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REVIEW

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# Role of capping agents in the application of nanoparticles in biomedicine and environmental remediation: recent trends and future prospects

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**Abstract**

Capping agents are of utmost importance as stabilizers that inhibit the over-growth of nanoparticles and prevent their aggregation/coagulation in colloidal synthesis. The capping ligands stabilize the interface where nanoparticles interact with their medium of preparation. Specific structural features of nanoparticles are attributed to capping on their surface. These stabilizing agents play a key role in altering the biological activities and environmental perspective. Stearic effects of capping agents adsorbed on the surface of nanoparticles are responsible for such changing physico-chemical and biological characteristics. Firstly, this novel review article introduces few frequently used capping agents in the fabrication of nanoparticles. Next, recent advancements in biomedicine and environmental remediation approaches of capped nanoparticles have been elaborated. Lastly, future directions of the huge impact of capping agents on the biological environment have been summarized.

**Keywords:** Capping agents, Nanotechnology, Biomedicine, Environment, Nanoparticles

## Introduction

The particles ranging in size between 1 and 100 nm and possessing properties varying from the bulk material are defined as nanoparticles. In the last few decades, nanoparticles have been employed in various applied fields of science [1–3]. Usually, the nanoparticles are produced in large quantities on a commercial scale that are uncapped and having a larger size. These nanoparticles become hazardous to the environment when released in the form of large aggregates. Therefore, the choice of suitable capping moieties is key in stabilizing the colloidal solutions and their uptake into living cells and the environment. The surface chemistry and size distribution of nanoparticles get altered after capping with biocompatible surfactants [4–7]. Capping agents should be biodegradable, well-dispersed and biosoluble, biocompatible, and non-toxic in nature so that they can be easily utilized in the living system. Hence, their non-specific interaction with biological components reduces leading to alleviated cellular toxicity [8].

Evaluation of promising therapeutic potential and environmental influence of nanoparticles is of great interest to the researchers. The biological properties of nanoparticles are enhanced by surface capping. Capping agents are emerging therapeutic agents that show their clinical significance in synergy with the biocompatible nanoparticles to which they have been attached. The covalent bonding between the chains of capping ligands and the nanoparticles' surface leads to steric hindrance providing ultimate stability to the nanocomposite. The percentage of atoms present on the surface increases at the nanoscale which gets further boosted by capping. Moreover, the agglomeration

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of nanoparticles gets minimized for a longer period of time employing appropriate capping agents [9].

Capping agents significantly modify the properties of colloidal suspensions of nanoparticles which makes them attractive candidates for biomedical applications such as drug delivery and theranostics in cancer. The biological reactivity and functionality with mitigated side-effects of nanocrystals are defined by their surface chemistry, morphology, and size which is attributed to suitable capping moieties. The small-sized nanoparticles have been explored in biomedicine and environmental remediation due to their novel characteristics obtained after surface tailoring [10, 11].

There are rising concerns regarding the safety and long-term toxicity of nanoparticles in the biological system that need to be resolved. Biocapping with aqueous plant extracts is an effective way of getting controlled growth of nanoparticles with minimum toxicity. However, since surface manipulation of nanocrystals is necessary to obtain monodisperse nanoparticles, polydispersion, and purification from by-products is a hurdle to the employment of this method on an industrial scale [12].

This review gives insight into the development of capped nanocomposites with ameliorated colloidal stability and biological functionalities. According to our knowledge, this is the first comprehensive report outlining the potential effects caused by the capped nanomaterials in the areas of biomedicine and environmental remediation.

## Capping agents in nanotechnology

The frequent use of capping agents in colloidal dispersions to regulate nanoparticles controls the growth, agglomeration, and physico-chemical characteristics in a precise way [13]. The capping agent is an amphiphilic molecule comprising of a polar head group and a non-polar hydrocarbon tail. Owing to the amphiphilic nature of capping agents, they confer the functionality and enhance the compatibility with another phase. The non-polar tail interacts with the encircling medium while the polar head interacts with the metal atom of the nanosystem [14] as shown in Fig. 1.

Different types of capping agents have been used in nanoparticles' synthesis including surfactants, small ligands, polymers, dendrimers, cyclodextrins, and polysaccharides. All of these have been successfully utilized as capping agents having the capability to induce subtle changes in nanoparticles elucidating tremendous therapeutic and environmental cleansing effect [15]. Figure 2 is representing the various types of capping agents.

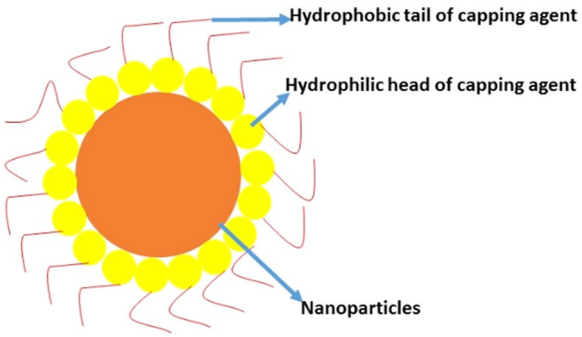


**Fig. 1** Nanoparticles covalently bound with capping agents

### Polyethylene glycol (PEG)

PEG is a great biocompatible polymer with structural formula $H–(O–CH_2–CH_2)_n–OH$. Synthesis of PEG takes place through the poly-condensation of ethylene glycol in the presence of a catalyst either acidic or basic, producing a lower molecular weight product. It is soluble in both aqueous and organic solvents. This feature enhances both its biocompatibility and processability. It is less toxic and non-immunogenic. Hence, coupled as a surface modifier with other compounds including biomaterials, micelles, and particles for active molecule transport, and also for physical and chemical hydrogels. In vivo, PEG is not detached hydrolytically. Nevertheless, its hydrophilic properties grant a greater water affinity and biodegradability to the polymer [16].

PEG has been used as a capping agent in nanotechnology extensively for several purposes such as the biomedical field for sustained and targeted drug delivery. The coating of metal and metal oxide nanoparticles with PEG takes place in wet-chemical synthesis [17]. PEG has been reported in various studies as a capping agent for metal nanoparticles involving gold (Au) [18], silver (Ag) [19], zinc (Zn) [20] to reduce cytotoxicity, improve stability, and biocompatibility associated with metal nanoparticles.

