii) <i>C. albicans</i> Gram-negative: <i>E. coli</i>	[77]
Starch/CuO	Antibacterial activity against (i) <i>Bacillus aureus</i> (ii) <i>Shigella sonnei</i> (iii) <i>Straptophylococcus epidermidis</i> (iv) <i>Enterococcus</i> (v) <i>pseudomonas aeruginosa</i> POA ₁ (vi) <i>E. coli</i>	[78]

Polyurethane/starch/CuO	Antibacterial activity against <i>S. aureus</i>	[79]
Cellulose/CuO	Antibacterial activity against Gram-positive: <i>pneumonia</i> Gram-negative: <i>pseudomonas</i>	[80]
Cellulose/graphene oxide/CuO	Antibacterial activity against	[81]
Peroxidase/CuO	Antibacterial activity against <i>E. coli</i>	[82]
Gum acacia/Ni/CuO	Antibacterial activity (i) <i>Enterobacter</i> (ii) <i>Klebsiella</i> (iii) <i>pneumonia</i> (iv) <i>pseudomonas aeruginosa</i> (v) <i>staphylococcus aureus</i>	[83]
Polyvinyl alcohol/gelatin/CuO	Antimicrobial activity	[84]
Chitosan/CuO	Antibacterial activity Gram-positive i) <i>S.aureus</i> ii) <i>S. pyogenes</i> Gram-negative i) <i>E.coli</i> ii) <i>K.aerogenes</i> anti-cancerous activity against human breast cancer (MCF-7) cell line	[34]
Starch/CuO	Anti-cancerous activity against MCF-7 cells	[78]

Using the colony farming unit (CFU) technique, the in-vitro antibacterial properties of both carboxymethyl chitosan/CuO nanocomposite biopolymers and pure carboxymethyl chitosan biopolymers against gram-negative and gram-positive *E. coli* and *S. aureus* were investigated, respectively. Pure carboxymethyl chitosan biopolymer showed poor antibacterial effect against both types of bacteria, while good antibacterial activity was demonstrated by biopolymer incorporating CuO nanoparticles [74]. Chitosan is not as thermally stable as chitosan-CuO-neem seed (NS) nanocomposite. The chitosan-CuO-NS showed cytotoxicity against the MCF-7 cell line and good antibacterial activity against gram-negative and gram-positive bacterial pathogens. It also showed antioxidant activity utilizing DPPH and 2,2-azino-bis-3ethylbenzothiazoline-6-sulphonic acid (ABTS) radical scavenging tests [34].

3.4. Biomedical applications of biopolymer/CuO nanocomposites

Due to their useful applications, nanomaterials have recently received significant attention in the field of biomedicine. Nanoparticle production has important applications in the medical field, including cell imaging, drug delivery, and antibacterial and biosensing [7]. Drugs can be targeted to specific cells fixed to specially designed carriers. Nanoparticles, whose structures are less than 100 nm in one dimension, have recently demonstrated a significant capability as drug carriers. The NPs are advantageous for biomedical use because of their tiny sizes and distinctive

physiochemical and biological characteristics (such as an improved reactive area and the capacity to pass cell and tissue barriers) [85 - 86].

Biopolymer/CuO nanocomposites have tremendous promising prospects in biomedical applications, and Table 5 provides an overview of recent advancements.

Table 5. Applications of biopolymer/CuO nanocomposites in the biomedical field.

Biopolymer/Metal	Application	Reference
Chitosan/CuO	Drug delivery (curcumin)	[88]
Carboxymethyl - chitosan - starch/CuO	Drug delivery (amoxicillin)	[89]
Chitosan - PVA - graphene oxide/CuO	Wound healing	[87]
PVA/CuO	Drug delivery (ibuprofen)	[90]
Starch/CuO	Drug delivery	[33]
Oxidized starch/CuO	Colon specific naproxen (npX) delivery	[39]
Carboxymethyl/starch / CuO	Wound healing	[32]
Chitosan/CuO	Anti-proliferative activity against human lung cancer cells A549	[92]
Starch/CuO	Treatment of gastrointestinal system	[92]

