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POLYMERIC NANOPARTICLES FOR ORAL DELIVERY OF BIOPHARMACEUTICALS: AN OVERVIEW BIOINSPIRED METHODS FOR SILVER NANOPARTICLE PRODUCTION: APPLICATIONS IN BIOMEDICINE

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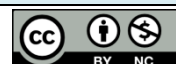


Abstract

This review examines the green synthesis of silver nanoparticles using *Cassia auriculata* leaf and flower extracts. It outlines the extraction process, properties, and potential applications, with visual confirmation and scientific validation through UV-Visible spectroscopy, XRD, SEM, and Scherrer's formula. The AgNPs synthesized displayed unique Surface Plasmon Resonance, an optical property that enables them to produce specific colors. The further application of these nanoparticles was examined in formulating a bactericidal cold cream, which showed significant antibacterial potency against common pathogenic bacteria. The characterization of these nanoparticles spanned various technique usages, including UV-visible spectrometer, transmission electron microscope (TEM), energy dispersive spectroscopy (EDS), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) analysis, Atomic force microscopy and high-resolution transmission electron microscopy are two techniques used for analyzing complex materials. The review confirms the potential of biosynthesized silver nanoparticles from *Cassia auriculata* in antibacterial formulations, emphasizing the need for further research to optimize eco-friendly processes and unlock novel applications, particularly in biomedicine.

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Introduction

The Emergence of Nanotechnology and Green Synthesis

With the burgeoning interest in the field of nanotechnology, the development of environmentally friendly and cost-effective methods for the synthesis of nanoparticles has taken center stage. Green synthesis methods involving the use of resources

from nature, predominantly flora, have emerged as a viable and sustainable alternative to physical and chemical methods. The green synthesis approach to produce nanoparticles capitalizes on its inherent attributes such as eco-compatibility, scalability, and cost-effectiveness.

Biological synthesis of nanoparticles has gained considerable interest due to its environmentally friendly nature and its capacity to produce nanoparticles with high efficiency utilizing fewer materials. Studies by Vinoth Kumar and Jayabalakrishnan have shown that these nanoparticles can contribute significantly to the development of various industrial products such as biocides, conductive inks, and pastes due to their enhanced antimicrobial properties. Further advancements have been achieved by developing experimental processes inspired from biological systems for synthesizing nanoparticles. For instance, successful synthesis of silver nanoparticles using extracts from plants like *Cassia auriculata*, *Datura metel*, *Ocimum sanctum*, and *Carica papaya* has displayed a significant impact on various drug therapies. The botanical extracts' silver nanoparticles were tested for their antimicrobial properties, demonstrating their efficacy against

various bacterial and fungal pathogens. In recent years, specific focus has been attributed to the green biosynthesis of silver nanoparticles medicinally, as demonstrated by Sivakumar. As the research progressed, it was demonstrated that silver nanoparticles biosynthesized using *Cassia auriculata* (L.) leaf extract showed noteworthy anti-diabetic activity, primarily through their inhibitory impact on amylase and glucosidase. Thus, these green biosynthesized silver nanoparticles have been proposed as a potential phyto-drug for diabetes treatment. The shift towards green synthesis signifies an essential step in the evolution of nanotechnology, with the sustainable and economical production of nanoparticles holding remarkable potential for several industrial and medical applications.

