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Biosynthesis of nanoparticles for wound healing property: A Review

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ABSTRACT

Physicians and the entire medical community have a problem when it comes to the treatment and management of wounds. For this purpose, a number of medications and formulations are available. Nanoparticles that are either bio- or green-synthesized among them are becoming more significant. To create nanoparticles, metallic ions such as zinc oxide and silver are used as starting materials. In the current work, the wound-healing capabilities of nanoparticles are examined. The biosynthesis of plant materials, bacteria, etc. produces the nanoparticles. When challenged, zinc oxide nanoparticles exhibit antibacterial, anti-inflammatory, and wound-healing properties. Zinc oxide nanoparticles produced through biosynthesis are useful in preventing tissue epithelialization, re-epithelialization, tissue scarring, stem cell activation, platelet activation, debris removal and angiogenesis. At the time of healing process for wounds, they either work together or separately to carry out the aforementioned process. In order to cure wounds, a wide variety of biosynthesized zinc oxide nanoparticles are used.

Keywords: *Wound healing, Zinc oxide nanoparticles, Microorganisms, Biosynthesis of zinc oxide nanoparticles*

INTRODUCTION

A wound is a separation or breaking of tissue or tissue components. It can be divided broadly into open wounds and closed wounds. Open wounds occur when the body's natural defences are violated, allowing foreign objects to enter the tissues. Closed wounds prevent the damaged tissues from being exposed to the environment, allowing the healing process to proceed unhindered by impurities. Both types of wound healing present more of a difficulty, particularly in surgical cases.

The physiological process of healing a wound is intricate and involves the regeneration and repair of tissue. Many medications and preparations with both natural and synthetic origins are used to treat wounds[1]. Nowadays, wound management solutions made with nano-silver and nano-zinc, which are employed for their antibacterial qualities, are used. One such composition that works well for managing wounds through various applications is nanoparticles. Researchers are looking into the potential of nanoparticles in the treatment of wounds. Zinc oxide nanoparticles, however, have not undergone enough testing to determine whether they can speed up healing[2]. Due to their small size and versatility, metal oxide nanoparticles are of considerable interest.

Silica hydrogel biomaterials aid in wound epithelialization, provide a moist environment, and absorb exudates. During surgery, bacterial wound infections can be brought on by both airborne diffusion from a contaminated environment and direct contact with the pathogen through contaminated surgical equipment. When the pH of a wound is neutral at the start of an infection, several microbial populations are present; these populations change as chronic wounds develop. Anaerobic bacteria are made more likely to exist as the pH rises and becomes more alkaline[3].

Bacterial resistance to antibiotics is one of the biggest problems that doctors and other healthcare professionals face when treating and managing wound infections. This is because pathogenic bacteria are constantly evolving antibiotic resistance mechanisms, making it difficult to treat infections brought on by these bacteria. Particularly Staphylococcus aureus and other Staphylococci species colonise wound infections. This has a significant impact on the pathophysiology and aetiology of wound infections. This happens as a result of polluted surface, liquid, and atmospheric exposure. Making an acidic environment in a wound bed has another benefit in that it aids in wound healing. Utilising citric acid has been found to accelerate the healing of wounds by enhancing antibacterial activity, preventing infection, and encouraging angiogenesis and epithelialization[4]. Chemical and physical approaches can be replaced by the biosynthesis of NPs in a more efficient and sustainable way. The green chemistry process of plant-mediated synthesis of NPs combines nanotechnology and plants. Research is significantly impacted by the large specific surface area to volume ratio of metal nanoparticles compared to the analogous bulk materials[5–9].

Metal oxide nanoparticle production is essential to the growing field of nanotechnology because of its peculiar properties linked to a single species. Numerous attempts have been made to create nanoparticles from various metal and plant species. Regarding their qualities and effectiveness in healing the wound, zinc oxide nanoparticles are discovered to be the best. Table-1 shows some of the plant species with different metallic nanoparticles.

