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RESEARCH ARTICLE

Anticancer Activity of Zinc Oxide Nanoparticles Synthesised Using Nutmeg Oleoresin

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ABSTRACT

Introduction: Nutmeg is well known in Indian medicine for having aromatic, analgesic, antioxidant, antibacterial, antifungal, antidiabetic, hypolipidemic, hepatoprotective, and anti-inflammatory properties. Oleoresin is a natural mixture of resin and essential oil derived from the leaves of the olea europaea tree. Oleoresins are organic solvent-extracted mixtures of essential oils and resins extracted from spices.

Aim: The aim of the current study was to analyse the anticancer activity of zinc oxide nanoparticles synthesized using nutmeg oleoresin on HepG2 Cell line.

Materials and method: Nutmeg oleoresin was obtained from synthite industries Ltd,Kerala. MTT assay was performed with nutmeg oleoresin mediated zinc oxide nanoparticles to assess the anticancer activity.The cells were treated with different concentration of nutmeg oleoresin (20,40,60,80,100,200µg/ml) for 24 hours and the cell viability was analysed using MTT assay.

Result and discussion: The results of MTT assay showed a dose dependent increase in anticancer activity of nutmeg oleoresin against the cancer cell line. The IC50 value was 40µg/ml.

Conclusion: The present study within the limitations conclude that nutmeg oleoresin possesses a good level of cytotoxic activity against cancer cell lines. Hence the extract may be further explored in animal models to establish its activity.

KEYWORDS:
Anticancer, oleoresin, MTT assay, zinc oxide nanoparticle, eco friendly, green synthesis

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INTRODUCTION

The tropical tree nutmeg (Myristica fragrans) belongs to the Myristicaceae family. The seed kernel of nutmeg is found inside the fruit. Nutmeg is well known in Indian medicine for having aromatic, analgesic, antioxidant, antibacterial, antifungal, antidiabetic, hypolipidemic, hepatoprotective, and anti-inflammatory properties (1) Oleoresin is a natural mixture of resin and essential oil derived from the leaves of the olea europaea tree. Oleoresins are organic solvent-extracted mixtures of essential oils and resins extracted from spics. Oleoresins contain both volatile and non-volatile elements, and they more accurately represent flavour consistency than distilled volatile oils. Nutmeg is known for its anti-inflammatory, antioxidant and antimicrobial role (2)

Nanotechnology is supposed to be the foundation for several major technological breakthroughs in the twenty-first century. This field's research and development is rapidly expanding around the world. The production of new materials in the

manometer scale, particulate materials with at least one dimension of less than 100 nm, is a significant performance of this activity. (3)Nanotechnology has a wide range of uses in fields including chemistry, cosmetics, catalysts, electricity, plasmonics, onto-electronics, and medicine. Because of their applications, nanoparticle synthesis and growth play a significant role in the field of nanotechnology. (4–6) Nanoparticles are particles with a size of less than 100 nanometers. These have gained popularity in recent years and have been shown to have a wide range of technological and biological applications. Cancer is characterised by rapid cell proliferation and the ability to spread to other areas of the body, causing vital processes to deteriorate. Chemotherapy, radiotherapy, and surgery are all options for cancer care, depending on the type of cancer. Many plants have recently been studied in various models to determine their anticancer function. Cell lines are often used to evaluate anticancer activity. (7,8)

Among the noble nanoparticle zinc oxide nanoparticles have unique properties such as chemical stability, anti-cancer, anti-inflammatory, antimicrobial, anti -oxidant, antiviral and antifungal activity which has made it the particle of interest to the scientific community. (9,10). Our team has extensive knowledge and research experience that has translated into high quality Our team has extensive knowledge and research experience that has translate into high quality publications(11–15),(16),(17),(18),(19),(20),(21),((13,22,23),(24–28) .,(29),(30) The aim of the current study was to analyse the anticancer activity of zinc oxide nanoparticles synthesized using nutmeg oleoresin.

MATERIALS AND METHOD

Study Setting

The study was carried out in the Cancer and Stem Cell Research Lab, Dept of Pharmacology, Saveetha Dental College after getting approval from the institutional review board . The ethical clearance was obtained from research department of Saveetha Dental College with the ethical number - IHEC/SDC/UG-1949/21/122

Plant Extract

Nutmeg oleoresin was obtained from synthite industries Pvt Limited, Kerala (product number 4010000484).

Chemicals

DMEM medium, 0.25% Trypsin-EDTA solution, sodium bicarbonate solution, bovine serum albumin (BSA), low melting agarose, MTT from Sigma Chemicals Co., St. Louis, USA. fetal bovine serum (FBS) and antibiotic/antimycotic solution, DMSO were from Himedia, Sodium phosphate monobasic and dibasic, sodium chloride, sodium hydroxide, sodium carbonate, hydrochloric acid and methanol were purchased from Sisco Research Laboratories (SRL) India.

