MINI REVIEW

RECORDS OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Green Nanoparticles as a Novel Application of Nanotechnology in Medicine: Study of zinc, Copper and Magnesium Nanoparticles

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Abstract

The objective of this review study is to shed light on the effective role played by nanotechnology, especially nanoparticles, in the medical field. We take nanoparticles of zinc, nanoparticles of magnesium, and nanoparticles of copper, as examples. The conventional methods of developing NPs are costly and produce very toxic product, so the need of hour is to reduce the risk of toxicity in the environment from the different chemicals used in the physical and chemical methods. The alternate approaches found to develop NPs is “green synthesis. The green synthesis of nanoparticles is a novel way to synthesize nanoparticles by using biological sources. It is gaining attention and attracted the scientists from different fields due to its simplicity, and environmentally-friendly nature. In green synthesis, we use many plants that can contribute to converting metals into the nanoform, such as the purslane plant, which converts zinc and copper into the nanoform, which contributes to increasing the potency and biological and pharmaceutical activity of the two metals, as well as the basil plant, which contributed to the conversion of magnesium. To magnesium oxide, which has great effectiveness and great influence in the medical field **.**Green synthesis could produce nano-sized materials that could be a solution to many pathological conditions, such as those related to inflammation or oxidative stress.

Keywords: Nanotechnology, Nanoparticules, Green synthesis, Medical application

1. Introduction

Nanotechnology is an area of emerging interest in the field of science and technology due to its wide variety of applications in the field of biomedicine, optics, and electronics (Mubarak et al., 2019). The emergence of nano-medicine has enriched the knowledge and strategies of treating diseases, and especially some incurable diseases, such as neurodegenerative diseases. The application of nanoparticles in medicine is in the core of nano-medicine (Leng et al., 2018).

Nowadays, nanotechnology involving green synthesis of nanoparticles has become an eye-catching idea (Chartarrayawadee et al., 2020). Recently, plant-mediated route or green approach for preparing metal and metal oxide nanoparticles has received enormous attention due to the ease of preparation and environmental friendliness when compared to physical and chemical methods (Enobong et al., 2019).Biosynthesis of nanoparticles using plant extracts is gaining importance in biomedical applications because of their unique properties (Poka et al., 2019). Metallic nanoparticles (MNPs) have considerable interest owing to unique properties of nanoparticles (NPs) such as small size and the greater surface area to volume ratio (Yao et al., 2019). Magnesium, zinc and copper known as potential metal involved in metabolic organism regulation, where the zinc oxide nanoparticle (ZnNPs) is considered as one of the most promising and novel magic materials because of its unique catalytic and antimicrobial properties as well as its low cost and extensive applications in diverse areas (Erjun et al., 2006). Also the copper nanoparticles (CuNPs), from their unique physical and chemical properties and the low cost of preparation, have been of great interest recently (Honary et al., 2012) copper nanoparticles have potential applications in diverse fields including biomedicine (Rubilar et al., 2013). Magnesium is involved in several essential physiological, biochemical, and cellular processes regulating cardiovascular function (Kolte et al., 2014).

Magnesium oxide (MgO) is a category of the practical semiconductor metal oxides, which is extensively used as catalyst and optical material (Nemade & Waghuley, 2014). Magnesium oxide (MgO) is widely used in the chemical and pharmaceutical industry (Meenakshi et al., 2012).

The aim of this review study is to shed light on the effective role played by nanotechnology, especially nanoparticles, in the medical field. We take as examples zinc nanoparticles, magnesium nanoparticles, and copper nanoparticles, to determine the methods of phyto- preparation for them and to know their role in treating many diseases.

Nanotechnology

Nanotechnology is one of the most promising technologies of the 21st century. It is the ability to observe measure, manipulate, assemble, control, and manufacture matter at the nanometer scale generally from 1 to 100 nm (Bayda et al., 2019).Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization, and application of materials and devices whose smallest functional organization, in at least one dimension, is on the nanometer scale or one billionth of a meter (Saini et al .,2010).

