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Biomedical applications of different green synthesized nanoparticles as a potent anticancer agent

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Cancer is the leading cause of death worldwide. Millions of people die of cancer because of poor economic condition. Chemotherapy and surgical removal of tumor is last option in carcinoma but there are several drawbacks of chemotherapy and surgery. Because even after the chemotherapy there are high chances of cancer reversion, chemotherapy is highly expensive, and it has a lots of side effects. Nanotechnology is revolutionizing the medical field. Nanotechnology is the ability to work at the atomic, molecular, supramolecular levels (on a scale of ~1-100nm). A natural antioxidant flavonoid luteolin 30, 40, 5, 7-tetrahydroxyflavone nanoparticles present in vegetables is non-toxic and highly effective in cancer treatment. PLGA-PEG nanoparticles loaded with cisplatin has potent role in treating prostate cancer. This nanoparticle is commonly applied against LNcapcel a human prostate cancer cell line. Copper oxide nanoparticles active against A549 lung cancer cell. Photodynamic therapy is also good in cancer treatment. An analogue to surgery and chemotherapy in carcinoma treatment is through the applications of photodynamic therapy (PDT). Here we are providing an overview of nanoparticles characteristics their use in medical field especially in cancer therapy. In this review the anticancer activity of nanoparticles like zarconia, silver, gold, luteolin, titanium, copper oxide nanoparticle are studied. These nanoparticles possess anticancer activity against human cancer cell lines like lung, head, neck, intestinal etc.

Keywords Nanotechnology, Nanoparticles, Anticancer, Antioxidant.

INTRODUCTION

Nanotechnology is the capacity of working at the atomic, molecular, supramolecular levels (on a scale of ~1-100nm) also the study of the devices that will help to design and create the structure of nanoparticles and elaborate their functions in different fields (Roco et al. 200). Treatment of the cancer is one of the promising therapeutic advantages of nanotechnology (Jain .2005). It has been estimated in 2008 that approximately 7.6 million people died of different types of cancer worldwide (Rosarin et al. 2012). The available therapies for cancer are surgical removal of cancer and chemotherapy but these are limited by

their low specificity towards target tumor and are highly toxic. And even after the surgery or chemotherapy there are high chances of cancer reversion (Hong et al. 1997). Nanotechnology has resolved this issue up to much extent the use of nanoparticles in nutritional supplements has less side effects and high anticancer and antioxidant activity (Amin et al. 2009). A natural antioxidant flavonoid luteolin, 30, 40, 5, 7-tetrahydroxyflavone nanoparticles present in vegetables is non-toxic and highly effective in cancer treatment (Lin et al 2008).PLGA-PEG nanoparticles loaded with cisplatin has potent role in treating prostate cancer. This nanoparticle is commonly applied against LNcapcel a human prostate cancer cell line. Copper oxide nanoparticles active against A549 lung cancer cell. Photodynamic therapy is also good in cancer treatment (Agostinis et al. 2011; Dougherty et al. 1998). Specialists have played out the cytotoxicity of ZrO_2 NPs (Fahdawi et al. 2015; Sathishkumar, et al. 2013). Invitro cytotoxicity of silver nanoparticles is additionally seen against human cellular breakdown in the lungs a549 cells at various grouping of the applied nanoparticles (Sankar et al. 2013). The cytotoxic impact of AgNPs bio generated by Klebsiellaoxytoca DSM 29614 under high-impact (AgNPs-EPSaer) and anaerobic conditions (AgNPs-EPSanaer) was explored after 24 h of therapy on two human bosom malignant growth cell lines (SKBR3 and 8701-BC) and three human colon disease cell lines (HT-29, HCT 116 and Caco-2) by utilizing the MTT assay (Nakkala et al 2014). Nanozarconia removed from *Euclapytus globulus* leaf extract shows anticancer movement against two cell lines the human colon disease HCT-116 and human cellular breakdown in the lungs A549 Cell Lines (Balaji et al. 2017). Photodynamic treatment (PDT), as a malignant growth treatment technique, has a progression of favorable circumstances over methodologies, for example, medical procedure, chemotherapy and radiotherapy, as examined somewhere else (Monge et al. 2014; Ju et al. 2007).