Bio-nanocomposites incorporating oxidized starch/CuO, designed to be pH-sensitive and antibacterial, were prepared and investigated for their potential as a drug delivery system targeting bacterial infections in the colon. Drug release was examined at pH 7.4 and total naproxen (NPX) release as a ratio of time was calculated to determine the prepared system capacity to transport NPX to the colon. Zone inhibition and NPX loading capabilities for the developed system were equivalent, superior, compatible, and suitable. It implies that synthetic oxidized starch/CuO bio-nanocomposite may be promising medication delivery technology with built-in antibacterial activity [39]. In comparison to nanocomposites and nanoparticles, the chitosan/PVA/CuO/graphene oxide patch demonstrated strong antibacterial activity against the test bacterium, which is frequently seen in wounds. According to the results of the cell viability experiments, the nanocomposite and CS/PVA/CuO/GO patch exhibited good cell viability and boosted NIH₃T₃ cell proliferation at a concentration of 5 g mL⁻¹. The maximum inhibition control (MIC50) value of the nanocomposite is close to 10 g mL⁻¹. It has stronger antibacterial action at this dose. The increased cell migration supports the possible use of CS/PVA/GO/CuO patch combined with GO/CuO nanocomposite for wound healing applications [87]. By depositing reduced CuO NPs on starch in an alkaline medium, a green method of creating CuO/starch nanocomposite has been developed. The cytotoxic and anticancer effects of the starch/CuO nanocomposite against pancreatic cancer (MIA, AsPC-1, and PaCa-2), gastric cancer (KATO III and AGS), and colon cancer (HCT-8 and HCT-116) were evaluated for biological applications. Cancer line viability decreased in the presence of the starch/CuO nanocomposite depending on the dose. The strongest antioxidant effects against 2,2-diphenyl-1-picrylhydrazyl (DPPH) were demonstrated by the starch/CuO nanocomposite [92]. By using the 3-(4,5-dimethyl thiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT) test, the synthetic chitosan-CuO nanocomposite and rutin were assessed for their ability to inhibit the proliferation of A549 human lung cancer cells.

The antiproliferative effect of rutin and synthesized nanocomposite against a human lung cancer cell line was concentration-dependent [93]. The study demonstrated that as the concentration of CS-CuO nanocomposite increased from 3.1 to 200 g mL⁻¹, there was a significant reduction in the viability of A549 lung cancer cells.

4. CATALYTIC ACTIVITY OF COPPER OXIDE /BIOPOLYMER NANOCOMPOSITES

Since NPs have a high specific surface area ratio, which enhances their selectivity and activity while keeping the fundamental characteristics of a heterogeneous catalyst, nano-catalysis has recently emerged as a viable and affordable alternative to conventional catalysis [94]. Biopolymers support the synthesis of transition metal NPs because they serve as both stabilizing and reducing agents in an alkaline medium [95]. Due to the biodegradability and biocompatibility of biopolymers such as chitosan, guar gum, alginate, cellulose, PVA, etc. the catalytic activity of synthetic metal oxide NPs (such as CuO, Fe₃O₄, TiO₂, etc.) is enhanced. CuO is decorated on the surface of the biopolymer to increase the catalytic activity leading to the creation of an efficient catalyst for a range of chemical processes.

Table 6 shows the overview of the catalytic activity of CuO embedded with various biopolymers.

Table 6. Catalytic activity of biopolymer/CuO nanocomposites.

Biopolymer/Metal	Catalytic species	Reference
Chitosan/CuO	4-nitrophenol to 4-aminophenol	[96]
Tantalum Ta/chitosan/CuO	Methylene blue in the presence of NaBH ₄	[97]
Chitosan/CuO	1,3,4 hydrazonyl chloride to 1,3,4 trisubstituted pyrazole	[98]
Na-Alginate/CuO	Carboxylic acid to amide	[76]
Agar/CuO	Nitrophenol to aminophenol	[99]
Cellulose/CuO	Catalysis of 4- nitrophenol	[72]
Cellulose acetate/CuO-	Catalysis of 4- nitrophenol	[100]
Chitosan/PVA/CuO	A catalyst for the synthesis of 1,2,3 triazole	[105]

The catalytic activity of tantalum Ta/chitosan/CuO [97] was observed in all media at 4 % Ta/chitosan/CuO. Greater surface areas were associated with the highest catalytic efficiency because they offered a more active site. In an acidic environment, the catalytic efficiency increased due to enhanced adsorption of H⁺ ions onto the nanorods (NRs) surface. Conversely, under basic conditions, the greater presence of -OH groups promotes the oxidation of reduced products, leading to a reduction in catalytic effectiveness. Biopolymer/CuO exhibits good catalytic activity as compared to single CuO NPs.