Cell Culture

The cells were grown in a T255 culture flask containing DMEM medium supplemented with 10% FBS. Upon reaching confluence, the cells were detached using Trypsin EDTA solution

Mtt Assay Analysis

In vitro cytotoxicity assay The effect of ginger oleoresin on cell viability was measured by MTT assay following the method by Mosmann. Briefly, the cells (1 × 105 cells per ml) were seeded in a 96 well microtiter plate (100 µl per well) with replications. Treatment was conducted for 24 hours with different concentrations (20,40,60,80,100,200µg/ml) of ginger oleoresin. After incubation, 20 µl of 5 mg/ml MTT stock solution was added to each well and incubated for 4 h at 37 °C. The obtained formazan crystals were solubilized with DMSO and the absorbance was measured at 570 nm using a microplate reader (SpectraMax M5, Molecular Devices, USA). Cell viability (%) has been shown as a ratio of absorbance (A570) in treated cells to absorbance in control cells (0.1 % DMSO) (A570). The IC50 was calculated as the concentration of sample needed to reduce 50 % of the absorbance in comparison to the DMSO-treated control.

Cell Viability Estimation

Cell viability is calculated using the formula:

Cell viability (%) = {A570od of (sample)/A570 od of (control)} x 100

Statistical Analysis

All data obtained were analyzed and the results were computed statistically (SPSS/10 Software Package; SPSS Inc., Chicago, IL, USA) using one-way ANOVA. In all tests, the level of statistical significance was set at $p < 0.05$

RESULT

In the present study, the cytotoxic effect of nutmeg oleoresin against cancer cell line HepG2 was evaluated using MTT assay. MTT assay provided a quick, simple and cost effective way for testing the cytotoxic activity of nutmeg oleoresin. In this study, cancer cell lines were treated with different concentrations of the extract of nutmeg oleoresin for 24 hours. Nutmeg oleoresin extract caused a dose dependent increase in the cytotoxic activity of cancer cell line. As the concentration of the extract increased, the percentage of cell viability decreased which depicted significance in cytotoxic activity of nutmeg oleoresin against cancer cell line (figure 1). Morphological changes and apoptosis of cancer cells were observed using nutmeg oleoresin under inverted phase contrast microscope at 20x magnification (figure 2).

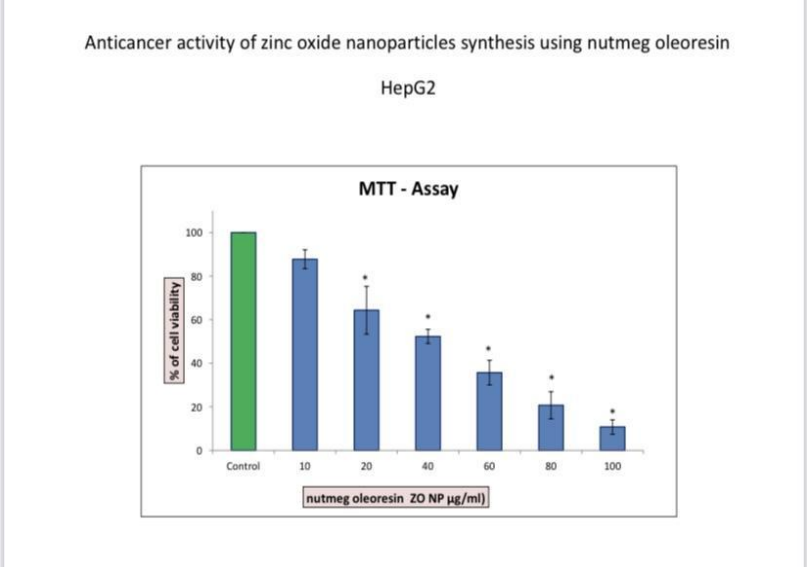

Fig.1: The cytotoxic effects of nutmeg oleoresin against cancer cells.X- axis represents control in green colour and different concentration of nutmeg oleoresin in blue color; whereas Y-axis represents percentage viability produced by the control and nutmeg oleoresin at different concentrations. Cells were treated with nutmeg oleoresin(10- 100µg/ml) for 24 hours Data are shown as means ± SD (n = 3). * compared with the control , p value was 0.001 at 40µg/ml which was statistically considered as significant ($p < 0.05$).