### Polyvinylpyrrolidone (PVP)

PVP, also known as povidone or polyvidone, is a polymer $(C_6H_9NO)_n$ soluble in water. PVP is composed of polymerization of monomer *N*-vinylpyrrolidone. It is light, flaky, and hygroscopic powder. It absorbs approximately 40% of water by its mass. It consists of outstanding moistening properties. Hence, it makes films forming a compelling coating agent. PVP with its exclusive physico-chemical properties like solubility both in water and organic solvents, biocompatibility, chemical stability and non-toxicity makes it a potential biomaterial in many considerable medical and non-medical purposes. PVP

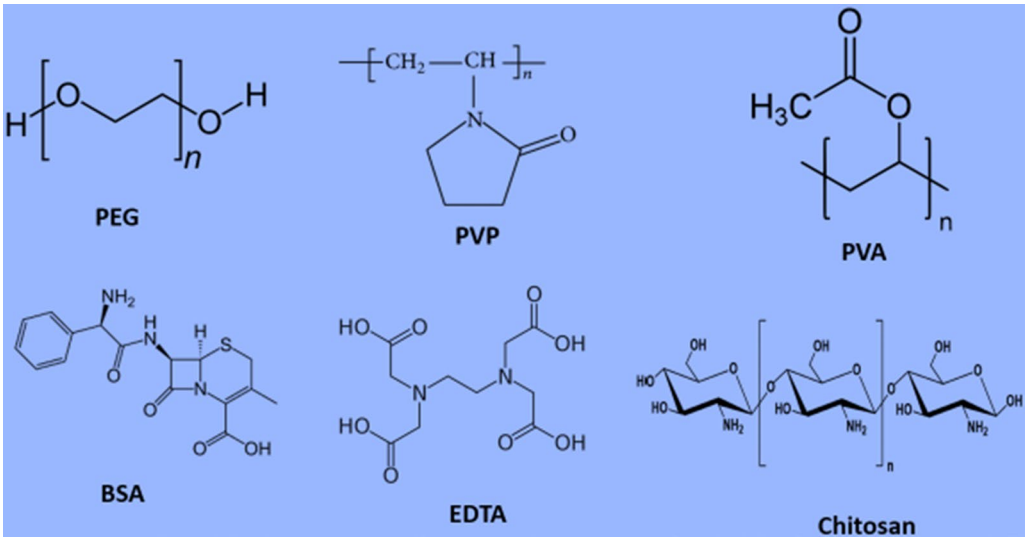


**Fig. 2** Different types of capping agents utilized in nanotechnology

is extensively used in various medical products, cosmetics, and haircare products. The popular uses of PVP in a pharmaceutical industry include manufacturing of drugs as a common ingredient in tablets, granules, pellets, soft gelatine capsules, gels, hydrogels, films and coatings, membranes and mats of nanofibers, powders, syrups, oral or injectable solutions, coatings for medical devices, contact lenses and many others [21, 22].

PVP is one of the significant capping agents that have been utilized in nanotechnology to overcome drawbacks associated with conventional methods of preparation of nanoparticles such as their toxicity, size, and agglomeration. Hence, ecofriendly nanoformulations are obtained using PVP having more applicability [23, 24]. In various researches, PVP has been employed as a capping agent around metal nanoparticles such as Iron (Fe), silver (Ag), gold (Au), zinc (Zn), etc. [25].

#### Polyvinyl alcohol (PVA)

PVA is one of the high performance capping agents used in nanotechnology [26, 27]. PVA, which is essentially made through hydrolysis of polyvinyl acetate, is a synthetic polymer owning great hydrophilicity, biocompatibility, and biodegradability. PVA has been used as a stabilizing agent, for shape and size control of Ag nanoparticles to protect against water [28]. PVA is used in various biomedical arenas. PVA hydrogels hold considerable potential for their usage in tissue engineering and artificial grafts [29]. To improve the optical emission, crystallinity, and size dispersion, ZnO nanoparticles capped with PVA were prepared by the sol–gel method [30]. Iron oxide or magnetite nanoparticles are most likely to agglomerate due to magnetic forces, and it compromises the effectiveness and potential use of these nanoparticles. Therefore, PVA has been employed as a capping agent and glutaraldehyde as a cross-linker in the fabrication of iron oxide nanoparticles. This has not only prevented the agglomeration but also the oxidation of iron oxide nanoparticles via a two-step method in which first the iron oxide nanoparticles were prepared, and then coated and crosslinked with PVA and glutaraldehyde [31].

#### Bovine serum albumin (BSA)

One of the most abundant and well-characterized ubiquitous proteins present in the plasma of mammals is serum albumin (SA). The key role of this protein is to maintain the level of pH in the blood, regulating the colloidal osmotic pressure and transporting different substances of various natures such as ionic, hydrophilic, and hydrophobic. The molecular weight of bovine serum albumin (BSA) is ~ 66 kDa and consists of 582 amino acids, with 35 threonine and 32 serine amino acids. Due to the presence of charged functional groups, including carboxyl, sulfhydryl, and amino, BSA finds numerous binding sites. These sites also assist in the binding of different therapeutic systems like drugs, poly-conjugated dyes, and nanoparticles. As a capping agent, BSA increases the bioavailability of loaded nanoparticles. It is taken up by cells through certain receptors present on the surface of tumor cells as a source of nutrient and amino acid. The mild reducing property of BSA is due to the hydroxyl group, just like PVP, capable of fabricating metal nanoplates, for instance, palladium (Pd), gold (Au), platinum (Pt), and silver (Ag) [32, 33].

Jyothi Kumar et al. (2019) reported the stabilization of Au nanoparticles by using BSA as a capping agent. BSA has exhibited excellent stabilizing as well as size control properties in bio-conjugated Au nanoparticles [34]. In another study, a sensor was developed for the detection of heparin and protamine using Au nanoparticles and BSA capped cadmium sulfide quantum dots (CdS QDs) based on the inner filter effect [35]. BSA also acts as a structure-directing agent as well as controlling the assembly, nucleation, and growth of nanoparticles. Cuprous oxide ($Cu_2O$) nanoparticles capped with BSA have been reported to produce a hierarchical structure emulating biomineralization via the facile method [36].

