wjpmr, 2024, 10(3), 99-108

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

NANOPARTICLES: APPROACH FOR CANCER TREATMENT

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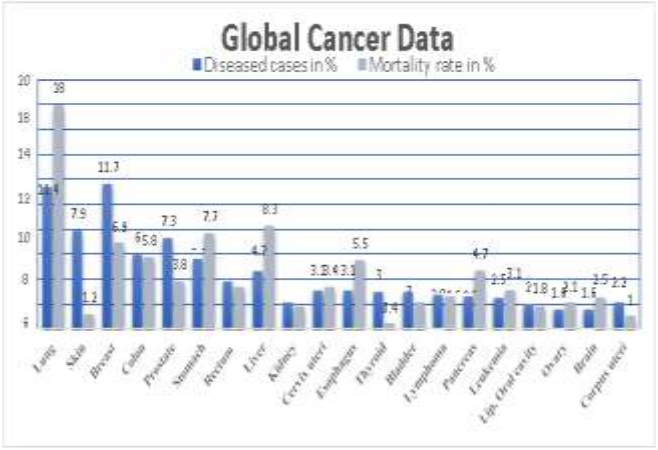
Article Received on 09/01/2024 **Article Revised on 29/01/2024** **Article Accepted on 19/02/2024**

INTRODUCTION

Throughout this pursuit of knowledge, mankind has conceived and built the elements of this physical world on scales ranging from the gigantic to the most minute scale of mass, length, shape and structure. Up to this date, the study of nanoparticles has been majorly involved in to the various fields. Especially talking about the pharmaceutical field this concept of quantum atom, ranging between 1 nm (i.e., 10^{-9} m) to 1000 nm these very minute particles help in nanotechnology and preparation of nanomedicine, used for disease diagnosis, treatment and therapies. However, this study is known as 'nanoscience' or 'nanotechnology'.[1][2] In terms of size comparison with other microparticles and microorganism, the nanoparticles are much smaller than the cells and compared to virus or antibody the nanoparticles are equal size. Nanoparticle a promising frontier for the cancer treatment. Cancer one of the most life- threatening diseases for the mankind, global cancer rates according to The Global Cancer Observatory (GCO) observe the number of mortality and diseased cases, approximately 19.3 million diseased case and mortality rate over 10 million because of cancer which was recorded in year 2020.[3]

As specified data in Graph



In India the statistics are recorded by, India's cancer statistics are meticulously recorded and maintained by the National Cancer Registry Programme (NCRP) of the National Center for Disease Informatics and Research (NCDIR) in Bengaluru. The NCDIR is an institute under the Indian Council of Medical Research (ICMR). The data is collected through two main types of registries: 36 PBCRs (Population-based cancer registries) and 236 HBCRs (Hospital-based cancer registries). For the year 2020, the approximate projected diseased cases of cancer in India were 1,392,179, which is equivalent to around 1.4 million cases. Unfortunately, accounting for approximately a million deaths due to various types of cancers lives lost to the disease. These numbers highlight the significant burden of cancer in the country and underscore the importance of continuous efforts in cancer research, prevention, and treatment. However, the nanoparticles are applicable for both diagnoses and treatment of cancer, also known as nanotherapeutics.[3][4] Upon application of the nanoparticles-based imaging agents gave a deep exposure to unreachable tissue area make it easier to diagnose and prioritize the tissue targeting, on the other hand talking about cancer treatment nanoparticles gives numerous mechanisms for the targeting of the cancer cells, those are: by acting on DNA, by mitochondrion disruption, by protein

denaturation of the cancer cells which ultimately results in cancer cell death and show anti-cancerous effect.[2][5][6]

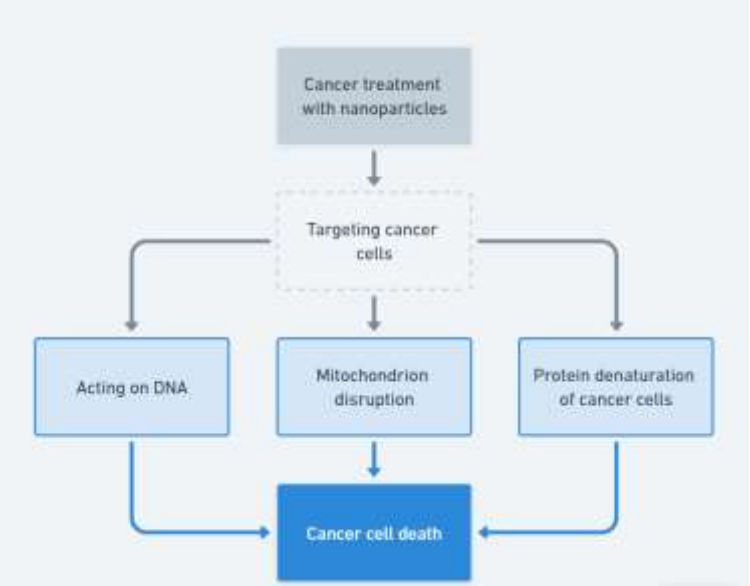


Figure 2

Because of these nanoparticles and their pivotal properties helps in bio-medical application. Cancer stands as a predominant cause of human mortality, overshadowing infectious disease. Traditional chemotherapeutic agents, including anti-metabolites and alkylating agents, wield numerous deleterious effects upon patients. Consequently, researchers are inclined towards the exploration of targeted therapy to mitigate these side effects. A novel avenue involves the application of nanomaterials to regulate the release of anti-cancer drugs, amplifying there in vivo efficacy. The utilization of nanoparticles as carriers for anti-cancer drugs, also showcases intrinsic anti-tumor effects. Metallic Nanoparticles are metal derived nanoparticles which are induced to give anti-cancer property, some of the metallic nanoparticles are Gold, Silver, Iron, Titanium, platinum, Zinc etc.[5][6][7]

