

## **EDIBLE PLANT DERIVED NANO-LIPIDS INCORPORATED IN THE MANAGEMENT OF CANCER: A REVIEW**

**Swathi Bollineni<sup>1\*</sup>, Gudela Haritha<sup>1</sup>, Vuddanti Meghana<sup>1</sup>, G. N. J. V. L. Sarada Sri<sup>1</sup>,  
Natta Prathiba<sup>2</sup> and Kantamaneni Padmalatha<sup>3</sup>**

<sup>1</sup>Pharm-D, V year, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India, 521108.

<sup>2</sup>Associate Professor, Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India, 521108.

<sup>3</sup>Professor and Principal, Department of Pharmacology, Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India, 521108.

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### **\*Corresponding Author**

**Swathi Bollineni**

Pharm-D, V year,  
Department of Pharmacy  
Practice, Vijaya Institute of  
Pharmaceutical Sciences for  
Women, Enikepadu,  
Vijayawada, Andhra  
Pradesh, India, 521108.

### **ABSTRACT**

Nanomedicine is a branch of study concerned with organic medical applications at the nanoscale. The primary goals of nanotechnology in drug delivery include, more specific drug targeting and delivery, reduction in toxicity while maintaining therapeutic effects, greater safety and bio-compatibility, and faster development of new safe medicines. According to the researchers, plant-derived exosome-like nanoparticles (PENs) are likely to become viable therapeutic modalities for disease management or pharmaceutical administration. Edible plant derived nanoparticles(epNPs) have been prepared from various edible plants such as corn, citrus, grapefruit, ginger, and broccoli were studied in this review. Increased solubility and the ability to improve storage stability, enhanced permeability and bioavailability, fewer side effects, prolonged half-life, and tissue-

targeted administration are some of the benefits of NLCs over conventional carriers. The systematic literature review concluded that Nanotechnology-based drug delivery systems showed considerable potential in improving cancer treatment. Combining natural medicines with chemotherapy could be a viable cancer-eradication strategy in the near future. Many natural chemicals have emerged as alternative cancer preventative and treatment options. The

therapeutic efficacy of nanoparticles is dependent on efficient cellular absorption and cytotoxicity.

**KEYWORDS:** Nanoparticles, Effective drug delivery, Edible plants derived nanoparticles (epNPs), Nano-structured lipids carriers (NLCs), Plant-derived exosome like nanoparticles (PENs), Effective disease and mainly cancer therapy.

## INTRODUCTION

Nanoparticles are being used in pharmaceutical research to lower drug toxicity and side effects.

"Nanomedicine is the application of nanoscale devices to the detection, prevention, and treatment of disease."

The nano drug-delivery technology improved cellular absorption and lowered hazardous side effects compared to conventional drugs, potentially making chemotherapeutics more effective in cancer treatment.

NLCs (Nanostructured lipid carriers) are drug delivery systems with a solid and liquid lipid matrix at their core. The basic goal of drug trapping in nanoparticles is to improve drug delivery to or uptake by target cells. Site-specific medicine delivery is possible due to the small size and limited size distribution. An active medicine can be released in a regulated and continuous manner. Lipophilic and hydrophilic medications can both be used. It can be sterilized using an autoclave or gamma radiation, both of which produce no hazardous byproducts. It is both affordable and reliable. The hot dispersion process makes industrial scale manufacture simple.<sup>[7]</sup>

Plant exosomes, also known as nanovesicles, are naturally occurring nanocarriers with unique morphological and compositional characteristics. PELNV lipid bilayer structures require lipids to function. Phospholipids and glycerol lipids are two separate categories of lipids discovered by lipid profiling. PELNV stability, absorption and other biological functions are all dependent on these lipids.<sup>[9,10]</sup>

Transmission electron microscopy (TEM) is used to investigate the ultrastructure of PELNVs in their subcellular state. Using atomic force microscopy (AFM), individual PELNVs can be

investigated structurally and in terms of size. Dynamic light scattering (DLS) can be used to determine the size and zeta potential of scattered PELNVs.

