REVIEW ARTICLE

Tannin Loaded Nanoparticles and its Therapeutic Applications – A Comprehensive Review

M. Narmadha, M. Surendar, S. Sathesh Kumar*

Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai, Tamil Nadu, India

Abstract

Cancer is one stage of a condition that occurs due to uncontrolled growth of cells and is caused by many factors ranging from genetic mutations to different lifestyle factors such as exposure to chemicals, radiation, tobacco usage, and physical exercise so on. They are so many surgeries and therapies treatment is available for cancer but this treatment only reduces the symptoms of the disease, and complete cannot be expected. These chemical drugs are more prominent to destroy cancer cells in our body but they increase side effects includes nausea and vomiting it will lead to damage to the vital organs such as the kidney, heart, and lung. Phytoconstituents are one of the promising treatment prospects for minimizing the side effects and to improve effectiveness of the chemotherapeutic drugs and it is used for natural products, which have been traditionally used to treat many types of cancer. Many plant extracts were described that pharmacological activities are characteristic of their phytoconstituents includes tannins, flavonoids, saponin, alkaloids, and terpenes. Tannins are secondary metabolites of plants. Tannins are popularly known as natural polyphenolic molecules possess many pharmacological actions such as antibacterial, anti-cancer, antioxidant, chemo-preventive, and anti-inflammatory actions. One of the problems that present the use of tannins is their poor bioavailability. Nanoparticles have been introduced a different type of formulation and evaluation methods to identify their bioavailability of a drug. The present study concentrates on tannin-loaded nanoformulations to increase the bioavailability in the treatment of cancer.

Key words: Cancer, Nanoparticles, Phytoconstituents, Polymers, Tannins

INTRODUCTION

Cancer is many types of disease that begins in the cells and leads to uncontrolled growth of cells. In 2012, the more number of cancers are raising faster rate and 1.41 million new cancer cases were identified worldwide.[1] In 2020, cancer death was increased by 12 million. Meanwhile, in the Globocan report, the most common type of cancer, which caused more number mortality in lung, stomach, liver, and brain cancer. They are so many treatments are available in cancer such as surgery, radiation, chemotherapy, and so on. This chemotherapy has many side effects it will lead to harm to the organs such as the kidney, heart, and lung.[2]

Phytoconstituents are secondary metabolites it naturally occurs from plant sources. Application of nanoparticles in phytoconstituents will increase therapeutic efficacy and bioavailability and biocompatibility of chemotherapeutic agents and it also reduces the hazard of cancer.[3] Phytoconstituents have some physiological activities includes antioxidant properties, anti-inflammatory properties, anti-cancer properties, and anti-tumor properties. It is responsible for color, organoleptic properties, and smell. Phytoconstituents are bioactive compounds; it protects the plants from infection, infestation, fungi, and parasites. The consumption of natural sources of phytoconstituents-rich food provides several beneficial effects that promote human health. They are so many phytoconstituents that are present in secondary metabolic includes tannins, flavonoids, saponins, catechin, epigallocatechin (EGC), and polyphenols.[4]

Address for correspondence:
S. Sathesh Kumar, Department of Pharmaceutics, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies, Pallavaram, Chennai - 600 117, Tamil Nadu, India.
E-mail: sathesh2000@gmail.com

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Tannins are usually denoted as plant polyphenols, but the tannin name was originally given to plant extracts showing astringency, without recognizing their chemical structures. For a large scale of biological processes, there are several natural substances.[5] In particular, polyphenols, which have been researched for many years and are still a very active area of study because of their prospective use in medicine, are all considerable concerns. Polyphenols have aromatic rings and hydroxyls group that differs in the sum of aromatic rings and the position of phenolic groups. In several clinical states, including cancer, coronary, and neurodegenerative diseases, polyphenols have different biological functions and it is used for beneficial effects. The physiological functions of polyphenols are antioxidant properties that affect the intracellular redox status has been proposed as the molecular mechanism of action.[6] Tannins show a variety of different bioactivities under this general character, which also has antioxidant properties. More emphasis has been focused on tannins recently with the use of certain herbs such as *Emblica phyllanthus* and *Sanguisorba officinalis*, as well as red wine with major tannins. Tannins have some useful effects, such as inhibition of lipid peroxidation, as well as antiviral, antibacterial, and antimutagenic effects, which have been verified. The anti-cancer ability of tannins, however, remains largely uncharted. Plant phenolics are generally associated with the defense of pathogens, rodents, and predators from ultraviolet radiation or violence, as well as with plant colors. In all plant organs, they are omnipotent and thus an essential part of the human diet. Widespread constituents of plant foods (fruits, grains, cereals, olives, legumes, chocolate, etc.) and drinks (tea, coffee, beer, wine, etc.) are phenolics and are partly responsible for the overall organoleptic properties of plant foods. Tannins are secondary metabolites of plants that may be hydrolyzable or condensed.[7] Hydrolyzable tannins are classified into two types they are gallotannins and ellagitannins. Hydrolyzable tannins are mainly al-glucose, are simply esters of gallic acid and polyolas a base unit, gallotannins contain gallic acid, while ellagitannins have subunits of gallic acid and hexahydroxydiphenol moieties.[8] Hydrolyzable tannins are derivatives of polygalloyl glucose and/or polygalloyl quinic acid that contain between three and 12 residues of gallic acid per molecule.[9]

