ROLE OF PHYTOCHEMICAL COMPOUND WITH NANOPARTICLE: AS COMBINATORIAL

[1]Rishika Chauhan, [2]Dr. Anuj malik

[1]Research Scholar, Dept of Pharmaceutics, M.M College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, Haryana, India

[2]Dept of Pharmaceutics, M.M College of Pharmacy, Maharishi Markandeshwar (Deemed to be University), Mullana, Ambala, Haryana, India

Corresponding Author

Dr. Anuj malik

Abstract

This article focuses on how using phytochemicals Compounds with nanotechnology can improve such problems in a controlled manner by enhancing biodistribution of bioactive drugs, cellular metabolism, and encapsulating bioactive compounds. Phytochemicals have cut pharmaceutical manufacturing costs and are cost-effective. This review focuses on phytochemical substances and nanoformulation to improve therapeutic value, stability, and bioavailability. Studies may reveal phytochemicals alter nano- formulation. This review focuses on nano-phytochemicals. Nanotechnology, nanomedicine, and nanodrugs have grown over decades. This article discusses nanotechnology's function in phytochemicals.

Keywords: - phytochemical compound, cancer medicines, nanomedicine, combination therapy

Introduction

Phytochemistry investigates plant chemicals. Phytochemicals are valuable plant derivatives or compounds. Scientists, physicians, and researchers find phytochemical substances therapeutic. The world wants bioactive plant components and formulations. Medicine comes from plants, herbs, and shrubs. Throughout history, phytochemicals have prevented/cured disease. 67% of plants are therapeutic, but 50% of phytochemicals are unknown.

Pharmaceutical companies still use phytochemicals as medicine due to their effectiveness, low cost, and lack of toxicity (Tomiyama K et al.,). Future phytochemical research and medication discovery will be influenced by nanoformulation (Kumar et al., 2015). Culture, poverty, cost effectiveness, and ineffectiveness of modern medicine drive the use of phytochemicals as nanomedicine (Tenovor et al., 2006).

Nanoformulation incorporating phytochemical compounds is a godsend for industry and research and will lead to their vast application, high-loading medication, site drug delivery, and more. Nanolipidcarrier (NLC), liposomes, metal nanoparticles, silver nanoparticle polymer nanoparticles, nanostructured lipids, solid lipid nanoparticles (SLN). Nanoformulation affects poorly soluble molecules in medicines and phytochemicals.

The history of phytochemicals shows that they act as inhibitors, enzymes, and protein receptors. Phytochemicals:

• Antioxidant phytochemical molecules generate O2.

• Phytochemicals protect enzymes.

• Healthy tissue absorbs phytochemicals.

• Phytochemicals VD (volume of distribution).

• Benefits from preclinical models.

• Immune-boosting physiochemicals [31].

• Phytochemicals [35].

• Ist pass degrades orally administered phytochemicals.

Phytochemicals defend cells.

Combining phytochemicals increases their effectiveness.

Avicenna marina species from mangrove tree used in the treatment of ulcer (Subashree et al; 2010) and same species of Avicenna marina have found in different region exhibit anti-parasitic, antibacterial, antifungal activity (Khategi et al; 2003). Avicenna marina inhibits skin cancer, according to a 2001 study.

Phytochemicals have limited absorption, toxicity, decreased solubility, and GI stability. Polar, large compounds are hard to traverse the blood brain barrier, blood vessel endothelium, and GI tract. Nanoformulation can overcome this difficulty by encapsulating phytochemicals with nanotechnology and creating them in different sizes, shapes, and functions with varying compositions.

Phytochemicals are important in every business, especially cancer treatment. According to WHO, every sixth death in India is due to cancer. Cancer was the second-leading cause of death in 2015, with 7.7 million deaths. Colon, stomach, thyroid, breast, and cervix are common in women. Cancer is a group of diseases characterised by abnormal cell development that spreads. In a normal body, cells develop and divide to produce new cells while old ones die. In malignant bodies, this process fails because to an imbalance in cell creation. This causes cancer and tumour growth. Malignant or benign tumours don't spread through lymph or blood.