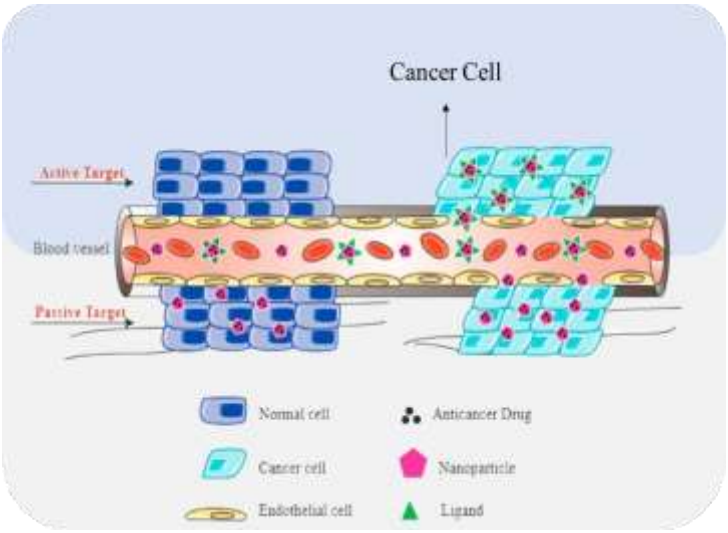
Rationale

The rationale for undertaking this work lies in the critical need for innovative approaches to combat the global challenge of cancer. With cancer emerging as a leading cause of mortality worldwide, there is a pressing demand for novel and targeted therapeutic strategies. The study is on nanoscience and nanotechnology, specifically focusing on nanoparticles, to explore their potential in revolutionizing cancer diagnosis and treatment. The unique properties of nanoparticles, particularly their ability to operate at the molecular level, offer unprecedented opportunities for precise targeting and efficient drug delivery. The escalating cancer statistics in India underscore the urgency for advanced treatments, making it imperative to investigate and harness the potential of nanoparticles in this context. The targeted drug delivery mechanisms, both active and passive, present a compelling rationale for mitigating systemic toxicity and enhancing treatment efficacy. By examining specific types of nanoparticles, including Platinum, Silver, and Gold, the research aims to unravel their distinct properties and applications in anticancer therapy. Additionally, the exploration of environmentally friendly green synthesis methods using plant extracts adds a dimension of sustainability to the study. Ultimately, this work aspires to contribute valuable insights and solutions to the ongoing global effort to alleviate the burden of cancer and improve patient outcomes through cutting-edge nanomedical interventions.

Targeting

Addressing cancer with non-targeted drugs presents significant challenges due to the widespread distribution of most chemotherapeutic drugs throughout the body. This broad distribution leads to systemic toxicity, causing adverse effects and intolerability in patients. Consequently, these issues often result in discontinuation of treatment. Tumor cell targeting represents a crucial feature of nanocarriers employed in drug delivery, as it plays a pivotal role in improving treatment efficacy while minimizing harm to healthy non-cancerous cells and tissues. Numerous studies have developed into drug delivery utilizing targeted nanoparticles. Understanding the mechanistic interactions between tumors, cancer cells, and nano-carriers is essential for the rational design of efficient drug delivery systems.[8]

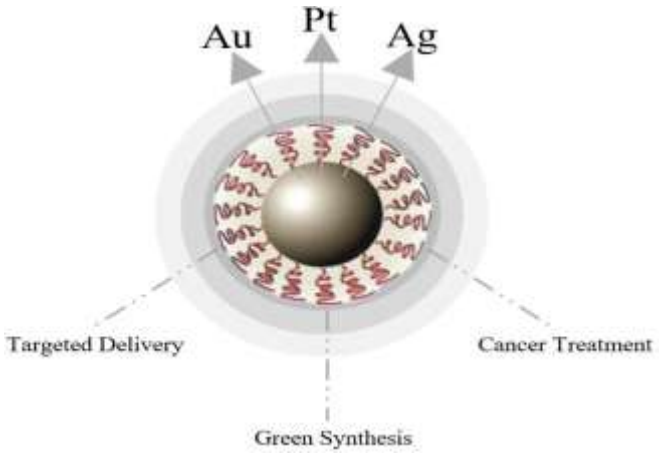
The mechanisms of targeting can be broadly classified into two distinct categories: active targeting and passive targeting.



i. **Active targeting:** Active targeting involves the intentional modification of nanocarriers to recognize and selectively bind to specific receptors or markers on the surface of cancer cells. This customization allows for precise drug delivery to the tumor site. Ligands, antibodies, or peptides that have an affinity for cancer cells are often integrated into the nanocarrier design to facilitate this targeted approach.

ii. **Passive targeting:** Passive targeting relies on the unique physiological characteristics of tumors to enhance drug delivery. Tumors typically exhibit abnormal vasculature with leaky blood vessels, a phenomenon known as the enhanced permeability and retention (EPR) effect. Nanocarriers take advantage of this feature by passively accumulating in the tumor due to increased permeability and reduced lymphatic drainage. This accumulation enhances drug concentration at the tumor site, maximizing the therapeutic effect.