CONDENSED TANNINS

Condensed tannins are also called proanthocyanins; it contains oligomers and polymers and flavan-3-nuclei. Condensed tannins are derived from flavan-3-nuclei includes (+)-catechin, (−)-epicatechin, (+)-gallocatechin, EGC, and (−)-EGC gallate (EGCG).The group of condensed tannins is O-methylation, C-methylation, O-glycosylation, and O-galloylation.[10] The other condensed tannins are proanthocyanins. Proanthocyanidins are found in flowers, nuts, vegetables, bark, and seeds of different plants. Their astringency protects plants against pests and pathogens. Epicatechin, Catechin, and EGC -3-gallate are the main compounds for proanthocyanidins.[11] Biosynthesis of proanthocyanidin is a primary step for leucoanthocyanidin which involves reductase catalyzes catechin synthesis. Procyanidins are also called prodelphinidins such as catechin, EGC -3-gallate, and epicatechin. Anthocyanins have the amount of sugars from anthocyanidins.[12,13] Proanthocyanidins produce anthocyanins which are boiling in acidic media. The product of tannic pathways of proanthocyanidins and anthocyanins is concerned with the same metabolic intermediates.[14,15] To form colloidal solutions, tannins dissolve in water, but their solubility varies with their polymerization.[16] Alcohol and acetone are soluble in them. The consistency of the aqueous solution varies with the composition and is usually mild, for example, tannin such as geraniin decomposes to gallic acid, ellagic acid, and corilaginic acid within 30 min during extraction with boiling water (i.e. in the state of decoction). Tannin interacts with ferric chloride, as all phenols. Hydrolyzable tannins are glucose polyesters and they eliminate gallic acid sugar, and hexahydrodiphenic acid.[17,18]

Nanotechnology is multidisciplinary research based on nanoparticles they are a wide-range of properties. Nanoparticles show unique and novel properties in the size ranges from 1 to 100 nm.[19] Nanoparticles have their high surface energy, a large amount of surface atoms, high target specificity, and high solubility, and nanoscale materials show their special properties. Nanoparticles are used to increase the bioavailability and solubility of drugs.[20]

Polymeric nanoparticles also show unique and novel properties in the size ranges from 10 to 1000 nm where the substance is dissolved, suspended, encapsulated, or bound to a matrix of nanoparticles. Nanoparticles, nanospheres, or nanocapsules may be obtained, depending on the method of manufacturing. In a wide variety of fields, includes computing, photonics, material processing, sensing, medicine, biotechnology, pollution control, and environmental technologies, the area of polymer nanoparticles (PNPs) is increasingly expanding and plays an important role. By simple manipulation to train carriers to bring the drugs to a particular target, PNPs are ensuring drug delivery vehicles; such an advantage enhances drug safety. Their nanometer-size facilitates efficient permeation and stabilization in the bloodstream across cell membranes. With the improvement of countless and varying molecular designs, polymers are very convenient materials that can be combined for many possible medical uses into special NP constructs.[21]

Non-biodegradable and biodegradable NPs are also used to develop the treatment rate of many water-soluble/insoluble pharmaceutical drugs and biological effects and it also increasing bioavailability, solubility, and retention time. Patient risks and toxicity risks are minimized by the NP-drug formulation. Nanoencapsulation (nanomedicines) improves the potency, accuracy, and tolerability, and therapeutic effects of the pharmaceutical drugs are involved. Those

nanomedicines have many uses in terms of protection against premature degradation and connection with the biological system: Improvement of absorption into the selected tissue, bioavailability, survival time, and increases intracellular penetration. Polymers are used in NPs such as chitosan, sodium alginate, poly-co-glycolic acid, polyanhydrides, polyvinyl alcohol, polyacrylic acid, and polymethacrylic acid.[22]