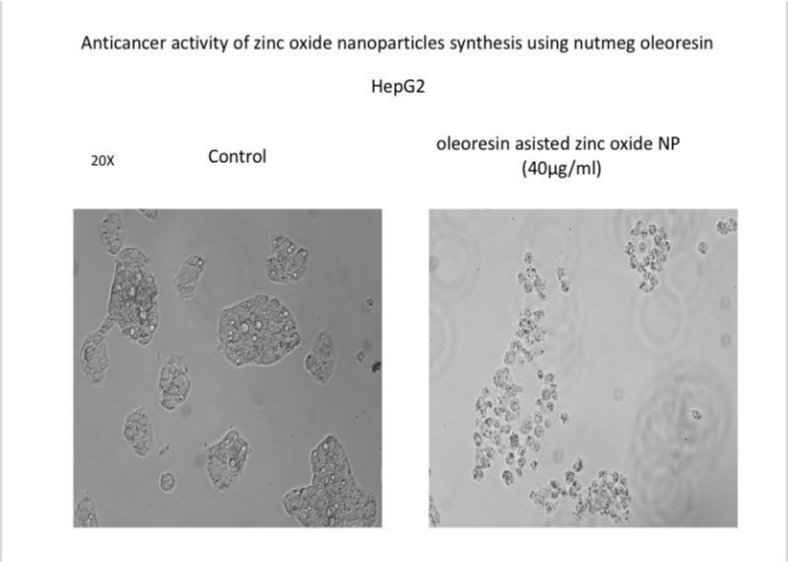

Fig.2: Assessment of cell morphology of cancer cells treated without or with nutmeg oleoresin. Cells were treated with nutmeg oleoresin (40 µg/ml) for 24 h along with the control group. Images were obtained using an inverted Phase contrast microscope at 20X magnification

DISCUSSION

In the present study, the cytotoxic effect of nutmeg oleoresin against cancer cell line HepG2 cell line was evaluated using MTT assay. MTT assay provided a quick, simple and cost effective way for testing the cytotoxic activity of nutmeg oleoresin. In a previous study conducted it was stated that, Production of metallic nanoparticles through green route was striking on the area of nano-science. The rushed biological complex of ZnONPs by Cardiospermum halicacabum proposes an environmentally friendly, simple and dexterous way for amalgamation of nanoparticles. ZnONPs are able to endure on ions solitary with presence of tough oxidizers. Conclusions represent Cardiospermum halicacabum coddle ZnONPs that further mediate apoptotic markers, and also aggravates cancerous cell apoptosis, toxicity to cancerous cells, and ROS development. This may also help as a viable candidate for cancer treatment and therapy.(31)

In another study, it was stated that the synthesized MN-ZnONPs have a spherical shape, average size and present different functional groups. MN-ZnONPs also showed improved anticancer activity in AGS cells by lowering MMP, increasing cell viability, and decreasing intracellular ROS levels and cytotoxicity. Furthermore, the prepared MN-ZnONPs in- duced apoptosis by enhancing pro-apoptotic, preventing anti-apoptotic proteins and arresting cell cycle in AGS cell lines. Based on those findings, this could be concluded that the MN-ZnONPs was an ultimate agent to treat and protect gastric cancer.(32)

The MTT assay, first defined by Tim Mosmann in 1983, is the most widely used viability assay in the world. The assay is based on metabolically active cell transferring of soluble yellow tetrazolium salt to insoluble purple formazan crystals. The tetrazolium salt can only be taken up by living cells. Internalized tetrazolium salt was converted to purple formazan

crystals by an enzyme ,mitochondrial dehydrogenase located in the mitochondria of living cells. (33,34)

The natural combination of ZnO nanoparticles utilizing plant extract gives an ecological well disposed, straightforward and proficient course for amalgamation of nanoparticles. Using plant concentrates instead of concoction methods avoids the use of harmful and toxic lessening and settling agents. Plant mediated ZnO nanoparticles indicated best anticancer action. ZnO np were successfully synthesized in a chemical and green approach using Zerumbone as a reducing and capping agent. Further, green ZnO np showed enhanced anticancer and antioxidant activity than chemical ZnO np. Finally, cost effectiveness, biocompatibility, and predictability to modify these ZnONPs make them viable choices in future biomedical applications particularly in cancer. (35)

Previously our team has conducted various studies based on similar topics (36)(37)(38)(39)(40)(41)(42)(43)(44)(45)(46)(47)(47,48)(49)(49,50)(51)(52)

Limitation of the study was that the study was conducted only at the in-vitro level. In future , the study may be extended in animal models.

CONCLUSION

The nutmeg oleoresin mediated nanoparticles have shown good anticancer activity and the IC50 value was (40 µg/ml). (53-62).Hence,nutmeg oleoresin mediated zinc oxide nanoparticles may be used for its anticancer activity however more invivo studies only can support its ultimate use in humans.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest in the study.

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