Antimalarial Evaluation of Magnesium Nanoparticlres of Bioactive Compounds Derived From Crinum Jagus Rhizome

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Research Article

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Abstract

Magnesium Nanoparticles (MgNPs), are biocompatible and have shown promise in various biomedical applications, including antimicrobial and antimalarial treatments. Synthesis of magnesium nanoparticles from crude extract and isolated compound of *crinum jagus* rhizome and their antimalarial activity were reported. Magnesium nanoparticles mediated by crude extract and isolated compound were characterized by UV-visible spectroscopy, SEM and TEM analyses. The UV-visible absorption results of the magnesium nanoparticles synthesized from the crude extract showed absorption that varies slightly across the wavelength range of 343 nm to 353 nm, with a peak absorption value of 1.52934 at 345 nm. UV-visible absorption data for the magnesium nanoparticles synthesized from the isolated compound (lupeol) shows significant absorption in the range of 343 nm to 353 nm. The absorption values are relatively high, with a peak at 345 nm where the absorbance is 0.88005. MgNPs synthesized from the crude extract exhibited the best antimalarial activity (IC50 = 0.1310), significantly outperforming both the lupeol-based MgNPs (IC50 = 0.9103) and chloroquine (IC50 = 0.2762). The enhanced activity of the crude extract-based MgNPs may be attributed to the synergistic effects of multiple bioactive compounds present in the crude extract. The antimalarial activity observed in this study highlights the potential of combining traditional plant-based medicine with nanotechnology. The significantly lower IC50 values (0.1310) for the crude extract MgNPs compared to chloroquine (0.2762) demonstrate the promising future of this approach in overcoming drug resistance and improving the efficacy of antimalarial treatments.

Introduction

Synthesis of metal nanoparticles through the utilization of plant extracts represents a notably straightforward, practical, cost-effective, and ecologically sustainable approach that reduces the necessity for toxic chemical substances (Vanlalveni et al., 2021). The fabrication of green nanoparticles possesses a multitude of applications within the realms of environmental science and medicine (Kankonkar, 2022). Nanotechnology-oriented methods have been posited as a mechanism for the formulation of plant extracts, facilitate in crossing the biological barriers, to increase bioavailability of poorly water-soluble phytochemicals, to encapsulate mixture compounds of different phytochemicals, to provide targeted delivery of phytochemicals to specific organs resulting in low toxicity (Syahnita, 2021). However, health-related adversities stemming from pathogenic microorganisms threaten many people's lives globally (Thatyana et al., 2023). NPs are synthesized by using various metals such as gold, silver, iron, zinc, copper, palladium, platinum, and metal oxides (Simon et al., 2022). Magnesium nanoparticles (Mg-NPs) have emerged as a promising material due to their unique properties, including high biocompatibility, biodegradability, and catalytic potential. In recent years, the green synthesis of Mg-NPs using plant extracts has gained considerable attention as an eco-friendly and sustainable approach (Patra *et al*., 2023). This method not only eliminates the use of toxic chemicals but also harnesses the natural reducing, capping, and stabilizing agents found in plant secondary metabolites such as alkaloids, flavonoids, and phenolics, leading to nanoparticles with enhanced biological activity (Patra *et al*., 2023). Plant-mediated Mg-NP synthesis offers significant advantages over conventional methods by being cost-

effective, simple, and environmentally benign. The plant extracts serve dual roles: acting as a reductant to convert magnesium ions into nanoparticles and stabilizing the formed nanoparticles to prevent agglomeration (Kumar & Khan, 2022). The use of different plant species and parts (leaves, stems, roots) has resulted in diverse nanoparticle sizes and morphologies, which directly influence their functional properties, such as antimicrobial, antioxidant, and catalytic activities (Jeevanandam et al., 2021). Magnesium nanoparticles synthesized from plant extracts have shown significant potential in biomedical applications, particularly in antimicrobial therapies and drug delivery systems, due to their ability to interact effectively with biological systems (El-Husseiny *et al*., 2021). The use of plant-based resources not only eliminates the need for toxic chemicals but also enhances the biocompatibility of the nanoparticles, making them suitable for medical applications such as drug delivery, wound healing, and antimicrobial activities (Sharma et al., 2023; Rajeshkumar & Bharath, 2020). Plant extracts contain a variety of bioactive compounds, including alkaloids, flavonoids, and phenolic acids, which facilitate the reduction of magnesium ions into nanoparticles while preventing their agglomeration (Khalil et al., 2022). This green synthesis approach is both sustainable and scalable, allowing for the production of nanoparticles with controlled size, shape, and enhanced surface properties, which are critical for their effectiveness in specific applications (Kumar et al., 2021). Recent studies have highlighted the potential of magnesium nanoparticles synthesized from plant extracts in addressing key challenges in nanomedicine and environmental science, particularly due to their high reactivity, biodegradability, and lower cytotoxicity compared to other metal nanoparticles (Nasrollahzadeh et al., 2022). The global rise in drug-resistant malaria strains has necessitated the development of new treatment strategies. Antimalarial drugs such as chloroquine and artemisinin-based therapies are becoming less effective due to the increasing adaptability of *Plasmodium* species, the parasites responsible for malaria (Sankar, 2023). Recent studies suggest that MgNPs synthesized from plant extracts exhibit promising antimalarial properties, potentially by enhancing drug delivery and targeting parasitic cells more effectively (Teli *et al*., 2021). The phytochemicals present in plant extracts, when combined with the properties of magnesium nanoparticles, offer synergistic effects that can disrupt the lifecycle of the malaria parasite, thereby improving treatment outcomes (Sharma, (2022). In line with this, biomedical application of magnesium nanoparticles synthesized from crude extract and isolated compound of *crinum jagus* rhizome and their antimalarial evaluation was studied.

