



Voyage into Curcumin Embedded Delivery Systems of Natural Polymers to Ameliorate Solubility and Bioavailability Limitations

Roopa G¹, Roopa Karki², Jayanthi C^{1*}, Mukunthan S¹, Hanumanthachar Joshi¹, Goli Divakar²

¹Department of Pharmaceutics, Sarada Vilas College of Pharmacy, Mysore, Karnataka, India

²Department of Pharmaceutics, Acharya and BM Reddy College of Pharmacy, Bangalore, Karnataka, India

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Corresponding Author:

E-mail : jnthc3@gmail.com

Mob.: +918105387034

Abstract

The turmeric (*Curcuma longa*) plant, a perennial herb of the ginger family, is an agronomic crop in south and southeast tropical Asia. The rhizome is coined as the most useful part of the plant and a staple in all cooking and treatment of medicinal purposes include antioxidant, anti-viral, anti-bacterial, anti-fungal, anti-carcinogenic, anti-mutagenic and anti-inflammatory. It has a wide array of affinity to biological proteins and inhibits various kinases. Curcumin modulates the activity of several transcription factors, regulates the functioning of inflammatory enzymes, cytokines, adhesion molecules, and apoptic proteins. Recent preclinical and animal studies revealed the anti-proliferative, anti-invasive and antiangiogenic activity^{5,6}. Clinically, Curcumin is proven to be safe while administering at larger doses, but due to poor aqueous solubility, quick systemic elimination, scanty tissue absorption and degradation at alkaline pH, which restrains its bioavailability, following strategies are used to enhance the bioavailability: (i) adjuvants like piperine which interferes with glucuronidation, (ii) liposomal curcumin, (iii) nanoparticles, (iv) Curcumin phospholipid complex and (v) structural analogues of curcumin. (VI) Micronisation and nanonisation (VII) self-microemulsifying drug delivery systems (SMEDDS), (vii) cyclodextrin inclusions, (IX) solid dispersions (X) Nanoemulsions, nanospheres, nanobeads, nanofibres⁷. The intention of this comprehension is to present a retrospective and prospective gist of applications of innovative delivery systems of Curcumin employed by the researchers to optimize Curcumin delivery using natural polymers with the objective of enhancing solubility and bioavailability, which might revolutionize the therapy of challenging chronic disorders of mankind.

1 Introduction

The turmeric (*Curcuma longa*) plant, a perennial herb of the ginger family, is an agronomic crop in south and southeast tropical Asia. The rhizome is coined as the most useful part of the plant and a staple in all cooking and treatment of medicinal purposes include antioxidant, anti-viral, anti-bacterial, anti-fungal, anti-carcinogenic, anti-mutagenic and anti-inflammatory. Turmeric has been embedded long in ancient Ayurveda for its incredible list of healing properties to promote the holistic health of mankind. It has been recommended to ameliorate various routine ailments such as gastrointestinal problems (stomach ache, dysentery, ulcer etc), hepatic disorders including jaundice,

arthritis, sprains, wounds, acne, skin and eye infections¹⁻³. This marvelous phytochemical has proved itself as a prophylactic for neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases⁴. It has a wide array of affinity to biological proteins and inhibits various kinases. Curcumin modulates the activity of several transcription factors, regulates the functioning of inflammatory enzymes, cytokines, adhesion molecules, and apoptic proteins. Recent preclinical and animal studies revealed the anti-proliferative, anti-invasive and antiangiogenic activity^{5,6}. Clinically, Curcumin is proven to be safe while administering at larger doses, but due to poor aqueous solubility, quick systemic elimination, scanty tissue absorption and degradation at alkaline pH, which restrains its

bioavailability, following strategies are used to enhance the bioavailability: (i) adjuvants like piperine which interferes with glucuronidation, (ii) liposomal curcumin, (iii) nanoparticles, (iv) Curcumin phospholipid complex and (v) structural analogues of curcumin. (VI) Micronisation and nanonisation (VII) self-microemulsifying drug delivery systems (SMEDDS), (vii) cyclodextrin inclusions, (IX) solid dispersions (X) Nanoemulsions, nanospheres, nanobeads, nanofibres⁷. The intention of this comprehension is to present a retrospective and prospective gist of applications of innovative delivery systems of Curcumin employed by the researchers to optimize Curcumin delivery using natural polymers with the objective of enhancing solubility and bioavailability, which might revolutionize the therapy of challenging chronic disorders of mankind.