Over 350 nanomedicines have been patented in the last 25 years. Nanomedicine as entangled phytochemicals treats cancer. Curcumin from Curcuma longa treated cancer in vitro and in vivo (Tsai JR, Ameri A et al., 1998). Another study used luteolin nanoformulation to treat lung cancer cells (Akiyama H et al., 2001). Patent drug for cancer treatment introduces phytochemical nanoformulation such as paclitaxel (abraxane) (Wang y et al., 2015) and (Doxil) doxorubicin first liposomal anticancer medicine bearing phytochemical (Shan S et al., 2006, Thakkar HP et al.). Cancer is detoxified by phytochemicals. These chemicals have cancer-fighting pharmacological and physiological effects (astebial et., al 2002). Anticancer drug preparation using phytochemical compounds shows more significant action against cancerous cells. Phytochemical compound as nanoparticle or combinatorial of nanoparticle with phytochemical such as gold nanoparticle, silver nanoparticles shows more response against cancer disease due to their non-toxic, non-irritant, self-assembled nature (Mahesh et al., 2017). Anticancer S. borealis AuNPs in green. Genistein and capsaicin work better together than either medicine alone (wang et al., 2009). Quercetin and doxorubicin phytochemical nanoparticles were used to encapsulate drugs and target receptors in breast cancer (Lu et al., 2016). Gymnema sylvestre is AgNP, per Arunachalam et al. G. Using HT29 human adenocarcinoma colon cancer cells, silver NPs anticancer activity was compared. (2013) Green production of (SeNPs) selenium nanoparticles was produced by using fenugreek seed extract. Combining Selenium Nanoparticles with doxorubicin showed greater antitumor efficacy than independent therapies. Inhibits cell growth dose-dependently. SeNPs are used in catalysis, anticancer, antioxidant, rectifiers, and xerography.

Only botanists and biologists paid attention to phytochemical substances a decade ago, but 21st century study demonstrates their medical effects (kende H et al., 2006). Cancer treatment using phytochemical nanoformulation.

Phytochemicals are used as drug sources due to their wide therapeutic characteristics, and their chemomolecular composition can overcome bioavailability, low solubility, etc. phytophenolic Brassica oleracea contains rutin, kaempferol, naringenin, fisetin, catechin, and myricetin. Quercetin, a phenolic component from Haplopappus multifolius leaves, displays DPPH (1,1-diphenyl-2-picrylhydrazyl) in mice (Torres R et al., 2006). Another investigation of phenolic component from Thunbergia laurifoli Clostridium leptum and Bacteroides are found in Morinda oleifera leaves (Patil VV et al., 2019, Nayak BS et al., 2012).

Table 1 Medicinal functions of different class of phytochemical compounds.

S. No.	Phytochemical compound (Class)	Role	Reference
•	Glycoside (cardiotonic glycoside)	Cardiac function	[55], [93]
•	Flavoind	Oxidative stress damage, anticancer property	[63]
•	Sterol	Vitamin, hormone	[18], [74]

•	Quinine	Antibacterial effect	[74]
•	Tannin	Astringent, antibacterial, antifungal activity, antiseptic property, antimicrobial function, astringent	[5], [79], [93]
•	Polyphenols	Potential to defend against oxidative stress damage	[81]
•	Triterpenes	Anthelminthic, antiseptic, diuretic, expectorant, antibacterial activity	[78], [87], [77]
•	Alkaloids	Anaesthetic effects	[12], [39]
•	Coumarins	Antibacterial property, anticoagulant action	[40], [84]
•	Flavonoid glycoside	Bronchodilation action, stimulant	[84], [73]
•	Phenol	Antifungal activity	[39]
•	Saponins	Corticosteroids, steroidal function, and haemolyzing function	[19], [87]
•	Terpenoids	Antibacterial, antifungal	[5], [84]

B kumar et al. (2014) studied antibacterial, antioxidant, and biomedical applications of phytochemicals. Sacha inchi leaf extract is used to make non-toxic, non-irritant AgNPs. Ag nanoparticles have radical-scavenging and antioxidant properties. Bovine serum albumin-coated catechin and epicatechin nanoparticles increased stability and antioxidant activity. EI-Zayat. The researchers synthesised two distinct NP formulations using Ephedra aphylla extract and showed its effectiveness against cancer cells and DPPH using six tumour cell lines. Selenium or zinc NP improves biological properties, they found. Oedera genistifolia silver nanoparticles (Ag NPs) show good antibacterial profile and phytochemical evaluation against human cervical cancer and Gram-negative (-) and Gram-positive (+) bacteria. Antibacterial medicine using seabuckthorn silver nanoparticles has increased stability and lengthy activity against bacterial infection (Kalaiyarsan et al., 2017). Using selenios acid, Venugopal et al. (2019) generated selenium nanoparticles from Withania somnifera. Their work focuses on phytochemical selenium nanoparticles' antioxidant and antibacterial effects on Bacillus subtilis (12.2 mm), Staphylococcus aureus (19.66 mm), and Klebsiella pneumoniae (14 mm). Se NPs back green projects.

(Mittal K et al., 2016) reported on the antibacterial and anticancer potential of synthetic silver nanoparticles by medicinal plants such Syzygium cumini, Catharanthusroseus, Azadirachta indica, quercetinand gallic acid generating selenium NPs and silverselenium nanoparticles. All phytochemical NP have equal bactericidal efficacy against diverse strains, and selenium silver NP has a greater potential than chloramphenicol.

