Pesquisa Brasileira em Odontopediatria e Clínica Integrada 2023; 23:e220068
https://doi.org/10.1590/pboci.2023.073
ISSN 1519-0501 / eISSN 1983-4632

ORIGINAL ARTICLE

Curcumin Mediated Gold Nanoparticles and Analysis of its Antioxidant, Anti-inflammatory, Antimicrobial Activity Against Oral Pathogens

Sreedevi Dharman[1], Gopal Maragathavalli[1], Rajeshkumar Shanmugam[2], Karpagavalli Shanmugasundaram[3]

[1]Department of Oral Medicine & Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University,Chennai, Tamil Nadu, India.
[2]Nanobiomedicine Lab, Department of Pharmacology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India.
[3]Department of Oral Medicine & Radiology, Seema Dental College & Hospitals, Rishikesh, Uttarakhand, India.

Correspondence: Sreedevi Dharman, Department of Oral Medicine and Radiology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, No.162 Poonamallae High Road, Velappanchavadi, Chennai, 600077, Tamil Nadu, India. **E-mail:** sanjamrut@gmail.com

Academic Editor: Wilton Wilney Nascimento Padilha

Received: 04 May 2022 / Review: 15 November 2022 / Accepted: 02 January 2023

How to cite: Dharman S, Maragathavalli G, Shanmugam R, Shanmugasundaram K. Curcumin mediated gold nanoparticles and analysis of its antioxidant, anti-inflammatory, antimicrobial activity against oral pathogens. Pesqui Bras Odontopediatria Clín Integr. 2023; 23:e220068. https://doi.org/10.1590/pboci.2023.073

ABSTRACT

Objective: To green synthesise gold nanoparticles using curcumin and to analyse its antioxidant, anti-inflammatory, and antimicrobial activity among oral pathogens. **Material and Methods:** Biosynthesised Curcumin Gold nanoparticles (CuAuNP) were evaluated by UV-visible spectrophotometer (UV-Vis), Transmission Electron Microscopy (TEM), and evaluation of antioxidant, anti-inflammatory and antibacterial activity against oral pathogens. **Results:** Synthesized CuAuNP were characterized using UV-visible spectrophotometry and showed peak absorption at 530nm. CuAuNp showed a 90.3% maximum scavenging ability of DPPH at a concentration of 50 µg/mL. CuAuNP exhibited 79.6 % of the highest anti-inflammatory activity at 50µg/mL than the standard drug diclofenac. TEM image clearly showed uniformly dispersed spherical-shaped gold nanoparticles with a size of about 20 nm. The biosynthesized nanoparticle was tested for its antimicrobial effect, and it showed a potent effect against *S. aureus*, *E. faecalis*, and *C. albicans* at 100µg/ mL. *Enterococcus faecalis* has a maximum zone of inhibition of 14 mm at 100µg/ mL of CuAuNp. Among gram-positive bacteria, a maximum zone of inhibition of 12 mm at 100µg/ mL was seen in *S. aureus* compared to *S mutans*. *Candida albicans* showed a maximum zone of inhibition of 18 mm at 25 µg/mL of CuAuNp. **Conclusion:** Curcumin-mediated gold nanoparticles with 20 nm size were effective and had strong antioxidant and anti-inflammatory activity at 50µg/ mL, antimicrobial action inhibiting microbes at 100µg/ mL concentration that can be used in treating various Oral mucosal lesions.

Keywords: Metal Nanoparticles; Curcumin; Anti-Infective Agents.

Introduction

Conventional Drug delivery has a low profile in biodistribution, targeting, aqueous solubility, therapeutic index, and low bioavailability. These limitations are currently solved by nanotherapeutics that have promising effects [1]. The renowned visionary talk given by the American physicist Richard Feynman, "There's plenty of room at the bottom" in 1959, is accepted to have given an applied birth to the area of nanotechnology [2]. Nanotechnology tends to have an innovative progression that prompts material organization at the nanometer scale (one billionth of a meter). In recent years, the biosynthesis of metallic nanoparticles has become a significant focus in nanotechnology for its medical applications [3].

In the previous two decades, noble metal nanoparticles (MNPs), particularly gold nanoparticles (AuNPs), have progressively accomplished extraordinary consideration from the scientific community because of their remarkable natural, physical, synthetic, and optical properties [4]. This unique property of gold with chemical inertness, resistance to surface oxidation, and less cytotoxicity make them get prioritised for nanotechnologies and applications [5]. They have discovered numerous applications in different regions in biotechnology [6], drug delivery [7], biosensing, and catalysis [8].

Properly functionalised gold nanoparticles act as a drug reservoir for small molecules with prolonged blood presence. The tunability of AuNPs allows complete control of surface properties for targeting and sustained release of bioactive molecules [9].

Depending on the reducing agents, nanoparticles can be synthesised by physicochemical and biological approaches. The physicochemical methods are generally costly and tedious. However, the biological methods use enzymes or secondary metabolites from plants from microorganisms, fungi, and polyphenolic-rich compounds to overcome the drawbacks of the physicochemical approach [10].

Green chemistry uses naturally occurring functionally rich biomaterials such as plant extract, which could be an alternative for producing nanoparticles in eco-friendly methods. Curcumin is one of the most useful plant-based biomaterials, safe with minimal toxicity from turmeric. It has the potential for green synthesis due to its polyphenol trigger during the reduction process [11]. Its curative aspects include antioxidant, anticancer, anti-inflammatory, antimicrobial, and radioprotective properties [12]. Curcumin is effective against proinflammatory cytokines, cyclooxygenase, and Prostaglandin E. in wound healing [13].

