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REVIEW ARTICLE **OPEN ACCESS**

A Comprehensive Study of Curcumin with Their Novel Technologies

Jayant Bidkar*, Sumit Mule, Ganesh Dama, Shital Bidkar, Kranti Musmade
SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi, Otur, Tal. Junnar, Dist. Pune, Maharashtra, India.
Correspondence Email: jayantbidkar@gmail.com

ABSTRACT
A Novel Drug Delivery System (NDDS) is a new technique that combines innovative development, formulations, new technology, and novel methodologies for safely delivering pharmaceutical compounds in the body.The lipid-compatible molecular complex is known as phytosomes. Phytosomes technology is used to improve the absorption of phytoconstituents that are difficult to absorb. The use of medication delivery systems with the ability to pass the biological membrane can improve phytoconstituent bioavailability. Traditional herbal extracts have a worse pharmacokinetic profile than phytosomes.In recent years, the effective pharmacological activity of Curcumin in inflammatory disorders, cardiovascular disease, cancer, Alzheimer's disease and neurological disorders have been shown. However, the clinical application of Curcuma is severely limited by its main disadvantages such as instability, poor solubility, low bioavailability and high metabolism rate. Multifarious nanotechnology-based delivery strategies have been used to enhance the oral bioavailability, biological activity or targeting delivery ability of Curcumin . This review presents the potential nanoformulation based delivery systems for Curcumin containing liposomes, metallic nanoparticles, nanosuspensions, nanoemulsions, solid proliposome, which grant promising results for Curcumin to improve its therapeutic activities.
Keywords: *Curcumin, Phytosome, Novel drug delivery system, Herbal, bioavailability, biosynthesis.*

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INTRODUCTION

Curcumin is the main curcuminoid in turmeric, a renowned Indian spice that belongs to the ginger family (Zingiberaceae). Desmethoxycurcumin and bis-desmethoxycurcumin are the other two curcuminoids. Turmeric's yellow hue is due to the curcuminoids, which are polyphenols [1]. Turmeric has a long history of use as a spice in Asian cuisines as well as in other parts of the world.

In Persian, for examples, it is known as Zard choobe. It increases the colour tone and flavour of dishes like rice, yoghurt, and poultry. Consumers, on the other hand, prefer to combine it with other spices to enhance the flavour. With special reference to China, India, Iran, and Indonesia, certain communities around the world employ turmeric and its variant fractions to make certain traditional remedies to treat human ailments. Turmeric has been used as a tonic for a long time. It's also used to treat a range of ailments, including dyslipidemia, stomach problems, arthritis, and hepatic encephalopathy [2-4].

While curcumin supplementation appears to have a plethora of therapeutic benefits, the majority of these are related to its antioxidant and anti-inflammatory properties [5, 6].

Curcumin is available in capsules, pills, and ointments, among other forms. The US Food and Drug Administration (FDA) has designated curcuminoids as "Generally Recognized as Safe" (GRAS). The goal of this review is to give a quick summary of curcumin's potential health advantages [7, 8].

MORPHOLOGY

A perennial herb that grows to be around 1 m tall. The rhizome (underground stem) is thick, with the bases of previous leaves ringed around it. Turmeric reproduces only through its rhizomes. Large, oblong, up to 1 metre long, dark green on top, pale green underneath. Each pseudostem (leafy sprout) has 8-12 leaves. Yellow-white flowers on a 10-15 cm long spike-like stalk. Flowers do not produce viable seed because they are sterile. Brown, ovoid, and little. This isn't feasible [13-15].

Taxonomical classification of Curcumin

kingdom	plantae
clade	trichophytes
Clade	angiosperms
Clade	monocots
clade	Camelid
order	zingibereles
family	zingberaceae
genus	Curcuma
species	amada

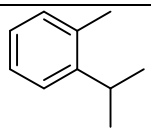
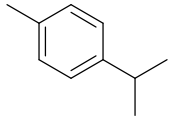
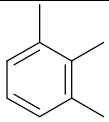
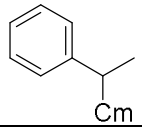
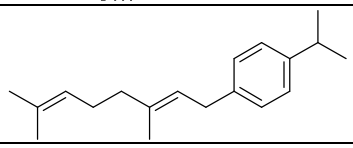
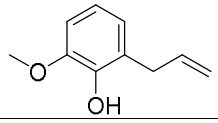
Common names

Language	Common name
Kannada	Ambarasini, Huli Arsin
Hindi	Aamaa-haldi, Amiyaa haldi
Malayalam	Mangayinji
Tamil	Mankayyinji
Telugu	Mamidi Allamu
English	Mango-ginger
Kannada	Aamrardrakam
Oria	Anada

