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Comparative Evaluation of Green-Synthesized Silver Nanoparticles from Ficus glomerata and Artocarpus heterophyllus Bark Extracts: Physicochemical Characteristics, Safety and Antitumor Potential

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ABSTRACT: **Background**: Plant-mediated synthesis of silver nanoparticles (AgNPs) combines the reducing and stabilizing capacity of phytochemicals with the physicochemical and biological properties of silver. The two source manuscripts evaluated bark-derived AgNPs from Ficus glomerata (FG-B) and Artocarpus heterophyllus (AH-B), respectively, using broadly comparable in vitro and in vivo cancer models.

Objective: To prepare a structured comparative assessment of the phytochemical content, nanoparticle characteristics, acute oral safety and anticancer performance of FG-B AgNPs and AH-B AgNPs using the reported data from both manuscripts.

Methods: Reported total phenolic and flavonoid contents, differential scanning calorimetry (DSC), dynamic light scattering (DLS), zeta potential, X-ray diffraction (XRD), scanning electron microscopy (SEM), acute oral toxicity, MTT cytotoxicity against MCF-7 cells, Trypan Blue Exclusion (TBE) against HeLa cells, and Ehrlich Ascites Carcinoma (EAC) outcomes were extracted and compared descriptively. Both manuscripts used 50 mg/kg AgNP treatment in the EAC model and 2000 mg/kg for acute oral toxicity.

Results: FG-B extract contained higher total phenolics (91.3 ± 1.4 mg GAE/g) and flavonoids (72.5 ± 1.0 mg QE/g) than AH-B (84.5 ± 1.2 mg GAE/g and 67.2 ± 0.9 mg QE/g, respectively). FG-B AgNPs were larger by DLS (67.9 ± 1.1 nm) than AH-B AgNPs (51.1 ± 0.9 nm), while both exhibited moderately negative zeta potentials (−23.88 ± 1.4 and −21.69 ± 1.6 mV, respectively). AH-B AgNPs showed FTIR evidence of hydroxyl, carbonyl, amide and aromatic functional-group involvement, whereas FTIR was not reported in the FG-B manuscript. MTT IC_{50} values were 19.4 ± 1.2 µg/mL for FG-B and 23.6 ± 1.4 µg/mL for AH-B. TBE IC_{50} values were 15.4 ± 0.6 and 18.6 ± 0.7 µg/mL, respectively. In the EAC model, FG-B AgNPs reduced reported viable tumor cells from 10.5 ± 0.6 to 4.1 ± 0.3 $\times 10^6$ cells/mL, while AH-B AgNPs reduced them from 11.3 ± 0.6 to 5.8 ± 0.4 $\times 10^6$ cells/mL. Both formulations produced apoptotic morphology and DNA laddering and showed no mortality or overt toxicity at 2000 mg/kg.

Conclusion: Within the limitations of a descriptive cross-manuscript comparison, FG-B AgNPs demonstrated stronger reported in vitro cytotoxicity and greater reduction in viable EAC tumor cells, while AH-B AgNPs provided the smaller DLS particle size and additional FTIR evidence of phytochemical capping. Both preparations showed favorable

short-term safety and promising antitumor activity. A controlled head-to-head study using identical synthesis conditions, analytical methods, doses, cell passages and statistical design is required to establish comparative superiority.

1. INTRODUCTION

Cancer therapy continues to require approaches that can improve therapeutic selectivity while limiting systemic toxicity. The source manuscripts emphasize that conventional chemotherapy and radiotherapy can be constrained by adverse effects, organ toxicity and drug resistance, creating interest in phytochemical and nanotechnology-based approaches. Ficus glomerata Roxb. (syn. Ficus racemosa) and Artocarpus heterophyllus Lam. are medicinally relevant members of the Moraceae family with reported phytochemical richness and traditional use [12,14,16,35,38].

Green synthesis of AgNPs uses plant metabolites as reducing and stabilizing agents and can avoid some of the harsher reagents associated with conventional chemical synthesis. Phenolics, flavonoids, proteins and other metabolites can participate in reduction of Ag^{+} and stabilization of the resulting nanoparticles [24,31,43]. The two supplied manuscripts independently developed bark-mediated AgNP formulations and assessed their physicochemical properties, acute oral safety and anticancer activity.

