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The Prospects of Phyto-Nanoparticle-Based Anti-Respiratory Virus Agents: A Review

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ABSTRACT

Infections caused by viral agents create major public impairments to well-being, especially given the fact that the appearance of opposing viruses and the undesirable outcomes linked to their extended exploits keep on slowing down the implementation of successful antivirus agent therapy. These have, in turn, contributed to the need for developing safer and more effective advantages over traditional antiviral drugs. Currently, nanomaterials have surfaced as new vaccines because of their unique physicochemical properties. Phyto-nanotechnology offers novel antiviral therapies a motivating opportunity. This reduces the level of metal ions into phyto-nanoparticles, which in essence strike a wide range of viral targets and thus reduce the risk of developing resistance compared to traditional antiviral agents. In essence, this reduces the phyto-materials into nanoparticulate form, which has the ability to hit a huge spectrum of virus targets while also lowering the danger of antiviral resistance associated with traditional antiviral drugs. The current study emphasizes the creation of nanoparticles from natural products and their usage in the treatment of a variety of viral illnesses, including respiratory viral infections.

Keywords: *Infectious virus, Respiratory, Natural products, Phyto-nanoparticles, Viral treatment, Infections.*

INTRODUCTION

Viral respiratory tract diseases are driven by a range of viruses that have common characteristics and affect both the upper and lower respiratory tract compartments. Thus, respiratory viral infections are a major public health problem for human communities, causing millions deaths annually worldwide [1]. Many cases of lower respiratory tract infections (LRTIs), about 80 percent are known to be caused by viruses [2]. Usually, these viruses may reach the body through the respiratory route via aerosols, particles in the air, or other respiratory pliable particulates, and they tend to reproduce effectively in the mucous membranes where they trigger specific symptoms varying from febrile to bronchiolitis and pneumonia [3]. Viral-induced lower respiratory tract infections are also a vital determinant of income loss for animal production industries since such viruses also predispose livestock to microbial infections [4]. Respiratory viruses such as influenza viruses, respiratory syncytial viruses (RSV), parainfluenza viruses, and adenovirus are capable of infecting the nasal and respiratory cavities [5]. The influenza virus, which is responsible for seasonal flu outbreaks, causes a major disease effect in infants and the elderly, accounting for 3-5 million cases of severe poor health with almost 290,000–650,000 deaths worldwide each year [6]. Respiratory syncytial virus and human parainfluenza virus were identified as the primary cause of severe respiratory infection leading to high hospitalization rates in children, particularly causing 40-45% of pediatric hospitalization [7,8]. Adenovirus illnesses affect infants and toddlers and can be fatal in immune-compromised patients.

Generally, respiratory viruses are serious medical conditions for infants, young children, immune-compromised patients, and the elderly [9]. In a key report, these vulnerable patient populations account for 74 percent of deaths associated with lower respiratory tract infections [10,11]. Unfortunately, there is very limited interventions against respiratory viruses.

ANTI-RESPIRATORY VIRAL INTERVENTIONS

Efforts have substantially been devoted to the development of competent interventions against lower respiratory tract infections caused by some viruses. These interventions included inactivated, fragmented trivalent, or quadrivalent seasonal vaccines against influenza A and B viruses like influvac, vaxigrip,nasovac, [12], and nasal flumist in children [13]. However, live attenuated influenza virus vaccine, due to its nature, suffers from safety concerns and poses a risk to elderly and immunosuppressed people [12]. Additionally, inactivated pathogenic vaccines and virus-derived subunit vaccines make the immune system weak and there are frequent to allow adjuvant improve efficacy. However, some viruses, such as the influenza virus, have a high level of antigenic drift (genetic changes), which reduces vaccine efficacy and should be considered [12,13]. As a result, vaccinations would be less susceptible to antigenic drift, improving protection and effectiveness. Nanoparticles/Nanomaterials have now emerged as new antiviral agents, as a result of their special physicochemical properties and the promise they provide. Particles used as nanoplatforms with significant antigenic moieties are attractive as an adjunct to a standard vaccine.