PELNVs are incubated with drug molecules at a specific temperature in a procedure known as passive drug loading. Exogenous therapeutic molecular medicines, including proteins, expression vectors, siRNA, and DNA, could be loaded into ELNVs. To load therapeutic drug molecules onto ELNVs, various techniques have been devised.<sup>[4]</sup>

PA (Phosphatidic acid) is the main lipid mediator in many PELNVs, modulating membrane fission and fusion. PA, which causes cytoskeleton rearrangement and protein modulation in vesicular endocytosis, can also alter PELNV absorption. The lipid bilayer architectures of PELNVs require lipids for stability, absorption, and other biological functions.

PELNVs have been discovered to exert anti-inflammatory benefits through modulating the immune responses of their hosts. Unlike artificially created liposomes, they have apparently proven successful in overcoming mammalian barriers such as diffusing through the blood-brain barrier (BBB), which prevents any activation of inflammatory response or necrosis.<sup>11</sup> PELNV's lipid bilayer shape secures their payload and prevents proteinases and nucleases from decomposing it.

Phagocytosis, macropinocytosis, clathrin-mediated endocytosis, and caveolae-mediated endocytosis have all been implicated in the cellular internalization of PELNV based nanopharmaceuticals.<sup>[4]</sup>

Biocompatibility, stability, biodistribution, longer half-life, and cellular internalization are among the many benefits of PELNV based nanoplateforms. PELNVs are remarkably non-immunogenic and have potent immune-modulatory properties that promote tissue homeostasis and contribute to an organism's overall health.<sup>[4]</sup> The main advantage of employing them for drug administration is that they can lessen the negative effects of a loaded medicine when given to test participants.

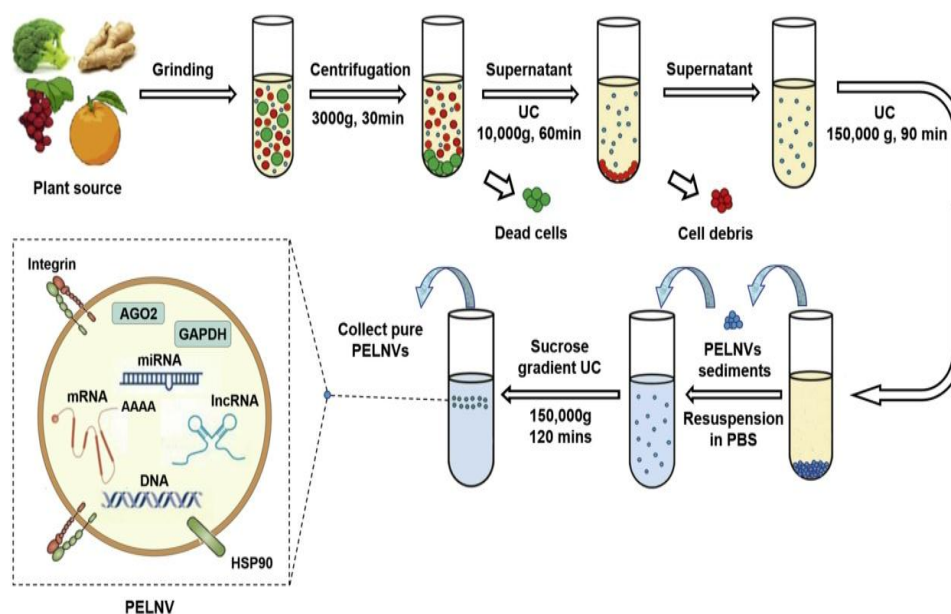


Fig. 1: Isolation and Preparation of PELNVs (Haseeb anwar dad *et al.*),<sup>[4]</sup>

