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Review Article

Role of Phytoconstituents in the *Aloe*-Mediated Nanoparticles

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Abstract

Currently, green, single-pot biomimetic, and/or biological methods of Nanoparticle (NP) synthesis are preferred over chemical and physical methods because of their rapidity, eco-friendliness, non-pathogenicity, and economic attributes. In addition, these biosynthesis methods exclude the use of high temperature, energy, pressure, and toxic chemicals. Through biosynthetic methods, nanotechnology is related to biotechnology. This has advanced nanobiotechnology which is the development of eco-friendly and biosynthetic nanomaterials/nanoparticles. Therefore, nowadays, biogenic or green synthesis of NPs using plants has emerged as a potential nano-factory, and their applications are based on phytochemicals. The chemical constituents identified in *Aloe* plants include vitamins, minerals, enzymes, polysaccharides, fatty acids, indoles, hydrocarbons, carboxylic acids, aldehydes, ketones, phenolic compounds, phytosterols, pyrimidines, alkaloids, etc. Each of these chemicals has potential biological activities that make them essential for in nanotechnology. *Aloe* phytochemicals play a crucial role in the fabrication of *Aloe*-based NPs by acting as reducing, capping, and stabilizing agents that control the shape and size of the formed NPs. In addition, these phytochemicals play a significant role in the applications of *Aloe-based* NPs owing to their biological properties. Moreover, it is important to understand the role of phytoconstituents from different *Aloe* species and in every part of the plants using nanotechnology.

Keywords: *Aloe* species; Phytoconstituents; Nanoparticles; Fabrication; Applications

Introduction

The development of nanotechnology is a modern multidisciplinary science involving the fields of chemistry, physics, biology, and engineering, the production of Nanoparticles (NPs), both in nature and by humans [1]. The area of nanotechnology is one of the most dynamic views in current-day material science [2]. The word "nanotechnology" refers to the use of matter with dimensions ranging from one to a hundred nanometers at the molecular or atomic level [3]. "Nano" is a Greek word. "Nanos", means "dwarf, tiny, or very small". Nowadays, the terms like "creation," "exploitation," and "synthesis" are associated with nanotechnology [4]. A nanoparticle is characterized as a little item that acts in the general unit as far as its transport and properties in nanotechnology [5]. There are various chemical and physical methods to synthesize Nanoparticles (NPs). Among them, the sol-gel process, chemical precipitation, chemical vapor deposition, hydrothermal, and microwave methods have been reported mostly [6]. However, these methods are not effective in many aspects. Therefore, currently, green synthesis, single-pot biomimetic, and/or biological methods of synthesis are preferred over chemical and physical methods due to their rapidity, eco-friendliness, non-pathogenic, and economical attributes. Besides, these biosynthesis methods exclude the use of high temperature, energy, pressure, and toxic chemicals [7]. Therefore, nowadays, biogenic or green synthesis of (NPs) using bacteria, fungi, actinomycetes, algae, and higher plants have emerged as potential nano factories [8-10] and their applications are based on the phytoconstituents of these living things. Through biosynthesis methods, nanotechnology is related to biotechnology. This has been advanced in nanobiotechnology which is the development of eco-friendliness and biosynthetic nanomaterials/ nanoparticles [11].

The green synthesis of nanomaterials such as silver [12], zinc oxide [13], magnesium oxide [14], gold [15], cerium oxide [16], copper oxide [17], titanium dioxide [18], activated carbon [19], palladium [20] and tin oxide [21] has been conducted extensively in recent years. The reasons that make green synthesis very important are due to the simple work-up procedure, environmentally benign nature, reusable, low cost, and ease of isolation [22]. Nanoparticles have a novel or superior behavior with defined shape and size. This is because of the high surface area to volume ratio. The physicochemical parameters of Nanoparticles (NPs) are different from that of bulk or large material and single atom and molecule [23,24]. The size of Nanoparticles (NPs) is 1-100 nm with their unique surface, optical, electrical, magnetic, and biological properties [25].

Out of various biomaterials employed for these purposes, plant extracts have attracted much attention due to their effectiveness, availability, and green characteristics [26,27]. Additionally, it has been noticed that the NPs prepared using plant extracts are more stable, cheap, monodispersed, and take less time to reduce [28]. The influence of the added particles like phytocomponents such as polysaccharides, flavanones, terpenoids, etc. attached to the nanoparticle can change its overall properties, especially the antimicrobial property [29]. In addition to plant extracts have an intense array of antioxidants such

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Table 1: Reports of *Aloe* species phytoconstituents.