Table.1: Chemical Constituents of Curcumin [16]

Sr. No.	Parts of Plants	Chemical constituents
1.	rhizome	β-Curcumene (42.0%), (-)-xanthorrhixol (36.6%), and ar-curcumene (7.5%)
2.	Leaf	Camphor (17.9%), epi-curzerenone (10.8%), curzerenone (9.5%), and isoborneol (7.3%)
3.	Root	α-Pinene (14.5%), caryophyllene oxide (9.4%), and alconfor (5.1%)

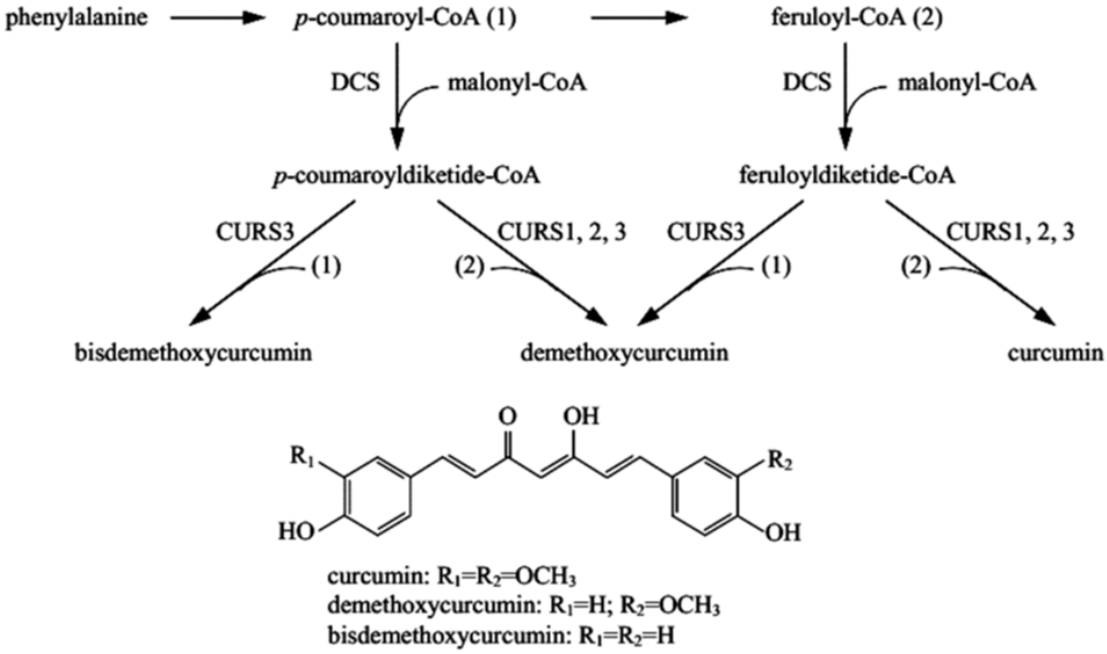
Table. 2: Some Important Chemical constituents

o-cymene	
p-cymene	
hemellitol	
β-curcumene	
β-tumerone	
m-eugenol	

Biosynthesis

Curcumin's synthesis pathway is unknown. Peter J. Roughley and Donald A. Whiting postulated two curcumin biosynthetic methods in 1973. The first mechanism involves cinnamic acid and 5 malonyl-CoA molecules forming a curcuminoid through a chain extension reaction. Two cinnamate units are linked by

malonyl-CoA in the second process. Cinnamic acid, which is generated from the amino acid phenylalanine, is the beginning point for both[17,18,19,20].



Medicinal Properties

Anti-oxidant Activity

Curcumin's antioxidant activity is enhanced by scavenging reactive oxygen species (ROS) such as superoxide radicals, hydrogen peroxide, and nitric oxide (NO) radicals, as well as preventing lipid peroxidation. Curcumin can also stop ROS-producing enzymes including LOX, COX, and xanthine oxidase from working. Because of its lipophilic nature, curcumin is also thought to be a chain-breaking antioxidant, possibly working as a peroxyl radical scavenger. Binding free radicals, hydrogen atom donors, and electron donors to neutralise free radicals are some of the mechanisms that can explain antioxidant activity. To do so, researchers used laser flash photolysis and pulse radiolysis to figure out how curcumin's antioxidant activity works. [21,22,23]