#### Ethylene diamine tetra acetic acid (EDTA)

EDTA is a water-soluble polymer commonly used as a chelating agent to dissociate cells from the extracellular matrix (ECM) by binding to divalent metal ions. Also, EDTA has been utilized as a complexing agent for the removal of metal ions [37]. EDTA has gained significant importance in nanoscience, being used as a stabilizer in the fabrication of nanoparticles. It efficiently controls the morphology and size of nanoparticles. It has been used as a capping agent in the preparation of various metal nanoparticles including gold (Au), zinc (Zn), copper (Cu), chromium (Cr), and cadmium (Cd) [38, 39]. Rahal et al. [40] synthesized nickel oxide (NiO) nanoparticles capped with EDTA via co-precipitation method and results showed that EDTA capped nanoparticles were smaller in size as compared to the pure NiO nanoparticles with enhanced surface magnetization properties. EDTA was also employed in the synthesis of magnetic iron oxide nanoparticles to enhance the mono dispersion via high-temperature hydrolysis reaction resulting in more water solubility and enhanced magnetic properties [41].

#### Chitosan

Chitosan is a co-polymer comprising D-glucosamine and *N*-acetyl-D-glucosamine produced via alkaline deacetylation of chitin naturally occurring in the crustaceans or hydrolysis of chitin by the enzymatic action of deacetylase. After cellulose, this is the second most abundant biomaterial [42]. Although chitin is not soluble in dilute acids, chitosan is an acid-soluble polymer [43]. Lately, chitosan due to its exceptional biological properties has drawn substantial consideration in the biomedical field. In terms of biological applications, its fascinating properties include biocompatibility, biodegradability, non-toxicity, anti-carcinogenicity, immune-enhancing, and antimicrobial activity. It degrades both in vitro and in vivo into small monomers without producing any adverse effects [44]. In nanoscience, chitosan has been extensively used in the preparation of metal nanoparticles as a stabilizer and promoting wet-chemical synthesis, although the bonding between chitosan and metallic nanoparticles is still a debate. For instance, the linkage between platinum (Pt) nanoparticles and chitosan has been suggested to be via amino and secondary hydroxyl groups [45].

Chitosan has been used as a capping agent to stabilize the colloidal dispersion, and to control the morphology and optical properties of metal nanoparticles including gold (Au) [46], silver (Ag) [47], copper (Cu) [48], etc. Capping of Au nanoparticles with chitosan is used as a temperature manipulation sign. Au nanoparticles transform its color and intensity with variation in storage temperature and its duration. This difference in color and intensity is principally owing to the change in shape and size of chitosan capped Au nanoparticles, potentially used for the development of sensors in food [49].

#### Plant extracts

Fabrication of nanoparticles using extracts from plants as potential capping and reducing agents is often known as green synthesis. The extracts from leaves, fruit, roots, and seeds of the plants can influence the properties of the formulated nanoparticles by enhancing their functionality optimally for biomedical applications [50–52]. Much work has been conducted using a green synthesis approach to tailor the properties of nanoparticles. Figure 3 illustrates the process of green synthesis of nanoparticles.

Anddresa et al. [53] used *Virola oleifera* exudate as a potential capping and stabilizing agent for the formulation of gold (Au) nanoparticles. With the capping agent,

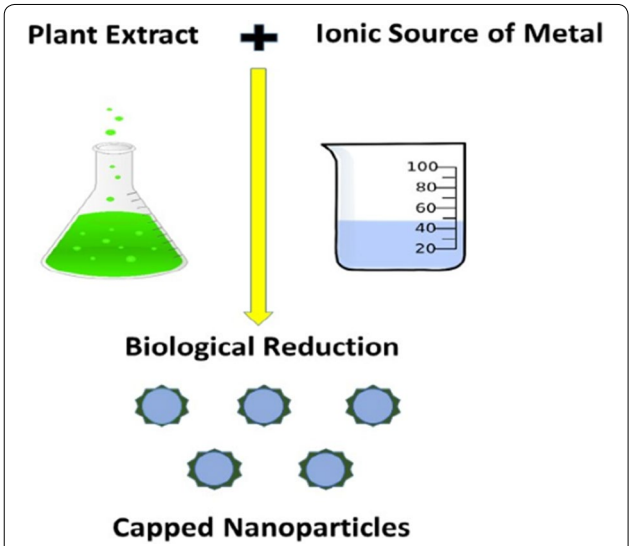


**Fig. 3** Schematic representation of the green synthesis of nanoparticles

the zeta potential of the formulated Au nanoparticles was observed to shift from a negatively charged to a positively charged surface. The capped Au nanoparticles showed a low toxicity effect and high antioxidant activity. Rashid et al. [54] used four different plants (*Rumex dantatus*, *Bergenia ciliata, Rumex hastatus, and Bergenia stracheyi*) as potential capping agents to formulate silver (Ag) nanoparticles. The different formulated Ag nanoparticles showed strong antibacterial activity against six bacterial strains. The activity of the formulated nanoparticles was increased with the rise of their concentration. Moreover, an eco-friendly synthesis protocol using an extract of the bark of *Solanum trilobatum* as a potential capping agent for the formation of Ag nanoparticles was demonstrated by Ramanathan et al. [55]. The *S. trilobatum* capped Ag nanoparticles showed an enhanced antimicrobial and antifungal activity against *E. coli*, bacillus species, and *Aspergillus niger.* Madubuonu et al. [56] used two different extracts of *Psidium guajava* and *Moringa oleifera* for the preparation of iron oxide (FeO) nanoparticles for antibacterial and photocatalytic activity. From their observation, the composite extract gave a better activity than the individual extracts by providing mutual stability to FeO nanoparticles.

Angel et al. [57] prepared nickel oxide (NiO) nanorod via *Phoenix dactylifera* as a potential reducing and capping agent. The formulated nanorod showed strong toxicity over A549 cells, and good antibacterial and photocatalytic activity. Similar results were observed by Aisida et al. [51], they synthesized iron (Fe) nanorod using the green extract of *Moringa oleifera* as a potential reducing agent for antibacterial activity against six human pathogenic strains. They observed a strong susceptibility of the pathogens against Fe nanorods. Tahir et al. [58] used *Artemisia vulgaris* (AV) leaves extract as a potential reducing agent to synthesize Ag nanoparticles. The obtained AV-Ag nanoparticles showed strong antibacterial activity. The antioxidant and the cytotoxicity effect of AV-Ag nanoparticles showed a promising potential against MCF-7 and HeLa cell lines. A similar report was published by Nithya et al. [59] using ionic liquids from *Justicia adhatoda* extract as a templating and stabilizing agent to enhance the surface morphology of three different precursors; Au, Ag, ZnO nanoparticles and their composites. The composite samples exhibited strong antibacterial and anticancer activity against *E. coli, Staphylococcus aureus*, and HeLa cancer cells. Senthilkumar et al. [60] reported the synthesis of zinc oxide (ZnO) nanoparticles capped with *Tectona grandis* leaves extract for antiarthritic, anticancer, antioxidant, antibacterial activity, and in vitro cytotoxicity. The obtained results enhanced the antibacterial activity against both the Gram-positive and Gram-negative bacterial strains. The sample also showed enhanced denaturation of protein as well as proteinase activity at 200 μg $ml^{-1}$ dosage. The anticancer activity was also tested against osteoblast MC3t3-E1 cell lines with a profound reduction in the size of the tumor.

