



Green Synthesis of Magnesium and Potassium Hydroxide Nanoparticles from *Garcinia Kola* Heckel Stem-Bark and Their Preliminary Cytotoxic and Antioxidant Activities

Seide Modupe Akoro^{1,*}, Taiwo Samson Aiyelero¹, Oyinlade Cecilia Ogundare¹, Mutiat Adetayo Omotayo¹, Ajibade, Sunday Olugbenga², Olajide Korede Alade³ and Deborah Oluwaseun Akinluyi³

¹Department of Chemical Sciences, College of Basic Sciences, Lagos State University of Science and Technology, Ikorodu, Lagos State, Nigeria.

²Department of Chemical Sciences, Redeemer's University, Ede, Osun State

³Department of Chemical Sciences, College of Basic Sciences, Lagos State Polytechnic, Ikorodu, Lagos State, Nigeria.

(* Corresponding author: akoro.sm@lasustech.edu.ng

Abstract

Green synthesis of nanoparticles from medicinal plants has become a focus point in the search for healing and other benefits for mankind. This work is aimed at synthesizing, characterizing and determining the preliminary cytotoxic and antioxidant properties of magnesium and potassium hydroxide nanoparticles using aqueous *Garcinia kola* stem-bark extract. Magnesium and potassium hydroxide nanoparticles were synthesized using 50% *Garcinia kola* stem-bark aqueous extract. The nanoparticles were characterized using Fourier Transform Infrared Spectroscopy (FTIR) spectroscopy, UV-visible spectrophotometry X-ray diffraction (XRD) spectroscopy, Energy-Dispersive X-ray spectroscopy (EDX) and Scanning Electron Microscopy (SEM). The preliminary cytotoxic and antioxidant investigations were carried out using the brine shrimp lethality bioassay and Thin Layer Chromatography (TLC) bio-autography with DPPH (1, 1-diphenyl-2-picrylhydrazyl) respectively. The magnesium and potassium hydroxide nanoparticles (GbMgN and GbKN) were synthesized from aqueous *G. kola* extract (GbAQ). FT-IR detected O-H stretch (3231 cm^{-1} , 3384 cm^{-1}), C=C stretch (1640 cm^{-1} , 1580 cm^{-1}) and C-O stretch (1066 cm^{-1} , 1364 cm^{-1}) in GbMgN and GbKN respectively. FTIR of the GbAQ extract showed O-H stretch (3260 cm^{-1}), C-H stretch (2937 cm^{-1}) and aromatic C=C stretch (1606 cm^{-1} , 1513 cm^{-1} , 1401 cm^{-1}), UV-visible data gave $\lambda_{\text{max}} = 270\text{ nm}$ for GbMgN and $\lambda_{\text{max}} = 230\text{ nm}$ for GbKN which is consistent with magnesium and potassium nanoparticles. XRD study revealed the crystalline groups of GbMgN and GbKN, EDX analysis showed the percentage elemental compositions and the morphological assessment from SEM analysis confirmed that the nanoparticles are of different shapes. The average grain size of the synthesized nanoparticles was calculated to be 52.80 nm and 36.29 nm respectively for GbMgN and GbKN. The bioassay results showed both nanoparticles have cytotoxic activity. The Mg-nanoparticles and the aqueous extract showed DPPH scavenging activities. The results suggested GbMgN and GbKN as possible sources of new drugs in the management of cancer and other inflammatory conditions.

Keywords: Cytotoxic and Antioxidant activity, *Garcinia kola* stem-bark, potassium and magnesium nanoparticles, XRD, EDX, SEM.

Introduction

From the beginning of Mankind, the forests and trees have provided people with food and medicines [1]. Diverse natural bioactive compounds are produced by the numerous trees from the forest and their other natural habitats [2, 3]. These bioactive compounds contained in plants are used by humans as medicine in the management of diseases, especially in most African countries where about 80% of the population is reported to rely on one form of traditional herbal medicine or the other [4, 5].

Natural products are chemical substances or compounds produced by living organisms and they form the foundation for drug discovery [3, 4]. The natural products from plants known as phytochemicals or secondary metabolites have remained a source of succor to Man and animals in the management of diseases [4]. Natural products also remained the source of modern medicines because of their biological and pharmaceutical activities [3, 4] which vary from one plant to another [4-6].