Antibacterial Activity

The essential oil from the rhizomes has antimicrobial properties. The antibacterial activity of mango ginger is due to difurocumenonol, amadannulen, and flavonoids. The antibacterial activity of mango ginger chloroform rhizomes extract was tested against *P.aeruginosa, S. aureus, E. coli, S. typhi, E. fecalis, B. subtilis, B. cereus, K. pneumoniae, Y. enterocolitica, E. aerogenes, P. mirabilis, and L. monocytogenes*. Furthermore, they discovered that the antibacterial activity of Difurocumenonol and amadannulen compounds. Myrcene and pinene, two components of volatile oils, have antifungal action against Curvularia palliscens, Aspergillus niger, Aspergillus terreus, Fusarium moniliforme, and Fusarium falcatum, respectively.[24]

Hepatoprotective Activity

Turmeric, like silymarin, has been discovered to have hepatoprotective properties. Turmeric has been shown to protect the liver from a range of hepatotoxic insults in animal tests, including carbon tetrachloride (CCl4), galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. Turmeric's hepatoprotective benefits are mostly due to its antioxidant capabilities and capacity to reduce the generation of pro-inflammatory cytokines. Curcumin treatment significantly reduced liver injury in rats with CCl4-induced acute and subacute liver injury when compared to controls. When administered to ducklings infected with Aspergillus parasiticus, turmeric extract reduced fungal aflatoxin production by 90%. Aflatoxin-induced biliary hyperplasia, lipid alterations, and necrosis were likewise reversed by turmeric and curcumin.[25]

Wound Injury

The skin acts as a natural barrier against the elements and performs a number of important defensive functions. When the skin's integrity is damaged by acute or chronic injuries, the body undertakes a multi-step and dynamic process at the wounded location that results in partial tissue repair and restoration of the skin's barrier function. The primary goal of wound healing is to restore tissue integrity and maintain homeostasis. Hemostasis, inflammation, proliferation, and remodelling are the four phases of wound healing that overlap yet are clearly defined. Hemostasis occurs when platelets aggregate and blood clots as a result of an injury. For cell migration, the blood clot acts as a temporary extracellular matrix.[26,27]

Cytotoxicity Activity

Curcumin has a dose-dependent chemopreventive impact in numerous animal tumour bioassay systems, including colon, duodenal, stomach, esophageal, and oral carcinogenesis, according to recent research. On mouse skin, it has been demonstrated to reduce tumours caused by benz(a) pyrene and 7, 12 dimethyl benz(a) anthracene, tumour promotion caused by phorbol esters, carcinogen-induced tumorigenesis in the fore stomach, and N-ethyl-N′-nitro-Nnitrosoguanidine-induced duodenal cancers. The use of turmeric in Indian cooking has been linked to a lower incidence of colon cancer among Indians. [28,29,30]

Novel Drug devlivery system in phytosomes

Natural therapies are now used to treat the majority of common diseases and nutritional issues.Several plant extracts and phyto components, despite having great bioactivity in vitro, have poor lipid solubility, incorrect molecular size, or both, leading in poor absorption and bioavailability in humans. As a result, great effort has gone into the development of phytosomes, a new idea in herbal delivery that is more absorbed, utilised, and produces better effects than traditional herbal extracts. Herbosomes are another name for phytosomes. Phyto refers to a plant, while some refers to a cell. Phytosomes are a type of microorganism that resembles a cell. The phospholipids in phytosomes, primarily phosphatidylcholine, form a lipid-compatible molecular complex with other elements. Phytosomal complexes were initially studied for cosmetic purposes. However, Indena, a leading provider of nutraceutical components such as milk thistle, ginkgo biloba, grape seed, green tea, hawthorn, and ginseng, created and maintained the PHYTOSOME technique. Recently, one of the most popular beverages has been green tea. its active ingredients Major supplement companies are interested in using EGCG in weight-loss supplements. Phytosomes are superior than liposomes since the component and phospholipid complex formation ratios are 2:1 and 1:1, respectively.Much superior absorption and stability profiles, respectively. Phytosomes are both anti-inflammatory and antioxidant. In animal models used in research It increased resistance to the development of atherosclerotic lesions and boosted a protective mechanism. prostaglandin, which protected the ventricular heart pump muscle from harm caused by a lack of blood flow. Development In India, phytosomes are in the early phases of development.

