

Cancer Therapy with Platinum Nanoparticles: A Systematic Review

Dr. Nagaraju Potnuri¹, Dr. Ajendra Kumar², Sushama Rawat^{3a,b}, Dr. Prasanthi Samathoti⁴, Dr. Vivekanand B. Jadhav⁵, Rajeev Ranjan⁶, Pranjali Bajrang Chole⁷, Dr. Nihar Ranjan Kar⁸, Dr. Aniketa Sharma^{9*}

¹*Principal and Professor, Mandesh Institute of Pharmaceutical Science & Research Center Mhaswad (V), Man (Tal), Satara-415509 Maharashtra, INDIA*

²*Assistant professor, Chemistry, S.M.S.G. College, Sherghati, Gaya(Bihar)- 824211*

^{3a}*Assistant Professor, Nirma University Institute of Pharmacy, S G Highway, Ahmedabad – 382481, Gujarat.*

^{3b}*Jaipur National University, School of Pharmaceutical Sciences, Jaipur -302017*

⁴*Associate Professor, MB School of pharmaceutical sciences, Sree sainath nagar, A.Rangampeta, Tirupati, Andhra Pradesh, pin: 517102*

⁵*Associate Professor, Department of Chemistry, Shri Muktanand College, Vaijapur Road, Gangapur, Tq.-Gangapur, Dist.-Aurangabad, Pin-431109, Maharashtra*

⁶*Assistant Professor, University Department of Chemistry, DSPM University, Ranchi 834008*

⁷*Research Scholar, CHRIST (Deemed to be University), Bangalore, Karnataka, India. 560029*

⁸*Assistant Professor, Centurion University of Technology and Management, Gopalpur, balasore, Odisha, India, Pin-756044*

⁹*Assistant Professor, Department of Medicine, Dr.YSP Govt.Medical College Nahan District Sirmour H.P.*

***Corresponding Author Details:Dr. Aniketa Sharma**

Email: aniketa.shonyo786@gmail.com

Abstract: Cancer is defined as an abnormal and uncontrolled growth of cells, which may lead to the development of potentially fatal malignancies. This condition imposes significant financial burdens on both individuals affected by cancer and the healthcare system. The phytochemical elements has the capacity to function as agents for chemoprotection and chemotherapy in many forms of cancer, since they have historically been used for the purpose of preventing and treating a broad spectrum of diseases. These benefits, which have also been shown in the literature, include notable antioxidant, anti-inflammatory, antiproliferative, antineoplastic, and immunomodulatory properties. One of the challenges associated with the utilisation of polyphenolic chemicals is their restricted bioavailability. A variety of formulations have been developed to enhance the bioavailability of these drugs, among which nanonization has gained significant recognition. The primary objectives of this study were conducting a comprehensive examination of existing scientific literature pertaining to the molecular mechanisms via which natural polyphenols exert their anticancer effects. The use of nano formulations in the field of medicine has shown promising potential as chemo preventive and anticarcinogenic agents.

Keywords: Poly phenol, Platinum nano particles, Flavonoids, cancer treatment, diagnostic agent.

1.Introduction:

Despite the continuous advancements in cancer prevention and treatment strategies, cancer remains a significant global public health issue. This syndrome is characterised by uncontrolled cellular growth that is not amenable to cessation. In addition, it is observed that malignant tumour cells possess a tendency to undergo metastatic dissemination, therefore infiltrating and affecting organs beyond the primary tumour location. The treatment of cancer often involves the use of a variety of therapeutic approaches, including both pharmaceutical and nonpharmacological interventions. These interventions may include immunotherapy, chemotherapy, and hormone therapy. Nonpharmacological interventions include a range of therapeutic modalities, such as radiation treatment, surgical procedures, stem cell therapy, and the use of heat. In this study, we aim to investigate the effects of climate change on biodiversity in a tropical region. However, it is important to note that the aforementioned approaches, including chemotherapy, possess notable drawbacks. One such limitation is the inadequate localization of therapeutic agents to the tumour site, resulting in various adverse effects and potentially hazardous off-target repercussions. According to the second source,

The unit of measurement known as the nanometer, which represents one billionth of a metre, is often used in the field of nanotechnology to quantify the dimensions of particles. According to the source provided, [3]. One of the primary advantages of nanoparticles is the significant ratio between their surface area and volume, resulting from the arrangement of their atoms or molecules. These qualities modify the biological and physical characteristics of nanoparticles, hence enhancing their surface activity. According to the source provided, it is stated that [4].

Polyphenolic compounds, which belong to a significant category of plant secondary metabolites, include several health-promoting qualities, including antioxidant, anti-inflammatory, and anti-cancer activity. The user's text is already academic and does not need to be rewritten. Curcumin, resveratrol, and other flavonoids are representative natural polyphenols that have been the subject of previous research on their anticancer properties. Consequently, these compounds have garnered considerable attention from scientists, prompting more exploration. The primary objective of the present research is to analyse available evidence about the use of natural polyphenol Nano formulations as medicines with anticarcinogenic and chemotherapeutic properties. Additionally, the study aims to elucidate the molecular processes behind the anticancer effects of these formulations.

1. Polyphenols nano formulation for anticancer therapy

Polyphenols have garnered significant attention in the field of cancer due to their diverse therapeutic and pharmacological effects. Various methods have been used to develop polyphenol nano formulations, such as liposomes, dendrosomes, nano capsules, and nanosheets.

The bulk of these nanostructures have significant anticancer efficacy. The polyphenols that have been investigated in nanoformulations for their potential anticancer effects include luteolin, quercetin, curcumin, coumarin, baicalein, resveratrol, Epigallocatechin gallate, honokiol, chrysin, and honokiol. The user has provided a numerical input in the form of a list containing the numbers 7 and 8.

Polyphenol Nano formulations have been shown to exhibit efficacy against cancer by inducing

cytotoxic effects at different stages of the cancer cell cycle, activating apoptotic enzymes, reducing tumour vascular permeability to prevent invasion and metastasis of malignant cells, causing damage to mitochondria, and inducing apoptosis in neoplastic cells. Induction of apoptosis is a significant mechanism by which Nano structured polyphenols exert their effects on cancer cells, hence serving as a crucial signal in the context of anticancer treatment.

Apoptosis, a regulated process of cell death that eliminates unwanted cells from the body, may be induced by several herbal remedies as a means to combat cancer. The Bcl-2 and Bax proteins, which belong to the Family proteins of apoptosis-regulating proteins, exhibit contrasting functions in the process of apoptosis. The protein Bcl-2 functions to inhibit apoptosis, while the protein Bax serves to increase the process of programmed cell death. The process of apoptosis, which is controlled by an elevation in the Bax/Bcl-2 ratio, is widely acknowledged as a primary mechanism via which these pharmaceutical agents induce cell death in cancerous cells. The given input consists of the numbers 9 and 10.