Anticancer, antibacterial, and antileishmanial activity of green synthesized hematite were observed by Naz et al. [61]. They used *Rhus punjabensis* extract as a potential reducing agent to form hematite nanoparticles. The formulated nanoparticles also showed significant cytotoxic effect against HL-60 leukemic and DU-145 prostate cancer cell lines with $ED_{50}$ values of 11.9 and 12.79 μg/ml, respectively. Aqueous extract of *Hygrophila spinose* was used to synthesize Au nanoparticles by Swaha et al. [62]. The formulated nanoparticles showed a small particle size with the help of the capping agent and exhibited potential anticancer activity against ovarian, breast, and brain cancer cell lines. Antioxidant and free radical scavenging activities of Ag nanoparticles prepared from the extract of *Piper longum* were presented by Renuka et al. [63]. The anticancer activity conducted against HeLa cells (cervical cancer cell line) showed non-toxicity of the fabricated Ag nanoparticles and gave a maximum IC50 value. Besides, antilarvicidal activity of the nanoparticles with efficient mortality was obtained against *Anopheles stephensi*, *Aedes aegypti* and *Quinque fasciatus* having $LC_{50}$ and $LC_{90}$ values of 8.969 ppm and 16.102 ppm, 14.791 ppm and 28.526 ppm, and 18.662 ppm and 40.903 ppm, respectively after 72 h of exposure.

#### Influence of capped nanoparticles in biomedicine

Capping or stabilizing agents are essential in the fabrication of nanoparticles to enhance their biomedical functionality by reducing their toxicity and enhancing their biocompatibility and bioavailability in living cells. They prevent clusters or aggregates of nanoparticles, enhance their colloidal stability, and prevent uncontrolled growth of nanoparticles (especially the metal and metal oxide nanoparticles). The different types of capping agents also determine the particle size and morphology, and their magnetic, optical, and catalytic properties. For biomedical applications such as drug delivery in cancer therapy [64–66] and antimicrobial activities, [51, 56, 67], the bioconjugate of the nanoparticles is very important. This involves the use of biocompatible, non-toxic, and biodegradable moieties as potential capping agents. Table 1 provides an overview of a few capped nanoparticles and their applications in the biomedical field.

The capped nanoparticles have been extensively studied for their applications in biomedicine including antimicrobial, antioxidant, anticancer, and antidiabetic activities as shown in Fig. 4.

**Table 1 The nanoparticles with their capping agents conferring them with different biological activities**

| Capping agents | Nanoparticles | Biological activity | References |
|---|---|---|---|
| Chitosan | Liposomes | Antidiabetic | [68] |
| *Parkia speciosa* extract | Ag | Antioxidant | [69] |
| PVA | Ag | Anticancer | [70] |
| PEG | $TiO_2$ | Anticancer | [71] |
| Chitosan | ZnO | Antibacterial, antioxidant, antidiabetic, cytotoxic | [72] |
| Chitosan | FeO | Antibacterial and antioxidant | [73] |
| Chitosan + PEG + PVP | $Fe_3O_4$ | Anticancer drug delivery | [74] |
| PVP | $WO_3$ | Anticancer | [75] |
| PVA | Mg | Anticancer | [76] |
| PVA/Guar Gum | $Fe_3O_4$ | Anticancer | [77] |
| PVA | Cu | Antibacterial | [78] |
| *Aloe vera* extract | $Fe_3O_4$ | Anticancer | [79] |
| Cellulose | Ag | Antibacterial | [80] |
| Alginate | ZnO | Antibacterial | [81] |
| Ethylene glycol | ZnO | Antifungal | [82] |
| Dodecanethiol | Ag | Antifungal | [83] |

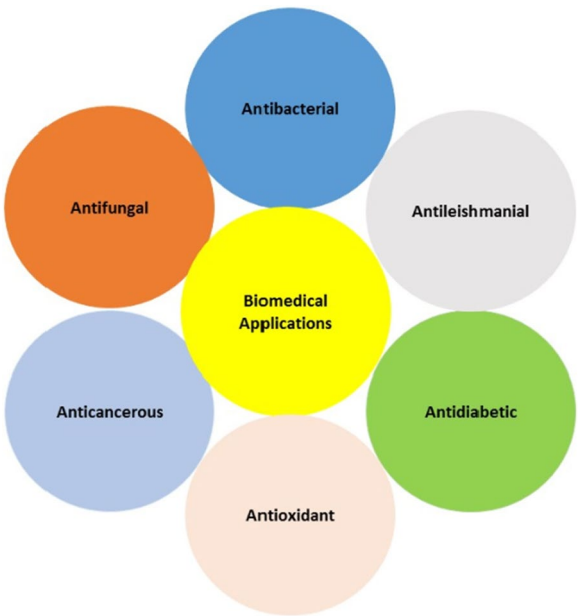


**Fig. 4** Capping agents of nanoparticles affecting different areas of biomedicine

### Antimicrobial activities: antibacterial, antifungal, antileishmanial

Microorganisms are the major culprit of infectious ailments throughout the globe. Scientists from all around the world are trying to fight against developing microbial infections. For instance, generally used conventional drugs are incompetent to show their effectiveness against microbial infections. The most common factor behind this is the overuse of these drugs, hence microbes develop resistance against drugs [84]. Moreover, some antimicrobial drugs are particularly toxic and irritant so there is great attention in searching novel ways to formulate safe and cost-effective antimicrobial agents. Currently, prevention and inhibition of microbial infections have been the most active research area in healthcare. This urges the growth and development of an effective and novel materials with superior antimicrobial properties. A good substitute for this purpose is nanotechnology [85]. Former reports have shown that antimicrobial preparations in the form of nanoparticles could be employed as an effective antibacterial agent [86]. Plenty of development has been done in the pharmaceutical industry using monodispersed nanoparticles to treat antimicrobial ailments. Various types of nanomaterials are in practice as an antimicrobial agent. However, the fabrication of nanoparticles with the desired shape and size is still challenging [87]. Hence, the synthesis, characterization, surface decoration, and functionalization of nanomaterials decipher the promise of developing new generation antimicrobial (bactericidal) materials [88].