Owing to its marvelous health benefits, curcumin is sold in various countries, including the United States, India, Japan, Korea, Thailand, China, Turkey, South Africa, Nepal, and Pakistan in the form of tablets, capsules, soaps, cosmetics, ointments and energy drinks. Few of the branded popular products are Vico turmeric Cream, Santoor soap and Band aid etc. Curcumin tablets and capsules are useful in various disorders like Osteoarthritis, rheumatoid arthritis, allergic conditions, Diabetes, Muscular injury, Cancer –all types, Alzheimer's disease, Prostate enlargement, all kinds of inflammatory conditions in the body⁸. The breast inflammation in women with lactational mastitis are being treated with curcumin ointments and are also helpful in wound healing⁹.

Curcumin energy drinks can be employed for rejuvenation and regulation the body activities, and to reduce inflammation precipitated by sugary foods and saturated fat. Prepare the body to combat disorders due to chronic stress and sleeplessness¹⁰.

2 Pharmacokinetics of curcumin

2.1 Preclinical pharmacokinetics

Minimum 10, ADME evaluations were conducted in rodents for the previous tri decades in rodents. There was a 75% of fecal excretion and trace amounts in the urine following a dose of 1 g/kg when diet enriched Curcumin was administered to rats¹¹. Subsequent study of oral Curcumin to rats showed 60% availability of Curcumin in blood providing substantiation for the existence of glucuronide and sulphate conjugates in urine¹². The same group studied Curcumin bioavailability utilizing 3H-radiolabelling after administering orally and noticed that remarkable quantities were present in faecal matter by excreting 33% unchanged¹³. Significant availabilities of Curcumin as tetrahydrocurcumin and hexahydrocurcumin glucuronides were found in rodents when administered by intravenously and intraperitoneally¹⁴⁻¹⁵. Following I.V administration greater than after intravenous dosing, more than 50% of the dose was found in the bile in 5 h; extending a proof that Curcumin transforms

and undergoes enterohepatic recirculation in the process of intestinal absorption¹⁶. This hypothesis proposed by Holder, Plummer and Ryan¹⁷ founded on their examination of Curcumin disposition in rats.

Comparatively a recent investigation of intraperitoneal curcumin (0.1 g/kg) in mice revealed that parent Curcumin primarily gets metabolized to dihydrocurcumin and tetrahydrocurcumin, which gets physiologically transformed to monoglucuronide conjugates¹⁸. Pharmacokinetic evaluation following oral curcumin in rats employing high performance liquid chromatography (HPLC) revealed the presence of little quantities of curcumin in plasma with greater levels of curcumin glucuronide and curcumin sulphate, and little amounts of hexahydrocurcumin, hexahydrocurcuminol and hexahydrocurcumin glucuronide¹⁹.

2.2 Pharmacokinetic studies in humans

Insubstantial curcumin pharmacokinetics in humans in contrast to animals is observed and efforts have been made to review them extensively²⁰. Most of the pharmacokinetic investigations showed very poor gastrointestinal absorption, per oral bioavailability with biotransformation to various metabolites, some of them being Curcumin glucuronide, curcumin sulfate, including dihydrocurcumin (DHC), tetrahydrocurcumin (THC), hexahydrocurcumin (HHC), and octahydrocurcumin (OHC). THC, a moderately hydrogenated analogue of curcumin not a component in turmeric, is the primary metabolite of curcumin. HHC and OHC, which are also the partially reduced form of curcumin, though regarded as Curcumin metabolites, but were not exhaustively evaluated as THC. THC, a colorless compound and exhibits pronounced hydrophilic nature compared to curcumin also manifests strong antioxidant property which is accountable for the curcumin's in vivo antioxidant property. Investigators from Thailand prepared succinyl analogues of all three primary curcuminoids. Curcumin diethyl disuccinate hydrolysis in a phosphate buffer (pH 7.4) and in human plasma exhibited pseudo first order kinetics. The K^{obs} and $t_{1/2}$ of this chemical moiety in phosphate buffer was significantly higher than the parent of curcumin, implying better chemical stability. At the same time, this ester acted as a prodrug in human plasma²¹. Chinese researchers prepared intravenous injection of curcumin didecanoate and revealed extended concentration of Curcumin in plasma utilizing reversed phase high pressure liquid chromatography²². Pharmacokinetic study of curcumin phosphatidylcholine (CU-PC) complex by Indian researchers revealed enhanced bioavailability, improved pharmacokinetics²³, which was also substantiated by the greater absorption of the complex compared to Curcumin by an everted intestine sac. The same group showed greater bioavailability and $t_{1/2}$ and also hepatoprotective action in rats and isolated rat hepatocytes respectively²⁴. Research group of University of Athens, Investigators of Athens University, Greece

