e-ISSN: 2248-9126
Vol 9|Issue 1| 2019 |11-22. Print ISSN: 2248-9118

Indian Journal of Pharmaceutical Science & Research

www.ijpsrjournal.com

CURCUMIN DRUG DELIVERY SYSTEM

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ABSTRACT

Curcumin (diferuloylmethane) is the natural polyphenolic compound. It is bioactive and major phenolic component of turmeric. It is derived from the rhizomes of the plant 'Curcuma longa' Linn of family Zingiberaceae. It is water-insoluble and has potent anticancer, anti-inflammatory, and antioxidant activities. Besides this it also plays significant and pleiotropic role in cardiovascular diseases, Alzheimer's disease, and other neuromuscular diseases. It controls inflammation, oxidative stress, cell secretion, cell survival, homeostasis, and proliferation. The clinical implication of curcumin is hindered as due to low solubility, physicochemical instability, and poor bioavailability, rapid metabolism, and poor pharmacokinetics. These issues can be overcome by utilizing efficient delivery systems. A number of formulations exist that can be translated toward medicinal use upon successful completion of pre-clinical and human clinical trials. Nano-systems can deliver the active constituents at sufficient concentration directing it to desired site of action. In this article a brief overview of different drug delivery systems of curcumin and their recent advances have been discussed.

Keywords: Curcumin, Nanoparticles.

INTRODUCTION

Origin

First of all Curcumin is the component of turmeric. It is prepared by pulverizing the dried rhizomes of the plant 'Curcuma longa' belonging to Zingiberaceae family. The plant grows naturally in India and other parts of South-east Asia. Alcoholic extract of curcuminoids contains 3-5% of curcuminoids. It also contains up to 5% resins and essential oils [1].

Curcumin has the history of administration in traditional systems of India, China and Iran [2]. The plant 'Curcuma longa' is found in abundance in countries like India, Sri Lanka, Myanmar, Thailand, Malaysia, Indonesia, China and some African countries [3,4].

More than 10 different curcuminoids are isolated from Curcumin. They are Curcumin I, desmethoxycurcumin (Curcumin II), and bisdesmethoxycurcumin (Curcumin III).

Sesquiterpenoids such as turmerone and curlone are components of turmeric essential oils and have biological components of turmeric essential oils. They have biological properties similar to those of curcuminoids. However, differences in activity among the curcuminoids congeners and other oils remain to be determined.

Therefore, when commercially available 'Curcumin' or 'turmeric' is used for the activities of these preparations in the literature are compared; the results may depend on the origin or quality of the preparations [5].

USES

Anticancer activity

Breast Cancer

Breast cancer is the most common and frequently diagnosed cancer affecting women worldwide. It causes significant inhibition of tumour regression in a xenograft mouse model of human breast cancer [6].

Ovarian Cancer

Ovarian cancer composed of different types of cancer depending on the cells from which they form. The major difficulty in treating advanced ovarian cancer is chemo radiotherapy resistance. When curcumin conjugated with Monoclonal antibody enhance the site specificity and

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sensitivity of the chemo radiotherapy resistance of ovarian cancer cells [7]. It inhibits proliferation and clonogenic potential of cisplatin resistant cells (A2780CP) in the presence of low levels of cisplatin. Curcumin has been found to completely inhibit the effect of C-reactive protein (CRP) which has a tendency to damage the vascular endothelial cells [8].

Pancreatic Cancer

Curcumin acts as a potential agent to inhibit the tumour growth. The therapeutic effectiveness of nanocurcumin was confirmed by cell viability and clonogenic assays[9].

Cervical Cancer

Cervical cancer is the most common and deadliest cancers among women worldwide and is related with Human Papillomavirus (HPV) infection. Nanocurcumin effectively inhibits cell growth & further induces apoptosis. Then it arrests the cell cycle in cervical cancer cell lines [10]. Curcumin modulates the in vitro expression and function of P-g in multidrug-resistant human KB-V1 cells [11, 12].

Anti-inflammatory Activity

Curcumin inhibits TNF-dependent NF-κB activation, as well as other activation pathways induced by various agents of which some were used to producer active oxygen intermediates that were also shown to be putout by curcumin [13]. COX-2, the inducible form of cyclooxygenases, predominates at inflammatory sites, and a great number of papers indicated a critical role of COX-2 in tumour promotion. Curcumin down-regulates the expression of enzyme and inhibits the expression of pro-inflammatory enzyme 5-LOX. It also induces down-regulation of various inflammatory cytokines such as TNF, IL-1, IL-6, IL-8, interferon and some other chemokine [14, 15].

