Article preview

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Kolanut-mediated magnesium oxide nanostructures for biomedical applications: Antimicrobial, antioxidant,

larvicidal, anticoagulant and thrombolytic activities

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panelA. Lateef [a b], K.O. Ismaheel [a], O.O. Ajani [a], D.A. Adebayo [a], S.T. Fagbemiro [a], T.B. Asafa [b c], E.B. Gueguim-Kana [d], L.S. Beukes [d], S.H. Abbas [e], H.M. Irshad [f]
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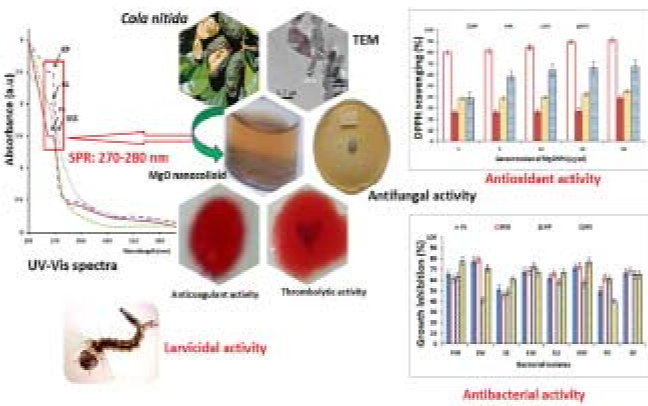
Highlights

- First report of MgO nanostructure synthesis by *Cola nitida*.
- MgO nanostructures displayed SPR at 270–280 nm.
- MgO nanostructures inhibited growth of multi-drug resistant bacteria the particles had antifungal, DPPH scavenging and larvicidal activities.
- MgO nanostructures prevented blood coagulation and lysed blood clots.

Abstract

This study was aimed at using hot water extracts of pod (KP), seed (KS), leaf (KL) and seed shell (KSS) of *Cola nitida* (kola nut) for the synthesis of nano-sized magnesium oxide and evaluation for biomedical applications. The nano-sized MgO were biosynthesized for the first time using kola nut extracts and characterized by UV–visible spectroscopy, Fourier transform infra-red spectroscopy (FTIR), transmission electron microscopy (TEM), selected area electron diffraction (SAED) and energy-dispersive X-ray (EDX). The antimicrobial, antioxidant, larvicidal, anticoagulant and thrombolytic activities of the nano-sized MgO were evaluated. The crystalline polygonal-shaped nano-sized MgO absorbed maximally in the range of 270–280 nm and FTIR spectra indicated the involvement of phenolic compounds and proteins in their biosynthesis. At 40 µg/ml, nano-sized MgO showed growth inhibition of 41.2–79.3% against eight multi-drug resistant strains of *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella granulomatis*, and inhibition of 60.2–88.4% on *Rhizopus stolonifer, Trichoderma longibrachiatum, Aspergillus flavus* and *Aspergillus fumigatus*. DPPH scavenging activities of 26.1–90.4% were obtained for 1–40 µg/ml of MgO nanostructures, while mortality of 13.33–100% against anopheline larvae was achieved at 30 μg/ml. The nanostructures also prevented blood coagulation and completely dissolved preformed blood clots within 10 min which is herein reported for the first time. This report has shown that *Cola nitida* can be employed for sustainable synthesis of nano-sized MgO with potent biomedical applications.

Graphical abstract



Introduction

Nanotechnology as a discipline of production, manipulation and utilization of structures at nanoscale is rapidly evolving on daily basis with profound applications in different areas of human endeavours that include engineering, agriculture, foods, environment, energy, industries, security and healthcare among others (Elegbede and Lateef, 2019; Zain et al., 2022). It is now being increasingly deployed to address various developmental challenges that confront mankind and used as a viable tool to deliver on the sustainable development goals (SDGs) of the United Nations (Pokrajac et al., 2021; Lateef et al., 2021a; Lateef, 2022). More so, the impacts of nanotechnology have been enhanced through green chemistry approach that seeks to promote sustainable production of nanomaterials with improved biocompatibility within eco-friendly framework under ambient conditions. The green synthesis of nanoparticles utilizing metabolites derived from living resources such as plants, microbes and animals has blossomed in the last two decades (Akintayo et al., 2020; Dutta and Das, 2021; Lateef et al., 2021b), and continues to define advances in nanotechnology.

Among the biological resources that are abundantly available for exploitation in the green synthesis of nanoparticles, plants have prime position. This is due to their renewable and abundant nature, and simplicity in their growth under natural environment and lesser requirement for purification of metabolites when compared with microorganisms. Series of components of plants ranging from leaf, stem, root, fruit, seed, pulp, peels, shell, pod and various wastes emanating from their processing have been used for the green synthesis of metal nanoparticles (Aguda and Lateef, 2021; Alharbi et al., 2022). The phytosynthesis of nanoparticles which is devoid of the utilization of noxious chemicals and procedures has contributed to improved biocompatibility of such nanoparticles, to enhance their biomedical applications (Lateef et al., 2019). The range of nanoparticles that have been synthesized using green approach is limitless and growing every day. Among such nanoparticles are magnesium oxide nanoparticles (Kumar et al., 2021).