Syzygium cumini AgNPs destroyed bacterial and tumour cells dose-dependently at 10 g/mL. Se-NP antibacterial preparation was studied (Mohammed S. Al-Saggaf et al., 2020). SeNPs used SCE root extract for green photosynthesis. SCE/Se-NPs inhibited Salmonella typhimurium, E. coli, and S. aureus. The current study aims to physiologically synthesise SeNPs using Mucuna pruriens seed extract/powder (Menon et al., 2021). Environmental and antimicrobial nanoparticles were biosynthesized.

Amanda et al., 2018 studied protein corona role on silver nanoparticles and phytochemical encapsulates (HSA), EGCG, and curcumin (Cur). Their study compares NPHAS to citrate-stabilized AgNPs, however NPHAS is preferred. (Alberene et al., 2017) This study used the coprecipitation method Vinblastine sulphate with iron oxide and showed the chemotherapy against cancer was combined with the iron oxide NPs and tested on MCF-7 a breast cancer cell line. Vin- Fe_3O_4 inhibits MCF-7 development more effectively. Yordan et al., 2020 review phytochemistry Gut microbiota modulators and oxidative stress modulators target the intestinal barrier and membrane. (Anter et al., 2019) synthesised Chitosan oligosaccharide (COS) NP using tripolyphosphate (TPP) as a cross-linker. The NPs formula with COS showed the most drug entrapment efficiency and promise in stomach ulcer therapy. Hussein et al., 2020 studied microalgae's role in silver nanoparticle antibacterial activity (AgNPs). Synergistic effects of AgNPs on susceptible and multidrug-resistant bacteria.

Dietary phytochemicals prevent skin cancer, say researchers. Cell cycle, metastasis, angiogenesis, and cancer cell proliferation are affected by phytochemicals. Gingerol is integrated into solid lipid nanoparticles (SLN) with enhanced chemical stability (Ratcharin et al., 2012). Banjeer et al. found that dietary phytochemicals alter miRNA expression. Curcumin, ellagic acid, indole-3-carbinol, quercetin, resveratrol, diallyl disulphide, 3,3′ diindolylmethane, sulforaphane, and genistein alter BC miRNA in vitro and in vivo.

Table 2 Three different nanoformulation prepared by phytochemical compounds

Applications	Silver NP formulation	Gold NP	Selenium NP	Year (References)
Anticancer				
		Sasa borealis		Mahesh et al. (2017)
	Gymnema sylvestre			Arunachalam et al. (2014)
	Nepeta deflersiana			Sheddi et al. (2018)
			fenugreek seed	Ramamurthy et al. (2013)
			Allium sativum	Anu et al 2017
	Suaeda maritima (L.) Dumort	Suaeda maritima (L.) Dumort		Rajendran et al. (2016)
	Dropanax morbifera	Dropanax morbifera		Wang C et al. (2016)
			Asteriscus graveolens	Zeebaree et al. (2020)
Anti-oxidant				
	Plukenetia volubilis			B kumar et al. (2014)
	Dracaena mahatma			Shankar et al. (2018)
			Selenium	Hui yan et al. (2019)
			Withania somniferum	Venugopal et al. (2019)
			Allium sativum	Vyas et al. (2017)
Anti-microbial				
	Ginkgo biloba			Nishanthi R et al. (2016)

	Bauhinia acuminata and Biophytum sensitivum			Antony et al. (2017)
	Pelargonium endlicherianum			Seker et al. (2017)
	Mangosteen			Veerasamy et al. (2011)
			Allium sativum	Rana et al. (2018)
	Annona reticulata			Parthiban et al. (2018)
			Saussurea costus (SCE)	Mohammed S. Al-Saggaf et al. (2020)
			Mucuna pruriens	Menon et al. (2021)
			Aloe vera	Fardsadegh et al. (2019)
Anti-bacterial				
	Seabuckthorn			Kalaiyarsan et al. (2017)
	Oedera genistifolia			Okaiyeto et al. (2019)
	Ficus hispida			Ramesh et al. (2018)
	Callistemon citrinus			Larayetan et al. (2019)
			Clausena dentata	Sowndarya et al. (2017)
	Millettia pinnata			Rajkumar et al. (2017)
	Taraxacum laevigatum			Taher et al. (2017)

Metallic nanoparticles have biological uses due to their properties. Metallic nanoparticles include silver, gold, and selenium. Plant and microbe extracts were used to document metallic nanoparticles' roles.

Each group of phytochemical substances has a distinct function and application. Nanoformulation can enhance solubility, phytochemical stability, medication bioavailability, absorption, and protection from premature bodily breakdown.

