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RESEARCH ARTICLE
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Anticancer activity of Green synthesized selenium nanoparticles from Garcinia Mangostana Crude extract against MCF-7 Breast cancer cells

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ABSTRACT

Background: Nano-biotechnology has evolved and plays a crucial role in the detection and treatment of many diseases in the current scenario. An eco-friendly and efficient method (photoinduced) has been used for green synthesis of stable selenium nanoparticles (SeNPs) using aqueous extract as a reducing and stabilizing agent, derived from fruit extract of garcinia mangostana.

Aim: The aim of this study was to evaluate the anticancer activity of green synthesized GM selenium nanoparticles (Se-NPs) against breast cancer cells (MCF-7).

Methods And Materials: The preparation of selenium-induced Garcinia Mangostana nanoparticles were examined by ultraviolet-visible spectroscopy with a wavelength of range from 25-650nm. The selenium nanoparticle pellet was stored in sealed vials after being calcined for two hours at 70°C in a hot air oven.In-vitro antitumor activity of Se-NPs was evaluated by MTT assay. Inverted microscope was used to evaluate the morphology of the cells.

Results: The synthesized Selenium Nanoparticles have anticancer against MCF-7 cell lines. The cytotoxicity study exhibited a dose-dependent effect against breast cancer cells (MCF-7) using MTT assay, the inhibitory concentration (IC50) was found to be 50µg/mL . Inverted phase contrast microscope showed low viability of cell at a concentration of 60ul in the breast cancer cell line.

Conclusion: In conclusion, the results of this study demonstrated that Garcinia Mangostana induced selenium Nanoparticles extract may be a potential therapeutic agent for human breast cancer treatment.

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Keywords: *garcinia mangostana, selenium nanoparticle, MTT assay, antitumor activity, green synthesis*

INTRODUCTION

Breast cancer is the most common cancer in women globally, and its prevalence has increased over time(1). When compared to other types of cancer, breast cancer is the second largest cause of mortality in women. Around 20.3 million females worldwide died from breast cancer in 2020, making it the leading cause of cancer-related DALYs, deaths, and YLLs, of which 93.3% were caused by YLLs and 6% by YLDs(1). Radiation, chemotherapy, and surgery are frequently employed in the management of cancer. Chemotherapeutic drugs employed in the treatment also have undesirable effects on normal tissues, such as gastrointestinal disorders, thrombocytopenia, and bone marrow depression (2,3). This sparked a new interest in the development of alternative strategies such as treatments aided by nanotechnology (4,5) (6). Therefore, developing effective alternative drugs for breast cancer is an urgent need, which could reduce mortality and improve the quality of life of Breast carcinoma patients (7),

Traditional medicine has been employing medicinal plants to manage human health care for centuries. The commercial production and formulation of numerous herbal-based products and nutritional supplements increased due to the high demand for products made from medicinal plants. One of the most well-known herbal remedies, Garcinia Mangostana Linn, produces fruits that contain a group of natural substances called "mangosteen" that were extracted from the fruit's epicarp. For centuries, people have utilized the fruit shell of the mangosteen to treat conditions like cancer, diabetes, and diarrhea. Due to the presence of anthocyanins and other antioxidants, mangosteen has been found to have cardioprotective, anti-inflammatory, anticarcinogenic, and antibacterial properties (8)(9)(16). A study by Moongkarndi et al, a crude methanolic extract (CME) from mangosteen pericarp was found to significantly inhibit the proliferation of the human breast cancer cell line SKBR3 in a dose-dependent manner with an ED50 of 9.25±0.64μg/ml.

Over the past ten years, nanotechnology has experienced tremendous growth, and recent developments in its use in medicine have opened up fascinating possibilities for the future of healthcare. The antitumor effects of selenium have been established, and selenium supplements have been employed in various anticancer treatments (10). SeNPs' promotion of cancer cell apoptosis is typically thought to be a key mechanism in their suppression of malignant tumors (11). SeNPs have been discovered to control important apoptotic proteins, such as the p53 gene, ROS [6] cells, and the caspase family (12). Antitumor effects of SeNPs in lung cancer, prostate cancer, and glioma cancers have already been reported. In previous work of the authors, SeNPs were found to play an important role in inhibiting lung cancer cells but had little effect on normal cells. Therefore, it was proposed to test for the inhibitory effects of SeNPs on other cancers. SeNPs are suggested to have potent antitumor activity on cervical carcinoma (13), hepatocarcinoma (14), and colorectal cancer. There are several disadvantages to using physical and chemical methods to create nanoparticles, including time consumption, expense, and harmful by-products. A transparent, less harmful, and environmentally friendly nano component was produced to satisfy these criteria through green nanoparticle synthesis. (15). Since the usage of SeNPs as a drug carrier has recently gained considerable attention (16)(17).