Aloe spp.	Part of Pant	Phytoconstituents Present	Ref.
A.vera	Leaf (gel)	Tannins, saponins phlobatannins, flavonoids, anthraquinones, terpenoids, steroids, alkaloids, carbohydrates, and glycosides	[44]
A. gilbertii	Root	Alkaloids, anthraquinones, terpenoids, and flavonoids	[45]
A. eleganis	Root	anthraquinones, terpenoids, phenols, saponins, tannins, glycosides	[45]
A. tormentorii	Leaf	alkaloids,anthraquinones, terpenes, phenols, flavonoids, coumarins, saponins, and tannins	[46]
A. adigratana Reynolds	Leaf (Gel)	Alkaloids, glycosides, steroids, carbohydrates, fixed oils and fats, amino acids and proteins, flavonoids, tannins, terpenoids, and saponins,	[47]
A. arborescens	Leaf	Alkaloids, terpenoids, steroids, flavonoids, tannins, and reducing sugars	[48]
A. ferox	Leaf	Phenols, flavonoids, flavonols, proanthocyanidins, tannins, alkaloids, and saponins	[49]
A. striata	Leaf	Flavonoids, terpeneoids, and aromatic compounds	[50]
A.vera	Leaf	Alkaloids, glycosides, reducing sugars, phenolic compounds, steroids, terpenoids, flavonoids, tannins, and saponin glycosides	[51]
A. turkanensis	Whole Leaf	Tannins, anthraquinones, terpenoids/steroids, saponins, and alkaloids	[52]
A. perryi	Flower	Glycosides, phytosterols, proteins, and amino acids, flavonoids, phenols, and carbohydrates	[53]
A. pulcherrima Gil. and Seb.	Leaf (latex)	Anthraquinones, Flavonoids, Saponins, Glycosides, Tannins, Phenols, and Alkaloids	[54]

as polyphenols [30,31], reducing sugars [32], nitrogenous bases, and amino acids [**33**], which can produce nanoparticles of metal and metal oxide from metal ions [34].

Aloe species can store water and important chemical constituents in their swollen and succulent leaves because of their ability to survive in conditions such as hot and dry, which makes them a unique source of phytochemicals [35]. *Aloe* plants have been widely known and used for centuries as topical and oral therapeutic agents due to their health, beauty, medicinal, and skin care properties [36]. The range of chemical constituents of the *Aloe* species can be used in preparing beauty and cosmetics, medicinal and pharmaceutical, personal care and toiletry products, and bittering agents in alcoholic drinks, and they are also grown as ornamental plants [37]**.** The phytoconstituents and bioactivity of *Aloe* spp. have attracted research interest since the trade in 'drug *Aloe*s', prepared from the leaf exudate, expanded rapidly in the 19th century [38]. But nowadays, the applications of *Aloe* plants do not limed to the *Aloe* alone; it is incorporated into different substances to give novel ideas such as chemical synthesis and drug delivery [39]. Currently, many researchers are focused on the incorporation of *Aloe* extracts into substances such as metal/metal oxides at the nanoscale. This is due to the *Aloe* species having a variety of phytocomponents responsible for the target application. Therefore, these phytochemicals have a great role in *Aloe*-based nanotechnology [11].

However, due to several complexities in the identification of exact chemical components responsible for the synthesis and applications of nanoparticles, the green synthesis of nanoparticles becomes challenging. Moreover, there is a lack of a comprehensive review that presents a general idea about the roles of phytochemicals in both fabrication and applications of *Aloe*-mediated NPs. Herein; the review summarizes the recent update on these ideas somewhat. In addition to that almost all kinds of literature, fabricated NPs from leaves of *Aloe* especially, *A. vera*. But other parts of the plants like flowers and roots are also rich in bioactive compounds. Therefore, it is very important to synthesize NPs from other than leaves of *Aloes* and identify the roles of responsible phytoconstituents in them.

Aloe Phytoconstituents

The chemical constituents that have been identified in *Aloe* plants include vitamins, minerals, enzymes, simple and complex polysaccharides, fatty acids, indoles, hydrocarbons, dicarboxylic acids, aldehydes, ketones, phenolic compounds, phytosterols pyrimidines, and alkaloids with potential biological and toxicological activities [40-42]. The biological properties of *Aloe* such as anti-inflammatory, antimicrobial, antitumoral, and antioxidant are due to various compounds of *Aloe* extracts. These properties and activities are synergistic rather than one single class of compounds [43]. If the same climatic, geographic, harvesting time, solvent system, extraction, etc. conditions are applied to the same *Aloe* species, the part of the plants makes difference in the presence and absence of the phytochemicals. Table 1 shows the different *Aloe* species' phytochemicals from the different parts of the plants.

Several constituents from various classes such as alkaloids, anthrones, chromones, flavonoids, glycoproteins, naphthalenes, and pyrones have been isolated from different *Aloe* spp [55]. Aloin, *Aloe*sin, *Aloe*nin, *Aloe*resin, *Aloe*-emodin, apigenin, acemannan, and chrysophanol are some examples of such bioactive compounds (Table 2 and Figure 1).

The chemical structure of some *Aloe* species phytochemicals components is represented in (Table 2) is shown in (Figure 1) [36,64-66]**.**

The most commonly used medicinal *Aloe* parts, leaves are heterogeneous and can be divided into three major parts, (i) the outer green epidermis, primarily consisting of structural components, known as skin/peel; (ii) the outer pulp region below the epidermis, consisting of vascular bundles where the yellow bitter latex/sap is derived; and (iii) the inner leaf pulp, consisting of *Aloe* gel and containing parenchyma cells. Regarding the different compositions of these leaf portions, they are also likely to have distinct classes of bioactive compounds, which are believed to contribute to the different biological properties of leaves [58]. Although leaves are the most used part of the plant, recently some studies have reported the

Table 2: The main phytoconstituents of *Aloe* spp.