Researchers have generated nanoliposomes, nano micelles, nanoemulsions, lipid nanocarriers, phytosomes, solid lipid nanoparticles, poly (lactic-co-glycolic acid) (PLGA) nanoparticles, and polyvinyl acid nanoparticles using phytochemical substances as nanoformulations.

Phytochemical compound promising applications as nanoformulation

Phytochemical Compound	**P.C class**	**Genius/species**	**Application**	**Reference**	**Nanoformulation**
Ursolic acid	Terpenoids	Holy basil	Hepatocellular carcinoma	[55]	Nanocarrier
Ginsenoside Rg3		Panax ginseng	In vitro and in vivo study	[36]	Silver nanoparticle
Curcumin	Polyphenol	Curcuma longa	Anticancer	[93]	Liposomal NP
Isoflavone	Polyphenolic	Soybean	Skin treatment (skin cancer)	[31]	Micelle’s nanoparticle
Cyanidin-3-glucoside	Anthocyanin	Delonix elata	antiulcer, antioxidant, anti-inflammatory, antiarrthymic	[92]	Copper nanoparticles
	Combination of phytochemical	Ficus krishnae	Antibacterial, anticancer	[10],[34]	Silver NP

Quercetin	Poly phenol	Onion	Prostate cancer	[52]	Quercetin NP
Curcumin	Polyphenol	Curcumin longa	Alzheimer disease, arthritis, anticancer	[50]	Nanolipidcarrie r
Withanolides	Alkaloids	Withania somnifera	Anticancer	[27]	Silver NP
Picroside I and II	Glycosides	Picrorhiza kurrooa	Hepatoprotecti on	[24]	PLA NP
Lycopene	Carotenoids	tomatoes	Antioxidants, anti-inflammatory, anticancer	[52]	SLN nanoparticle
Sennosides A	Dianthrone glycosides	Cassia angustifolia	Antibacterial	[99]	Ag NP
6-mercaptapuri ne	Purine		Antileukemia	[27]	Gold nanoparticle
Vincristine	Alkaloids	Catharanthus rosea	Anticancer	[60]	Chitosan NP
Doxorubicin	Anthracycli ne	Ocimum basilicum	Anticancer	[57]	NP
Vinblastine	Alkaloids	Catharanthus rosea	Anticancer	[47]	Polymeric, iron oxide NP
Pluchea	Alkaloids, phenolic, terpenes	Pluchea indica	Wound healing, antioxidant	[98]	NP
Paclitaxel			In vivo prevention of arterial restenosis	[21]	Lipid polymeric nanoparticle (LNP)

According to studies and literature reviews, phytochemicals have been employed in medicine since ancient times. Nanomedicine, antimicrobials, and therapeutics are biomedical nanoformulations. Observing the side effects of standard synthetic medication motivated scientists or researchers to adapt historical medical systems. Nanoformulation impacts phytochemicals' metabolism, bioactive properties, therapeutic use, and side-effect-free formulation, influencing phytochemical research. Nanocurcumin compositions with taxol have been studied.

Researchers use CADD, drug screening, molecular docking, etc. to learn about these compounds. Phytochemicals heal wounds, treat diabetes, Alzheimer's, heart disease, cancer, lesions, and prevent tumours. Some pharmaceutical companies sell 99.9% pure phytochemical substances with a COA, thus extraction, isolation, and purification can be omitted.

In healthy or sick hosts, phytochemicals may increase intestinal probiotic growth [18, 78]. Some phytochemicals have bacteriostatic or bactericidal properties [32]. Nanoformulation enhances solubility and bioavailability. Low-dose nanoformulated phytochemicals are effective. Entangling, encapsulating, or conjugating phytochemical nanocarriers improves absorption, dispersion, and therapeutic effect.

Conclusion: -

The present review focuses on phytochemicals and their derivatives that can be used with any other medicine for many purposes, including targeted sites, drug resistance in cancer cells, chemotherapy, preclinical models, invitro, and other uses. Scientists and researchers develop safe, cost-effective, and large-scale phytochemicals and medicinal substances. Using phytochemicals, nanoformulation delivers s.c. or i.v. medications (subcutaneous and intravenous). Safe and effective phytochemical- and nanoformulated medications are coming. Nanoformulations improve phytochemical potency, although their production is unknown. Nanoformulated phytochemicals are the future of pharma. Recent research indicates phytochemicals' utility in drug delivery and herbal medicine. Invented, patented, and popularised herbal therapies. Nanodrugs improve phytopharmaceuticals (NDDS). Effective nano-herbal drugs. Most plants and derivatives haven't been studied, therefore nanophytoformulation seems promising. Nanotechnology improves bioavailability, bioeffectiveness, pharmacokinetics, pharmacodynamics, and controlled release of bioactive components.

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