Types of nanoparticles



1. Platinum: The Platinum nanoparticles (PtNPs) have multifunctional applications and have been found enhanced efficacy of malignant bone tumors osteosarcoma.[9][10][11] Nanocarriers have been specifically engineered to enhance the concentration of therapeutic compounds in the proximity of malignant bone tumors, aiming to improve the effectiveness of treatment. This targeted approach is designed to address the challenges associated with conventional drug delivery, offering a more precise and efficient means of combating bone-related malignancies. Platinum-based anticancer drugs, as well as platinum nanoparticles (PtNPs), have been found to induce the breakage of DNA strands within cells.[12][13][14] Unlike soluble platinum-based drugs, PtNPs exhibit an additional capability of effectively scavenging hydrogen peroxide and superoxide, demonstrating antioxidant activity. Furthermore, PtNPs possess imaging capabilities, contributing to their potential use in cancer theragnostic.[14][15][16][18] However, it's noteworthy that PtNPs also display cytotoxicity, which hinders their widespread application in medicine and healthcare. Consequently, the development and testing of more biocompatible PtNPs for cancer treatment remain a

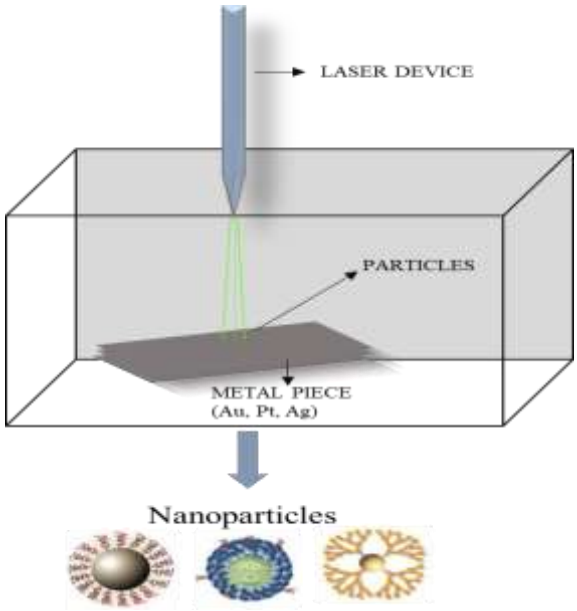
significant challenge.[19][20] Moreover, the efficacy of nanomedicine for cancer treatment may face limitations due to short circulation times and the limited persistence of nano-drug conjugates and nanoparticles (NPs) within tumor tissues. Nanoconjugates are often rapidly removed from the body after recognition by the human immune system. To address this issue, NPs are commonly pegylated by attaching the Food and Drug Administration (FDA)-approved polyethylene glycol (PEG). This pegylation process aims to increase circulation and retention time, while also reducing nonspecific serum protein adsorption, thus avoiding rapid clearance by the reticuloendothelial system (RES). This strategy is crucial for optimizing the performance of nanomedicine in cancer treatment.[21][22] The borohydride reduction technique to produce PEGylated platinum nanoparticles (PtNPs) in colloidal form at room temperature. These PtNPs exhibited stability during storage for over 2 years and for approximately 1 week in both phosphate-buffered saline (PBS) at pH 7.4 and serum. In vitro studies with various normal cell lines and a chicken egg embryo model demonstrated the biocompatibility of PtNPs. Subsequently, the researchers developed a PtNP-based delivery system for doxorubicin (PtNPs-DOX). Various analytical methods were employed to characterize PtNPs-DOX and the PtNPs. In a series of in vitro assays, PtNPs-DOX exhibited the ability to suppress the growth of tumor cells, specifically B16F10 and A549 cells.

Annexin-V staining confirmed the induction of apoptosis in tumor cells by PtNPs-DOX. Moving to in vivo studies, intraperitoneal (IP) administration of PtNPs-DOX in a mouse model with subcutaneous melanoma significantly inhibited tumor proliferation when compared to the free drug. The anti-tumor activity was further substantiated by a decrease in the expression of Ki-67 and SOX2 proliferation markers, coupled with an increase in the expression of the tumor suppressor protein p53 in malignant melanoma. These findings, determined through Western blotting and immunofluorescence, highlighted the potential of PtNPs-based drug delivery systems in anticancer nanomedicine applications Further investigations into the application of PtNPs in drug delivery for anticancer purposes are warranted based on the promising results of this study.[23]

Production of platinum nanoparticles

Platinum nanoparticles (PtNPs) are produced through physical, chemical methods using a top-down approach, involving the mechanical degradation of bulk metallic materials. While this process is energy-intensive and time-consuming, it proves effective in regulating the size and controlling morphologies of NPs. Various physical methods, Laser ablation and Solvothermal, are employed for production of PtNPs. Chemical methods such as Reduction in Nonpolar Solvents, Fusion Approach, Wet Chemical Reduction. And Green Synthesis using Plant Extracts, using Microorganisms.

i. **Laser ablation:** Laser ablation, a simple but expensive process, involves irradiating a solid surface with a laser beam to gradually remove material. Although it incurs high costs for sufficient energy, its overall energy efficiency is good. Laser ablation of solid metal faces challenges of aggregation and inadequate degradation, leading researchers to explore pulsed laser ablation in liquid (PLAL) for PtNPs generation.[24][25][26][27][28] as shown in (figure 5).