Nanoparticles are ultrafine particles of matter with sizes between 1 and 100 nm in diameter [7-9]. The term is sometimes used for larger particles, up to 500 nm, or fibers and tubes less than 100 nm in only two directions [7-8]. Nanoparticles are different and distinguished from micromolecules, fine particles, and coarse particles with sizes 1-1000 μm , 100 - 2500 nm, and 2500 - 10,000 nm

respectively because of their smaller size. This peculiarly small size of the nanoparticles explains their colloidal properties, ultrafast optical effects and ultrafast properties [7-9]. These properties have made nanoparticles significant in medicine, agriculture, and pharmaceutical products, as well as in therapeutic agents such as air sanitizers, sprays, face masks, wet wipes, detergents, shampoos, toothpaste, lip care products, and in general healthcare delivery [8-11].

Plant extracts, microorganisms, polymers, sugar, and vitamins are becoming very interesting in the formation of nanoparticles and natural product chemistry [12-16]. Green synthesis of nanoparticles has eliminated the risk associated with toxic chemicals and the excessively high temperature and pressure involved in physicochemical methods of preparation [17]. The various advantages of this method have caused the drive towards it in the production of metallic nanoparticles with various pharmaceutical applications [17, 18, 19]. Previous researchers had reported the green synthesis of hydroxide nanoparticles from plants and they were well characterized [9, 20, 21]. Martin *et al.* [22] reported the synthesis of Zn-Mg layered hydroxide nanoparticles with anti-inflammatory activity. Previous work associated deficiency in magnesium and potassium elements and their nanoparticles with oxidative stress and anticancer properties [23-25]. High potassium levels have been related to the ability to initiate a stem-cell-like ability in T cells

during immunotherapy treatment showcasing the ability to treat cancer. [26].

Garcinia kola is a tropical African plant reported for its usage as a ceremonial and medicinal plant [27-29]. This has been reported as an antiparasitic, antidiabetic, antimicrobial, antiviral, and anti-inflammatory antidote to various infections [27-29]. The cytotoxic activity and GC-MS profile of the seed and stem-bark of *G. kola* n-hexane extract were reported [29]. Metal nanoparticles have been synthesized using *G. kola* [8]. Hassan *et al.* [30] and Akintelu *et al.* [31, 32] reported the synthesis and characterization of Silver Nanoparticles from *G. Kola* seed leaves and Pulp Extracts.

In this study, we report the synthesis and characterization of magnesium and potassium hydroxide nanoparticles from the aqueous *G. kola* extract. The comparative preliminary cytotoxic and antioxidant activities of the synthesized nanoparticles were determined using the simple brine shrimp bioassay and Thin Layer Chromatography (TLC) bio-autography respectively. The bioassay results for nanoparticles were compared with that of the aqueous *G. kola* stem-bark aqueous extract.

Materials and Methods

Chemical and general instrumentation

All the solvents and chemicals used in this work were of analytical grade purchased either from Sigma-Aldrich Chemical Company or Fisher Scientific Chemical Company. *Artemia salina*

(Aqua master, China) was used for the cytotoxicity assay. The Infra-red data was obtained using the FTIR (Agilent Technologies); UV-visible data was obtained using UV-visible spectrophotometer (Jenway); the XRD pattern was obtained from X-ray diffractometer (Empyrean Malvern Panalytical); SEM-EDX images were obtained using scanning Electron Microscope Energy Dispersive X-ray Spectroscopy Phenom Pro model.

Sample collection and preparation of aqueous extract

The *Garcinia kola* Stem-bark was collected and authenticated at the University of Lagos Herbarium (LUH 3260). The plant material was washed and shredded into smaller pieces before it was air-dried for about 5 weeks until dried. The aqueous plant extract was obtained by macerating 50 g of the plant materials in 500 mL of water for 72 h. The extract was filtered using a Whatman filter paper and the filtrate was poured into a glass bottle and then kept in the refrigerator for preservation until further use.

Synthesis of magnesium and potassium nanoparticles (GbMgN and GbKN) from aqueous *G. kola* stem-bark extract

Magnesium sulphate (8 g) was weighed into a dried 250 mL beaker; *G. kola* aqueous extract (170 mL) was poured into the beaker containing the magnesium sulphate. The mixture was placed on the magnetic stirrer hot plate with a magnetic bar

in it to stir continuously for 1 h at 80°C. To the reaction mixture, NaOH solution (4 mL; 1M) was added. This altered the pH to 10. The *G. kola* nanoparticles obtained were separated using the centrifuge. After drying in an oven at 105 °C, to form Mg (OH)₂-x (where x is the complex from the phytochemicals present in the plant extract) [33], the synthesized nanoparticle (GbMgN) was subsequently weighed. Potassium nitrate (8 g) was weighed into a beaker, and 170 mL of the aqueous *G. kola* extract was poured into the beaker. The beaker was placed on a magnetic stirrer and stirred for 1 h at 60 °C. The initial pH was noted and the addition of NaOH (1.5 mL; 1M), caused the pH to change to 10. The potassium nanoparticles (GbKN) were separated using the centrifuge and the yield was calculated after drying in the oven at 105 °C to form KOH-x (where x is the complex from the phytochemical present in the plant extract) [8, 34]. The solubility in water was determined.