Anti-HIV Activity

Curcumin exhibit effective inhibition of HIV-1 replication in vitro. It down regulates gag gene expression as a result inhibits the synthesis of pro-viral genes [16].

Parkinson's disease

Curcumin can mitigate S-induced cytotoxicity provided with system in neuron degeneration. In Parkinson's disease curcumin reduced ROS levels that has been generated by oligomer a-syncline [17, 18].

Chronic Obstructive Pulmonary Disease (COPD)

Reactive oxygen species play an important role in causing inflammation through stress kinases and redox sensitive transcription factors such as nuclear factor (NF)-κB and activator protein. Activation of (NF)-κB increases acetylation and inhibits deacetylation activity which leads to inflammatory gene expression and attenuated glucocorticoid sensitivity. The polyphenols present in curcumin play a role in controlling the activation of NF-κB and thus it can be used in lung epithelial cells to control the expression of inflammatory gene [19].

Alzheimer's disease

AD is characterized by the presence of extracellular deposition of aggregated amyloid-ß (Aß) peptide and intra-neuronal accumulation of hyper phosphorylated Tau protein and activation of caspase pathway [20]. Curcumin suppresses oxidative tissue damage and reduced amyloid-ß deposit [21].

Heart Failure

Curcumin possess a HAT inhibitory activity. It inhibits activity of HAT .NF-κB factor is also involved in cardiomyocyte hypertrophy. So curcumin which has already been known to inhibit NF-κB can also be used in preventing myocarditis[22].

PHYSICOCHEMICAL PROPERTIES

Curcumin is a yellow-orange powder. It has the molecular formula of $C_{21}H_{20}O_6$ (MW 368.39). It has a melting point of183˚C.

It is insoluble in water at acidic and neutral pH, but the solubility increases at alkaline pH as ionization of its phenolic hydroxyl group takes place. Its solubilityis limited in common organic media such as ethanol and vegetable oils, which makes ordinary liquid formulation difficult [23, 24].

The stability of aqueous solutions of curcumin (water or water/organic medium mixture) is pH-dependent, being reasonably stable at pH 1-6 and unstable at pH >7. Under pH conditions, more than 90% of curcumin is degraded within 30 min. In alkaline aqueous solution, hydrolytic degradation products such as vanillin, ferulic acid and feruloyl methane were detected [24].Curcumin is also sensitive to oxygen. Autoxidation proceeds in aqueous solution, and bicyclopentadione was identified as a main degradation product. Furthermore, curcumin in solution decomposes with light (UV and visible).Therefore, to prevent loss during experiments, strict attention should be paid to the environment (pH, air and light) [25].

CLINICALSTUDIES CURRENT STATUS AND ISSUES

Many trials on curcumin are designed to study its curative effects on diseases and condition such as dermatitis, stomatitis, chronic colitis, rheumatoid arthritis, central nervous system diseases such as Alzheimer's disease & depression. The oncology trials are also performed in conjunction with chemotherapy or radiation therapy.

Many clinical studies of curcumin have been already conducted worldwide. There are a few examples

with positive outcomes. During phase II clinical trial on 25 patients with advanced pancreatic cancer, one patient was given a dose of 8 g of curcumin orally for two months showed tumour regression and increased serum levels of cytokines [26]. In other clinical trials, curcumin demonstrated some therapeutic effect in high-grade prostatic intra-epithelial neoplasia (phase I) [27] and multiple myeloma (monoclonal gammopathy of undetermined significance and multiple myeloma). Most of the clinical studies had small patient enrolments However, in recent trials; quality has been improved [28].

CURCUMIN DELIVERY METHODS

To achieve optimum results due to application of a drug to alleviate pathological disorder requires a specific method of administration generally tailored, so that the drug reaches the pathologic lesion in therapeutic amounts.

Oral Administration

Curcumin has negligible bioavailability. Less than 1% of oral curcumin enters the plasma and the small amount of curcuminthat enters the bloodstream is rapidly conjugated via glucuronidation and sulfation to inactive products in the liver. When turmeric extracts taken orally may have potential utility for prevention of multiple diseases; there remain issues of aqueous solubility, poor intestinal bioavailability resulting from metabolic inactivation in the gut wall, and negligible detectable blood levels. Curcumin bioavailability is also limited because of reducing enzymes (dihydrocurcumin reductase) in E coli in the gut [29].

