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Anticancer activity of synthesized green silver nanoparticles against human colon cancer cell lines

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ABSTRACT

This study was conducted to discuss the anticancer efficacy of synthesized AgNPs on human cancer cell (HT29) using curcumin leaf extract. A nano silver prepared by green synthesize were described by appearing a peak at 434nm using UV-visible spectroscopy. The surface morphology of prepared nanoparticles was analyzed using TEM. TEM images showed that Cur-AgNPs were measured in size of 30nm–40 nm. The MTT assay revealed that different doses of Cur-AgNPs were effectively cytotoxic against 29-HT cell lines in a time-dependent manner. Dose-dependent apoptosis and necrosis showed a similar pattern to the MTT assay. Based on the data obtained in, Cur-AgNPs have therapeutic value and a promising plan for colon cancer treatment.

Key words: Plant extract, Cur-AgNPs, Cancer Cell Line, cytotoxic activity, green chemistry, Drug delivery

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INTRODUCTION

Cancer is a type of diseases in which abnormal cells differentiate out of control [1], invade other tissues nearing their end, then spread to the other organs through blood & lymphatic vessels [2]. Cancer is one of the leading causes of death, and its prevalence is increasing worldwide. In the last century, the development of cytotoxic drugs has changed the way cancer is treated, resulting in increased patient survival rates and quality of life. However, due to the limited therapeutic indications of some drugs, the potential for damage to healthy and normal tissues as well as cancer cells, and the emergence of resistance, the creation of agents that combine efficacy, safety, and convenience remains a major problem [3].

The causes why a cell becomes cancerous are genetic varations related to the cell division and the order of death. Tumor suppressor genes as well as oncogenes have an important role in the development of cancer (Fig. 1). Tumor suppressive genes (such as p53) and tumor oncogenes (such as bcl-2) are responsible for regulating cell growth [4].

Deletions and mutations in these genes also contribute to the progression of cell cycle control points, as well as to increased cell migration. Tumor suppressor genes are often absent or absent in cancer, which promotes cancer growth and progression [5,6].

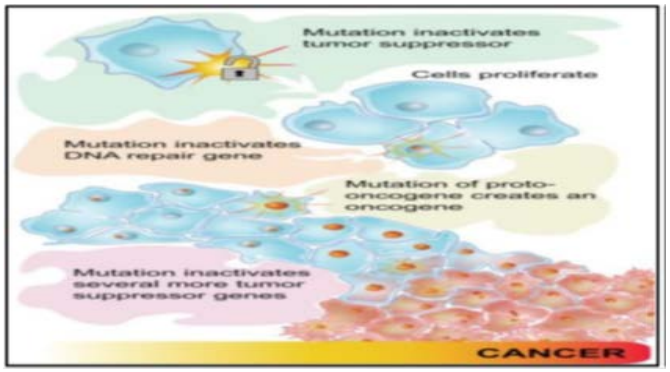

Fig 1. Cancer progression

cancer or tumer common therapys contain surgery, radiation therapy as well as chemotherapy. However, side effects and limitations of classical therapys affect results. example of this, standard chemotherapy may cause serious side effects, including local effects, like tissue necrosis and thrombophlebitis, as well as systemic effects, such as myelosuppression, kidney and liver dysfunction and immunosuppression [7]. In addition, malignancies can evolve multidrug resistance (MDR), that may lead to failure of chemotherapy [8]. Therefore, it is necessary to develop new medicines to evolve the therapeutic influences. Recently, nanomaterials have attention more interest as cancer drugs due to their special chemical and physical characteristics, which has led to the emergence of a new field of anticancer drugs - cancer nanomedicine [9,10].

Nanomaterials are defined as physical substances with one dimension at the smallest between (1nm to 100nm), have attracted a lot of attention due to their unique features that set them apart from their bulk counterparts. Nanoscale structures frequently have distinctive optical, electrical, or mechanical features. They are gradually becoming commodities and being commercialized. Inorganic non materials like quantum dots, nanowires, and Nano rods may be used in optoelectronics because of their fascinating optical and electrical properties [11-14]. Recently, a variety of nanoparticles have been applied for biomedical application like tissue manufacturing, drug delivery, and biosensor [15-20]. They have been employed as quantum dots and as chemical catalysts such as nonmaterial base catalysts. Size-related characteristics can be seen in nanoparticles [21]. Additional methods chemical and also physical were used to prepare the nanoparticles. However, there are a number of methods that have disadvantages including toxic solvents, the use of high energy consumption, hazardous products... etc., so elemental need to grow environmentally friendly methods for the manufacture of metallic nanoparticles. The progress of environmentally friendlytechnology in the production of materials is great important to develop their applications. At present, various types of nanoparticles were synthesized by green methods with chemical composition, size and morphology synthesized by various methods and their application have been explored in many innovative technological fields. The method is advantageous over