Throughout history, natural therapies have been extensively used as supplementary and alternative treatments for managing various forms of cancer and achieving optimum physiological functioning. The efficacy of traditional drugs delivered in presently available dosage forms for cancer treatment is limited. Consequently, it is essential to acknowledge the indispensability of limitations in the realm of cancer therapy. The current situation necessitates the advancement of precise and safe administration of medication treatments that exhibit improved therapeutic efficacy. Consequently, there is a need to explore innovative approaches in drug delivery. The user's text is not sufficient to rewrite in an academic manner. Please provide more information. One notable difference between free polyphenol molecules and those included in Nano formulation is in their heightened anti-neoplastic efficacy and greater absorption, hence facilitating passive targeting of malignant cells. The user's text does not contain any information to rewrite. In the present scenario, this particular condition requires the administration of reduced pharmaceutical dosages in order to get an optimum response, while also mitigating the pharmacokinetic challenges often associated with conventional formulations. Multiple studies have shown that polyphenols possess notable anticancer properties that may be strategically harnessed, namely by selectively inducing cytotoxic effects on neoplastic cells while sparing normal cells. In contrast, conventional anticancer medications have not exhibited comparable selectivity. The user's text does not contain any information to rewrite.

2. Synthesis of plant-mediated nanoparticles

Because the form, size, chemical compositions, electrical surface morphology, and capping agent of PtNPs have a significant influence on their industrial and biological capabilities, researchers have developed novel synthetic ways to control these properties. [14, 15]

Nanoparticles (NPs) may be made using a variety of methods, including biological, mechanical, and chemical ones. Conventional physical and chemical processes for NP synthesis are hazardous and may cause environmental harm because they produce toxic by-products. Additionally, NPs made utilising such dangerous techniques are not suitable for use in the medical sector, especially in clinical applications, owing to health concerns.

The general synthesis procedures for PtNPs include physical, chemical, and biological processes, as shown in Figure 1.

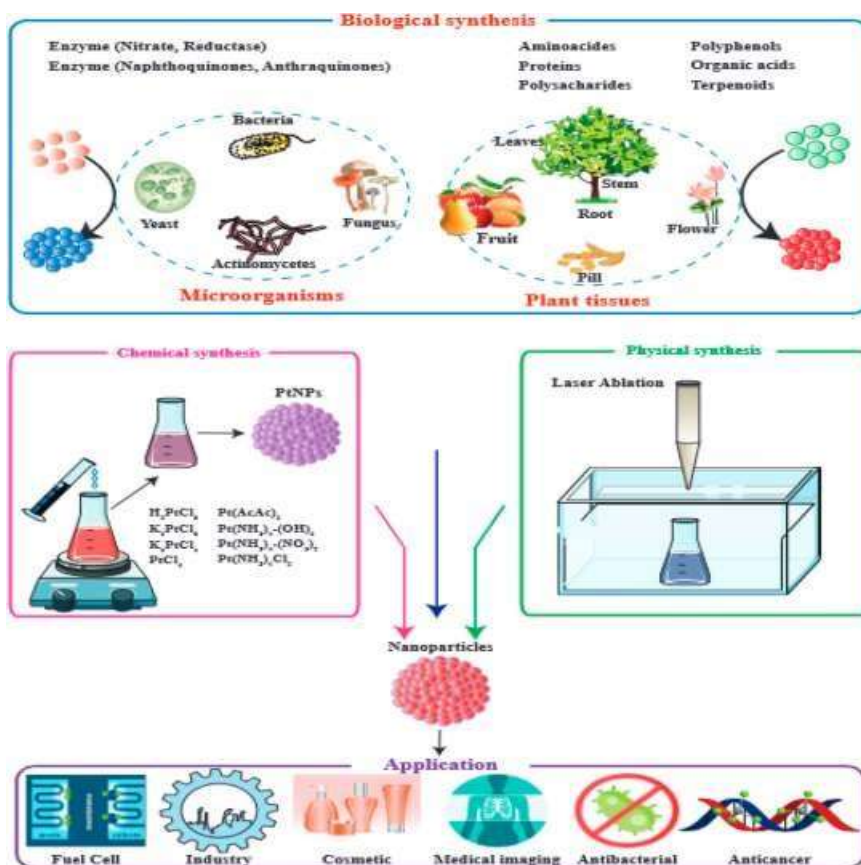


Figure 1. Applications of PtNPs and their methods of preparation

3.1 Physical processes

Aerosol-assisted deposition [16], laser ablation techniques [17], flame synthesis [18], and electron-beam-induced reduction [19] are recently well-liked physical methods that attempt to get beyond some of the restrictions of chemical procedures (e.g., organic solvents, dangerous reagents, etc.). PtNPs are volatilized during the laser ablation process from a solid source. The laser beam may be used either constantly or occasionally. To achieve exact PtNP characteristics, this flexible approach depends on temperature, pulse, and ambient gas pressure control.

Avoiding unfavourable stabiliser, coating, and solvent contaminations is the main advantage of this approach, which may be important in nanomedicine.[20] However, it is challenging to alter the size, shape, and manufacturing yield of Pt NPs, and nothing is understood about how they are made. The use of Pt NPs is restricted by these limitations.[21] Such Pt NPs' cellular environment lifespan may likewise provide challenges. The NPs produced by laser ablation stay stable in aqueous solution even in the absence of stabiliser because to the electric repelling influence caused by charges on the surface of the NPs.[22] However, Pt NPs may precipitate and aggregate when incubated in complex environments such cell culture medium and high ion concentration solutions, which might be troublesome for biological research. Cathodic corrosion, which transforms a bulk alloy electrode into a suspension of NPs with the same composition, is another straightforward physical technique for producing PtNPs for various applications.[23] All methods, meanwhile, have comparable drawbacks such limited manufacturing yield and size adaptability.

Vapour deposition, flame spray pyrolysis, ball milling, arc discharge, laser ablation, and sputter deposition are a few of the physical techniques that have been utilised.[24]

3.1.1 Laser Ablation

By shining a laser beam on a solid surface (or rarely a liquid surface), material is gradually removed by laser ablation. It serves as an easy and affordable alternative to electrical heating. Although it has a high cost of energy generation, laser ablation has an acceptable total energy efficiency. A material absorbs the transmitted laser energy when it is exposed to a laser flux, turning it into plasma. Because of the challenges with aggregation and inadequate degradation associated with laser ablation of solid metal (pulsed laser ablation in liquid), several researchers have shown the creation of PtNPs by PLAL in prior investigations. [25, 26, 27]

3.1.2 Solvothermal Processes

As a result of the reactants becoming more soluble, solvothermal processes allow reactions to occur at lower temperatures. Using polar solvents at pressures and temperatures above their typical boiling points, it is a low- temperature process.^[28]

3.1.3 Inert Gas Condensation

IGC methods are used to evaporate metals in vacuum chambers under a 100 Pa inert gas pressure.

IGC is a very effective technique for producing superior platinum and silver nanoparticles. In the IGC procedure, metal atoms are struck by gas atoms, which results in the loss of kinetic energy and crystallisation of the latter into tiny particles in liquid nitrogen. The process for making gold nanoparticles is similar.[29]

3.2 CHEMICAL PROCESSES

Pt NPs were produced using chemical methods both in solution phase and on the solid surface of the supporting material. Materials for supporting, including such nanotubes or even silica, can be used to create the solid support. Chemical techniques are simple and cheap to explore with. Platinum metal precursors like chloroplatinic acid and platinum chloride are reduced to produce Pt NPs. A solvent that is organic or aqueous contains the precursor. A reducing agent is required to convert soluble precursors into solid NPs. This starts a process of chemical conversion. Sodium borohydrate is a common reducing agent for chloroplatinic acid (NaBH₄).^[30, 31]

Temperatures, reducing/capping agents, size, and shape must all be carefully managed during the production of Pt NPs. The ingredients and circumstances for the generation of Pt NPs have been optimized through several investigations. The three main components in the production of Pt NP are the metal precursor, a reducing agent, and a capping/stabilizing agent. Aggregate should be avoided in the strategy. Chemical processes have a number of advantages, such as low cost, strong surface chemistry flexibility, simple chemical modification, good yields, reasonable sized control, heat resistance, and reduced dissipation. Low quality, the use of risky different chemicals, and the possible danger that organic solvents pose to humans and the environment are some of the downsides.^[32, 33]

3.1.1 Reduction in Nonpolar Solvents

The most popular method for making metal nanoparticles (NPs) involves chemically reducing metallic ions contained inside inverting micelles in a non-polar solvent (MNPs).