Materials and Methods

Preparation of Crinum jagus Rhizome

Rhizomes of *Crinum jagus*, were collected in June 2023, from Dabawa of Dutsin-Ma Katsina, Nigeria. The plant was authenticated by botanists in the Department of Biological Science, Faculty of life sciences, Federal University of Dutsin-ma, it then dried and ground into powder. The plant extract was obtained by soaking 200g of the plant material in 500ml methanol and macerated for 72hrs, then filtered and concentrated (Oubannin et al., 2024). The crude extract (2g) was subjected to chromatographic techniques, (silica gel column chromatography and thin layer chromatography, to isolate specific compounds. Lupeol, a triterpenoid, is separated by eluting the mixture with an appropriate solvent

system (mixture of hexane and ethyl acetate). The isolated lupeol is characterized and confirmed using Nuclear Magnetic Resonance (NMR) spectroscopy and Mass Spectrometry (MS) (Musa et al., 2023). The crude extract and isolated compound were then used for synthesis of magnesium nanoparticles (Dhage et al., 2023).

Biosynthesis Magnesium Nanoparticles

About 0.1M magnesium sulfate ($MgSO_4$) solution was prepared in distilled water. In a typical reaction, 50 mL of the $MgSO_4$ solution was mixed with 5 mL of the *Crinum jagus* rhizome extract and stirred vigorously for 15–30 minutes at room temperature using a magnetic stirrer. The addition of 1M NaOH was done dropwise until the pH of the solution reached 10, promoting the reduction of magnesium ions (Mg^{2+}) to form magnesium nanoparticles (Sharma et al., 2021). The solution was continuously stirred for 2 hours, during which a color change was observed, indicating the formation of magnesium nanoparticles of the crude extract (Patel et al., 2022). Another 0.1M magnesium sulfate ($MgSO_4$) solution was prepared in distilled water. In a typical reaction, 50 mL of the $MgSO_4$ solution was mixed with 1 mL of the isolated compound and stirred vigorously for 15–30 minutes at room temperature using a magnetic stirrer. The addition of 1M NaOH was done dropwise until the pH of the solution reached 10, promoting the reduction of magnesium ions (Mg^{2+}) to form magnesium nanoparticles of the isolated compound. The solution was continuously stirred for 2 hours, during which a color change was observed, indicating the formation of magnesium nanoparticles (Labaran et al., 2024).

In-Vitro Schizont Growth Inhibition Assay

Parasite Culture

P. falciparum infected blood was obtained from Kadpoly Clinic cultured in human erythrocytes using RPMI-1640 medium supplemented with 15% human serum and the culture maintained at 37°C in an incubator with 5% CO_2. *P. falciparum* infected blood was obtained from Kaduna polytechnic Medical Center, using complete malaria culture media (CMCM) in gas combination (5% CO_2, 5%$O_2$and 90% N_2 gases at 37^{o}C) the blood was cultured and subsequently synchronized using 5% sorbitol following standard protocols mark III according to WHO. Different concentrations of crude extract nanoparticles and the isolated compound (ranging from 1.5 µg/ml to 100 µg/ml) were prepared and used in screening against cultivated isolate of the *P falciparum* clinical strain to assess growth inhibition (Bahl et al., 2021). Ten (10 µM) of Chloroquine phosphate and Quinine were prepared and used as the positive control to benchmark the efficacy of the plant extracts. The percentage growth inhibition was calculated, and the IC_{50} values was determined for the crude extract nanoparticles and isolated compound using Prism 5 software (Feix et al., 2023).

Microscopy Analysis

After 40 to 48 hours of incubation, thin blood smears was prepared from each sample, stained with Giemsa, and examined under a microscope. The schizont count was recorded to determine the percentage of schizont inhibition (Barnes *et al.*, 2022). The percentage schizont inhibition for each concentration of MgNPs was calculated and plotted to generate dose-response curves. The IC50 value, representing the concentration required to inhibit 50% of schizont growth, was determined using non-linear regression analysis (Mertens et al., 2024).

The inhibition of parasite growth in the drug treated groups was calculated as follows: -

Percentage viability = Number of schizonts in test well X 100

Number of schizonts in control wells

% inhibition = Number of schizoids in control wells - Number of schizonts in test well X 100

Number of schizonts in control wells.