Characterization of the synthesized magnesium and potassium nanoparticles

Infrared spectroscopy was adopted in the determination of the functional groups present in the synthesized nanoparticles by scanning on an Infrared spectrophotometer (Agilent) at wavelength (650 - 4000 cm⁻¹). The UV-visible data were obtained using UV-visible spectrophotometer (Jenway) reading in a wavelength region of 200 nm to 800 nm. The crystalline nature of the synthesized nanoparticles was examined through XRD pattern

obtained from X-ray diffractometer using the angle at 2θ. The composition of elements in the synthesized nanoparticles was determined using EDX spectrometer. The morphological study of the synthesized nanoparticles was carried out by scanning on a SEM machine.

Cytotoxicity assay

The cytotoxic activity of the Nano particles and extracts was carried out according to methods described by Vanhaecke *et al.* [35] and Akoro *et al.* [36]. *Artemia salina* leach (brine shrimp eggs) was used as the test organism. Sea water was taken into a small tank and shrimp eggs were added to the tank and then covered. The shrimps were allowed to hatch for 24 h. Constant oxygen supply was maintained to the hatching set-up throughout the hatching period and good illumination was maintained. Samples preparation was done by preparing the various concentrations (100 µg/mL, 200 µg/mL, 400 µg/mL, 800 µg/mL) from the stock solution (10 mg of nanoparticle or crude extract in 10 mL of 5% DMSO) by serial dilution and all sample concentrations were done in triplicate. Ten brine shrimps (nauplii) larvae were taken by using a Pasteur pipette and then placed into each of the sample vial containing the nanoparticles or crude extract solution and then mixed properly. The number of shrimps in each sample vial was counted after 24 h and the total number of death was determined. The percentage mortality at each dose level and that of the control (brine shrimps in 1% dimethyl sulfoxide without the extract) were

determined. The LC_{50} was determined from the graph of logarithm to base ten of concentration against percentage mortality [35, 36].

Preliminary antioxidant activity using DPPH

The preliminary antioxidant activity of the nanoparticles and the aqueous extracts was determined using Thin Layer Chromatography (TLC) bioautography. The nanoparticles and extract (1600 $\mu\text{g/mL}$ each) were spotted on the TLC plate and then sprayed with 2% DPPH (1, 1-diphenyl-2-picrylhydrazyl) in ethanol. [37]. A yellow colour against a purple background indicates DPPH scavenging activity. The experiment was carried out twice.

Preparation of the extract solution

The solution of each nanoparticle (0.016 g) was dissolved in 1% dimethyl sulfoxide (DMSO) to prepare the stock solution from which other concentrations were prepared.

Results and Discussion

The *G. kola* stem-bark magnesium hydroxide Nanoparticles (GbMgN; 5.16 g) and potassium hydroxide Nanoparticles, (GbKN; 8.60 g) were prepared and characterized. Both Nanoparticles were brown crystalline solids that were soluble in water. The aqueous *G. kola* (GbAQ) extract was also obtained as a brown solid.

Fourier Transform Infrared Spectroscopy (FTIR) analysis

Infrared spectroscopy data of the nanoparticles (GbMgN and GbKN), and the aqueous *G. kola* extract (GbAQ) were obtained and the results are illustrated in Figure 1. The FTIR spectrum of GbMgN (Figure 1A) showed three distinct peaks at 3231 cm^{-1} , 1640 cm^{-1} , and 1066 cm^{-1} which indicate the presence of O-H stretching vibration with the broad band of carboxylic O-H alcohol at 3235 cm^{-1} , C=C stretching vibration at 1640 cm^{-1} , and C-O stretch at 1069 cm^{-1} . The FTIR spectrum of GbKN (Figure 1B) however showed bands at 3384 cm^{-1} , 1580 cm^{-1} and 1364 cm^{-1} indicating the presence of O-H stretching vibration for alcohol, C=C stretching frequency at 1580 cm^{-1} and C-O stretch for alcohol at 1364 cm^{-1} . Comparing the FTIR spectra of both nanoparticles with that of the dried aqueous *G. kola* extract, GbAQ (Figure 1C), the spectrum revealed O-H stretch at 3260 cm^{-1} , C-H stretch at 2937 cm^{-1} , aromatic C=C stretch at 1606 cm^{-1} , 1513 cm^{-1} and 1401 cm^{-1} [9, 34]. The variation in signals between the GbAQ signals and that of the nanoparticles may be due to the stabilization of nanoparticles through coordination with -OH, C=C and C-O [9].