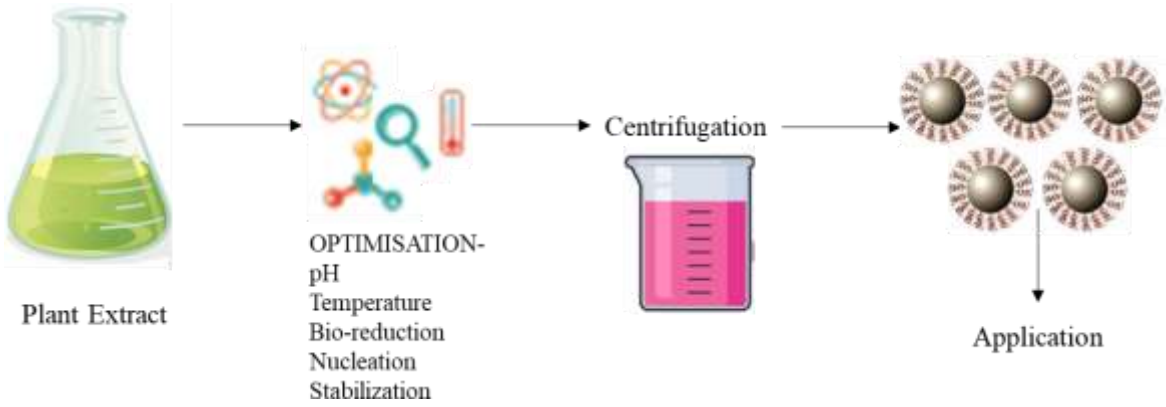
ii. **Solvothermal:** The milling process involves gradually decreasing particle size and mixing to form new phases. Solvothermal processes carry out reactions at lower temperatures using polar solvents at high pressure. Inert Gas Condensation (IGC) methods, involving metal evaporation in vacuum chambers with inert gas, are efficient for producing high- quality PtNPs.[29][30]

iii. Reduction in nonpolar solvents: The chemical reduction of metal ions within reversed micelles in a nonpolar solvent is a widely recognized method for generating metal nanoparticles (MNPs) The process involves initially dissolving a metal salt in water, which is then encapsulated within reverse micelles. Subsequently, a chemical reduction occurs within these micelles, leading to the formation of MNPs. Given the significance of particle size, precise control over the volume of the reverse micelles, as well as the ratio of water to solvent, is crucial in this technique. This control ensures the desired size and properties of the resulting nanoparticles.[31]

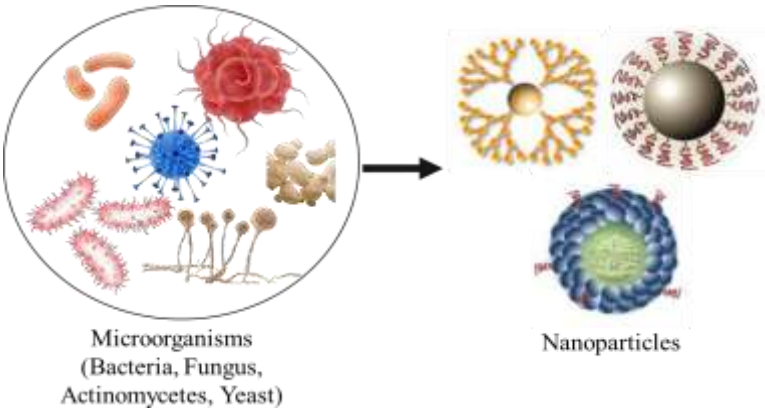
iv. Fusion approach: In the early 1920s, Adam and his colleagues successfully synthesized bulk-type PtO2 through a fusion approach at 450°C. Following this synthesis, the material underwent modifications to transform it into platinum nanoparticles (PtNPs) using various techniques. However, it's worth noting that many of these techniques often involve the use of toxic chemicals.[32]

v. Wet chemical reduction: Wet chemical reduction is commonly employed to finely control the size of particles. Various chemical reducing agents can be utilized for this purpose, including methoxy polyethylene glycol, sodium borohydride, trisodium citrate dihydrate, potassium bitartrate, elemental hydrogen, and ascorbate. The size and shape of the produced nanoparticles (NPs) depend on several factors, including temperature, the choice of the reducing agent, and the concentration of the precursor platinum compound.[33][34][35][36][37]

vi. By using plant extracts: Plant derivatives encompass a range of primary and secondary compounds that can serve as natural reducing agents and capping agents. These derivatives have found application in the green synthesis of various metal nanoparticles (MNPs), as reported in several studies. The biosynthesis of MNPs mediated by plants is a straightforward and swift process involving a combination of plant derivatives and a solution of metal ions at optimal the reaction medium, change in color shoes formation of nanoparticles,[38][39] as shown in (figure 6).



vii. By using microorganisms: Both single-celled and multicellular organisms have the capability to produce inorganic materials, either outside (extracellularly) or inside (intracellularly) their cells. In the case of bacteria, metal nanoparticles (MNPs) can be generated through a reduction process that is controlled by intracellular signaling pathways. Bacterial enzymes play a crucial role in converting metal ions into MNPs during this process. One of the main advantages of using bacteria for nanoparticle production is the simplicity of handling,[40] as shown in (figure 7).



2. **Silver:** Silver nanoparticles have proven to be highly effective due to their strong antimicrobial efficacy against bacteria, viruses, and other eukaryotic microorganisms. They stand out as the most widely used nanomaterials, finding applications as antimicrobial agents, in textile industries, water treatment, sunscreen lotions, and more.[7][41][42] Silver nanoparticles are extensively explored for various scientific purposes because of their distinctive physicochemical and biological properties. These properties include a large surface area to volume ratio, excellent surface plasmon resonance, ease of functionalization or conjugation with different types of ligands to achieve desired tailored properties, toxicity against pathogens, efficient cytotoxicity towards cancer cells, catalytic applications, and more.[6][43][44] Various mechanisms have been identified in research that help justify the anticancer properties of silver nanomaterials. Silver nanoparticles efficiently interact with cancer cells, taking advantage of the enhanced permeation and retention effect (EPR) displayed by cancer cells. This effect facilitates the entry and accumulation of silver nanoparticles within cancer cells, leading to the death of cancer cells or impeding their uncontrolled division. Additionally, silver nanoparticles can impact signaling physiological pathways, both downregulating and upregulating them, resulting in early apoptosis or slowing down the rapid division of tumor cells. Some studies suggest that silver nanomaterials activate p53, caspase-3, and p-Er K1/2, eventually leading to apoptosis and regulating cell division through a series of events within the cells.[45][46][47] The mechanistic pathway of silver nanoparticles on the breast cancer cell line (SKBR3) using advanced techniques and procedures. Their findings provide conclusive insights into the anticancer potential of silver nanoparticles on human cancer cell lines (SKBR3). They reported significant inhibition of cell motility and the inhibitory action on metalloproteinases (MMPs). Treatment with silver nanoparticles induced notable morphological changes in cancer cells, including shrinkage, irregularity in shape, blebbing of cytoplasm, changes in the shape of intracellular vacuoles, and chromatin condensation. Alongside these changes, the production of reactive oxygen species (ROS) caused oxidative stress and cell death. Furthermore, they reported the upregulation of LC3-II, ATG7, beclin-1, ATG5, and downregulation of HSP90, AKT, P62, p-AKT autophagic markers.[46]