Results

Table 1
Sample C In vitro schizont growth inhibition activity of the drug against P falciparum clinical strain

	Sample C			**Chloroquine**		
Concentration	**% viability**	**% Inhibition**	**IC50**	**%viability**	**% Inhibition**	**IC50**
1.56	15.12 ± 1.38	84.86 ± 1.38	0.1310µg/ml	33.59 ± 0.80	66.41 ± 0.80	0.2762µg/ml
3.125	7.44 ± 0.82	91.62 ± 0.82		32.02 ± 0.77	67.98 ± 0.77	
6.25	7.20 ± 0.52	92.56 ± 0.52		30.38 ± 0.87	69.62 ± 0.87	
12.5	6.02 ± 0.50	93.04 ± 0.50		25.58 ± 0.99	74.42 ± 0.99	
25.0	5.29 ± 1.15	94.47 ± 1.15		17.58 ± 1.18	82.42 ± 1.18	
50..0	4.08 ± 0.10	95.68 ± 0.10		11.99 ± 0.51	88.01 ± 0.51	
100.0	3.41 ± 0.25	96.41 ± 0.25		6.37 ± 1.45	93.63 ± 1.45	

Table 2
Sample I In vitro schizont growth inhibition activity of the drug against *P falciparum* clinical strain

	Sample I			**Chloroquine**		
Concentration	**% viability**	**% Inhibition**	**IC50**	**%viability**	**% Inhibition**	**IC50**
1.56	30.11 ± 0.97	55.49 ± 0.97	**0.9103 µg/ml**	33.59 ± 0.80	66.41 ± 0.80	**0.2762µg/ml**
3.125	12.55 ± 1.34	87.45 ± 1.34		32.02 ± 0.77	67.98 ± 0.77	
6.25	7.02 ± 0.31	92.98 ± 0.31		30.38 ± 0.87	69.62 ± 0.87	
12.5	6.60 ± 0.006	93.40 ± 0.006		25.58 ± 0.99	74.42 ± 0.99	
25.0	6.40 ± 0.29	93.60 ± 0.29		17.58 ± 1.18	82.42 ± 1.18	
50..0	4.77 ± 0.33	95.23 ± 0.33		11.99 ± 0.51	88.01 ± 0.51	
100.0	4.26 ± 0.18	95.75 ± 0.18		6.37 ± 1.45	93.63 ± 1.45	

Table 3
Calculations of IC50 for Extract, Isolate and Chloroquine Using Prism Software

log(inhibitor) vs. response Variable slope	Extract	Isolate	Chloroquine
Best-fit values			
BOTTOM	-249600	-122.5	-81460
TOP	78.92	93.66	93.87
LOGIC50	-0.8828	-0.04081	-0.5588
HILLSLOPE	3.965	2.858	5.259
IC50	0.1310	0.9103	0.2762
Span	249660	216.2	81556
Goodness of Fit			
Robust Sum of Squares	8.732	27.52	7.596
RSDR	11.10	0.2308	2.170
Number of points			
Analyzed	24	24	24

Table 4
Wavelength (nm) and absorptions of crude extract's MgNPs

Wavelength(nm)	Crude Extract's NPs (Abs)
353	1.38526
351	1.44576
349	1.49422
347	1.49524
345	1.52934
343	1.51109

Table 5
Wavelength (nm) and absorptions of isolate's MgNPs

Wavelength(nm)	Isolate'sNPs (Abs)
353	0.84201
351	0.84215
349	0.83646
347	0.86019
345	0.88005
343	0.85078

Discussion

Antimalarial Evaluation

Magnesium Nanoparticles (MgNPs), are biocompatible and have shown promise in various biomedical applications, including antimicrobial and antimalarial treatments (Fatiqin et al., 2021). Nanoparticles offer a higher surface area-to-volume ratio, which can enhance drug solubility and bioavailability (Uddin et al., 2024). In this study, the MgNPs synthesized from the crude extract of *Crinum jagus* rhizome exhibited the best antimalarial activity (IC50 = 0.1310), significantly outperforming both the lupeol-based MgNPs (IC50 = 0.9103) and chloroquine (IC50 = 0.2762) (Table 3). The enhanced activity of the crude extract-based MgNPs may be attributed to the synergistic effects of multiple bioactive compounds present in the crude extract (Mohammed & Hawar, 2022). This is consistent with existing research suggesting that crude extracts often provide enhanced therapeutic effects compared to isolated compounds due to the presence of a broader range of bioactive compounds that work together to combat pathogens (Kekani & Witika, 2023). Chloroquine, one of the most commonly used antimalarial drugs, has been used as a standard control in numerous studies on novel antimalarial agents (Stevens et al., 2021). In this finding that the crude extract MgNPs had a significantly lower IC50 than chloroquine suggests that the nanoparticles derived from *Crinum jagus* crude extract could be a potent alternative or complementary treatment for malaria, particularly in chloroquine-resistant strains of *Plasmodium* (Lokole et al., 2024). These results align with similar studies that demonstrate the potential of nanoparticles in enhancing the bioactivity of plant-derived compounds (Moraes-de-Souza et al., 2024). In contrast, the lupeol-based MgNPs had a higher IC50 (0.9103), which may suggest that while lupeol is bioactive, the isolated compound lacks the synergistic support from other compounds present in the crude extract. This finding emphasizes the importance of considering the whole plant extract in drug development, particularly when using nanoparticle delivery system.

