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A Review On Curcumin and It's Use as Novel Drug Delivery System

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Abstract

Curcumin is a principal compound obtained from turmeric, that is, Curcuma longa which is an Indian rhizomatous medicinal plant from the family Zingiberaceae. Curcumin is a yellow pigment commonly used as a spice in the food processing industry. Curcumin, Demethoxycurcumin, and Bisdemethoxycurcumin are the major active constituents of the turmeric and are collectively known as curcuminoids. In recent studies, it has been demonstrated that curcumin has a variety of biological activities, pharmacological performances, provide protection, and promote health. This paper reviews the current research progress on its versatile bioactivity, such as antioxidant, anti-inflammatory, and immune-regulatory activities, cancers, diabetes, liver, and cardiovascular systems. The curcumin belongs to the biopharmaceutical classification system Class IV that indicates low solubility and low permeability. The systemic bioavailability of orally administered curcumin is low in humans and only traces of it have been found in the liver. Here, we emphasized its broad therapeutic activity in treating life-threatening diseases by improving solubility as well as permeability with the help of a novel drug delivery system**.**

Key words: Novel Herbal Drug Delivery Systems Herbal Nanotechnology, Phytosomes; Liposomes; Nanoemulsions; Nanoparticles Bioavailability Enhancement, Phytoconstituents, Targeted Drug Delivery.

1. Introduction

In recent time, there is no single drug delivery system, which fulfil all the criteria but with the advancement of technologies the attempts have been made to achieve all the priorities with in a single approach for that we are focusing on sustained and controlled release formulation along the natural origin of drug for safe and effective management of many life-threatening diseases. In the novel, researchers want to introduce the dosage form that does not bring any kind of side effects and has the maximum possibility of curing the disease completely safely as well as of natural origin. Hence, in this paper, we try to introduce curcumin proniosomes that has its great importance in today's world.The curcumin which is natural origin obtained from turmeric its iupac name is Curcumin, 1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6- heptadiene-3, 5-dione), having small molecular weight, hydrophobic polyphenolic compound, isolated from the rhizomes of Curcuma longa, family Zingiberaceae.curcumin a drug effective in various respiratory conditions (asthma, bronchial hyperactivity, and allergy) other disorders including anorexia, coryza, cough, hepatic diseases, cancer, Alzheimer, Parkinson's, and sinusitis.

In biopharmaceutical classification system (BCS) curcumin belongs Class IV means poor solubility and

poor permeability but because of its abundant list of merits we try to formulate curcumin proniosomes.In many of studies, it is reported that high dose of curcumin up to 12g/day is safe.

On oral administration no amount of curcumin was observed while high amount was observed in feces because of high rate of metabolic excretion.Proniosomes are dry formulation of water soluble particles which are coated vesicular structure of proniosomes, that prolong the existence of drug in the systematic circulation and enhances the penetration into tissue and reduce toxicity. The proniosomes are prepared by the modification in niosomes which literally help to formulate novel drug delivery systems.

Uses of turmeric:

1. Curcumin having rich amount of potassium which keeps you healthy.
2. Curcumin having collagen protein which maintain skin elasticity and keep joints healthy.
3. Curcumin is used as a dietary supplement.
4. Curcumin is used in cosmetic formulation.
5. Curcumin is used in Ayurveda formulation.
6. Curcumin is used in many life-threatening diseases.

Pharmacokinatics:

In many of the Pharmacokinetic studies in animals it is demonstrated that 40–85% of oral dose of curcumin passes through the gastrointestinal (GI) tract remains unchanged and undergoes rapid metabolic reduction resulting in poor bioavailability. Example: On oral dose administration of 0.1g/kg into rats yields 2.25 µg/ml of free curcumin in plasma,while on 40mg/kg i.v dose in rats completely disappears from plasma.

Bioavailability of curcumin:

In many of the research papers, we studied that curcumin belongs to the BCS ClassIV category and it observed that systemic bioavailability of orally administered curcumin is low in humans. In many of researches on human and animals the clear result indicates on oral administration of curcumin the trace elements of it and its metabolites were observed in systemic circulation as well as in liver, Piperine has been reported to increase the bioavailability of curcumin.The further researches in mice with novel drug delivery systems, the nano-particulate curcumin results show more bioavailability and had a longer half-life than native curcumin.THERACURMIN, a nano-particulate curcumin, in their result also shows improved bioavailability in humans. They also compared various published reports that clearly emphasized on the plasma curcumin levels in human subjects after oral intake increases.