Due to the instability (agglomeration), toxicity, size, and shape defects, nanomaterials are generally surface modified to enhance their antimicrobial properties. Literature supports the positive effects of surface modification on the antimicrobial potential of nanoparticles. For example, chitosan functionalized silver (Ag) nanoparticles exhibited superior antibacterial activity due to higher solubility and release of $Ag^{+1}$ ions [89]. Spherical Ag nanoparticles functionalized with core–shell magnetic chitosan microspore demonstrated efficient antimicrobial

activity and act as smart antifouling agents [90]. Ag nanoparticles coated with PVA/aminopropyltriethoxysilane revealed superior fungicidal activity [91]. Moreover, the capping of Ag nanoparticles with PVP and glucantime (antimicrobial drug) produced promising results against *Leishmania amazonensis* [92]. In another study, the PVP-360 capped Ag nanoparticles demonstrated obvious improvements in the antibacterial activities [93]. This was ascribed due to the effective prevention of agglomeration that resulted in the efficient stabilization of nanoparticles. The PVP and PEG-modified Ag nanoparticles [94], ZnO nanoparticles, and CuO nanoparticles [9, 95] exhibited pronounced antibacterial activities. Moreover, the functionalization of Ag nanoparticles with EDTA, PEG, PVP, and PVA was tested for antimicrobial potential [96]. Results showed that PVP coated Ag nanoparticles possess superior antimicrobial activity due to their smaller size as compared to other coated nanoparticles. Literature also stated that comparatively small particles demonstrate relatively higher antibacterial activity [97]. Besides this, ZnO nanoparticles capped with chitosan elucidated significant antimicrobial activity against fungus (*Candida albicans*) and bacterial strains (*Micrococcus luteus* and *Staphylococcus aureus*). Moreover, ZnO–Chitosan nanoparticles also displayed marked biofilm inhibition activity against *M. luteus* and *S. aureus* [98]. Chitosan functionalized gold (Au) nanoparticles were effective against the bacterial endotoxin lipopolysaccharide (LPS) [99]. From these findings, we could say that antimicrobial activities of nanoparticles are exclusively dependent on their physical attributes, i.e., adsorption of nanoparticles to the cell wall and their interaction, and denaturation of cell wall proteins which subsequently lead to the production of porous structures and marked alterations in the structure of cell membrane. This eventually enhances the permeability of the cell membrane and allow the movement of extracellular fluids inside the cell. Precisely, Ag nanoparticles impair the cell membrane via electrostatic attractions and effect certain membranous enzymes, damages the proton motive force (PMF), and finally cause cell lysis [100, 101]. From the literature discussed above, we can conclude that the functionalization of nanomaterials is crucial in the enhancement of their antimicrobial properties and useful in treating infectious diseases.

Figure 5 explains the mechanism of antibacterial action of capped nanoparticles.

#### Antioxidant activities

Antioxidants are compounds produced naturally to defend the human body from the side effects of free radicals. Antioxidants scavenge the free radicals that produce reactive oxygen species (ROS), like nitric oxide (NO), hydroxyl radical ($OH^-$), and superoxide anion ($O_2^-$) in healthy organisms as a defense system. Accumulation of ROS leads to varied chronic pathologies, for example, the development of cancer,

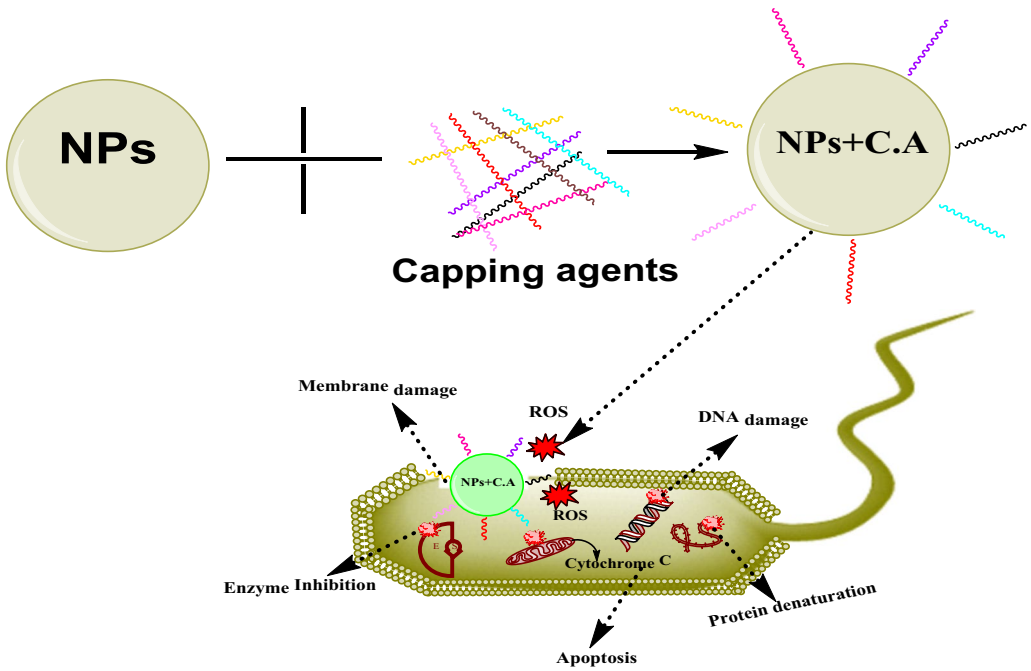


**Fig. 5** Proposed mechanism of antibacterial action of capped/modified nanoparticles

cardiovascular, and neurodegenerative illnesses. Natural antioxidants are obtained from vegetables like quercetin. Quercetin (3,5,7,3′-4′-pentahydroxy flavone) is one of the flavonoids consisting of significant pharmacological activities including antioxidant potential. Despite its advantages, its clinical use is compromised due to low bioavailability and oral absorption due to less solubility in water. Therefore, gold (Au) nanoparticles are surface-functionalized with the capping of quercetin to enhance the bioavailability of the compound, hence the antioxidant activity. Nitric oxide (NO), 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) free radical scavenging assays were performed to evaluate the antioxidant activity of quercetin capped Au nanoparticles. Results demonstrated that capped Au nanoparticles exhibited higher antioxidant activity as compared to quercetin alone [102].