Magnesium oxide nanoparticles (MgONPs) are synthesized using biological route and evaluated for different purposes such as antimicrobial, antioxidant, seed germination, photocatalytic, anticancer, water treatment, and insecticidal applications (Khan et al., 2020; Abinaya et al., 2021; Hassan et al., 2021). Beyond these, they are also useful in the production of ceramics, batteries, catalysts, sensors and supercapacitors (El-Shafai et al., 2021; Kokulnathan et al., 2021). Researches on the synthesis and applications of MgONPs are still unfolding considering the available literature in this area. Therefore, there is need to explore more green routes in the fabrication of nano-sized MgO and extend the frontiers of their applications. In biomedicine, their limited applications include use as antimicrobial, anticancer, antioxidant and insecticidal agents (Abinaya et al., 2021; Kumar et al., 2021). However, for instance, there are no studies reporting the anticoagulant, wound-healing and thrombolytic activities of MgONPs. In view of the importance of magnesium in human health, its nanoparticles will engender profound health benefits. As a cofactor, magnesium supports activities of more than 300 enzymes and it is involved in a number of physiological processes that include bone formation, control of glycemic index and blood pressure, contraction of muscles, production of energy and transport of materials in the cell (Al Alawi et al., 2018). Its deficiency, hypomagnesemia can herald some diseases such as diabetes, hypertension, heart failure, osteoporosis, stroke, seizure, Alzheimer's disease, cancer and migraine (Angkananard et al., 2016; Chen et al., 2016; Barbagallo et al., 2021).
Among several plants that have been explored for the synthesis of mono, bimetallic and metal oxide nanoparticles is kola nut (*Cola nitida*). In our previous investigations, its various parts (leaf, pod, seed and seed shell) have been extracted to synthesize silver (AgNPs), silver-gold alloy (Ag-AuNPs), calcium (CaNPs), titanium oxide (TiO_2NPs), and titanium-silver alloy (Ti-AgNPs) nanoparticles with profound potential applications in biomedicine, agriculture, environmental cleansing, desulphurization and paint manufacturing (Lateef et al., 2015; 2016a; Olajire et al., 2017; Akinola et al., 2020, 2022; Azeez et al., 2020, 2021). Variously, the nanoparticles displayed antimicrobial, antioxidant, dye-degradation, plant-growth promotion, anticoagulant, thrombolytic and larvicidal activities. *Cola nitida* is a perennial plant mostly found in west and central African countries that include Nigeria, Angola, Liberia, Gambia, Togo, Republic of Benin, Sierra-Leone, Tanzania Ghana, Mozambique, Gabon and Cote d'Ivoire (Akinola et al., 2020) with Nigeria being the world largest producer of kola nuts (FBA, 2019) accounting for 52% world production. It has also been cultivated in other countries particularly in Trinidad and Tobago, Australia, Madagascar, Jamaica, India, Mauritius, Malaysia and South America (Adebola, 2011). The most important part of the plant for

which it is cultivated is the kola nut fruit, which is very rich in phenolic compounds (Adamu et al., 2020) that confer on it antimicrobial, anti-inflammatory, antioxidant, and anti-cancer activities (Solipuram et al., 2009). It is of important rites in Africa, consumed widely as stimulant, used in the traditional treatments of cough, asthma and cardiovascular diseases (Savi et al., 2019), and also employed as flavouring agent in the food industry (Nyadanu et al., 2020). Its leaf, nut, root and stem bark are valuable in ethnomedicine in Africa (Ekalu and Habila, 2020).

The processing of kola nut generates wastes in the form of kola nut pod and seed shell which are often discarded without any appreciable usage. Efforts have been made mostly to valorize the pod to produce adsorbents, catalyst, animal feeds and viable microbial products such as enzymes and oligosaccharides (Lateef et al., 2012; Betiku et al., 2019; Yahya et al., 2021; Oloruntola, 2022). This study further examines the potential roles of *C. nitida* in nanobiotechnology, with the view of using the extracts obtained from its different parts (leaf, pod, seed and seed shell) for the synthesis of magnesium oxide nanoparticles, which is hitherto unreported. We also evaluated the phytosynthesized nano-sized MgO against multi-drug resistant bacteria, fungi and determined their abilities to scavenge free radicals using DPPH. For the first time, we reported their abilities to prevent blood coagulation and to lyse blood clots (thrombolysis) without the destruction of red blood cells. These newly reported activities can promote the biomedical applications of nano-sized MgO and in the development of novel nanopharmaceuticals.

Section snippets

Plant materials for the preparation of extracts

The leaf (KL), pod (KP), seed (KS) and seed shell (KSS) of *C. nitida* were obtained as previously reported (Akinola et al., 2022) from a plant in Ogbomoso, Southwest, Nigeria. The dried samples that were obtained through air-drying at ambient temperature and milling were extracted with water at 60 °C for 1 h using 1% (wt/vol). This was followed by filtration using Whatman filter paper No. 1 and centrifugation at 4000 rpm for 20 min to obtain the various extracts that were used without further

Statistical analysis

Data obtained for antimicrobial, antioxidant and larvicidal activities were subjected to statistical analysis using SPSS Package Version 20, and the means ± SE were analyzed by ANOVA to determine the significance difference ($p < 0.05$). Thereafter, Duncan's multiple range test was applied to separate the means.

Phytosynthesis of nano-sized MgO and their properties

The various extracts of *C. nitida,* namely leaf (KL), pod (KP), seed (KS) and seed shell (KSS) mediated the formation of MgO nanostructures as observed through change in color of MgO solution from colourless to varying shades of brown color (Fig. 1). The transformation in color occurred within 1 h and stabilized at 24 h. Some authors have reported green synthesis of MgONPs depicting transformation in color to brown, pale white, turbid white, black, and pale yellow colloidal solutions (Narendhran

Conclusion

The present study has shown the feasibility of fabrication of nano-sized MgO using the pod, leaf, seed and seed shell extracts of *Cola nitida* under benign conditions. The brownish colloidal colloids had SPR in the range of 270–280 nm and presented polygon structure. It was established that phenolics and proteins in the various extracts were responsible for bioformation of MgO nanostructures and subsequent capping. They inhibited growth of multi-drug resistant Gram positive and Gram negative

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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