Two main steps of nanoparticle synthesis are reducing and stabilising agents. Using a reducing agent causes electrons from curcumin to reduce metal from M^{x+} to M^{0}, transforming from bulk metal to its electrical state. Using stabilising agent stabilises nanoparticles and protects them from aggregation. Repulsive force controls the size and shape of nanoparticles [14]. Despite its promising medicinal properties, curcumin shows poor bioavailability with undetectable concentrations in blood and extra-intestinal tissues. These limitations are due to low absorption, chemical instability, fast metabolism, and high systemic elimination [15]. Our previous research concentrated on the synthesis of novel turmeric gold nanoparticles [5] and curcumin-mediated silver nanoparticles [16] for its application in oral mucosal lesions. In this present study, curcumin was used as a reducing and stabilizing agent to synthesize gold nanoparticles. This study aimed to green synthesise gold nanoparticles using curcumin, characterized by UV-Visible spectrophotometry, TEM analysis, and evaluation of its antioxidant, anti-inflammatory, and antimicrobial activity against four oral pathogens.

Material and Methods

Materials

Curcumin, Gold chloride, DPPH(2,2diphenyl-1-picrylhydrazyl), Ascorbic Acid, and Bacterial media were purchased from (HiMedia Laboratories, Mumbai, India).

Synthesis of Curcumin Mediated Gold Nanoparticles

0.1g of curcumin was dissolved in 5 mL dimethyl sulphoxide, and 45 mL of distilled water was added. 1mM of gold (III) chloride trihydrate ($HAuCl4.3H_2O$) was measured and dissolved in 75 mL of distilled water, and 25 mL of prepared curcumin extract was added. The reaction mixture was stirred for 48 hours at 800 rpm in a magnetic stirrer. The synthesized gold nanoparticles were separated by centrifugation at 8000rpm for 10 minutes. Colour change was visually observed every 1 hour. The obtained pellets were purified by washing them with ethanol and water 2-3 times. The purified pellet was stored in the refrigerator for further use.

Characterization of Gold Nanoparticles

The green synthesized nanoparticles were characterized for their optical properties using a UV-visible double-beam spectrophotometer. The morphological characteristics, such as the size and shape of the nanoparticles, were analysed using transmission electron spectroscopy (TEM). The functional groups were responsible for synthesising curcumin-mediated gold nanoparticles were characterised using Fourier Transform infrared spectroscopy.

Antioxidant Activity

The antioxidant potential of the CuAuNP was determined using a DPPH (2,2-diphenyl-1-picrylhydrazyl) assay. 1ml of CuAuNP with different concentration (10µL, 20µL, 30µL, 40µL, 50µL) of solutions were added to 1ml DPPH (80µg/mL) 0.2mm solution in methanol (0.1g/L) and incubated at 30 minutes in room temperature. Methanolic-coloured DPPH is reduced to a non-coloured solution. The reduction in absorbance was measured at 517nm. The standard solution was the ascorbic acid. Inhibition percentage was calculated using the absorbance of sample solution: (Absorbance of control-Absorbance of sample/ Absorbance of control) x100.

The absorbance of DPPH and methanol is the absorbance of control, and the absorbance of DPPH and sample extract is the absorbance of the sample.

Anti-inflammatory Activity

Anti-inflammatory activity was performed by Albumin denaturation assay. Different concentrations of CuAuNP of 10µL, 20µL, 30µL, 40µL, and 50µL respectively, were added to 2ml of 1% aqueous Bovine Serum Albumin (BSA) mixed with 400µL of methanolic extract, pH of the reaction mixture was 6.8 and 20 min incubation was done and heated at 57° C for 20 min in a water bath. The mixture was cooled, and absorbance was observed at 660nm. BSA mixture with 30% methanol solution is controlled. Different concentration of diclofenac sodium is standard. The experiment was repeated thrice.

Percentage inhibition is: =(Absorbance of control-Absorbance of sample)/ Absorbance of control x 100.

Antimicrobial Activity

The antimicrobial activity was done by using the agar well diffusion technique. 10µL of fresh microbial cultures such as *Streptococcus mutans*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Candida albicans* were inoculated in sterile Hi-Veg broth medium and incubated for 18 hours in an orbital shaker at 120-150rpm. Mueller Hinton agar was prepared (For *Candida albicans*, Rose Bengal Agar was used). The antimicrobial activity was done to analyze the efficacy of Cucumber-intervened gold nanoparticles against oral pathogens at different

concentrations. The oral pathogens were swabbed on the surface of each sterile MHA plate (For *Candida albicans* RBA plates). A gel puncher was used to cut four wells into each plate. The first three wells were loaded with three different concentrations (25µL, 50µL,100 µL) of biosynthesized gold nanoparticles. A standard antibiotic (Amoxicillin) was loaded in the fourth wall. The plates were incubated at 37 °C for 24 hours (*Candida albicans*- 48 hours of incubation). After incubation, the plates were observed and measured for a zone of inhibition around each well.