other risky procedures due to the regenerative properties of the plant extracts, the ecologically friendly aqueous medium, and the moderate reaction conditions. Due to their energy efficiency, cheap cost, and benign behaviour in the process of creating metallic nanoparticles, several plant extracts and products have gained interest in recent years [22-29].

Compared to classical anticancer drugs, the nanometallic (MNPs) materials can be utilized as new therapeutic factors or drug deliveries in association with common therapies, and unwanted side-effects can be reduced by providing a targeted methods [30]. They can be utilized as new therapeutic factors or drug vectors in association with common treatments, which is an improvement over conventional anticancer drugs and allows prevention of negative side effects [7,10], Therefore, the aim of our study is to investigate the antibiological effect of silver nanoparticles in vitro against Human Colon Cancer Cell Lines.

Silver Nano bodies have been displayed to show good anticancer effects in almost of cancer like breast cancer, colon cancer, cervical cancer, ovarian cancer, lung cancer, pancreatic ductal adenocarcinoma, hepatocellular carcinoma, osteosarcoma, melanoma etc. Many articles emghasize that the anticancer effects of AgNPs with diverse shapes, sizes and doses/concentrations are discrepant in various cancer cells [31-40]. As well as, another agent like exposure time, pH of lesions, tumor microenvironment, cell lines and AgNPs effect in the anticancer activity [36, 38, 41]. In general, AgNPs show broad spectrum as anticancer activity in size-, time-and dose/concentration-dependent manners. Silver nanoparticles at smaller size can obtain to increasing the endocytosis, and reason more significant genotoxicity and cytotoxicity. Compared with another forms, spherical silver nanoparticles exhibit better cytotoxicity because more their surface-to-volume ratio. Almost higher concentrations of silver nanoparticles induce apoptosis more than lower [42].

MATERIALS AND METHODS

Preparation of Curcumin-silver nanoparticle (Cur-AgNPs)

Curcumin (≃95% w/w) was gained from India. Curcumin extract was obtained according to the study Jagannathanet el al. (2018) [43]. 0.5g of the plant powder was addition to 0.1l of deionized water, and the mixture was heated at 80 C for 30 minutes. Then, the solution was filtered by using Whatman No. 1 filter paper to gain a homogeneous solution of curcumin in water. Cur-AgNPs were prepared according to the procedure described by Manonmani et al. (2015) [44], 10 ml of silver nitrate

(AgNO3; 0.1 M) and 3 ml of curcumin solution were mixed in a conical flask (50 ml) and boiled in a water bath at 60 °C for 1 hour. The Ag-NPs composition was investigated and detected by the colour changes of the mixture which changed from light yellow to brown.

Characterization of synthesized curcumin silver nanoparticles

The optical property of Cur-AgNPs was detected by UV-visible spectrophotometer (Model-Shimadzu UV 1800, Japan). The prepared solution was centrifuged for about 15 min. After, to get filtered and purified Cur-AgNPs, the compound was washed by ethanol and dried by vacuum oven (VO-27, Korea). The particle size and surface morphology and size of AgNPs were analyzed utilizing Transmission Electron Microscopy [(TEM) (JEM-2010 (Jeol)], and the sample was prepared by coating AgNPs solution onto carbon coated copper TEM grids, then the film was permitted to dry prior to measurement by utilizing TECHNAI 10 activated at an accelerating voltage at 80KV, the resolution about 0.22 nm.

Assessment of in vitro cytotoxic activity of the Cur-AgNPs on human cell line: Thiazolyl Blue Tetrazolium Bromide (MTT) assay was performed to determine the cytotoxic property of the synthesized Cur-AgNPs against HT29 cell line according to [45]. Cell lines were inoculated into a 96-well microtiter plate. Cur-AgNPs stock solutions(5 mg/mL) were prepared in sterile distilled water and diluted to the required concentrations (5, 10, 20, 50, 100, 150, 200 and 250 µg/mL).