Nanoparticles Induce Apoptosis of The Cancerous cell:

Inducing apoptosis or autophagy and the regulatory pathways of autophagy made a massive development in autophagy applied studies. Nowadays nanomaterials has been absorbed to result in autophagy and lots of nanomaterials are seen in autophagososmes in dendritic cells, alveolar macrophages, non-small mobile lung cancer cells, human mesenchymal stem cells, murine macrophages and human lung adenocarcinoma dealt with with nanoparticles, apoptosis is prompted through silver nanoparticles, zarconia nanoparticles, luteolin nanoparticles and many more. A hypothesized mechanism involved in autophagy perturbation brought about via NMs is stated in (Figure.1).

Anticancer Activity of Luteolin Nanoparticle

Luteolin has proven anticancer results towards lung most cancers, head and neck most cancers, prostate, breast, colon, liver, cervical, and pores and skin cancer (Ju et al. 2007; Panzarini et al. 2013). Its mechanism of motion is with the aid of suppressing the survival pathways of the cellular with the aid of inducing mobile apoptosis and at remaining cell death. Another mechanism of luteolin anticancer activity is arresting cell cycle and also apoptosis of carcinoma cells in lung (Ju et al. 2007; Chiu et al. 2008). the oral carcinoma squamous cellular is also destroyed (Yang et al. 2008; Amin et al. 2010).

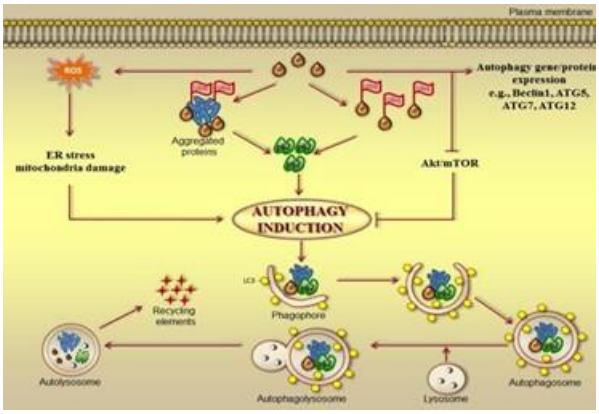

Figure 1: Nanoparticle-induced autophagy adapted from Panzarini et al. 2013

Anticancer Activity of Zarconia Nanoparticles:

Nanoparticles extracted from *Euclaptus globules* is nanozarconia which suggests Emmenceanti carcinoma activity in opposition to two cell strains human colon most cancers HCT-116 and human lung cancer A549 CELL LINES and the activity became studied and confirmed by using assays like MTT assay and blue exclusion of tryphan. There are varieties of mechanism via which zarconia nanoparticles shows anticancer activity by the formation of ROS (Reactive Oxygen Species) which leads to lack of the integrity of the membrane and those ROS result loss of membrane proteins and DNA (Balaji et al.

2017).

Mechanism of Action

Nanozarconia generate the reactive oxygen species which damage the DNA and plasma membrane of the cell as shown in (Figure 2) (Balaji et al. 2017).

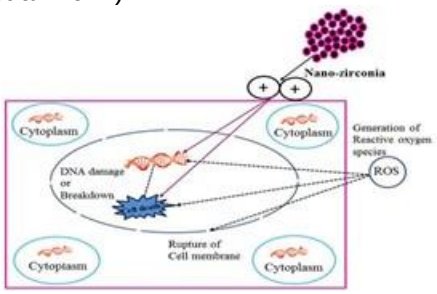

Figure 2: Showing Autophagy Induce By (Nan0-zarconia) By Formation of Reactive Oxygen Species (ROS) adapted from (Balaji et al. 2017).

Anticancer Activity of Silver Nanoparticles:

The nanoparticles silver acquired from living specie of *Klebsiella oxytoca* DSM 29614 also known as biogenerated nanoparticles and was investigated by treating two human cell lines with nanoparticles for 24h and the usage of each aerobic (AgNPs-EPSaer) and anaerobic situations (AgNPs-EPSaer). The 2 human cellular strains are i.E two human breast most cancers mobile strains (SKBR3 and 8701-BC) and three human colon cancer cell traces (HT-29, HCT 116 and Caco-2) and the first time became absolutely confirmed through using MTT assay. The nanoparticles received for the duration of aerobic situation i.E: The AgNPs-EPSaer is more lively than nanoparticles received during anaerobic conditions i.E:AgNPs-EPSanaer, with SKBR3 and 8701-BC cellular lines being extra touchy to AgNPs-EPSaer treatment in evaluation to HT-29, HCT 116 and Caco-2 colon most cancers cell traces. The mobile proliferation of the SKBR3 became greatly inhibited via AgNPs-EPSaer with an inhibitory attention of (IC_{50}) cost of 5µg/ml, whilst an IC_{50} value of 8µg/ml became observed for 8701-BC cell line. These values had been located properly within the clinically proper concentration of 100µg/ml (Nakkala et al. 2014).