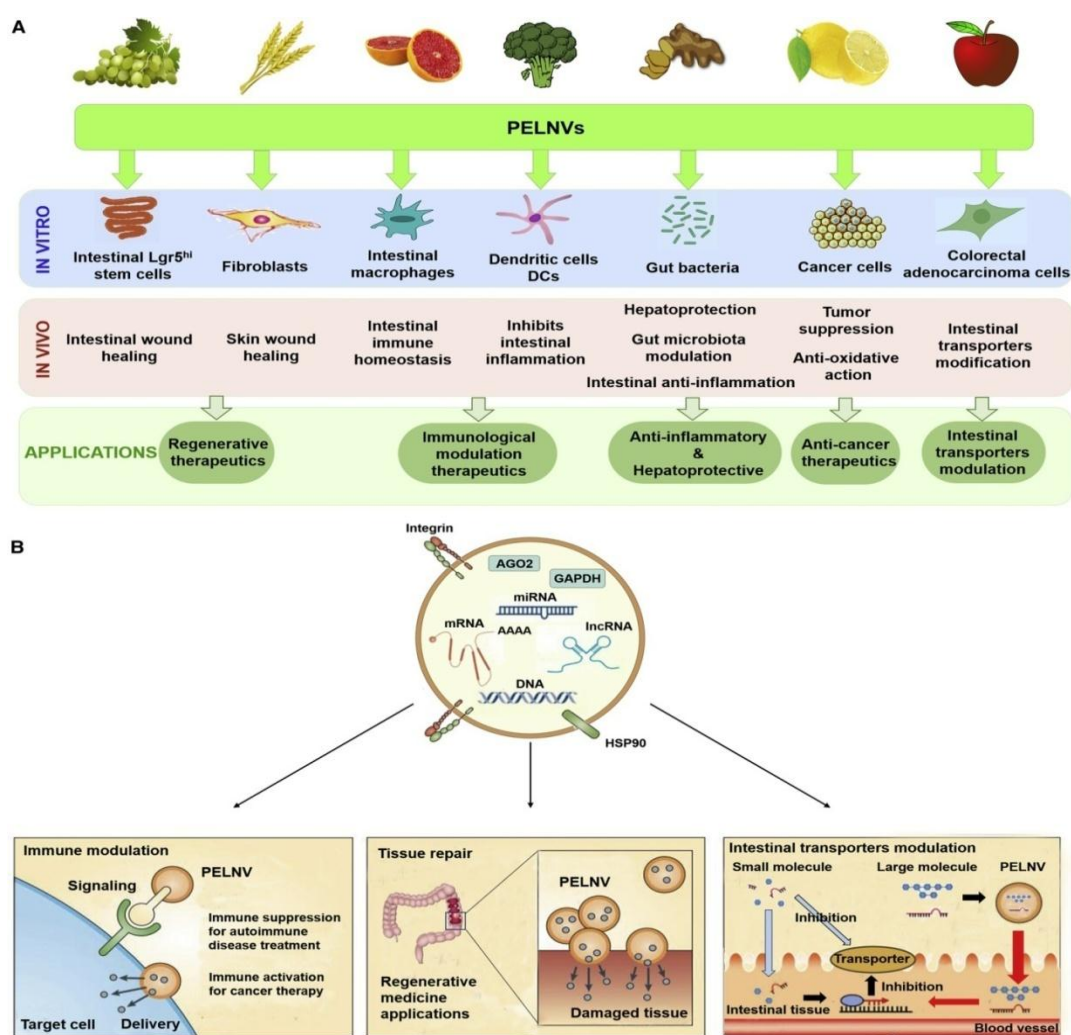


Fig. 2: Outline of PELNV Biological Functions and Translation into Therapeutic Applications from a Variety of Plant Sources (Haseeb Anwar Dad *et al.*),<sup>[4]</sup>

## DISCUSSION

### Study 1:

In 2015, **Stefania Raimondo *et al.***, conducted a study on **“Citrus limon-derived nanovesicles inhibit cancer cell proliferation and suppress CML xenograft growth by inducing TRAIL-mediated cell death”**

This study determined the use of a portion of lemon juice in cancer therapy. Citrus Limon L. (Rutaceae) juice includes nanoparticles with morphological, dimensional, and proteomic profiles that allow them to be classified as exosome-like nanovesicles with in vitro anticancer activity. They also have anticancer action in vivo, inhibiting the growth of a CML xenograft model and triggering a TRAIL-mediated apoptotic mechanism.

The Citrus Limon L. nanovesicles were purified on a 30 percent sucrose gradient after being separated from fruit juice using an ultracentrifugation process. The integrity and size of isolated vesicles measured 50–70 nm and were exosome-like in structure and size, according to electron microscopy analyses.

By labeling citrus nanovesicles with the lipophilic dye PKH26, researchers were able to show that they are internalized by human cancer cells. The A549 human lung cancer cell line and the LAMA84 chronic myeloid leukemia cell line were treated with 20 µg/ml nanovesicle for 3 or 6 hours at 37°C. HS5 (Human bone marrow stromal cells), HUVEC (Human Umbilical Vein Endothelial Cells), and PBMC (Human peripheral blood mononuclear cells) were used to test the specificity of lemon nanovesicles against tumor and non-cancer cell lines. Citrus nanovesicles were effective against the cancer cell lines A549, SW480, and LAMA84, but had no effect on normal cell proliferation. The effects on cancer cell growth were discovered to be dependent on nanovesicle integrity and stability.

