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Green Synthesis of Silver Nanoparticles via Various Plant Extracts for Anti-Cancer Applications

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Abstract

The development of eco-friendly and reliable techniques for synthesis of metal nanoparticles is a vital step in the area of nanotechnology. The researchers pay more attention on silver nanoparticles (Ag-NP's) because of their unique properties and applications in various fields such as medicine, catalysis, water treatment, nanoelectronics, pollution and textile field. The silver nanoparticles are synthesized by various chemical and physical methods. The major drawbacks of chemical and physical methods are the synthesis process is expensive and many toxic chemicals are used. To overcome these problems green nanotechnology comes to play very crucial role for synthesis of silver nanoparticles. Use of various plants for synthesis of biogenic silver nanoparticles referred as Green Nanotechnology.

This review emphasis on green synthesis of silver nanoparticles (Ag-NP's) using various plant extracts and its applications in cancer treatment. Generally chemotherapy, surgery and radiation treatment are the most prevalent therapeutic option for cancer. Unfortunately, these treatments have various side effects due to lack of targeted delivery and cancer specificity. To overcome these limitations of presently cancer treatments, nanoparticle could ensure targeted drug therapy having very few side effects. In this review, we focused on silver nanoparticle, synthesized from natural plant extracts, as it is cost effective, eco-friendly, stable and safe in cancer treatment.

Keywords: Green nanotechnology; Biogenic silver nanoparticles; Chemotherapy; Cancer treatment

Abbreviations: Ag NP's: Silver Nano Particles; ROS: Reactive Oxygen Species; PEG: Polyethylene Glycol; WHO: World Health Organization; DNA: Deoxyribonucleic Acid

Introduction

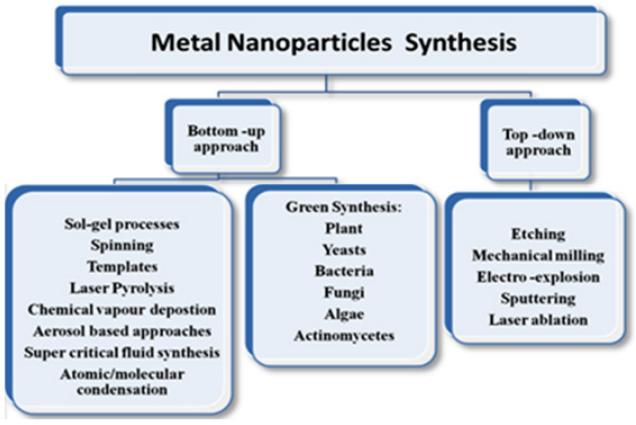

Figure 1: Different approaches of synthesis of metal nanoparticles.

Nanotechnology is the capability to examine, see and manipulate the things on atomic or molecular scale usually under 100nm. At this scale many effects are arises such as large surface to volume ratio, minimizing effects of gravity, quantum effects etc. Metal nanoparticles have fascinated researchers due to their impending applications in various fields like biomedical applications and sensitive diagnostic assays, radiotherapy enhancement, and thermal ablation, gene delivery, as non toxic carriers for gene and drug-delivery applications, optical imaging and labelling of biological systems [1-3]. These tiny particles are known as nanoparticles, which are synthesized by generally two methods top down and bottom up (Figure 1). The top down suggest the nanoparticles preparation by lithographic techniques, ball milling, etching, sputtering, etc. The most effective approach for synthesis of nanoparticles is the bottom up methods, in which nanoparticles are grown from simpler molecules and size or shape of nanoparticles can be controlled

or modulated by varying in concentration of chemicals and reaction condition (temperature, pH etc.).