NANOPARTICLES

Nanoparticles are subsequently particles of between one and a hundred nanometers (nm)in size with an interfacial layer surrounding them. Nanoparticles are substances with at least one dimension smaller than 100 nanometers, and their odd and intriguing qualities have piqued people's interest. Nanoscale compounds can come from both natural and synthetic sources. The enormous number of particle surface and large area-to-volume ratio give them unique physiological (such as surface plasmon resonance, and fluorescence optimization) as well as chemical (for example, catalytic advancement) features. Furthermore, when a particle's diameter falls, the useful surface area of the particle grows considerably, enhancing the particle's original qualities. Many organisms, like viruses and proteins, are nano-sized [14,15], and the advantage of these substances is mostly in size (at most one diameter must be nanoscale). Nanoparticles can be injected subcutaneously, intramuscularly, or through mucosal sites (oral and intranasal) and can penetrate capillary and mucosal surfaces [16,17]. Recent developments have allowed, for example, the size, shape, dissolution, surface chemistry, and hydrophilicity of nanomaterials with certain physicochemical features to be controlled and managed, allowing nanomaterials with tailor-made biological traits to be manufactured [18,19]. Furthermore, nanomaterials can also be modified for the integration of a wide range of molecules, including antigens, making them a promising choice for vaccine development [20,21].One way researchers try to ease the attacks of pathogens is through the use of nanoparticles to target drug efficacy and drug delivery. Because of their tiny sizes, nanomaterials are expected to go a long way toward supplying active components of drugs to enter the body organs and thus affect the survival of pathogens.

FUNCTIONALISED METAL NANOPARTICLES

The exploitation of nanoparticles from metals provides an exciting opportunity for new antiviral therapies. Although some metals can be tested for antiviral activity, few attempts have been made to establish metal nanoparticles' relationships with viruses, and these metals, include; gold, silver, platinum, copper, zinc, titanium, magnesium, and alginate, and most have been effective against various microorganisms including viruses. However, several studies have recently shown that metallic nanoparticles may be active antivirals against human immunodeficiency virus (HIV-1), hepatitis B viruses, respiratory syncytial viruses, herpes simplex viruses, monkeypox viruses, influenza viruses, and Tacaribe viruses. Silver nanoparticles (AgNPs) (PVP-coated 69 nm +/-3 nm) are the composition scale of respiratory syncytial virus metal nanoparticles, and they have a mechanism for viral attachments to communicate with each other [22,23,24]. Influenza virus metal nanoparticles composition scale sialic-acid gold nanoparticles functionalized (14 nm) and have action mechanisms in plasma membrane-binding virus inhibition [25,26]. The influenza virus is an infection that causes worldwide epidemics every year and its propensity can produce novel viruses that can move from animals to people. The findings on the use of functionalized AgNps to stop influenza virus replication according to a report showed a significant result [26]. Silver nanoparticles have achieved a unique focus and choice for potential applications in the fields of biological systems, living organisms, and medicine [27,28]. Silver nanoparticles were chiefly studied for their antimicrobial potential against bacteria but were also confirmed to be active against various types of viruses, including human immunodeficiency virus, hepatitis B virus, herpes simplex virus, respiratory syncytial virus, and monkeypox virus. The exact mechanism of silver is assumed to be completely reliant on Ag^+ which restricts bacteria's growth by suppressing respiration enzymes and electron transport molecules while interfering with DNA processes.The continual release of silver ions boosts the antibacterial efficacy of silver nanoparticles when used for impregnation. The early methods for making noble metal nanoparticles are still in use today, and they serve as a benchmark for comparing other synthesis processes. The most frequent approaches are excess-reduction agents like sodium citrate, sodium borohydride etc.[29]. Nanoparticles were produced from silver, gold, lead, and Copper by lowering the number of metal salts in dry ethanol [30]. Aqueous polyethylene glycol solutions [air-saturated] were also used to produce gold, silver, and lead [31]. Methods of reduction can also be applied to make Platinum, lead, Copper, and other metals, albeit specific techniques rely on the donor ion's reduction potential [32]. When various complexes are reduced in the presence of metallic ions, atoms form first, followed by aggregation into oligomeric clusters. As reduction chemicals, commonly available sugars such as glucose, fructose, and sucrose are used in the creation of various metal nanoparticles such as gold, lead, platinum, and silver [33,34]. This method also has several advantages: (a) monosaccharides and sucrose are all readily available sugars that can be used as reducing agents. (b) sugars do not require a stabilizing or capping agent to maintain nanomaterial; (c) sugars are indeed cost-effective and eco-friendly; and (d) nanomaterials could also be properly maintained in desiccators for months before being re-distributed. A range of additional physiochemical techniques have been used for modifying nanomaterials. Ultraviolet irradiation, aerosol technology, lithography, laser ablation, ultrasonic fields, and photochemical reduction techniques have all been developed for the synthesis of noble metal nanoparticles of specific form and structure, the challenge with the nanomaterials produced with this process is that materials can be too costly and it requires toxic substances which are poisonous, carcinogenic, and irritating to a human cell. As a result, developing environmentally friendly and sustainable ways is a major concern. Biological nanoparticles, however, are not monodispersed due to their stability, and synthesis rates are slow. To solve these issues, many elements must be improved, such as microbial growth methods and extraction procedures, while others, such as form, scale, and nature, can be easily regulated by adjusting pH, temperature, and nutritional medium composition. Because of their vast biodiversity, organisms' usefulness as biomolecules for synthesizing safe nanoparticles is still to be properly assessed, bearing in mind that there are three phases to making metal nanoparticles: the selection of a solvent, environmentally-friendly reduction substance selection; and non-toxic chemicals for nanoparticle stability [35,36].