Curcumin is highly lipophilic and crosses the blood–brain barrier. Only very small amounts of orally administered curcumin are detected in the blood and the brain [30].

Intraperitioneal Administration

Intraperitioneal (IP) curcumin administration effectively inhibits inflammation and collagen deposition. It further reduces fibrotic progression. The IP route has been preferred because of simplicity of administration, and avoidance of volume limitations as compared to intravenous administration [31].

Subcutaneous Administration

Curcumin's poor oral bioavailability (<1%) results in barely detectable plasma concentrations, assuming the processing of plasma samples for analysis accounts for curcumin stabilization. The inability to achieve effective systemic concentration following oral administration limits curcumin's therapeutic potential in systemic cancers and neurologic disorders. Extended systemic presence of curcumin following subcutaneous administration using a sustained release microsphere formulation could deliver effective therapeutic levels[32].

Intramuscular Administration

Curcumin distribution in the plasma and brain was measured following intramuscular, gavages, and intraperitoneally application. Plasma levels of curcumin intramuscular injection were compared to Intraperitioneal injection respectively. Brain tissue levels following intramuscular injection vs. intraperitoneally injection were similarly increased respectively [33].

Intravenous Administration

Formulation is required for the curcumin to give intravenously. Several formulation methods are available. It allows repeated systemic injections of curcumin reported in the preclinical studies [34-37].

Intra-arterial Administration

Curcumin was applied to endovascular stents by a method called as dip coating method for reducing restenosis [38].

Topical Administration

Curcumin was applied for the ophthalmic and cutaneous disorders such as skin ulcers or in combination with neem paste for scabies. [39].

Intranasal Administration

Curcumin is absorbed through the nasal mucosa across the cribriform plate and further transported into the brain. For this a mucoadhesive micro emulsion was developed by the water titration method. The micro emulsion was transparent, and stable. The micro emulsion was non ciliotoxic because it was having excised sheep nasal mucosa. The intranasal administration of this formulation can deliver an effective amount of curcumin to the olfactory mucosa, and may be useful to treat neurodegenerative disorders [40-42].

Rectal Suppository Administration

Rectal suppositories directly deliver drug into the blood stream via absorption. The suppository base consists of blend for effective delivery of the drug. The breakdown of suppository takes place in between 5-6 min with absorption in 20-30 min [43].

Intrathecal Administration

In this the curcumin is delivered directly into the cerebrospinal fluid. It is delivered to reduce the nociceptive effects of pathogenic substances in human brain and spinal cord based upon curcumin-induced anti-nociceptive activity when administered systemically [44-46].

Controlled Release Implant Administration

A comparison of bioavailability of curcumin given by implants showed significantly higher levels of curcumin in the plasma, liver, and brain [47].

CURCUMIN FORMULATIONS AS SUITABLE DRUG DELIVERY SYSTEM

There are emerging list of formulations as first line therapeutic drugs to improve human health which have been approved or are under consideration by Food and Drug Administration (FDA). These help to overcome challenges and also make the translation of curcumin easy from bench to clinical application.

Nanoparticles (NP)

Nanoparticles are the particles ranging in size from 1 to 100 nm. They have distinct physical and chemical properties that can be exploited for drug delivery [49]. Encapsulating drugs within nanoparticles improve the solubility and pharmacokinetics of the drugs. Sometimes they also enable targeting slow release of drugs. They are useful for poorly water soluble drugs or lipophilic drugs [50].

The selection of a nanoparticle preparation method for effective encapsulation of active agents involves choosing the right polymer composition, stabilizer, solvent, and drug solubility and preparation technique [51]. The size, polydispersity index and entrapment efficiency are also depended on composition materials used [52].

Many materials have been explored to use as nanoparticle carriers such as poly lactic-co-glycolic acid (PLGA), human serum albumin (HSA), chitosan, poly (e-caprolactone) (PCL), glycerol monooleate (GMO), etc. PLGA is the most generally used, because of its solid state solubility, compatibility, biodegradability, and versatile degradation kinetics. The curcumin encapsulated nanoparticles in these materials could be prepared by several techniques such as emulsion, precipitation and solvent evaporation techniques [48, 53, 54].