Metal oxide nanoparticles exhibit great antioxidant potential but the use of uncapped nanoparticles is hindered due to their toxicity. For example, CuO nanoparticles capped with PEG and PVP were synthesized by co-precipitation method and antioxidant assays were carried out including antioxidation assay, reducing power assay, and DPPH-free radical scavenging assay. Both CuO-PEG and CuO-PVP nanoparticles exhibited excellent antioxidant, reducing power and DPPH-free radical scavenging activity. Most interestingly, the antioxidant activities were higher in capped nanoparticles as compared to uncapped ones [95, 102]. Similar results were obtained from another study in which ZnO nanoparticles were capped with PEG and PVP showing higher antioxidant activity by capped nanoparticles as compared to uncapped nanoparticles. This can be attributed to the alteration in the surface chemistry, morphology, and size of nanoparticles which substantially contribute towards the improvement of the biological properties of nanoparticles [9]. Antioxidant capacities of chitosan capped selenium (Se) nanoparticles have also been studied. Se was stabilized to its zero state via chitosan capping to harness its full potential of an antioxidant agent by increasing bioavailability and lowering the toxicity. Lipid peroxide, DPPH, and ABTS assays revealed that chitosan capped Se nanoparticles scavenge free radicals at diverse levels. A month-old chitosan capped Se nanoparticles apprehended such a higher ABTS scavenging ability that the value could reach up to $89.44 \pm 5.03\%$. In the cell culture assays using BABLC-3T3, the accumulation of the intracellular ROS could be inhibited by chitosan capped Se nanoparticles with better penetration and lower toxicity [103].

#### Anticancer activities

Despite the presence of conventional cancer treatments including radiotherapy, chemotherapy, or surgical removal, there are many side effects such as hair loss, pain, nausea, vomiting, and damage to normal cells. Nanotechnology is an alternative approach to develop combinational chemo-immunotherapies against different types of cancers. The goal of incorporating nanoparticles in treating cancer is to provide targeted drug delivery to overcome the side effects of conventional therapies (Fig. 6). Although nanoparticles exhibit tremendous tumor and cancer-killing properties, they cannot be applied clinically due to their toxicity. Hence, capped nanoparticles are utilized to treat different types of cancer such as breast, colorectal, liver, ovarian, and lung cancer [104].

Nanoparticles act as potential drug delivery systems because they escalate the retention time of the drug in the blood, lower the efflux, and undergo targeted delivery. Methotrexate (MTX) is an anti-cancer drug that can cause renal and hepatic toxicity at higher administration doses. Methotrexate silver nanoparticles (Ag-MTX) capped with PEG were synthesized via chemical reduction method. Biocompatibility and anticancer activity were evaluated. PEG capped Ag-MTX nanoparticles displayed increased anticancer activity against the MCF-7 cell line. Also, the hemolytic activity of nanoparticles was significantly reduced as compared to MTX administered alone. Therefore, PEG-Ag-MTX nanoparticles were proved to be the prospective nano-carriers of methotrexate with reduced side effects [105]. Moreover, magnesium (Mg) nanoparticles coated with PEG act as a drug delivery vehicle for anticancer drug, 2-Methoxyestradiol (2ME). These drug carrier nanoparticles were tested against prostate cancer cell lines and results revealed the decrease in tumor activity of cells, and this drug carrier system can be used to treat prostate cancer [106].

Magnetic ($Fe_3O_4$) nanoparticles are promising candidates for drug delivery as they are biocompatible and can be directed under an external magnetic field for magneto-therapy. $Fe_3O_4$ nanoparticles have been used as a drug carrier for various anticancer drugs such as doxorubicin, daunorubicin, 5-bromotetrandrine, and anti-HER2 immunoliposomes to assess their therapeutic potential in breast cancer. Dual paclitaxel (PTX)/superparamagnetic iron oxide (SPIO)-loaded poly (lactic-co-glycolic acid) (PLGA)-based nanoparticles were developed for cancer therapy. These nanocarriers showed effective antitumor activity in vitro against the CT26 cell line. These nano-entities have not only antitumor characteristics but also imaging properties, therefore, concurrently achieving multifuctionalities including targeting, imaging,

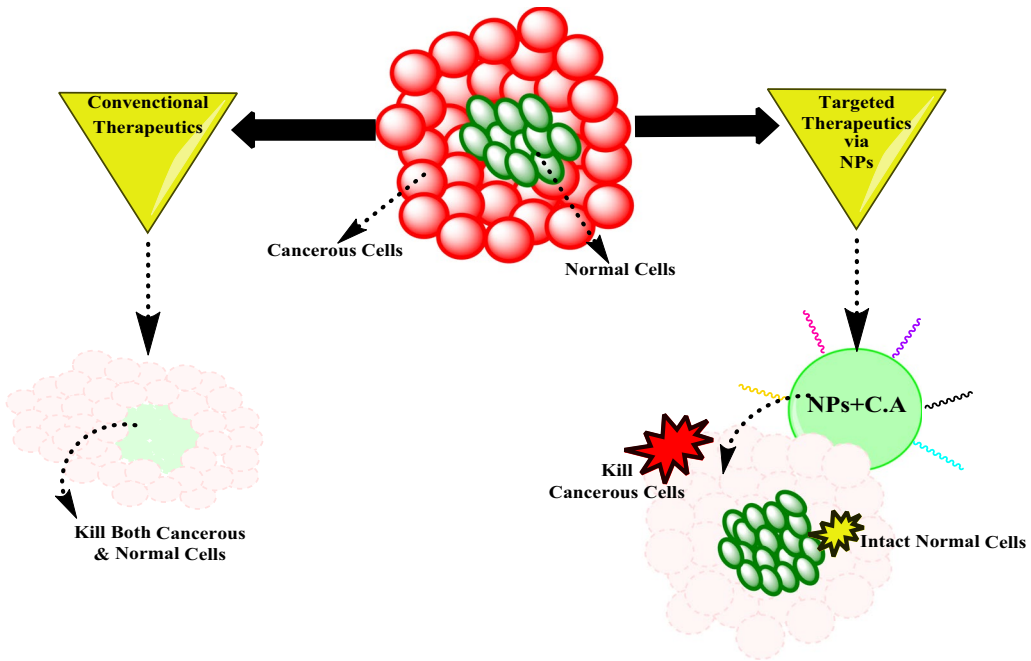


**Fig. 6** Comparison of mode of anticancer action of conventional therapeutics versus capped/modified nanoparticles

drug delivery, and real-time monitoring of therapeutic response [107].