PHARMACEUTICAL AND MEDICINAL APPLICATIONS

Many preceding examinations on the pharmaceutical use of tannins have been reported that anti-cancer, anti-tumor, and antioxidant properties are particularly well recorded. The antiviral properties are also well recorded for various kinds of 12 different hydrolysable tannins and proanthocyanidins, anthocyanins, and condensed tannins.[23] Tannins will give the best antiviral response when they have lower least inhibitory concentration (minimum inhibitory concentration [MIC]) values. MIC means the least inhibitory concentration. The different tannins that have the least cytotoxic concentration (microcrystalline cellulose) to rectify the microscopic change of natural cell morphology were also found. Poor toxicity in tannins should be analyzed by patients' cells. The efficacy of different tannins that have polyphenolic can be precious against different kinds of viruses. While many studies have examined that many tannins are collected from various plant extracts it has anti-cancer properties and these tannins are also used for many medical applications. Condensed tannins are also called proanthocyanins, it is used to cure intestinal problems.[24]

TANNIN LOADED NANO FORMULATIONS

Abdelhady *et al*. reported by Poly (lactic-co-glycolic acid) (PLGA) NPs incorporated with *Callistemon citrinus* phenolics showed anti-cancer properties against three breast cancer cell lines. *Callistemon citrinus* has 34 species that are generally grown in many parts of the world. *Callistemon citrinus* is used for many treatments such as gastrointestinal disorders, infectious diseases, and many pains. *Callistemon citrinus* is bioactive compounds that include phenolic antioxidants, tannins, flavanols, flavanones, and terpenoids. *Callistemon citrinus* has many medicinal properties against cardiovascular diseases, inflammation, anti-cancer, and antidiabetic activities. Nanotechnology is used to deliver different therapeutic drugs to a specific site of action. Polylactic-co-glycolic acid (PLGA) has many advantages when compared to other techniques. PLGA has been selected because of its benefits in pharmaceutical research. PLGA NPs can increase biodegradability, bioavailability, and non-toxicity. PLGA NPs were fabricated with *Callistemon citrinus* and berberine is prepared by the nanoprecipitation method. *Callistemon citrinus* and berberine shown their effectiveness against very invasive MDA-MB 231(Human Mammary Carcinoma), slightly invasive Michigan Cancer Foundation (MCF)-10A (nontumorigenic epithelial cell line), and minimally invasive MCF -7 breast cancers.[25] PLGA-loaded *Callistemon citrinus* polyphenolic is used to treat breast cancer. The combination of *Callistemon citrinus* extracts with berberine will increase their cytotoxic in encapsulated forms. *Callistemon citrinus* and berberine loaded PLGA NPs were evaluated by particle size, stability of PLGA NPs, *in vitro* studies, and scanning electron spectroscopy (SEM).[26,27]

Tannic acid is incorporated with modified pectin to form tannic acid cross-linked nano complexes to increase the targeted delivery of medications in pancreatic cancer cells. Pancreatic cancer is a harmful cause of disease. In a later period, pancreatic cancer has been diagnosed successfully but surgeries are more difficult to perform, chemotherapy is a suitable one nowadays for cancer treatment.[28] The present chemotherapies have some side effects include drug resistance and low therapeutic efficiency. The delivery of carriers is more efficient than chemotherapies. The carrier should be biocompatible, biodegradable, and low immunogenic profile. Nanotechnology-based carriers have many advantages include it will improve bioavailability, solubility, and retention time.[29] Where NP technology also increases targeting capability and reduces side effects and dose frequency. Pectin has excellent water-soluble properties and is an appropriate transporter for drug delivery system applications. Pectin is generally occurring from polysaccharides and it is derived from apple and citrus and also reduces the digestive problem, gastrointestinal problem, and metabolic disorders problem.[30] Pectin nanocomplexes are appropriate for colon targeting and tumor cells and it is a more beneficial treatment for pancreatic cancer. Cross-linking agents are $Ca^{2+}$and Zn^{2+} used in pectin gel particles. In this method, tannic acid is incorporated with modified pectin to form nanocomplexes of tannic acid. Tannic acid is used as cross-linked nanocomplexes to improve bioavailability and increase entrapment efficiency. Pectin tannic acid nanocomplex also passes therapeutic agents such as gemcitabine, 5-FU (5-Fluorouracil), and IRI (irinotecan), for increased therapeutic activity in pancreatic cells. Pectin tannic acid nanocomplex was prepared by self-assembly method. MPT-NC (modified pectin and tannic acid) was evaluated by SEM (scanning electron microscopy), transmission electron microscopy (TEM), Fourier transform infrared (FTIR), and particle size, *in vitro* drug profile.[31]