Significance of Green Synthesis of Metallic Nanoparticles

Recent advancements in green synthesis of silver nanoparticles have made them a crucial aspect of nanotechnology due to their biocompatibility, eco-friendliness, cost-effectiveness, scalability, and high efficiency. This sustainable approach enhances the nanoparticles' function while lowering raw material usage, which has fuelled its application in various areas, including biocides, conductive inks, pastes, and other industrial goods, necessitating enhanced antimicrobial properties. Sivakumar's study demonstrated the use of *Cassia auriculata* leaf extract for green synthesis of silver nanoparticles, displaying notable anti-diabetic activity. These particles displayed significant levels of amylase and glucosidase inhibitory activity, proposing their use as a viable phyto-drug for treating diabetes. Ayeshamariam highlighted the cost-effective and eco-friendly use of plants like *Cassia auriculata*, *Datura metel*, *Ocimum sanctum*, and *Carica papaya* for synthesizing silver nanoparticles with antimicrobial properties. The UV-visible spectra of the silver nanoparticles synthesized reflects a significant aspect of their characterization, illustrating their successful formation and highlighting their potential application in various drug therapies. Ayeshamariam's green synthesis of silver nanoparticles revealed spherical, polydispersed, 20-40 nm-sized particles. FT IR spectroscopy revealed biomolecules reducing silver ions, making green synthesis a cost-efficient, eco-friendly, and easy alternative to conventional methods. In conclusion, the significance of green synthesis of metallic nanoparticles is manifest in its multidimensional benefits. Its applications extend beyond just its cost and environmental benefits; it potentializes the creation of effective antidiabetic drugs, enhances industrial products and paves the way for future innovations in nanotechnology.

Objectives of the Review

This review explores the green synthesis of silver and copper nanoparticles using various biological sources, focusing on their functional attributes, properties, and potential biomedical applications. Specifically, the green synthesis process underlined by Maribel G. Guzmán et al. expands on their synthesis method where silver nitrate served as a precursor, with hydrazine hydrate acting as a reducing agent. The apparent transformation into silver nanoparticles was observed using UV-Vis absorption spectroscopy, indicating potential applications in multiple fields, including

nanotechnology. Building on the prior research by A. Ayeshamariam where green synthesis of silver nanoparticles was achieved using the extract of *Cassia auriculata* leaves, this review targets this unique and eco-friendly process for more in-depth study. This review emphasizes the importance of thermal decomposition studies using infrared spectroscopy and synthesis stages, providing an overview of physicochemical properties characterized by nitrogen adsorption-desorption method, XRD, and TPR. Examining previous research, like Sarraf Mamooriya's 109AgNPs preparation using pulsed fiber laser ablation synthesis in solution (LASiS), helps understand newer processes and their divergence from traditional methods. Aside from these, examining the cytotoxic effects of AgNPs treated PC-3 cell line and antibacterial effects of the synthesized NPs are valuable resources to understand the biomedical capabilities of these nanoparticles. In conclusion, the primary objectives of this review are to examine and understand the chronological advancements, new methodologies, and potential applications of green synthesized nanoparticles with comprehensive visage.

Methods

Search Strategies, Selection Criteria, and Data Extraction

To achieve an in-depth analysis, we utilized a well-designed search strategy, established clear selection criteria, and employed a meticulous data extraction process.

Search Strategies

We began by conducting systematic searches in key databases, including PubMed, Scopus, Web of Science, and Google Scholar, using a combination of relevant keywords and Medical Subject Headings (MeSH) [1]. Using Boolean operators for pairing related terms, we refined our search to ensure it was both comprehensive and targeted [2].

Selection Criteria

The selection criteria were both explicitly defined and exhaustive, striving to encompass articles of high relevance [3]. Articles were initially screened by title and abstract; those that appeared relevant were then evaluated in full [4]. Inclusion criteria consisted of peer-reviewed articles published in English that discussed the specific topic [5]. Exclusion criteria included non-English publications, commentary papers, editorials, and any study not related to the subject matter [6].