Nanotechnology is one of the most promising technologies of the 21st century. It is the ability to convert the nanoscience theory to useful applications by observing, measuring, manipulating, assembling, controlling and manufacturing matter at the nanometer scale (Bayda et al., 2020). Nanotechnology has opened up by rapid advances in science and technology, creating new opportunities for advances in the fields of medicine, electronics, foods, and the environment (Morais et al.,2014). Nanotechnology has emerged as one of the leading felds of the science having tremendous application in diverse disciplines (Gatoo et al.,2014). It employs knowledge from the fields of physics, chemistry, biology, materials science, health sciences, and engineering. (Godwin et al., 2015).Researchers use bionanotechnology techniques as eco-friendly and cost-effective routes to fabricate nanoparticles and nanomaterials (Linhai et al.,2018). In recent years there has been a rapid increase in nanotechnology applications to medicine in order to prevent and treat diseases in the human body (Gopal et al., 2010).

3. Application of nanotechnology

Recently, nanotechnology has been a subject of great interest, offering considerable advantages in many areas an increased interest in nanotechnology applications can be observed in various fields (figure 1) medicine, materials science, pharmacy, environmental protection, agriculture **(Baranowska-Wójcik et al., 2019),** nutrition, and energy (Elumalai et al., 2019). Their reactivity, toughness and other properties are also dependent on their unique size, shape and structure**.** Due to these characteristics, they are suitable candidates for various commercial and domestic applications, which include catalysis, imaging, medical applications, energy-based research, and

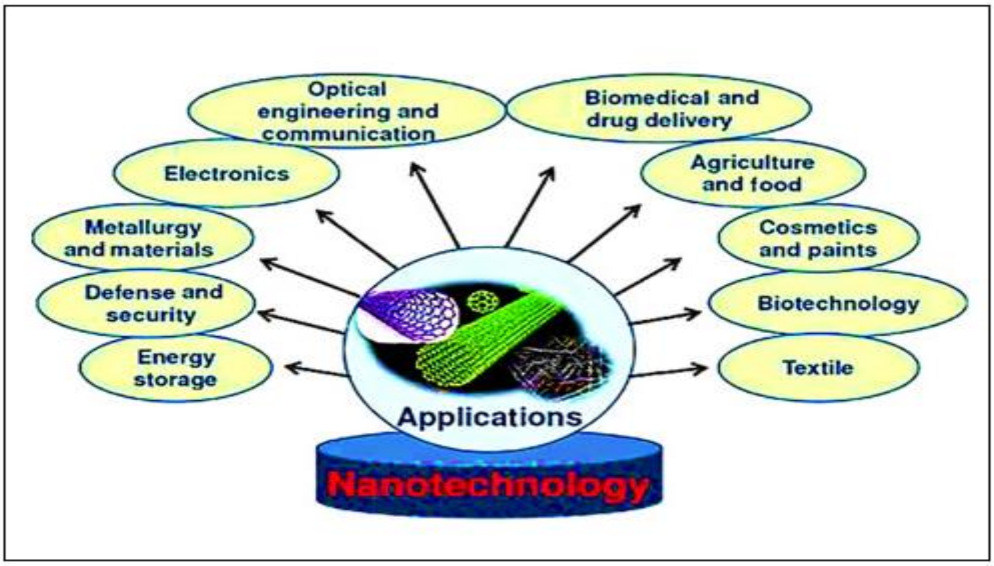

Figure 1: Applications of nanotechnology (Nasrollahzadeh et al., 2019)

environmental applications (Khan et al., 2019). Medical applications of nanotechnology (commonly known as nanomedicine) are expected to significantly improve disease diagnostic and therapeutic modalities and subsequently reduce health care costs. The use of nanotechnology in medicine has the potential to significantly improve human health and wellbeing due to highly accurate and sensitive diagnostic tests (Satalkar et al., 2015).