Numerous studies have recognized that different extracts of mangosteen have demonstrated antitumor properties on in vitro analysis in various cell lines (19)(9). Interestingly, α-mangosteen was observed to induce mitochondrial dysfunction. Moreover, it induced cell-cycle arrest and apoptosis in human colon cancer DLD-1 cells (12). However, no evidence has been reported to date on the synergistic effect of SeNPs with the Garcinia mangostana extracts against human breast carcinoma (MCF-7) cells. Therefore, the present study aims to explore and evaluate the anticancer potential of Garcinia mangostana pericarp extracts synergic with SeNp against breast carcinoma cell lines

MATERIAL AND METHODS

Preparation of extract

From the Amazon online purchasing service, a dried packet of garcinia mangostana pericarp was bought. The pericarp was dried at 60°C for 24 hours prior to extraction. 5g of dried pericarp were ground into a fine powder using liquid nitrogen and a mortar and pestle. This powder was then dissolved in 100ml of distilled water and heated for 10 minutes at 60–80°C using a heating mantle to produce the extract. To filter the boiled extract, Whatman No. 1 filter paper was used. The filtrates were kept at 5°C for future research. Using an aqueous extract of G. mangostana, the bio-reduction procedure was carried out. SeNP, 0.2M sodium selenite was dissolved in 60ml of distilled water and stirred for a short period of time using a magnetic stirrer. G. mangostana extract, filtered to 40 mL, was then added to it. The solution mixture was agitated in a magnetic stirrer for 72 hours at 650–800 rpm. The color variations in the reaction mixture were monitored constantly using a double-beam UV-visible spectrophotometer with a wavelength range of 300-600nm. The mangostana extract-mediated selenium nanoparticles was centrifuged for 10 minutes at 8000 rpm. The selenium nanoparticle pellet was stored in sealed vials after being calcined for two hours at 70°C in a hot air oven.

Characterization of selenium nanoparticles

The optical properties of G. mangostana's selenium nanoparticles were determined using a double beam UV-vis spectrophotometer (UV-2450, Shimadzu) in the frequency range of 300-600 nm.

Anticancer activity of G mangostana-induced SeNPs

cell culture

The National Centre for Cell Science (NCCS), located in Pune, India, provided the breast cancer cell line (MCF-7). The cells were cultured in T25 culture flasks with antibiotics (100 U/ml penicillin and 100 g/ml streptomycin) at 1% in DMEM supplemented with 10% FBS. Cells were kept at 37 degrees in a humid environment with 5% CO2.

Determination of cytotoxicity of G.mangostana induced SeNPS by 3-(4, 5-dimethyl thiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay: Using the MTT assay (3-(4, 5-dimethylthiazol- 2-yl)-2, 5-diphenyltetrazolium bromide), cell cytotoxicity was determined. The MCF-7 cells are seeded in 96-well plates (5x 103 cells/well) and left for 24 hours. The old media was aspirated the following morning and replaced with a new fresh medium that contained different concentrations of SeNPS extract (0-200 µg). The plate is placed in an incubator at 37 degrees for 24 hours. After incubation of 24 hours, MTT solution is added to each well and again incubated for 4 hours under dim lighting. The ability of living cells to transform yellow tetrazolium salt into a purple formazan product was used to measure cell viability. After that, the formazan product was dissolved in DMSO, and the absorbance at 570 nm was measured.

cell viability is calculated using the formula:

% Growth inhibition = A570 nm of treated cells/ A570 nm of control cells× 100

RESULTS

Green synthesis of Selenium nanoparticle

Visual observation and characterization of Selenium nanoparticle

Visual identification of color change is a preliminary tool that confirms the ability to synthesize nanoparticles (22). Green synthesis of selenium nanoparticles using Garcinia Mangostana fruit extract was initially confirmed by visual observation. (Figure 1) The fruit extract was exposed to a selenium ion solution, and the selenium nanoparticle was formed. At first, no difference in color was seen. At 60°C, the reaction mixture is agitated once again using a magnetic stirrer at 650–800 rpm. The intensity of the brown color increased after 24 hours, showing that the g. mangostana extract had reduced sodium selenite to selenium nanoparticles, as illustrated in figure 1. The UV spectrum of Selenium Nanoparticles was characterized in the range of 300-600 nm. UV-Vis absorption spectrum shows the surface

plasmon resonance band centered at 450 nm which is the characteristic peak for selenium nanoparticles.

MTT assay

MTT assay was used to test the selenium nanoparticles' cytotoxicity. The enzyme mitochondrial succinate dehydrogenase reduces the yellow color of MTT to produce purple-blue formazan, which is measured using a colorimetric assay. Based on the viability of cancer cells, the effect of Gm-selenium nanoparticles was examined (breast cancer cell line). This test was conducted with GM-Se nanoparticle concentrations ranging from 0-200 ug/ml. The findings of inhibitory concentration (IC50) at 50 ug/ml show that selenium nanoparticles reduce the viability of MCF-7 cells in a dose-dependent manner

Morphological assessment using an inverted microscope

Using an inverted phase contrast microscope, the morphology of breast cancer cells was examined. The appearance of a nucleus in the cell in the control sample indicated that the cells were alive. The cell begins to die after introducing the sample at various concentrations. At a concentration of 20 µl, the nucleus in the cells could not be seen. At a concentration of 40 µl, some of the cells begin to rupture and die, resulting in low cell viability in the microscope when compared to a concentration of 20 µl. At a concentration of 60 µl, the cells quickly perished as a result of the cytotoxicity effect induced by the reactive oxygen species brought on by the high concentration of selenium oxide.(figure 2)

DISCUSSION

Plants have been explored successfully for rapid biosynthesis of metal nanoparticles such as gold (18), silver (19), selenium (20), MgO (20) CuO (21) and ZnO (22)nanoparticles. The nanoparticles are used extensively in cancer drug delivery as the drugs which are bound with nanoparticles are able to penetrate deep into the organs (20). SeNPs have been suggested to have antitumor activity, and many studies have shown that they have high specific toxicity for cancer cells (23). To date, whether or not SeNPs have different inhibitory potential against different types of tumors has not been made clear. Mangosteen has been noted to be an abundant source of a class of polyphenols known as xanthones. The diverse structure and chemical properties of xanthones have been reported to have a variety of health promoting properties including anti-inflammatory, anti-oxidant, and anti-cancer activity (25),

In several studies, crude extracts from pericarp of mangosteen were evaluated for their cytotoxic activity against human breast adenocarcinoma cell line. In one study, Moongkarndi et al (26), a crude methanolic extract (CME) from mangosteen pericarp was found to significantly inhibit the proliferation of human breast cancer cell line SKBR3 in a dose-dependent manner with an ED50 of 9.25±0.64µg/ml. According to previous literature, it has been demonstrated that the compound Garcinia mangosteen isolated from the pericarp induces cell-cycle arrest and apoptosis in many types of human cancer cells.(27) Additionally, mangosteen has been demonstrated to inhibit cell invasion and migration in breast and prostate cancer cells with the concomitant downregulation of MMP-2 and MMP-9.(27) However there is a paucity in the literature regarding the combined antitumor activity of selenium nanoparticles and Garcinia Mangostana pericarp extract. The present study was done to evaluate the anticancer activity of selenium nanoparticle induced Garcinia Mangostana fruit extract.

Our study results showed that there was a color change observed visually indicating the green synthesis of selenium nanoparticle induced Garcinia Mangostana. These results were consistent with previous studies that have described the synthesis of SeNPs employing various reductant agents (28)These different colors of Selenium Nanoparticles are related to the excitation effect of surface plasmon resonance.