Polymeric Nanoparticles

These are the colloidal systems which work as the vectors to control the drug release. They can increase the solubility of constituents, reduce therapeutic dose, and improve absorption of the active components. They have an advantage that when it is used in blood they are stable, non-toxic, non-immunogenic, non-thrombogenic, and non-inflammatory. They also do not activate neutrophils and avoid reticulo-endothelial system. They range from 10 to 1000 nm in diameter. They can appear as Nano capsules and Nano spheres. Nano capsules consist of an oily core surrounded by a polymeric membrane. The active constituent can be adsorbed in polymeric membrane or dissolved in oily core. Nano spheres are made from the polymeric structure which can be retained or adsorbed. The methods used to produce polymeric nanoparticles are the in situ polymerization method, with dispersed monomers (alkyl cyanoacrylate), precipitation of preformed polymers, such as poly (lactic acid) (PLA), poly (lactic-co-glycolic acid) (PLGA), poly (ε-caprolactone) (PCL), methacrylic acid copolymers, and acrylic or methacrylic esters [55-58].

Solid-Lipid Nanoparticles

These were introduced in the mid-1990s as novel drug delivery systems capable of protecting the labile drugs from light/pH/heat-mediated degradation, controlled release, and excellent biocompatibility. These are spherical lipid NPs with a high specific surface area that can be easily modified to

(i) attain a favourable zeta potential,
(ii) Pseudo zero-order kinetics,
(iii) Rapid internalization by cancer cells, and
(iv) Impart stealth properties to lessen uptake by the reticuloendothelial system[59, 60].

They can cross blood brain barrier and provide an alternative vehicles for poorly lipophilic drugs which cannot cross blood brain barrier[61]. They are less toxic as compared to polymeric nanoparticles.They can be stabilized by surfactants. Theymay be used in the pharmaceutical field for various routes of administration, such as oral, parenteral, and percutaneous. They not only protect entrapped drug from photochemical or pH-mediated degradation but also enables drug targeting and large scale production [62, 63].They are made up of natural or synthetic lipids such as lecithin or triglycerides [64].

Liposomes

These are the spherical bilayer vesicles with an aqueous interior formed by self-association behaviour of amphiphilic phospholipids with cholesterol molecules. Depending upon their bilayer structure and size, liposomes can be categorized as multilamellar, large unilamellar, or small unilamellar. Depending upon the driving force for drug release, they can be classified as conventional liposomes, pH-sensitive liposomes, cationic liposomes, immunoliposomes, and long-circulating liposomes. They are used for parenteral administration [65, 66].Liposome has a phospholipid bilayer structure, which is similar to that of biological membrane. So it allows for both stabilization of the compound in physiological pH and increasing its solubility in aqueous environment. Their diameter varies from 25 nm to2.5 nm. They are able to deliver drugs into cells by fusion or endocytosis [67].

Nano emulsions

These are the colloidal, optically isotropic, transparent or slightly opalescent formulations. It consist of surfactant, surfactant oil, and water. It is also known as micron emulsion [68]. It has a huge surface tension thus have a significant surface energy. They have a droplet size of 20 to 100 nm[69].

Micelles

These are the self-association of amphiphilic into small aggregates having diameter less than 100 nm. These aggregates have hydrophobic core surrounded by

hydrophilic layer in aqueous solution. The hydrophobic drugs are thus dissolved in the core forming aqueous solution of parenteral dosage form[70].It is a Nano sized vesicular membrane which becomes soluble in water by gathering the hydrophilic heads outside in contact with the solvent and hydrophobic tails inside. The shape or morphology of micelles is from amphiphilic block copolymers such as spherical, rod like, and star like, as well as vesicles. The hydrophobic core area hands out as a pool for hydrophobic drugs, while the hydrophilic shell area stabilizes the hydrophobic core and makes the polymers water soluble. Polymeric micelles can serve as transporters of water-insoluble drugs such as curcumin, which can augment the drug's efficiency by targeting definite cells or organs; therefore, fewer drugs accumulate in healthy tissues and their toxicity reduces, and occasionally higher doses can be administered [71].

Phospholipid Complex

A molecular complex of curcumin with phosphatidylcholine can be formed by refluxing in organic solvents. It can reduce the hydrophobicity of curcumin. It can also increase the permeability by interacting with membrane components.

It has better hepatoprotective activity, owe to its superior antioxidant property, than free curcumin [72].