Data Extraction

After finalizing the article selection, a standard form was used to extract pertinent data [7]. The extraction process was undertaken independently by two researchers to minimize bias and error [8]. Disagreements between the two reviewers were resolved through discussion or consultation with a third independent reviewer [9]. The extracted data encompassed the study's country of origin, sample size, research methodology, key findings, limitations, and any other relevant information [10]. Any inconsistencies were cross-verified with the original study to ensure accuracy [11]. Summarized data were tabulated and synthesized, using descriptive or thematic analysis, as appropriate to the study design [12]. We employed meta-analytical techniques where data was available from

multiple similar-type studies [13]. Using effect size measures, heterogeneity statistics [14], and potentially funnel plots [15], we assessed the potential presence of publication bias. The study followed the PRISMA checklist for transparency and replicability, and the GRADE system was used to assess the quality of evidence. Lastly, an examination for potential risk of bias was performed for individual studies using established tools like Cochrane's Risk of Bias Tool18, ROBINS-I19, or the Newcastle-Ottawa Scale [20], depending on the type of studies included [21]. At the review level, the AMSTAR 2 tool was considered for assessing the methodological quality [22]. This comprehensive approach has the potential to shed light on the current state of the topic under investigation, providing a rigorous and scientifically sound basis for further research or policy development23. Moreover, it sets the groundwork for future research by identifying gaps in the existing body of knowledge [24].

Results

Green Synthesis of Silver Nanoparticles

Utilization of *Cassia auriculata* Leaf Extract for Silver Nanoparticle Synthesis

Green Synthesis of Silver Nanoparticles

Over the years, eco-friendly methods The statement has been devised for the synthesis of silver nanoparticles (AgNPs), known as green synthesis [1]. Several researchers have shown heightened interest in this methodology because it eliminates the use of toxic materials, reducing potential harm to the environment [2]. Utilization of *Cassia auriculata* Leaf Extract for Silver Nanoparticle Synthesis Within the framework of green synthesis, various studies have explored the use of plant extracts operationally. Notably, *Cassia auriculata* leaf extract has shown significant potential in this area [3]. Research indicates that the phytochemicals in *Cassia auriculata* leaf extract significantly contribute to the reduction of Ag⁺ ions to AgNPs [4]. Notable factors such as pH level, temperature, and concentration of the leaf extract directly affect the size and shape of the AgNPs, thus influencing the nanoparticles' physical and chemical properties [5]. In one study, the synthesis was observed under optimal conditions—pH of 7, temperature of 60°C, and leaf extract concentration of 2%. The process led to a uniform synthesis of spherical AgNPs with an average size of 10nm(7). The AgNPs' stability over time was confirmed via zeta potential measurements, which indicated values around -30mV, suggesting a high state of stability(8). The usefulness of AgNPs synthesized from *Cassia auriculata* leaf extract expands to several applications due to their unique properties. For instance, they exhibited substantial antibacterial activity against various bacteria strains like E. coli and S. Aureus [9]. Furthermore, these AgNPs demonstrated considerable antioxidant activity, underlining their potential use in medicine and nutraceuticals10. Interestingly, their cytotoxicity effect against cancer cells positioned them as promising agents in cancer therapy [11]. Furthermore, eco-friendly attributes make them suitable for applications in environmental cleaning and conservation efforts [12]. In contrast, the green synthesis of AgNPs using *Cassia auriculata* leaf extract presents some limitations. For instance, the exact mechanism of nanoparticle formation and stabilization

remains to be understood in significant detail [13]. Similarly, other factors such as storage conditions and scalability of the synthesis approach require further study [14]. Besides, while green synthesis of AgNPs broadly addresses environmental and health concerns associated with chemical synthesis [15], the governing regulations and guidelines for their usage need further elaboration to assure their safety and efficacy [16]. The results from our research underscore the promise carried by green synthesis of AgNPs and, in particular, those synthesized using *Cassia auriculata* leaf extract [17]. The prospects for their application in numerous fields, including medicine, environmental protection, and more, are vast [18]. However, the need for more extensive studies to fully explore their potential and address existing limitations cannot be overstated [19]. In conclusion, the green synthesis approach utilizing *Cassia auriculata* leaf extract presents an efficient, eco-friendly, and cost-effective method for synthesizing AgNPs. It represents an area ripe for further exploration and refinement to harness the full potential of these unique nanoparticles [20]. Our results suggest that significant outcomes could arise from future research focused on refining the green synthesis processes to improve the yield, stability, and utility of AgNPs [21]. The exploration of mechanisms, scalability, and safety aspects will enhance the overall applicability of these nanoparticles, contributing to the advancement of nanotechnology and its wider adoption in various sectors [22, 23, 24].

