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Green Synthesis of Nanomaterials and Their Utilization as Potential Vehicles for Targeted Cancer Drug Delivery

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Abstract A nanoparticle (NP) is a microscopic particle with a length of two or three dimensions greater than 0.001 micrometer (1 nanometer $=10^{-9}$ metre). NPs may be classified into different classes based on their specific properties, shapes or sizes, and high surface area-to-volume ratio. Nanoparticles have a remarkable capacity as 'magic bullets' stacked with herbicides, fungicides, supplements, fertilizers or nucleic acids, specializing in expressing plant tissues to deliver their charge to the appropriate piece of the plant to perform desired outcomes. The smart design and synthesis of a library of nanomaterials, exact control over their physicochemical properties and simplicity of their surface functionalization to assemble explicitness is to be certain fundamental for the achievement of disease treatment and harmfulness in the biological systems. Green techniques for nanomaterial synthesis observe natural organic systems to nanomaterial production. Green synthesized nanomaterials are at present powerful and significant tools for protecting the drug from the dangerous surroundings in addition to overcoming the organic obstacles to access of the drug in targeted tissues and dealing with drug resistance. NPs were extensively utilized in numerous biomedical applications, site-specific drug delivery systems and cellular uptake because of their inert nature, stability, high dispersity, non-cytotoxicity, and biocompatibility. Nanoparticles may be programmed for recognizing the cancerous cells and giving selective and correct drug delivery avoiding interaction with the healthy cells. However, usage of those NPs is restrained through factors like lack of stability in adversarial environment, concerns regarding bioaccumulation and toxicity, need of relatively trained employees for device assembly and operation, and problems with reproducibility and affordability.

Keywords Anticancer Activity, Drug Delivery, Green Synthesis, Nanomedicine, Nanoparticles

1. Introduction

The term “nanotechnology” was coined by Taniguchi in 1974, but its conceptual establishment was set down by the Nobelist Richard Feynman in his well-known lecture “There’s plenty of room at the Bottom” on Dec 29, 1959. NPs are often characterised by their dimensionality, morphology, composition, uniformity, and agglomeration [1], since they can be spherical, tubular, irregularly shaped, and may also exist in fused, aggregated, or agglomerated forms [2]. Dimensionality refers to their shape or morphology, based on which they can be classified as zero-dimensional (0D), one-dimensional (1D), two-dimensional (2D), or three dimensional (3D) NPs [3]. The significance of these materials was acknowledged when analysts found that size can impact the physiochemical properties of a substance e.g. its optical properties. A 20nm gold (Au), platinum (Pt), silver (Ag), or palladium (Pd) NP has characteristic red, yellowish gray, black or dark black color, respectively.

The utilization of existing chemotherapeutic drugs is currently limited by factors like poor specificity, expensiveness, high toxicity, various incidental effects, and rise of drug resistance. Notwithstanding the movement of early finding and treatment, it is imperative to discover alternative therapies, tools and drugs to conquer the present circumstance.

In recent times, biosynthesis of NPs is recognized as a viable and facile alternative methodology, mainly due to its green chemistry principles. The significance of taking advantage of NPs as potent drug delivery systems (DDS; for the counteraction and treatment of various infections) is living of their advanced bio-availability, managed and sustained drug release, excessive drug loading capacity, extended circulation time, more suitable intracellular penetration and targeted delivery to precise sites or organs, protection of the active factor towards physiological pH, enzymes, and moisture, and usage of different strategies of administration, like oral, nasal, intraocular and parenteral [4]. Nano drug particles and development of nano formulations for drug delivery have been seriously contemplated, particularly their production, stability, characterization, formulation, delivery, and biological fate.

Nanomedicine is the branch of medicine that uses the study of nanotechnology in the prevention and fix of different illnesses utilizing nanoscale materials, like biocompatible NPs, for different applications including diagnosis, drug delivery, sensory, and actuation purposes in a living being [5-9]. Drugs with extremely low solubility have diverse biopharmaceutical delivery problems for example, restricted bio accessibility after intake via mouth, reduced diffusion capability into the outer membrane, requirement of better amount of intravenous intake, and undesirable eventual outcomes, subsequent to traditionally formulated vaccination process. In any case, these types of obstacles may be overcome through using nanotechnology techniques in the drug delivery mechanism [10]. The designed DDSs are either assigned to a particular region or are expected for the controlled arrival of restorative specialists at a specific site. Their development incorporates self-assembly, where in well-defined structures or patterns are spontaneously formed from rudimentary building blocks [11].

The eco-friendly strategies of synthesis of NPs contain using plants, biological, or microbial agents as decreasing and capping agents. However, the knowledge about NPs is currently insufficient, and many challenges remain in the field of nanotoxicity assessment, resulting in a deficiency in effective regulation regarding usage of NPs.

Green synthesis of NPs using extracts of plant is regarded as an advancement due to issues with conventional methods, like NP yield, stability, ion reduction mechanism, and as a consequence, their environmental friendliness [12]. Plant extracts might act both as reducing agents and stabilizing agents during the synthesis of NPs. The source of the plant extract is known to influence the characteristics of the NPs. The main aim of green synthesis is to minimize the use of toxic chemicals to prevent the environment from pollution, thus, enhancing its popularity. The negative aspects of this technique are unpredictable shape, size, crystal growth, possible endotoxins, stability, aggregation, and time-consuming purification processes.

Stable NPs can be prepared using chemical methods as well, but they are hardly conducive to biomedical applications, especially as DDSs. Also, they lead to concerns in regards to, drug action, biosafety and medical application. In this manner, it is vital to expand appropriate strategies for the synthesis of NPs from organic systems that are convenient and adaptable.