Class of phytoconstituents	Components	Ref.
Carbohydrates	Pure mannan, acetylated mannan, acetylated glucomannan, glucogalactomannan, galactan, galactogalacturan, arabinogalactan, xylan, pectic, cellulose, acemannan, glucose, galactose, manose, fucose, and aldopentose	[56,57]
Anthraquinones	*Aloe*-emodin, *Aloe*saponarin, desoxyerythrolaccin, chrysophanol, 1,5-dihydroxy-3-hydroxy methylanthraquinone, helminthosporin, 7-hydroxy*Aloe* emodin, nat*Aloe* emodin and its ester nat*Aloe* emodin-8-methyl ester, *Aloe*chrysone, *Aloe*saponol, bianthracene O-glycosides: *Aloe* emodin-11-O-rhamnoside, *Aloe*saponol-6-O-glucoside, *Aloe*saponol-8-O-glucoside, *Aloe*saponol-O-methyl-4-O-glucoside, and elgonicardine	[58,36]
Anthrones	Aloin A and B (collectively called aloin and also often referred to as barbaloin), 5-hydroxyaloin A, 7-hydroxyaloin, 10-hydroxyaloin B, 5-hydroxyaloin A 6'-O-acetate, 7-hydroxyaloin-6'-O-monoacetate, homonataloin, nataloin, aloinoside, barbendol, *Aloe*-emodinanthrone, chrysophanolanthrone, *Aloe* emodin-10-C-rhamnoside, 8-O-methyl-7-hydroxyaloin, 6′-O-cinnamoyl-8-O-methyl-7-hydroxyaloin, 6'-O-p-coumaroyl-7-hydroxyaloin, 7-hydroxyaloin-4',6'-O-diacetate, 6'-O-cinnamoyl-5-hydroxyaloin A, microstigmin A, littoraloin, littoraloside, microdontin, homonataloside, and deacetyllittoraloin,	[57,59]
Chromones	*Aloe*sin, iso-*Aloe*resin, 7-O-methyl*Aloe*sin, 8-[C-β-D-[2-O-(E)- cinnamoyl]glucopyranosyl]-2-[(R)- 2-hydroxypropyl]-7-methoxy-5-methylchromone, 8 -C-glycosyl-7-O-methyl*Aloe*diol, and 8-C-glucosyl-7-methoxy-(S)-*Aloe*sol	[36,57]
Coumarins	Feralolide and dihydroisocoumarin glycoside	[57]
Flavonoids	Naringenin, dihydroisorhamnetin, apigenin, isovitexin, isorhamnetin, genistein, saponarin, kaempferol, and quercetin	[36,60]
Alkaloids	N-methyltryamine, O,N-dimethyltryamine, γ-coniceine, coniine	[59]
Pyrans and pyrenes	Bisbenzopyran, *Aloe*nin, *Aloe*nin aglycone, *Aloe*nin acetal, *Aloe*nin B, and *Aloe*-2″-p-O-coumaroyl ester,	[59]
Benzene, naphthalene and furan derivatives	Protocatechuic acid, methyl-p-coumarate, pluridone, isoeleutherol, isoeleutherol-5-O-glucoside, feroxidin, feroxidin A, feroxidin B, plicataloside, 5-OH-3-methylnaphto[2,3-c]furan-4(1H)-one, 3-methylnaphto[2,3-c]furan-4(9H)-one, and 3-methylnaphto[2,3-c] furan-4,9-dione	[57]
Sterols	Cholesterol, campesterol, β-sitosterol, and lupeol	[57,59]
Proteins	Lectins, lectin-like substance	[57]
Enzymes	Alkaline phosphatase, amylase, cyclooxidase, cyclooxygenase, lipase, oxidase, phosphoenolpyruvate carboxylase, and superoxide dismutase	[60,61]
Vitamins	B1, B2, B6, B12, C, E, β-carotene, choline, folic acid,α-tocopherol	[61,62]
Inorganic compounds	Calcium, chlorine, chromium, copper, iron, magnesium, manganese potassium, phosphorous, sodium, and zinc.	[57,62]
Miscellaneous including lipids	Arachidonic acid, γ-linolenic acid, triglicerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, and uric acid	[61,63]

bioactive roots [67] and flowers [68] of the plant. *Aloe* species have become of great interest to researchers who have tried to identify the compounds responsible for these beneficial effects.

Aloe-Based Nanoparticles

Recently, *Aloe*-based nanoparticles have been utilized for their wide applications. The fabrication of NPs by using *Aloe* species is due to chemical compounds present in the *Aloe* genus [69]. In works of literature, numerous *Aloe*-mediated NPs have been fabricated along with their various applications. In *Aloe*-based NPs the leaf gel [70], leaf skin (peel) [71], whole leaves [72], and/or flower [73] of *Aloe* species with metal/ metal oxide have been conducted. the metal and metal oxide of *Aloe* based NPs such as silver NPs, gold NPs, selenium NPs, copper NPs, iron NPs, iron oxide NPs, silver oxide NPs, zinc oxide NPs, magnesium oxide NPs, titanium oxide NPs, and indium oxide NPs with various applications such as cytotoxicity, UV protection, antibacterial activity, catalytic activity, antibiofilm potential, photocatalytic activity, antifungal, and antioxidant activities have been described. *Aloe*-based NPs fabrication is affected by various factors such as type of metal, different *Aloe* spp., method of NPs formation, temperature, pH, and type of solvent used [28]. In addition to that, the part of the *Aloe* plant such as leaf skin, leaf gel, leaf latex, whole leaf, root, and flower is also a great factor to make difference in the fabrication of *Aloe*-based NPs due to the phytochemicals present in each part are different.