A direct comparison is scientifically useful because both studies used methanolic bark extracts, AgNPs, MCF-7 and HeLa cell systems, an EAC mouse model, a 2000 mg/kg acute oral toxicity dose and a 50 mg/kg AgNP treatment dose in EAC. However, the manuscripts were not originally designed as a single controlled head-to-head experiment. Accordingly, the present paper treats the comparison as a structured descriptive analysis and explicitly identifies methodological differences and internal reporting discrepancies that should be resolved before journal submission [6,9].

2. MATERIALS AND METHODS

2.1 Comparative study design

The present manuscript was prepared by harmonizing the experimental descriptions and reported results contained in the two supplied manuscripts. The FG-B study investigated AgNPs synthesized using Ficus glomerata bark extract; the AH-B study investigated AgNPs synthesized using Artocarpus heterophyllus bark extract. The comparison focused on endpoints available in both manuscripts and separately identified endpoints available in only one manuscript.

2.2 Plant extraction

In both source studies, bark was washed with deionized water, air-dried, powdered, and extracted by maceration/stirring of 10 g material with 200 mL methanol overnight at room temperature. The extract was filtered, freeze-dried and stored at 4 °C in an amber/dark container until use.

2.3 AgNP synthesis and characterization

FG-B AgNPs were described as being synthesized by a laboratory-standardized green method with modifications to a reported Ficus-mediated protocol; nanoparticle formation was indicated by a pale-yellow to dark-brown color change. AH-B AgNPs were prepared by combining 10 mL extract with 27.5 mL of 0.02 M silver nitrate and subjecting the mixture to microwave irradiation at 400 °C for 6 min under dark conditions. Both studies used DLS/zeta-potential analysis, XRD and SEM. The AH-B study additionally reported FTIR.

2.4 Phytochemical and thermal evaluation

Total phenolic content was determined by the Folin–Ciocalteu method and expressed as mg gallic acid equivalents (GAE)/g extract. Total flavonoid content was determined by the aluminium chloride colorimetric method and expressed as mg quercetin equivalents (QE)/g extract [19,27,36]. DSC was performed on 2–3 mg samples over 0–300 °C under nitrogen at 40 mL/min, with triplicate measurements reported.

2.5 Acute oral toxicity

Both studies used female Swiss albino mice and OECD Test Guideline 425 with a 2000 mg/kg oral limit dose and 14-day observation [25,29]. Clinical signs, behavior, body weight and gross pathology were assessed; liver and kidney histology were examined in the AH-B study, and liver/kidney tissues were also assessed in the FG-B study.

2.6 In vitro anticancer assays

Both formulations were evaluated against MCF-7 breast cancer cells using MTT and against HeLa cervical cancer cells using Trypan Blue Exclusion [7,22,41]. The source manuscripts reported IC_{50} values and 48-h viability observations. Because the original manuscripts do not provide a unified raw-data set, the present comparison uses the reported summary values only.

2.7 EAC model

Both studies used intraperitoneal inoculation of 1×10^6 EAC cells in Swiss albino mice, initiated treatment on day 9 and continued treatment for 7 days, with AgNPs administered at 50 mg/kg and cyclophosphamide at 25 mg/kg as standard treatment [20,26,32,39]. Outcomes included tumor/ascitic-fluid burden, viable tumor-cell count, survival and histopathological/apoptotic observations.

2.8 Comparative data analysis

Comparisons were descriptive. Where useful, relative differences were calculated from the reported means, for example percentage reduction in viable tumor cells = [(control − treated)/control] × 100. These calculations do not constitute independent statistical testing. No p-values were generated from summary data.

3. RESULTS

3.1 Comparative phytochemical profile

Parameter	Ficus glomerata bark	Artocarpus heterophyllus bark	Comparative interpretation
Total phenolic content	91.3 ± 1.4 mg GAE/g	84.5 ± 1.2 mg GAE/g	FG-B reported higher
Total flavonoid content	72.5 ± 1.0 mg QE/g	67.2 ± 0.9 mg QE/g	FG-B reported higher
Extract solvent	Methanol	Methanol	Comparable
DSC behavior	Predominantly amorphous	Predominantly amorphous	Comparable

FG-B showed approximately 8.0% higher reported TPC and 7.9% higher reported TFC than AH-B when calculated from the manuscript means. Both extracts were described as phytochemically rich and predominantly amorphous by DSC.