Tannic acid-loaded paclitaxel NPs are used for improved anti-cancer properties in breast cancer cells. Paclitaxel is derived from taxes brevifolia and it is used to cure many ovarian, pancreatic, and breast cancer lung carcinomas. In this method, paclitaxel is used to cure breast cancer. Paclitaxel has adverse side effects and low pharmacodynamics parameters so we are combing the eleven pharmaceutical excipients with the paclitaxel nanoformulation with help of the self-assembly method. The 11 pharmaceutical excipients are ascorbic acid,

β-cyclodextrin, carboxymethyl-β-cyclodextrin, mannitol, hydroxypropyl β-cyclodextrin, tocopherol, sorbitol, tannic acid, and tween 80.[32] In this method, we have screened 11 pharmaceutical excipients that are water-soluble molecules such as ascorbic acid, β-cyclodextrin, carboxymethyl-β-cyclodextrin, Mannitol, Hydroxypropyl-β-cyclodextrin, tocopherol, sorbitol, tannic acid, tween 80, and tannic acid paclitaxel (TAP) have reached the best nanoformulation. The 11 pharmaceutical excipients were prepared by the self-assembly technique. In these 11 pharmaceutical excipients, tannic acid-loaded paclitaxel NPs have more therapeutic effects in breast cancer. The drug is loaded with a self-assembly technique. TAP NPs have greater β-tubulin stabilization in BC (breast cancer) cells for apoptosis. The tannic acid provides better paclitaxel NP self-assembly development versus strong hydrogen bonding the ten furthermore polymer excipients are tested. Pharmaceutical excipients and paclitaxel was evaluated by zeta potential, particle size, quenching assay, biocompatibility, liquid chromatography/mass spectrometry (LC-MS/MS) analysis (LC-tandem MS), and encapsulation efficiency.[33]

Kim *et al*. reported by tannic acid is coated with zeolite Y NPss as a novel drug nanocarrier with controlled-release behavior and anti-protozoan activity against *Trichomonasgallina*. Zeolite is composed of silicon, aluminum, oxygen nanochannels, and cages and it also solid hydrated crystalline.[34] The pores present in the zeolite are attached to the surface and enter the molecules to diffuse from outside and inside of zeolite particles. New drug nanocarrier was fabricated by zeolite NPs and it is layered with tannic acid on NPs to form a nanocomposite carrier.[35] Zeolite is super cages that are used for loading various compounds. Metronidazole is used as a model drug for loading the drugs in nanocarriers. Metronidazole acts as an anti-protozoan drug was encapsulated with nanocarriers. Metronidazole loaded with tannic acid-altered zeolite Y NPs is very active for an anti-trichomonal agent.[36]

EGCG is loaded with chitosan NPs (EGCG) that were developed by the ionic gelation method. EGC -loaded chitosan NPs increase the absorption and bioavailability of the drug. This method will increase the bioavailability of EGCG.[37] EGCG is a subtype of catechin. EGC is also used for the prevention of cancer, human immunodeficiency virus, chronic diseases, and neurodegeneration. EGC has low stability in the gastrointestinal tract (GIT). When we are loading the EGC into NPs it will be delay degradation in digestive fluids. Chitosan polymers have many advantages compared to other techniques. Chitosan polymer has been selected because of its benefits in pharmaceutical research.[38] Chitosan polymer can increase biodegradability, bioavailability, non-toxicity, non-immunogenicity, and low cost. Polymeric NPs will improve the bioavailability of the drug. Several methods have been used in the characterization of polymeric NPs include the solvent evaporation method, nanoprecipitation method, and emulsification coacervation. Poloxamer is also used in this method; it will reduce the aggregation and increase the stability. EGC is coated with the coating material of chitosan by the ionic gelatin method. Negatively charged chitosan communicates with positively charged sodium tripolyphosphate to prepare coacervates. The ratio of EGCG and chitosan is 1:0:1, 1:0:2, 1:0:4, and 1:0:5. Chitosan was soluble in the isolated aqueous solution of acetic acid at 5.5 PH. Poloxamer 188 was soluble in the above solution. Deionized water is added deliberately to the aqueous solution carrying chitosan and it is stirred with a magnetic stir. Sodium tripolyphosphate was mixed into the solution. Cross-linking of CS (chitosan) and tripolyphosphate produces the NPs. EGC incorporated into chitosan NPs was evaluated by particle size, DSC, FT-IR, Powder X-ray Diffractometer, and *in vitro* drug release study.[39]