Results

Visual Observation

The initial colour of the gold chloride solution was pale yellow, and after adding curcumin extract, it quickly changed to dark yellow within 15 minutes at 38 °C. After 2 hours of synthesis, the curcumin-mediated gold nanoparticles showed dark greenish-yellow colour. This colour change indicates the ability of curcumin extract to reduce, which leads to the reduction of gold chloride to gold nanoparticles. The colour change process of curcumin-mediated gold nanoparticles was evident in (Figures 1A, B, C, D) which showed Curcumin with DMSO extract, Gold (III) chloride trihydrate Solution, Curcumin Gold Chloride Mixture, and Curcumin Gold Chloride nanoparticle.

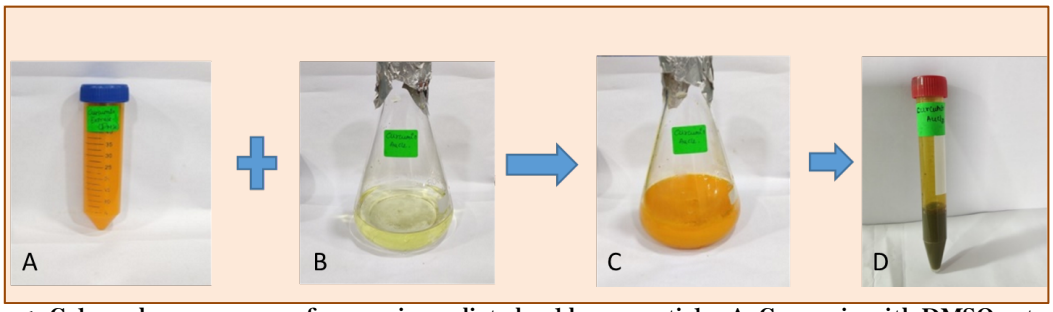

Figure 1. Colour change process of curcumin mediated gold nanoparticles A. Curcumin with DMSO extract B. Gold (III) chloride trihydrate Solution C. Curcumin Gold Chloride Mixture D. Curcumin Gold Chloride nanoparticle.

UV-vis Spectroscopy

Green synthesised Cu Au Np was analysed by Ultraviolet (UV)-visible spectrophotometer (ELICO SL201 UV-V is spectrophotometer). Blank was the control solution, and the nanoparticle solution was simultaneously scanned from 400-650nm. The absorption spectra of biosynthesized gold nanoparticles showed their maximum absorption peak at 530 nm (Figure 2). The absorption peak at 530nm is due to the excitation of surface plasmon resonance, which further confirmed the presence of reduced gold nanoparticles by curcumin extract, ascertaining the synthesis of CuAuNP. They were monitored at different intervals of 1, 2, 6, and 24 hours. Further purification was carried out by centrifugation at 6,500rpm for 15 min, and the nanoparticles were collected in the form of pellets which were further used for analytical characterisation.

Transmission Electron Microscopy

Transmission Electron Microscopy (TEM) (Make; PHILIPS Model; CM 200) was assisted in analysing the shape and size of the synthesized gold nanoparticles (CuAuNP), which was depicted in Figures 3 and 4. TEM images are obtained with various magnification ranges by a high-resolution megapixel camera. CuAuNp aqueous solution was deposited on a carbon-coated copper grid and was analysed. The shape of the nanoparticles was found to be spherical and uniformly dispersed in nature, with a size of about 20nm. They were spherical shaped

with smooth edges and were well dispersed. AuNps, which are well dispersed, are surrounded by curcumin extract that serves as a capping agent.

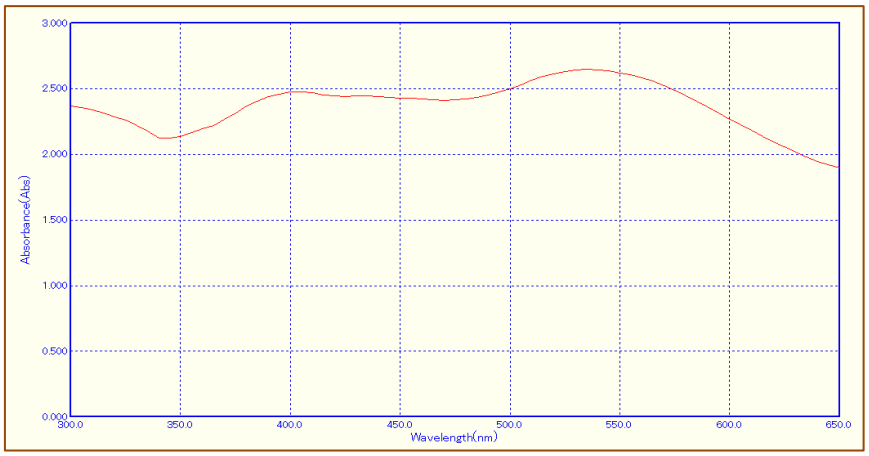

Figure 2. UV-visible spectra of curcumin-mediated gold nanoparticles.

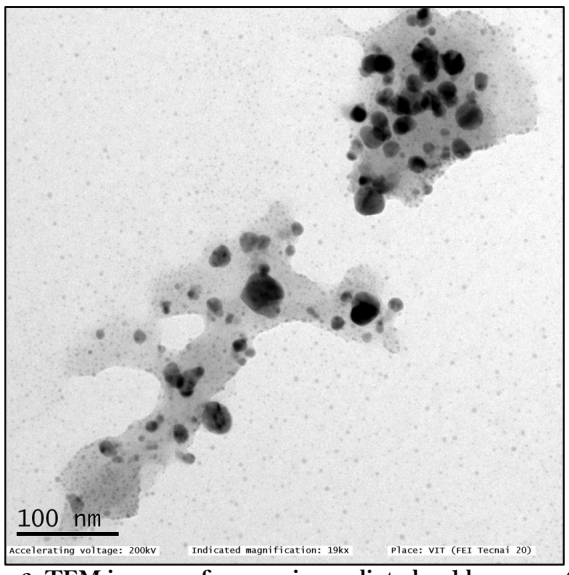

Figure 3. TEM images of curcumin-mediated gold nanoparticles.