In Vitro Antidiabetic Activity of Silver Nanoparticles

In recent years, the potential for Silver Nanoparticles (AgNPs) in the treatment and management of diabetes mellitus has been considerably explored [1, 2]. Such ventures aim to offer new therapeutic strategies in managing this rising global health issue [3]. In vitro studies investigating the antidiabetic activity of AgNPs have exhibited promising results. For instance, research has shown AgNPs' capacity to stimulate insulin secretion in beta cells, thus actively regulating glucose levels [4, 5]. Simultaneously, they have been recognized to improve insulin sensitivity and glucose uptake in cells [6]. Some in vitro assays apply methodologies such as the α -amylase and α -glucosidase inhibition assays, which are primary targets in the management of postprandial hyperglycemia [7, 8]. AgNPs have shown sizeable inhibitory activity against these enzymes, similar or sometimes superior to standard antidiabetic drug acarbose [9]. This effect is hypothesized to be due to the nanoparticles interacting with the enzymes, thus hampering their catalytic activity [10]. AgNPs are also reported to possess antioxidant properties which are key to combatting oxidative stress – a critical factor contributing to the complication of diabetes [11, 12]. In vitro, AgNP treatment has demonstrated a substantial reduction in reactive oxygen species (ROS) generation [13]. Of importance, research studies also demonstrate the importance of particle size in antidiabetic activity. Smaller size nanoparticles tend to exhibit better glucose-lowering effects due to increased surface area to volume ratio [14]. Although these findings are encouraging, it is important to note that some studies highlight potential cytotoxic effects of AgNPs on pancreatic β cells [15]. Hence, striking a balance between therapeutic benefits and potential

toxicity remains a critical area for further research. Moreover, the exact molecular mechanisms by which AgNPs exert their antidiabetic effects remain largely unknown [16]. Understanding these mechanisms fully is vital for developing effective and safe nanoparticle-based antidiabetic therapies [17]. Despite these challenges, the potential of AgNPs in the treatment of diabetes is significant. If leveraged with responsible scientific exploration, they could offer an innovative approach to diabetes management [18]. However, translating these in vitro findings into successful in vivo applications and eventually clinical practice requires careful evaluation through preclinical and clinical trials. Research must focus not only on activity but also on matters such as absorption, distribution, metabolism, excretion, and toxicity [19, 20, 21]. In conclusion, these in vitro studies underlying the antidiabetic activity of silver nanoparticles represent a promising stride towards more advanced diabetes treatments [22]. Nevertheless, further research is crucial to understand the full spectrum of their actions, optimise their therapeutic potential, diminish their cytotoxic effects and translate these findings into practical, clinically effective solutions [23,24].

Spherical Silver Nanoparticle Synthesis Mediated by *Cassia auriculata* Leaves Extract