### Antidiabetic activities

Diabetes is a metabolic disorder characterized by elevated levels of glucose in the blood. It has affected more than 100 million people worldwide. Consequently, there is a requirement to develop medicines at nanoscale inhibiting the levels of carbohydrate-hydrolyzing enzymes with a greater extent of specificity and achieving the utmost therapeutic effectiveness with negligible side-effects. Antidiabetic activity of PEG and PVP coated CuO nanoparticles was carried out using the α-amylase inhibition assay. Capped CuO nanoparticles showed higher inhibition, i.e., CuO-PEG and CuO-PVP nanoparticles revealed 32.23% and 37.75%, respectively as compared to uncapped CuO nanoparticles achieving only 19.17% of enzymatic inhibition. It is due to a decrease in size and more surface area owing to the major movement of atoms towards the outer surface of capped nanoparticles [95]. Also, the antidiabetic assay against PEG and PVP capped ZnO nanoparticles declared efficient antidiabetic activity in comparison to uncapped ZnO nanoparticles [9].

Folic acid-functionalized chitosan nanoparticles were synthesized by the ionotropic gelation method. The effects of these nanoparticles on stability, oral bioavailability, and hypoglycemic activity were observed following oral administration in vivo. Formulated nanoparticles demonstrated the persistent release of insulin up to 24 h. Encapsulated insulin remained stable both conformationally and chemically. Uptake studies in Caco-2 cell lines deduced remarkably higher effects, so was the bioavailability through oral administration [108]. Chitosan-EDTA coated (CEC) liposomes encapsulating insulin were synthesized by reverse-phase evaporation method and the shape obtained was either spherical or ellipsoidal. The hypoglycemic effect was evaluated by the oral administration of nanoparticle formulations in mice. Proteolytic activity of pepsin and trypsin was repressed by CEC-coated liposomes that enhanced the enteral absorption of insulin [109].

### Impact of capped nanoparticles in environmental remediation

Environmental pollution increases day by day and now it becomes one of the most serious global menace facing by society as it produces irreversible damage. Continuous urbanization and the breakneck leap of industrialization have disturbed the balance of environmental composition through the release of hazardous materials, smoke, and noxious gases which consequently lead to the toxic effects on living things. Furthermore, over usage of natural resources due to overpopulation, a large number of vehicles, and higher release of smoke from industry and many other factors lead to nature's destruction [110,

111]. Examples of some hazardous materials include heavy metals, pesticides, herbicides, fertilizers, residual pharmaceutical products, poisonous gases, effluents generated by the industries, sulfur-containing compounds, oil spills, matter particulates, sewage, pathogens, organic compounds, etc. These materials release into the environment and eventually contaminate the soil, water, and air, hence compromising the ecosystem and health (like Alzheimer's, dementia, or deafness) [110, 112]. Currently, under present circumstances, sustaining the pure and healthy air and water environment is a key challenge.

Fortunately, novel technologies are now in practice to remediate undesirable products from the air, water, and soil [113]. Among them, nanotechnology exhibits great potential to build and use novel and cost-effective techniques for the detection and monitoring of contaminants, degradation via catalysis, adsorptive removal, and cleaning of the environmental pollutants [113]. In comparison to the bulk materials, nanotechnological products have novel physical and chemical attributes due to their smaller size (< 100 nm) [114, 115] that results in a higher surface to volume ratio which makes them efficient catalyst. Furthermore, higher interfacial reactivity and specific functionalization make nanoproducts as newly miniaturized, precise, and sensitive nanosensors for targeted detection and remediation of undesirable materials. Recently, a myriad of nanomaterials such as carbon nanotubes, polymers, dendrimers, metallic oxide nanoparticles, and many more have been synthesized and employed for the purification of water, air, and soil.

However, researchers have to make sure that nanoparticles should not induce environmental degradation itself while using them in the environmental remediation. Mostly, nanomaterials tend to form aggregates, adsorb into bigger particles or surfaces, or even decomposed [116, 117] that can be toxic to human health and the environment. Meanwhile, the contact of nanomaterials to their environment takes place through their surfaces [118], and hence nanoparticles can even have a higher susceptibility for toxicity. To overcome these limitations and endure their characteristic properties, nanoparticles are generally functionalized, although materials that are used for functionalization have different effects on the physico-chemical properties of nanoparticles [119, 120]. Among them, polymer functionalization of nanoparticles has recently gained significant momentum in the field of environmental remediation due to the integration of both nanoparticles and polymers together under the same system. Polymer-coated nanoparticles are expedient because of their surface properties and pore space, together with their excellent and long-lasting mechanical strength. Moreover, polymer-coated nanoparticles retain their innate features and provide stability and biocompatibility, hence providing a superior surface coating. Furthermore, selectively can also be attained via specific chemical functionalization in order to target certain pollutants. Mainly, due to these properties, the promising use of polymer-coated nanoparticles for remediation and cleaning of environmental pollutants is in practice (Figs. 7 and 8). The basic mechanism of action of polymer-coated nanoparticles comprises of adsorption, catalytic degradation (pollutants), and antibacterial effect especially used in the purification of drinking water [121]. Various types of polymer functionalized nanoparticles used in the environmental remediation are presented in Table 2. These nanomaterials are target specific and do not produce any waste, therefore, there is no requirement to dispose of after treatment, and propose a greener route for environmental remediation [122].