Antioxidant Activity

DPPH free radical scavenging potential of various concentrations of green synthesized AuNP is shown in Figure 4. The antioxidant potential of CuAuNp was performed using free radical DPPH. Methanolic violet-coloured DPPH is reduced to a yellow or non-coloured solution by hydrogen or electron. Antioxidants are bio compounds in plant extract with functional groups assigned on AuNp, which reacts with free oxygen radicals and reduces DPPH. Biosynthesised AuNP exhibited 90.3% maximum inhibitory activity of DPPH radical at the highest concentration of 50µg/ml. Dose-dependent antioxidant activity was described as comparable with the DPPH scavenging potential of ascorbic acid (Standard).

Anti-Inflammatory Activity

Different concentrations of methanolic CuAuNp extract exhibited inhibition of protein denaturation (Figure 5). CuAuNp showed protein denaturation inhibitory activity of 41.7%, 57.5%, 67.6%, 77.4%, and 79.6%, respectively, comparable with commercially available synthetic, anti-inflammatory drug Diclofenac. Maximum protective activity and highest inhibition of CuAuNp was 80 % at a concentration of 50µg/mL. When the extract concentration increased, there was a dependent rise in anti-inflammatory activity comparable with the standard.

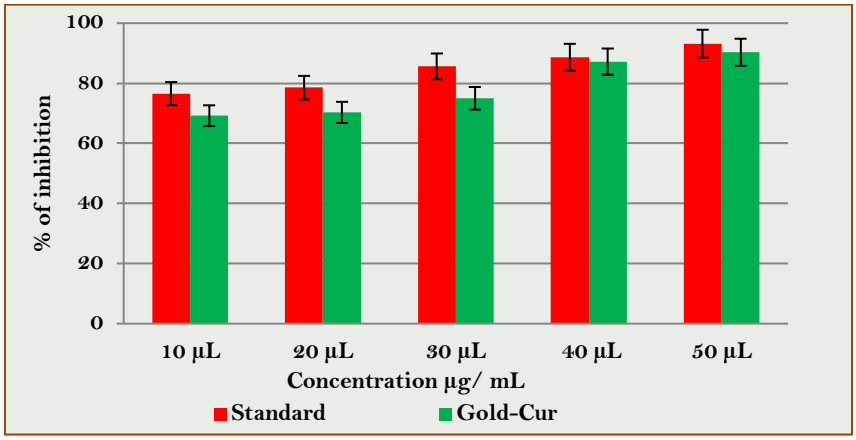

Figure 4. The bar diagram shows the antioxidant activity of CuAuNPs compared with standard: DPPH free radical scavenging assay.

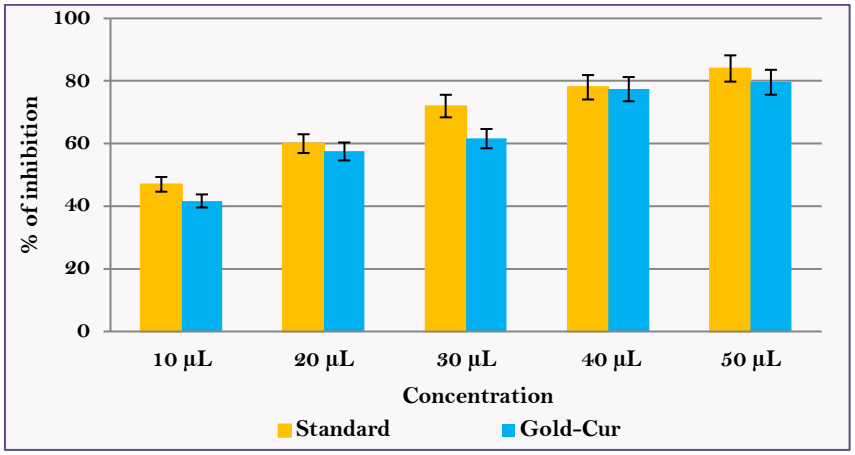

Figure 5. The bar diagram shows the anti-inflammatory activity of CuAuNPs compared with the standard bovine serum albumin assay.

Antimicrobial Activity

The antimicrobial effect of biosynthesized gold nanoparticles was tested against four oral pathogens: *S. aureus, S. mutans, E. faecalis, and C. albicans.* They were two gram-positive, one gram-negative, and one fungal pathogen. Wells of 5 mm were loaded with different concentrations of 25 µL, 50 µL, and 100 µL of CuAuNP. Results demonstrated that the gold nanoparticles, when compared with the standard (Amoxicillin, *C. albicans*-Fluconazole) group, hold an average antimicrobial effect against all four pathogens, which increased its effect dose-dependently, as depicted in Figures 6 and 7. A maximum zone of inhibition was observed in *S. aureus* and *E. faecalis* at 100µg/ mL and *C. albicans* at 25µg/ mL.