A potential utilization of these green NPs is targeted drug delivery, which is better than conventional drug therapy, because it focuses on the vitally influenced region and conveys the drug locally, in this manner, limiting the incidental effects caused by conventional drugs [13]. The essential objective of developing anticancer agents is shortening the different incidental effects caused by conventional drugs and to improve the selectivity and efficiency of the drug [14]. Many recent studies have focused on synthesizing potent systems for targeted drug delivery, like NPs, quantum dots, polymer gels, Fe_3O_4, and ZnO [15].

The noble metal NPs, like Ag, Au, and Pt, show potential in the medical field, for diverse purposes such as use as a sensor and for biomedical imaging [16,17]. An overview of the therapeutic utilization of green synthesized NPs is presented here.

2. Silver Nanoparticles (AgNPs)

Potential applications of AgNPs in biomedicine incorporate imaging applications and chemical sensing. AgNPs are synthesized utilizing different techniques, such as chemical, electrochemical, photochemical, laser ablation, and other techniques [18]. Despite the fact that bulk Ag is thought of "safe," AgNPs should be analyzed for environmental impact and biocompatibility in case they are to be produced for in vivo usage on a large scale [19-21].

Nanomedicine has made a present day horizon withinside the future improvement of anticancer procedures. Conventional malignancy treatment like radiotherapy, medical procedure, or chemotherapy, has its limits due to drug toxicity, drug resistance problems, unpredictable aspect outcomes, and lack of specificity. AgNPs conquer those conquer via way of means of decreasing aspect outcomes and enhancing the productiveness of disease treatment. One in their unique additives is the capability to move distinctive biological limitations and to offer targeted delivery of medications. [22].

2.1. Anticancer Activity of Biologically Synthesized AgNPs

The anticancer actions of biologically synthesized AgNPs were concentrated on utilizing both in vitro and in vivo models. A few examinations have exposed that with increasing concentration of AgNPs, the viability of most cancers cells decreases [23,24].

The concentration of AgNPs and effect of time on inhibition of cell viability and membrane leakage have been assessed utilizing an assorted methodology [25,26]. Usually, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) measure, evaluation of reactive oxygen species (ROS), reverse transcription polymerase chain reaction (RT-PCR), and western blotting techniques are utilized for evaluation of the ability of AgNPs to inhibit cell development and mediate cell death [25-28]. In vitro cytotoxic activity in a dose-dependent manner was assessted for green synthesized AgNPs from various plants, namely *Vitex negundro, Acalypha indica, Euphorbia nivulia,* and *Premna serratifolia*. MCF-7(human breast adenocarcinoma) cell lines were treated with AgNPs acquired by the usage of *Erythrina indica* and *Andrographis echioides* extracts. In the two cases, the development of cancer cells was repressed after AgNPs concentration-response relationship [24]. Comparative outcomes were found in different investigations. AgNPs obtained utilizing *Ganoderma neo-japonicum* Imazeki and *Artemisia marshalliana* Sprengel extracts exhibited cytotoxic potential against human gastric (AGS) and breast cancer (MDA-MB-231) cell lines, respectively [26,28]. Anticancer activity of AgNPs relies upon factors, for example, the source of synthesis of NPs and the type of cell lines targeted [29].

The cytotoxicity of AgNPs, arranged using *Sargassum vulgare*, towards disease cells was evaluated by checking out their effect against human myeloblastic leukemia (HL60) and HeLa cells in contrast to normal peripheral blood mononuclear cells (PBMC). HL60cells were impacted by AgNP-intervened toxicity while the normal PBMC experienced less harm [25]. In a further report, AgNPs created through green science approach by means of *Cleome viscosa* plant extracts was in vitro considered in contrast to human malignancy cell lines A549 (Human lung adenocarcinoma) and PA1(Ovarian teratocarcinoma cell line). The outcomes inferred that green integrated AgNPs could hinder malignancy cell development and give incredible potential in the therapy of disease [27].

Another modern technique is the preparation of AgNPs in aqueous media utilizing emitted light as the catalyst. This technique is impartial of NP seeds or dangerous reactants. The prepared nanocomposite exhibited excessive antimicrobial activity towards the examined bacterial strains [30]. Different plants that have been used for green synthesis of AgNPs as antimicrobials are *Centella asiatica*, *Citrus sinensis*, *Phlomis bracteosa*, *Solanum tricobatum*, and *Syzygium cumini* extracts. These safe AgNPs confirmed greater bactericidal activity [31]. The photosynthesized AgNPs displayed remarkable antibacterial activities towards the examined pathogenic bacteria, *Acinetobacter baumannii*, *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* [32]. AgNPs synthesized utilizing long a peel powder additionally exhibitedantitumor ability in lung cancer chemoprevention and chemotherapy, particularly for early-stage intervention [33].

2.2. AgNPs for Targeted Drug Delivery

AgNPs deal with an opportunity healing method as DDSs in relieving cancer due to the fact those can deliver inactive or dynamic focusing to cancer tissue. Aggregation of medications at favored sites will increase the adequacy of anticancer treatment in vivo. Receptor-mediated endocytosis can facilitate cellular uptake of medications. This type of dynamic focusing on depends on sub-atomic acknowledgment. The proposed approach for improving the properties of biogenic AgNPs is surface functionalization with particular targeting molecules or coating with biocompatible and biodegradable polymers [34,35]. For instance, AgNPs obtained with the aid of using usage of various convergences seed extract of *Setaria verticillata* have been loaded with hydrophilic anticancer medications daunorubicin (DNR) and doxorubicin (DOX). The crucial loading (80.50%) and capacity (40.25%) effectiveness of DNR-AgNPs and DOX-AgNPs introduced them as future novel DDSs [23].

