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A Review on Different approaches for Cancer Treatment through Green Chemistry using Silver Nanoparticles

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Abstract: **Over the last decade, there has been a progressive growth in the field of nanoparticles on a large scale. Metal nano-particles have become advantageous these days because of their anticancer properties. These metal nano-particles are synthesized through green chemistry with the help of fruits, plants, flowers and even algae extract. The cancer treatment forms includesurgery, radiotherapy, hormonal therapy, chemotherapy, and nowadays nanotherapy. The new nano therapy provides minimumside effects as compared to other treatments and has claimed to be much beneficial. The eco-friendly nanoparticles using green chemistry enter the cancer cells and kill them,also show antibacterial and antimicrobial activity. Despite many nanoparticles used in cancer therapy, the main focus of the paper is to address silver nanoparticles preferably used nowadays and useful in the days to come.**

Index Terms: **Anticancer, Green chemistry, Metal NPs, Nanotechnology, Silver NPs.**

I. INTRODUCTION

Richard. A. Frey, Father of Nanotecnology and a Nobel Prize winner, delivered the lecture in the meeting of American Physical Society (1959) that was "There is plenty of room at the bottom ". (Ferrari, 2005). Then further, the research on the synthesis and applications of nanoparticles (NPs) is active. NPs are ranging in size 1-100 nm. Now these entities have improving the world and targeted various scientific areas including cancer (Vaid et al. 2020).

The various treatments including chemotherapy, radiations, surgery, immunotherapy, cancer vaccinations, stem cell transformation, photodynamic therapy and their connective treatments have several side effects such as toxicity, limited bioavailability, fast clearance, non-specificity (Berciaud et al.2005; Raza et al.2016; Chahal et al.2018). NPs can be synthesized using different methods, but the green chemistry is most reliable and supportable. Through this method, the synthesis of NPs does not cause any harm to the environment and human health. (Perveenand Al-Taweel, 2017). In NPs synthesis usually biological materials such as plants, fruits extracts, micro-organisms and naturally occurring polymers are used. The synthesis of NPs is done by through the metals such as gold, silver, copper. In this review preferably silver NPs is described. The Ag NPs are enter into cells and kill the cancer cells by the different pathways. These are Apoptotic, Autophagy and Necrotic pathways).

II. SYNTHESIS OF METAL NPs BY THE GREEN CHEMISTRY

Synthesis of metal NPs by the biogenic method is more beneficial than the chemical method. The biogenic synthesis are carried out in Ambient physicochemical conditions.The process is environmental-friendly, Energy efficient and there is more control on morphology. While in chemical methods byproduct is formed, there is less control on morphology, usage of harmful stabilizing agents. In green synthesis not only bacteria, fungi and yeasts are induced for the production of NPs but also the extracts of different plants and informational bio-macromolecules such as proteins, polypeptides, DNA and RNA. (Faramarzi & Sadighi, 2013).

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Table I. Silver NPs synthesized utilizing green chemistry approach exhibiting anticancer activity. (Vaid et al. 2020.)

Cancer Type	Cell Line	Biological Material	Size	Reaction Condition	Shape	Mechanism Of Action	References
Cervical Cancer	HeLa	Moringaoliefera- (Aqueous stem bark extract)	40 nm	NA/60° C	Spherical and Pentagonal shape	Increased ROS generation thus inhibiting cell replication by apoptosis induction.	Vasanth et al.(2004).
Cervical Cancer	HeLa	Ecklonia cava (Aqueous extract of marine algae)	15-30 nm	72h/37° C	Mostly Spherical	Necrotic and Apoptptic Cell Death	Venkatesan et al.(2016)
Breast Cancer	MCF-7	Cassia fistula (Aqueous fiower extract)	21-30 nm	15min/Room Temp.	Speric al	Apoptotic cell death accompanied by loss of membrane integrity	Ramya et al.(2015)
Breast Cancer	MCF-7	Padinatetrastromatica (seaweed Extract)	40-50 nm	17h/37° C	Mostly Round	Caspase-3 mediated apoptotic death through DNA damage	Selvi et al.(2018)
Lung Cancer	A549	Trichoderma harzianum fungus (Culure Supernatant)	20-30 nm	28h/28° C	Spherical	Apoptotic and Necrotic Cell Death	Guilger et al.(2017)
Lung Cancer	H1299	Dimocarpuslongan Lour.(Aqueous Peel extract)	8-22 nm	5h/18°C	Spherical	Suppression of anti-apoptotic proteins and an increase in caspase-3 dependentapoptotic pathways	He et al.(2016a)
Colon Cancer	HT29	Zingiberofficinale and Curcuma longa (Aqueous rhizome extract)	20-51 nm	30min/Room Temp	Spherical	Apoptotic cell death by ROS generation and DNA fragmentation .	Venkatadri et al.(2020)
Colon Cancer	HT29	Aspergillusniger JX556221 (Aqueous Cell-free filtrate)	20-25 nm	5h/Room Temp	Spherical	Apoptotic cell death by ROS generation and caspase-3 activation	Chengzheng et al.(2018)
Liver Cancer	Hup7	PenicilliumshrariiAJP05 fungus (Cell-free filtrate)	3-20 nm	50min/Room Temp.	Spherical	DNA damage initiated by ROS generation	Fageria et al.(2017)

Some of the medicinal plants extract and their bioactive compounds having potential to use as direct anticancer agents. The biological materials used for the synthesis act as reducing and capping agent. (Mohamadet al. 2014). The NPs exhibit their different properties and that explain the difference in their anticancer potential. In the NPs medicinal plants not only reduced the toxicity but also increased the medicinal properties.(Li et al.2008 ; Phogat et al., 2007). Nanoparticle synthesis involves two methodologies- "Top-down synthesis" and "Bottom-up synthesis"(Sepeur,2008 ;Mital et al., 2013). A

top-down synthesis approach is a catabolic that involves the production of NPs by the siz reduction. It can be done by physical and chemical methods. A bottom-up synthesis approach is an Anabolic that involves the production by building up NPs from small entities.That further happen by chemical methods and biogenical methods. (Mitalet al. 2013).

III. MECHANISM OF METAL NPs AGAINST CANCER

Due to nps the Anticancer pathways are activated. The large and small nps enter the cancer cell by the various path and proceed in endosome /lysosomal complex to generate metal ions. A. Apoptotic pathway: - The increased production of ROS (reactive oxygen species) leads to the activation of pro-apoptotic proteins. Apoptotic cell death by initiating DNA damage in the form of DNA fragmentation. B. Autophagy pathway:- The over production of ROS caused by metal ions and increased production of p53 protein induces the formation of autophaolysosomal, and conversion of LC3I to LC3I I(light chain 3 II) takes place and results in cell death. C. Necrotic pathway:- Programmed necrosis is another form of programmed cell death pathway. It is also mediated through ROS , where pre-necrotic complex influence mitochondria leading to cell death.

CONCLUSION

This review paper provides the study of various cancer treatment by using silver nanoparticles. The nanoparticles mainly play an important role in medicinal field. The apoptotic ,autophagic and necroptotic pathways are activated by the NPs causing cancer cell death. In future 3D tumourmodel studies are being explored and clinical trials are going on in medicinal field due to which treatment of cancer will become easy.

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