In the synthesis of *Aloe* mediated NPs, *Aloe* extract is prepared separately before being added to precursors. The extracts can be prepared from different parts of the plant such as the leaf, flower, and root. The mature, healthy, and fresh *Aloe* parts are used to utilize for this purpose. The selected part of the plant is washed with distilled water to remove any dirt or debris on the surface [70]. If the synthesis of NPs is based on whole leaf, the leaf extract is prepared by cutting it finely, if the skin of the plant the is targeted, the extract is prepared by peeling off the leaf carefully using a sharp knife and if the gel is needed, the leaf is slit longitudinally into half, the skin is discarded, the gel is scraped off by sharp-edged spoon/knife from the inner leaf into a container. If the latex/sap part of the *Aloe* is the target extract, the cut leaf is kept 45^{o} to obtain latex. Flower and root parts of the plant are also used to prepare *Aloe* extract. The identified *Aloe* extracts are ground to be kept for the next steps. In the literature, there are different methods to make extracts to store for further use. Among the different methods, boiling the prepared extract with distilled water for certain minutes is the common method [73-75].

The NPs that are prepared from the addition of plant extracts like *Aloe* extract to precursors such as metals and metal oxides green synthesis. Based on the aim of nanoparticle synthesis, a different form of green synthesis can be followed. During the synthesis of NPs, the formation of NPs is indicated by physicochemical properties. Among the many physicochemical properties reduction, a color change is mandatory to show the completion of NPs [76]. This shows that there is the reduction in the chemical reaction between *Aloe* extracts and precursors because *Aloe* species possess reducing agent phytochemicals.