UV-Visible Spectroscopy of the Crude Extract's MgNPs

The UV-Visible absorption results of the magnesium nanoparticles synthesized from the crude extract of *Crinum jagus* rhizome show a distinct absorption pattern, which provides valuable insights into the optical properties and potential applications of the nanoparticles. The data shows that the absorption of the crude extract's nanoparticles (NPs) varies slightly across the wavelength range of 343 nm to 353 nm, with a peak absorption value of 1.52934 at 345 nm. As the wavelength decreases from 353 nm to 345 nm, there is a general increase in absorbance. From 345 nm to 343 nm, the absorbance slightly decreases from 1.52934 to 1.51109. The peak absorbance of 1.52934 at 345 nm suggests that the magnesium nanoparticles synthesized from the crude extract exhibit strong optical activity in the UV region (Table 4). Nanoparticles often exhibit enhanced absorption in the UV-Visible range due to surface plasmon resonance (SPR), which is the collective oscillation of electrons in response to light (Mika & Zakari, 2024). The absorption data provides clues about the size and shape of the nanoparticles *(*Wan Mat Khalir *et al.*, 2020). The peak absorbance in the UV region typically indicates small-sized nanoparticles (Sreenivasagan et al., 2021). The sharpness and specific wavelength of the absorption peak suggest that the magnesium nanoparticles may be spherical and monodispersed (uniform in size and shape) (Chutrakulwong et al., 2024). A higher absorbance value indicates a higher concentration of nanoparticles or better light absorption due to their surface properties (Melkamu & Bitew, 2021). Since these nanoparticles were tested for antimalarial activity, their strong absorption at these wavelengths could contribute to their biological interaction with cells, enhancing the efficacy of drug delivery.

UV-Visible Spectroscopy of the Isolated Compound's MgNPs

The UV-Visible absorption data for the magnesium nanoparticles synthesized from the isolated compound (lupeol) shows significant absorption in the range of 343 nm to 353 nm. The absorption values are relatively high, with a peak at 345 nm where the absorbance is 0.88005, indicating a strong interaction of the nanoparticles with UV light at this wavelength (Table 5). This peak suggests optimal nanoparticle stability and resonance due to surface plasmon activity, which is typical for metal nanoparticles (Akinwumi Gentle et al., 2020). The slight fluctuations in absorbance values across the measured wavelengths, such as 0.86019 at 347 nm and 0.84201 at 353 nm, may reflect variations in particle size or distribution (Table 5). The trend observed within this narrow range is characteristic of magnesium nanoparticles, and the high absorbance values confirm the successful synthesis of lupeol-based magnesium nanoparticles with distinct optical properties (Al-Abdullah, 2023). The consistency of absorbance, with values ranging between 0.83646 and 0.88005, further supports the formation of uniform nanoparticles with good optical behavior (Adeleye et al., 2023).

Scanning Electron Microscope (SEM)

The SEM images obtained from the different temperatures, are presented in Fig. 5 and Fig. 6 which showed the platelets of magnesium nanoparticles for the crude extract and isolated compound of *Crinum jagus* rhizome. The bioactive compounds present in this plant played a vital role acted as reducing and capping agents. The presence of this bioactive molecules from the plant extract and the

isolated compound were confirmed by UV-visible spectroscopy analysis of the samples which indicates the formation of the nanoparticles (Fig. 7 and Fig. 8). Figure 6a, b, and c showed the TEM images of the crude extract nanoparticles obtained at higher temperature of synthesis (90^{o}c). The MgNPs showed size range of 3.22nm-50nm indicating multiple spread nature of the nanoparticles. Figure 6d, e and f showed the TEM images of the isolated nanoparticles obtained at 60^{o}c with the nanoparticles size ranged between 3.22nm-100nm indicating single dispersity.

Conclusion

Magnesium nanoparticles mediated from the crude extract and isolated compound of *Crinum jagus* rhizome characterized by (UV-visible spectroscopy, SEM and TEM) analyses were reported. The UV-Visible absorption results of the magnesium nanoparticles synthesized from the crude extract shows that the absorption of the crude extract's nanoparticles (NPs) varies slightly across the wavelength range of 343 nm to 353 nm, with a peak absorption value of 1.52934 at 345 nm. UV-Visible absorption data for the magnesium nanoparticles synthesized from the isolated compound (lupeol) shows significant absorption in the range of 343 nm to 353 nm. The absorption values are relatively high, with a peak at 345 nm where the absorbance is 0.88005. The MgNPs synthesized from the crude extract of *Crinum jagus* rhizome exhibited the best antimalarial activity (IC50 = 0.1310), significantly outperforming both the lupeol-based MgNPs (IC50 = 0.9103) and chloroquine (IC50 = 0.2762). The enhanced activity of the crude extract-based MgNPs may be attributed to the synergistic effects of multiple bioactive compounds present in the crude extract. The antimalarial activity observed in this study highlights the potential of combining traditional plant-based medicine with nanotechnology. The significantly lower IC50 values (0.1310) for the crude extract MgNPs compared to chloroquine (0.2762) demonstrate the promising future of this approach in overcoming drug resistance and improving the efficacy of antimalarial treatments. Therefore, further research and clinical trials is recommended to explore the full therapeutic potential of these nanoparticles.