4. Metal nanoparticles

The prefix 'nano' is referred to a Greek prefix meaning 'dwarf' or something very small and depicts one thousand millionth of a meter (10-9 m) Bayda et al., 2020). Where nanoparticles have been shown to have utility in various fields of science (Sharma et al .,2017) and possess unique (physical and chemical properties due to their high surface area and nanoscale size (Khan et al.,2019). The metal nanoparticles exhibit many properties that are very useful or can be manipulated for numerous new scientific studies and multitudes of technological applications (chetehouna et al., 2024). Recently, there are advances in the use of metal nanoparticles in the study of biomolecular interactions, developing bioassays and biomedical devices, and various other biomedical applications such as immunodiagnostics, drug delivery, therapeutics, and gene transfer (Mei & Wu, 2017). Nanoparticles have great interest due to their extremely small size and large surface to volume ratio (figure 2), which lead to differ in their property such as the biological one, compared to bulk of the same chemical composition (Iravani, 2011).

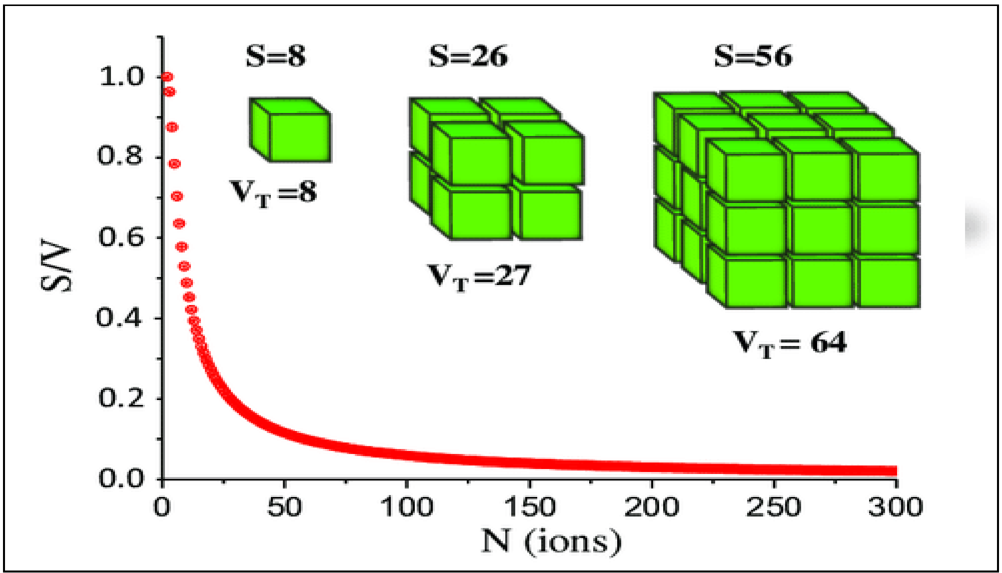

Figure 2: Ratio of surface to volume ions in a cubic lattice, for very small nanoparticles (Pineiro et al., 2020)

5. Green synthesis of nanoparticles

Nowadays, nanotechnology involving green synthesis of nanoparticles has become an eye-catching idea and has gained much importance and significance in recent years due to its great facility, clean processing, non-toxic chemicals used, cost-effectiveness, and being environmental and ecofriendly (Chartarrayawadee et al .,2020). The conventional methods of developing NPs are costly and produce very toxic product, so the need of hour is to reduce the risk of toxicity in the environment from the different chemicals used in the physical and chemical methods. The alternate approaches found to develop NPs is "green synthesis". (Gour & Jain, 2019). Green synthesis method, provides a faster metallic nanoparticle production by offering an environmentally friendly, simple, economical and reproducible approach. Given the wide range of applications of metallic nanoparticles produced, biological methods play a major role in the synthesis of metallic nanoparticles (Nadaroğlu et al., 2017). The green synthesis of nanoparticles is a novel way to synthesize nanoparticles by using biological sources. It is gaining attention and attracted the scientists from different fields due to its simplicity, and environmentally-friendly nature (Sara et al., 2023), especially in light of efforts to find greener methods of inorganic material synthesis (Philip, 2009), due to the growing need to develop environmentally benign technologies in material synthesis (Bar et al., 2009). The biosynthesis for obtaining nanoparticles using naturally occurring reagents such as vitamins, sugars, plant extracts, biodegradable polymers, and microorganisms as reductants and capping agents (figure 3) could be considered attractive for nanotechnology (Derouiche et al., 2022).