synthesized a stable liposome curcumin formulation employing egg-phosphatidylcholine (EPC) having drug to lipid molar ratio of 1:14²⁵ and noticed 14% release of the drug in fetal bovine serum followed by 96 hours of incubation. Twenty nine folds of greater bioavailability was revealed by a phospholipid lecithin formulation of standardized curcuminoids (Meriva®) in comparison to unformulated curcuminoid mixture²⁶ with demethoxycurcumin showing highest bioavailability, observed in a randomized double-blind cross over clinical study in human beings²⁷.

BCM-95 (also known as Biocurcumax) curcuminoids in association with turmeric oil (turmerons) in a certain ratio enhanced the bioavailability 7–8 times more, higher retention time contrast to free curcumin. This could be due to curcumin being a lipophilic molecule gets dissolved in the Turmeric oil which might alter diffusion and partition coefficient of curcumin resulting in enhanced transmembrane permeability similar to enhancement of bioavailability of oil soluble vitamins when administered orally with oils or emulsions. The authors linked the enhanced bioavailability with the synergistic effect of turmeric oil components (essential oils) which are themselves bioactive²⁸⁻²⁹. Six healthy adult male human volunteers were administered with 2 g of curcumin with or without 5 mg of piperine (as biopiperine) for one week and subjected to randomized cross-over study design, later crossed over to the counter treatments followed by collection of blood samples for the determination of plasma curcumin profiles. Investigators observed curcumin with piperine doubled the AUC i.e. 15.55 hr x ng/mL from 8.44 hr x ng/mL for curcumin alone. This enhanced bioavailability is due to retardation of hepatic and intestinal glucuronidation since piperine plays a vital role in inhibiting this metabolic pathway, resulting in increased rate, extent of absorption and decreased elimination rate constant^{30,31}. Curcumin was given orally at a dose of 2g/ kg in humans, resulted in either undetectable or extremely low (0.0006 (0.005µg/ml at 1hr) serum levels. In a human clinical trial, 3.6g of curcumin via oral route was to produce a plasma curcumin level of 11.1nmol/L after an hour of dosing. The concentrations of curcumin in traditional and malignant body part tissue of patients receiving 3600 mg of curcumin were 12.7 (5.7 and 7.7) 1.8 nmol/g, severally, and these doses had pharmacologic activity in colorectum as measured by effects on levels of M(1)G and cyclooxygenase macromolecule. Another study by constant cluster showed no curcumin in liver tissues of patients, with internal organ metastases from body part cancer, who received 450-3600mg of curcumin daily for one week before surgery³²⁻³³.

Bioavailability of Curcumin: Shoba et al. Reported that the absorption and elimination $t_{1/2}$ of curcumin administered orally at a dose of 2g/kg, and the serum curcumin levels in human were below the limit of detection³⁴.

3 Conventional and novel techniques to enhance solubility/Dissolution, stability, Bioavailability and controlled delivery of Curcumin using Natural polymers

3.1 Microparticles

Microcapsules, microsphere technology have been well exploited in food, cosmetics and pharmaceutical industries and recently have been well explored for drug delivery, especially when provided with protection; selective permeation characteristics and organ targeted release properties. These techniques of embedding a bioactive in polymeric materials would moderate safety and efficacy providing new therapeutic solutions. Phytochemicals like Ptothecin, rutin, zedoary oil and andrographolide have been presented in the form of Microcapsules³⁵. Investigators have ventured to present curcumin in the form of microspheres or microcapsules³⁶. Augmented dissolution and oral bioavailability of Curcumin has been recorded by the microparticles formulated by ionic crosslinking of chitosan with tripolyphosphate (TPP). The enhanced pharmacokinetic parameters in rats (C_{max} 270.24 ng/ml, T_{max} 1.30 h) was observed in comparison to native curcumin (C_{max} 87.06 ng/ml, T_{max} 0.66 h). The AUC of microparticles was 8.4 times higher than pure drug. This affirms the feasibility of employing microparticles to enhance dissolution hence bioavailability of poorly aqueous soluble drug Curcumin³⁷. Curcumin starch microspheres prepared by cross linking with N, N'-methylene bisacrylamide and were studied as Curcumin vectors and demonstrated the sustained release of 80.53% Curcumin at the end of 25 hours³⁸. Gastroretentive floating microspheres of Curcumin were prepared by emulsion solvent diffusion method employing hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), Eudragit S 100 polymer in varying proportions and concluded enhanced bioavailability with the sustained release of Curcumin³⁹. Curcumin encapsulation in the lauroyl sulphated chitosan showed the dose dependent anti-oxidant effect. Pharmacokinetic evaluations exhibited 11.5 folds increased bioavailability followed by oral administration of Curcumin in rats against pure curcumin⁴⁰.