PHYTO-NANOPARTICLE

In the hunt for a technique that might give a faster and better production of metallic nanoparticles, it appears that biologically active synthesis employing filtered supernatant of diverse plant extracts has a substantial influence where metal ions are reduced by releasing reductase enzymes into the solution. Phyto-nanoparticle synthesis was used to reduce silver ions in one of the biometric techniques for the production of silver nanocrystals.

The enzyme mediates the process, and the enzyme's presence in the plant is related to its production [37,38]. Modern nanoparticle studies, derived from medicinal plants, tend to produce positive results. Thus, one of the most innovative techniques offering a tremendous change in the production of nanoparticles is medicinal plants in the fast-evolving fields of nanotechnology, science, and technology [39,40]. Indeed, Phyto-nanotechnology is gaining tremendous global attention and relevance [41,42]. Production of nanoparticles using medicinal plants has a major advantage over the chemical approach in terms of their interaction and impact on the environment; it is environmentally friendly and causes no damage. The time needed for particle formation is also within reasonable limits and makes it one of the best options available in this field to produce the particles with the ease of obtaining the necessary plants. Plants were the primary sources of medication, and for the medicinal behavior of most plants, secondary metabolite was ascribed [43,44]. The production of diverse nanoparticles using components from various parts of the plant, such as seeds, fruits, leaves, roots, and so on, has been the focus of phyto-nanotechnology. The utilization of extracts from plant materials and enzymes in the synthesis of nanoparticles has turned nanotechnology into a potential study subject [45,46]. The chemical reaction usually involves organic compounds such as flavonoids, alkaloids, terpenoids, polyphenols, etc., reacting with metal nanoparticles with metal ions. In this method, the chemical constituents of medicinal plant components act as reduction substances as well as the nano-particle stabilizing agent. In a variety of ways, one of which is to employ proteins from plant extracts to reduce metal ions to nanoparticles in a single process. The procedure is rapid, straightforward, and scalable.