BCS:

The BCS is used for determining the exact value of drug solubility and its permeability through the membrane. Before the development and designing of new formulation researchers follow this system to obtain the future goals. This system is broadly divided into four major classes: high/low solubility and permeability of drugs.

Solubility:

According to the guidance of USFDA and WHO a drug is considered to be highly soluble when the highest dose (if the API appears on the WHO Model List of Essential Medicines) or highest dose strength of any market formulation as an oral solid dosage form (if the API does not appear on the WHO Model List of Essential Medicines) which is soluble in 250ml or less than in aqueous media over the pH range.

Permeability:

Permeability The extent of absorption of a drug substance in humans is directly the measurements of the rate of mass transfer across the intestinal membrane. A drug substance is considered highly permeable when the extent of absorption is observed/determined to be 90% or more. All this is guided in the BCS.

Types of BCS:

This BCS is classified into four major categories on the basis of solubility and permeability of drug from the intestinal membrane, as shown below.

- ClassI: High Solubility-High Permeability
- ClassII: Low Solubility-High Permeability
- ClassIII: High Solubility-Low Permeability
- ClassIV: Low Solubility-Low Permeability.

Therapeutic Properties of Curcumin

Anti-inammatory activity:

Curcumin has a list of beneficial activities, one of them is anti-inammatory activity.it has natural origin with potent benefits. It acts in managing the anti-inammatory activity by suppressing the activation of transcription factor NF-kB, because the factor produces an inflammatory gene. Curcumin also acts by controlling the regulation of transcription factor NF-kB, because the factor produces inflammatory genes. Curcumin also acts by controlling the regulation of cyclooxygenase-2 enzymes.

Anti-obesity activity:

Curcumin was significantly recorded as a main aspect in treating the obese patients. Several clinical trials have been conducted on curcumin obesity effects. In a most recent study, it is reported that on oral administration of curcumin 1.6g/day with 8 mg piperine significant reduction in body mass index, body fat, and body weight. These studies were also in nonalcoholic fatty liver disease patients and show nearly the same result.

Anti-alzheimer activity:

Many investigations have been done to identify the effect of curcumin on Alzheimer's disease patients. The main cause of Alzheimer's disease is increased Aβ40 levels in serum or Aβ-deposits as a plaque in the brain. Now in recent studies curcumin shows remarkable results on Alzheimer's disease patients with curcumin (100 mg/day) stated significant improvements in Neuropsychiatric Inventory after 12 weeks

Curcumin Novel drug delivery systemAsian Pacific Journal of Health Sciences.were ensured a higher bioavailability, improved memory good acute, and chronic activities immediately after a single dose, while after 4-week administration enhanced memory, mood, and alertness.

Anticancer property of Curcumin:

Curcumin is considered to be a very potent anticancer agent. Cancer is a result of successive alterations resulting in apoptosis, uncontrolled cell proliferation of cells. Curcumin can suppress the cancer of the skin, oral cavity, mammary gland, intestine, colon, etc. In many studies, it is highlighted that cancer is cured by inhibiting cell proliferation, inhibiting cytochrome and last but not least by Induction of glutathione S-transferase activity.

Anti-oxidant activity:

Curcumin has been shown to improve systemic markers against oxidative stress. It can modulate the activity of those agents which are responsible for the oxidative stress are glutathione, catalase, and superoxide dismutase enzymes and free radicals. Curcumin protects biomembranes against peroxidative damage, it means free radical mediated chain reaction which is the reason for cell damage. Curcumin attributes its activity by hunting the reactive free radicals. Curcumin has a variety of functional groups including the B-diketo group, carbon–carbon double bonds, and phenyl rings containing varying concentrations of hydroxyl and methoxy groups which make the curcumin a highly recommendable agent against oxidative stress.

Anti-diabetic activity:

Curcumin is a naturally occurring compound and has received most attention in managing most of the diseases. On considering these parameters, its contribution is also seen in managing diabetes. Diabetes is the consequence of hyperglycemia and changes in energy metabolism. Diabetes in association with depletion of cellular antioxidant defense mechanism systems and enhanced the production of reactive oxygen species.

Anti-diabetic activity:

Curcumin improves the function of the endogenous antioxidants which improves glucose-lowering activity and also stimulation of the pancreas to produce and secrete more insulin that will assist to manage the diabetes.