The concept of green chemistry was introduced to nanoparticles synthesis strategy to decline the use toxic chemicals and eliminate the production undesirable or toxic products. The well known process for synthesis of metal nanoparticles is a chemical reduction of organic and inorganic solvents act as reducing agents viz. Sodium Borohydride, Hydrazine, Ascorbic acid, N-dimethylformaide and Poly (ethylene glycol) (PEG) [4,5] etc. Green nanotechnology or green synthesis is nothing but an organic synthesis of nanoparticles using plant extracts and the synthesized nanoparticles are then known as biogenic nanoparticles. In numerous studies huge number of medicinal plants are used to synthesize the Silver NPs [6,7] like Mulberry Leaves [8] Alternanthera dentate [9], *Ocimum sanctum* [10], *Azadirachta indica* [11], *Brassica rapa*, *Coccinia indica, Vitex negundo, Melia dubia* are used have already been used to synthesize and stabilize metallic nanoparticles, very particularly biogenic silver (Ag) nanoparticles.

Applications of green synthesized or bio reduced silver Nanoparticles (Ag-NP's) as anti-cancer therapeutics

Cancer is one of the most serious problems and health issue in this world. It has been observed that more than one out of three people will develop some form of cancer in their entire lifetime. Based on the origin, there are variety of cancer exist, such as thyroid, prostate, bladder cancer, kidney cancer, pancreatic, breast cancer, melanoma, leukemia with all types, oral cancer, colon-rectal combined cancer, etc. In cancer cells are divided into other new cells and grow hysterically, forming invasive tumours and invading nearby healthy parts of the body. Conventional cancer treatments like chemotherapy, radiotherapy or surgery will damage the cancer cells and some healthy cells in the body (Figure 2).

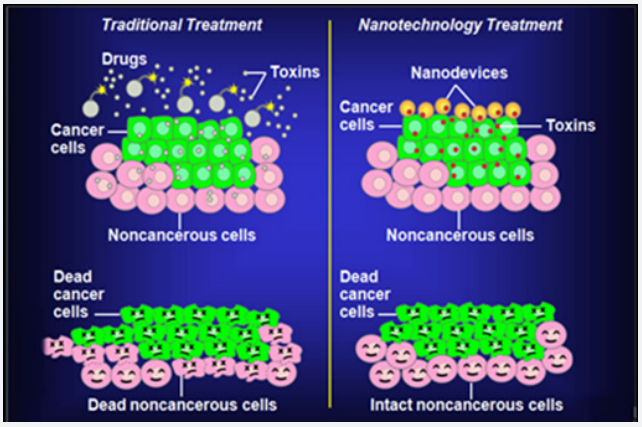

Figure 2: Comparative study of Traditional and nanotechnology cancer treatment.

Table 1: Application of plant extract used in different cell lines [13].

S. No	Plant name	Source of extract for synthesis of silver nanoparticle (SNP)	Cancer cell lines (Human)	Size of silver nanoparticle (Ag) nm	Ic50µg/ml
1	*Citrullus colosynthis*	Fruits, leaves, Seeds, roots	HCT-116, MCF-7, Hep-G2, Caco-2	Fruits-19.267, seeds-16.578, leaves-13.376, roots-7.398	(Fruits) Hep-G2 =17.2 & MCF-7= 22.4(leaves) Hep-G2=10.2, (roots) HCT-116=21.2 & Hep-G2=22.4
2	*Origanum vulgare*	leaves	A549	63-85	100
3	*Sesbania grandiflora*	leaves	MCF-7	22	20
4	*Cissus quadrangularis*	stem	Hep-2	20-56	64
5	*seaweed Ulva lactuca*	Whole microalgea	Hep-2, MCF-7, HT-29	5-30	Hep-G2=12.5, MCF-7=37 & HT-29=49
6	*Brassica oleracea*	Cauliflower florets	MCF-7	48	190.501
7	*Seaweed Gelidiella sp.*	Whole seaweed	Hep-2	31.25	40-50

These treatments are expensive and severe side effects like bone marrow problems, hair loss, nausea, emesis and fatigue [12]. To diminish or avoid these side effects, nanoparticles are used as anti-cancer therapeutics. As there are numerous methods like, chemical precipitation sol-gel process, reverse micelles technique, hydrothermal method and biological methods used to synthesize silver nanoparticles but biological methods/Green synthesis are eco-friendly, easy, cost effective and don't involve the use of any toxic and expensive chemicals. The various plants are used in synthesis of silver nanoparticles for anticancer activity against human cancer cell lining (Table 1) [13].