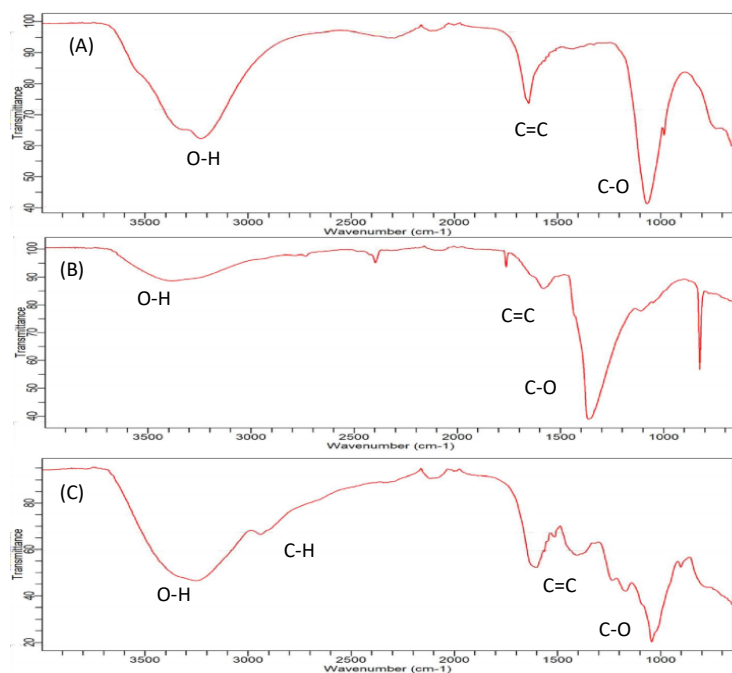


Figure 1: FT-IR spectra of GbMgN (A), GbKN (B), and GbAQ (C)

UV-VISIBLE SPECTROSCOPY

The UV-vis spectroscopic analysis gave λ_{\max} of 270 nm for GbMgN and 230 nm for GbKN. The λ_{\max} values obtained are within the expected range, as

reported by Vega-Jiménez *et al.* [21] for a series of Mg nanoparticles, including the oxide and hydroxide. The value for the potassium nanoparticles is consistent with that earlier reported by Weng *et al.* [38].