5. TOXICITY OF BIOPOLYMER/CuO NANOCOMPOSITE

Chitosan/CuO and alginate/CuO nanocomposites have been investigated for their toxicity effect, particularly concerning their biomedical applications. Chitosan, known for its

biocompatibility, can mitigate some of the cytotoxic effects of CuO nanoparticles. However, studies have shown that higher concentrations of CuO in chitosan-based nanocomposites can lead to increased cytotoxicity due to nanoparticle-induced oxidative stress. In contrast, alginate, another biocompatible polymer, has been explored for its ability to stabilize CuO nanoparticles and reduce their cytotoxic potential. Alginate/CuO nanocomposites have shown promise in maintaining low cytotoxicity while retaining antimicrobial efficacy, making them suitable candidates for biomedical applications requiring controlled release and biocompatibility assessments [108 - 109].

6. RESEARCH DIRECTION IN THE COMING TIME

Future aspects of bio-nanocomposites such as chitosan/CuO, alginate/CuO, starch/CuO, cellulose/CuO, graphene oxide/CuO, etc. synthesized by different methods, such as green synthesis, alco-thermal, co-precipitation, *in situ* methods, hold significant promise across various fields. In the realm of antibacterial applications, these composites can be further optimized for enhanced efficacy and specificity, particularly in targeting drug-resistant bacterial strains. This is crucial for developing next-generation antibiotics and reducing the global burden of infectious diseases. Additionally, the heavy metal removal capabilities of these bio-nanocomposites present an eco-friendly solution for water purification, addressing critical environmental issues related to industrial pollution. Their catalytic activity, especially in organic reactions, can be leveraged to create more efficient and sustainable chemical processes. Advancements in these areas could lead to widespread adoption in environmental remediation, healthcare, and industrial applications, ultimately contributing to improved public health and environmental sustainability. Further research should focus on refining synthesis techniques for better control over particle size and distribution, enhancing the biocompatibility of these composites, and exploring their multifunctional roles in complex real-world scenarios.

7. CONCLUSIONS

In summary, CuO NPs have been extensively explored and are attracting a great deal of interest from material researchers and technologists today, due to their unique features and possible usage in a variety of industries. The incorporation of CuO NPs into natural biopolymers such as chitosan, guar gum, tamarind, alginate, starch, and cellulose, has led to the development of biopolymer/CuO nanocomposite with enhanced biological and antimicrobial properties. These nanocomposites have shown great potential in diverse applications including antimicrobial, wound dressing, organic impurity removal, and heavy metal removal from wastewater. Various synthesis methods, including co-precipitation, green synthesis, solvent casting method, and *in situ* methods have been employed to create nanocomposite. Over the past decade, research has demonstrated the significant potential of biopolymer/CuO nanocomposite in medical, environmental, and industrial applications. This review provides a comprehensive overview of the synthesis methods and applications of biopolymer/CuO nanocomposite highlighting their advantages and potential features developments. Researchers interested in the usage of CuO NPs supported by biopolymers will find this review to be helpful.

List of abbreviation

CuO	-	Copper oxide
NPs	-	Nanoparticles
PAA	-	Polyacrylic acid
Q _{max}	-	Maximum adsorption capacity
CMC	-	Carboxymethyl cellulose
Poly AMPA	-	Poly(2-acrylamide-2-1-methyl-1-propane sulfuric acid)
DXN	-	Doxycycline
RSM	-	Response surface methodology
CFU	-	Colony forming unit
DPPH	-	2,2 diphenyl-1-picrylhydrazyl
ABTS	-	2,2 azino-bis 3-ethyl benzoline-6-sulfonic acid
NPX	-	Naproxen

Acknowledgements. We would like to thank the Department of Chemistry, Gurukula Kangri (deemed to be University) Haridwar for providing us research facilities.

Credit authorship contribution statement. **Rajdeep Malik:** Formal analysis and Supervision. **Nazreen:** Writing - Original Draft, Formal analysis, Correspondence, Writing and Editing. **Jagran Meena:** Investigation, Review and Editing, Correspondence.

Declaration of competing interest. The authors declare that there are no conflicts of interest related to the work presented in this manuscript. None of the authors have financial, personal, or other relationships with other people or organizations that could inappropriately influence or bias the work.

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