Production of silver nanoparticles: Silver nanoparticles can be synthesized through three different methods: physical, chemical, and biological.[48]

i. Physical methods include spark discharging, pyrolysis, tube furnace (evaporation– condensation), laser ablation, gamma-irradiation, microwave processing, and others. While these methods may have certain drawbacks such as high energy consumption, low yield, and non-uniform distribution of nanoparticles, they have the advantage of not using environmentally hazardous chemicals, as shown in (figure 5).

ii. Chemical methods for synthesizing silver nanomaterials encompass techniques like the Sol-Gel method, co-precipitation, pyrolysis, Sono-chemical, and electrochemical methods.

iii. Green Synthesis one of the biological approaches to silver nanoparticle synthesis is the green synthetic approach, which involves creating nanoparticles exclusively from plant extracts. Currently, there is a notable emphasis on adopting green synthetic approaches due to their eco-friendliness, cost-effectiveness, and the vast diversity of plant resources available, along with the abundance of bioactive phytocompounds in plant extracts. It's essential to highlight those plants serve as extensive reservoirs of naturally occurring bioactive phytocompounds. These compounds not only contribute to the synthesis of nanoparticles but also provide versatile properties, including desired functionalization, long-term stability, biodistribution, and nanolithography, enabling a broad spectrum of bioactivities. Additionally, factors such as temperature, pressure, pH, the type of reducing agent, and precursor agents play a significant role in controlling the shape, size, surface area to volume ratio, size distribution, morphology, and bioactivity of the synthesized silver nanomaterials.[49][50][51][52] as shown in (figure 6,7).

3. **Gold:** In recent years, there has been considerable research interest in the synthesis of nanoparticles (NPs) due to their exceptional biomedical applications, as well as electronic, optical, and chemical properties. Metallic NPs have been synthesized by,[53] The in vitro cytotoxicity of the synthesized gold nanoparticles (AuNPs) and Hygrophila spinosa aqueous extract (HSAE) against MCF-7 and MDA-MB-231 (breast), SKOV-3 (ovarian), NCI/ADR (multi-drug resistant), and U-87 (brain) cancer cell lines was determined at concentrations ranging from 12.5 to 200 µg/mL using the MTT assay. AuNPs exhibited dose-dependent cytotoxicity against all the tested cancer cell lines. At a concentration of 200 µg/mL, the percentage cell viability for synthesized AuNPs against MCF-7, MDA-MB-231, SKOV-3, NCI/ADR, and U-87 cell lines was 43.78%, 39.34%, 21.45%, 31.48%, and 27.89%, respectively. The synthesized AuNPs demonstrated higher cytotoxicity in the ovarian cancer cell line compared to breast, brain, and multi-drug resistant cell lines. Green Synthesized AuNPs exhibited significantly greater anticancer activities compared to HSAE, possibly due to increased cellular uptake

and retention of the nanoparticles. Additionally, the nanoparticles are not substrates for the P-glycoprotein efflux pump.[54]

i. Physical methods using various metals such as Ag, Au, Cu, and Zn. Among these, gold nanoparticles (AuNPs) have garnered significant attention for their applications in cancer therapy and imaging, angiogenesis, diagnosis of genetic diseases and disorder.[55][56] AuNPs have been specifically designed for the targeted delivery of anticancer agents like paclitaxel, doxorubicin, and methotrexate,[57] as shown in (figure 5).

ii. Chemical methods are the most commonly employed approach for the synthesis of metallic NPs, involving the reduction of metallic ion solutions with reducing and capping agents such as sodium citrate, sodium borohydride, trisodium citrates, N,N-dimethyl formamide, 2-mercaptobenzimidazole, sodium hydroxide, and sodium dodecyl sulfate.[58] It's worth noting that many of the materials used in these synthesis processes can be harmful to both human health and the environment.

iii. Green synthesis the green synthesis of gold nanoparticles (AuNPs) using plant extracts and its biomedical applications are currently garnering significant interest in the field of nanotechnology. In the present study, AuNPs were synthesized utilizing an aqueous extract from Hygrophila spinosa (HSAE). The plant materials were cut into small pieces and allowed to dry in the shade for 15 days. Once dried, the material was coarsely powdered and stored in an air-tight container for future use. A total of 100 grams of the coarse powder material was subjected to extraction via soxhlation using 95% ethanol (300 mL). The ethanol extract obtained was concentrated using a rotary evaporator, dried, and then preserved in an air-tight container until further use. For the next step, 5.0 grams of the above extract were added to 100 mL of distilled water, subjected to sonication for 5 minutes, and then filtered using Whatman filter paper. Subsequently, the filtrate underwent an additional filtration step through a 0.25 µm membrane filter, and the resulting extract was stored in an air-tight container for further use,[53][59] as shown in (figure 6,7).