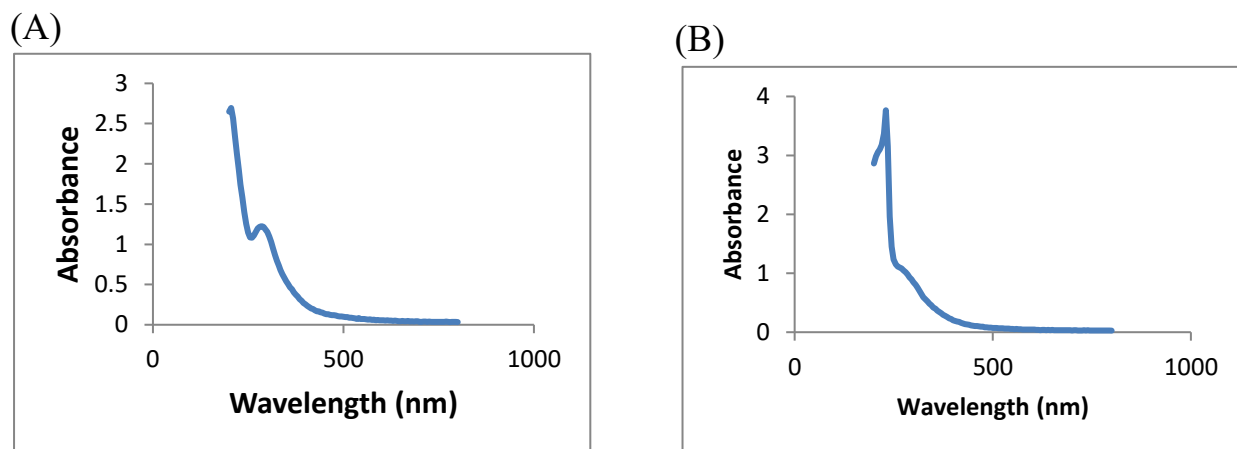


Figure 2. UV-VIS spectra of GbMgN (A) and GbKN (B) nanoparticles

X-ray diffraction (XRD) analysis

The crystalline nature of the structures of the two synthesized nanoparticles, GbMgN and GbKN were determined using XRD (Figure 3). The spectra pattern of GbMgN (Figure 3A) indicates a multi-phase crystal structure having peaks at 2θ of 19.8°, 33.45°, 38.95° which are the hexagonal crystal of Mg(OH)₂ corresponding to planes (001), (100) and (101) respectively [39], and the cubic centered structure of MgO at 37.44°, 42.75°, 62.5° corresponding to planes (111), (200), (220) respectively [40]. These peaks could have arisen from phase interference during drying to obtain the Mg(OH)₂.

The XRD pattern of the potassium nanoparticle, GbKN (Figure 3B.) indicated the most prevalent phase as shown in the peaks are at 2θ 19.8°, 21.5°, 24.6°, 30.0°, 34.0° and 39.5°. The most prevalent phase of the nanoparticle is the Sodium Magnesium Sulphate phase (49%) observed peaks at 2θ of 24.6°, 30.0°, 34.0° and 39.5° which possibly arises during synthesis from the interaction of the sulphate ion, and the sodium on the addition of sodium hydroxide in the pH control mechanism.

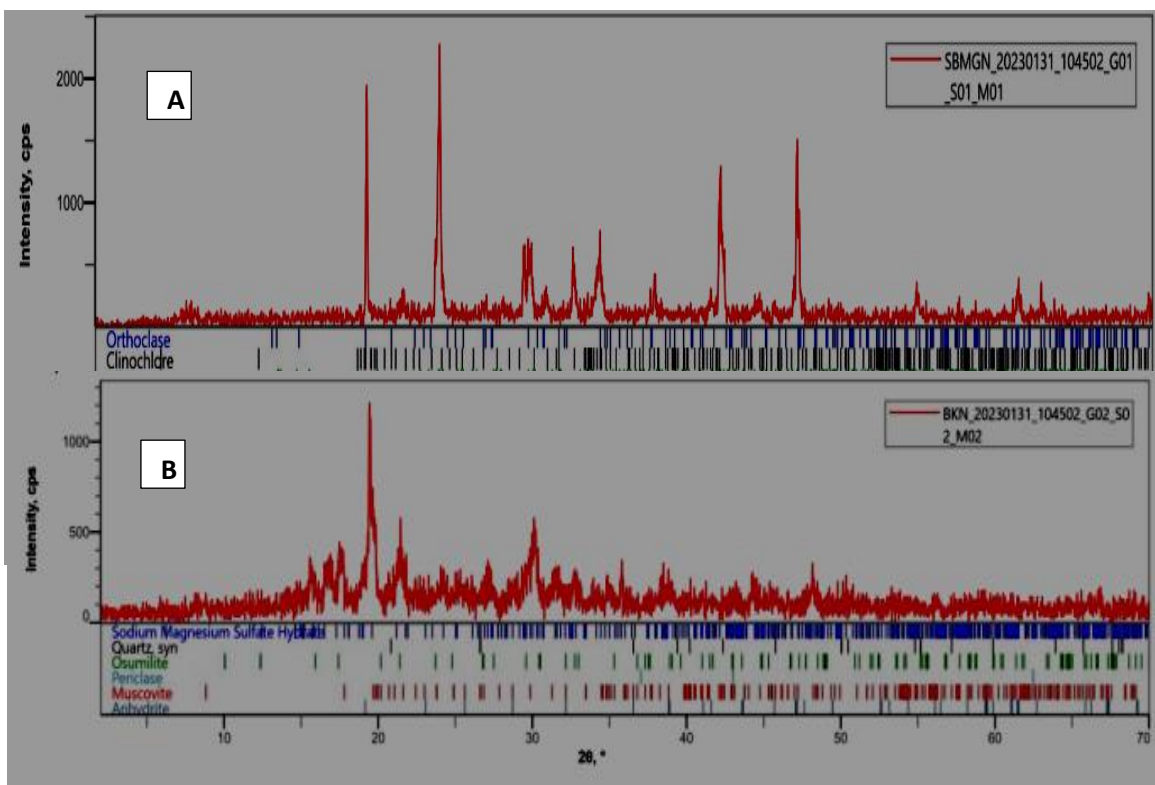


Figure 3: XRD patterns of the synthesized GbMgN (A) and GbKN (B) nanoparticles

SEM-EDS (scanning electron microscopy and energy dispersive x-ray spectroscopy) analysis