The approach has also gained the benefit that it does not pose a significant threat to health and the climate, as it mainly includes water-soluble plant metabolites. These metabolites are mainly used for processing nanoparticles made from silver and gold. Plant extracts use green synthesis nanoparticles as reducing agents. Plant extracts' ability to reduce metal ions has been known, but the nature of the reduction agents involved has remained unclear. The use of live plants, whole plant extracts, and plant tissue to reduce metal salts to nanoparticles has gotten a lot of attention [47,48,49], presumably due to its simplicity. The mediated production of green plant extracts [50,51,52] is becoming increasingly popular. The plants utilized in the synthesis process are important because they contribute to or influence the character of the nanoparticle that results. Polyphenols and bioactive chemicals are abundant in medicinal plants' components, which aid in the reduction process. Plants with a high polyphenol content can be used to make phyto-nanoparticles. Phyto-nanoparticle production has various advantages over chemical synthesis in diverse ways which include: the minimum amount of time, a production that is cost-effective, economical, and low-cost, scaling up to make vast numbers of metal nanoparticles is simple, no high-temperature, high-pressure, high-energy, or hazardous compounds are used, availability of raw materials and the possibility to reduce toxicity while also lowering the possibility of contamination.

SOME PLANTS UTILIZED IN THE SYNTHESIS OF PHYTO-NANOPARTICLE

Plant-based nanoparticle syntheses may be competitive with biological entities that may avoid the time-consuming procedure of employing microorganisms and sustaining their culture, which could result in the loss of their ability to synthesize nanoparticles. By the way, the utilization of plant extract for synthesis could have a huge impact today and in the next decades. Plant extracts are the greatest choice for phyto-nanoparticle manufacturing and environmental remediation applications because they have tremendous opportunities for heavy metal accumulation and detoxification. Biologically, silver nanoparticles are synthesized to generate anti-respiratory virus agents using extracts from medicinal plants, such as *Garcinia kola Haeckel*. *Garcinia kola* (GK) is a major component of herbal preparations used in traditional African medicine for the treatment of a variety of respiratory tract diseases [53,54]. These plants have powerful pharmacological properties, including antioxidant, antibacterial, antiviral, antifungal, and anti-inflammatory activity [55,56]. *Garcinia kola*'s anti-oxidant property is accredited to its extremely high ascorbic acid content [57]. Some benzophenones, xanthones, biflavonoids, alkaloids, phenols, tannins, and saponins have been discovered in *Garcinia kola*'s phytochemical content [58,59].In folk remedies, *Garcinia Kola* is used to treat ailments such as laryngitis, bronchitis, gastritis, and oral pharyngeal infection [60]. Other plants include *Moringa oleifera* (MO). This plant is highly appreciated and used as a food source, as well as for boosting good health and treating numerous maladies in traditional medicine. It has long been used to treat bronchial infections. This is extremely rich in polyphenols that are used for the synthesis of phyto-nanoparticles. Other plants include *Psidiumguajava* L, *Allium sativum Linn*, *Brassica oleaceae*, *Hibiscus rosa-sinensis* L, *Thyme vulgaris* L, *Cinnamomum camphora*, *Musa paradisiacal*, *Medicago sativa* (alfalfa), and others.

Table 1:Notable examples of plant-based nanoparticle production.

Origin of plant	Nanoparticle	Scale of nanoparticle[nm]	Organic forms	References
Aloe vera	gold & silver	___	round, triangular	[61]
Moringa oleifera	silver	10	Spherical	[62]
Medicago sativa[alfalfa]	silver	2-10	crystalline	[63]
Musa paradisiaca	silver	___	crystalline, irregular	[64]
Hibiscus rosasinensis	gold&silver	14	round, prism	[65]
Cinnamomum camphora	palladium	3.2–6	_____	[66]
Carica papaya	Copper oxide	60-80	Round	[67]
Psidium guajava[guava]	gold	25-30	mostly round	[68]