MNPs are synthesized from a metal salt solution dissolved in water, which are then combined into reverse micelles and chemically reduced. Since size of the particles is crucial, the quantity of micelles as well as the liquid ratio should be properly controlled.^[34, 35]

3.1.2 Fusion Approach

Adam and his colleagues used a fusion technique at 450°C to manufacture bulk type PtO₂ in the early 1920s. Various procedures were used to convert the material into PtNPs. However, hazardous substances are frequently used in these approaches.^[36]

3.1.3 Wet Chemical Reduction

To more effectively control particle size, wet chemical reduction is often used. Chemical reducing agents that can be employed include potassium bitartrate, sodium borohydride, methyl polyethylene glycol, elemental hydrogen trisodium, citrate dihydrate and ascorbate. Temperature, reducing agent, and precursor platinum compound concentration all influence the size and structure of the NPs generated.^[37]

Other Chemical Methods

Some other techniques for chemical synthesis include sol-gel, chemical vapor deposition (CVD), sono decomposition, hydrolysis, confined reaction, thermal decomposition, pyrolysis, micro emulsion, photochemical reduction, hydrothermal, polyol synthesis, chemical vapor deposition, electrochemical process and plasma enhanced chemical vapor.

3.2 Biological synthesis of platinum nanoparticles

Microbially synthesis of Pt NPs by multicellular and unicellular organisms can result in low-cost, monodisperse, environmentally friendly, less or non-toxic, low-waste, and large-scale production alternative to physical and chemical approaches. Mild reducing agents quickly decrease noble metal nanoparticles made via biological synthesis. It has been found that plants, fungi, bacteria, seaweeds and cyanobacteria all produce narrow size distribution and stable Pt NPs. Pt NPs have also been produced using bio-derived materials like hydrophilic sugar solutions. Using an extracts of the Indian brown seaweed *Padina gymnosperm*, Ramkumar et al. created polyvinylpyrrolidone (PVP) polymer doped Pt NPs with diameters of 10–60 nm. It was revealed that PVP/Pt NPs are excellent antibacterial agents against harmful microorganisms.^[38]

The morphology of PtNPs produced by biological processes is determined by the platinum precursor content as well as the temperature or pH of the reaction mixture. PtNPs of small size form at high temperatures and pH. One of the limits of biological synthesis is the ability to control the size and form of PtNPs that are produced. Plant extracts utilized in green synthesis also contain a variety of active compounds that can pose complications during isolation and purification. However, as compared to alternative approaches, the advantages of biological synthesis outweigh the drawbacks. These platinum nanostructures are still in their early stages of development, but they already display attractively well-structured particles that show promise as a therapeutic

agent.^[39]

3. Plant-based nanomaterials

Greener synthesis techniques are being devised and studied to avoid the usage of harmful compounds during the synthesis of NPs, as previously stated. Plant-mediated NPs synthesis is an environmentally friendly and green synthesis method that adheres to green chemistry principles. Plant extracts have long been utilized to make metallic nanoparticles.^[40]

Additionally, Pt NPs have been made from plant resources.^[41, 42, 43] Since they are created in an environmentally benign way, NPs made from plant extracts are especially suited to situations where NPs must interact with biological beings.

Additionally, the use of potentially hazardous compounds that might otherwise pollute the environment is avoided while using plant material in synthesis. NPs are made from plant extracts that include a variety of phytochemicals that have medicinal benefits.

These phytochemicals help to stabilize NPs and might improve the quality of man-made NPs. In order to synthesize NPs, a medicinally relevant plant extract is chosen above other biological techniques. It has already been discovered that certain plant extracts can create Pt NPs.^[44, 45] It has been reported that *Gloriosa superba* dried tuber powder was used to make a plant tuber extract used in the manufacture of Pt NPs. The precursor PtCl₆²⁻ ions may be transformed into 0.8–3 nm spherical Pt NPs by the tuber extract in just 5 hours. Similar to this, leaf extract from the long-used medicinal herb *Barleria* was used to make 1-2 nm Pt NPs. There are fewer studies demonstrating the use of plant extracts in the manufacture of Pt NPs than for other types of metallic nanoparticles.^[46]

Scanning electron microscope (SEM) transmission electron microscopy, Fourier transform infrared UV-visible spectroscopy, and EDS profiling have all been used to confirm that Pt NPs were synthesized from the extract of *Fumariae herba*.^[47]

The original NPs had a diameter of 30 nm and were either hexagonal or pentagonal in form. Similarly, *Jatropha gossypifolia* and *Jatropha glandulifera* leaf extracts were used to make 100-200 nm small square and dodecahedron-shaped Pt NPs.^[48] Similar to that, black cumin seed extract was used to make 1-6 nm sphere Pt NPs (*Nigella sativa* L).^[49]

Application of platinum nanoparticles

Potentially innovative materials are being created as a result of nanotechnology. Metallic NPs, in particular, are of interest because of their diverse range of disciplinary uses. Pt NPs have a diverse set of physical, chemical, and biological applications as well. Their unusual physical and chemical features are responsible for their multi-functionality.^[50] The uses of Pt NPs are discussed in the next section.

5.1 Biological applications

Due to their unique electrical and physiochemical characteristics, Pt NPs offer a wide range of biological uses. They have become the most efficient technology biomaterials for applications in imaging, diagnostics, and drug delivery. The sections below describe how Pt NPs can be used in biology.^[51]

5.2 Cancer therapy

5.2.1 Chemical cancer treatment

Although most cancer medications are Pt-based, Pt has been employed in cancer treatment.^[52] The next generation of Pt medicines with changed nano formulations is now being developed. Bacitracin-Pt NPs (Bac– PtNPs) with a spherical form have been created to exhibit strong anti-tumor action in vivo and in vitro. Bac- PtNPs with a spherical shape had cubic crystalline structure and were water stable. Bacitracin's functional groups acted as bonding moieties and aided in the development of Pt NPs. Titanium dioxide and Silicon dioxide nanostructures containing 3–4% Pt have been shown to have anti-cancer activity, and they are now used to treat cancer.^[53] These nanostructures drastically decreased the size and mass of a rat tumor after treatment.^[54] Pt NPs have additionally demonstrated their ability to pass the blood-brain barrier and encourage cellular death in tumors when used in the treatment of brain cancer.^[55]

5.3 Photothermal therapy and radiotherapy

Due to the obvious side effects of chemotherapeutic, malignant tumors are being treated using a more effective and site-specific method. The introduction of Pt NPs makes photothermal therapy non-invasive.^[56] When Pt NPs were exposed to radiation, they increased cellular temperature, resulting in protein denaturation, membrane rupture, DNA/RNA damage, and eventually apoptosis. Researchers mostly used noble NPs, graphite NPs, copper sulphide, and carbon nanotubes for the therapy of cancer. These nanoparticles have the capacity to absorb near-infrared laser light and convert it to heat. Combining Pt NPs' cytocompatibility and catalytic abilities has improved the photothermal treatment. Pt NPs with a size of 5-6 nm is indicated for photothermal therapy.^[57]