Biosynthesis of nanoparticles is more unique and reliable not only because of its less toxicity as compared to some of physicochemical production methods but also because it can be used to produce large quantities of nanoparticles that have well shape and size. The biological synthesis approaches may actually produce nanoparticles of a better defined size and morphology as compared to some of other physicochemical methods of production (Khandel et al., 2018).

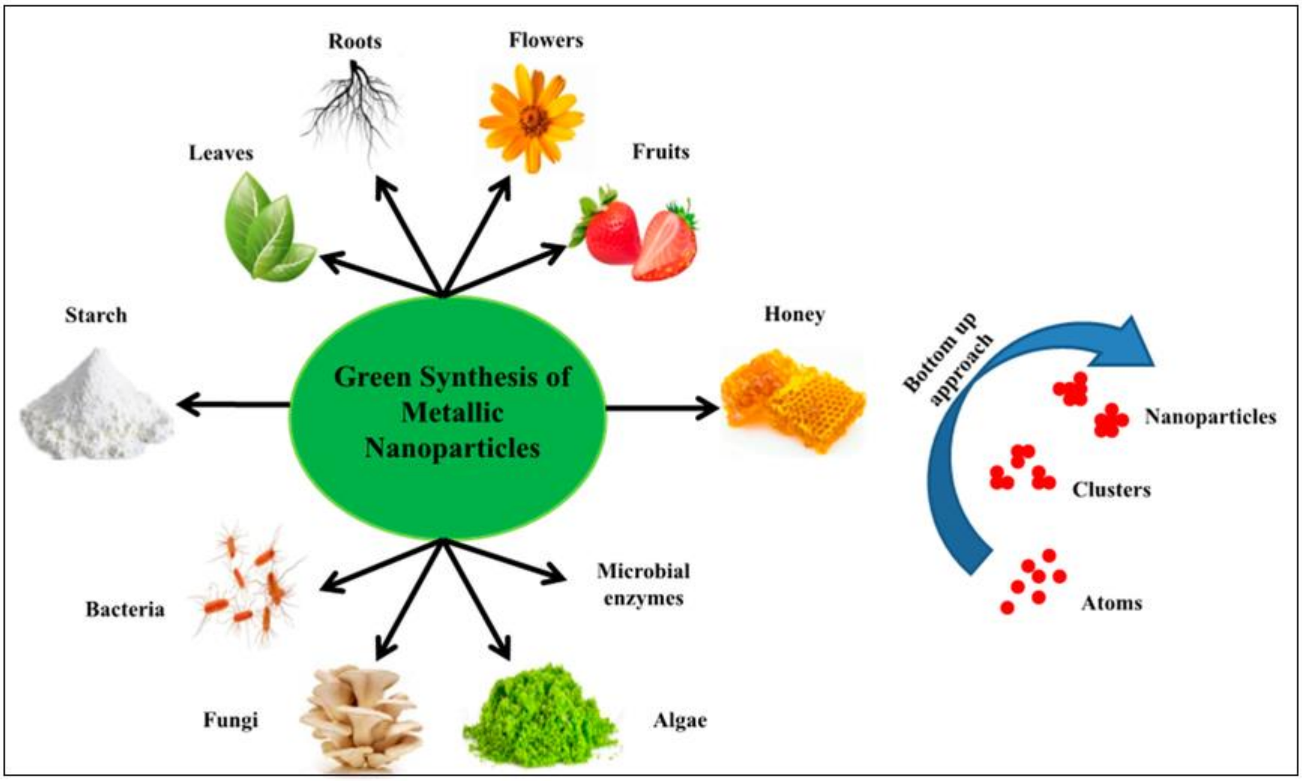

Figure 3: Green synthesis of nanoparticles (kumar et al., 2020).