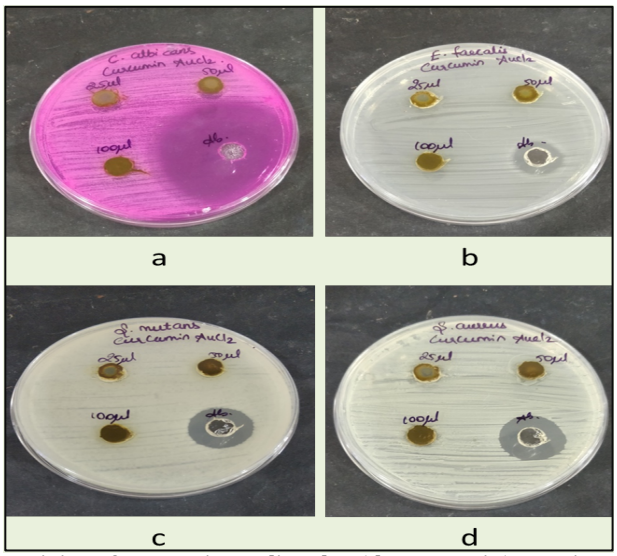

Figure 6. Antimicrobial activity of Curcumin mediated gold nanoparticles against (a) *Candida albicans*, b) *Enterococcus faecalis*, c) *Streptococcus mutans*, and d) *Staphylococcus aureus*.

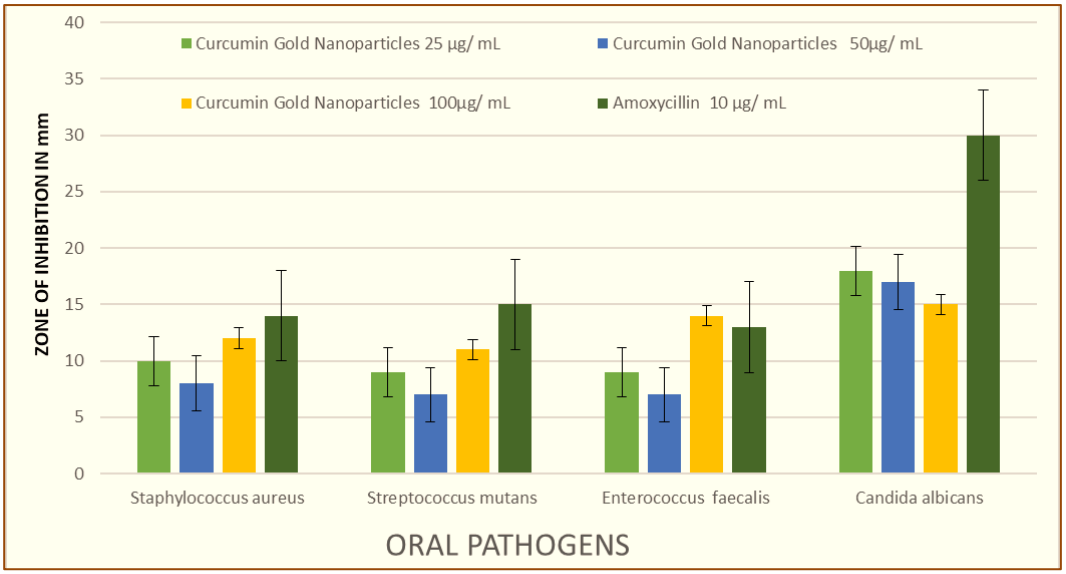

Figure 7. The bar diagram shows the zone of inhibition in mm for different concentrations of curcumin-mediated gold nanoparticles against oral pathogens.

Discussion

Phytomedicine is developing today for treating various oral diseases [17]. The most important advantage is that there are less severe side effects, and it is also effective in curing diseases. Nanomedicine is also a blooming field that helps treat chronic diseases [18]. Among various nanomaterials, gold nanoparticles have unique physicochemical properties and are an efficient drug in Nanomedicine. An essential property of them is they accurately target cells. Several drugs are coated with gold nanoparticles to improve efficacy [19].

Curcumin is one of the most useful phytochemicals derived from "turmeric" and has the potential for the green synthesis of Au NPs. During the reduction process, Polyphenol in turmeric may trigger the synthesis of Au NPs [20]. Time consumption, cost, and low curcumin solubility are the drawbacks of physicochemical methods [21]. Eco-friendly, cost-effective, green methods are warranted in the synthesis of Gold Nanoparticles,

wherein in our study, gold (III) chloride trihydrate is used as a Gold precursor, and curcumin is used as a reducing and capping agent.

Visual observation was used as an initial identification tool to confirm the synthesis of nanoparticles [22]. Colour change from yellow to ruby red showed the synthesis of gold nanoparticles synthesised from *Curcuma wenyujin* [23]. In our study, the initial color of the gold chloride solution was pale yellow, which changed to dark yellow within 15 min and dark greenish yellow, which indicated the reducing ability of curcumin extract that led to the reduction from gold chloride to gold nanoparticles. Similarly, Brazilian red propolis mediated the green synthesis of gold nanoparticles, which was observed by a colour change from pale yellow to dark red [24]. The different colors of AuNPs, from light pink to dark red, depend on these nanoparticles' size, shape, and structural characteristics [25].