Mechanism of Autophagy induced by AgNPS

Silver NPs own great capability as an anticancer agent. Numerous reports have documented the great potential of AgNPs to elicit cytotoxicity in cancer cells, through various mechanisms involving oxidative pressure, DNA damage, cellular cycle arrest, apoptosis, or necrosis. AgNPs are also amazing sensitizers for cancer chemotherapy and radiotherapy and display widespread antitumor interest in numerous animal models. However, whether or not AgNPs can result in autophagy and how this might affect the anticancer hobby of AgNPs have now not been suggested. In this report, we confirmed for the first time that AgNPs effectively induced cytoprotective autophagy, and that inhibition of autophagy extensively promoted the antitumor hobby of AgNPs, as illustrated in (Figure 3.0) (Lin et al. 2020).

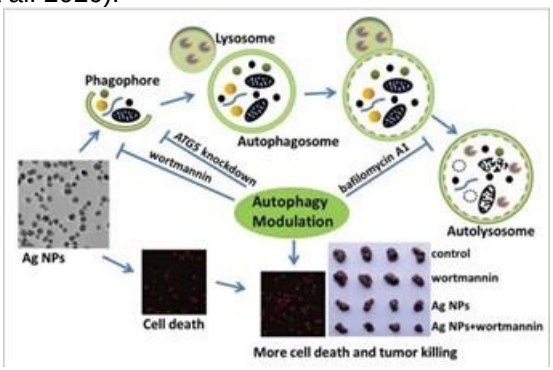

Figure 3: Shows Ag NPs induced cytoprotective autophagy and that inhibition of autophagy enhanced the antitumor efficacy of Ag NPs. (Lin et al. 2020).

1.5 .Anticancer Activity of Copper oxide Nanoparticles:

The cytotoxic impact of the green synthesized nanoparticles was concentrated against human lung carcinoma A549 cells with various concentrations (50 to 500µg/ml). The results of the lung cancer respond to nanoparticles copper oxide is dose dependent concentration revealed highly cytotoxicity against A549 cell. At the point when we take lower grouping of the copper oxide nanoparticles is lower with 70% practicality of cell at (50µg/ml) and cell suitability is diminished up to 6 percent with nanoparticles of focus (500 µg/ml). The half maximal inhibitory focus (IC_{50}) of copper oxide nanoparticles against A549 cells was discovered to be 200µg/ml. The improved cytotoxicity might be because of the presence of bioactive particles in *F. religiosa* leaf separate, play as epitomizing operator in copper oxide nanoparticles (Sankar et al. 2013). The copper oxide nanoparticles changes the state of the lung carcinoma cells by hatching the cell with nanoparticles for 36h,anyway the untreated cell does not show any various morphological changes like amassing of cell and restraint of the

correspondence the cell and buildup of the chromatin and these progressions prompts cell passing in nanoparticles treated cells (Jeyaraj et al. 2013). Copper oxide nanoparticles extricated from *F. religiosa* by arrangement of ROS and the responsive oxygen species actuate the apoptosis pathways of the cell modification of Δψm against A549 cells, prompts cell demise. Expanded centralization of the ROS results in free extreme assault at the membrane phospholipids and loss of Δψm. The elevated level of ROS may change the mitochondrial function and furthermore leads to apoptosis (Ling et al. 2003; Gibellini et al. 2010). The copper oxide nanoparticles investigate apoptosis of tumor cell in mice as appeared in (Figure 4) (Wang et al. 2013).