5.4 Antibacterial agent

The existence of multidrug-resistant germs poses the biggest risk and challenge to the development of antibacterial medications. In the production of bactericidal agents, metal-based nanoparticles (NPs) like Pd, Cu, Ag, Cu, Au, ZnO and TiO₂ are frequently used. The therapeutic potential of these NPs has been constrained by the unfavorable effects of their use. Platinum ions have been found to have strong antibacterial activity against

E. coli.^[58] On the other hand, it is yet unclear if Pt NPs have antimicrobial potential. Pt NPs have been demonstrated to have a significant bacteriotoxin effect by upregulating intracellular ATP synthesis, limiting growth, and harming DNA.^[59] An enzyme that stops cellular development is expressed more frequently as a result of increased ATP synthesis brought on by exposure to Pt NPs. Pt nanoparticles of small size been shown to be bacteriotoxin at low concentrations. With larger NPs soaking onto the cell membrane and smaller NPs readily penetrating bacterial cells, TEM study showed that size played a critical role.^[60] Additionally, it has been discovered that Pt NPs have antibacterial action against both gram-positive and gram-negative pathogens.^[61] Pt ions can penetrate gramme negative bacteria's peptidoglycan-based cell wall. Pt NPs may

potentially be able to treat drug-resistant *E. coli*.^[62, 63]

5.5 Nanomedicine

Pt NPs are scavengers of oxygen radical's species found in the environment and antioxidants. They are an excellent component of nanozymes for treating diseases brought on by oxidative stress. Saponins were used to functionalize Pt NPs, resulting in saponins-Pt conjugates with substantial antioxidant activity. The conjugates blocked the MAP kinase pathway and regulated the synthesis of macrophage inflammatory protein-2 (MIP-2).^[64] Pt NPs have been shown to inhibit cancer and heart disease due to its in vitro enzyme-like properties. Pt NPs have a high in vivo tolerance due to their stability in acidic cellular vesicle settings.^[65]

Reactive oxygen species (ROS), which can kill cells when exposed to UV-A, X-Ray, or acoustic radiation, have been discovered to be inhibited by platinum nanoparticles (Pt NPs).^[66, 67] Pt NPs are said to mimic the enzymatic activities of catalase and horseradish peroxidase when they are included in dendrimers.^[68] When enclosed within the cavity of apoferritin, Pt NPs have the ability to quench peroxidase and oxidative ions both in suspension cultures fluid and inside the cell. Additionally, it can increase antioxidant activity.^[69]

5.6 Nanodignosis

Pt NPs are frequently employed to make medical diagnoses.^[70] Fluorescence For diagnostic purposes, Pt NPs are utilized in biocompatible bio-imaging probes. Pt nanoparticles are a part of catalytic nanomotors, which are utilized in the construction of molecular devices and the detection of moving particles.^[71] Pt NPs are a suitable source of replacement enzymes that can be used in diagnostic procedures.^[72] high catalytic activity even at high pH, affinity for horseradish peroxidase (HRP) substrates, Stability, temperature and protease resistance are just a few of the benefits of platinum nanoparticles (Pt NPs).

Some of the compounds that can be found in the human body include metal ions, penicillin antibiotics, medications, hydrogen peroxide, glucose, viruses, cholesterol, L-cysteine, choline, acetylcholine, proteins, bacteria, and antibodies.^[73] In the enzyme-linked immunosorbent test for the colorimetric detection of rabbit IgG utilizing the substrate 3,3',5,5'- tetramethylbenzidine (TMB) and peroxide, Pt NPs act as Heparin enzymes when they bind with anti-RigG antibody (H₂O₂). Using encapsulating Pt NPs in a microporous silica matrix, level free DNA is detected.^[74] Utilizing 4-mercaptophenylboronic acid synthesized Au@Pt NPs, the TMB oxidation process is used in the incredibly sensitive test for the identification of *E. coli*. Mercury in the environment has also been detected using sensors based on Pt NPs.^[75]

Polyphenols and flavonoids-based Pt-NPs and their biomedical applications

In-depth discussion is given regarding the biological efficacy of the flavonoid and

polyphenols used in MNP synthesis. The total flavonoids identified in *Alternanthera tremella* and *Coriandrum sativum* leaf extracts^[76] were tested against *P. acnes*, *Malassezia furfur*, and human breast adenocarcinoma cells and were found to be effective as antiacne, antidandruff, and anti-breast cancer agents.^[77, 78]

6.1 Mechanisms of flavonoids-mediated NP synthesis

Flavonoids are a class of polyphenols that includes chalcones, flavones, isoflavones, flavanones, flavanols, and anthocyanins,^[79] among others. Flavonoids have a variety of pharmacological actions, including antioxidant,^[80] anti-inflammatory,^[81] immunomodulatory,^[82] and anti-cancer properties.^[83] Higher plants can be used to extract flavonoids. The human diet has a wide variety of these vibrant fruits and vegetables, including Ericaceae (blueberries), Rutaceae (citrus fruits), Apiaceae (parsley), *Theobroma cacao*'s and Rosaceae (apples),^[84] as well as the renowned delightful product, dark chocolate.^[85] They come in red, orange, or yellow hues (apple), Numerous studies have shown that flavonoids have anticancer properties.^[86]

The flavonoids known as baicalin is found in the roots of *Scutellaria lateriflora* and *Scutellaria baicalinensis*. Berberine nanoparticles with dual-targeted ligands of folate and hyaluronic acid reduced cell survival and inhibited tumor development in human lung cancer A549 and paclitaxel-resistant lung cancer A549/PTX cells in a xenograft mice model of A549/PTX87.^[87,88] Chrysin is a flavonoid that may be extracted from numerous plants, such as *Passiflora* species, and different mushrooms, such as *Pleurotus ostreatus*.^[89] Chrysin has a number of pharmacological effects, including anti-inflammatory, antioxidant, and anticancer properties.^[90] Human hepatocellular carcinoma HepG2 cells' ability to proliferate was decreased by chrysin nanosuspension, indicating that it has anticancer effects.^[90]

Despite being present in several plants, green tea has the largest amount of EGCG.^[91] In both human and animal cells, the flavonoid demonstrated anticancer effects in a variety of ways. The EGCG produced as Ca/Al-NO₃ layered double-hydroxide nanoparticles inhibited colony formation, induced apoptosis, and decreased cell survival in human prostate cancer PC-3 cells.^[92] In another study, it was found that chitosan nanoparticles of EGCG caused human melanoma Mel 928 cells to undergo apoptosis through increased Bcl-2 levels, increased G2/M phase cell cycle arrest, and poly (ADP-ribose) polymerase (PARP) proteolytic processing, initiation of gene transcription and p27, inhibition of cyclin and D3, and decreased Bcl-2 and caspase-3.^[93,94]