6. Magnesium oxide nanoparticle

The metal elements are able to form a large diversity of oxide compounds (Meenakshi et al., 2012). MgO NPs are one such metal oxide NP, exhibiting increased utilization in recent time (Verma et al. 2020). Nanoscale MgO possesses unique optical, electronic, magnetic, thermal, mechanical and chemical properties due to its characteristic structures (Narendhran et al., 2019). Magnesium oxide (MgO) is a category of the practical semiconductor metal oxides, which is extensively used as catalyst and optical material (Nemade & Waghuley, 2014). MgO is an important inorganic oxid (Tang et al.,2014) .And that has many applications(Camtakan et al .,2012).6- Magnesium oxide (MgO) is widely used in the chemical industry (Meenakshi et al., 2012).

6.1. Method of phytosynthesis of MgNPs using Ocimum basilicum

In the experiment, 5 ml of fresh leaves extract and 20 ml of distilled water was added to a 250 ml beaker and heated at 60ºC. 5 gram of Magnesium Nitrate is added to the solution and heated at 80°C with continuous stirring for 4hours. The Magnesium nitrate ions were reduced to Magnesia or Magnesium Oxide nanoparticles by using leaves extract. The formation of Magnesium oxide nanoparticles (MgNPs) have been observed by color change of the solution from yellow to yellowish-brown color (Samir et al., 2020).

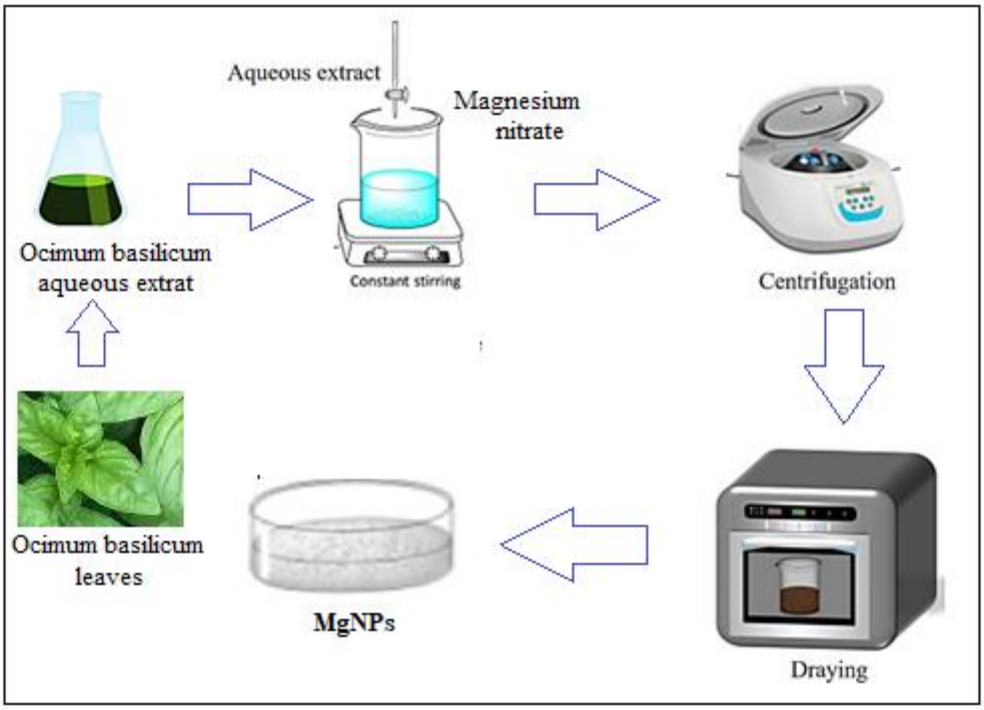

Figure 4. The method of phytosynthesis of Magnesium nanoparticles using Ocimum basilicum aqueous extract.