UV-visible spectrophotometry was used to detect the synthesis of nanoparticles at various time intervals [14]. Existing works also reported obtaining the absorption peak at 530nm for gold nanoparticles synthesized by using Brazilian red propolis extract, which was similar to our study where gold nanoparticles showed their maximum absorption peak at 530 nm due to the excitation of surface plasmon resonance that confirmed the presence of reduced gold nanoparticles by curcumin extract. In a curcumin and potassium carbonate study, curcumin was used as a reducing agent, where Au^{3+} was easily reduced to Au^{0}. A minor peak was obtained at 425nm, which was reduced considerably, and a major peak was obtained at 525nm, which increased gradually after 4 hours. This change was due to the reaction of curcumin in solution with a reduction of Au^{3+} to Au^{0} [26].

Previous research works reported that the TEM results of synthesized gold nanoparticles from *Curcuma wenyujin* extract showed a nanoparticle size around 20nm [23].

Antimicrobial application is due to ultrasmall size and shape as small as 250 times than bacteria, causing an electrostatic interaction between Au from the nanoparticles and negative charge on the cell wall of microbes resulting in distortion such as permeability, osmolarity, electron transport leading to cell death [27]. Small nanoparticles have a great bactericidal effect by binding with a larger bacterial cell membrane surface area. There are several theories. One among them is nanoparticles, which have a strong predilection for reacting with sulfhydryl and phosphorous groups on the cell walls, thus causing significant damage resulting in the release of bacterial cell contents [28]. Another hypothesis is that Au NPs enter the bacterial cell membrane, thus attaching to NADH dehydrogenase, generating highly reactive oxygen species and exhausting the ATP, thus interrupting the respiratory chain. These radicals interact with intercellular constituents and DNA, destroying microbes [29]. Higher concentrations of Nps interact with cytoplasmic organelles and bacterial nucleic acid [30].

Bacterial cell wall composition shows the difference in antimicrobial activity. AuNPs show superior activity against Gram-negative bacteria than Gram-positive bacteria. A thick peptidoglycan layer of polysaccharide chain crosslinked by short peptides causes a hard, rigid structure for NPs to penetrate. Similarly, in our study, there was minimal antimicrobial activity against gram-positive microbes such as Streptococci mutans, and average antimicrobial activity was against gram-positive *S. aureus*, gram-negative *E. faecalis* 100µg/Ml, fungal pathogen *C. albicans* at 25 µg/ mL which increased its effect in a dose-dependent manner. *Enterococcus faecalis* has a maximum zone of inhibition of 14 mm at 100µg/ mL of Cu Au Np. Among gram-positive bacteria, the maximum zone of inhibition of 12 mm at 100µg/ mL was seen in *S. aureus* compared *to S mutans.*

In contrast, Nirmala Grace and Padalia [31] enhanced nanoparticle antimicrobial activity by having surface modification by coating with aminoglycoside antibiotics, thus increasing gram-positive bacterial activity [31,32]. Similarly, Wang et al. [33] revealed gentamycin-resistant E coli in their study. The drug promotes NP

dissolution and increases Ag ion concentration, causing bacterial growth inhibition and cell death [33]. In accordance with our study, Thangamani and Bhuvaneshwari [34], Au NPs synthesised using *Simarouba glauca* leaf extract NP size decreased with various morphological variations such as a prism, spherical like particles and found antimicrobial activity against *S. aureus*, *S. mutans*, *B. subtilis*, *E. coli*, *Proteus vulgaris*, and *K. pneumonia*. Nanoparticles with sizes ranging from 6-71 nm had superior antibacterial properties against *E. coli*, *P. aeruginosa*, and *K. pneumonia* with 200 µg/mL completely inhibited microbial growth [34]. Similar to our study, Cu Au Nps is effective against Gram-negative microbes such as E. coli at a low concentration of 100 µg/mL. Antimicrobial activity can be used to fight and control fungal pathogens. Balasubramanian et al. [35] synthesised Au NPs from the *Jasminum auriculatum* leaf extract, which showed an antifungal effect against *Aspergillus fumigatus*. Similarly, our study with a minimal concentration of 100 µg/mL was effective against *Candida albicans* with the maximum zone of inhibition of 18 mm seen at 25 µg/mL of Cu Au Np.

Conclusion

Curcumin is an antioxidant-rich natural polyphenol that is highly used for human consumption and well-being. In this study, curcumin was intervened with gold nanoparticles observed by a colour change to dark greenish-yellow. The synthesised nanoparticle was characterised by a UV-Visible spectrophotometer, which showed a surface plasmon peak at 530nm with TEM showing spherically shaped at 20 nm, confirming the presence of curcumin. The antimicrobial activity of the nanoparticle showed its resistance against *C. albicans* at 25µg/ mL, *S. aureus, and E. faecalis* at 100µg/ mL. The biosynthesized nanoparticle can be used as an effective medicine in treating oral mucosal lesions in the future.

Authors' Contributions

SD	https://orcid.org/0000-0001-6475-0909	Conceptualization, Methodology, Software, Validation, Formal Analysis, Investigation, Resources, Data Curation, Writing - Original Draft and Writing - Review and Editing.
GM	https://orcid.org/0000-0002-8108-3607	Conceptualization, Methodology, Writing - Review and Editing, Visualization, Supervision, and Project Administration.
SR	https://orcid.org/0000-0001-7059-8894	Conceptualization, Methodology, Investigation, Resources, Data Curation, Writing - Review and Editing, Visualization, Supervision and Project Administration.
KS	https://orcid.org/0000-0002-3605-1286	Conceptualization, Methodology, Investigation, Resources, Data Curation, Writing - Review and Editing, Supervision and Project Administration.