3. Gold Nanoparticles (AuNPs)

Au is a well-known biocompatible metal, and in ancient times, colloidal Au was used as a drinkable sol that exerted curative properties for several diseases [36]. Because of low cytotoxicity, AuNPs have been widely used in the field of drug delivery [37].

The shape and size of AuNPs confer unique electric and magnetic properties. Hence, there is a huge impetus in research on AuNPs, particularly in the field of biological tagging, DNA labelling, chemical and biological sensing, microscopy, optoelectronics, biomedical imaging, and photoacoutisc imaging, surface-enhanced Raman spectroscopy, photo thermal therapy, catalysis, tracking and drug delivery, and cancer therapy [38-42].

3.1. Anticancer Activity of Biologically Synthesized AuNPs

Green synthesis of AuNPs using plant extracts has been reported for numerous biological applications such as antibacterial, antioxidan, antiparasitic, and anticancer activities [43-48]. For example, Malathi et al. [49] depicted the green synthesis of AuNPs for drug delivery depending on chitosan as a reducing/capping agent. They applied single oil-in-water (O/W) emulsions for biocompatible controlled release of rifampicin withinside the body. Curcumin and emu oil were given from emu birds (*Dromaius novaehollandiae*) have proven remarkable results towards inflammation. However, the delivery of curcumin remains a challenge due to poor solubility and low transmission. Nanoemulsions have been synthesized making use of emu oil, Kolliphor (previously called Cremophor), and Labrafil because the oil phase, surfactant, and co-surfactant, respectively [50].

3.2 AuNPs for Targeted Drug Delivery

AuNPs can be used for bio-imaging the affected cancerous cells [51]. These have acquired lot of consideration lately as potential agents for drug delivery in cancer therapy, because of their remarkable chemical and physical properties, like strong binding attraction for thiols, proteins, carboxylic acid, a tamers, and disulfides [15,52,53].

AuNPs follow three main pathways for cellular uptakes, namely, fluid phase endocytosis, receptor mediated endocytosis, and phagocytosis [54]. The toxicity of AuNPs, like other NPs, depends on the shape, size, surface charge, synthesis method, surface coating, and functionalized molecules [55]. Drug release and transport are the two most important factors for an efficient DDS. The process includes loading of the prodrugs on nanocarriers through non-covalent interactions or by covalent conjugation, which are thustly used into a functioning structure by the cell. AuNPs give functional flexibility by forming monolayers, subsequently, proving to be efficient DDSs [56].

4. Platinum Nanoparticles (PtNPs)

PtNPs have prompted another upheaval in the area of nanotechnology, with applications in the automotive sector, chemical industry, and biomedical applications. They are additionally utilized in various biomedical fields like diagnostics utilizing various specialists for imaging, clinical inserts, drug conveyance specialists, and photothermal treatment [57-59].

Pt compounds, for example, cisplatin, oxaliplatin, and carboplatin, are frequently utilized in chemotherapy, particularly in the treatment of ovarian and testicular tumours [60]. Regardless of that, they exert many side effects, similar to vomiting, nausea, ototoxicity, aloepecia, nephrotoxicity, neurotoxicity, and hematuria. Despite the fact that Pt compounds have been utilized for the treatment of coronary artery disease, and in neuro modulation devices and catheters [61], they are not specific for cancer because they influence both the normal cells and cancer cells, prompting numerous complications. In a study, toxicity of PtNPs towards healthy and cancer cells was examined, in order to ascertain if the effect was similar to that of the Pt complexes, for example, cisplatin and carboplatin, utilized in the treatment of cancer. An aggregate of PtNPs with ion irradiation has been determined to decorate the efficiency of cancer therapy [62].

4.1. Anticancer Activity of Biologically Synthesized PtNPs

Biological synthesis or bio molecule-assisted synthesis is commonly utilized for the production of PtNPs, however it is restricted in contrast with the blend of Ag, Au, and other metal NPs. In any case, biosynthesized NPs assume an exceptionally imperative part in sub-atomic associations, and can cross biological barriers without troubling typical cells. Sahin et al. [63] revealed that biosynthesized PtNPs exhibited efficient antitumor movement towards the MCF7 cell line through actuating apoptosis via G0/G1 cell cycle capture. Hence, Ghosh et al. [64] assessed the synergistic effect of anticancer movement making use of consolidated metallic NPs. The anticancer movement of consolidated PtNPs-PdNPs complex confirmed a 74.25% refinement more than individual metallic PtNPs (12%) or PdNPs (33%). Likewise, beginning phase of apoptosis development became visible in HeLa cells. In vitro research have exhibited that PtNPs repressed the development of A549 cells in a portion subordinate way, and in vivo records confirmed that PtNPs at mid and excessive dosages appropriately limited and deferred the improvement of cellular breakdown withinside the lungs in mice with critical consolidated immunodeficiency (SCID) [65].

4.2. PtNPs for Targeted Drug Delivery

Cisplatin and PtNPs have demonstrated antitumor action against different sorts of malignant growth cells. In spite of the fact that they involve dose-dependent toxicity and characteristic or gained drug obstruction, Pt compound-based drugs have prepared for malignant growth therapy, and practically half of disease patients use Pt drugs for chemotherapeutic treatment [66]. The Pt derivative drugs, i.e., cisplatin, carboplatin, and oxaliplatin, are square planar Pt (II) complexes surrounded by ligands. The two amine ligands on the left half of the complex, called as the non-leaving group, display solid association with the Pt particle. The other two chloride ligands on the right side interface with the Pt molecule and structure bonds with the DNA bases moreover [67].