3.2 Self-microemulsifying drug delivery systems

Self-micro emulsifying drug delivery system (SMEDDS) has gained momentum in recent years as a fascinating strategy to enhance solubility, dissolution and oral bioavailability of poorly aqueous-soluble drugs⁴¹. SMEDDS is a mixture of oil, surfactant, co-surfactant and drug, which produces a micro emulsion in GIT when taken orally, with particle size of about 100 nm, enhances solubility and bioabsorption of hydrophobic drug⁴². Poorly water-soluble drugs like curcumin, acyclovir, and fenofibrate have been shown to enhance their bioavailability using this technology⁴³⁻⁴⁵. Fast disintegrating SMEDDS tablet containing Curcumin was sealed in an impermeable capsule and the mouth of the capsule was covered with methoxylated

pectin (H-pectin)/lactose. This system exhibited increased solubility of Curcumin, also showed pulsatile release characteristics with specific lag time with the objective of formulating colon specific drug delivery system⁴⁶.

Single phase optically isotropic nanostructures and nanoemulsions generally is expected to exhibit high permeability and flux compared to oleic acid and oil-based microemulsions as the mechanism of enhanced absorption will be different. Nano systems primarily poses higher intracellular uptake whereas microemulsions might increase rate and extent of absorption due to increased solubility and dissolution owing to enhanced surface area⁴⁷.

3.3 Liposomes/phytosomes

Liposomes are spherical vesicles possessing lipid bilayer which encapsulates an aqueous phase containing drug. They are well proved to entrap poorly soluble drugs which can be administered in an aqueous form⁴⁸. Liposomes are nanoparticles which are non-toxic, non-immunogenic, complete biodegradable with structural versatility and clinically approved nano vectors⁴⁹.

Very important advantage of liposomes is easiness of tailoring surface modification, to suit the target site⁵⁰. Liposomes have the ability to get a drug pay load of different categories of pharmacological agents/or diagnostic agents as they contain aqueous and lipoidal chambers. Liposomes are classified as multilamellar, large unilamellar, or small unilamellar based on their the bilayer structure and size, Liposomes are classified as multilamellar, large unilamellar, or small unilamellar liposomes. Conventional liposomes, cationic liposomes pH-sensitive liposomes, long-circulating liposomes and immunoliposomes have been categorized according to their gradient of release of the drug. Curcumin cyclodextrin complex encapsulated in liposomes has been investigated as a promising delivery system in the treatment of various types of cancers including osteosarcoma⁵¹. Considerably, increased ($p < 0.05$) penetrability through artificial and isolated bovine mucus membranes was observed upon enrobing Curcumin-liposomes with chitosan and Carbopol the mucoadhesive natural and synthetic polymers respectively in comparison with pure drug. This has been attributed to increased bioadhesiveness hence as a potential novel delivery system for vaginal administration of curcumin⁵². Curcumin-phytosomes (Cur-PSs) in the form of chitosan microspheres (Cur-PS-CMs) prepared by ionotropic gelation produced prolonged delivery and oral bioavailability compared to (Cur-PSs) or (Cur-PS-CMs). This hybrid technology can be considered as an ideal controlled delivery system for lipophilic molecule with poor aqueous solubility and meager oral bioavailability⁵³. Curcumin incorporated in Egg phosphatidylcholine (EPC) liposomes at a drug to lipid molar ratio 1:14 exhibited high incorporation efficiency approximately 85%, which also exhibited improved cytotoxicity against

colorectal cancer cell lines. Increased plasma concentration of curcumin from its liposomal preparation could be attributed to enhanced dissolution of curcumin from liposomal vesicles and augmented intracellular uptake of nanosized liposomal vesicles⁵⁴.