Transdermal Curcumin Delivery

Curcumin has very poor permeability [73]. It is therefore classified as BCS Class IV molecule because of its poor solubility and poor intestinal permeability. It has high first pass metabolism delivered by oral route. Transdermal delivery (skin route) represents an attractive alternative to oral delivery for local and systemic therapeutic uses. It is used for various types of skin diseases such as scleroderma, psoriasis, and skin cancer. Transdermal drug delivery can avoid first-pass metabolism and also is considered as a convenient route for drug administration [74].

Cyclodextrin Inclusions

Cyclodextrin are cyclic oligosaccharides with a hydrophilic outer surface and lipophilic central cavity. Three types of Cyclodextrin exist: α-Cyclodextrin, β-Cyclodextrin, and γ-Cyclodextrin which are composed of six, seven, and eight α-(1, 4)-linked glycosyl units, respectively.β-Cyclodextrin is most useful because of greater accessibility and low price. They have a special ability of enabling drugs to increase their water solubility, reduce bitterness, and enhance stability and improving bioavailability [75, 76]. One of the main drawbacks of the Cyclodextrin, especially γ-Cyclodextrin is their relatively low aqueous solubility, which creates difficulties in their development as carriers of curcumin. Another problem is the expensive and long process of partition of the main types of Cyclodextrin in the enzyme dissolution of the starch. Use of organic solvents such as toluene or acetone is required, and also the presence of these solvents is associated with the emergence of unwanted immunological or toxic effects [76].

Solid Dispersions

It is defined as the dispersion of one or more active ingredients in an inert carrier or matrix in the solid state prepared by melting (fusion), solvent or melting-solvent methods. Nowadays it was found that these solid dispersions can increase bioavailability of poorly water-soluble drugs such as curcumin [77-80]. Solid dispersion technology transforms crystalline materials to amorphous materials.

Crystal and amorphous solid dispersions have also been designed by wet-milling and subsequent freeze-drying with the aim of improving physicochemical and pharmacokinetic profiles of curcumin [81].

Niosomes

These are microscopic lamellar constructions of non-ionic surfactants of alkyl or dialkylpolyglycerols ether category with cholesterol. They were first introduced in 1970s [82, 83]. It can provide the drug molecules a wide range of solubilities due to presence of hydrophilic, lipophilic and amphiphilic moieties. They behave similar to that of liposomes. They can be used asan alternative to liposomal drug carriers. Type of surfactant, encapsulated drug nature, storage temperature, detergents, and use of membrane spanning lipids affects Niosomes stability. They can be used in anti-cancer and anti-infectivedrug targeting agents. They can increase the bioavailability of poorly water-solubledrugs such as curcumin and also increase the skin penetration of drugs [84]. It can be apotential drug delivery system inordertosuppress degradation of curcumin and increase its life-time.

Niosomes are very stable and promising prolonged delivery systems for curcumin [85].

Niosomes enhances permeation of curcuminoids. Such formulations have superior properties for transdermal drug delivery system [86].

Dendrimers

These are the group of branched globular polymers which are created with structural control. They were introduced in the mid-1980s. They were also referred to as structural proteins. Dendrimers are the series of polymeric architecture with different chemical and surface related properties. The Dendrimers structure composed of core, branched interiors with numerous surface functional groups. It can serve as the platform of which additional substrates can be added to this spherical molecule in a highly controlled manner [87, 88].

Nanogels

These are the cross-linked three dimensional polymer networks created through covalent linkages and

further customized to gel networks with biocompatible and degradable properties. The porosity in these cross-linked networks not only provides the reservoir for loading drugs but also prevent them from environmental degradation [89].The swelling of nanogels in an aqueous setting is controlled by using the polymer chemical structure, cross-linking degree,and the polyelectrolyte gel's charge density and/or by pH value, ionic strength, and chemical nature of low molecular mass. Nanogels can be chemically modified to incorporate various ligands for targeted drug delivery, triggered drug release, or preparation of composite materials. Nanogels can be developed as carriers for drug delivery and can be planned to spontaneously absorb biologically active molecules via creation of salt bonds, hydrogen bonds, or hydrophobic interactions that can enhance oral and brain bioavailability of low-molecular-weight drugs and bio macromolecules [90]. Nanogels demonstrate potential for systemic drug delivery that have a common features including a smaller particle size (10-200 nm), biodegradability and/or biocompatibility, prolonged half-life, high stability, higher amount of drug loading and/or entrapment, and molecules protection from immune system [89].