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Figures

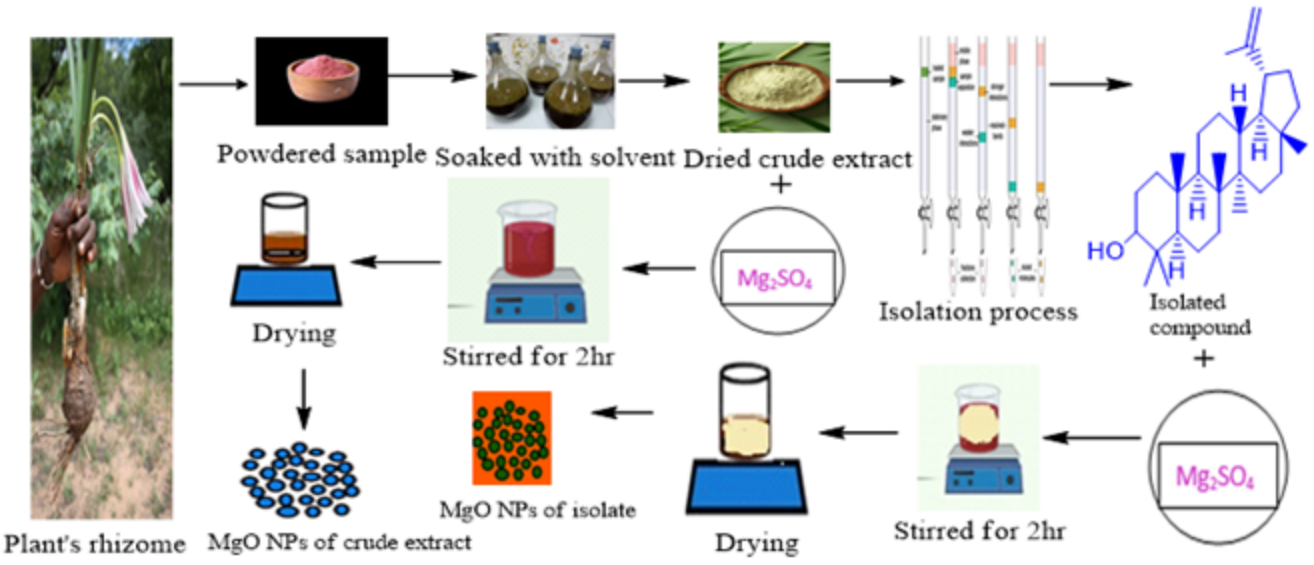

Figure 1

Procedure for the Preparation of MgO Using Crude Extract and Isolated Compound

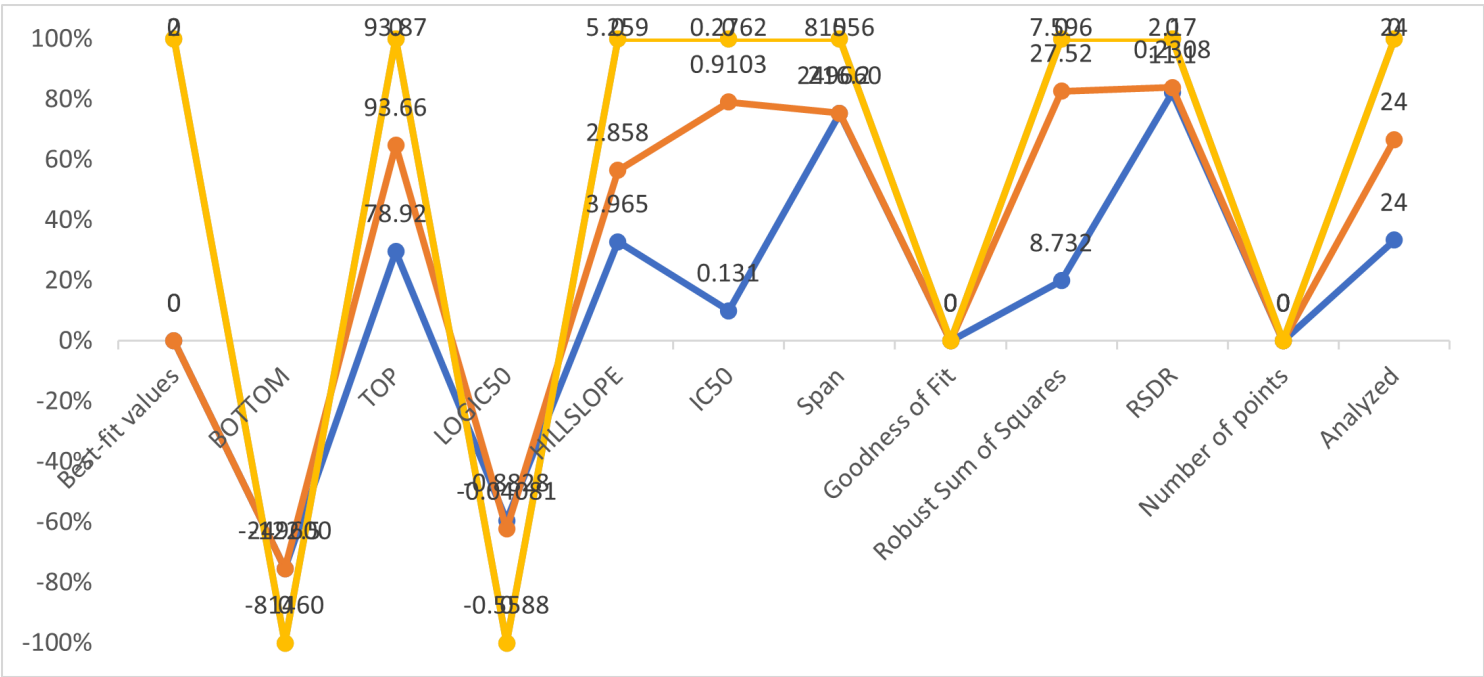

Figure 2

Graphical representation of the anti-plasmodia effects the extract C I and Chloroquine showing their respective IC50