Curcumin has been encapsulated with liposome-PEG-PEI complex (LPPC) which is cationic and produce curcumin/LPPC. It had a mean size less than 270 nm and a zeta potential of nearly 40 mV. The LPPC encapsulation efficiency for curcumin was about 45%. The authors to their astonishment found that the cytotoxic activity of the curcumin/LPPC increased 5-times and 20- times on curcumin-sensitive cells and curcumin-resistant cells respectively. They could also observe the cessation of cell cycle at G2/M phase, which instantaneously resulted in apoptosis. The enhanced cytotoxic activity of curcumin/LPPC is attributed to its faster accumulation in the cell. The growth of tumor in mice possessing CT-26 or B16F10 cells was inhibited following the In vivo, administration of curcumin/LPPC⁵⁵. The growth of tumor in mice possessing CT-26 or B16F10 cells was inhibited following the In vivo, administration of curcumin/LPPC.

3.4 Nanoparticles (NPs)

Nanoparticles (NPs) size range from 1 to 100 nm, bestowed with characteristic physicochemical properties which can be explored for novel drug delivery technology⁵⁶. Embedding drugs in NPs has the ability to improve solubility and pharmacokinetics of the drug, including sustained release and targeting. Natural polymers (proteins, polysaccharides, etc), synthetic biodegradable polymers (polyvinyl alcohol, polylactic acid, etc.) are the commonly used NPs vector materials. The following nano drug delivery systems, polymer NPs, solid lipid NPs, magnetic NPs, polymer micelles, and albumin NPS are the most explored delivery systems of Curcumin investigated and exploited commercially.

3.5 Polymer Nanoparticles / nanoconjugates

Programmed therapeutic success can be observed using polymer nanoparticles which have prolonged circulation in the blood owing to very small dimensions and good physiological compatibility. Chitosan, poly (D, L-lactide-co-glycolide) (PLGA), and PEG are the extensively investigated polymers. The other polymer vectors like poly (butyl) cyanoacrylate, silk fibroin, N-isopropylacrylamide (NIPAAm), and hydrophobically modified starch, have also been proved for ameliorating the physicochemical and bioavailability limitations of Curcumin. Curcumin chitosan nanoparticles (CS-NPs) prepared by ionic gelation using tripolyphosphate (TPP) possess mucoadhesive and demonstrated promising efficacy in the treatment of colon cancer owing to sustained retention and delivery. Embedded Curcumin had an effect on the adsorption of mucin because of H-bonding and π - π interactions of phenolic moieties of

curcumin with mucin⁵⁷. Srilatha T et al prepared liposomal nanoparticles by embedding curcumin using double emulsion (w/o/w) solvent evaporation employing poly- ϵ -caprolactone a biodegradable polymer which involves thin film hydration – sonication where soya lecithin and cholesterol are the phospholipids. Nanoparticles were examined for hepatoprotective function in CCl₄ induced hepato toxicity and drug concentration in various tissues were determined. Results revealed higher levels of drug in the liver were found with nanoparticles compared to pure drug⁵⁸.

Curcumin loaded cationic nanoparticles using chitosan and poly (ϵ -caprolactone) were prepared by nano-precipitation method. Cell uptake studies demonstrated these nanoparticles as potential Curcumin delivery to cancer cells⁵⁹. A programmable thermo-responsive nanoparticle based on ionic modifications of hydroxypropyl cellulose was developed and evaluated: cationic (using trimethylammonium groups) and anionic (using styrenesulfonate groups). Polycation-polyanion interactions self-assemble them into nanoparticles on their own accord in aqueous medium. Well proven anti-cancer and anti-inflammatory photochemical Curcumin was successfully encapsulated into these nanospheres whose release profile was observed to be temperature dependent⁶⁰. Albumin is the blood's natural vector for hydrophobic molecules, like fatty acids, hormones, and fat-soluble vitamins. This protein has been thoroughly examined as a drug carrier because of its safety and very low immunogenic potential. This polymeric drug loading provides a better solution to overcome poor water solubility of hydrophobic drug molecules. Human serum albumin (HSA) entrapped Curcumin nanoparticles (CCM-HSA-NPs) formulated for I.V dosing by albumin bound technique exhibited 300 times increased aqueous solubility than free Curcumin stability studies observed insignificant loss of bioactivity. In vivo distributions and vascular endothelial cells permeation studies revealed the exemplary antitumor activity of CCM-HSA-NPs in comparison to free Curcumin. This has been attributed to increased aqueous solubility, enhanced tumor accumulation, and greater transport into vascular endothelial cell⁶¹.

A combinatorial nanomedicine of 5-fluorouracil's (5-FU) and Curcumin in N,O-carboxymethyl chitosan nanoparticles (N,O-CMC NPs) were developed which proved enhanced anticancer effects in colon cancer cells (HT 29) with an in vitro sustained release behavior in pH 4.5 and 7.4 for a duration of 4 days and improved plasma concentrations upto 72 h under in vivo conditions⁶².