The cherry extract (CE) is loaded with polymeric NPs based on chitosan or PLGA or human umbilical endothelial cells. The CE has anti-inflammatory properties and polyphenols also rich in this source. Cherries extract reduces the risk of atherosclerosis and polyphenols will reduce inflammation and dysfunction. Cherry fruit is loaded into the NPs it will improve bioavailability and increase their health effects. Natural cherry was removed from Prunus. Human umbilical endothelial cells were acting as substrate.[40] The cherries extract has polyphenols, anthocyanins, flavonoids, and antioxidant properties. CE polyphenols content was undergoing double emulsion method. In this preparation, the CE is loaded with chitosan derivatives and PLGA NPs.[41] PLGA NPs have more anti-inflammatory properties. In this method, it was exposed that the loading of CE in NPS improves polyphenols and anti-inflammatory activity and their absorption, and increases the CE oral bioavailability. CE-loaded NPs were characterized by zeta potential, particle size, SEM, TEM, and DSC analysis.[42]

EGC naturally occurs from plant resources. EGC has more anti-cancer and antioxidant properties. In this method, we enhance the anti-cancer efficiency of EGC so it was encapsulated with gold NPs (GNPs). The NPs were prepared by a green synthesis method.[43] EGC-loaded GNPs are used to reduce side effects. ECG inhibits cell proliferation and apoptosis. ECG has low stability and low oral bioavailability. To enhance ECG bioavailability and efficacy, we are using different types of techniques in NPs they are gold, polymeric, and lipid-based NPs. EGCG-GNPs also rise the EGCG efficacy on melanoma cells and prostate cancer (PCa) in mice models.[44] GNPs were increasing high yield, stability, and biocompatibility. EGCG-encapsulated GNPs are to improve their anti-cancer efficacy against Ehrlich's ascites carcinoma. The EGCG-GNPs were evaluated by particle size and zeta potential, polydispersity index, efficiency, and fabricated capacity, and it is characterized in mice carrying Ehrlich ascites carcinoma.[45]

Chow *et al*. reported by catechins are found in green teas, myrobalan, blueberries, and gooseberries. The biological

activities of catechin are cardioprotective, neuroprotective, and anti-cancer effects. This catechin has low solubility, bioavailability, and absorption so we are encapsulating the catechin and EGC in chitosan NPs to increase the bioavailability.[46] Here, we are using mouse jejunum and it is developing in chambers then encapsulation is enhanced the intestinal absorption. Chitosan is the polymers and chitosan-loaded NPs will increase the absorption in the GIT. In studies, it will provide the bioavailability and absorption of catechin. Catechin and EGC were evaluated by zeta potential and particle size.[47]

Catechin and quercetin are loaded with polymeric NPs using the solvent displacement method. Quercetin and catechin have many advantages such as antioxidant, antiradical, anti-inflammatory, antimutagenic carcinogenic, antiangiogenic, antibacterial, antiviral, and antiaging effects.[48] Catechin and quercetin have low stability and water solubility in the gut. Quercetin or catechin is loaded with polymeric NPs and a biocompatible copolymer of (PLGA) is characterized by physicochemical and antioxidant properties. The design and development of nanotechnology for the protection, loading, and release of bioactive tannins have the potential to increase human health or increase the half-life of pharmaceutical research. Both tannins are usually encapsulated with the monocrystalline state with PLGA NPs matrix. The use of PLGA NPs develops the antiradical and chelating properties of two bioactive compounds and it also increases the half-life and bioavailability, bioaccessibility of catechin and quercetin. The encapsulation of polymeric NPs for bioactive compounds displays useful effects on human health.[49]