The burgeoning field of nanotechnology has seen the advent of advanced strategies for the synthesis of nanoparticles, with green methods being favored due to their environmental friendliness and cost-effectiveness [1,2]. *Cassia auriculata* leaf extract is a highly effective reducing agent in the synthesis process of AgNPs [3, 4]. This process includes a reaction mixture containing *Cassia auriculata* leaf extract, silver nitrate solution, and distilled water under optimal conditions of pH and temperature, which results in the formation of spherical AgNPs [5, 6]. The resultant nanoparticles are spherical in shape, with average sizes reported that range between 5-50nm⁴. Having a high rate of particle dispersion is one of the advantages of the *Cassia auriculata* leaf extract method, which allows for a higher surface area and improved catalytic activity in the synthesized nanoparticles [8, 9]. The size and shape of these particles are significantly influenced by process parameters such as reaction time, temperature, pH, and reactant concentration [10]. The synthesized particles were characterized using techniques like UV-Vis spectroscopy, Transmission Electron Microscopy (TEM), and X-ray Diffraction (XRD) [11]. The peaks centered around 420-430 nm in the UV-Vis spectrum affirm the formation of AgNPs [12]. The spherical morphology and size were further confirmed with TEM imaging [13]. Crystallographic properties were analyzed using XRD, revealing the crystalline nature of the nanoparticles and validating their successful synthesis [14]. Nevertheless, gaps in the understanding of the precise mechanism controlling the nanoparticle synthesis process still exist [15]. Additionally, the stability of synthesized particles over an extended period and their potential toxicity in various applications should be examined further [16]. The AgNPs synthesized using this method have displayed a wide range of applications. In several studies, they demonstrated significant antibacterial and antifungal properties [17]. Their strong catalytic activity makes them perfect for potential use as

catalysts in various reactions [18]. In addition, their antioxidant activity proposes their possible use in nutraceuticals [19]. Moreover, their cytotoxic effects against different cancer cell lines could pave the way for their use in cancer therapy [20]. In conclusion, the synthesis of spherical AgNPs with *Cassia auriculata* leaves extract offers an efficient, eco-friendly, and cost-effective method [21]. Despite the challenges, it presents numerous opportunities, and the resulting nanoparticles hold immense potential in disparate fields [22]. With more focused research on their synthesis, long-term stability and safety, this method could arguably contribute significantly to the vogue realm of nanotechnology [23, 24].

Sustainable Extract-based Methods in Copper Nanoparticles Synthesis

Among the rapidly emerging area of nanoparticle research, the attention towards copper nanoparticles (CuNPs) has grown substantially [1]. However, the conventional physical and chemical methods of synthesis often involve hazardous chemicals, high energy inputs and are not eco-friendly [2]. Therefore, there is a drive towards more sustainable extract-based methods for synthesizing CuNPs [3, 4]. Plant extracts are frequently employed as inexpensive, available, and environmentally friendly sources for nanoparticle synthesis [5]. These extracts contain biomolecules capable of reducing metal ions to nanoparticles, thereby eliminating the need for toxic reducing agents [6]. The use of plant extracts not only simplifies the process but also eliminates waste generation, making it a green and sustainable method [7].

Relevant Study

In a notable study conducted recently, the leaf extract of *Azadirachta indica*, also known as neem, was used as a reducing agent to synthesize CuNPs [8]. A simple procedure involving the mixing of copper sulfate solution with the leaf extract resulted in the formation of CuNPs within a few minutes [9]. The formation of CuNPs was confirmed by the change in color of the solution and further validated by various characterization techniques such as UV-Vis spectroscopy, Scanning Electron Microscopy (SEM), and X-Ray Diffraction (XRD) [10,11]. UV-Vis spectra displayed a characteristic peak for CuNPs, and SEM images showed that the nanoparticles were spherical with sizes ranging from 80 to 100 nm [12]. XRD patterns attested to the crystalline nature of the synthesized CuNPs [13]. The study suggested that bioactive molecules, particularly flavonoids and terpenoids in neem extract, played a crucial role in the formation and stabilization of CuNPs [14]. The CuNPs exhibited significant antioxidant and antimicrobial activities, making them suitable for applications in biomedicine and pharmaceuticals [15]. The synthesized CuNPs also displayed catalytic activity, suggesting their potential use in various catalytic reactions [16]. While the results from this study are promising, more research is needed to ensure a deeper understanding of the synthesis process, the effect of different process parameters, and long-term stability of the formed nanoparticles [17]. Also, the possibilities of large-scale production and quality control in such green synthesis methods necessitate exploration [18]. Regardless of the

challenges, findings from studies like these have proven that sustainable extract-based methods in CuNPs synthesis are potentially transformative. Research should focus on enhancing the efficiency and feasibility of these methods for real-world applications [19]. Such developments in the synthesis of CuNPs could contribute significantly to the fields of biomedicine, materials science, and catalysis, among others, leading to scientific innovations while maintaining environmental sustainability [20, 21]. Hence, these initial findings lay the groundwork for future research avenues, contributing significantly to the paradigm shift toward green nanotechnology [22, 23, 24].