6.2. Pharmacological application of MgNPs

Nanomaterials such as nanostructured surfaces, nanoparticles, and nanocomposites represent new viable sources for future therapeutics for cardiovascular diseases (Jiang et al., 2017). Nanoparticles can easily cross the cell membranes and interact with intracellular metabolism (Kumar et al., 2017). Due to their small size, therefore accumulate in organs (Staroń et al., 2020). Magnesium oxide nanoparticles (MgO) are considered a promising alternative to heavy metal based nanoparticles, because (MgO) contains metal ion Mg^{2+} (mineral) that is essential for human health (El-Shaer et al., 2019). Magnesium is involved in several essential physiological, biochemical, and cellular processes regulating cardiovascular function (Kolte et al., 2014). Magnesium (Mg^{2+}) is involved in several essential physiological, biochemical, and cellular processes regulating cardiovascular function (Kolte et al ., 2014). Deficiency of magnesium may result in many disorders, including cardiac arrhythmias (Cieoelewicz et al ., 2013). Where it is considered .Mg^{2+} is the most abundant divalent cation in living cells and it plays a vital role in many cellular processes (Chakrabort et al ., 2002).Also magnesium status is closely linked with liver function .where Magnesium deficiency is commonly associated with liver diseases (Liu et al ., 2019). Considered .Magnesium is essential for the stability of cell function, RNA and DNA synthesis, and cell repair, as well as maintaining the antioxidant status of the cell ,and it is an important cofactor for the activation of a wide range of transporters and enzymes (Uwitonze et al ., 2019). Mg was found to reduce the production of free radicals by inhibiting NADPH oxidase, which could stimulate the production of reactive oxygen species Also, Mg 2+ is also an essential cofactor in glutathione biosynthesis (Zhang et al ., 2016).

7. Zinc nanoparticles (ZnNPs)

The ZnNPs, characterized by its small size facilitates the absorption of zinc by the body, which make it attractive in the biomedical application (Jiang et al., 2018). Where zinc (Zn) is a well-known as essential trace element that is highly distributed and plentiful, it plays an important role in many cellular functions including neurotransmission, gene regulation, structural maintenance, enzymatic activity and protect the blood-brain barrier (BBB) from oxidative damage and prevent the progress of neurodegenerative diseases. Thus, ZnO NPs have drawn the attention of many biotechnologists as it has useful properties with potentially unlimited therapeutic applications (Derouiche et al., 2022).

7.1. Method of phytosynthesis of zinc nanoparticles using purslan

In order to prepare ZnNPs, as shown in figure 06, 200 ml of aqueous zinc sulfate was mixed with 20 ml of purslane leaves aqueous extract. The ions, which initiated the reaction, were afforded by the zinc sulfate in de-ionized water. The reaction mixture was incubated with constant stirring in the dark at 60 °C to avoid photo-catalysis. An observed off-white color marked the formation of ZnO NPs at the end of 24 h. The resultant product was further purified by centrifugation and washed in double-distilled water and ethanol, respectively, dried and kept in an amber-coloured sample bottle until use (Derouiche et al., 2022).

7.2. Pharmacological application of ZnNPs

The anti-inflammatory activity of ZnNPs as reported by (Nagajyothi et al., 2015), who reveled this activity in ZnNPs synthesized from *Polygala tenuifolia* root extract, by the reduce of the mRNA and protein expressions of interleukin 6 (IL-6) and tumour necrosis factor alpha (TNF- α) on polysaccharides induced inflammation in RAW 264.7 macrophage. Also, the copper nanoparticles have a good anti-inflammatory activity as what demonstrated by (Angajala et al., 2014). The information obtained from (Jarosz et al., 2017) suggest that zinc supplementation may lead to down-regulation of the inflammatory cytokines (IL-1β and TNF-α) through up-regulation A20 to inhibit induced NF-κB activation.

The mechanism of what could be the ZnNPs enter in the target cells where it dissociates and slowly but consistently released as Zn^{+2} ions (Hassan et al., 2019). It is well known that Zn is a powerful antioxidant metal; it is the core constituent of the antioxidant enzymes such as SOD (Abd El-Fatah et al., 2017). The activity of antioxidant, which then detoxify the free radicals. These factors protect cells from ROS damaging (Atef et al., 2016).