Angamuthu et al. reported the highest peak absorption of UV-Vis absorption spectrum at 370 nm (29), Malhotra et al. reported a similar high

absorbance peak at 390 nm as well (30) Furthermore, Chen et al. found the absorption maxima at 380 nm (31). Our study results were in concordance with previous literature which showed similar results of UV-Vis absorption spectrum of the surface plasmon resonance band centered at 450 nm, which is the characteristic peak for Selenium Nanoparticles. It reveals the reduction of selenium ions to metallic Selenium Nanoparticles in the reaction mixture, and the Surface Plasmon Resonance (SPR) of SeNPs is responsible for the creation of such a peak.

MTT assay in the present study revealed the inhibitory concentration (IC50) at 50 ug/ml, indicating that selenium nanoparticles reduce the viability of MCF-7 cells in a dose-dependent manner. Similar results have been seen with Garcinia mangostana and SKBR3 human breast cancer cell lines by Moongkarndi et al with IC value of 60 ug/ml. (26)DLD-1 human colon cancer cells by Akao et al (32) and B16-F10 melanoma cells by Cunha et al showed an IC value of 40 ug/ml and 60 ug/ml respectively (33).Similar studies have reported that various edible fruit extracts have anticancer activities against the Hep-G2 cell line, including cranberry, lemon, apple, strawberry, red grape, banana, and grapefruit.(34) Rowanberry, raspberry, lingonberry, arctic bramble, and strawberry, according to McDougall et al.(35), also demonstrated significant action against HeLa cell line.

Using an inverted phase contrast microscope, at the concentration of 60 µl the morphology of the cells quickly perished as a result of the oxidative stress brought on by the high concentration of selenium oxide. This was consistent with previous literature, Garcinia mangostana extract which induces the apoptosis of SKBR3 breast cancer cells, with morphological alterations like cytoplasmic membrane shrinkage, loss of contact with surrounding cells, membrane blebbing, and an apoptotic body. (26) This leads to early apoptosis in the formation of intracellular ROS. Such an oxidative stress situation damages numerous cellular components (proteins, DNA, and other organelles), which leads to apoptosis, or programmed cell death (36).These findings imply that mangostin inhibits Ca2+ ATPase to cause apoptosis in cells by activating the mitochondrial pathway. (37) Reactive oxygen species were produced together with early apoptosis in the GML extract-induced SKBR3 human breast cancer cell line. This was expected because one of the key mechanisms causing early apoptosis is the buildup of intracellular ROS. Both findings suggested that ROS influences both intrinsic and extrinsic apoptotic pathways by regulating the expression of Bcl-2 and FasL, two key molecules in these processes.

In this present study, we noticed that the synthesized pericarp extract of Garcinia Mangostana induced selenium nanoparticles has a potent anticancer property which are of great importance as therapeutic agent in preventing cancer

CONCLUSION

Selenium nanoparticles have become a significant class of nanomaterials with numerous commercial and medical uses. One of the innovative methods in the field of cancer therapy is the development of biocompatible molecules employing nanotechnology as an anticancer agent. Garcinia mangostana extract is a simple, inexpensive, environmentally friendly, and widely applicable method of manufacturing. Utilizing the MTT assay, we have seen that Selenium induced Garcinia mangostana Nanoparticles reduced the proliferation of MCF-7 breast cancer cells in a dose-dependent manner. The current findings showed that a fruit extract of garcinia induced selenium nanoparticles may have potential as a therapeutic agent for treating human breast cancer. Future research can be done in evaluating the role of Garcinia Mangostana in various other cancer cell lines.