Lemon-derived nanovesicles activated TRAIL-mediated apoptosis, causing cancer cells to die. They discovered that nanovesicle therapy reduced pro-angiogenic factors such VEGF-A, IL6, and IL8 in treated mice as compared to untreated mice. Trail and Dr5 mRNA were found to be upregulated, while anti-apoptotic genes including Survivin and Bcl-xl were downregulated, according to a real-time PCR analysis of mRNAs obtained from in vitro xenograft tumors. They discovered that nanovesicle treatment increased the pro-apoptotic gene Bax while decreasing the anti-apoptotic genes Survivin and Bcl-xl in nanovesicle-treated animals.

NOD/SCID mice were injected intraperitoneally with citrus nanovesicles labeled with the lipophilic fluorescent tracer DiR, Free-DiR, or PBS one week after subcutaneous injection of CML cells to see if nanovesicles suppressed tumor growth by reaching the tumor site. Nanovesicles-DiR penetrated tumor tissue quickly and accumulated from 15 minutes to 1 hour and up to 24 hours, but Free-DiR never reached the tumor site.

The researchers discovered that using citrus nanovesicles to treat lung, colon, and leukemia cancer cells alters pro- and anti-apoptotic pathways, resulting in an increase in the mRNA levels of pro-apoptotic molecules Bad and Bax and a drop in pro-survival molecules like Survivin and Bcl-xl. They discovered that it slows cancer cell proliferation while having no effect on healthy cells.

Citrus nanovesicles significantly reduced tumor growth and confirmed in vivo that this impact was related not only to TRAIL-mediated apoptosis but also to suppression of angiogenic processes. TRAIL-mediated pathways and angiogenic inhibition are two putative mechanisms by which nanovesicles exert antineoplastic action in vitro and in vivo.

### **Study 2:**

In 2016, **Mingzhen Zhang *et al.***, conducted a study on “**Edible Ginger-derived Nanolipids Loaded with Doxorubicin as a Novel Drug-delivery Approach for Colon Cancer Therapy**”

They isolated nanoparticles in large quantities from *Zingiber officinale*, the edible ginger, and characterized ginger derived nanovectors (GDNVs). They discovered that GDNVs were efficiently taken up by colon cancer cells, and that the modification with the targeting ligand folic acid (FA) achieved active specific targeting to colon-26 tumors in vivo.

Phosphatidic acid, digalactosyldiacylglycerol, and monogalactosyldiacylglycerol were shown to be abundant in ginger-derived nanoparticles, according to lipid profile analyses. Because of its tiny negatively charged headgroup adjacent to the acyl chain area of the bilayer, strong affinity for divalent cations, and proclivity to generate intermolecular hydrogen bonds, PA has a function to govern membrane fission and fusion.

GDNVs were usually spherical in shape, with an average hydro dynamic diameter of 188.5 nm and decreased polydispersity, according to TEM images of pure nanoparticles. Based on



the examination of their zeta potential and size distribution, GDNVs were relatively stable when stored at 4°C for up to 25 days.

Both Colon-26 and HT-29 cells ingested GDNVs labeled with DiL with high efficiency. First, colon-26 cells were treated with endocytosis inhibitors (amiloride, indomethacin, chlorpromazine, and cytochalasin D). Cytochalasin D, an inhibitor of actin polymerization necessary for phagocytosis, dramatically reduced the uptake of DiL-GDNVs. At equal lipid concentrations, GDNVs have a lower influence on cell proliferation than cationic liposomes. This method distinguishes four distinct phenotypes: viable cells, early apoptotic cells, necrotic cells, and apoptotic cells.

In mice, intravenous injections of GDNVs or cationic liposomes had no effect on proinflammatory cytokines such interleukin (IL)-6, IL-1 $\beta$ , or tumor necrosis factor (TNF- $\alpha$ ). Organ slices stained with hematoxylin and eosin (H & E) revealed no signs of organ damage in either the GDNVs or DC-Chol/DOPE cationic liposome treatment groups. Hepatocytes in the liver appeared normal, there was no myocardial fibrillary loss or vacuolation in the heart, and lung samples revealed no pulmonary fibrosis. At concentrations up to 200  $\mu$ mol/l lipids, hemolysis of nanoparticles in blood was not seen for GDNVs or cationic liposomes: Triton X-100, used as a positive control, achieved 100% hemolysis. After intravenous injection, GDNVs would be nontoxic to erythrocytes.