TABLE 1

Plant names	**Nanoparticles**
Hibiscus subdariffa	ZnO
Burkholderia cepacia	Fe_3O_4
Padina pavonica	CuO
Calotropis procera	ZnO
Arachis hypogaea	Cu_2O
Azadirachta indica	Cu_4O_3
Aloe barbadensis	Cu_4O_3
Glycosmis mauritiana	Fe_3O_4
Cassia fistula	ZnO
Phyllanthus amarus	CuO
Gum karaya	CuO
Aloe barbadensis	ZnO
Ocimum basilicum	ZnO
Solanum lycopersicum	CuO
Sapindus mukorossi	Fe_2O_3
Camellia sinensis	Fe_2O_3
Hibiscus rosa-sinensis	Cu_4O_3
Aloe barbadensis	Fe_2O_3
Aloe barbadensis	CuO

Optical microscopy examinations of the epithelial surface of the mice's wounded skin after 11 days of treatment with zinc oxide nanoparticles reveal the skin's healing process. The nanoparticles successfully closed wounds in an attractive manner and could act as a strong anti-microbial adhesive for the tissues. When used as a dressing, zinc oxide nanoparticles accelerated several wound healing processes in mice, including tissue scar formation, tissue necrosis, bacterial elimination, apoptosis, debris removal, platelet activation, re-epithelialization, angiogenesis and stem cell activation. In mice, the zinc oxide nanoparticles dressing was found to have features that better inhibited bacterial growth, were biocompatible, and hastened wound healing, all of which point to its medicinal potential [10,11].

Microscopic studies demonstrated that mouse tissues underwent hemostasis, proliferation, inflammation, and remodelling during the healing process. In mice skin wounds, zinc oxide nanoparticles have the potential to close wounds effectively and cosmetically while acting as effective antibacterial adhesives for the tissues. After 11 days, a microscopic examination of the wound's skin revealed that zinc oxide nanoparticles had the highest level of healing potential. A complex series of cellular and molecular processes that result in resurfacing of the damaged skin's tensile strength, restoration, reconstitution and carry out wound healing, which is a typical healing response to tissue damage[12].

Hemostasis is the first phase of wound healing, followed by inflammation, proliferation, and maturation, which often results in the creation of a scar. Migration of plasma proteins and cells into the wound matrix, which is predominantly made of fibrin, is described. During the first 2 to 4 days after healing, inflammatory cells such as neutrophils and macrophages clear wounded tissues (inflammatory phase). They also produce mitogenic and chemotactic proteins and protect against infections[13-17]. During the proliferative phase, epithelization and angiogenesis take place simultaneously. Additionally, the fibroblasts already present in the surrounding tissues begin to grow on the fibrin component to produce collagen, which is a crucial development in this phase[18]. During the maturation stage, the newly formed collagen molecules later cross-link with the pre-existing protein and collagen molecules, boosting the scar's tensile strength[19].

The maturation phase begins during the second weekend of recovery and lasts an indeterminate amount of time[20]. Despite recent advances in wound healing, researchers are still exploring for medications and other remedies that can help minimise the amount of scar tissue and ultimately aid in the remodelling of the lesion. Much progress has been made in the production of artificial nanoparticles for a variety of biological applications[21].

On the other side, a major increase in the number of antibiotic resistances in predatory and medically notable bacterial pathogens have led the scientific community to pursue the creation of novel drugs on a continual basis. Novel antibacterial treatments have improved in recent years as a result of the continuous selection of antibiotic - resistant features; yet, none of these drugs have enhanced efficacy towards multi-drug resistant organisms.

Additionally, the nanoparticles' antibacterial properties and the development of novel uses in this field make them a viable alternative to pharmaceutical antibiotics. The difficult task of developing novel antiviral drugs that attack the virus while preserving the viability of the host cell has millions of unfavourable impacts every year. For instance, the ability of nanoparticles to reduce skin infections and burn injuries has been researched. Fast wound healing with optimum function and minimal scarring is the ultimate goal[22–27].

Zinc oxide nanoparticles are a biosafe material having a wide bandwidth, high excitation energy, antibacterial, antifungal, anti-diabetic, anti-inflammatory, wound-healing, antioxidant, and optical characteristics. Green methods utilising plants, fungi, bacteria, and algae have been utilised due to the high concentration of hazardous chemicals and harsh environment used in the physical and chemical manufacturing of these NPs[28].

Many techniques, including metallorganic chemical vapour deposition, zinc oxidation, hydrothermal synthesis, vapour phase deposition, chemical vapour deposition, vapor-liquid-solid, can be used to create zinc oxide nanoparticles. Green chemistry concepts are used to generate ZnO NPs. Plant extracts are recognised to be vital in the production of various nanoparticles, such as graphene and silver. A number of plants are used to create zinc oxide nanoparticles[29,30,31].

The two most popular processes for creating zinc oxide nanoparticles are hydrothermal synthesis and vapor-liquid-solid synthesis. Microorganisms, phyto extracts, and natural biomolecules have lately been employed in the synthesis of nanoparticles due to their non-hazardous, inexpensive, biodegradable, and environmentally benign qualities. Nevertheless, surface capping agents can make zinc oxide nanoparticles more dispenseable, which is easily accomplished using environmentally friendly synthesis techniques. A variety of environmentally friendly technologies have been used to create zinc oxide nanoparticles.