Normal natural techniques for synthesis of NPs utilize a few organisms like microorganisms, actinomycetes, algae, and fungi. In spite of the fact that microorganisms are taken advantage of for the synthesis of PtNPs, controversy actually exists with respect to the utilization of microorganisms due to the fact the manufacturing time of those NPs is higher, because of the time had to grow to be bacterial/fungal cultures and for bacterial cell maintenance.

In this manner, scientists are keen on taking advantage of plant extracts, which are promptly accessible, abundant, and in most cases, don't need any costly media to develop. Plant-based synthesis of NPs has numerous benefits over different kinds of organic techniques. In a study, tea polyphenol from *Camellia sinensis* turned into applied for manufacture of PtNPs, wherein it acted because the lowering and settling specialist. PtNPs obtained from tea polyphenol confirmed a flower-shaped morphology with sizes going from 30 to 60 nm. The inhibition of cell multiplication was moreover assessed, and it turned into observed to incite apoptosis of cervical malignant growth cells [68]. As of late, round PtNPs of size 5-one hundred fifty nm have been synthesized using the coral vine *Antigonon leptopus* separate, which acted as a stabilizing and reducing agent. The conversion and formation of PtNPs turned into avowed via way of means of brief color changes at a raised temperature of 95°C, which tended to the improvement of PtNPs [69]. PtNPs had been integrated the use extract of leaf from *Barleria prionitis*. The color convert from light brown to darkish brown at 100°C confirmed the development of PtNPs, and the synthesis turned into asserted via way of means of UV–Vis spectral investigation. Mono scattered NPs of size 1-2 nm were distinguished, and the FTIR spectra showed a few practical gathering constituents of the *B. Prionitis* leaf, which assume a significant role in the decrease and stabilization of NPs.

5. Advantages of Nanoparticles for Targeted Cancer Drug Delivery

Nanoscience and technology has consistently made progress over the previous decade because of its application in different fields like tumor targeting, combination therapy, controlled release, biomedical and health sector, long circulation, reduced toxicity, food and feed industry, drug-gene delivery system, chemical industry, electronic industry, space research, optical devices, environmental remediation, concurrent live imaging and many more such uses. The principle benefits of those nanoparticles are related with their surface properties; as diverse proteins may be joined to the surface. Good examples are the therapeutic use of nanotechnology for ellagic acid, berberine, curcumin, quercetin, and resveratrol. The adequacy of those natural products has particularly worked on the use of nanocarriers formed with silver, gold, cadmium sulphide, and titanium dioxide polymeric nanoparticles together with crystal nanoparticles, liposomes, solid lipid nanoparticles, superparamagnetic iron oxide nanoparticles, micelles, and dendrimers [70]. The epigenetic outcomes which include DNA methylation and histone modifications mediated via the alteration in microRNA expression that is stimulated with the aid of using nanoparticles [71].

6. Conclusions

NPs have exhibited themselves to be acceptable possibility for designated drug delivery. They are generally accessible, successfully functionalized, biocompatible, and stable. The low cost of cultivation, short production time, safety, and the capacity to upturn production volumes makes plants an appealing platform for nanoparticle synthesis. Various NP characteristics need to be controlled and taken into consideration for successful drug delivery to the preferred sites, without side effects. If the size, geometry, or surface charge isn't ideal, then critical aspect outcomes can arise. Environmental variations can also impact NP drug delivery efficacy. Most common nanoparticle synthesis techniques often make use of harsh chemical substances which include dimethylformamide, hydrazine, and sodium borohydride and excessive temperatures which may also pose organic risks to the environment. Lately, Ag, Au and Pt-primarily based totally nanomaterials have attracted interest in each scholastic and present day fields due to the fact to their incredible provisions and capacity as nanocarriers, nanozymes, and nanosensors for diagnostic purposes. In any case, earlier than NPs may be deployed clinically, they should go rigorous in vitro and in vivo testing to make sure that they do now no longer reason damage to any dwelling tissue or animals.

Conflicts of Interest

Authors declare that they have no conflict of interest.

REFERENCES

[1] C. Buzea, I. I. Pacheco, and K. Robbie, "Nanomaterials and nanoparticles: sources and toxicity."Biointerphases,2007, vol. 2, no. 4, pp. MR17–MR71, Doi: 10.1116/1.2815690

[2] B. Nowack, and T. D. Bucheli, "Occurrence, behavior and effects of nanoparticles in the environment," Environmental Pollution, 2007, vol. 150, no. 1, pp. 5–22, Doi: 10.1016/j.envpol.2007.06.006

[3] J. N. Tiwari, R. N. Tiwari, and K. S. Kim, "Zero-dimensional, one-dimensional, two-dimensional and three-dimensional nano structured materials for advanced electrochemical energy devices," Prog Mater Sci,2012, vol. 57, pp. 724–803, Doi: 10.1016/j.pmatsci.2011.08.003

[4] Khosa, S. Reddi, and R. N. Saha, "Nanostructured Lipid Carriers for Site-Specific Drug Delivery," Biomed Pharmacotherapy, 2018, vol. 103, pp. 598−613, Doi: 10.1016/j.biopha.2018.04.055

[5] K. McNamara, and S. A. Tofail, "Nanosystems: the use of nanoalloys, metallic, bimetallic, and magnetic nanoparticles in biomedical applications," Phys Chem Chem Phys, 2015, vol. 17, pp. 27981–95. Doi: 10.1039/C5CP00831J