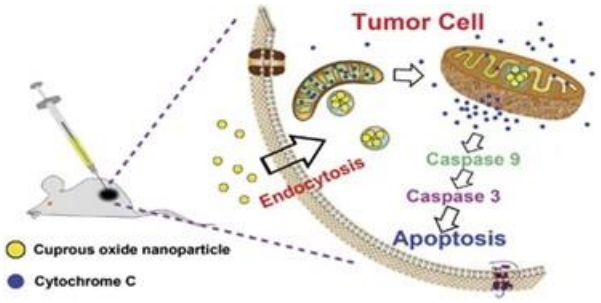

Figure 4: Shows the Copper Oxide Nanoparticles Inducing Apoptosis (Wang et al. 2013)**.**

Anticancer Activity of Solid Lipid Nanoparticles Containing *Curcumin*

Breast cancer cell lines MDA MB 438 and MCF-7 were gotten from American Type Culture Collection (HB-8065, Manassas, VA) and were refined in DMEM/F12+GlutaMAXTM medium (Invitrogen, Carlsbad, CA) containing 10% fetal cow-like serum (Invitrogen, Carlsbad, CA), 100 units/mL penicillin (Invitrogen, Carlsbad, CA) and 100 µg/mL streptomycin (Invitrogen, Carlsbad, CA). Brooding the cell with 37°C and with 5% CO_2 and 95% mugginess level. Curcumin against carcinomic action was concentrated by the (3-(4, 5-dimethylthiazol-2-yl)- 5-(3-carboxymethoxyphenyl)- 2-(4-sulfophenyl)- 2H-tetrazolium) (MTS) test. The cells were cultivated in 96-well microtiter plates at and the counter malignancy action of curcumin was inspected utilizing thickness of 5,000 cells/per well in a last volume of 100 µL medium. After 24 h, the cells were treated with a medium containing DMSO dissolved or DDAB-pluronic F127-epitomized curcumin at various focuses. Different cells were untreated as negative control, or treated distinctly with DMSO or DDAB in addition to pluronic F127 at the greatest fixation used to break down and epitomize curcumin, separately. After 72 h, the MTS arrangement (Cell Titer 96 Aqueous One Solution Reagent (Promega)) was included at 5 µl per well and brooded for 4 hours at 37°C. Absorbance at 490 nm was recorded with an Absorbance Microplate Reader (Molecular Devices, Sunnyvale, CA). Relative cell suitability was communicated as A560–A670 standardized to that of the untreated wells. Information was introduced as mean standard deviation with four-well rehashes (Dev et al. 2012).

Mechanism of Action

Curcumin nanoparticles form the reactive oxygen species which arrest the cell in cell cycle and at last induce the apoptosis of the cell as shown in figure 5 (Wang et al. 2018).

Figure 5: shows curcumin nanoparticles arrest the cell cycle and induce apoptosis (Wang et al. 2018)**.**

Anticancer Activity of Titanium oxide Nanoparticles:

The anticancer agents like Titanium (IV)-based anticancer edifices were first to be utilized as anticancer clinical preliminaries after the platinium mixes (Buettner et al. 2012).. The intercellular permeability and solvency and disintegration pace of the particles was expanded by the diminishing the molecule size to nanometric area because of this explanation the passage into the cell was improved (Judefeind et al. 2009). By quickly changing over the micro emulsion of the unpredictable oil-in-water into dry powder made out of the nanoparticles we can obtained the nanoparticles of salan–TiIV edifices Cytotoxicity of the reasonable and stable fluid scattering was estimated on colon HT-29 and ovarian OVCAR-1 malignancy.

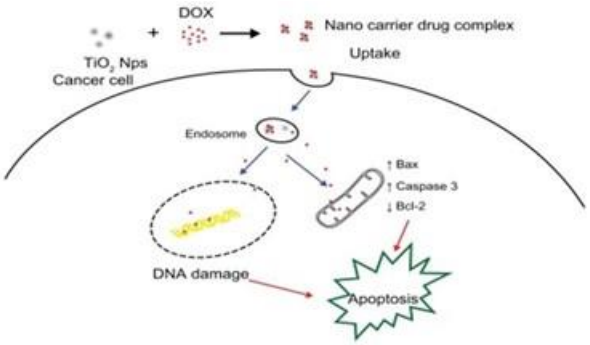

Figure 6: Shows the apoptosis induce by TiO2 nanoparticles (Ju et al. 2007).

The unstable beads that contain the complex gave a powder by quick transformation into fumes i.e: by dissipation (Margulis et al. 2010; Garrett & Workman 1999). Titanium oxide prompt apoptosis of malignant growth cell by the arrangement of responsive oxygen which finally harm the DNA and the destructive cell is taken out this ways as appeared in (Figure 6) (Ju et al. 2007).