CONCLUSION

In conclusion, the utilization of nanoparticles represents a groundbreaking approach in the field of cancer treatment. The staggering global statistics on cancer incidence and mortality underscore the urgent need for innovative solutions. Nanotechnology and their application in nanomedicine facilitate precise diagnosis exposure, while in cancer treatment, nanoparticles demonstrate diverse mechanisms such as DNA interaction, mitochondrion disruption, and protein denaturation, resulting in targeted cell death. Targeting strategies, both active and passive, play a pivotal role in enhancing drug delivery efficacy and minimizing adverse effects. Examining specific types of nanoparticles, such as Platinum, Silver, and Gold, reveals their unique properties and applications in anticancer therapy. Notably, the green synthesis of nanoparticles using plant extracts emerges as an environmentally friendly and bioactive method. Despite challenges like cytotoxicity, the remarkable potential of nanoparticles in cancer therapeutics, especially when harnessed through targeted approaches and innovative synthesis methods, signifies a transformative frontier in the ongoing battle against this formidable disease.

REFERENCES

1. Gadad, A. P., S M, V. K., Dandagi, P. M., Bolmol, U. B., & Pallavi, N. P. Nanoparticles and their Therapeutic Applications in Pharmacy. *International Journal of Pharmaceutical Sciences and Nanotechnology*, 2014; *7*(3): 2509–2519. https://doi.org/10.37285/ijpsn.2014.7.3.2
2. Khan, M. F., & Khan, M. A. Plant-Derived Metal Nanoparticles (PDMNPs): Synthesis, Characterization, and Oxidative Stress-Mediated Therapeutic Actions. *Future Pharmacology*, 2023; *3*(1): 252–295. https://doi.org/10.3390/futurepharmacol3010018
3. Chhikara, B. S., Parang, K., & Etters, L. *Global Cancer Statistics 2022: the trends projection analysis*, 2023; *10*(1): 1–16.
4. Mathur, P., Sathishkumar, K., Chaturvedi, M., Das, P., Sudarshan, K. L., Santhappan, S., Nallasamy, V., John, A., Narasimhan, S., & Roselind, F. S. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. *JCO Global Oncology*, 2020; *6*: 1063–1075. https://doi.org/10.1200/go.20.00122
5. Abed, A., Derakhshan, M., Karimi, M., Shirazinia, M., Mahjoubin-Tehran, M., Homayonfal, M., Hamblin, M. R., Mirzaei, S. A., Soleimanpour, H., Dehghani, S., Dehkordi, F. F., & Mirzaei, H. Platinum Nanoparticles in Biomedicine: Preparation, Anti-Cancer Activity, and Drug Delivery Vehicles. *Frontiers in Pharmacology*, 2022; *13:* 1–23. https://doi.org/10.3389/fphar.2022.797804
6. Abass Sofi, M., Sunitha, S., Ashaq Sofi, M., Khadheer Pasha, S. K., & Choi, D. An overview of antimicrobial and anticancer potential of silver nanoparticles. *Journal of King Saud University - Science*, 2022; *34*(2): 101791. https://doi.org/10.1016/j.jksus.2021.101791
7. Saba, H. A Review on Nanoparticles: Their Synthesis and Types. *Research Journal of Recent Sciences Res. J. Recent. Sci. Uttar Pradesh (Lucknow Campus)*, 2014; *4:* 1–3.
8. Desai N, Momin M, Khan T, Gharat S, Ningthoujam RS, Omri A. Metallic nanoparticles as drug delivery system for the treatment of cancer. Expert opinion on drug delivery, 2021; 2, 18(9): 1261-90.