Sreekanth et al. [14] synthesized the silver nanoparticles from *Saccharina japonica* extract act as reducing and capping agent and their cytotoxic effect on cervical carcinoma cells was examined. They use the confocal laser scanning microscopy and Fluorescence microscopy to examine the apoptotic features such as reduction in nuclear volume and cytoplasm condensation. This study revealed that, 0.16 and 0.32mg/ml silver nanoparticles could be toxic to healthy cells. In their work, *Saccharina japonica* extract mediated silver nanoparticles showed a clear cytotoxic effect on HeLa cells and clear concentration- response relationship was also observed. The fluorescence microscopy

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study was performed to determine the cytotoxic effect of Ag-NP's. Cytotoxicity was directly related to apoptosis induction.

Jeyaraj et al. [15] reported the green synthesis of Ag-NP's from *Podophyllum hexandrum* Royal leaf extract with spherical shaped with average size of 14nm. They determine the cytotoxic effects of green synthesized Ag-NP's on human cervical carcinoma cells by quantification of ROS, RT-PCR, MTT assay, and western blotting techniques. Their study suggested that because of DNA damage, green synthesized Ag-NP's can inhibit the cellular mechanism of HeLa. In this study, apoptosis was noticed with the morphological changes in the cell shape and chromatin condensation. The ability of green synthesized silver nanoparticles to induce apoptosis was examined by using acridine orange and ethidium bromide staining. The stained cells in this study were examined to early apoptotic, nonviable cells, late apoptotic cells and viable cells. By comparing the positive control cisplatin the green synthesized silver nanoaprticles shows the greater apoptotic effect.

Furthermore, the effects green synthesized silver nanoparticles against HeLa cells gross nuclear morphology was observed under fluorescence microscopy after Hoechst 33258 staining. After the treatment with 20mg/ml Ag-NP's for 24hours, HeLa cells shows the apoptotic characteristics like cell shrinkage, nuclear condensation, and fragmentation [15]. Rosarin et al. [16] studied the Anti-proliferative effect of amla extract mediated silver nanoparticles against Hep2 cell lining. They synthesize the spherical and cubic PE-AgNP's with an average size of 188nm. This study indicates that, Ag-NPs are capped with biomoecules of amla with enhanced cytotoxicity laryngeal cancer cells through oxidative stress and apoptotic function on Hep2 cancer cells.

Future prospective

The plant extract mediated synthesis of silver nanoparticles is an essential aspect of nanotechnology and the applications of nanoparticles in various sectors. Green synthesis of metal nanoparticles are not time consuming compared to other biological process. According to world health organization (WHO) the second leading cause of death in the world is cancer. As cancer is abnormal tissue growth, cell divisions occur rapidly in an autonomous fashion.

Conclusion

Biological synthesis of silver nanoparticles in nano-biotechnology area has increased its importance to create eco-friendly; cost effective, stable nanoparticles and their applications in medicines, agriculture and electronics are wider. From variety research on nanotechnology for synthesis of silver nanoparticles it is found that it is safer and better by using natural plants. With the huge plant diversity much more plants are still not explored for the synthesis of nanoparticles and its applications in pharmaceutical and agricultural industries. Fluorescence and confocal study have confirmed apoptosis induction in the tumour cells. Additionally, ROS was increased in the cancer cells, which further confirm the anticancer activity of Ag-NP's. Taking all these data together, it is concluded that green synthesized Ag-NP's might be a potential candidate for the prevention and treatment of cancer.

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