Reported methods of Noval drug delivery of Curcumin

Shyam S. Bansal *et. al :*Chemopreventives have been proven to alter a number of proteins involved in diverse molecular pathways that regulate inflammatory and carcinogenic responses in a cell over the last four decades of research. Chemopreventives influence a variety of enzymes, transcription factors, receptors, and adhesion proteins. Despite the fact that all these natural chemicals showed great efficacy in cell culture investigations, they had limited efficacy in clinical trials. Their introduction into the therapeutic context is hampered by their poor solubility, quick metabolism, or a combination of the two, which results in poor bioavailability when given orally. Alternative solutions should be investigated to overcome these restrictions and simplify their transition to clinics.[31]

Asish K Dutta *et al :* Curcumin, the main component of the common dietary spice turmeric, has a wide range of biological and pharmacological actions, making it a potential agent for the treatment and prevention of a wide range of human disorders. Curcumin's safety and efficacy at very high dosages have been demonstrated in several investigations; nonetheless, curcumin's relative bioavailability is a key problem. It has a very poor water solubility, and whether it metabolises into active or inactive metabolites is unknown. In this study, we have examined the different innovative curcumin drug delivery systems that have been described in order to improve the solubility, bioavailability, and efficacy of curcumin, such as nanoparticles, micellar formulations, liposomes, and cyclodextrin inclusion complexes.[32]

Shweta Vashist *et al:* Curcumin is a key component of turmeric, which is derived from Curcuma longa, an Indian rhizomatous medicinal plant belonging to the Zingiberaceae family. Curcumin is a yellow pigment that is often utilised in the food processing business as a spice. The principal active ingredients of turmeric are curcumin, demethoxycurcumin, and bisdemethoxycurcumin, which are together known as curcuminoids. Curcumin has been shown to have a variety of biological activities, pharmacological performances, give protection, and promote health in recent studies. This study summarises current studies on its diverse bioactivity, including antioxidant, anti-inflammatory, and immune-regulatory actions, as well as malignancies, diabetes, the liver, and the cardiovascular system. Curcumin is classified as Class IV in the biopharmaceutical classification system, which signifies limited solubility and permeability.[33]

Kaviya.L *et. al:* The widespread use and misuse of currently available treatment drugs has resulted in the emergence of resistance strains of common diseases as well as a rise in the prevalence of side effects. As a result, looking for phytochemicals extracted from plants is seen as a viable option. Because just a small number of plant species have been studied phytochemically to date, there is a lot of room for new bioactive chemicals and medications to be discovered. In the field of nanoformulation, the creation and development of herbal nanoparticles has become cutting-edge research.[34]

Dongmei Sun *et. al:* Monocyte-derived myeloid cells have an important role in autoimmune and inflammatory illnesses, as well as malignancies. Exosomes can transfer anti-inflammatory drugs like

curcumin to activated myeloid cells in vivo, according to new research. This method allows anti-inflammatory medications like curcumin to target inflammatory cells while also avoiding undesired side effects that restrict their effectiveness. We show that curcumin given by exosomes is more stable and highly concentrated in the circulation, using exosomes as a delivery mechanism. We show that exosomes determine target selectivity, and that improving curcumin activity is accomplished by directing curcumin to inflammatory cells, which has therapeutic but not harmful consequences.[35]

Jiajiang Xie *et. al :*The construction of a therapeutic drug-phospholipid complex using a mix of natural active ingredients and phospholipid (PC) has become a global trend in nanomedicine. It can serve as a unique bridge between classic dosage forms and innovative drug delivery systems because it is an amphiphilic molecular complex. We picked a pharmacologically safe and low toxic chemical curcumin (CUR) to increase drug-loading ability, accomplish controlled/sustained drug release, and improve anticancer efficacy in this paper based on drug-phospholipid complex approach and self-assembly technique. A co-solvent approach and a nanoprecipitation method were used to make a novel CUR-soybean phosphatidylcholine (SPC) complex and CUR-SPC complex self-assembled nanoparticles (CUR-SPC NPs).[36]

Dongmei Sun *et. al*: Monocyte-derived myeloid cells have an important role in autoimmune and inflammatory illnesses, as well as malignancies. Exosomes can transfer anti-inflammatory drugs like curcumin to activated myeloid cells in vivo, according to new research. This method allows anti-inflammatory medications like curcumin to target inflammatory cells while also avoiding undesired side effects that restrict their effectiveness. We show that curcumin given by exosomes is more stable and highly concentrated in the circulation, using exosomes as a delivery mechanism. We show that exosomes determine target selectivity, and that improving curcumin activity is accomplished by directing curcumin to inflammatory cells, which has therapeutic but not harmful consequences. In addition, we demonstrate the therapeutic utility of this method in a lipopolysaccharide.[37]