Chitosans

Chitosan is a linear polysaccharide composed of randomly disseminated deacetylated and acetylated units. It is prepared by deacetylation of chitin, a structural component of crustacean's exoskeleton and fungi cell walls. Chitosan is the only one exhibiting a cationic character due to its primary amino groups that responsible for various effects in drug delivery systems. It displays particular properties, for example, solubility in various media, poly-oxysaltcreation, Polyelectrolyte behaviour, metal chelation, and structural uniqueness. So far, curcumin-loaded chitosan NPs improve the bioavailability and prolong the retention time of curcumin due to accumulation of NPs in endoplasmic reticulum system and the carriers' features such as shape, size, charge, and hydrophobicity [91].

Chitosan showed promising features as auxiliary agent in drug delivery (e.g, slimming, wound dressing, and tissue engineering) [92].

Gold Nanoparticles

They have optical and chemical uniqueness. They are widely used in immunochemistry, immunohistochemistry and immunoblotting for electron microscopy. They can be generated in various shapes. They have low cytotoxicity, tune able surface features and stability in in-vivo conditions and can be easily synthesized and functionalized. They can also act as drug pool for small drug molecules, proteins, DNA, or RNA with improved long life in the blood circulation [93].

Silvers

Silver is an important material used for anti-microbial activitySilver nanoparticles are used as an antiviral, anticancer agent, anti-inflammatory and also help in HIV and wound healing [94]. In small concentrations it is safe for human cells but very dangerous to bacteria and viruses. Silver Nanoparticles have good opto-electronic activities originated from the surface plasmon resistance. They are used in optoelectronics, biological labelling and biological and chemical sensing [95].

Nanocrystals

Curcumin is highly crystalline compound.Advanced nanotechnology has been applied to fabricate pharmaceutical grade curcumin nanocrystals [96, 97]. The minimum possible size and physical stability which are crucial factors in stabilization are affected by the ability of stabilizers. High-pressure homogenization (HPH) and pearl milling are the chief techniques for producing nanocrystal drug, as for curcumin nanocrystal. Since the dissolution rate of combined nanocrystals decreases, the nanocrystal physical stability gets really acceptable [98].

Implantable Drug Delivery Systems

Polymeric implantable drug delivery systems have exhibited tremendous potential for systemic delivery of various therapeutic agents, including curcumin at a controlled rate [99, 100].These implants with homogeneous entrapment of drugs in a polymeric matrix achieve sustained localized delivery coupled with complete bioavailability into systemic circulation by slowly releasing the encapsulated drug at the site of implantation [101]. Due to their slow release kinetics, they can provide drug release ranging from months to years which can improves the patient compliance, especially for poorly bioavailable and rapidly metabolized compounds like curcumin [102].

There are 2 types of implantable drug delivery systems reservoir type and matrix type. In reservoir type implants, drug core is coated by a semipermeable polymeric membrane which controls the rate of drug release and is dependent upon the rate of water influx into the system. Matrix type implants on contain uniformly distributed drug into the polymeric matrix [103]. Matrix type implants are devoid of any dose dumping phenomenon and provide desirable biphasic drug release mediated by diffusion. This biphasic release consists of a burst release followed by a slow controlled release. Initial burst release delivers the drug for distribution to a large volume, to rapidly reach the therapeutic concentration and a slow, controlled release maintains the therapeutic concentrations for prolonged periods of time [104].

Fig 1. Chemical structure of curcuminoids, desmethoxycurcumin and bidesmethoxycurcumin