Cur-Ag-NP stock solution was added to the cultures to obtain their respective concentrations of Ag-NP and incubated for 48 h at 37 °C. Untreated cells were used as a control. Then the culture cell incubated with MTT ("3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, a tetrazole) tetrazolium salt chromatography test 3-[4,5-dimethylthiazol-2-yl]] -2,5-diphenyltetrazolium bromide (MTT)" is used to determine cell viability in cell proliferation and cytotoxicity assays. MTT is reduced in metabolically active cells to produce insoluble formazone purple. Cells were harvested at the exponential point from tissue culture and stained with trypan blue calculated using a cytometer, after a recovery period of 24, 48 and 72 h, the data were read at 520 nm using a spectrophotometer, the spectral absorbance of the lysates was determined using an ELISA reader microplate, and the cytotoxicity data were standardized by determining the absorbance and calculating the corresponding AgNP concentrations. The resulting data was utilized to plot a dose-response curve in which the amount of extract desired to kill fifty percent of the cell number (IC50) was revealed by [45, 46].

$$Cell\ viability\ (\%) = Mean\ OD / control\ OD \times 100$$

RESULT AND DISCUSSION

Characterization of synthesized curcumin silver nanoparticles

Reduction of silver ions Ag+ to form AgNPs by adding the curcumin solution could be followed by the change of color from light-yellow to brownish. The solution of reaction transferred to brown color after the addition of silver nitrate solution is a clear pointer to the synthesis of silver nanobodies [47]. Thus, the presence of AgNPs was characterized using a UV-Vis spectrum [48]. A single broad peak was detected at 434 nm (Figure 1), which is consigned to surface plasmon of Cur-AgNPs. Several studies have detected absorption highest of colloidal silver solution between 412 to442 nm, which corresponds to plasmon excitation of different nanometal [48-50]. The prepared nanosilver was established and confirmed by a TEM image recorded from the silver nanobodies deposited on carbon coated copper TEM grid are displayed in Figure 2. This image showing spherical Cur-AgNPs with low density dispersion and are in the range of 25nm-45nm in size. Characterization of NPs by TE M has been stated by [51] (Figure 3).

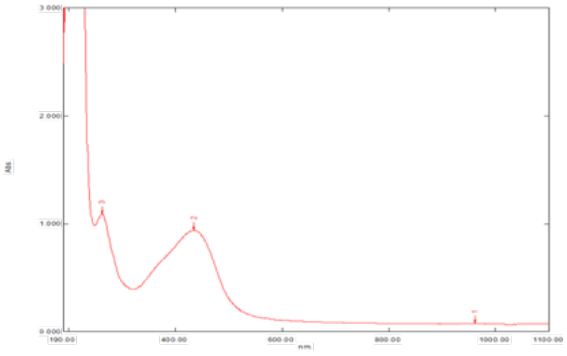

Fig 2. Ultraviolet-visible spectrum of synthesized Cur-AgNPs

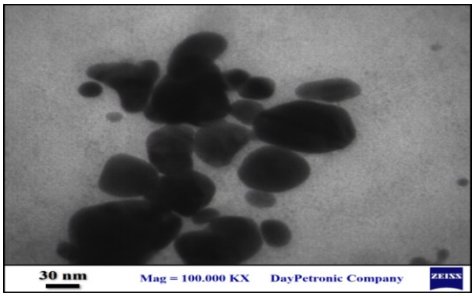

Fig 3. Transmission electron microscopy image of Cur- AgNPs at 30 nm scale

Assessment of in vitro cytotoxic

Activity of the Cur-AgNPs using MTT assay: The MTT assay showed that the sample has minimal cytotoxicity against HT29 cell line at 24, 48 and 72 hrs, however, a little cytotoxicity of that leads to deformation of the cell morphology. The cell proliferation of the treated cell was significantly lower compared with untreated control cells. The MTT assay showed that Cur-AgNPs induced a dose-dependent cytotoxic effect on HT29 cell line that the inhibition rate was as shown in Figure 4.