Because Dox has a slightly positive charge and most ginger-derived lipid components have a negative charge, ginger-derived lipids can form bilayers with the help of sonication, and Dox can be encapsulated within ginger lipids through electrostatic contact. Tumor cells extracellular milieu is acidic (pH 6.5–6.7), and their Dox release remains constant until they reach pH 6.5. A pH of 5.5, on the other hand, did not result in greater release. Dox-GDNVs were able to release loaded medications faster than commercially available liposomes in an acidic pH close to the tumor microenvironment. Dox-GDNVs with a better pH-dependent drug-release profile may have fewer severe side effects like leucopenia, thrombocytopenia, anemia, and gastrointestinal toxicities. GDNVs produced from ginger-derived lipid have a high loading efficiency and a pH-dependent release profile for the chemotherapeutic medication Dox.

The reduced percentage of viable cells observed after treatment with free Dox compared to Dox-GDNVs shows that free Dox penetrates cells quickly through passive diffusion across

the plasma membrane to directly exert antitumor effects in the nucleus. Dox-GDNVs had a time-dependent release profile, delaying Dox release from GDNVs and producing a long-lasting cytotoxic effect.

The fluorescence intensity of DiR-labeled FA-GDNVs in tumors was 2.8 times that of GDNVs, indicating that FA-GDNVs can target tumors, most likely through active (FA-FRs interaction) mechanisms. Up to 48 hours after intravenous injection, FA-GDNVs were stable and detectable. The longer nanoparticles are in the bloodstream, the more likely they are to penetrate tumor tissues.

Immunohistochemical detection of the cellular proliferation marker Ki67 and TUNEL (terminal deoxynucleotidyl transferase dUTP nick-end labeling) assays were used to assess the anticancer activity of Dox-FA-GDNVs against implanted Colon-26 cells. When compared to tumors from mice treated with free Dox, the fraction of Ki67-positive cells in Dox-FA-GDNVs was significantly lower.

They discovered that edible ginger may release nanoparticles, and that their lipids can be used to deliver therapeutic drugs (Dox) with great biocompatibility. They added FA to GDNVs, a ligand for high-affinity folate receptors (FRs), which are expressed at high levels in many tumors but in low amounts in nontumor cells. During GDNV manufacturing, FA can be introduced into the lipid bilayer. In a Colon-26 xenograft tumor model, it slowed tumor growth.

### Study 3:

In 2015, **Xingwang Zhang *et al.***, conducted a study on **“Enhanced bioavailability of tripterine through lipid nanoparticles using broccoli-derived lipids as a carrier material”**

The researchers wanted to build lipid nanoparticles out of broccoli lipids to increase the oral bioavailability of tripterine (Tri), a natural anticancer candidate. Broccoli is a pleasant green plant that belongs to the Brassicaceae family. A solvent-diffusion technique was used to develop Tri-loaded Broccoli Lipid Nanomaterials (Tri-BLNS), which have an entrapment efficacy (EE) of over 98 percent and a particle size of 75nm. Tri is a natural cancer-prevention proteasome inhibitor. Low oral bioavailability is caused by insolubility and inadequate intestinal absorption. Anticancer effects have been demonstrated in vitamins and



minerals such as 3, 30-diindolylmethane, glucoraphanin, and indole-3-carbinol. Vitamin A, carotene, and lipids are all lipophilic components found in broccoli.

To extract the liposoluble components of broccoli, 1-octanol was used, which has a comparable solubility parameter to biomembrane and may be beneficial in absorption enhancement. The researchers compared broccoli lipid nanoparticles (Tri-BLNs) to common lipid nanoparticles (Tri-CLNs). To collect lipids, dried broccoli was soaked in 1-octanol (1:8, w/v) and kept for 12 hours in a water bath at 75°C with stirring. Precirol ATO-5 as the lipid substance and 0.1 percent Tween 80 as the surfactant were used to make Tri-CLNs utilizing the same process. The average particle size of Tri-BLNs was 75.6 nm, with a fairly tight dispersion (PDI = 0.037). Tri-CLNs had a particle size of 151.3 nm with a PDI of 0.125, which was more than twice that of Tri-BLNs.