Mohi-ud-din *et. al :* Curcumin, a hydrophobic polyphenolic molecule found in Curcuma longa Linn. (Turmeric), has been used to treat Amyotrophic lateral sclerosis, multiple sclerosis, Parkinson's disease, Prion disease, stroke, anxiety, depression, and ageing. Curcumin's medicinal potential is limited by the Blood-Brain Barrier (BBB), which prevents it from reaching the brain. This study summarises current developments in curcumin's therapeutic efficacy, as well as numerous creative ways for overcoming its low bioavailability across the blood-brain barrier. In addition, the study summarises several toxicological research as well as curcumin's significance in CNS illnesses.[38]

Takuro kurita *et. al:*Curcumin, a polyphenolic substance derived from the turmeric plant (Curcuma longa L), has been shown to modulate several intercellular signalling pathways involved in inflammation, cancer cell proliferation, growth, invasion, drug sensitivity, angiogenesis, and metastasis. Curcumin has shown great efficacy in cell culture experiments, but only modest benefit in clinical investigations when given in traditional oral formulations. This disparity is mostly due to its low oral bioavailability, which could be due to poor solubility, a poor pharmacokinetic profile, or a combination of the two. Alternative medication delivery tactics and systems should be investigated to overcome these obstacles. Following a brief discussion of curcumin's physicochemical properties and pharmacokinetic profiles, this article discusses current improvements in curcumin oral delivery systems.[39]

O. Sreekanth Reddy *et. al :* The goal of this study is to use a simple ionotropic gelation procedure to make Curcumin encapsulated microbeads from Sodium Alginate/Polyethylene Glycol/Kaolin using glutaraldehyde as a crosslinker. To confirm the creation of microbeads, Fourier transform infrared spectroscopy was used to characterise the produced microbeads. The homogeneous molecular dispersion of CUR in the microbeads was confirmed by differential scanning calorimetry and X-ray diffraction investigations. CUR encapsulation efficiency in microbeads was found to be between 40 and 49 percent. Dynamic swelling experiments and in vitro release kinetics were carried out at 37 oC in simulated intestinal (pH 7.4) and stomach (pH 1.2) fluids. The findings imply that both swelling and cumulative release studies are influenced by the pH of the test media, which could be useful for medication administration in the intestine.[40]

Adhimoolam Karthikeyan *et. al :* Curcuma longa is a popular spice and medicinal plant in Asia. Curcumin (diferuloylmethane), a hydrophobic bioactive substance discovered in the rhizome of Curcuma longa, is a hydrophobic bioactive ingredient. It has gotten a lot of press in recent years because of its wide range of biological and pharmacological effects. Its low water solubility, poor bioavailability, and quick metabolism, on the other hand, are important roadblocks to successful therapeutic applications. As a result, researchers have tried to improve curcumin's biological and pharmacological activity while also addressing its disadvantages via effective delivery techniques, including nanoencapsulation. So far, research efforts and data from the literature have revealed that nanorange formulations of curcumin (Nanocurcumin) offer a promising potential for increasing all of curcumin's biological and pharmacological benefits, which was previously impossible.[41]

Yoichi Sunagawa *et. al:* Curcumin inhibits the activity of p300 histone acetyltransferase, which has been linked to the progression of heart failure. In rat models of heart failure, native curcumin at a dose of 50 mg/kg reduced the decline of systolic function. We created a unique drug delivery system (DDS) that significantly raises plasma curcumin levels in order to provide more efficient oral pharmacological therapy against heart failure with curcumin. DDS curcumin, but not native curcumin, recovered left ventricular fractional shortening in post-myocardial infarction rats at a dose of 0.5 mg/kg. As a result, our DDS strategy will be relevant in human clinical settings.[42]

CONCLUSION

In recent years, there is a continuous growth and interest in natural derived products. Several chemical constituents from curcuma shows low solubility and poor bioavailability. To enhanced solubility, bioavailability and targeted drug delivery, nanotechnology-based formulations were developed. This present review has described comprehensive information considering pharmacological property and most importantly have explained rational delivery approaches. The primary pursuit in developing such approaches is to improved bioavailability and therapeutic activity of Curcuma ambda.

FUTURE PERSPECTIVE

Herbal or herbs of optimum concentration are required for maximum benefit or effectivity. Controlling the pharmacokinetic and pharmacodynamic properties of drug is required for targeted drug delivery. According to that, novel drug delivery system developed. In consideration of limitation associated with low solubility, poor bioavailability, nanoformulation have been proved to be advance platform to improve bioavailability and therapeutic activity. Meanwhile, more research on developing nano-based formulation should be performed in the future to overcome pharmacokinetic and pharmacodynamic problems related to the herbal drugs.

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Disclosure of conflict of interest

The author have no conflicts of interest.

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