9. Schroeder A, Heller DA, Winslow MM, Dahlman JE, Pratt GW, Langer R, Jacks T, Anderson DG. Treating metastatic cancer with nanotechnology. Nature Reviews Cancer, 2012; 12(1): 39-50.
10. Cole LE, Vargo-Gogola T, Roeder RK. Targeted delivery to bone and mineral deposits using bisphosphonate ligands. Advanced drug delivery reviews, 2016; 1, 99: 12-27.
11. Jiang C, Wang Y, Wang J, Song W, Lu L. Achieving ultrasensitive in vivo detection of bone crack with polydopamine-capsulated surface-enhanced Raman nanoparticle. Biomaterials, 2017; 1, 114: 54-61.
12. Yamagishi Y, Watari A, Hayata Y, Li X, Kondoh M, Yoshioka Y, Tsutsumi Y, Yagi K. Acute and chronic nephrotoxicity of platinum nanoparticles in mice. Nanoscale research letters, 2013; 8: 1-7.
13. Dasari, S., and Tchounwou, P. B. Cisplatin in Cancer Therapy: Molecular Mechanisms of Action. Eur. J. Pharmacol, 2014; 740: 364–378. doi:10.1016/j.ejphar. 2014.07.025
14. Johnstone TC, Suntharalingam K, Lippard SJ. The next generation of platinum drugs: targeted Pt (II) agents, nanoparticle delivery, and Pt (IV) prodrugs. Chemical reviews, 2016; 9, 116(5): 3436-86.
15. Kajita M, Hikosaka K, Iitsuka M, Kanayama A, Toshima N, Miyamoto Y. Platinum nanoparticle is a useful scavenger of superoxide anion and hydrogen peroxide. Free radical research, 2007; 1, 41(6): 615-26.
16. Pelka J, Gehrke H, Esselen M, Türk M, Crone M, Bräse S, Muller T, Blank H, Send W, Zibat V, Brenner P. Cellular uptake of platinum nanoparticles in human colon carcinoma cells and their impact on cellular redox systems and DNA integrity. Chemical research in toxicology, 2009; 20, 22(4): 649-59.
17. Hu K, Berenjian S, Larsson R, Gullbo J, Nygren P, Lövgren T, Morein B. Nanoparticulate Quillaja saponin induces apoptosis in human leukemia cell lines with a high therapeutic index. International journal of nanomedicine, 2010; 2: 51-62.
18. Park EJ, Kim H, Kim Y, Park K. Intratracheal instillation of platinum nanoparticles may induce inflammatory responses in mice. Archives of pharmacal research, 2010; 33: 727- 35.
19. Gehrke H, Pelka J, Hartinger CG, Blank H, Bleimund F, Schneider R, Gerthsen D, Bräse S, Crone M, Türk M, Marko D. Platinum nanoparticles and their cellular uptake and DNA platination at non-cytotoxic concentrations. Archives of toxicology, 2011; 85: 799-812.
20. Yamagishi Y, Watari A, Hayata Y, Li X, Kondoh M, Yoshioka Y, Tsutsumi Y, Yagi K. Acute and chronic nephrotoxicity of platinum nanoparticles in mice. Nanoscale research letters, 2013; 8: 1-7.
21. Treuel L, Brandholt S, Maffre P, Wiegele S, Shang L, Nienhaus GU. Impact of protein modification on the protein corona on nanoparticles and nanoparticle–cell interactions. ACS nano, 2014; 28, 8(1): 503-13.
22. Pelaz B, del Pino P, Maffre P, Hartmann R, Gallego M, Rivera-Fernandez S, de la Fuente JM, Nienhaus GU, Parak WJ. Surface functionalization of nanoparticles with polyethylene glycol: effects on protein adsorption and cellular uptake. ACS nano, 2015; 28, 9(7): 6996- 7008.
23. Mukherjee S, Kotcherlakota R, Haque S, Bhattacharya D, Kumar JM, Chakravarty S, Patra CR. Improved delivery of doxorubicin using rationally designed PEGylated platinum nanoparticles for the treatment of melanoma. Materials Science and Engineering: C, 2020; 1, 108: 110375.
24. Waag F, Streubel R, Gökce B, Barcikowski S. Synthesis of gold, platinum, and gold- platinum alloy nanoparticle colloids with high-power megahertz-repetition-rate lasers: the importance of the beam guidance method. Applied Nanoscience, 2021; 11: 1303-12.
25. Fedorova EA, Stadnichenko AI, Slavinskaya EM, Kibis LS, Stonkus OA, Svintsitskiy DA, Lapin IN, Romanenko AV, Svetlichnyi VA, Boronin AI. A Study of Pt/Al 2 O 3 Nanocomposites Obtained by Pulsed Laser Ablation to Be Used as Catalysts of Oxidation Reactions. Journal of Structural Chemistry, 2020; 61: 316-29.
26. N Madlum K, Jasim Khamees E, Abdulridha Ahmed S, Akram Naji R. Antimicrobial and cytotoxic activity of platinum nanoparticles synthesized by laser ablation technique. Journal of Nanostructures, 2021; 1, 11(1): 13-9.
27. Jan H, Gul R, Andleeb A, Ullah S, Shah M, Khanum M, Ullah I, Hano C, Abbasi BH. A detailed review on biosynthesis of platinum nanoparticles (PtNPs), their potential antimicrobial and biomedical applications. Journal of Saudi Chemical Society, 2021; 1, 25(8): 101297.
28. Mathew G, Narayanan N, Abraham DA, De M, Neppolian B. Facile green approach for developing electrochemically reduced graphene oxide-embedded platinum nanoparticles for ultrasensitive detection of nitric oxide. ACS omega, 2021; 18, 6(12): 8068-80.
29. Jameel MS, Aziz AA, Dheyab MA. Impacts of various solvents in ultrasonic irradiation and green synthesis of platinum nanoparticle. Inorganic Chemistry Communications, 2021; 1, 128: 108565.
30. Mathiesen JK, Quinson J, Dworzak A, Vosch T, Juelsholt M, Kjær ET, Schröder J, Kirkensgaard JJ, Oezaslan M, Arenz M, Jensen KM. Insights from in situ studies on the early stages of platinum nanoparticle formation. The journal of physical chemistry letters, 2021; 25, 12(12): 3224-31.
31. Stepanov AL, Golubev AN, Nikitin SI, Osin YN. A review on the fabrication and properties of platinum nanoparticles. Rev. Adv. Mater. Sci, 2014; 1, 38(2): 160-75.
32. Adams DM. Inorganic solids: an introduction to concepts in solid-state structural chemistry. (No Title), 1974.