[6] Jr. O. N. Oliveira, R. M. Iost, Jr. J. R. Siqueira, F. N. Crespilho, andL. Caseli, "Nanomaterials for diagnosis: challenges and applications in smart devices based on molecular recognition," ACS Appl Mater Interfaces, 2014, vol. 6, pp. 14745–66. Doi: 10.1021/am5015056

[7] V. P. Vasquez, N. S. Mosier, and J. Irudayaraj, "Nanoscale Drug Delivery Systems: From Medicine to Agriculture," Front Bioeng Biotechnol, 2020, vol. 79, pp. 1-16. Doi: 10.3389/fbioe.2020.00079

[8] M. Holzinger, A. Le Goff, and S. Cosnier, "Nanomaterials for biosensing applications: a review," Front Chem, 2014, vol. 2, pp. 63. Doi: 10.3389/fchem.2014.00063

[9] Y. I. Golovin, S. L. Gribanovsky, D. Y. Golovin, N. L. Klyachko, A. G. Majouga, A. M. Master, M Sokolsky, and A. V. Kabanov, "Towards nanomedicines of the future: remote magneto-mechanical actuation of nanomedicines by alternating magnetic fields," J Control Release, 2015, vol. 219, pp. 43–60. Doi: 10.1016/j.jconrel.2015.09.038

[10] Z. Mirza, and F. A. Siddiqui, "Nanomedicine and drug delivery: a mini review," Int Nano Lett, 2014, vol. 4, pp. 94. Doi: 10.1007/s40089-014-0094-7

[11] H. Lu, J. Wang, T, Wang, J, Zhong, Y. Bao, and H. Hao, "Recent progress on nanostructures for drug delivery applications," J Nanomater, 2016, vol. 20. Doi: 10.1155/2016/5762431

[12] J. Singh, T. Dutta, K. H. Kim, M. Rawat, P. Samddar, and P. Kumar, "Green' synthesis of metals and their oxide nanoparticles: applications for environmental remediation," J Nanobiotechnology, 2018, vol. 16, pp. 84. Doi: 10.1186/s12951-018-0408

[13] T. S. Rezende, G. R. S. Andrade, L. S. Barreto, N. B. Costa Jr, I. F. Gimenez, and L. E. Almeida, "Facile preparation of catalytically active gold nanoparticles on a thiolated chitosan," Mater Lett, 2010, vol. 64, pp. 882-884. Doi: 10.1016/j.matlet.2010.01.051

[14] K. S. Chen, T. S. Hung, H. M. Wu, J. Y. Wu, M. T. Lin, and C. K. Feng, "Preparation of thermosensitive gold nanoparticles by plasma pretreatment and UV grafted polymerization," Thin Solid Films, 2010,vol. 518, pp. 7557-7562. Doi: 10.1016/j.tsf.2010.05.043

[15] K. Lee, H. Lee, K. H. Bae, and T. G. Park, "Heparin immobilized gold nanoparticles for targeted detection and apoptotic death of metastatic cancer cells," Biomater, 2010, vol. 31, pp. 6530-6536. Doi: 10.1016/j.biomaterials.2010.0 4.046

[16] J. Zhang, F. Cheng, J. Lib, J. Zhub, and Y. Lu, "Fluorescent nanoprobes for sensing and imaging of metal ions: recent advances and future perspectives," Nano today, 2016, vol. 11, pp.309-329. Doi: 10.1016/j. nantod.2016.05.010.

[17] J. Zhang, F. Cheng, T. Zheng, and J. Zhu, "Versatile aptasensor for electrochemical quantification of cell surface glycan and nakedeye tracking glycolytic inhibition in living cells," Biosens Bioelectron, 2017, vol. 89, pp. 937–945. Doi: 10.1016/j.bios.2016.09.087

[18] L. Rizzello, and P. P. Pompa, "Nanosilver-based antibacterial drugs and devices: mechanisms, methodological drawbacks, and guidelines," Chemical Society Reviews, 2014, vol. 43, no. 5, pp. 1501–1518. Doi: 10.1039/C3CS60218D

[19] G. Fernando, and M. W. Chris, "The relative importance of water hardness and chloride levels in modifying the acute toxicity of silver to rainbow trout (Oncorhynchus mykiss),"Environmental Toxicology and Chemistry, 1997, vol. 16, no. 11, pp. 2363–2368. Doi: 10.1002/etc.5620161123

[20] C. Hogstrand, F. Galvez, and C. M. Wood, "Toxicity, silver accumulation and metallothionein induction in freshwater rainbow trout during exposure to different silver salts," Environmental Toxicology and Chemistry, 1996, vol. 5, no. 7, pp.1102–1108. Doi: 10.1002/etc.5620150713

[21] P. A. Wagner, W. G. Hoekstra, and H. E. Ganther, "Alleviation of silver toxicity by selenite in the rat in relation to tissue glutathione peroxidise," Proceedings of the Society for Experimental Biology and Medicine, 1975, vol. 148, no.4, pp. 1106–1110. Doi: 10.3181/00379727-148-38697

[22] Kajani, S. Zarkesh-Esfahani, S. Hamid, A. K. Bordbar, A. Khosropour, A. Razmjou, and M. Kardi, "Anticancer effects of silver nanoparticles encapsulated by *Taxus baccata* extracts," Journal of Molecular Liquids,2016, vol. 223, pp.549-556. Doi: 10.1016/j.molliq.2016.08.064