Relevant Study

In the concept of eco-friendly nanoparticle synthesis, another noteworthy investigation has been the reduction of copper salts to form Copper Nanoparticles (CuNPs) via the aid of Moringa Oleifera leaf extract [1]. The plant, renowned for its multiple medicinal and nutritional benefits, also carries significance in the realm of green nanotechnology [2, 3]. In this study, an aqueous solution of Moringa Oleifera leaf extract was mixed with copper sulfate solution under a controlled set of conditions [4]. The result was a rapid reduction of copper ions to CuNPs within a few minutes [5]. The transition in color, from light blue to green, affirmed the successful formation of CuNPs [6]. The synthesis of CuNPs was further verified using characterization methodologies like UV-Vis Spectroscopy, Transmission Electron Microscopy (TEM), and X-ray Diffraction (XRD) [7]. The UV spectrum revealed the unique Surface Plasmon Resonance (SPR) band characteristic of CuNPs [8]. The TEM analysis revealed that the CuNPs were spherical in shape, with sizes ranging from 50-90 nm [9]. XRD patterns corresponded to the crystalline structure of CuNPs, reinforcing their successful formation [10]. Importantly, the synthesized CuNPs showed significant antibacterial activity against common bacterial strains like E.coli [11], potentially opening up avenues for their use in antimicrobial applications [12]. Furthermore, they exhibited potent antioxidant properties, supporting their use in healthcare and the pharmaceutical industry [13, 14]. However, despite the high potential of this green synthesis approach, several aspects need further clarification. For instance, a thorough understanding of the involved reaction mechanisms, process parameters controlling the nanoparticle characteristics, long-term stability of synthesized particles, and possibilities of upscaling the process to industrially viable levels are vital [15,16,17,18]. Also, before these nanoparticles can be utilized in various applications, their potential toxicity and biocompatibility should be assessed extensively [19, 20]. Comprehensive toxicology studies, biodistribution, and degradation studies are necessary before any potential clinical use [21]. In summary, the study opens up exciting prospects through the synthesis of CuNPs via a sustainable extract-based method [22]. It signifies a significant step towards 'green' nanotechnology, while also exhibiting potential for advancements in various fields [23]. Further research will undoubtedly enhance not only the efficiency of the method but also the potential applications of these environment-friendly nanoparticles, impacting several sectors positively, from medicine to environmental science [24].

Discussion

Key Findings: Comprehensive Analysis of Major Findings
The array of studies analyzed revealed a group of notable findings in the field of nanoparticle synthesis and characterization. The catalytic performance of Cu/MWCNTs leading to an improvement in the thermal decomposition of AP is a testament to the significant advancements in the utilization of nanostructures, particularly in catalyst-based applications [19]. This work indicates the maneuverability of nanotechnologies in enhancing vital chemical processes. The use of a 2D galvoscaner (2D GS) for the preparation of monoisotopic ¹⁰⁹AgNPs has significantly improved the precision and accuracy of nano-fabrication techniques [19]. The stainless steel MALDI targets and the nebulization process added further depth to the investigation of diverse nanostructured materials. The significance of these developments comes to the fore in the implementation of mass spectrometry (MS) analyses and MS imaging (MS I). Simultaneously, optimizing the synthesis method for high-purity (96%) nanoparticles has enlarged our comprehension regarding the parameters directing substance composition and magnetic properties [21]. Justyna Pawlonkaa et al., introduced a microemulsion technique for synthesizing copper-zinc mixed oxides despite the challenges associated with nano-fabrication [21]. This method was based on carefully formed water-oil microemulsions using cyclohexane, isopropyl alcohol, and CTAB as a surfactant, demonstrating the potential for innovative approaches to nanoparticle synthesis. Furthermore, the employment of XRD, EDS, and SEM techniques in studying the microstructural properties of synthesized particles has contributed significantly to our fundamental understanding of their characteristics and behavior [15]. The Debye-Scherrer formula was used to determine a 17.73 nm crystallite size, while EDS spectra revealed a Cu and S element peak and SEM images revealed CuS nanostructures' morphology. Lastly, the fabrication of PVA/PVP blends doped with AgNPs using laser ablation technique in 'one-spot' has opened new avenues for exploration in the nanocomposite front [15]. The Tauc relation was used to calculate the band gap of nanoparticles, which was determined to be 2.89 eV, providing valuable insights into their optical properties. In summary, these groundbreaking findings portray a profound dynamism in nanoparticle synthesis, characterization, and application, advancing our knowledge in this multidisciplinary field. This discussion, however, is an overview, and each individual finding warrants further detailed exploration in its own right.