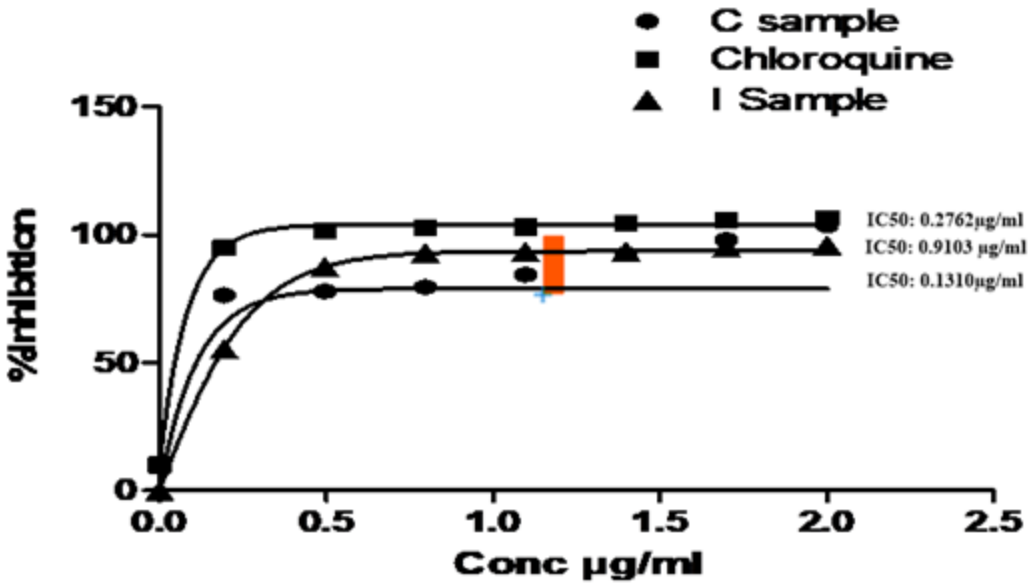

Fig. 3: Graphical representation of IC50 for C sample, chloroquine and I sample

Figure 3

See image above for figure legend

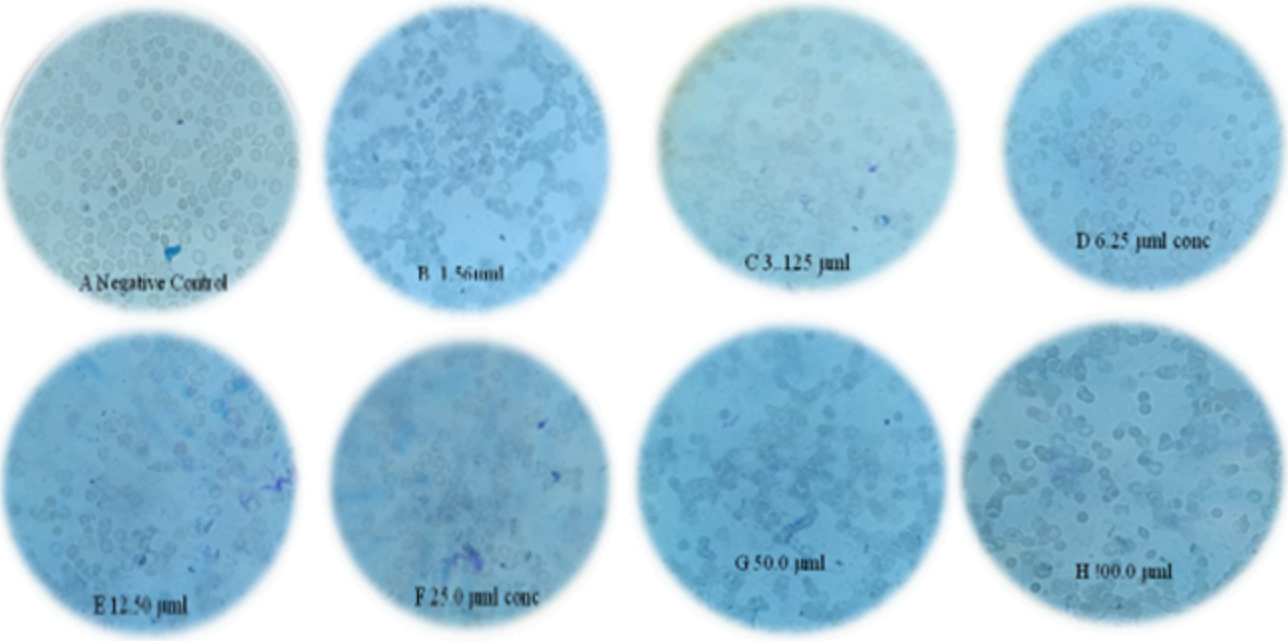

Figure 4

IC50 images of naturally synthesized magnesium nanoparticles of C sample, I sample and chloroquine