1.8 .Anticancer activity of Gold Nanoparticles:

Likewise, efforts are made to distinguish medicinal value of the gold nanoparticle. as a result of their endeavors gold nanoparticle is recognize to possess strong antileukimec anticancer movement. Secondly to coronary illness malignant growth is the main source of death (Chen et al. 2011).Gold nanoparticles show anticancer action against the HepG-2 and A549 cells affirmed by MTT examine (Rajeshkumar, 2016).

Mechanism of action

Au nanoparticles induce autophagy in the cell by releasing the electron from the cell to form ROS which at last destroy the cell as shown in (Figure **(**Raghunandan 2011**).**).

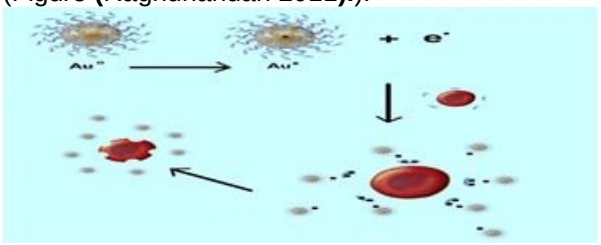

Figure 7: shows autophagy induced by gold nanoparticles by formation of ROS (Raghunandan 2011).

1.9. Aluminium Phthalocyanine Chloride Nanoemulsion for Photodynamic Therapy

In vitro cytotoxic action against Hep2, MCF7, HT29 and Vero cell line at various focuses was assessed and contrasted and the standard medication 5-fluorouracil. The in vitro screening of the AgNPs indicated likely cytotoxic movement against the human laryngeal disease (Hep-2) cell line, human bosom malignancy (MCF 7) cell line and human colon malignancy (HT 29) cell line. Less cytotoxicity of incorporated AgNPs against ordinary Vero cell line (Rajeshkumar, 2016). The nanoparticles along with their antitumour activity against different human cell lines is shown in the (Table 1)

Table 1: Shows different nanoparticles and their anticancer activity against different cells

Luteolin nanoparticle	lung cancer, head and neck cancer, prostate	Inducing cell death by apoptosis. (Monge et al.2014)
Zarconia nanoparticles	human colon cancer HCT-116 and human lung cancer A549 CELL LINES	Confirmed by MTT assay by the formation of reactive oxygen species inducing cell apoptosis. (Balaji et al.2017)
Biogenerated Silver nanoparticles	human breast cancer cell lines (SKBR3 and 8701-BC) and three human colon cancer cell lines (HT-29, HCT 116 and Caco-2)	Confirmed by MTT assay (Nakkala et al.2014)
Copper oxide nanoparticles	Against human lung carcinoma A549 cells with different concentration (50 to 500 µg/ml).	In vitro study. (Sankar et al.2013)
Circunium nanoparticles	Breast cancer cell lines MDA MB 438 and MCF-7	MTS assay. (Dev et al.2012)
Titanium oxide nanoparticles	on colon HT-29 and ovarian OVCAR-1 cancer	MTT assay. (Margulis et al.2010)
Gold nano particles	HepG-2 and A549 cells	MTT assay. Rajeshkumar, S. (2016).

CONCLUSION

Chemotherapy is too more expensive and surgical removal of cancer cell has a lot of chances of reversion. Chemotherapy has also a lot of side effects so there is a need of alternative and it is nanotechnology. the discovery of nanoparticles which has anticancer activity revolutionize the medical field and also drug delivery system to human body is improve also nanoparticle is targeted therapy and has no side effects. In this review the anticancer activity of nanoparticles like zarconia, silver, gold, luteolin, titanium, copper oxide nanoparticle are studied. These nanoparticles possess anticancer activity against much human cancer cell line like lung, head, neck, intestinal etc. The economic aspects of nanotechnology and the production of nanoparticles from different organisms like green plants and microorganism. The modification of these nanoparticles to be highly targeted, reducing their toxic effect making them suitable for the humans.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualization, S.Z.K. formal analysis, S.Z.K ,S.F and S.A.S,S.S; writing—original draft preparation, K.M,S.H,A and N.A; writing—review and editing, M.T.A and M.R., ; supervision, S.A.S., S.S and M.R.

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