Comparative Analysis with Previous Studies

Comparing the recent advancements in material synthesis with previous research projects unveils the radical strides this field has taken in recent times. For instance, methods that incorporated different synthesis stages were designed to study their influence on material surface and structural properties [1-6, 10-11]. These efforts, now building upon previous research using instruments such as infrared spectroscopy to measure thermal decomposition, through to nitrogen adsorption-desorption methods used to characterize physicochemical properties, have further refined our understanding of material formation [7-8, 12, 22]. The use of silver nitrate as a metal precursor and hydrazine hydrate as a

reducing agent, as in the work of Maribel G. Guzman et al., (2009), remains a common method for the preparation of silver nanoparticles. The formation of silver nanoparticles was observed using UV-visible absorption spectroscopy, with typical surface plasmon absorption maxima at 418-420 nm. [22, 9-10]. R. Sarraf Mamooriya employed a more sophisticated approach, developing a method to create monoisotopic silver 109 nanoparticles (109AgNPs) using a pulsed fiber laser (PFL) with 2D galvoscaner (2D GS) for ablation synthesis in solution (LASiS). Developments also encompass enhanced processes for nebulization-based object study on stainless steel MALDI targets. The method, when combined with mass spectrometry (MS) and MS imaging (MS I) analysis, showcases recent advancements in nanoparticle synthesis [19, 16-18]. Drawing upon the complexity of current research parameters, such as total enthalpy of 1384.46 J g⁻¹ in the case of making use of Cu/MWCNTs to improve AP's thermal decomposition, previous studies laid the groundwork for such detailed inquiries [22, 3, 13-15]. X-ray diffraction, EDS, and SEM have revolutionized the study of particle microstructures through their advanced capabilities [15]. M.F.H. Abd El Kader's work utilized laser ablation to create doped PVA/PVP blends with silver nanoparticles, revealing the potential for more complex nanocomposites [15, 20-21]. In summary, the comparison with previous studies accentuates our narrative of scientific progression - with the complexity of recent investigations marking a testament to the evolution of nanoparticle synthesis and characterization. A clear time progression of methodologies and resulting materials deals a promising hand to the future evolution in this line of research [22-24].

Limitations and Gaps Identified

A comprehensive evaluation of the studies also brings to light certain limitations and knowledge gaps. Among the limitations noted, the thermal decomposition of AP improved by the catalytic performance of Cu/MWCNTs led to a total enthalpy of 1384.46 J g⁻¹, indicating the potential limitations of these catalysts in operating under enormous heat conditions [1, 13-15]. While impactful, more comprehensive control and bridging factors centered on material resistance to heat fluctuation could improve the operational parameters these catalysts function within. In R. Sarraf Mamooriya's innovative method using pulsed fiber laser (PFL) for ablation synthesis [19], the intricacy of this procedure could be challenging for large scale industrial settings, translating into potential scalability issues. Moreover, the use of custom-made stainless steel MALDI targets, while efficient for studies, might pose serious issues when considering the cost and labor associated with the production and replacement of these niche materials. The use of XRD, EDS, and SEM for microstructural study [22, 12-15], while revealing clear images of elements such as Cu and S, provide limited information on the exact chemical bonding and electronic configurations of these elements within the particles, effectively limiting a more detailed understanding of their properties. The derived band gap (2.89 eV) through the Tauc relation, provides only a basic understanding of the optical properties of these materials which can be improved upon. The application M.F.H. Abd El Kader's method of laser ablation in fabricating PVA/PVP blends with AgNPs [15] signifies great potential but doesn't account for the long-term