All authors declare that they contributed to a critical review of intellectual content and approval of the final version to be published.

Financial Support

None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

Acknowledgements

We thank Nanobiomedicine Lab, Saveetha Dental College for providing insight and expertise that greatly assisted this research.

References

[1] Manju S, Sreenivasan K. Gold nanoparticles generated and stabilized by water soluble curcumin-polymer conjugate: blood compatibility evaluation and targeted drug delivery onto cancer cells. J Colloid Interface Sci 2012; 368(1):144-51. https://doi.org/10.1016/j.jcis.2011.11.024

[2] Dawadi S, Katuwal S, Gupta A, Lamichhane U, Thapa R, Jaisi S, et al. Current research on silver nanoparticles: synthesis, characterization, and applications. J Nanomaterials 2021; 2021:1-23. https://doi.org/10.1155/2021/6687290

[3] Chopra H, Bibi S, Singh I, Hasan MM, Khan MS, Yousafi Q, et al. Green metallic nanoparticles: biosynthesis to applications. Front. Bioeng. Biotechnol 2022; 10:874742. https://doi.org/10.3389/fbioe.2022.874742

[4] N Cyril, George JB, Nair PV, Joseph L, Sunila CT, Smitha VK, et al. Catalytic activity of Derris trifoliata stabilized gold and silver nanoparticles in the reduction of isomers of nitrophenol and azo violet. Nano-Struc Nano-Objects 2020; 22:100430. https://doi.org/10.1016/J.NANASO.2020.100430

[5] Dharman S, Kumar R, Shanmugasundaram K. Synthesis and characterization of novel turmeric gold nanoparticles and evaluation of its antioxidant, anti-inflammatory, antibacterial activity for application in oral mucositis-an invitro study. Int J Dentistry Oral Sci 2021; 08(05):2525-32. https://doi.org/10.19070/2377-8075-21000495

[6] Behzad F, Naghib SM, Kouhbanani MAJ, Tabatabaei SN, Zare Y, Rhee KY. An overview of the plant-mediated green synthesis of noble metal nanoparticles for antibacterial applications. J Ind Eng Chem 2021; 94:92-104. https://doi.org/10.1016/j.jiec.2020.12.005

[7] Luther DC, Huang R, Jeon T, Zhang X, Lee YW, Nagaraj H, et al. Delivery of drugs, proteins, and nucleic acids using inorganic nanoparticles. Adv Drug Deliv Rev 2020; 156:188-213. https://doi.org/10.1016/j.addr.2020.06.020

[8] Upoma BP, Mahnaz F, Sajal WR, Zahan N, Hossain Firoz MS, Azam MS. Bio-inspired immobilization of silver and gold on magnetic graphene oxide for rapid catalysis and recyclability. J Environ Chem Eng 2020; 8(3):103739. https://doi.org/10.1016/j.jece.2020.103739

[9] Venkatpurwar V, Shiras A, Pokharkar V. Porphyran capped gold nanoparticles as a novel carrier for delivery of anticancer drug: in vitro cytotoxicity study. Int J Pharm 2011; 409(1-2):314-20. https://doi.org/10.1016/j.ijpharm.2011.02.054

[10] Khodadadi S, Mahdinezhad N, Fazeli-Nasab B, Heidari MJ, Fakheri B, Miri A. Investigating the possibility of green synthesis of silver nanoparticles using vaccinium arctostaphlyos extract and evaluating its antibacterial properties. Biomed Res Int 2021; 2021:5572252. https://doi.org/10.1155/2021/5572252

[11] Verma AD, Jain N, Singha SK, Quraishi MA, Sinha I. Green synthesis and catalytic application of curcumin stabilized silver Nanoparticles. J Chem Sci 2016; 128:1871-8. https://doi.org/10.1007/s12039-016-1189-7

[12] Amalraj A, Pius A, Gopi S, Gopi S. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives - a review. J Tradit Complement Med 2016; 7(2):205-33. https://doi.org/10.1016/j.jtcme.2016.05.005

[13] Dharman S, G M, Shanmugasundaram K, Sampath RK. A systematic review and meta-analysis on the efficacy of curcumin/turmeric for the prevention and amelioration of radiotherapy/radiochemotherapy induced oral mucositis in head and neck cancer patients. Asian Pac J Cancer Prev 2021; 22(6):1671-84. https://doi.org/10.31557/APJCP.2021.22.6.1671

[14] De Souza CD, Nogueira BR, Rostelato MECM. Review of the methodologies used in the synthesis of gold nanoparticles by chemical reduction. J Alloys Compd 2019; 798:714-40. https://doi.org/10.1016/j.jallcom.2019.05.153

[15] Lopresti AL. The problem of curcumin and its bioavailability: could its gastrointestinal influence contribute to its overall health-enhancing effects? Adv Nutr 2018; 9(1):41-50. https://doi.org/10.1093/advances/nmx011

[16] Dharman S, Maragathavalli, Rajeshkumar, Shanmugasundaram K. Ecofriendly synthesis, characterisation and antibacterial activity of Curcumin mediated silver nanoparticles. Int J Dentistry Oral Sci 2021; 08(04):2314-8. https://doi.org/10.19070/2377-8075-21000457

[17] Chaudhary T, Chahar A, Sharma JK, Kaur K, Dang A. Phytomedicine in the treatment of cancer: a health technology assessment. J Clin Diagn Res 2015; 9(12):XC04–XC09. https://doi.org/10.7860/JCDR/2015/15701.6913