The morphology features of the synthesized magnesium nanoparticles (GbMgN) as displayed in the SEM micrograph (200x) reveal irregularly shaped aggregates of nanoparticles (Figure 4A). These aggregates likely result from a heterogeneous nucleation process occurring during synthesis, consistent with the findings of Ahmed and Kumar [41] who highlighted similar morphological characteristics in magnesium oxide nanoparticles synthesized under varying reaction conditions. The average grain size of the synthesized nanoparticle using ImageJ was calculated to be 52.80 nm. This aligns with the particle sizes for magnesium nanoparticles with similar morphological features as reported by Hornak [42].

In contrast, SEM analysis showed the morphology features of the synthesized Potassium nanoparticles (GbKN), as mono-dispersed as displayed in the SEM micrograph (Figure 4B). The shape of the nanoparticles is spherical and clustered and the average grain size calculated using ImageJ was 36.29 nm. Literature reports indicated different researchers presented varying sizes in green synthesized potassium nanoparticles: Sheoran *et al.* [43] reported biogenic potassium nanoparticles with sizes from 21-30 nm while Salama *et al.* [44] reported potassium nanoparticles with sizes less than 100 nm, Ismail *et al.* [45] reported KCl nanoparticle with size 80 nm. Constantino-Alcazar *et al.* [46] reported that potassium nanoparticles synthesized using Sideroxylon capiri extract exhibited spherical shapes with sizes ranging from 200 to 360 nm.

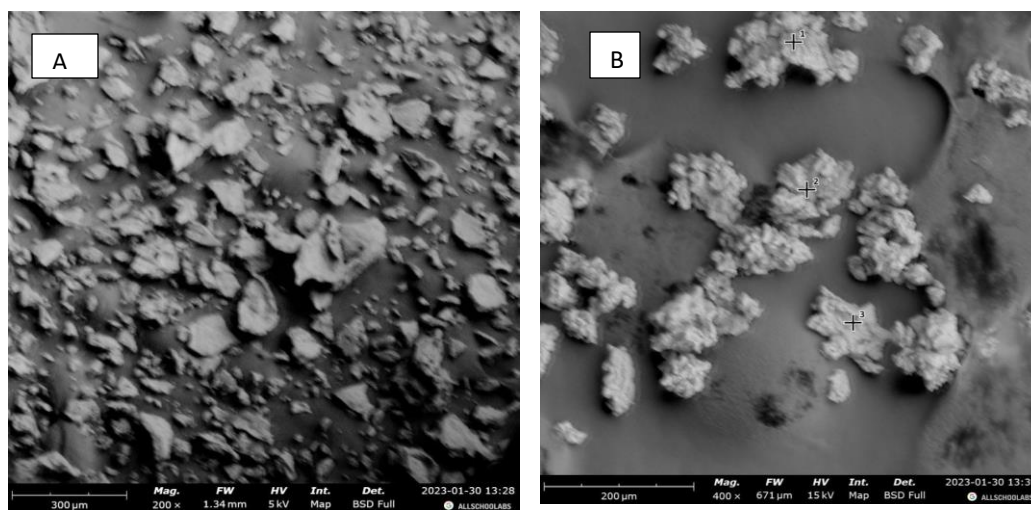


Figure 4. SEM micrograph of the synthesized GbMgN (A) and GbKN (B) nanoparticles

The EDX image of the synthesized GbMgN and GbKN nanoparticles (Figure 5) revealed distinct peaks of magnesium and potassium respectively. In

the GbMgN nanoparticles, the magnesium peak is observed at 1.2 keV. The other peaks correspond to carbon, oxygen, sodium and sulphur at 0.2 KeV

and 0.5 KeV, 1.0 KeV and 2.2 KeV respectively (Figure 5A). The nitrogen peak was also observed. The elemental contents for magnesium, carbon, oxygen, sodium, sulphur and nitrogen are 24.45%, 1.47%, 54.02%, 1.10%, 11.68% and 7.28% respectively (Table 1.0). The carbon, sulphur and nitrogen peaks may have originated from the plant material. The sodium peak may have originated from the sodium hydroxide and oxygen peak from

the atmospheric oxygen respectively. These findings are consistent with previous studies on the synthesis of nanoparticles from plant extracts such as those reported by Constantino-Alcazar *et al.*[46], and Sharma *et al.* [47]. These reports showed the EDX analysis revealed similar elemental distributions in the nanoparticles synthesized from plant extracts.