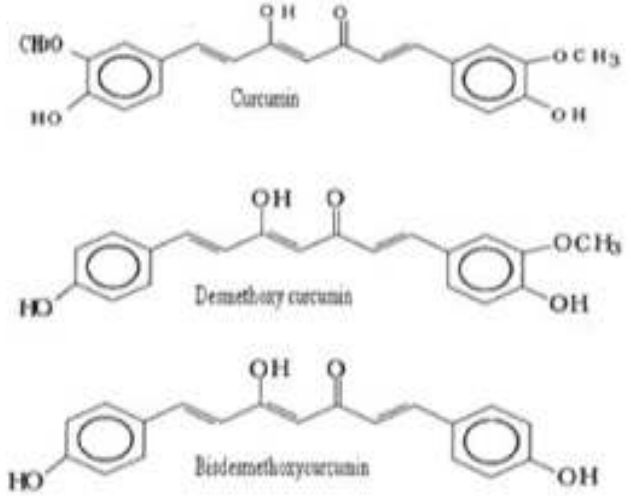


Fig 2. Curcumin Formulations

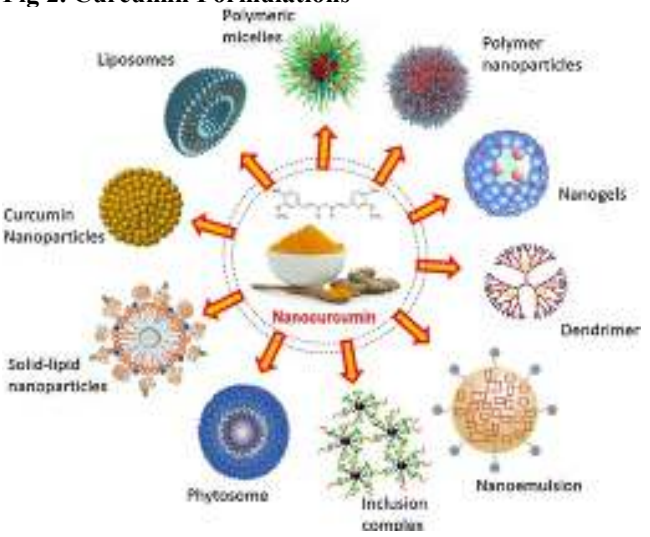
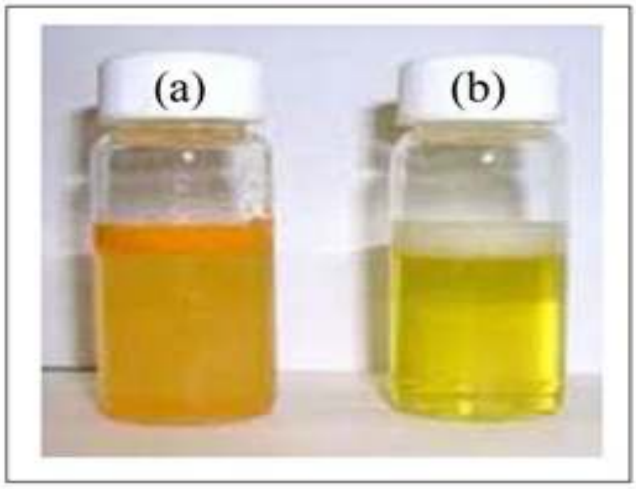