Green tea polyphenols, of which EGCG constitutes a major portion, were Nano synthesized using graphene nanosheets and demonstrated anticancer effect on colorectal cancer HT29 and SW48 cells via photothermal death.^[95] There is a lot of the yellow crystal flavonoid luteolin in the vegetables and plants that people eat.^[96] In human MDA-MB-231 cancer cells, phytotherapies containing luteolin decreased cell viability and reduced the expression of Nrf2 and its associated downstream gene Ho1, suggesting anticancer effects.^[97] Additionally, the formulation decreased the sensitivity of cells to the chemotherapeutic drug doxorubicin. Another study found that tumor development and colony formation suppression showed that

luteolin Nano synthesized with PLA- PEG polymer had anticancer properties against TU212 brain and neck epithelial cancer and lung cancer H292 cells. Additionally, similar results were demonstrated in a neck and head cancer xenograft mouse model, which led to tumorigenesis and size reduction.^[98] Another widely dispersed flavonoid is quercetin, which can be found in a variety of foods, including apples. Supplements containing quercetin are used to prevent cancer.^[99] By enhancing apoptosis and reducing mRNA transcription of Nrf2 downstream genes NQO1 and MRP1, phytotomies synthesized with quercetin nano showed anticancer effects in human breast cancer MCF-7 cells, but it had no effect on Nrf2. In a separate study, quercetin Nano, synthesized in lipid nanoparticles, was shown to have anticancer effects on human breast cancer and to prevent the proliferation of cancer cells. tissues MCF- 7.[100, 101,102]

Table 1 Summary of advantages and disadvantages of PtNP synthetic methods

Synt hesi s met hods	Advantages	Disadvantages
Chemical	Accurate control of NP size and shape High reaction yield High versatility in surface chemistry Biocompatible capping/reducing agents and non-toxic solvents Accurate control of NP size and shape High reaction yield Easy post-synthesis functionalization	Use of capping and reducing agents, organic solvents, and surfactants Possible toxicity related to residual reagents and capping agents Possible endotoxin and bacterial contamination Green reagents. Possible endotoxin and bacterial contamination
physical	Purity No solvent contamination No coating contamination	High amount of waste Highly diluted solution Difficult size and shape tunability. Possible NP stability issue in a biological environment
Biological	Green synthesis Absence of toxic reaction solvents Large-scale synthesis	Highly diluted solutions Difficult size and shape tunability Possible endotoxin and bacterial contamination Difficult purification procedures

PtNPs in Nano diagnostics

Pt NPs have generated interest in recent years for biomedical applications. As a brand-new, biocompatible bio- imaging probe, fluorescence Pt nanocrystals have been successfully developed for therapeutic use.^[103] A exciting idea is to build molecule devices and motion-based sensing systems using Pt nanoparticle in catalytic nanomotors. For instance, recently, the movement of chemical driven nanomotors based on basement Au-Pt nanostructures has been used to detect silver ions, DNA, and ribosomal RNA, acting as the basis for new diagnostic procedures. PtNPs have proven to be the best option for replacing the enzyme in diagnostic procedures. PtNPs have a number of benefits, including protease resistance, purification, ease of synthesis, stability, considerable catalytic properties even at high temperatures and pH levels, and affinity for HRP substrate.^[104]

DNA-stabilized PtNPs demonstrated an eight-fold greater affinity for tetramethylbenzidine compared to unsterilized HRP enzyme (TMB). Both an amperometry biosensor and a chemiluminescent interaction of luminol with H₂O₂ mediated by aptamer-PtNP complexes are utilized to detect thrombin.

PtNP-based colorimetric methods have been used to detect DNA, cancer cells, tumor markers, metal ions, penicillin antibiotics, medicines, acetylcholine, cholesterol, hydrogen peroxide, glucose, L-cysteine, choline and proteins, viruses, bacteria, and antibodies. Overall, the synthesis of Pt NPs and a thorough knowledge of their interactions with biological systems could have a substantial impact on the creation of point-of-care systems for the identification of environmental contaminants and biomarkers.

Conclusion

Platinum-based biomolecules have piqued interest for a number of years. For instance, the capacity of platinum-derived pharmaceuticals to eradicate tumour cells has been extensively investigated. Due to their non-selective actions on both cancer and healthy cells, these chemotherapeutic drugs have a number of drawbacks, including substantial dose-dependent acute and chronic adverse effects. The advancement of energy applications, electronics, biotechnology, and medicine delivery has benefited from the creation of nanomaterials with favourable environmental qualities. Platinum nanoparticles (Pt NPs) are a form of metal NP that have many benefits, including anti-tumor and anti-bacterial activity, making them desirable candidates for a variety of medicinal applications. PtNPs' remarkable behaviour in several applications has made methods for their synthesis and characterisation increasingly important. Therefore, polyphenols are good prospects for forthcoming cancer research. Nano formulation methods have been proposed as viable replacements for traditional drug delivery systems because they provide distinctive drug delivery properties. Through a number of processes, nanonization may boost the anti-cancer therapeutic benefits of natural polyphenols, bringing up a brand-new field of oncology study. There is still a lot of work to be done before these drugs may be offered, including evaluating their effectiveness and safety on healthy and cancer-bearing individuals in preclinical and clinical settings. The fact that each of the aforementioned formulations was tested in cell and/or animal cancer models must be emphasised.

Reference

4. Ochwang'i DO, Kimwele CN, Oduma JA, Gathumbi PK, Mbaria JM, Kiama SG. Medicinal plants used in treatment and management of cancer in Kakamega County, Kenya. *J Ethnopharmacol.* 2014; 151: 3:1040–1055.
5. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin.* 2010;60: 5:277–300.
6. Nagavarma B, Yadav HK, Ayaz A, Vasudha L, Shivakumar H. Different techniques for preparation of polymeric nanoparticles – a review. *Asian J Pharm Clin Res.* 2012; 5: 3:16–23.
7. Hede S, Huilgol N. “Nano”: the new nemesis of cancer. *J Cancer Res Ther.* 2006;2: 4:186.
8. Rasouli H, Farzaei MH, Mansouri K, Mohammadzadeh S, Khodarahmi R. Plant cell cancer: may natural phenolic compounds prevent onset and development of plant cell malignancy? A literature review. *Molecules.* 2016;21: 9:1104.
9. Hosein Farzaei M, Bahramsoltani R, Rahimi R. Phytochemicals as adjunctive with conventional anticancer therapies. *Curr Pharm Des.* 2016;22: 27:4201–4218.
10. Yallapu MM, Maher DM, Sundram V, Bell MC, Jaggi M, Chauhan SC. Curcumin induces chemo/radio-sensitization in ovarian cancer cells and curcumin nanoparticles inhibit ovarian cancer cell growth. *J Ovarian Res.* 2010;3:1:1.
11. Bondi M, Craparo E, Picone P, et al. Curcumin entrapped into lipid nanosystems inhibits neuroblastoma cancer cell growth and activates Hsp70 protein. *Curr Nanosci.* 2010;6: 5:439–445.
12. Gupta S, Afaq F, Mukhtar H. Involvement of nuclear factor-kappa B, Bax and Bcl-2 in induction of cell cycle arrest and apoptosis by apigenin in human prostate carcinoma cells. *Oncogene.* 2002;21:23:3727–3738.
13. Emi M, Kim R, Tanabe K, Uchida Y, Toge T. Targeted therapy against Bcl-2-related proteins in breast cancer cells. *Breast Cancer Res.* 2005;7: 6:1.
14. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems.
15. *Colloids Surf B Biointerfaces.* 2010;75: 1:1–18.
16. Doktorovova S, Gokce E, Ozyazici M, Souto E. Lipid matrix nanoparticles: pharmacokinetics and biopharmaceutics. *Curr Nanosci.* 2009;5: 3:358–371.
17. Fang X-B, Zhang J-M, Xie X, et al. pH-sensitive micelles based on acid-labile pluronic F68–curcumin conjugates for improved tumor intracellular drug delivery. *Int J Pharm.* 2016;502: 1–2:28–37.
18. Daniel MC, Astruc D. Gold nanoparticles: assembly, supramolecular chemistry, quantum-size-related properties, and applications toward biology, catalysis, and nanotechnology. *Chem. Rev.* 2004;104: 1:293-346.
19. Leong GJ, Schulze MC, Strand MB, Maloney D, Frisco SL, Dinh HN et al., Shape-directed platinum nanoparticle synthesis: nanoscale design of novel catalysts.. *Appl. Organomet. Chem.* 2014;28: 1:1-7.
20. Paschos O, Choi P, Efstathiadis H, Haldar P. Synthesis of platinum nanoparticles by aerosol assisted deposition method. *Thin Solid Films.* 2008;516: 12:3796-801.
21. Rakshit RK, Bose SK, Sharma R, Budhani RC, Vijaykumar T, Neena SJ et al.,