It has already been reported that numerous plants and plant component extracts can be used to make water dispersible ZnO NPs. The precursor Zn(CH2CO2)2. 2H2O was utilised to create zinc oxide nanoparticles from zinc acetate dihydrate. After being heated to 70oC, 100 ml of distilled water was added to the 100 ml of extract to dilute it. Then, in this solution, 20 g of zinc acetate salt was dissolved. It was then continuously heated and magnetically stirred at 70°C and 800 rpm, and 2M potassium hydroxide solution was added drop by drop until the pH reached 11. The creation of nanoparticles was confirmed by a progressive shift in the colour of the solution, which during the process went from solid brown to yellowish white.

Precipitation generation increased gradually until heavy precipitation was obtained. The resulting mixture was maintained at room temperature for three days. The pellet was washed with distilled water before being centrifuged twice at 4000 rpm for 25 minutes, and the supernatant was discarded. The generated viscous gel was put into an oven set to 90°C to create a dried mass that was brown in color before being pulverised to a fine powder. Biological organisms such as bacteria, fungi, actinomycetes, yeast, algae, and plants are used to make nanoparticles. At ambient pressure and temperature settings, it is demonstrated that biological agents significantly speed up the rate of metal ion reduction. Several studies have shown that ZnO nanoparticles speed up both acute and chronic wound healing. ZnO nanoparticles made by green synthesis or biosynthesis of different plants are effective against microbes, fungi, and wounds.

According to studies, *Aloe barbadensis*-derived zinc oxide nanoparticles have the ability to close wounds more quickly and boost recovery rates when compared to untreated controls. *Coleus amboinicus*-derived zinc oxide nanoparticles have better antibacterial and wound closure rates. Nanoparticles from *Wattakaka volubilis* have antibacterial and antihyperglycemic properties. Zinc oxide nanoparticles have antimicrobial properties and can be found in *Leptadenia hastata*, Achillea nobilis, and strawberry leaves. In comparison to chemically generated ZnO nanoparticles, *Lawsonia inermis* zinc oxide nanoparticles demonstrated a higher rate of wound healing. Zinc oxide nanoparticles from *Aerva javanica* have antibacterial properties. *Quercus infectoria* ZnO nanoparticles have antioxidant and anti-diabetic properties, and ZnO nanoparticles from *Solanum torvum* have wound-healing capabilities. Photocatalytic degradation is present in the *Serratia nematodiphila* strain.

Also created from microbes, zinc oxide nanoparticles have a variety of characteristics. These nanoparticles have excellent antimicrobial properties. Nanoparticles are produced chemically as well as by microbes and plants. These nanoparticles also have a variety of medical benefits, including antimicrobial, antibacterial, and wound healing characteristics. The effectiveness of plant-made nanoparticles in treating wounds has been demonstrated among the available nanoparticles[32–34].

Coleus amboinicus Lour, also known as Indian Borage, is a tender, fleshy perennial that contains a high concentration of flavonoids such as apigenin, genkwanin, quercetin, salvigenin, and luteolin, as well as phytochemicals such as caryophyllene (a bicyclic sesquiterpene), patchoulene, and carvacrol. The most common conditions for which this plant has been utilised in diagnostic procedures are hepatopathy, malarial fever, renal and cough, vesical calculi, hiccough, chronic asthma, anthelmintic bronchitis, convulsions, and colic[35]. The ability of the created nanoparticles to treat burn wounds and combat bacteria has been studied. Three fundamental conditions must frequently be met by wound dressings in order to be truly effective: they must keep wounds clean and free of infectious diseases, they must maintain wound moisture to expedite healing and prevent maceration, and they must absorb fluid exudates and toxic substances[36].

CONCLUSION

Plants can be used for the biosynthesis of ZnO nanoparticles, which offers a number of benefits including ease of use, low cost, good stability, quick processing, absence of harmful byproducts, environmental friendliness, and large-scale synthesis. Intense study is being done on the special catalytic, magnetic, electrical, optical, antibacterial, wound-healing, and anti-inflammatory properties of nanoparticles. The best choices for wound care and management are biosynthesized nanoparticles. Microorganism-derived nanoparticles are highly active against bacterial, fungal, and viral species.

However, more studies are required to explain the mechanism involved in it. This review's findings support the conclusion that zinc oxide nanoparticles derived from plants have superior therapeutic efficacy for wound healing through improved scar formation and a reduction in epithelialization time, while nanoparticles derived from microorganisms play a major role in antimicrobial efficacy.

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CONFLICT OF INTEREST

No conflict of interest

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