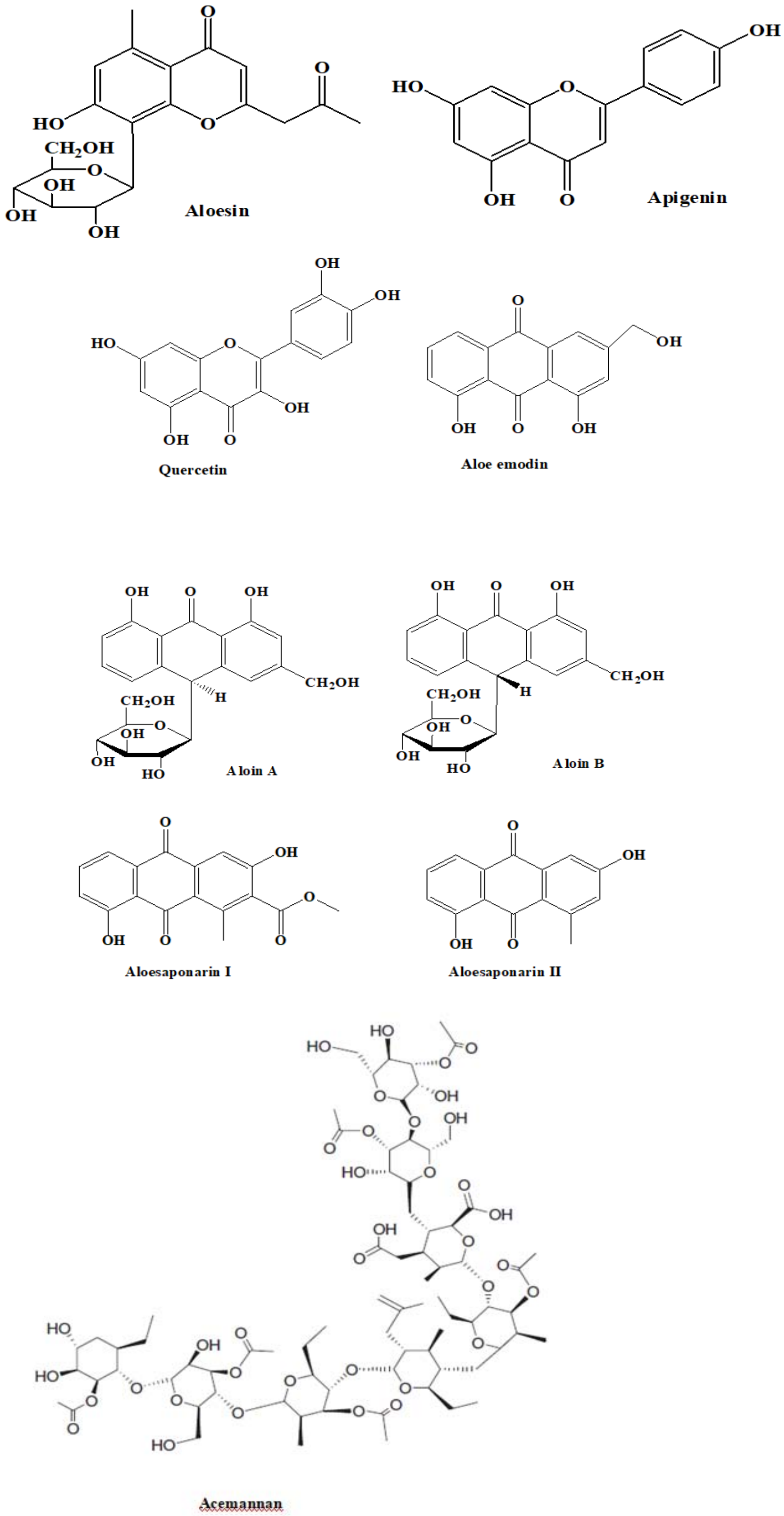

Figure 1: The chemical structures of some phytoconstituent components of *Aloe* species.

Role of Phytoconstituents in *Aloe* Based Nanoparticles

Role of Phytoconstituents in the Fabrication of Nanoparticles

It has been described that the plant chemical compositions are used for the NPs fabrication because they act as reducing, capping, and/or stabilizing agents [77]. Some of these bioactive molecules act as electron shuttles in metal reduction, while other constituents are responsible for the capping of resulting NPs, which not only controls the aggregation of NPs but also results in post-surface modification of NPs [78]. The phytochemicals that are responsible for these purposes of the *Aloe-based* NPs are anthrones, anthraquinones, chromones, polysaccharides, proteins, alkaloids, flavonoids, and Miscellaneous bioactive compounds, (Table 1, 2, and Figure 1). Hydroxyl and carboxylic groups present may act as reducing agents and stabilizing agents in the synthesis of nanoparticles [79]. The functional groups such as phenolics and alkaloids are responsible for capping and stabilizing nanoparticles reduced [80]. The size and stability of the formed nanostructure are also controlled by the reduction mechanism. The stability of nanoparticles can be attributed to the formation of stable bonding between metallic nanoparticles and phytochemicals present in the *Aloe* extract [81]. There are various roles of *Aloe* phytochemicals in the formation of *Aloe-based* NPs. However, roles such as reducing, capping, and stabilizing agents are very important in the characterizations and applications of *Aloe-based* NPs. These three properties are interrelated to one another. If the formed NPs are reduced or capped to precursor, then it stays stable. The stable NPs can be applied to the target applications.

Role of phytoconstituents in reducing NPs: Reducing agents have the role of driving electrons from the solution to the ions (usually metallic ones) to form atoms. In other words, they reduce the salts into the reduced form, which is usually insoluble [82]. A possible mechanism of the formation of *Aloe-based* NPs from *Aloe* spp. and the phytochemical involved are presented in (Figures 3 and 4). There is the presence of a -OH group in most phytochemicals obtained from *Aloe* spp. and this -OH served as a reducing agent, converting metal ions into metal/metal oxide NPs. Also, carbonyl functional groups are present in the phytochemical of *Aloe* spp. play a significant role in NPs fabrication [28]. In another study, the production of silver nanoparticles is demonstrated by the sharp peak around 400 nm for aloin-mediated silver nanoparticles in the UV–Vis spectrum, which indicates the availability of reducing functional groups in aloin [74]. The role of the functional groups in acemannan molecules in the formation of AgNP has been described as acting as a reducing and stabilizing agent, (Figure 4) [29]. The ZnO-biomolecule complex formation is due to the linkage between the Zn^{+2} ions and the functional group hydroxyl that present in the biomolecules like aromatic compounds like aloin (polyphenol) present in *A. vera* extract acts as the reducing agent for the ZnO NP synthesis [11].

Role of phytoconstituents in capping NPs: The environmentally friendly single-step protocols using plant extracts without involving any extrinsic surfactants, capping agents, and/or templates have been explored for metal NPs synthesis [83]. A capping agent is an amphiphilic molecule consisting of a polar head group and a nonpolar hydrocarbon tail and the functionality of the capping agent depends upon both the parts [84]. The surface chemistry and size distribution of nanoparticles get altered after capping with biocompatible