On MDCK-II cells, the cellular absorption of Tri-BLNs was assessed. Chlorpromazine (0.03 mM) and Filipin (1.5  $\mu$ M) were used to induce cellular absorption at 37°C and 4°C, respectively. Broccoli-lipid nanoparticles were suitable for oral delivery of Tri due to their small particle size and excellent encapsulation. The EE of Tri-BLNs neared 100%, with no free drug identified in the external aqueous phase by HPLC, demonstrating efficient drug solubilization by broccoli-derived lipids. The cumulative release percentage for Tri-BLNs and Tri-CLNs after 24 hours was only 2 and 0.8 respectively, according to the in vitro release profiles of Tri from Tri-BLNs and Tri-CLNs vs. time. Tri-CLNs were released a little more slowly than Tri-BLNs. Because broccoli-derived lipids are semi-solid at room temperature and slightly hydrophilic, Tri-BLNs provided a little rapid release. This could be owing to Tri's high hydrophobicity, which allows it to be stably incorporated into lipid nanoparticles thanks to a high affinity between the medication and the lipid materials. The type of drug solubility, as well as the lipolysis of lipid carriers, influences the release. For both lipid nanoparticles, lipolysis occurred quickly in the first 5 minutes. Tri-CLNs had about 100 percent lipolysis after 30 minutes, but tri-BLNs took 75 minutes to complete the procedure. This indicated that some Tri-BLN had managed to survive the hostile environment following administration. Because the lipids isolated from broccoli using 1-octanol are so complex, lipase cannot digest all of them. Lipase prefers to breakdown triglycerides into diglycerides or monoglycerides. Broccoli-derived lipids, on the other hand, have a high ratio of monoglycerides to triglycerides. In a synergistic impact, the inherent anticancer species found in broccoli can work with the supplied medications to eliminate malignant tumor cells.

Broccoli lipid nanoparticles show promise as chemotherapeutic drug carriers in the mouth. These broccoli-derived lipids should have the potential to improve the oral absorption of anticancer medicines with low bioavailability due to their high biocompatibility and functionality. Tri uptake rates were 7.88 percent, 10.72 percent, and 15.08 percent, respectively, with Tri solution, Tri-CLNs, and Tri-BLNs. Filipin's role in limiting cellular uptake was relatively minor, with only a 13% reduction in uptake. Chlorpromazine reduced the absorption of Tri by MDCK-II cells from Tri BLNs by 35% compared to the control group. These findings strongly show that energy is required to transport Tri through the clathrin-mediated endocytosis mechanism. Tri-BLNs and Tri-CLNs have been shown to enter into the cytoplasm of MDCK-II cells, allowing them to boost cellular absorption of Tri and hence increase its oral bioavailability. CLSM was used to better characterize cellular internalization using coumarin-6 as a fluorescent probe. The lipid nanoparticles made from broccoli-derived lipids were tiny and consistent in size, and they had better drug solubilization and loading capabilities. The nanocarriers greatly increased the oral bioavailability of Tri after delivery. The findings of increased absorption were further supported by research on cellular uptake and transport. This was mostly due to clathrin-mediated endocytosis, which reinforced active transport.

#### **Study 4:**

In 2021, **Daisuke Sasaki *et al.***, conducted a study on **“Development of nanoparticles derived from corn as mass producible bio nanoparticles with anticancer activity”**

Corn is the most extensively grown grain crop in the world, owing to its low cost of production and high yield. It contains several vitamins and minerals, as well as fibers, microRNAs, and xanthophylls like lutein and zeaxanthin, which have anticancer properties. The properties, functions, and activities of NPs produced from corn, or corn-derived NPs, were investigated in this work (cNPs). The edible section of maize used to make cNPs has a lipid makeup of 52.8 percent triglycerides, 18.4 percent glycolipids, and 28.8 percent phospholipids. In tumor-bearing mice, they tested the anticancer efficacy of cNPs.

Corn NPs (cNPs) were taken up by a variety of cells, including colon26 tumor cells and RAW264.7 macrophage-like cells, and colon26 cells growth was reduced selectively. They had an electric field of 17 mV, were 80 nm in diameter, and were negatively charged. The cNPs caused RAW 264.7 cells to secrete tumor necrosis factor.