[18] Chanda N, Kan P, Watkinson LD, Shukla R, Zambre A, Carmack TL, et al. Radioactive gold nanoparticles in cancer therapy: therapeutic efficacy studies of GA-198AuNP nanoconstruct in prostate tumor-bearing mice. Nanomedicine 2010; 6(2):201-9. https://doi.org/10.1016/j.nano.2009.11.001

[19] Tiwari PM, Vig K, Dennis VA, Singh SR. Functionalized gold nanoparticles and their biomedical applications. Nanomaterials 2011; 1(1):31-63. https://doi.org/10.3390/nano1010031

[20] Verma AD, Jain N, Singha SK, Quraishi MA, Sinha I. Green synthesis and catalytic application of curcumin stabilized silver Nanoparticles. J Chem Sci 2016; 128:1871-8. https://doi.org/10.1007/s12039-016-1189-7

[21] Silva AC, Santos PDF, Silva JTP, Leimann FV, Bracht L, Gonçalves OH. Impact of curcumin nanoformulation on its antimicrobial activity. Trends Food Sci Technol 2018; 72:74-82. https://doi.org/10.1016/j.tifs.2017.12.004

[22] Rajeshkumar S. Synthesis of silver nanoparticles using fresh bark of Pongamia pinnata and characterization of its antibacterial activity against gram-positive and gram-negative pathogens. Resource-Efficient Technologies 2016; 2(1):30-5. https://doi.org/10.1016/j.reffit.2016.06.003

[23] Liu R, Pei Q, Shou T, Zhang W, Hu J, Li W. Apoptotic effect of green synthesized gold nanoparticles from Curcuma wenyujin extract against human renal cell carcinoma A498 cells. Int J Nanomedicine 2019; 14:4091-4103. https://doi.org/10.2147/IJN.S203222

[24] Botteon CEA, Silva LB, Ccana-Ccapatinta GV, Silva TS, Ambrosio SR, Veneziani RCS, et al. Biosynthesis and characterization of gold nanoparticles using Brazilian red propolis and evaluation of its antimicrobial and anticancer activities. Sci Rep 2021; 11(1):1974. https://doi.org/10.1038/s41598-021-81281-w

[25] Majumdar R, Bag BG, Ghosh P. Mimusops elengi bark extract mediated green synthesis of gold nanoparticles and study of its catalytic activity. Appl Nanosci 2016; 6:521-8. https://doi.org/10.1007/s13204-015-0454-2
[26] Patra D, Moussawi RN. Curcumin Conjugated gold nanoparticles for nucleic acid sensing. IEEE Int Conf Nanotechnol 2016; 401-4. https://doi.org/10.1109/NANO.2015.7388621
[27] Rashmi BN, Harlapur SF, Avinash B, Ravikumar CR, Nagaswarupa HP, Anil Kumar MR, et al. Facile green synthesis of silver oxide nanoparticles and their electrochemical, photocatalytic and biological studies. Inorg Chem Commun 2020; 111:107580. https://doi.org/10.1016/j.inoche.2019.107580
[28] Ahmad A, Syed F, Imran M, Khan AU, Tahir K, Khan ZUH, et al. Phytosynthesis and antileishmanial activity of gold nanoparticles by Maytenus Royleanus. J Food Biochem 2016; 40(4):420-7. https://doi.org/10.1111/jfbc.12232
[29] Cui Y, Zhao Y, Tian Y, Zhang W, Lü X, Jiang X. The molecular mechanism of action of bactericidal gold nanoparticles on Escherichia coli. Biomaterials 2012; 33(7):2327-33. https://doi.org/10.1016/j.biomaterials.2011.11.057
[30] Manivasagan P, Venkatesan J, Senthilkumar K, Sivakumar K, Kim SK. Biosynthesis, antimicrobial and cytotoxic effect of silver nanoparticles using a novel Nocardiopsis sp. MBRC-1. Biomed Res Int 2013; 2013:287638. https://doi.org/10.1155/2013/287638
[31] Nirmala Grace A, Pandian K. Antibacterial efficacy of aminoglycosidic antibiotics protected gold nanoparticles - a brief study. Colloids Surf Physicochem Eng Asp 2007; 297(1-3):63-70. https://doi.org/10.1016/j.colsurfa.2006.10.024
[32] Padalia H, Moteriya P, Chanda S. Green synthesis of silver nanoparticles from the marigold flower and its synergistic antimicrobial potential. Arab J Chem 2015; 8:732-41. https://doi.org/10.1016/j.arabjc.2014.11.015
[33] Wang YW, Tang H, Wu D, Liu D, Liu Y, Cao A, et al. Enhanced bactericidal toxicity of silver nanoparticles by the antibiotic gentamicin. Environ Sci Nano 2016; 3(4):788-98. https://doi.org/10.1039/C6EN00031B
[34] Thangamani N, Bhuvaneshwari N. Green synthesis of gold nanoparticles using Simarouba glauca leaf extract and their biological activity of micro-organism. Chem Phys Lett 2019; 732:136587.
[35] Balasubramanian S, Kala SM, Pushparaj TL. Biogenic synthesis of gold nanoparticles using Jasminum auriculatum leaf extract and their catalytic, antimicrobial and anticancer activities. J Drug Deliv Sci Technol 2020; 57:101620.