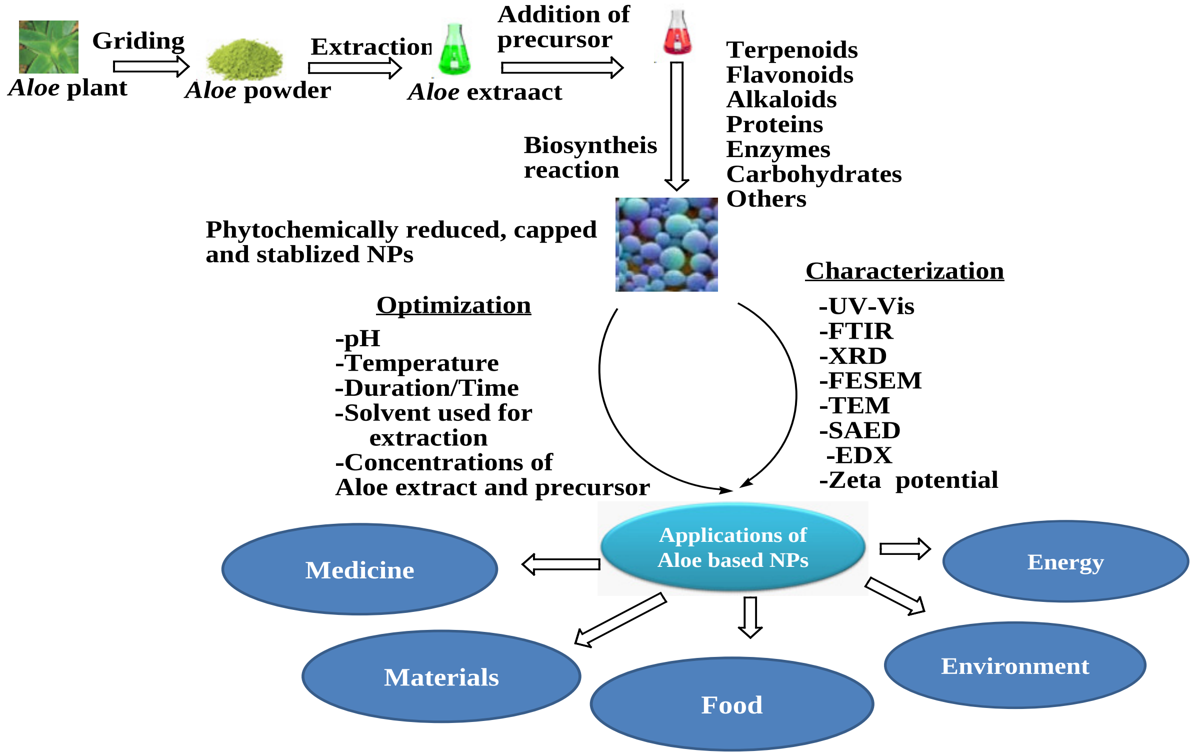

Figure 2: Diagram of biosynthesis, optimization, characterization, and applications of *Aloe*-based nanoparticles.

Table 3: Applications and responsible phytochemicals of *Aloe* based NPs.

Precursors	*Aloe* spp.	Part of *Aloe*	Applications	Responsible phytoconstituents	Ref.
Ag	*A.vera*	Leaf (Gel)	Antioxidant activity	Tannins, flavonoids, and proteins	[104]
Se	*A.vera*	Leaf	Antioxidant activity	Hydroxyl groups, methyl, carboxylic acid, and amine	[105]
ZnO	*A.vera*	Leaf	Antioxidant, antibacterial, and antiproliferative activities	Alkaloids, carbohydrates, flavonoids, phenolic, saponins, tannins, and terpenoids	[106]
Ag	*A.vera*	Leaf	Antibacterial and Antimalarial	Amine groups and carboxylic acids	[107]
Ag /Ag_2O	*A.vera*	Leaf	UV protection and antibacterial	Anthraquinone compounds, alcoholic compounds, proteins, polyphenols, terpenoids alkaloids, flavonoids, and polysaccharide	[108]
Au	*A.vera*	Leaf (gel)	Antibacterial Activity	Alcohol, phenol, carbonyl compounds, and amine	[109]
ZnO	*A.vera*	Leaf (skin)	Antibacterial Activity	Phenolic compounds, terpenoids and proteins	[110]
ZnO	*A.socotrina*	Leaf	Antibacterial Activity	Amines and hydroxyl groups	[39]
CuO	*A.vera*	Leaf	Antibacterial Activity	Hydroxyl groups, alkenes, and Alkanes	[111]
Se	*A.vera*	Leaf	Antibacterial and antifungal activities	Hydroxyl groups, carboxylic acid, and amine	[112]
Ag	*A.vera*	Leaf	Antifungal Activity	Amide and alcoholic hydroxyl groups	[74]
ZnO	*A.vera*	Leaf (gel)	Antimicrobial Activity	Alcohols, phenols, amines, and carboxylic acids	[113]
Ag	*A.vera*	Leaf (gel)	Antimicrobial Activity	Flavanones or terpenoids	[114]
Ag	*A.vera*	Leaf (gel)	Wound healing	Amino acids, organic acids, and mineral elements	[115]
TiO_2	*A.barbadensis*	Whole leaf	Antibiofilm Potential	Terpenoids, flavonoids, and proteins	[116]
Fe_3O_4	*A.vera*	Leaf (gel)	Cytotoxicity Assessment	Hydroxyl group, phenolics, and carbohydrate	[117]
TiO_2	*A.vera*	Leaf (gel)	Photocatalytic Activity	Amino groups, alcohols, phenols, and amines	[76]
Ag	*A.vera*	Leaf	Catalytic activity	Phenols, alcohols, carboxylic acids, amines, and minerals	[118]