In the next step, the dose-dependent Apoptosis and necrosis showed a similar pattern to the MTT assay (Figure 5 ,6), and all of these three experiments are in good agreement. Overall, the sample has minimal cytotoxicity, with a low apoptosis and necrosis percentage.

The anticancer activity of Cur-Ag Nps was highly supported by the studies of [50,52]. The cytotoxicity of silver nanoparticles could be owing to induction of reactive oxygen species (ROS) which pronounce the apoptosis pathway and its well-recognized mitochondrial interaction. Also, production of oxidative damage enunciated the genotoxic stress as well as gene up regulation which inductees the apoptosis [53,54]. Thus, it was observed from the present investigation that, the cytotoxic activity of silver nanoparticle synthesized from curcumin. This property of use for large scale silver nanoparticle production, and could result in economic viability, also being eco-friendly for cancer treatment. It would be further studied for its mode of penetration and suppression of cancer cell line and regulation of genes of guardian of cells. Further studies are needed to improve the pathway of AgNPs on cancer cells [55-58].

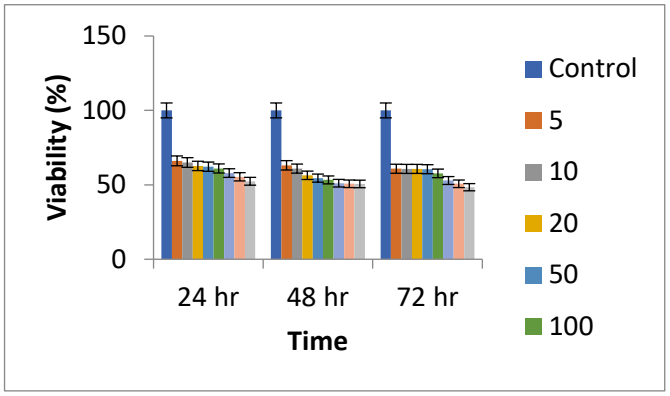

Fig 4. Results of MTT assay on HT29 cancer cell line. Percentage of cell viability in 24, 48 and 72hr.

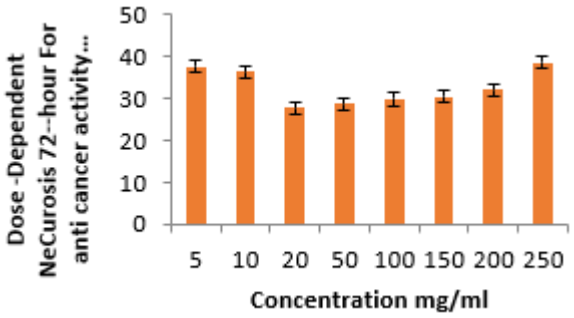

Fig 5. Dose-dependent necrosis of Cur- AgNPs

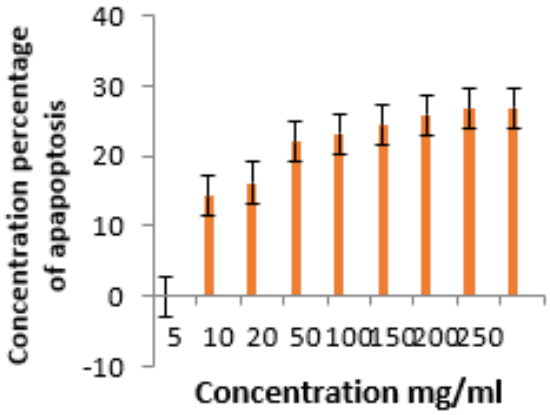

Fig 6. Dose-dependent Apoptosis of Cur-AgNPs

CONCLUSION

In this work the use of a sliver nanoparticles (AgNPs) to investigate the anticancer activity of synthesized on human cancer cell (HT29) Cur-AgNPs prepared by using curcumin plant extract. A nanosilver prepared by green synthesize were described by appearing a peak at 434nm using UV-visible spectroscopy. The surface morphology of prepared nanoparticles was analyzed using TEM. TEM images exhibited that Cur-AgNPs were measured 30nm-40nm in size. MTT assay revealed that various doses of Cur-AgNPs were potently cytotoxic against HT 29 cell lines in time dependent manner. The dose-dependent apoptosis and necrosis showed a similar pattern to the MTT assay. Based to the data obtained in this study, Cur-AgNPs can be considered a therapeutic value and promising plan for the treatment of colon cancer

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