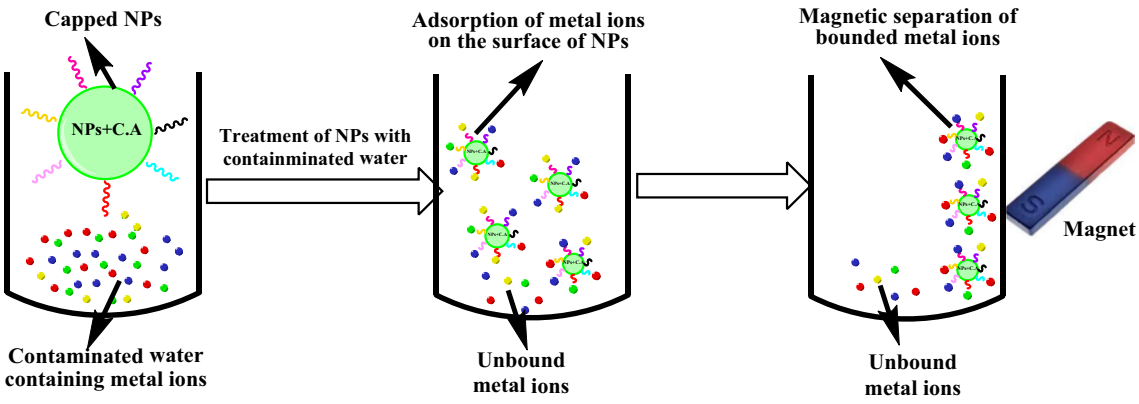


**Fig. 7** Magnetic separation of metal ions from the contaminated water by the use of capped/modified nanoparticles

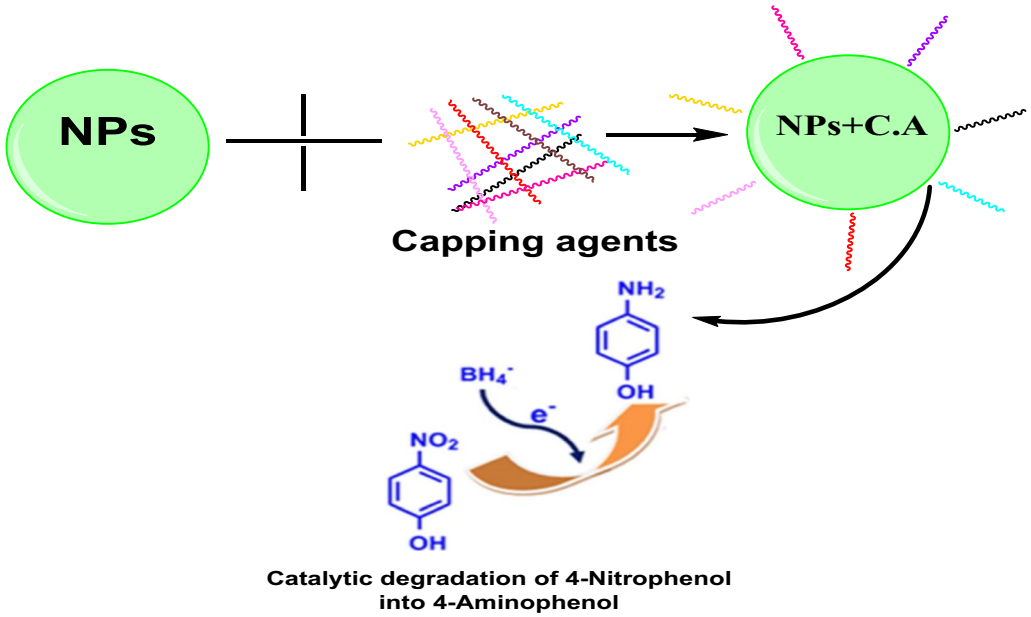


**Fig. 8** Capped nanoparticles undergoing catalytic degradation of 4-Nitrophenol into 4-Aminophenol

**Table 2 Polymer capped nanoparticles employed for environmental remediation applications**

| Nanoparticles | Capping agents | Principle | Substrate | Benefits | References |
|---|---|---|---|---|---|
| Ag | Chitosan | Catalysis | Methyl Orange | Efficient and occur in visible light | [89] |
| Ag | Core–shell magnetic chitosan | Adsorption | Cationic & anionic | Multi-dye adsorption, magnetic separation, and reusability | [90] |
| Ag | PVA | Biosorption | Manganese ions | Immobilized on *Trichosporon cutaneum R57* strain | [91] |
| Ag & ZnO | PVP | Photocatalyst | Methylene blue | Efficient as compared to simple ZnO nanoparticles | [123] |
| Ag | Chitosan | Adsorption | Atrazine (pesticide) | Efficient and reusable | [124] |
| Ag | Two different chitosan microparticles | Adsorption | Methyl parathion (pesticide) | Efficient and reusable | [125] |
| Ag & Au | Chitosan | Adsorption | Methyl parathion (pesticide) | Thermostable, highly hydrophilic | [126] |
| Au | PVP | Adsorption | Mercury | Efficiency can be controlled via optimizing the concentration of PVP | [127] |
| Fe | PVP | Catalytic adsorption | Bromate | Efficient and prolonged storage | [128] |
| Au | Chitosan | Sensor | Copper and Zinc ions | Detect even the lowest metal concentration | [129] |
| Magnetite | Chitosan & polythiophene | Adsorption | Mercury (II) | Efficient and sensitive | [130] |
| Silver tin sulfide | PEG | Catalysis | Eosin yellow & brilliant green dyes | Efficient, photostable, and recyclable | [131] |
| $TiO_2$ | PVA | Photocatalysis | Rhodamine B | Highly efficient, stable, and reusable | [132] |
| Ag | PVA | Sensor | Hydrogen peroxide | Simple, cost-effective and reliable | [96] |

## Conclusions and future implications

In essence, this novel survey unveils the favorable aspects of various capping agents in nanobiotechnology. Although designing the capped nanoparticles exhibiting significantly enhanced biomedical and environmental remediation properties as compared to the uncapped nanoparticles is very challenging, literature is increasing that highlights the unanticipated beneficial role of capping agents in different biological approaches. The controlled size, morphology, and surface composition achieved by nanoparticles' capping are crucial in determining the vital application of nanoparticles. However, such protocols need to be optimized that could efficaciously validate the capping phenomenon of stabilizers, and more reproducible experiments should be performed that could remove any discrepancies in getting the pure and controlled effect of the appropriate capping agents. Moreover, advanced characterization techniques should be utilized that would finely interpret the role of capping agents in the nanoparticle-stabilizer interface. Besides, in vitro and in vivo toxicity studies of capped nanocomposites should be conducted since the risk assessment of pharmacological and bioremediation activities are requisites to be strictly achieved in laboratory and clinical practices.

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**Authors' contributions**
RJ and MZ conceived the idea. RJ, SN, SOA, and NUA wrote the manuscript. RJ, MZ, and QA compiled the final draft and did the editing. RJ and QA were involved in funding. All authors read and approved the final manuscript.

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**Competing interests**
The authors declare that they have no competing interests.

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