- Correlations between morphology, crystal structure, and magnetization of epitaxial cobalt-platinum films grown with pulsed laser ablation. *J. Appl. Phys.* 2008;103: 2:023915.
22. Choi, I.D., Lee, H., Shim, Y.-B., Lee, D., A one-step continuous synthesis of carbon-supported Pt catalysts using a flame for the preparation of the fuel electrode. *Langmuir*, 2010; 26; 11212–11216.
 23. Ke X, Bittencourt C, Bals S, Van Tendeloo G. Low-dose patterning of platinum nanoclusters on carbon nanotubes by focused-electron-beam-induced deposition as studied by TEM. *Beilstein J. Nanotechnol.*, 2013; 4; 77.
 24. Dhand C, Dwivedi N, Loh XJ, Ying ANJ, Verma NK, Beuerman RW et al., Methods and strategies for the synthesis of diverse nanoparticles and their applications: A comprehensive overview. *RSC Adv.*, 2015; 5; 105003–105037.
 25. Scaramuzza S, Zerbetto M, Amendola V. Synthesis of gold nanoparticles in liquid environment by laser ablation with geometrically confined configurations: Insights to improve size control and productivity. *J. Phys. Chem. C*, 2016; 120; 9453–9463.
 26. Correard F, Maximova K, Esteve MA, Villard C, Roy M, Al-Kattan A et., Gold nanoparticles prepared by laser ablation in aqueous biocompatible solutions: Assessment of safety and biological identity for nanomedicine applications. *Int. J. Nanomed.* 2014; 9; 5415.
 27. Yanson AI, Rodriguez P, Garcia-Araez N, Mom RV, Tichelaar FD, Koper M. Cathodic corrosion: A quick, clean, and versatile method for the synthesis of metallic nanoparticles. *Angew. Chem. Int. Ed.*, 2011; 50; 6346–6350.
 28. Dhand C, Dwivedi N, Loh XJ, Jie Ying AN, Verma NK, Beuerman RW. Methods and Strategies for the Synthesis of Diverse Nanoparticles and Their Applications: a Comprehensive Overview. *RSC Adv.* 2015; 5:127.
 29. 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. *Appl. Nanosci.* 2021; 11 :4:1303–1312.
 30. Fedorova EA, Stadnichenko AI, Slavinskaya EM, Kibis LS, Stonkus OA, Svintsitskiy DA. A Study of Pt/Al₂O₃ Nanocomposites Obtained by Pulsed Laser Ablation to Be Used as Catalysts of Oxidation Reactions. *J. Struct. Chem.* 2020; 61:2: 316–329.
 31. N Madlum K, Jasim Khamees E, Abdulridha Ahmed S, Akram Naji R. Antimicrobial and Cytotoxic Activity of Platinum Nanoparticles Synthesized by Laser Ablation Technique. *J. Nanostructures.* 2021; 11 :1:13–19.
 32. Jameel MS, Aziz AA, Dheyab MA. Impacts of Various Solvents in Ultrasonic Irradiation and green Synthesis of Platinum Nanoparticle. *Inorg. Chem.* 2021; Commun128.; 108565.
 33. Maicu M, Schmittgens R, Hecker D, Glöß D, Frach P, Gerlach G. Synthesis and Deposition of Metal Nanoparticles by Gas Condensation Process. *J. Vacuum Sci. Technology A: Vacuum, Surf.* 2014; 32
 34. :2: 02B113.
 35. Park KW, Choi JH, Kwon BK, Lee SA, Sung YE. Chemical and electronic effects of Ni in Pt/Ni and Pt/Ru/Ni alloy nanoparticles in methanol electrooxidation. *J. Phys. Chem.*

- B. 2002; 106: 1869.
36. Mandal S, Vishvakarma P. Nanoemulgel: A Smarter Topical Lipidic Emulsion-based Nanocarrier. *Indian J of Pharmaceutical Education and Research*. 2023;57(3s):s481-s498.
 37. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of *Mallotus philippensis*. *Journal of Drug Delivery and Therapeutics*. 2022 Sep 20;12(5):175-81.
 38. Singh A, Mandal S. Ajwain (*Trachyspermum ammi* Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. *International Journal of Recent Advances in Multidisciplinary Topics*. 2021 Jun 9;2(6):36-8.
 39. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. *Plant Arch*. 2021;21:1345-54.
 40. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. *Journal of Pharmaceutical and Biological Sciences*. 2021 Jul 1;9(2):88-94.
 41. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. *Int J Sci Res Develop*. 2021;1:187-93.
 42. Ali S, Farooqui NA, Ahmad S, Salman M, Mandal S. *Catharanthus roseus* (sadabahar): a brief study on medicinal plant having different pharmacological activities. *Plant Archives*. 2021;21(2):556-9.
 43. Mandal S, Jaiswal DV, Shiva K. A review on marketed *Carica papaya* leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. *International Journal of Pharmaceutical Research*. 2020 Jul;12(3).
 44. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. *Solanum Nigrum* Linn: An Analysis Of The Medicinal Properties Of The Plant. *Journal of Pharmaceutical Negative Results*. 2023 Jan 1:1595-600.
 45. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis Of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. *Journal of Pharmaceutical Negative Results*. 2022 Dec 31:9189-98.
 46. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. *European Journal of Molecular & Clinical Medicine*.;10(01):2023.
 47. Chawla A, Mandal S, Vishvakarma P, Nile NP, Lokhande VN, Kakad VK, Chawla A. Ultra-Performance Liquid Chromatography (Uplc).
 48. Mandal S, Raju D, Namdeo P, Patel A, Bhatt AK, Gupta JK, Haneef M, Vishvakarma P, Sharma UK. Development, characterization, and evaluation of *rosa alba* l extract-loaded phytosomes.
 49. Mandal S, Goel S, Saxena M, Gupta P, Kumari J, Kumar P, Kumar M, Kumar R, Shiva K. Screening of *catharanthus roseus* stem extract for anti-ulcer potential in wistar rat.
 50. Shiva K, Kaushik A, Irshad M, Sharma G, Mandal S. Evaluation and preparation: herbal gel containing *thuja occidentalis* and *curcuma longa* extracts.