Jin *et al*. projected that NPs readily deliver the drugs to the specific target site of tumor cell DNA with no side effects.[50] The secondary plants are playing important role in the drug delivery system. Here, we are using proanthocyanins encapsulated with biodegradable chitosan NPs (PAC-CSNPs) it is used to target apoptosis in human colorectal carcinoma cells (HT-29). Proanthocyanin-loaded chitosan NPs were prepared by ionotropic gelatin technique.[51] PAC-CSNPs have mainly inhibited the cyclin-dependent kinases and protect the cell cycle/cell division from cancer cells. This study goals to build anti-cancer drugs that are more effective against colorectal carcinoma. PAC-CSNPs were evaluated by FTIR, TEM and SEM.[52]

The biopolymer NPs were fabricated from protein isolate (whey protein isolate) and beet pectin using thermal processing and electrostatic complexation. In this technique, blending the two biopolymers at pH 5.8, at the heating system (90°C and 5 min) to make protein NPs development, and then correcting the solution to pH 4.0 and coating the protein NPs with pectin.[53] The biopolymer NPs were incorporated with an anthocyanin-rich extract. Loaded anthocyanin had lower antioxidant activity than non-loaded anthocyanin; it undergoes thermal processing step during particle fabrication and combining the anthocyanins to biopolymers within the NPs. The fabrication of anthocyanins into biopolymer NPs was evaluated by particle size, zeta potential, and differential scanning calorimetry.[54]

Oliveira *et al*. prepared that EGC-3-gallate is fabricated with PEGylated-PLGA NPs to prevent the drug and increase brain delivery. EGC-3-gallates fabricated PEGylated-PLGA NPs are used to target temporal lobe epilepsy. NPs were formulated by the double emulsion method.[55]. It determines the effectiveness of the drug in cytotoxicity and Glial fibrillary acidic protein. EGC -3-gallate PEGylated-PLGA NPs are determined by optimization study, interaction studies, *in vitro* release profile, the stability of NPs, and cytotoxicity assays.[56]

Ahmed *et al*. reported that anthocyanins are loaded with β-Lg (lactoglobulin) NPs. Anthocyanins have several biological activities include antioxidant, anti-cancer, anti-tumor, anti-diabetic, and others. Anthocyanins are extracted from raspberry pomace. The NPs of β-Lg (lactoglobulin) will increase the solubility and bioavailability of a drug. NPs of β-Lg (lactoglobulin) were prepared under the desolvation method at PH 7.[57] The incorporation of anthocyanin will increase the antioxidant properties of β-Lg (lactoglobulin) NPs and it shows the highest anthocyanin concentration. Anthocyanin-loaded β-Lg (lactoglobulin) shows more stability in the gastrointestinal and high retention time than that of anthocyanin is encapsulated. Anthocyanin-loaded β-Lg (lactoglobulin) NPs shows more anthocyanins retention time, particle size, and high encapsulation efficiency. Anthocyanin-loaded β-Lg (lactoglobulin) NPs were evaluated with particle size, SEM, TEM, zeta potential, DSC analyzes, and *in vitro* studies.[58]

Anthocyanin is incorporated with polymeric NPs such as PLGA and PEG to increase their radical scavenging capabilities. Anthocyanin incorporated NPs were fabricated by the emulsification-solvent evaporation method. Anthocyanins constitute a subfamily of tannins that contain antioxidant action, anti-inflammatory action, anti-cancer action, and anti-tumor action.[59] Anthocyanin has low stability because of the hydroxy groups they are easily oxidized and reduce the biological properties of drugs. To overcome this problem, we are incorporating anthocyanin into polymeric NPs due to their properties it will increase the stability, bioavailability, and water-soluble drug and efficiency. Anthocyanin-loaded polymeric NPs were evaluated by TEM, particle size, zeta potential, and DSC analysis.[60,61]

Geraniin is loaded with PEG-b-PLGA NPs. Geraniin is one type of tannins it is separated from Phyllanthus Watsonii. The geraniin-loaded PEG-b-PLGA NPs are fabricated by the double emulsion method.[62] PEG-b-PLGA NPs show more bioavailability, biocompatibility, and improved drug content specificity. Geraniin-loaded PEG -b-PLGA NPs are used for the treatment of human epithelial colon cells and CCD 841 CoN cells. Geraniin-loaded PEG-b-PLGA NPs to evaluate

the cytotoxicity of PLGA-b-PEG NPs are encapsulated with geraniin to normal CCD 841 CoN colon epithelial cells.[63]