Endocytosis inhibitors such as methyl-beta-cyclodextrin (MCD), chlorpromazine (CPZ), ethyl-isopropyl amiloride (EIPA), and Filipin III were used to evaluate the uptake mechanism of cNPs in colon26 cells. The red fluorescence signals from DiI-labeled cNPs were found in all cell types, with colon26 cells uptake being the most efficient, but DiI-labeled PC-Lips were uptake most efficiently by RAW264.7 cells, showing efficient cNP uptake by these cells. The uptake mechanism of cNPs in colon26 cells was investigated using endocytosis inhibitors such as methyl-beta-cyclodextrin (MCD), chlorpromazine (CPZ), ethyl-isopropyl amiloride (EIPA), and Filipin III. MCD was discovered to be the most efficient inhibitor of DiI-labeled cNP uptake by colon 26 cells, showing that their uptake is mediated by cholesterol.

The immunological activity of cNPs, which are a xenobiotic product, was assessed by measuring cytokine release in RAW264.7 cells after cNPs were added. RAW264.7 cells strongly released the proinflammatory cytokine tumor necrosis factor (TNF) after incubation with cNPs, but there was no significant release of the anti-inflammatory cytokine interleukin (IL)-10. Following co-culture with RAW264.7 cells and cNP administration, the number of firefly luciferase (fluc) stably expressing-colon26 (colon26/fluc) cells was assessed to check if the cNP-induced reactions in RAW264.7 cells have an impact on tumor cell proliferation. The number of colon26/fluc cells decreased in a cell number-dependent way.

Researchers looked at how cNPs inhibited tumor growth in mice in a dose-dependent way and whether they caused toxicity. At 7 days following daily subcutaneous injections of cNP at a dose of 1000µg/mL, they examined the levels of aspartate aminotransferase (AST), alanine aminotransferase, and creatinine in the serum of mice. The cNP group's H&E-stained sections revealed no substantial alterations in these organs, showing that toxicity caused by cNPs was not present.

When compared to noncancerous cells colon26 cells preferred cNPs, which had more phospholipids than corn homogenized juice. Because MCD inhibits cholesterol-dependent endocytosis at the lipid raft domain, it's possible that this pathway is involved in the uptake of cNPs by colon 26 cells. The membrane structure of cNP is lipid bilayer. The hydrophobic interaction of the lipid bilayer of cNPs with the lipid rafts on the cell surface may aid in colon26 cell uptake. Furthermore, cancer cells have been found to possess larger quantities of lipid rafts than their non-tumorigenic counterparts, which contribute to oncogenic signaling and tumor growth.

The xanthophylls present in corn, are known to exhibit antitumor effects through regulation of the cell cycle or cell apoptosis. It has been reported that zeaxanthin induces cell cycle arrest at the G2/M phase and apoptosis through the ROS-mediated MAPK, AKT, NF- $\kappa$ B, and STAT3 signaling pathways.

The anti-tumor activity of materials in tumor-bearing mice can be evaluated by directly injecting them intratumorally. In the present study, cNPs exerted indirect antitumor effects by activating RAW264.7 cells. After daily subcutaneous injections of cNP, no significant adverse effects were observed, indicating that cNP are safe nanoparticles. cNPs inhibited tumor growth by inhibiting colon26 cell proliferation (direct effect) and indirectly by activating macrophages and other immune cells infiltrating the tumor (indirect effect).

### Study 5:

In 2016, Xiaoying Zhuang *et al.*, conducted a study on “**Grapefruit-derived Nanovectors Delivering Therapeutic miR17 Through an Intranasal Route Inhibit Brain Tumor Progression**”

Grapefruit-derived nanovectors (GNV) can carry miR17 for therapeutic treatment of mouse brain tumor. They showed that GNVs coated with folic acid (FA-GNVs) are enhanced for targeting the GNVs to a folate receptor-positive GL-26 brain tumor. Additionally, FA-GNV-coated polyethylenimine (FA-pGNVs) not only enhance the capacity to carry RNA, but the toxicity of the polyethylenimine is eliminated by the GNVs. Intranasal administration of miR17 carried by FA-pGNVs led to rapid delivery of miR17 to the brain that was selectively taken up by GL-26 tumor cells. Mice treated intranasally with FA-pGNV/miR17 had delayed brain tumor growth.