Figure 3: Mechanism of formation of Ag-NP from *A. vera.*

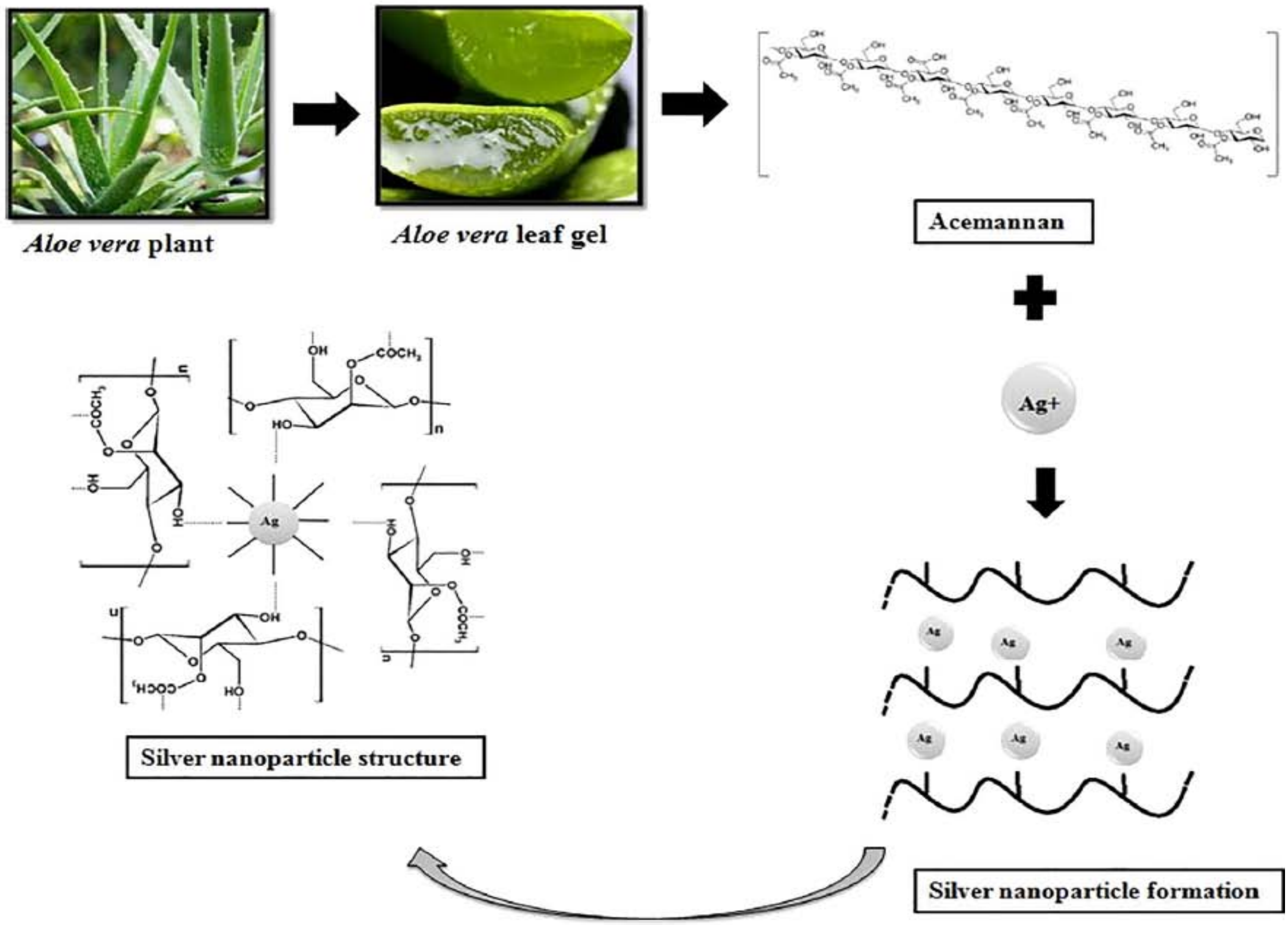

Figure 4: The possible mechanism involved in the synthesis of AgNP by *A. vera* gel extract.

surfactants [85]. The biological activities of nanoparticles are enhanced by surface capping as the role of phytochemicals. The controlled size, morphology, and surface composition achieved by nanoparticles' capping are crucial in determining the vital application of nanoparticles [86]. It has been reported that capping agent molecules prevent nanoparticles from aggregation and oxidation to stabilize the NPs [87]. *Aloe* species have phytochemicals and/or functional groups responsible for capping agents [88,89]. The presence of bioactive molecules in *Aloe* extract was associated with α-Fe_2O_3NPs surface, also illustrated by their stretching/bending vibrations. The appearance of prominent bands indicated the surface association of O–H bearing carbohydrates/alcohols, 1° and 2° amines, amide-I, proteins, and aromatic amines, respectively. Due to these capping agents, the overall, FTIR data suggested the stability of *Aloe* extract bioactive molecules capped/absorbed on the surface of NPs [90]. The authors proposed the capping of reduced silver by acemannan as the possible chemistry involved in the formation of AgNP as represented in (Figure 4). The surrounding acemannan is a surfactant and inhibits the AgNP agglomeration. In another study, the proteins responsible for the synthesis of CuNPs act as surface coating molecules that keep away from the internal agglomeration of the particles [73]. The biomolecules surrounding the NPs decomposed into gaseous products at high temperatures resulting in NPs during calcination or annealing [91]. By developing the green chemistry of phytochemical coating on metal nanoparticle surfaces, their toxicity could be reduced [92].