51. Thirumurugan A, Aswitha P, Kiruthika C, Nagarajan S, Nancy CA. Green synthesis of platinum nanoparticles using *Azadirachta indica*- an eco-friendly approach. *Mater Lett.* 2016; 170: 175-178.
52. Dobrucka R. Biofabrication of platinum nanoparticles using *Fumariae herba* extract and their catalytic properties. *Saudi J. Biol. Sci.* 2019; 26: 31-37.
53. Jeyapaul U, Kala MJ, Bosco AJ, Piruthiviraj P, Easuraja M. An Eco-friendly Approach for Synthesis of Platinum Nanoparticles using Leaf Extracts of *Jatropha Gossypifolia* and *Jatropha Glandulifera* and its Antibacterial Activity. *Orient. J. Chem.* 2018; 34: 783-790.
54. Aygun A, Gülbagca F, Ozer LY, Ustaoglu B, Altunoglu YC, Baloglu MC et al., Biogenic platinum nanoparticles using black cumin seed and their potential usage as antimicrobial and anticancer agent. *J. Pharmaceut. Biomed.* 2020; 179: 112961.
55. Stepanov AL, Golubev AN, Nikitin SI, Osin YN. A Review on the fabrication and properties of platinum nanoparticles. *Rev. Adv. Mater Sci.* 2014; 38: 160-175.
56. Pedone D, Moglianetti M, De Luca E, Bardi G and Pompa PP. Platinum nanoparticles in nanobiomedicine. *Chem. Soc. Rev.* 2017; 46: 4951-4975.
57. Johnstone TC, Suntharalingam K and Lippard SJ. The next generation of platinum drugs: targeted Pt
58. (II) agents, nanoparticle delivery, and Pt (IV) prodrugs. *Chem. Rev.* 2016; 116: 3436-3486.
59. Yin T, Wang Z, Li X, Li Y, Bian K, Cao W, He Y, Liu H, Niu K, Gao D. Biologically inspired self- assembly of bacitracin-based platinum nanoparticles with anti-tumor effects. *New J. Chem.* 2017; 41: 2941-2948.
60. Lopez T, Figueras F, Manjarrez J, Bustos J, Alvarez M, Silvestre-Albero J et., Catalytic nanomedicine: a new field in antitumor treatment using supported platinum nanoparticles. In vitro DNA degradation and in vivo tests with C6 animal model on Wistar rats. *Eur. J. Med. Chem.* 2010; 45: 1982-1990.
61. Prasek M, Sawosz E, Jaworski S, Grodzik M, Ostaszewska T, Kamaszewski M et al., Influence of nanoparticles of platinum on chicken embryo development and brain morphology. *Nanoscale Res. Lett.* 2013; 8: 1-9.
62. Au L, Zheng D, Zhou F, Li ZY, Li X, Xia Y. A quantitative study on the photothermal effect of immuno gold nanocages targeted to breast cancer cells. *ACS nano.* 2008;2(8):1645-52.
63. Gharibshahi E, Saion E. Influence of dose on particle size and optical properties of colloidal platinum nanoparticles. *Int. J. Mol. Sci.* 2012; 13: 14723-14741.
64. Beyth N, Hourri-Haddad Y, Domb A, Khan W, Hazan R. Alternative antimicrobial approach: nano- antimicrobial materials. *Evid. Based Complement. Alternat. Med.* 2015; 246012.
65. Zhao Y, Ye C, Liu W, Chen R, Jiang X. Tuning the composition of AuPt bimetallic nanoparticles for antibacterial application. *Angew. Chem. Int. Ed.* 2014; 53: 8127-8131.
66. Kebede MA, Imae T, Wu CM, Cheng KB. Cellulose fibers functionalized by metal nanoparticles stabilized in dendrimer for formaldehyde decomposition and antimicrobial activity. *Chem. Eng. J.* 2017; 311: 340-347.

67. Gopal J, Hasan N, Manikandan M, Wu HF. Bacterial toxicity/compatibility of platinum nanospheres, nanocuboids and nanoflowers. *Sci. Rep.*, 2013; 3: 1260.
68. Konieczny P, Goralczyk AG, Szmyd R, Skalniak L, Koziel J, Filon FL et al. Effects triggered by platinum nanoparticles on primary keratinocytes. *Int. J. Nanomed.* 2013; 8: 3963.
69. Bharathan S, Sundaramoorthy NS, Chandrasekaran H, Rangappa G, ArunKumar G, Subramaniyan SB et al. Sub lethal levels of platinum nanoparticle cures plasmid and in combination with carbapenem, curtails carbapenem resistant. *Escherichia coli. Sci. Rep.* 2019; 9(1): 5305.
70. Kim YJ, Kim DB, Lee YH, Choi SY, Park JS, Lee SY et al. Effects of nanoparticulate saponinplatinum conjugates on 2, 4-dinitrofluorobenzene-induced macrophage inflammatory protein-2 gene expression via reactive oxygen species production in RAW 264.7 cells. *BMB Rep.* 2009; 42: 304-309.
71. Jawaid P, Rehman MU, Hassan MA, Zhao QL, Li P, Miyamoto Y et al. Effect of platinum nanoparticles on cell death induced by ultrasound in human lymphoma U937 cells. *Ultrason. Sonochem.* 2016; 31: 206-215.
72. Jawaid P, Rehman MU, Yoshihisa Y, Li P, Zhao Q, Hassan MA et al. Effects of SOD/ catalasemimetic platinum nanoparticles on radiation-induced apoptosis in human lymphoma U937 cells. *Apoptosis* 2014; 19: 1006-1016.
73. Ju Y, Kim J. Dendrimer-encapsulated Pt nanoparticles with peroxidasemimetic activity as biocatalytic labels for sensitive colorimetric analyses. *Chem. Commun.* 2015; 51: 13752-13755.
74. Clark A, Zhu A, Sun K, Petty HR. Cerium oxide and platinum nanoparticles protect cells from oxidant-mediated apoptosis. *J. Nanopart. Res.* 2011; 13: 5547-5555.
75. Kawasaki H, Yamamoto H, Fujimori H, Arakawa R, Inada M, Iwasaki Y. Surfactant-free solution synthesis of fluorescent platinum subnanoclusters. *Chem. Commun.* 2010; 46: 3759-3761.
76. Sun Y, Wang J, Li W, Zhang J, Zhang Y, Fu Y. DNA-stabilized bimetallic nanozyme and its application on colorimetric assay of biothiols. *Biosens. Bioelectron.* 2015; 74: 1038-1046.
77. Hu X, Saran A, Hou S, Wen T, Ji Y, Liu W et al. Rodshaped Au@PtCu nanostructures with enhanced peroxidase-like activity and their ELISA application. *Chin. Sci. Bull.* 2014; 59: 2588-2596.
78. Chen T, Cheng Z, Yi C, Xu Z. Synthesis of platinum nanoparticles templated by dendrimers terminated with alkyl chain. *Chem. Comm. J.* 2018; 54: 9143-9146.
79. He SB, Wu GW, Deng HH, Liu AL, Lin XH, Xia XH et al. Choline and acetylcholine detection based on peroxidase-like activity and protein antifouling property of platinum nanoparticles in bovine serum albumin scaffold. *Biosens. Bioelectron.* 2014; 62: 331-336.
80. Yang ZH, Zhuo Y, Yuan R, Chai YQ. A nanohybrid of platinum nanoparticles-porous ZnO-hemin with electrocatalytic activity to construct an amplified immunosensor for detection of influenza. *Biosens. Bioelectron.* 2016; 78: 321-327.
81. Wang Z, Yang X, Feng J, Tang Y, Jiang Y, He N. Label-free detection of DNA by combining gated mesoporous silica and catalytic signal amplification of platinum