Physiologically soluble chitosan curcumin nanoparticles were developed, evaluated, for detoxification in arsenic poisoning⁶³. Galactosylated chitosan–polycaprolactone copolymers with a galactosylation degree of about 10% and varying PCL percentages lesser than 40 wt.% were synthesized to prepare nanoparticles for Curcumin delivery⁶⁴. Curcumin nanocrystals

posses a wide spectrum of potential and proven applications. They have enhanced surface area results in increased dissolution rate and better absorption. They are useful in pulmonary drug delivery system because lungs have comparatively large surface areas (43 to 102 m²), thin absorption barriers, and low proteolytic activities to aid faster drug absorption, in addition to have vascularisation and evade of hepatic first-pass effect. S. Onoue et al have formulated efficative nanocrystal solid dispersion of curcumin (CSD-Cur), amorphous solid dispersion (ASD-Cur), and nanoemulsions (NE-Cur). Bioavailability enhancement of 12 fold for ASD-Cur, 16 fold for CSD-Cur and 9-fold for NE-Cur were reported⁶⁵.

3.6 Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles (SLN), also considered as lipospheres or solid lipid nanospheres are a recent novel category of drug vector with the particles of submicron size (50 to 1000 nm) prepared from natural or synthetic lipids, lecithin, which are in the solid state at room and body temperature. SLN have been successfully prepared using various lipids such as lipid acids, mono-, di-, or triglycerides, glyceride mixtures or waxes, and stabilized by physiologically compatible surfactant(s) of non-ionic or ionic. Formulation and evaluation of SLN have been thoroughly reviewed by Muller et al⁶⁶, Mehnert and Mader^{67,68}. SLNs possess important benefits 1) protect sensitive drugs from chemical decomposition 2) retarded release to enhance accessibility of the drugs. 3) targeting for effectiveness. SLNs combine the merits of colloidal drug carrier systems like liposomes, polymeric nanoparticles, and emulsions, but reduce the demerits associated with them. Wenrui Wang et al⁶⁹ prepared curcumin-SLNs to enhance therapeutic potency in an ovalbumin (OVA)-induced allergic rat model of asthma. Curcumin SLNs were prepared by solvent injection method. The airway hyperresponsiveness as well as inflammatory cell infiltration and T-helper-2-type cytokines expressions namely interleukin-4 and interleukin-13, in broncho alveolar lavage fluid was decreased notably by the Curcumin SLNs compared to the asthma group and the group which was treated with curcumin. Hence Curcumin-SLNs could be benefitting delivery system for asthma therapy.

3.7 Nanoemulsions

Nano- and submicron-sized emulsions have attracted researchers focus as efficient delivery systems for hydrophobic drugs and other bio actives for various routes of administration such as oral, ocular, parenteral, dermatological-cosmetic preparations. Nanoemulsions are very fine oil-in-water dispersions, with globule size in the range of 100–600 nm, tailored for delivering oil-soluble substances, which have been dissolved in the oil phase of emulsion or amphiphilic drugs adsorbed at the oil–water interface⁷⁰⁻⁷¹. Whey protein isolate based Nanoemulsions of several ionic strengths and thermal treatments exhibited good stability⁷².

4 Conclusion

The promising therapeutic benefits of curcumin have been revisualized and found to be highly enterprising as observed by the retrospective and prospective studies. The Solubility/Dissolution and pharmacokinetic characteristics of curcumin have opened up challenging novel frontiers for the extensive medical use of curcumin in the management of daunting, miserable human disorders/ diseases, but surplus, extensive quantum of highly potential research has been conducted the world over to find remedies by employing novel delivery systems and physicochemical modifications to generate patentable drug products which would capture the minds of pharma capitalists. The exhaustive and extensive in vitro and in vivo studies reported, revealed the multifarious role of curcumin in diseased and health conditions of a human body. These therapeutic values are backed by the availability of diverse and large amount of molecular targets and mechanisms of action exhibited by curcumin in various host cells in vitro and in vivo. This is in addition to the time tested, and time trusted safety profile of curcumin for human use for diverse molecular targeting functionality so as to transform or program curcumin to be a really “simply go to” molecule for the prophylaxis of deadly chronic disorders of mankind.

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6 Conflict of Interest

Nil

7 Author's contributions

RG, RK, JC, MS carried out literature review. HJ and GD helped in drafting the manuscript. All authors have read and approved the final manuscript.

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