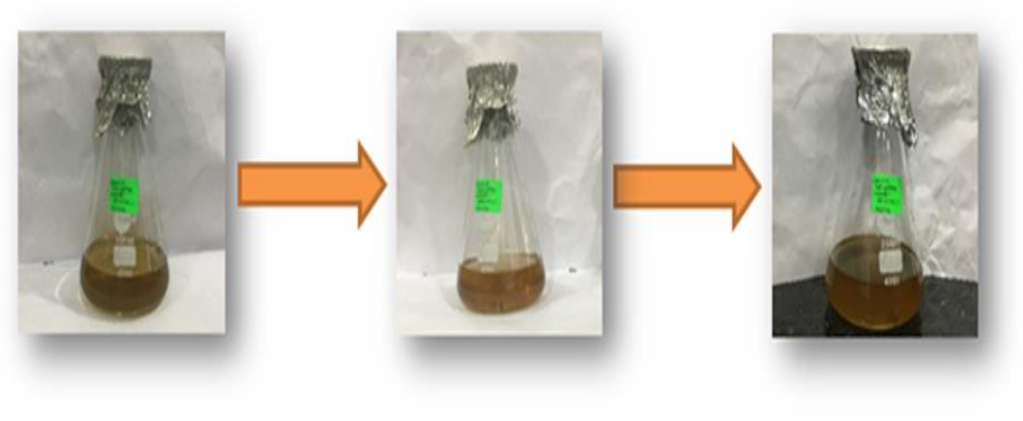

FIGURE 1: Visual observation of synthesized SeNP nanoparticles – color change observed

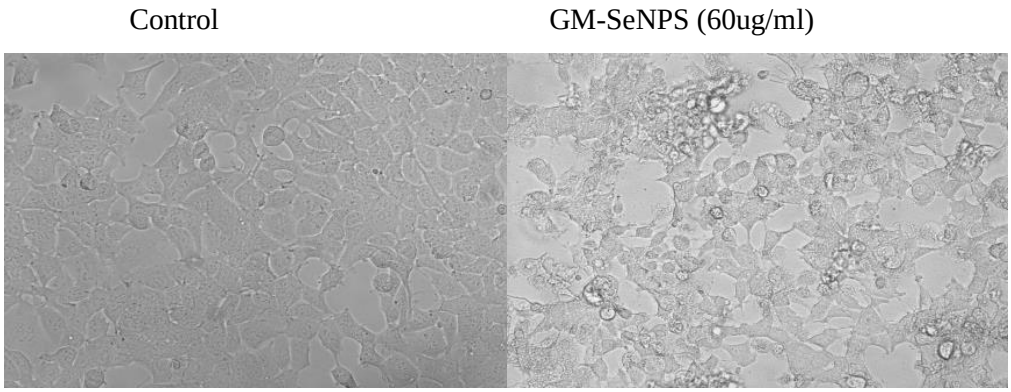

FIGURE 2: Assessment of cell morphology of MCF-7 Breast cancer cell line treated with GM-Se NP for 24 h along with the control group. Images were obtained using an inverted Phase contrast microscope in 20x magnification.

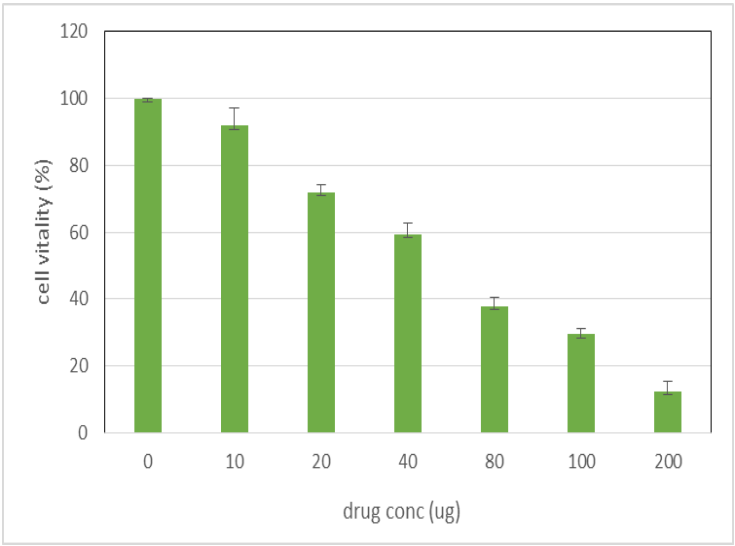

FIGURE 3: indicates the graph representing the anticancer activity of the seNPs-induced garcinia mangostana

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TABLE 1: represents the drug concentration and the anticancer activity

Drug Conc	24 hrs	SE
Control	100	0
10	91.8476	5.380218
20	71.78896	2.30135
40	59.42296	3.202299
80	37.82465	2.730741
100	29.24785	1.601731
200	12.36473	3.135533

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CONFLICT OF INTEREST

There is no conflict of interest

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