8. Copper nanoparticles (CuNPs)

Copper nanoparticles, due to their unique physical and chemical properties and the low of preparation, have been of great interest recently (Derouiche et al., 2022**)**. Additionally, Cu NPs are efficient catalysts, with high yields and easy product separation, and they can be reused repeatedly. Cu -free ions are potentially harmful to the human body at the cell, organ, and body levels. Therefore, Cu ions in living organisms should be regulated. Cu NPs can be easily oxidized to form copper oxides (CuOs), which are inorganic NPs (Ji et al.2023).

8.1. Method of phytosynthesis of copper nanoparticles using purslan

In order to prepare CuNPs, 1g of the copper sulfate was added into the defined amount of the prepared walnut aqueous extract (10mL) and the reaction solutions were mixed using a heater-stirred, adjusted at 500 rpm and 70°C, for 15 min. Finally, the samples were put in an electric furnace memmert adjusted at 200°C for 2 h. The obtained powders washed in double-distilled water and ethanol respectively, as farmed CuO NPs, were then used for further studies (Atoussi et al 2020) (figure 6).

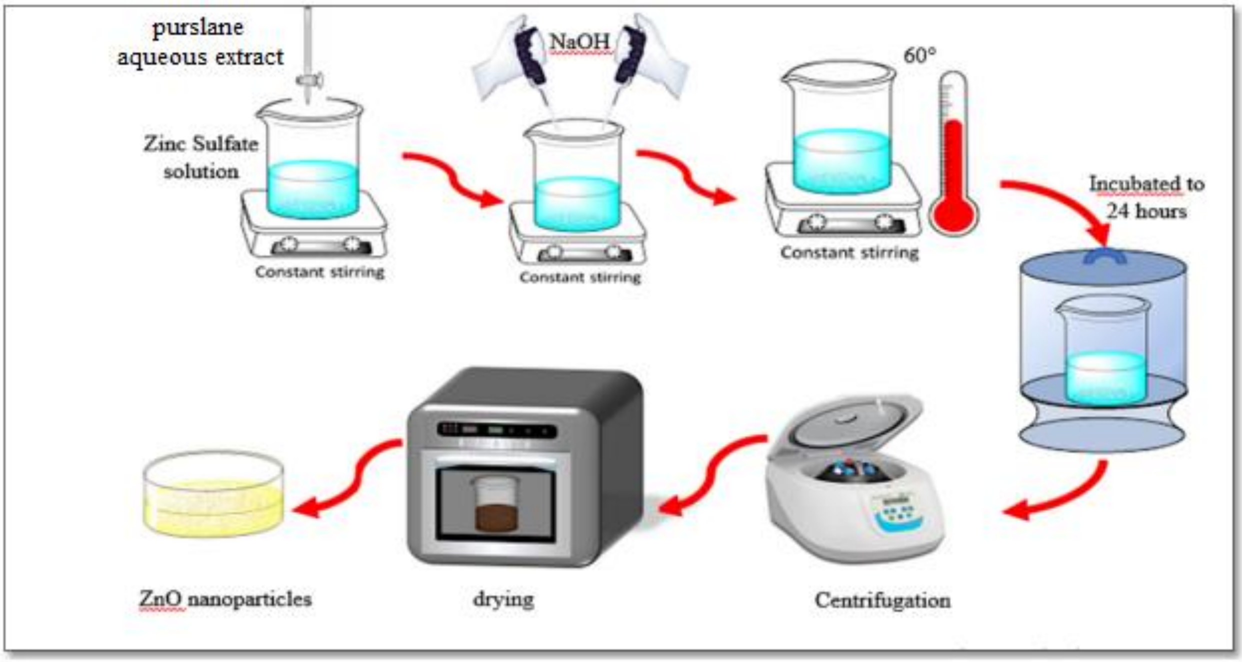

Figure 5. The method of phytosynthesis of zinc nanoparticles using purslan aqueous extract (Chetehouna et al 2020).