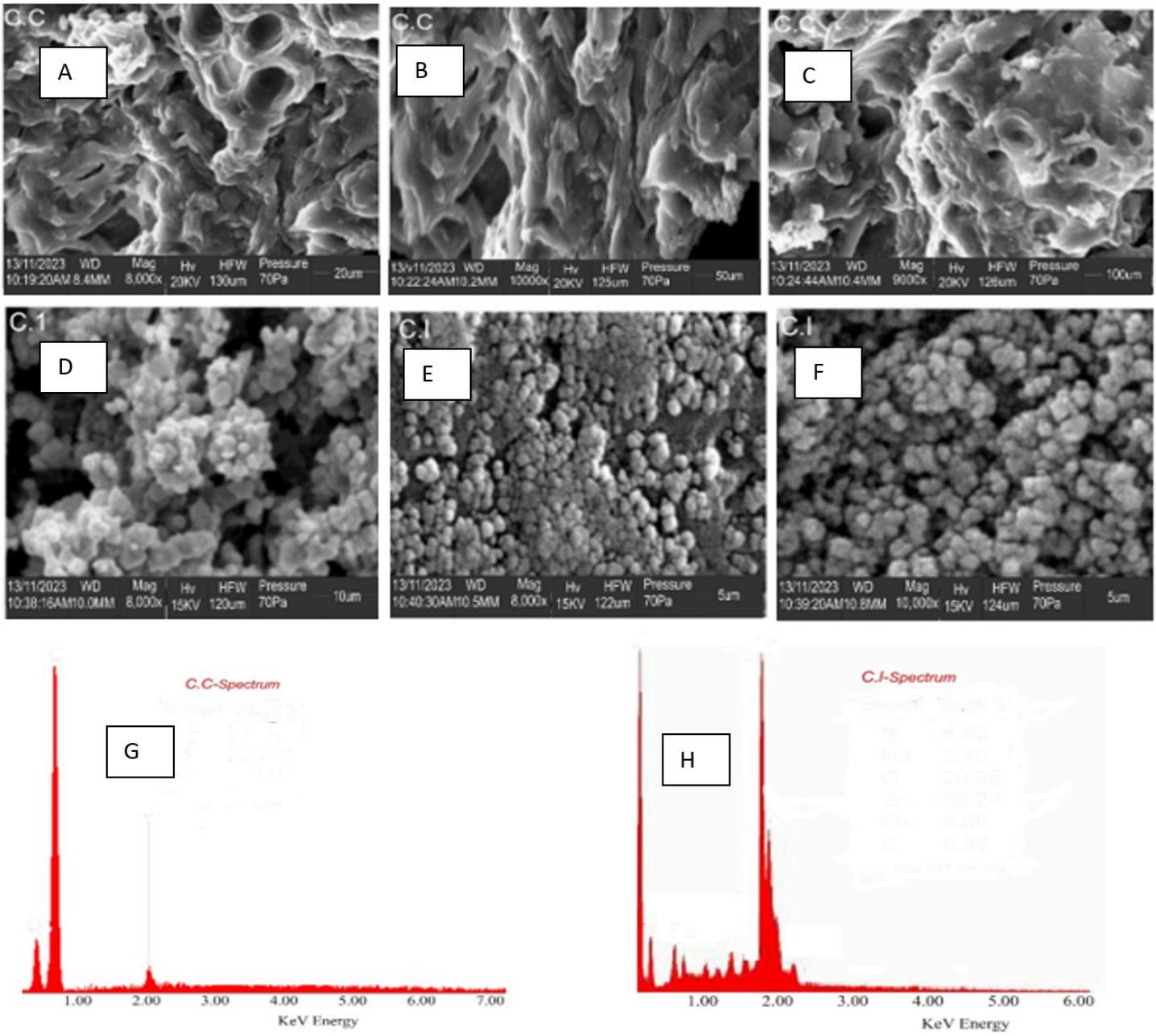

Figure 5

Scanning electron microscope of magnesium nanoparticles of the crude and isolated compound.