Lagoa *et al*. reported that tannic acid and Vitamin E (TA+E) are encapsulated with poly-D, L-lactide-co-glycolic to treat hepatoprotection in alcoholic liver disease mice model. PLGA NPs are fabricated by emulsion solvent evaporation it is characterized and delivered to mice. PLGA polymer has many beneficial effects such as it reduces toxicity and increases biocompatibility and biodegradable.[64] Vitamin E has poor absorption so we incorporated it with PLGA NPs for better absorption within the tissues. The research explained that PLGA (TA+E) defeated reactive oxygen species (ROS) formation and improved antioxidant potential. PLGA (TA+E) also ameliorated inflammatory responses and developed the apoptotic pathway by modulating the epidermal growth factor receptor (EGFR)-AKT and EGFR-STAT3 (EGFR and signal transducer and activators of transcription) pathways. This review of PLGA (TA+E) could give a useful milieu in protecting adrenoleukodystrophy. PLGA (TA+E) is evaluated by zeta potential, particle size, TEM, SEM, and DSC analysis.[65]

De and Robinson described that catechin-loaded polymeric NP. Polymeric NPs such as chitosan alginate will increase their therapeutic efficacies of catechin for drug delivery systems. Catechin is extracted from Cassia fistula and its anti-cancer properties.[66] The catechin is loaded with two polymeric nanocomplexes, and it's evaluated for two polymeric nanocomplexes for their sustained release and to enhance the anti-cancer action of catechin.[67] The catechin-loaded polymeric NPs are fabricated with the ionotropic gelation method. Catechin loaded polymeric NPs were evaluated by zeta potential, SEM, TEM, DSC analyzes, and particle size.[68]

NP formulations of poorly soluble polyphenols with anti-cancer properties were studied and reported to possess enhanced tumor targeting effect.[69] Polyphenols are derived from tannins, they have anti-cancer properties. Polyphenols have poor solubility, low bioavailability in their application of cancer prevention and treatment. To enhance the bioavailability of polyphenols so NPs are involved to increases the bioavailability, localization, and specific activity in tumor cells. The aim of this review is nanoparticulate carriers to deliver the polyphenols into the cancer site.[70,71]

Ariza *et al*. reported developing the bioavailability of phenolic compounds by loading them within lipid-based nanocarriers. Phenolic compounds are the main source of nutraceuticals in the pharmaceutical industries.[72] Phenolics have poor bioavailability, solubility, stability, and untargeted release. To overcome this problem, we introducing nanotechnologies to target the specific location of cancer. Phenolics are encapsulated into nanocarriers for better delivery of the drug into the targeted site of action. Lipid nanocarriers are formulated by different types of methods such as nanoemulsions, nanoliposomes, and lipid carriers. Lipid-based nanocarrier's formulation is best to approach then compared to micro-sized carriers, they will improve solubility and the bioavailability of phenolic compounds.[73]

EGC-3-gallate is incorporated with polymeric NPs such as PLGA-PEG-A to target PCa. EGC -3-gallate is a derivative of polyphenols it contains many biological activities such as anti-inflammatory, anti-cancer, anti-tumor, and antioxidant activities.[74]. Here, polymeric NPs are incorporated with EGC-3-gallate the showed over ten-fold dose use of its pro-apoptotic and anti-angiogenic effects are effective against PCa, in both *in vitro* and *in vivo*. In this study, to improve the targeted EGC-3-gallate loaded NPs to deliver cellular targeting and to evaluate the efficacy of EGC-loaded polymeric NPs.[75] Polymeric NPs were fabricated by nanoprecipitation technique and it is characterized by morphology and physicochemical properties of EGCG content and EGCG release. Drug-loaded polymeric NPs was reported to increase the pharmacokinetics and pharmacodynamic activities against prostate cancer (PCa). EGC-3-gallate encapsulated polymeric NPs are evaluated by *in vitro* release, Cytotoxicity of native EGCG and EGCG-loaded NPs and Docking analysis.[76]

Jia *et al*. reported that nanotechnology is used to improve the effectiveness of drugs and they also work better than chemotherapeutic agents. Compared to chemotherapeutic agents the phytoconstituents exhibited more benefits in nanoformulations. Polyphenols have more beneficial uses in human health such as anti-cancer properties.[77] Here, polyphenols are encapsulated with NPs for cancer treatment. Doxorubicin hydrochloride (DOX.HCL) also loaded with polyphenols NPs to increase retention time and anti-cancer efficacy and reduce toxicity in cancer therapy.[78] P-NPs could produce ROS and reduce the mitochondrial membrane; it has more cancer cell inhibition of DOX-loaded P-NPs than DOX. HCl on both HT-29 cells (human colorectal adenocarcinoma cell line) and Hela cells. DOX-loaded polyphenols-NPs *in vivo* can accumulate in tumor sites and maintain for a long time, showing enhanced anti-cancer efficacy as compared to DOX.HCl. DOX-loaded polyphenols-NPs are evaluated by SEM, TEM, particle size, and zeta potential.[79]