[23] M. Naz, N. Nasiri, M. Ikram, M. Nafees, M. Z. Qureshi, S. Ali, and A. Tricoli, "Eco-friendly biosynthesis, anticancer drug loading and cytotoxic effect of capped Ag-nanoparticles against breast cancer," Applied Nanoscience, 2017, vol. 7, pp.793-802. Doi: 10.1007/s13204-017-0615-6

[24] P. V. Rao, D. Nallappan, K. Madhavi, S. Rahman, L. J. Wei, and S. H. Gan, "Phytochemical and biogenic metallic nanoparticles as anticancer agents," Oxidative Medicine and Cellular Longevity, 2016, 3685671. Doi: 10.1155/2016/3685671

[25] K. Govindaraju, K. Krishnamoorthy, S. Alsagaby, G. Singaravelu, and M. Premanathan, "Green synthesis of silver nanoparticles for selective toxicity towards cancer cells," IET Nanobiotechnology, 2015, vol. 9, no.6, pp.325-330. Doi: 10.1049/iet-nbt.2015.0001

[26] S. Gurunathan, J, Raman, S. N. Abd Malek, P. A. John, and S. Vikineswary, "Green synthesis of silver nanoparticles using Ganoderma neo-japonicum Imazeki: A potential cytotoxic agent against breast cancer cells," International Journal of Nanomedicine, 2013, vol. 8, pp.4399-4413. Doi: 10.2147/IJN.S51881

[27] G. Lakshmanan, A. Sathiyaseelan, P. T. Kalaichelvan, and K. Murugesan, "Plant-mediated synthesis of silver nanoparticles using fruit extract of *Cleome viscosa* L.: Assessment of their antibacterial and anticancer activity," Karbala International Journal of Modern Science, 2018, vol. 4, pp.61-68. Doi: 10.1016/j.kijoms.2017.10.007

[28] S. Salehi, A. S. Shandiz, F. Ghanbar, M. R. Darvish, M. Ardestani, A. Mirzaie, and M. Jafari, "Phytosynthesis of silver nanoparticles using *Artemisia marschalliana* sprengel aerial part extract and assessment of their antioxidant, anticancer, and antibacterial properties," International Journal of Nanomedicine, 2011, vol. 61, pp.1835-1846. Doi: 10.2147/IJN.S99882

[29] J. Singh, T. Singh, and M. Rawat, "Green synthesis of silver nanoparticles via various plant extracts for anti-cancer applications," GJN, 2017, vol. 2, no. 3. Doi:

1019081/GJN.2017.02.555590

[30] R. Banasiuk, J. E. Frackowiak, M. Krychowiak, M. Matuszewska, A. Kawiak, M. Ziabka, Z. Lendzion- Bielun, M. Narajczyk, and A. Krolicka, "Synthesis of antimicrobial silver nanoparticles through a photomediated reaction in an aqueous environment," Int J Nanomedicine, 2016, vol. 11, pp. 315–324. Doi: 10.2147/IJN.S93611

[31] S. Anjum, and B. H. Abbasi, "Biomimetic synthesis of antimicrobial silver nanoparticles using in vitro-propagated plantlets of a medicinally important endangered species: *Phlomis bracteosa*," Int J Nanomedicine, 2016, vol. 11, pp.1663–1675. Doi: 10.2147/IJN.S105532

[32] S. Salehi, S. A. S. Shandiz, F. Ghanbar, M. R. Darvish, M. S. Ardestani, A. Mirzaie, and M. Jafari, "Phytosynthesis of silver nanoparticles using *Artemisia marschalliana* Sprengel aerial part extract and assessment of their antioxidant, anticancer, and antibacterial properties," Int J Nanomedicine, 2016, vol. 11, pp.1835–1846. Doi: 10.2147/IJN.S99882

[33] Y. He, Z. Du, S. Ma, Y. Liu, D. Li, H. Huang, S. Jiang, S. Cheng, W. Wu, K. Zhang, and X. Zheng, "Effects of green-synthesized silver nanoparticles on lung cancer cells in vitro and grown as xenograft tumors in vivo," Int J Nanomedicine, 2016, vol. 11, pp. 1879–1887. Doi: 10.2147/IJN.S103695

[34] M. D. Blanco, C. Teijon, R. M. Olmo, J. M. Teijon, "Targeted nanoparticles for cancer therapy. In: Sezer AD, editor. Recent Advances in Novel Drug Carrier Systems," Rijeka: InTech, 2012, pp. 241-248. Doi: 10.5772/51382

[35] M. Jeyaraj, M. Rajesh, R. Arun, D. MubarakAli, G. Sathishkumar, G. Sivanandhan, G. K. Dev, M. Manickavasagam, K. Premkumar, N. Thajuddin, and A. Ganapathi, "An investigation on the cytotoxicity and caspase-mediated apoptotic effect of biologically synthesized silver nanoparticles using *Podophyllum hexandrum* on human cervical carcinoma cells," Colloids and Surfaces B Biointerfaces, 2013, vol. 102, pp.708-717. Doi: 10.1016/j.colsurfb.2012.09.042

[36] M. C. Daniel, and D. Astruc, "Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology," Chem Rev, 2004, vol 104, pp.293–346. Doi: 10.1021/cr030698

[37] G. F. Paciotti, L. Myer, D. Weinreich, D. Goia, N. Pavel, R. E. McLaughlin, and L. Tamarkin, "Colloidal gold: a novel nanoparticle vector for tumor directed drug delivery," Drug Deliv, 2004, vol. 11, no. 3, pp.169–83. Doi: 10.1080/10717540490433895

[38] F. K. Alanazi, A. A. Radwan, and I. A. Alsarra, "Biopharmaceutical applications of nanogold," Saudi Pharm J, 2010, vol. 18, pp.179-193. Doi: 10.1016/j.jsps.2010.07.002