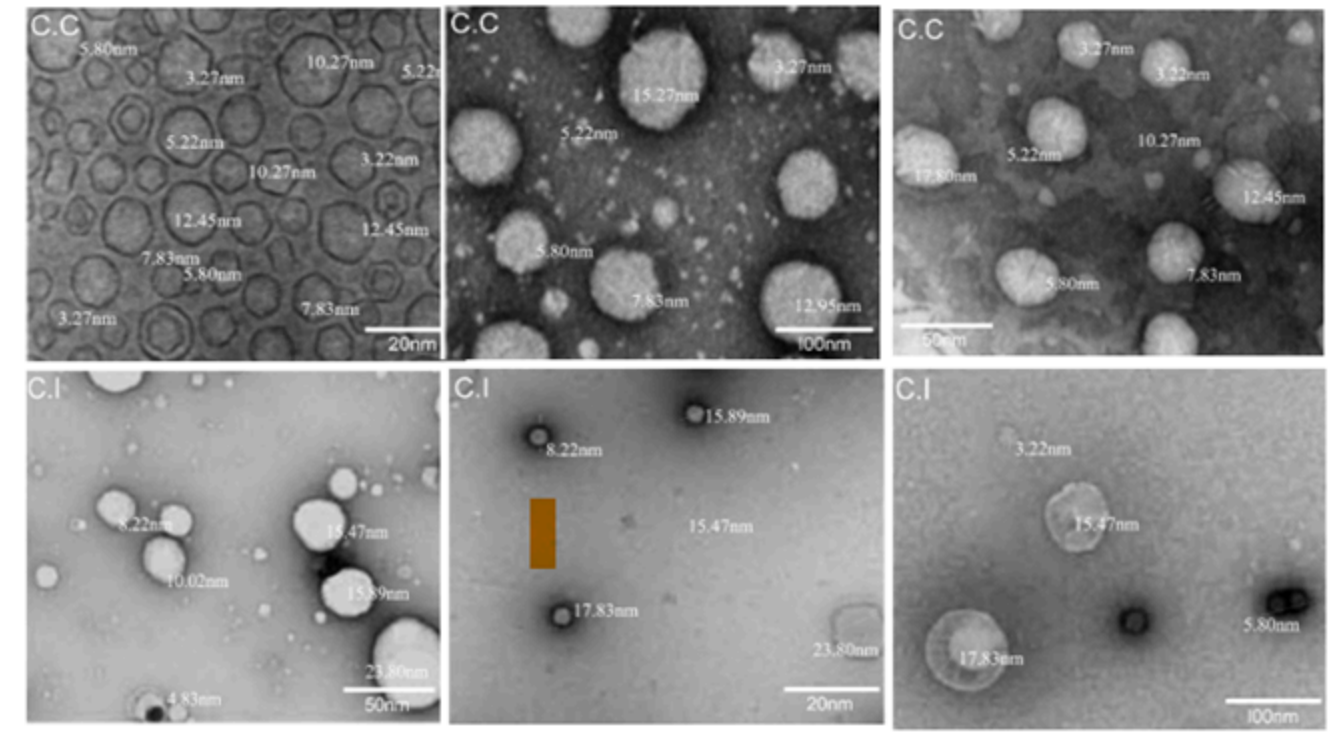

Figure 6

Transition electron micrographs of the prepared magnesium nanoparticles of C and I

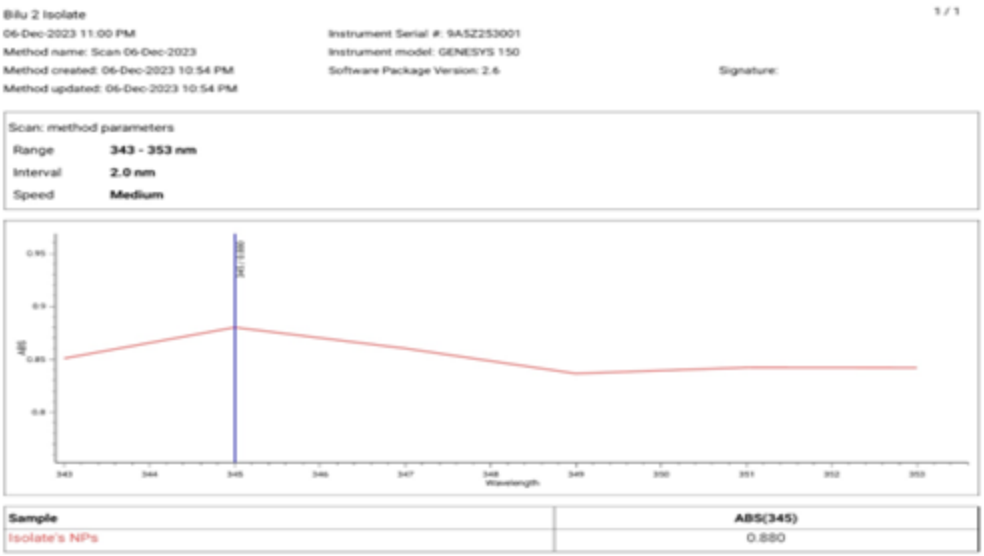

Figure 7

UV-Visible absorption spectrum of magnesium nanoparticles for sample C

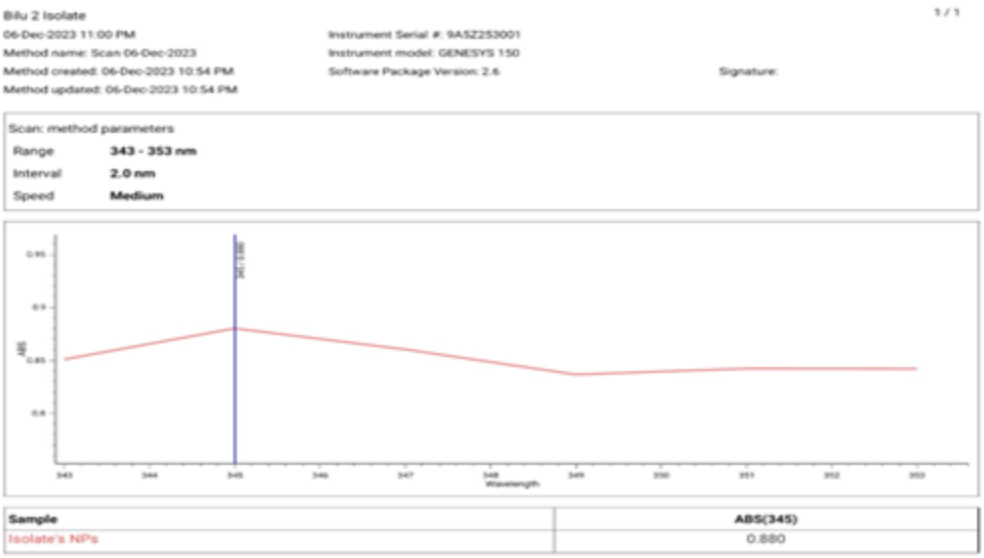

Figure 8

UV-Visible absorption spectrum of magnesium nanoparticles for sample I