Role of phytoconstituents in stabilizing NPs: It is well known that nanoparticles in their free form are thermodynamically unstable due to high surface energy. Due to Brownian motion, the high surface energy nanoparticles collide and the final state of nanoparticles is dictated by the type of interaction between the colloidal nanoparticles [93]. The intrinsically green approach involves the phytochemicals for the stabilization of NPs [94]. GC-MS analysis of *A. vera* leaf extract of ZnONPs revealed the predominance of compounds like ethanone, 1-phenyl, guanosine, pentadecanoic acid, and tetraconate in *Aloe* extract, which might be responsible for conferring stability to associated ZnONPs, besides proteins and other auxiliary phytochemicals [75]. The stability of CuO nanoparticles may be due to the free amino and carboxylic groups of *A. barbadensis* that have interacted with the copper surface [95]. The stability of NiO nanorods may be due to the free carboxylic and amino groups that interact with the surface of the nickel has been stated in the same way. In both cases, the proteins present in the medium prevent agglomeration and help the stability of NiO by covering the metal nanoparticles [96]. The formation of NPs complexes is due to the biomolecules present in *Aloe*. Due to these biomolecules having a strong chelating ability, it is readily attached and adsorbed onto the NP surfaces. As a result stability of NPs is achieved [11].

Role of Phytoconstituents in the Applications of *Aloe* Based Nanoparticles

In addition to other plant-based NPs [97], the *Aloe* plants have a variety of applications because they are rich in active components [28]. Researchers have demonstrated the possible mechanisms of action of medicinal plants and their active ingredients or active compounds/ phytochemicals, which may exert these mechanisms individually or in combination with other compounds present in the plants [98]. The influence of additional particles of *Aloe* phytocomponents attached to the nanoparticle can change its overall properties, especially in medical applications such as antimicrobial, anticancer, antioxidant, etc. [29]. Antibacterial activities of *Aloe*-based NPs have been described by many authors with the responsible phytochemicals and functional groups [99]. The enhanced antibacterial activity of AgNPs synthesized using *A. vera* extract was described as it is attributed to active components in the extract especially, acemannan as the main reason [28]. In another study, the addition of *A.vera* in the Nanofiber Membranes (NFMs) can increase the antibacterial effect of the NFMs. This might be due to the presence of substances such as acemannan, anthraquinones, and salicylic acid in *A.vera*, resulting in its better antimicrobial activity [100].

In the literature, the peak separation potential of Lithium Titanate (LTO) is lower than the Green Synthesis of Lithium Titanate (GSLTO); possibly due to the utilization of *A.vera* extract, which contains various phytochemical compounds like tannin, saponin, flavonoids, etc. has been stated [69]**.** These phytochemical species also take a role in the electrochemical performance of the GSLTO sample [101]. There are many different types of phytochemicals with different structures. It has been suggested that the structures of phytochemicals are associated with their different activities [102]. The synergistic activities of these phytochemicals [63] and a synergistic effect between particles and phytochemicals [29] make nanobiotechnology an interested and applicable scientific research. It is concluded that the insulin-loaded nanoemulsion topical gel with *A. vera* showed a synergetic effect toward efficient healing of the wound in diabetes, and is more effective than the application of topical insulin alone [103]. Although the role of some phytocomponets has been described well, still it needs more clarification on which phytocomponents are more responsible for the *Aloe*-based NPs. (Table 3) indicates the combination of phytochemicals as well as functional groups in the applications of *Aloe*-based NPs. In this case, the idea of responsible phytochemicals shows the role of these phytochemicals in investigated applications.

Limitations and Future Aspects

Despite being rich in all parts, the works of literature regarding *Aloe-based* NPs were limited to the leaf of *Aloe* species. Also among the leaf parts, the gel was under the consideration. But there was no clear evidence for the selection of leaf and/or gel only. Therefore, the *Aloe* plants' parts such as roots, flowers, etc. are rich in phytoconstituents and they can be used in the biosynthesis of *Aloe*-based NPs. Although many works have been done on *A.vera* and it is available everywhere, it should not be *A.vera* alone to make investigations like biosynthesis of NPs. Other *Aloe* species should be analyzed for their role in the *Aloe*-mediated NPs.

Conclusion

Currently, *Aloe*-based nanoparticles are very important in a broad area of study. The first reason for this idea is due to the unique nature of *Aloe* plants. They have a variety of chemical compositions with chemical and biological properties. Therefore, the incorporation of these *Aloe* biochemicals into another substance like metal or metal oxides make the biosynthesis of NPs which are very necessary for all aspects than other means of NPs syntheses. The second idea that brings the importance of *Aloe*-based nanoparticles is the new idea of nanotechnology. The combination of these points forms what is known as *Aloe*-based nanobiotechnology. Although the combination of *Aloe* phytocomplexes and precursors is known, *Aloe* phytoconstituents have a great role in the formation and applications of *Aloe*-based NPs. Nowadays; this science has wide applications in medicine, food, environmental protection, material preparations, etc.

Competing Interests

The author declares that he has no competing interests.

Authors' Contributions

All parts of the manuscript were prepared by the corresponding author.

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