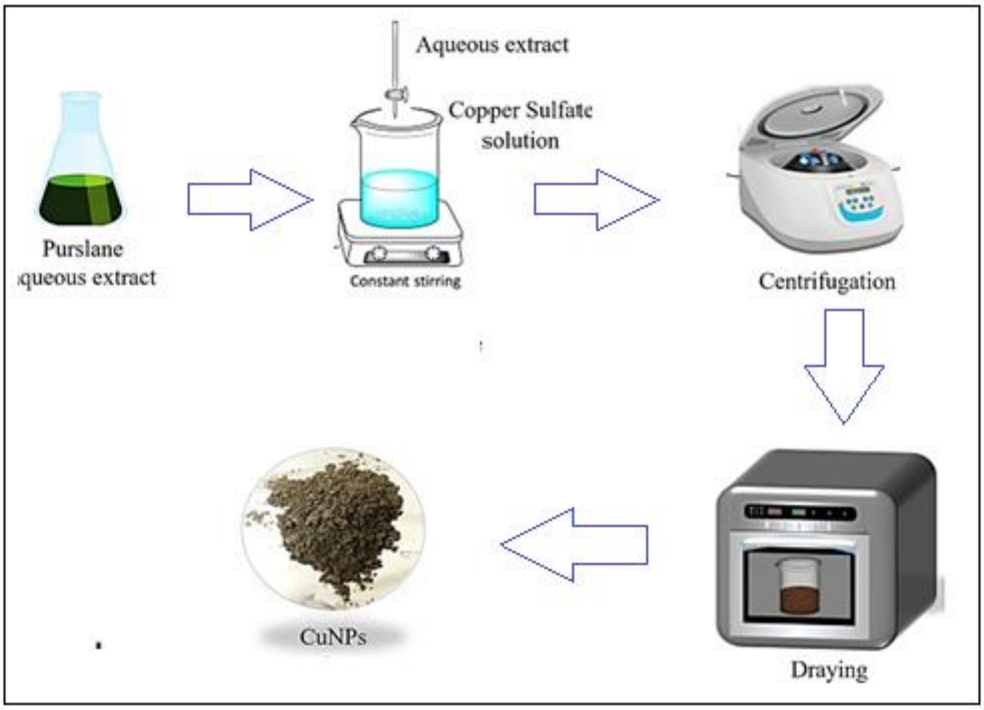

Figure 6. The method of phytosynthesis of copper nanoparticles using purslan aqueous extract.

8.2. Pharmacological application of CuNPs

According to the distinctive properties of copper, the copper oxide (CuO) based nanomaterials are gaining importance in biomedical sciences that includes both, diagnosis and therapy (Verma & Kumar, 2019). Thus, the research is increasingly carried out on replacement of standard Cu forms with nanoparticles (CuNPs), due to their very small size and specific surface area; it is assumed that, they may be differently utilized by the body than their macro counterparts. This suggests that they may be better absorbed in the body (Cholewińska et al., 2018). Moreover, copper is an essential trace element that is required as a cofactor for normal functioning of various metabolic enzymes. This property can be used to synthesize antitumor formulations that induce killing of tumor/diseased cells by altering the intracellular level of copper ions. Due to their nano size, they are easily accessible to the micrometer-sized human cellular entity and can readily interact with the biomolecules present on the cell surface and intracellularly (Verma & Kumar, 2019). The copper has an antioxidant role through involvement in maintaining antioxidant defenses, which may to ameliorate the state of oxidative stress (Buzadžić et al., 2002).

Conclusion

One of the many examples of the tremendous development in nanotechnology is its uses in the medical field in treating many diseases due to its great interaction with biological systems inside the human body, which is what we observed in metallic nanoparticles that have great effectiveness and are characterized by being environmentally friendly, especially those that are prepared by the biological method. An example of These are nanoparticles of zinc, copper, and magnesium, which have significant therapeutic properties in the body, and which we nominate to take their place to reduce the economic burdens of the pharmaceutical industry or mitigate the damage resulting from chronic diseases.

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