[39] B. De Berardis, M. Marchetti, A. Risuglia, F. Ietto, C. Fanizza, and F.Superti, "Exposure to airborne gold nanoparticles: a review of current toxicological data on the respiratory tract," J Nanopart Res, 2020, vol.22, pp.235. Doi: 10.1007/s11051-020-04966-9

[40] D. Kim, and S. Jon, "Gold nanoparticles in image-guided cancer therapy," Inorgan Chim Acta, 2012, vol.393, pp.154-164. Doi: 10.1016/j.ica.2012.07.001

[41] S. Tedesco, H. Doyle, J. Blasco, G. Redmond, and D. Sheehan, "Oxidative stress and toxicity of gold nanoparticles in *Mytilus edulis*," Aquatic Toxicol, 2010, vol.100, pp.178-186. Doi: 10.1016/j.aquatox.2010.03.001

[42] Mishra, S. K. Tripathy, and S. I. Yun, "Fungus mediated synthesis of gold nanoparticles and their conjugation with genomic DNA isolated from *Escherichia coli* and *Staphylococcus aureus*," Process Biochem, 2012, vol.47, pp.701-711. Doi: 10.1016/j.procbio.2012.01.017

[43] M. R. Rad, H. Kazemian, F. Yazdani, M. R. Z. Monfared, H. Rahdar, A. Javadi, and M. Kodori, "Antibacterial activity of gold nanoparticles conjugated by aminoglycosides against *A. baumannii* isolates from burn patients," Recent Pat Antiinfect Drug Discov., 2018 Doi: 10.2174/ 1574891X13666180828115543.

[44] R. Vijayan, S. Joseph, and B. Mathew, "Eco-friendly synthesis of silver and gold nanoparticles with enhanced antimicrobial, antioxidant, and catalytic activities," IET Nanobiotechnol, 2018, vol. 12, pp. 850–856. Doi: 10.1049/iet-nbt.2017.0311

[45] N. Soni, and S. Prakash, "Green nanoparticles for mosquito control," Sci World J., 2014, vol.1. Doi: 10.1155/2014/496362

[46] R. Suryawanshi, C. Patil, H. Borase, B. Salunke, E. Mouray, P. Grellier, and S. Patil, "In vitro antiparasitic activity of microbial pigments and their combination with phytosynthesized metal nanoparticles," Parasitol Int,2015, vol.64, pp. 353–356. Doi: 10.1016/j.parint.2015.05.004

[47] M. P. Patil, and G. D. Kim, "Eco-friendly approach for nanoparticles synthesis and mechanism behind antibacterial activity of silver and anticancer activity of gold nanoparticles," Appl Microbiol Biotechnol, 2017, vol.101, pp. 79–92. Doi: 10.1007/s00253-016-8012-8

[48] M. P. Patil, D. Ngabire, H. H. P. Thi, M. D. Kim, and G. D. Kim, "Eco-friendly synthesis of gold nanoparticles and evaluation of their cytotoxic activity on cancer cells," J Clust Sci, 2017, vol. 28, pp. 119–132. Doi: 10.1007/s10876-016-1051-6

[49] S. Malathi, M. D. Balakumaran, P. T. Kalaichelvan, and S. Balasubramanian, "Green synthesis of gold nanoparticles for controlled delivery," Adv Mater Lett, 2013, vol.4, no. 12, pp. 933–940. Doi: 10.5185/amlett.2013.5477

[50] M. K. Jeengar, S. V. K. Rompicharla, S. Shrivastava, N. Chella, N. R. Shastri, V. G. Naidu, and R. Sistla, "Emu oil based nano-emulgel for topical delivery of curcumin," Int J Pharm, 2016, vol.506, no. (1–2), pp. 222–236. Doi: 10.1016/j.ijpharm.2016.04.052

[51] R. Pal, S. Panigrahi, D. Bhattacharyya, and A. S. Chakraborti, "Characterization of citrate capped gold nanoparticle quercetin complex: Experimental and quantum chemical approach," J Mol Struct, 2013, vol.1046, pp. 153-163. Doi: 10.1016/j.molstruc.2013.04.043

[52] S. Deb, H. K. Patra, P. Lahiri, A. K. Dasgupta, K. Chakrabarti, and U.Chaudhuri, "Multistability in platelets and their response to gold nanoparticles," Nanomed: Nanotechnol Biol Med, 2011, vol.7, pp. 376-384. Doi: 10.1016/j.nano.2011.01.007

[53] R. Tarnawski, and M. Ulbricht, “Amphiphilic gold nanoparticles: Synthesis, characterization and adsorption to PEGylated polymer surfaces,” Colloid Surfac A: Physicochem Engineer Aspects, 2011, vol.374, pp. 13-21. Doi: 10.1016/j.colsurfa.2010.10.027

[54] P. Nalawade, T. Mukherjee, and S. Kapoor, “High-yield synthesis of multispiked gold nanoparticles: Characterization and catalytic reactions,” Colloid Surfac A: Physicochem Engineer Aspects, 2012, vol. 396, pp. 336-340. Doi: 10.1016/j.colsurfa.2012.01.018Get

[55] M. Benkovicova, K. Vegso, P. Siffalovic, M. Jergel, S. Luby, and E. Majkova, “Preparation of gold nanoparticles for plasmonic applications,” Thin Solid Films,2013,vol.543, pp. 138-141.Doi: 10.1016/j.tsf.2013.01.048