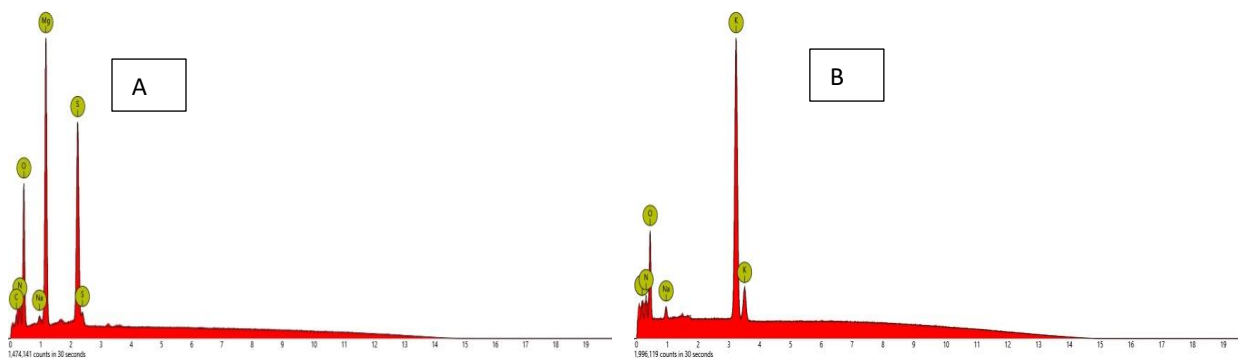


Figure 5. EDX image of the synthesized GbMgN (A) and GbKN (B) nanoparticles

TABLE 1. EDX elemental analysis of GbMgN

Element Number	Element Symbol	Element Name	Atomic Conc.	Weight Conc.
6	C	Carbon	1.47	0.89
7	N	Nitrogen	7.28	5.15
8	O	Oxygen	54.02	43.69
11	Na	Sodium	1.10	1.28
12	Mg	Magnesium	24.45	30.04
16	S	Sulfur	11.68	18.94

However, the EDX image of the synthesized GbKN nanoparticles (Figure 5B) revealed a distinct peak of potassium at 3.5– 3.2 keV. Other peaks detected are nitrogen (0.3 KeV), oxygen (0.5 KeV) and sodium (1.0 KeV).

TABLE 2. EDX elemental analysis of GbKN

Element Number	Element Symbol	Element Name	Atomic Conc.	Weight Conc.
7	N	Nitrogen	14.86	10.12
8	O	Oxygen	62.33	48.49
11	Na	Sodium	2.50	2.80
19	K	Potassium	20.31	38.60

The atomic percentage of potassium, oxygen, sodium and nitrogen are 20.31%, 62.33%, 2.50%, 14.86%, respectively (Table 2). The signal of the oxygen might have originated from atmospheric oxygen while the other metals are from the elemental contents of the plant material.

Cytotoxic activities of synthesized magnesium and potassium nanoparticles and aqueous solution of *G. kola* stem-bark extract

A preliminary Cytotoxic activity study using brine shrimp lethality assay on the magnesium and potassium nanoparticles showed mortality only at higher concentrations of nanoparticles (Figure 6) with LC₅₀ of 715.49±68.27 µg/mL for GbMgN and 668.47±0.00 µg/mL for GbKN suggesting toxicity based on the report of Meyer et al. [48]. GbAQ gave LC₅₀ of 501187.20 ±0.00 µg/mL.