- nanoparticles. *Analyst*. 2014; 139: 6088-6091.
82. Sathishkumar P, Gu FL, Zhan Q, Palvannan T, Yusoff AR. Flavonoids mediated 'green' nanomaterials: A novel nanomedicine system to treat various diseases current trends and future perspective. *Mater Lett* 2018; 210:26-30.
83. Sathishkumar P, Preethi J, Vijayan R, Mohd Yusoff AR, Ameen F, Suresh S, *et al.* Anti-acne, anti- dandruff and anti-breast cancer efficacy of green synthesised silver nanoparticles using *Coriandrum sativum* leaf extract. *J Photochem Photobiol B* 2016; 163:69-76.
84. Sathishkumar P, Vennila K, Jayakumar R, Yusoff AR, Hadibarata T, Palvannan T, *et al.* Phyto- synthesis of silver nanoparticles using *Alternanthera tenella* leaf extract: An effective inhibitor for the migration of human breast adenocarcinoma (MCF-7) cells. *Bioprocess Biosyst Eng* 2016; 39:651-9.
85. Williams CA, Grayer RJ. Anthocyanins and other flavonoids. *Nat Prod Rep*. 2004;21:4:539–573.
86. Parhiz H, Roohbakhsh A, Soltani F, Rezaee R, Iranshahi M. Antioxidant and anti-inflammatory properties of the citrus flavonoids hesperidin and hesperetin: an updated review of their molecular mechanisms and experimental models. *Phytother Res*. 2015;29:3:323–331.
87. Leyva-López N, Gutierrez-Grijalva EP, Ambriz-Perez DL, Heredia JB. Flavonoids as cytokine modulators: a possible therapy for inflammation-related diseases. *Int J Mol Sci*. 2016;17:6:921.
88. Peluso I, Miglio C, Morabito G, Ioannone F, Serafini M. Flavonoids and immune function in human: a systematic review. *Crit Rev Food Sci Nutr*. 2015;55:3:383–395.
89. Sak K. Cytotoxicity of dietary flavonoids on different human cancer types. *Pharmacogn Rev*. 2014;816:122.
90. Ayoub M, de Camargo AC, Shahidi F. Antioxidants and bioactivities of free, esterified and insoluble- bound phenolics from berry seed meals. *Food Chem*. 2016; 197:221–232.
91. Serafini M, Bugianesi R, Maiani G, Valtuena S, De Santis S, Crozier A. Plasma antioxidants from chocolate. *Nature*. 2003; 6952:1013.
92. Le Marchand L. Cancer preventive effects of flavonoids – a review. *Biomed Pharmacother*. 2002;56:6:296–301.
93. Xie Y, Song X, Sun X, *et al.* Identification of baicalein as a ferroptosis inhibitor by natural product library screening. *Biochem Biophys Res Commun*. 2016;473:4:775–780.
94. Liu A, Wang W, Fang H, *et al.* Baicalein protects against polymicrobial sepsis-induced liver injury via inhibition of inflammation and apoptosis in mice. *Eur J Pharmacol*. 2015;748:45–53.
95. Anandhi R, Annadurai T, Anitha TS, *et al.* Antihypercholesterolemic and antioxidative effects of an extract of the oyster mushroom, *Pleurotus ostreatus*, and its major constituent, chrysin, in Triton WR- 1339-induced hypercholesterolemic rats. *J Physiol Biochem*. 2013;69:2:313–323.
96. Rashid S, Nafees S, Vafa A, *et al.* Inhibition of precancerous lesions development in kidneys by chrysin via regulating hyperproliferation, inflammation and apoptosis at pre clinical stage. *Arch Biochem Biophys*. 2016;606:1–9.

97. Li X, Huang J-M, Wang J-N, Xiong X-K, Yang X-F, Zou F. Combination of chrysin and cisplatin promotes the apoptosis of Hep G2 cells by up-regulating p53. *Chem Biol Interact.* 2015;232:12–20.
98. Shin YS, Kang SU, Park JK, et al. Anti-cancer effect of (–)-epigallocatechin-3-gallate (EGCG) in head and neck cancer through repression of transactivation and enhanced degradation of β -catenin. *Phytomedicine.* 2016;23:12:1344–1355.
99. Shafiei SS, Solati-Hashjin M, Samadikuchaksaraei A, Kalantarinejad R, Asadi-Eydivand M, Abu Osman NA. Epigallocatechin gallate/layered double hydroxide nanohybrids: preparation, characterization, and in vitro anti-tumor study. *PLoS One.* 2015;10(8):e0136530.
100. Siddiqui IA, Bharali DJ, Nihal M, et al. Excellent anti-proliferative and pro-apoptotic effects of (–)- epigallocatechin-3-gallate encapsulated in chitosan nanoparticles on human melanoma cell growth both in vitro and in vivo. *Nanomedicine.* 2014;10(8):1619–1626.
101. Narayanan S, Mony U, Vijaykumar DK, Koyakutty M, Paul-Prasanth B, Menon D. Sequential release of epigallocatechin gallate and paclitaxel from PLGA-casein core/shell nanoparticles sensitizes drug-resistant breast cancer cells. *Nanomedicine.* 2015;11(6):1399–1406.
102. Abdolahad M, Janmaleki M, Mohajerzadeh S, Akhavan O, Abbasi S. Polyphenols attached graphene nanosheets for high efficiency NIR mediated photodestruction of cancer cells. *Mater Sci Eng C Mater Biol Appl.* 2013;33:3:1498–1505.
103. Meng G, Chai K, Li X, Zhu Y, Huang W. Luteolin exerts pro-apoptotic effect and anti-migration effects on A549 lung adenocarcinoma cells through the activation of MEK/ERK signaling pathway. *Chem Biol Interact.* 2016;257:26–34.
104. Sabzichi M, Hamishehkar H, Ramezani F, et al. Luteolin-loaded phytosomes sensitize human breast carcinoma MDA-MB 231 cells to doxorubicin by suppressing Nrf2 mediated signalling. *Asian Pac J Cancer Prev.* 2014;15: 13: 5311–5316.
105. Majumdar D, Jung KH, Zhang H, et al. Luteolin nanoparticle in chemoprevention: in vitro and in vivo anticancer activity. *Cancer Prev Res (Phila).* 2014;7:1:65–73.
106. Murakami A, Ashida H, Terao J. Multitargeted cancer prevention by quercetin. *Cancer Lett.* 2008;269:2:315–325.
107. Minaei A, Sabzichi M, Ramezani F, Hamishehkar H, Samadi N. Co-delivery with nano-quercetin enhances doxorubicin-mediated cytotoxicity against MCF-7 cells. *Mol Biol Rep.* 2016;43:2:99–105.
108. Rezaei-Sadabady R, Eidi A, Zarghami N, Barzegar A. Intracellular ROS protection efficiency and free radical-scavenging activity of quercetin and quercetin-encapsulated liposomes. *Artif Cells Nanomed Biotechnol.* 2016;44:1:128–134.
109. Tanaka SI, Miyazaki J, Tiwari DK, Jin T, Inouye Y, *Chem., Int. Ed.*, 2011; 50; 431–435.
110. Y. Fu, X. Zhao, J. Zhang and W. Li, *J. Phys. Chem. C*, 2014; 118; 18116–18125.