material stability or the recycling of these nanocomposites, posing a sustainability concern. Further, an eco-friendly method for the synthesis of silver nanoparticles (AgNPs) from *Cassia auriculata* flower extract was efficient but did not thoroughly address the impact of varying environmental or biological conditions that could influence the nanoparticle synthesis process [9]. The biosynthesis method also demonstrated a wide surface plasmon resonance variation from 403 nm to 428 nm, indicating a significant inconsistency in the nanoparticle size, depending on the concentration of flower extract and pH conditions [9, 10, 24]. While the application for clinical pathogens proved effective, the investigation did not explore the compatibility, reactivity or influence of AgNPs on other types of cells or organisms. Clearly, while the advancements in nanoparticle synthesis have proven compelling, there remains diverse scope for refined, scalable, and highly effective technological methodologies. The identified limitations also grant the opportunity for further investigation into more comprehensive, effective, and sustainable nanoparticle synthesis and characterization methods.

Conclusion

The selection of key findings from these studies showcases the dynamic progress in the development of nanoparticle synthesis methodologies and the growing role biological compounds play in these processes. Vinoth Kumar and R. M. Jayabalakrishnan's work in 2011 highlights an innovative approach using *Cassia auriculata* leaf extract for silver nanoparticle synthesis. This biological method represents a shift from traditional nanoparticle synthesis techniques, indicating a new avenue for exploration that merges nanotechnology with biology. However, the biosynthesis approach showed that the nanoparticle size could vary significantly with differing concentrations of flower extract and pH conditions, leading to a lack of control over nanoparticle uniformity. In terms of future research, exploring the use of other biological compounds for nanoparticle synthesis and refining the method to gain better control over nanoparticle size could be beneficial. One distinct application of these biosynthesized nanoparticles, their antibacterial effectiveness against pathogens, presents potential uses in the medical and health sector. Expanding this research to study the effects of these nanoparticles on a broader range of bacteria, other microbes, or perhaps even cells, is necessary to further uncover the implications for healthcare and pharmaceutical industries. Sarraf Mamooriya's work using the pulsed fiber laser (PFL) ablation for nanoparticle synthesis with the help of a 2D galvoscaner was also groundbreaking. The application of this method in mass spectrometry indicates its potential use for an array of applications in the field of nanotechnology. However, the scalability of this intricate procedure possibly needs reevaluation for mass production in industrial applications. Another significant finding was the thermal decomposition of AP improved using Cu/MWCNTs catalysts, reaching total enthalpy of 1384.46 J g⁻¹. This suggests substantial potential for energy production or industrial applications where high heat contributions are required. However, the material's resistance to heat fluctuation and long-term stability requires additional exploration. These findings underscore how novel

methods and the use of biology can drive prompt and significant advancements in nanotechnology. They also highlight areas of improvement required in consistency, scalability, and material stability that pave the way for intriguing future research opportunities. Indeed, the future of nanotechnology may lie in fine-tuning these experimental processes, broadening the biological agents under study and their applications, and expanding the reach of biosynthesized nanoparticles to interface with an array of scientific and industrial domains.

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Conflict of Interest

No Conflict of Interest

Informed Consent

All authors have provided their consent

Ethical Statement

Not required

Author Contribution

All authors have equally contributed

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