33. Leong GJ, Schulze MC, Strand MB, Maloney D, Frisco SL, Dinh HN, Pivovar B, Richards RM. Shape-directed platinum nanoparticle synthesis: nanoscale design of novel catalysts. Applied Organometallic Chemistry, 2014; 28(1): 1-7.
34. Tao AR, Habas S, Yang P. Shape control of colloidal metal nanocrystals. Small, 2008; 3, 4(3): 310-25.
35. Chen J, Lim B, Lee EP, Xia Y. Shape-controlled synthesis of platinum nanocrystals for catalytic and electrocatalytic applications. Nano Today, 2009; 1, 4(1): 81-95.
36. Lim SI, Ojea-Jiménez I, Varon M, Casals E, Arbiol J, Puntes V. Synthesis of platinum cubes, polypods, cuboctahedrons, and raspberries assisted by cobalt nanocrystals. Nano letters, 2010; 10, 10(3): 964-73.
37. Miyabayashi K, Nakamura S, Miyake M. Synthesis of small platinum cube with less than 3 nm by the control of growth kinetics. Crystal growth & design, 2011; 5, 11(10): 4292-5.
38. Azzazy HM, Mansour MM, Samir TM, Franco R. Gold nanoparticles in the clinical laboratory: principles of preparation and applications. Clinical chemistry and laboratory medicine, 2012; 1, 50(2): 193-209.
39. Marslin G, Siram K, Maqbool Q, Selvakesavan RK, Kruszka D, Kachlicki P, Franklin G. Secondary metabolites in the green synthesis of metallic nanoparticles. Materials, 2018; 3, 11(6): 940.
40. Gong P, Li H, He X, Wang K, Hu J, Tan W, Zhang S, Yang X. Preparation and antibacterial activity of Fe3O4@ Ag nanoparticles. Nanotechnology, 2007; 15, 18(28): 285604.
41. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnology advances, 2009; 1, 27(1): 76-83.
42. Sharma VK, Yngard RA, Lin Y. Silver nanoparticles: green synthesis and their antimicrobial activities. Advances in colloid and interface science, 2009; 30, 145(1-2): 83-96.
43. Jain PK, Huang X, El-Sayed IH, El-Sayed MA. Noble metals on the nanoscale: optical and photothermal properties and some applications in imaging, sensing, biology, and medicine. Accounts of chemical research, 2008; 16, 41(12): 1578-86.
44. Akter M, Sikder MT, Rahman MM, Ullah AA, Hossain KF, Banik S, Hosokawa T, Saito T, Kurasaki M. A systematic review on silver nanoparticles-induced cytotoxicity: Physicochemical properties and perspectives. Journal of advanced research, 2018; 1, 9: 16.
45. Gurunathan S, Park JH, Han JW, Kim JH. Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by Bacillus tequilensis and Calocybe indica in MDA-MB- 231 human breast cancer cells: targeting p53 for anticancer therapy. International journal of nanomedicine, 2015; 29: 4203-23.
46. Buttacavoli M, Albanese NN, Di Cara G, Alduina R, Faleri C, Gallo M, Pizzolanti G, Gallo G, Feo S, Baldi F, Cancemi P. Anticancer activity of biogenerated silver nanoparticles: an integrated proteomic investigation. Oncotarget, 2018; 2, 9(11): 9685.
47. Bethu MS, Netala VR, Domdi L, Tartte V, Janapala VR. Potential anticancer activity of biogenic silver nanoparticles using leaf extract of Rhynchosia suaveolens: an insight into the mechanism. Artificial cells, nanomedicine, and biotechnology, 2018; 31, 46(1): 104-14.
48. Iravani S, Korbekandi H, Mirmohammadi SV, Zolfaghari B. Synthesis of silver nanoparticles: chemical, physical and biological methods. Research in pharmaceutical sciences, 2014; 9(6): 385.
49. Chavan RR, Bhinge SD, Bhutkar MA, Randive DS, Wadkar GH, Todkar SS. In vivo and in vitro hair growth-promoting effect of silver and iron nanoparticles synthesized via Blumea eriantha DC plant extract. Journal of Cosmetic Dermatology, 2021; 20(4): 1283-97.
50. Argade PA, Bhutkar MA, Magdum CS. Albizzia lebbeck extract mediated synthesis and characterization of Zinc oxide Nanoparticle. Asian Journal of Pharmaceutical Research, 2019; 9(1): 1-6.
51. Shejawal KP, Randive DS, Bhinge SD, Bhutkar MA, Wadkar GH, Jadhav NR. Green synthesis of silver and iron nanoparticles of isolated proanthocyanidin: its characterization, antioxidant, antimicrobial, and cytotoxic activities against COLO320DM and HT29. Journal of Genetic Engineering and Biotechnology, 2020; 18: 1-1.
52. Voronov A, Kohut A, Vasylyev S, Peukert W. Mechanism of silver ion reduction in concentrated solutions of amphiphilic invertible polyesters in nonpolar solvent at room temperature. Langmuir, 2008; 4, 24(21): 12587-94.
53. Satpathy, S., Patra, A., Ahirwar, B., & Hussain, M. D. Process optimization for green synthesis of gold nanoparticles mediated by extract of Hygrophila spinosa T. Anders and their biological applications. *Physica E: Low-Dimensional Systems and Nanostructures*, 2020; *121*: 113830. https://doi.org/10.1016/j.physe.2019.113830
54. Gabizon AA. Selective tumor localization and improved therapeutic index of anthracyclines encapsulated in long-circulating liposomes. Cancer research, 1992; 15, 52(4): 891-6.
55. Sadeghi B, Mohammadzadeh M, Babakhani B. Green synthesis of gold nanoparticles using Stevia rebaudiana leaf extracts: Characterization and their stability. Journal of Photochemistry and Photobiology B: Biology, 2015; 1, 148: 101-6.
56. I.H. El-Sayed, X. Huang, M.A. El-Sayed, Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: applications in oral cancer, Nano Lett, 2005; 5: 829-834.
57. Rai M, Ingle AP, Birla S, Yadav A, Santos CA. Strategic role of selected noble metal nanoparticles in medicine. Critical reviews in microbiology, 2016;

2, 42(5): 696-719.
58. Shankar SS, Rai A, Ahmad A, Sastry M. Rapid synthesis of Au, Ag, and bimetallic Au core– Ag shell nanoparticles using Neem (Azadirachta indica) leaf broth. Journal of colloid and interface science, 2004; 15, 275(2): 496-502.
59. Duan H, Wang D, Li Y. Green chemistry for nanoparticle synthesis. Chemical Society Reviews, 2015; 44(16): 5778-92.