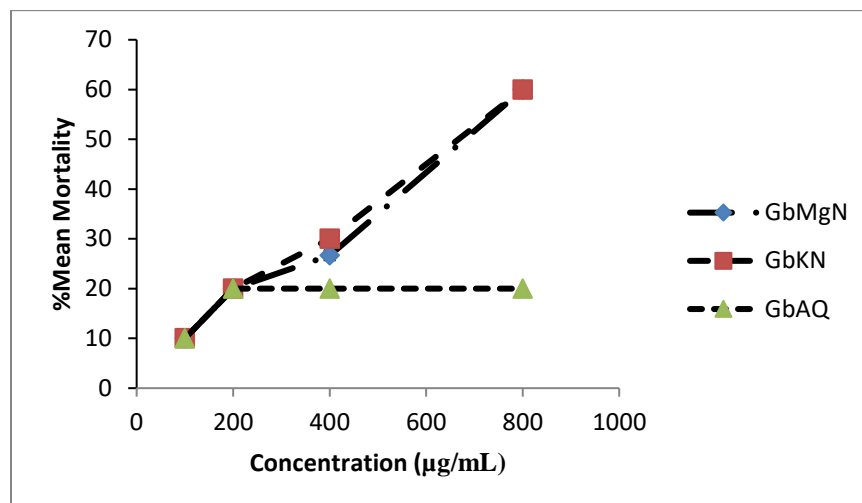


Figure 6. Mean Percentage Mortality of Brine Shrimp by GbMgN, GbKN and GbAQ

The aqueous extract GbAQ is not cytotoxic ($LC_{50} > 1000 \mu\text{g/mL}$). The nanoparticles may be a possible remedy for managing tumor cells considering the LC_{50} value. *Garcinia kola* has been reported to be an anti-parasitic, anti-inflammatory and antimicrobial agent against various infections [28-30].

Preliminary Antioxidant activity by GbMgN, GbKN and GbAQ

Preliminary antioxidant screening using DPPH bio-autography on the *G. kola* nanoparticles and the aqueous extract indicated activity in the magnesium nanoparticles, GbMgN, and the *G. kola* aqueous extract, GbAQ (Plate 1), with no activity in the potassium nanoparticles, GbKN as indicated by the yellow colour against the purple background suggesting DPPH scavenging activity (Plate 1).

Thin Layer Chromatography (TLC) bio-autography technique is a cheap but highly sensitive and selective protocol that utilizes the separation and analysis of TLC with the detection of biological activities of natural products [37]. The results of our work suggest a possible use of GbMgN in the management of oxidative stress and inflammatory conditions. Earlier reports indicated magnesium oxide and magnesium hydroxide nanoparticles show antioxidant and anti-inflammatory activities [49,50]. *Garcinia kola* is reported to have antioxidant and anti-inflammatory activities and is an antidote to various infections as an immune booster [27, 28, 51]. Magnesium-containing plants have been reported to boost energy, improve immunity, and reduce inflammation [52].

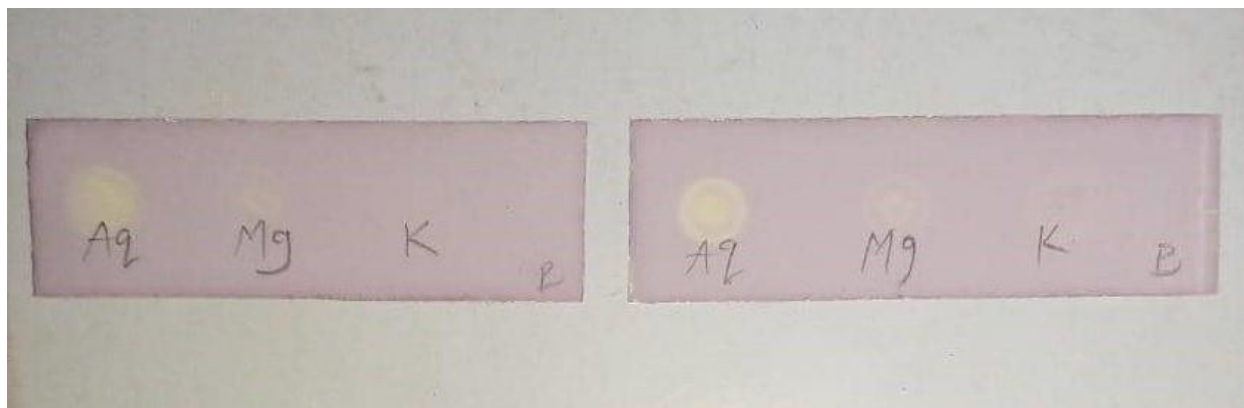


Plate 1. Chromatogram of preliminary antioxidant activity

Conclusion

In our study, the magnesium hydroxide nanoparticles (GbMgN) and potassium hydroxide nanoparticles (GbKN) were synthesized using *G. kola* stem-bark aqueous extract and properly characterized. The preliminary cytotoxic assay indicated a dose-dependent activity in both the magnesium and potassium nanoparticles while the antioxidant test was positive for the magnesium nanoparticles and the aqueous *G. kola* stem-bark extract only. These results suggested that the two synthesized nanoparticles may serve as anticancer agents while the magnesium nanoparticles may be a possible source of antioxidant and anti-inflammatory drugs. There is a need for further work to confirm the indicated activities of these nanoparticles in an *in vivo* study.

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