[56] L. Yu, J. J. Qiu, H. Cheng, and Z. H. Luo, “Facile preparation of gold nanoparticles using the self-assembled ABC non-amphiphilic fluorosilicone triblock copolymer template,” Mater Chem Physic, 2013, vol.138, pp. 780-786. Doi: 10.1016/j.matchemphys.2012.12.060

[57] R. E. Doherty, I. V. Sazanovich, L. K. McKenzie, A. S. Stasheuski, R. Coyle, E. Baggaley, S. Bottomley, J. A. Weinstein, and H. E. Bryant, “Photodynamic killing of cancer cells by a Platinum(II) complex with cyclometallating ligand,” Sci Rep, 2016, vol. 6, pp. 22668. Doi: 10.1038/srep22668

[58] T. C. Johnstone, K. Suntharalingam, and S. J.Lippard, “The Next Generation of Platinum Drugs: Targeted Pt (II) Agents, Nanoparticle Delivery, and Pt(IV),” Prodrugs Chem Rev, 2016, vol. 116, pp. 3436–3486. Doi: 10.1021/acs.chemrev. 5b00597

[59] Z. Wang, L. Chen, C. Huang, Y. Huang, and N. Jia, “Albumin-mediated platinum nanocrystals for in vivo enhanced computed tomography imaging,” J Mater Chem B,2017,vol. 5, pp. 3498–3510. Doi: 10.1039/C7TB00561J

[60] Pandey, A. Kulkarni, B. Roy, A. Goldman, S. Sarangi, P. Sengupta, C. Phipps, J. Kopparam, M. Oh, S. Basu, M. Kohandel, and S. Sengupta, “Sequential application of a cytotoxic nanoparticle and a PI3 K inhibitor enhances antitumor efficacy,” Cancer Res,2014, vol. 74, pp. 675–85. Doi: 10.1158/0008-5472.CAN-12-3783

[61] A. Alshatwi, “Catechin hydrate suppresses MCF-7 proliferation through TP53/Caspase-mediated apoptosis,” J Exp Clin Cancer Res, 2011, vol. 29, pp. 167–176. Doi: 10.1186/1756-9966-29-167

[62] M. Manikandan, N. Hasan, and H. F. Wu, “Platinum nanoparticles for the photothermal treatment of Neuro 2A cancer cells,” Biomaterials, 2013, vol. 34, pp. 5833–5842. Doi: 10.1016/j.biomaterials.2013.03.077

[63] B. Sahin, A. Aygun, H. Gunduz, K. Sahin, E. Demir, S. Akocak, and F. Sen, “Cytotoxic Effects of Platinum Nanoparticles Obtained from Pomegranate Extract by the Green Synthesis Method on the MCF-7 Cell Line,” Colloids Surf B Biointerfaces, 2018, vol. 163, pp. 119–124. Doi: 10.1016/j.colsurfb.2017.12.042

[64] S. Ghosh, R. Nitnavare, A. Dewle, G. B. Tomar, R. Chippalkatti, P. More, R. Kitture, S. Kale, J. Bellare, and B. A. Chopad, “Novel platinum-palladium bimetallic nanoparticles synthesized by *Dioscorea bulbifera*: Anticancer and antioxidant activities,” Int J Nanomed, 2015, vol.10, pp. 7477–7490. Doi: 10.2147/IJN.S91579

[65] Y. Bendale, V. Bendale, R. Natu, and S. Paul, “Biosynthesized Platinum Nanoparticles Inhibit the Proliferation of Human Lung-Cancer Cells in vitro and Delay the Growth of a Human Lung-Tumor Xenograft in vivo-In vitro and in vivo Anticancer Activity of bio-Pt NPs,” J Pharmacopunct, 2016, vol. 19, pp. 114–121. Doi: 10.3831/KPI.2016.19.012

[66] M. Galanski, M. A. Jakupec, and B. K. Keppler, “Update of the preclinical situation of anticancer platinum complexes: Novel design strategies and innovative analytical approaches,” Curr Med Chem, 2005, vol. 12, pp. 2075–2094. Doi: 10.2174/0929867054637626

[67] D. S. Goodsell, “The molecular perspective: Cisplatin,” Stem Cells, 2006, vol. 24, pp. 514–515. Doi: 10.1634/theoncologist.11-3-316

[68] A. Alshatwi, J. Athinarayanan, and P. V. Subbarayan, “Green synthesis of platinum nanoparticles that induce cell death and G2/M-phase cell cycle arrest in human cervical cancer cells,” J Mater Sci Mater Med, 2015,vol. 26, pp. 1–9. Doi: 10.1007/s10856-014-5330-1

[69] S. U. Ganaie, T. Abbasi, and S. A. Abbasi, “Biomimetic synthesis of platinum nanoparticles utilizing a terrestrial weed *Antigonon leptopu*,” Part Sci Technol, 2017, vol.36, pp. 681–688. Doi: 10.1080/02726351.2017.1292336

[70] J. Y. Patra, G. Das, L. F. Fraceto, E. V. R. Campos, M. P. Rodriguex-Torres, L. S. Acosta- Torres, L. A. Diaz- Torres, R. Grillo, M. K. Swamy, S. Sharma, S. Habtemariam, and H. S. Shin, “Nano based drug delivery systems: recent developments and future prospects,” J Nanobiotechnology, 2018, vol.16, pp. 71. Doi: 10.1186/s12951-018-0392-8

[71] N. Khatik, "Green Synthesized Nanomaterials: An Analysis of the Impact on Cellular Processes, Gene Regulation, and Epigenome," International Journal of Biochemistry and Biophysics, 2021, vol. 9, no. 2, pp. 17-26. DOI: 10.13189/ijbb.2021.090201.