Grapefruit-derived nanovectors (GNVs) are effective at delivering a wide range of therapeutic compounds, including medications. They created a GNV-based nanovector hybrid with polyethylenimine (PEI) (pGNV) for successful intranasal miRNA delivery to the brain in this investigation. PEI is used as an enhancer for delivering nucleic acids because it is more efficient in transporting RNA and DNA. Because of the positive charge on its surface, PEI particles are toxic. PEI polyplexes with a positive charge are necessary for high-efficiency transfection. The intracellular clearance of nucleic acids is faster when PEI is absent. Exosomes from edible plants, such as nanoparticles (GNVs), have been found to be delivered intranasally into the brain by scientists. Throughout this study, DIR fluorescent-

labeled GNVs were discovered in the brain, with the olfactory bulb, hippocampus, thalamus, and cerebellum being the most common locations. There were no signs of toxicity or behavioural changes, such as diarrhea, changed gait, or skin inflammation, swelling, body ulceration, or motor paralysis. PEI was explored to see if it could be utilized to boost the capability of RNA or DNA enclosed for intranasal delivery. According to the researchers, PEI reassembled into GNVs (pGNV/RNA) with a diameter of  $87.2 \pm 11.3 \text{ nm}$  (means  $\pm$  SEM), whereas PEI/RNA had a diameter of  $35.6 \pm 8.7 \text{ nm}$ .

Then they investigated if pGNV-carrying RNA might be delivered to the brain via an intranasal method. A positive fluorescent signal was seen as early as 1.5 hours after intranasal delivery, according to imaging results from frozen sectioned brains. This finding is consistent with a drop in DiR signal in the olfactory bulb of mice given pGNV and RNA 12 hours after delivery. FA-pGNVs (PGNVs that bind folic acid) would increase pGNV targeting to FR-expressing GL-26 tumor cells. In comparison to 20% of cells that picked up pGNV/RNA prior to co-culturing, over 80% of these cells took up FA-pGNV/RNA within 2 hours of co-culturing. Intranasal targeted delivery of miR17 to brain tumors was also done using a similar technique.

FA-pGNVs deliver miR17 to GL-26 cells more efficiently than pGNVs and are persistent for 48 hours after transfection. Mice were treated every three days for 21 days, starting on the fifth day after the tumor cells were implanted. After therapy, the mice's survival time climbed to an average of 47.5 days ( $P = 0.0012$ ). Therapeutic miR17 delivery to brain tumor cells through intranasal route. A number of challenges are avoided when using FA-pGNVs, including tissue targeting selectivity, toxicity, and the requirement for lifelong cancer monitoring. Researchers detected rapid transport of GNVs into the brain within 1.5 hours following intra-nasal injection. The FA-pGNVs eliminate a number of issues that have occurred with traditional therapeutic vectors like PEI and DOTAP, such as tissue targeting selectivity, toxicity, and scaling and production difficulties. Within 1.5 hours of intranasal treatment, GNVs were found to have moved rapidly into the brain in this investigation. Furthermore, they discovered that DiR-labeled pGNVs have a weaker signal than Syto60-labeled pGNVs. GNV phospholipid or cholesterol can be used as the lipophilic anchor for folate ligand.

## CONCLUSION

Nanotechnology-based drug delivery systems have showed considerable potential in improving cancer treatment. Unlike chemically generated nanoparticles, natural released nano-sized particles originating from various types of human cells, as well as exosome-like nanoparticles from edible plants, play an important role in intercellular communication. The therapeutic efficacy of nanoparticles is dependent on efficient cellular absorption and cytotoxicity.

Nanocarriers made from food-extractable components have been tested for medication delivery. Nanosized vesicles are important participants in cell-to-cell communication, affecting physiological and pathological processes such as cancer. For nanoparticles less than 100 nm, smaller particle size is advantageous to medication absorption. The relevance of plant-derived nanovesicles in cancer progression is uncertain.

Combining natural medicines with chemotherapy could be a viable cancer-eradication strategy in the near future. Many natural chemicals have emerged as alternative cancer preventative and treatment options. Natural chemicals are employed either alone or in combination with chemotherapy medications, allowing for a lower drug dosage. The therapeutic efficacy of nanoparticles is dependent on efficient cellular absorption and cytotoxicity.

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## Conflicts of interest

The authors confirm that this article content has no conflicts of interest.

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