Fig 3. Curcumin Nanoparticles



(a) : Raw Curcumi (b):Cucumin NP

Fig 4. Curcumin Liposomes

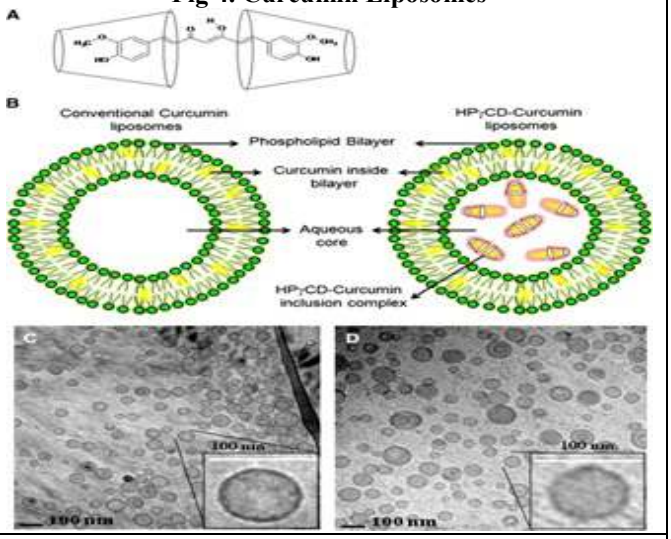


Fig 2. Preparation of CurcuminNanoemulsion

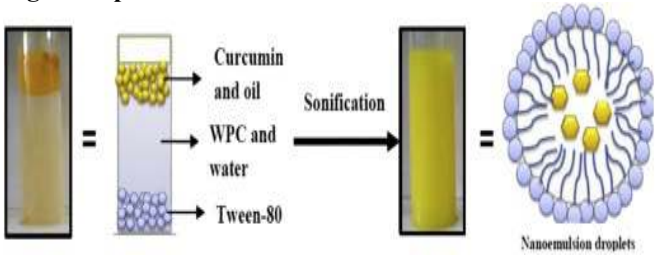


Fig 5. Curcumin Transdermal Delivery

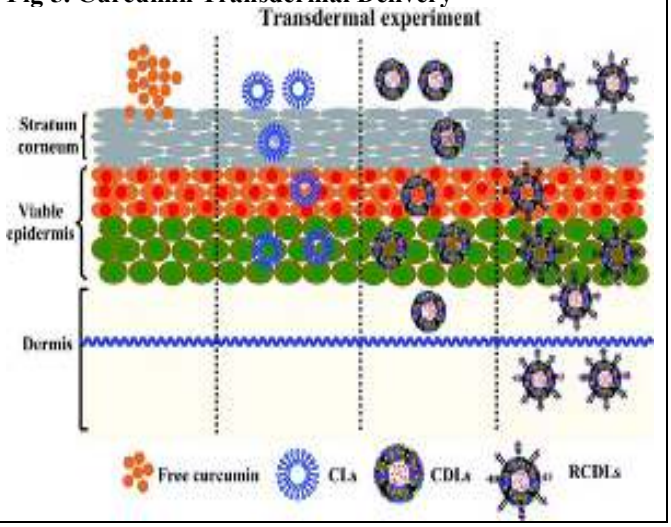


Fig 6. Curcumin Niosomes

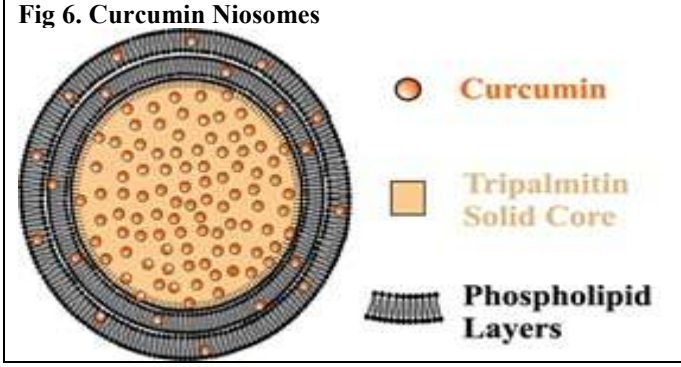
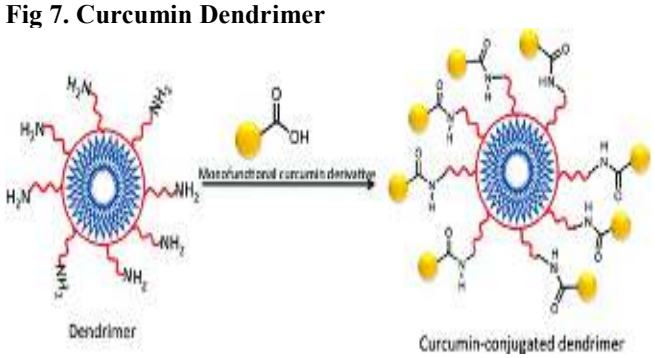


Fig 7. Curcumin Dendrimer



CONCLUSION, PROMISES AND FUTURE CHALLENGES

Curcumin, is derived from traditional natural compounds, has proven to be effectual in long-term application and preclinical trials. Curcumin shows excellent properties such as anticancer, anti-HIV, anti-diabetic, etc. Its inherent poor water solubility, higher metabolism rate and poor pharmacokinetics properties hamper its ability to emerge as a potent medicine for cancer and many diseases. Curcumin formulations will improve human health care. Interest in this area has been emerging worldwide over the last few years and different types of nano-formulations have been developed successfully. Curcuminnano-formulations may offer numerous advantages including improved bioavailability, better efficacy, and tumour targeting property, reduced systemic toxicity, compliance and convenience. Oral and intra-peritoneal dosages of these nano-formulations are more preferred which reduces patient visits and also the cost. There is no doubt that advance of novel delivery systems of curcumin with better therapeutic effectswill be vital for future improvement of curcumin as a therapeutic agent. It is an enormous implication to over come the current limitations of curcumin. It seems that only by multidisciplinary collaboration we can bring these promising traditional natural compounds to the forefront of therapeutic agents for different diseases. Therefore, the promise of nanotechnology-based medicine may become a reality with sufficient efforts and further researches. Human trials need to be conducted to establish curcumin's effectiveness in clinical applications as an improved therapeutic modality for treatment of different diseases.

ACKNOWLEDGEMENT

We would like to acknowledge our college, Dr D.Y Patil College of Pharmacy, Akurdi, Pune.

CONFLICT OF INTEREST

None.

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