3.2 Nanoparticle physicochemical characteristics

Parameter	FG-B AgNPs	AH-B AgNPs	Comparative interpretation
Mean DLS particle size	67.9 ± 1.1 nm	51.1 ± 0.9 nm	AH-B smaller by ~24.7%
Zeta potential	−23.88 ± 1.4 mV	−21.69 ± 1.6 mV	Both moderately negative; FG-B more negative
pH	6.5	6.3	Both near physiological range
Viscosity	13.1 ± 0.3 cP	12.5 ± 0.4 cP	Similar

14-day visual stability	No precipitation/aggregation	No precipitation/aggregation	Comparable
Redispersibility	>90% recovery	>90% recovery	Comparable
XRD	Crystalline; peaks reported at 16.8, 22.4, 27.9, 32.3, 37.5, 44.1, 64.2°	Ag peaks at 38.1, 44.3, 64.5, 77.4°	Both crystalline; AH-B pattern more directly assigned to fcc Ag
FTIR	Not reported	O–H, C–H, C=O/amide, C–O and metal–oxygen-associated bands	AH-B provides additional chemical-group evidence
SEM	Spherical morphology reported	Spherical, uniform/monodispersed morphology reported	Comparable overall morphology

The most conspicuous physicochemical difference was hydrodynamic particle size: AH-B AgNPs had the smaller reported DLS diameter. Both formulations had moderately negative zeta potentials and short-term physical stability. The AH-B manuscript additionally supplied FTIR evidence supporting participation of hydroxyl, carbonyl/amide, aromatic and carbohydrate-associated groups in nanoparticle formation/stabilization [6,9,24,43].

3.3 Acute oral safety

Safety endpoint	FG-B AgNPs	AH-B AgNPs	Comparative interpretation
Dose	2000 mg/kg p.o.	2000 mg/kg p.o.	Identical reported limit dose
Observation	14 days	14 days	Identical
Mortality	None reported	None reported	Comparable
Clinical toxicity	None reported	None reported	Comparable
Gross organ pathology	No abnormality reported	No abnormality reported	Comparable
Histology	No major liver/kidney injury reported	No hepatotoxicity/nephrotoxicity reported	Favorable short-term profile

Both source manuscripts reported no mortality or overt toxicity at 2000 mg/kg and described normal gross organ findings. [2,21,25,29].

3.4 MTT cytotoxicity against MCF-7

Endpoint	FG-B AgNPs	AH-B AgNPs	Comparison
IC_{50}	19.4 ± 1.2 µg/mL	23.6 ± 1.4 µg/mL	FG-B lower by ~17.8%
48-h viability at reported IC_{50}	44.5 ± 2.2%	51.2 ± 2.5%	FG-B lower viability
Comparator reported in IC_{50} text	Cyclophosphamide 7.5 ± 0.8 µg/mL	Cyclophosphamide 6.8 ± 0.4 µg/mL	Not directly comparable

FG-B showed the lower reported MTT IC_{50} and lower reported viability.

3.5 Trypan Blue Exclusion against HeLa

Endpoint	FG-B AgNPs	AH-B AgNPs	Comparison
IC_{50}	15.4 ± 0.6 µg/mL	18.6 ± 0.7 µg/mL	FG-B lower by ~17.2%
48-h viability at reported IC_{50}	25.1 ± 1.8%	35.3 ± 2.1%	FG-B lower viability
Morphology	Shrinkage, blebbing, granularity, nuclear fragmentation	Shrinkage, blebbing, granularity, nuclear fragmentation	Comparable apoptotic morphology

The TBE assay again favored FG-B on the reported summary endpoints. Both formulations caused dose-dependent loss of HeLa viability and morphological changes consistent with apoptosis.

3.6 EAC antitumor activity

Endpoint	FG-B AgNPs	AH-B AgNPs	Descriptive comparison
AgNP dose	50 mg/kg	50 mg/kg	Identical
Reported tumor volume: control → AgNP	9.1 ± 0.9 → 3.6 ± 0.4 mL	8.4 ± 0.6 → 4.3 ± 0.5 mL	Both reduced tumor burden
Reported ascitic fluid: control → AgNP	6.8 ± 0.7 → 2.8 ± 0.24 mL	6.2 ± 0.4 → 3.1 ± 0.3 mL	Both reduced fluid accumulation
Reported growth inhibition	58.7%*	52.3%*	FG-B higher*
MST	23.1 ± 1.7 days	25.6 ± 1.2 days	AH-B longer reported MST
% increase in life span	46.1%	48.8%	AH-B slightly higher
Viable tumor cells: control → AgNP	10.5 ± 0.6 → 4.1 ± 0.3 $\times 10^6$/mL	11.3 ± 0.6 → 5.8 ± 0.4 $\times 10^6$/mL	FG-B greater absolute/reported reduction
Approx. reduction calculated from reported means	61.0%	48.7%	FG-B greater descriptive reduction