The active components identified in these plant materials are thought to be responsible for reducing metals and producing nanoparticles in the form of secondary metabolites [69,70]. *Aloe vera* leaves have been utilized as therapeutic plants because of their anti-inflammatory qualities, UV defense, anti-arthritis activity, wound and burn healing properties, and antibacterial properties [71,72,73]. In addition, lignin, hemicellulose, and pectin are found in *Aloe vera* leaves and could be employed in the ion reduction of silver nanoparticles [74,75]. Plant extracts were used to produce silver and gold nanoparticles, resulting in pure metallic silver and gold nanoparticles. Plant extracts were used as both reducing and stabilizing agents in the production of gold nanoparticles. Pomegranate peel, on the other hand, has the most polyphenols and proanthocyanidins of all the extracts, juice, and seeds fractions, and has the highest antioxidant capacity [76]. Their antioxidant activity is recognized in polyphenols and proanthocyanidins [77,78]. Pomegranate peel water extract could thus be a suitable reduction chemical for gold nanoparticle formation in plants. Plant-made nanoparticles are firmer and have a faster synthesis rate than those produced by other species [79]. Nanoparticle properties and manufacturing time are influenced by plant extract features such as concentration, metal salt concentration, pH, temperature, and contact time. In removing metal-borne pollutants, plants have great potential to detoxify, reduce, and eliminate metals and this makes them promising, fast, and cost-effective. Nanoparticles of metal can be produced intracellularly and extracellularly, having different morphological characteristics. The synthetic process begins with the introduction of extracts from plant parts such as leaves, roots, and fruits into an aqueous metal ion solution [80-81]. The elements in the plant extract, such as sugar, flavonoid, protein, enzyme, polymer, and organic acid, operate as reduction agents in the bio-reduction of metal ions into nanoparticles. The following are some of the key aspects that should be considered to develop extremely reliable and well-defined nanomaterials: a) Choosing the best candidate: when choosing the best candidates for the production of metallic nanoparticles, researchers focus on the essential inherent properties of organisms such as activity enzymes and biochemical pathways. Plants with a high capacity for heavy metal buildup and detoxification, for example, are ideal candidates for producing nanoparticles. b) The most important factors for cell development and enzyme activity are: The importance of optimizing growing conditions cannot be overstated. It is important to optimize the nutrients, inoculums, scale, light, temperature, pH, mixing speed, and buffer strength. The presence of substrates or related chemicals at subtoxic levels would promote enzyme activity from the start of the process. c) Optimal reaction conditions: the utilization of metal nanoparticles to synthesize species on an industrial scale, as well as yield and production rate, are all critical factors to consider. As a result, we must optimize the reaction mixture's bio-reduction conditions. The substrate concentration, bio-catalyst concentration, source of electrons and their concentration, pH, exposure period, temperature, buffer power, mixing velocity, and light must all be monitored and optimized. Researchers have also used a range of complementary variables, such as visible light or microwave irradiation, as well as boiling, to modify reaction size, morphology, and pace. The morphologies and other features of nanoparticles can be greatly influenced by optimizing these important parameters.

Many obstacles must be solved in accomplishing this major breakthrough in the use of environmentally friendly methods to generate nanoparticles with the desired morphological characteristics and sizes. Metal nanoparticle bio-reduction using a mixture of biomolecules found in plant extracts (e.g., enzymes, proteins, amino acids, vitamins, polysaccharides, and organic acids like citrate) is environmentally friendly. PH alterations in plants result in changes in the charge of natural phytochemicals that further affect their binding capacity and metal ion reduction during nano optic synthesis. In effect, it will influence the morphology and yield of nanoparticles. Other conditions such as duration, the concentration of salts, and the location of nanoparticle synthesis depend on the species and extracts. Phyto-nanoparticle synthesis of plant-based metal nanoparticles will always be a feasible choice because plants play a significant and delicate role in the manufacturing of metal nanoparticles in the medical field today.

CONCLUSION

Respiratory viral agents, with several side effects of existing therapies, are the world's leading cause of death. The cost of therapy is constantly rising, limiting access to life-saving therapies. Alternative treatments are important to make care more affordable for all. Natural medicine was important with these alternative treatments. It is also possible to use certain natural medicinal plants to synthesize phyto-nanoparticles with specific anti-respiratory virus properties. Unlike those formed by other chemicals or species, plant-generated metal nanoparticles are steadier, eco-friendly, relatively safe, and cost-effective. Plants (particularly plant extracts) can remove metal ions more quickly than physicochemical or biological approaches. Furthermore, plant extracts are unquestionably superior to plant biomass or living plants for scaling up and industrial processing of well-dispersed nanoparticles in metals in a simple and healthy green manner. As science advances, these compounds could provide a future source of conveniently accessible and affordable medicines.

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