The phenolic compound is derived from polyphenols that naturally occur from plants it plays an essential role in cellular growth, coloration, and regulation of fruits' maturation; it is present in vegetal foodstuffs, flowers, and beverages.[80] Polyphenols contain polyphenolic groups it has many beneficial effects such as antioxidant, anti-cancer, anti-tumor, and anti-carcinogenic activities. Still, polyphenols have some disadvantages they are low bioavailability and low stability toward PH. Here, we are using solid lipid NPs and nanostructured lipid carriers are used as an essential tool for improving the bioavailability and stability of phenolic compounds. In this study, we are increasing the bioavailability and stability of phenolic compounds and the

Drug	Polymer	Method of Preparation	Activities of Tannins	Reference
Callistemon citrinus and Berberine	PLGA (Poly-lactic co- glycolic acid)	Nanoprecipitation Method	cardiovascular diseases, inflammation, anti-cancer, and antidiabetic activities	[26],[27]
Pectin tannic acid nano complex	Pectin	Self-assembly method	Antioxidant, anti-cancer, and anti-carcinogenesis	[28],[29]
Epigallocatechin -3- Gallate	Chitosan	Ionic gelation method	Antioxidant, Anti-cancer, and Anti-carcinogenesis	[38],[39]
Polyphenols	Chitosan	Double emulsion technique	Antioxidant, Anti-cancer, and Anti-inflammatory	[41],[42]
Catechin	Chitosan	Using chamber model	Cardio protective, Neuroprotective, and anti-cancer effects	[46],[47]
Catechin, Quercetin	PLGA	Solvent displacement method	Cardioprotective, Neuroprotective, and anti-cancer effects	[48],[49]
Proanthocyanidins	Chitosan	Ionotropic gelation method	Antioxidant and Anti-cancer activities	[51],[52]
Anthocyanin	Pectin	Thermal processing and electrostatic complexation	Antioxidant and Anti-inflammatory property	[53],[54]
Epigallocatechin -3-gallate	PEGylated-PLGA	Double emulsion method	Antioxidant, anti-cancer, and anti-carcinogenesis	[55],[56]
Anthocyanins	N-(3 Dimethylaminopropyl)-N Ethyl Carbodiimide Hydrochloride	Desolvation method	Antioxidant, anti-cancer, anti-tumor, and anti-diabetic	[57],[58]
Anthocyanins	PLGA-PEG nanoparticles	Emulsification-solvent evaporation technique	Antioxidant, anti-cancer, anti-cancer, anti-tumor, and antidiabetic	[60],[61]
Geraniin	PLGA-b-PEG	Double emulsion method	Anti-inflammatory property and anti-cancer activities	[62],[63]
Tannic acid and vitamin E	poly-D, L-lactide-co-glycolic	Emulsion Solvent Evaporation	Antioxidant, anti-cancer, and anti-inflammatory	[64],[65]
Catechin	Chiston Alginate	Ionotropic gelation method	Cardioprotective, neuroprotective, and anti-cancer effects	[67],[68]
Epigallocatechin -3-gallate	PLGA-PEG-A	Nanoprecipitation	Antioxidant, anti-cancer, and anti-carcinogenesis	[75],[76]

preparation of SLNs-loaded phenolic compounds includes micro emulsification and solvent evaporation method and double emulsion technique.[81,82]

CONCLUSION

Plants contain different types of tannins that possess strong antioxidant properties. Hence, dietary intake of tannins has been associated with the prevention of various types of cancer. Tannins have pharmacological actions such as antioxidant, anti-inflammatory, anti-cancer, anti-carcinogenesis, and antibacterial and antifungal activity. In this study, tannins-based nanoparticles will increase the bioavailability, solubility, stability, and drug loading and it also improves the target specificity of action. Tannic acid-based nanoparticles drug delivery system will increase the efficiency and safety of the drug. A tannic acid-based nanoparticle drug delivery system is used for the treatment of different types of cancer.

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