3.7 Apoptosis and histopathology

Both formulations produced cytological changes consistent with apoptosis in EAC-associated observations, including nuclear condensation, nuclear fragmentation, chromatin margination, cytoplasmic vacuolization and apoptotic bodies. DNA laddering was reported in both manuscripts as evidence of internucleosomal fragmentation [4,11,42]. In acute-toxicity histology, both studies reported preserved liver/kidney architecture and absence of major degenerative, inflammatory or necrotic lesions.

4. COMPARATIVE DISCUSSION

The comparative findings indicate that both bark extracts can support green synthesis of AgNPs with measurable physicochemical stability and anticancer activity. FG-B possessed the higher reported phenolic and flavonoid contents, which may contribute to reduction and capping capacity. Its AgNPs were larger by DLS but exhibited a somewhat more negative zeta potential. AH-B produced the smaller DLS particle size and, importantly, its manuscript included FTIR characterization that directly documented functional groups associated with nanoparticle formation and stabilization[6,9,24,43].

The biological findings consistently favored FG-B on the reported in vitro cytotoxicity endpoints. Its MTT IC_{50} of 19.4 µg/mL was lower than the AH-B value of 23.6 µg/mL, and its TBE IC_{50} of 15.4 µg/mL was lower than the AH-B value of 18.6 µg/mL. The reported 48-h viabilities also showed greater loss of viability with FG-B. These differences are directionally consistent across two cancer cell lines and therefore identify FG-B as a strong candidate for further mechanistic investigation.

The EAC findings are more nuanced. FG-B produced a larger reported reduction in viable tumor cells and a higher reported tumor-growth-inhibition percentage, whereas AH-B showed a longer reported mean survival time and slightly higher percentage increase in life span. This apparent divergence suggests that tumor-cell suppression and survival outcomes may not rank the two formulations identically. It also emphasizes the importance of harmonized dosing, tumor burden measurement, survival methodology and statistical analysis in a future head-to-head experiment.

The apoptosis-related findings provide a plausible common biological explanation for the anticancer effects. Both manuscripts report membrane damage, nuclear condensation/fragmentation and DNA laddering. Published literature cited within the source manuscripts indicates that plant-mediated AgNPs can generate oxidative stress and activate apoptotic signaling [4,11,18,42]. Nevertheless, the present comparative study should not claim a confirmed molecular mechanism because neither source manuscript provides a complete mechanistic panel of intracellular ROS, mitochondrial membrane potential, caspase-9/caspase-3 activation, Bax/Bcl-2 ratio or cell-cycle distribution.

From a formulation perspective, both preparations had moderately negative zeta potentials and short-term physical stability, with >90% redispersibility reported. The smaller AH-B DLS size could be advantageous for cellular interaction, while the higher phenolic/flavonoid content and stronger reported in vitro cytotoxicity of FG-B indicate a potentially stronger biofunctional phytochemical contribution. These properties should be evaluated together rather than treating particle size alone as a surrogate for therapeutic superiority [6,9].

5. CONCLUSION

The comparative analysis of the two supplied manuscripts indicates that Ficus glomerata bark and Artocarpus heterophyllus bark are both promising phytochemical sources for green synthesis of AgNPs. FG-B extract showed higher reported phenolic and flavonoid contents, while AH-B AgNPs showed a smaller DLS particle size and additional FTIR evidence of phytochemical involvement. FG-B AgNPs demonstrated stronger reported MTT and TBE cytotoxicity and a greater descriptive reduction in viable EAC tumor cells, whereas AH-B showed a longer reported mean survival time in the EAC study. Both formulations exhibited favorable short-term acute safety at 2000 mg/kg and apoptosis-associated cellular changes. These findings support further development of both systems, with FG-B emerging as the stronger candidate for mechanistic anticancer optimization based on the currently reported in vitro and tumor-cell-count outcomes. A properly controlled head-to-head experiment is required before claiming definitive superiority.

6. DECLARATIONS

Ethics statement: The source manuscripts state that animal experiments followed institutional ethical guidelines and OECD Guideline 425.

Conflict of interest: None.

Funding: No new funding was used for preparation of this comparative analysis.

Conflict of interest: None

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