Anti-pancreatitis activity:

Anti-pancreatitis activityThe curcumin is a prominent active substance which exhibits many activities and one of them is its anti-inammatory activity against pancreatitis. The mechanism through curcumin performs its activity by inhibiting the activation of factor NF-κB, as well as inhibiting mRNA, it is a key regulator of inammation. The pancreatitis correlates with the inflammatory responses. The blockage of key signals of the inflammatory responses improves the condition of pancreatit is patients.

Anti-rheumatoid activity:

Rheumatoid arthritis is a joint disorder that is more commonly observed in old age persons. A randomized, controlled trial is performed; curcumin was recommended in patients with rheumatoid arthritis. Curcumin 1200mg daily given to the patient and found effective in improving S joint swelling, morning stiffness, and other joint disorders.

Curcumin against bacterial activity:

Curcumin and the oil fraction both have the property to suppress the growth of several bacteria such as Streptococcus, Staphylococcus, and Lactobacillus. The aqueous extract of turmeric rhizome has antibacterial effects. Curcumin also prevents the growth of Helicobacter pylori strains.

Fig1: - Source of Curcumin

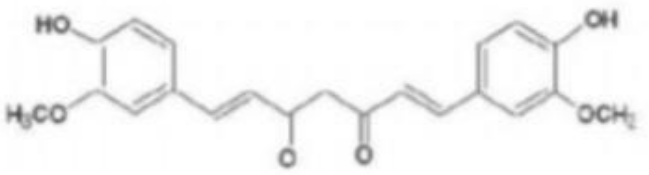

Figure 2: Structure of curcumin

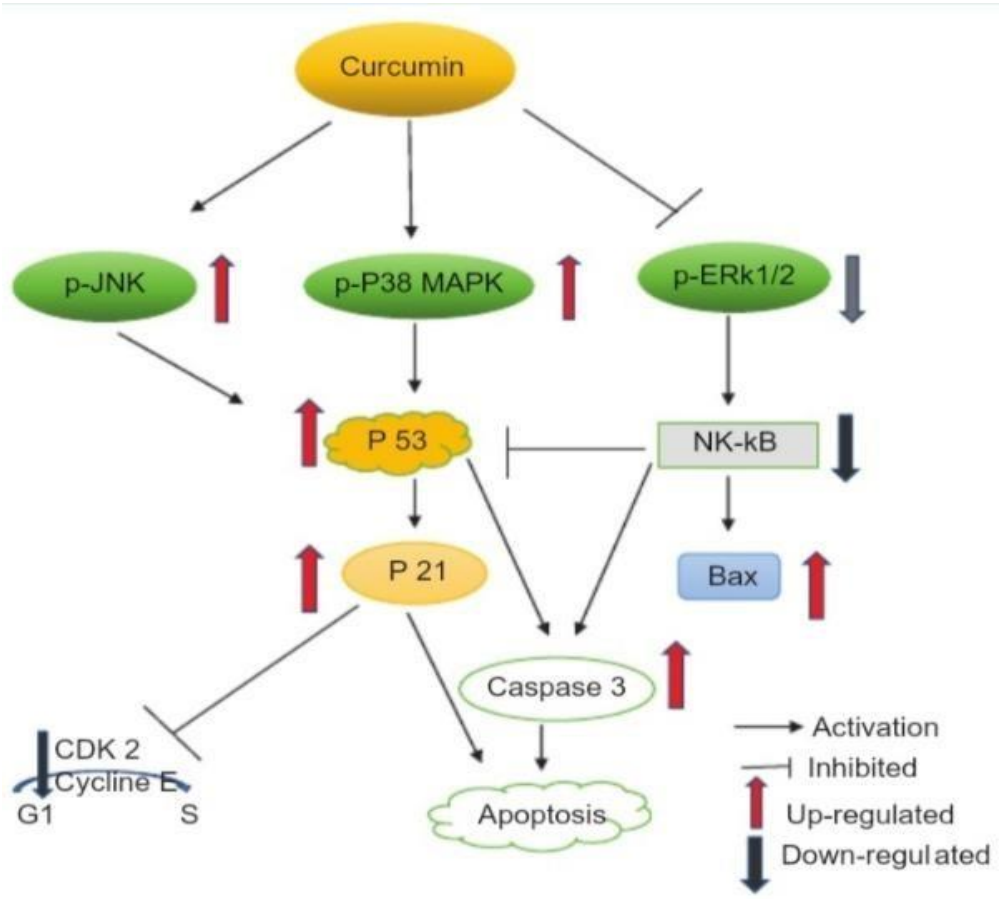

Fig3: -Representation of curcumin response again apoptosis.

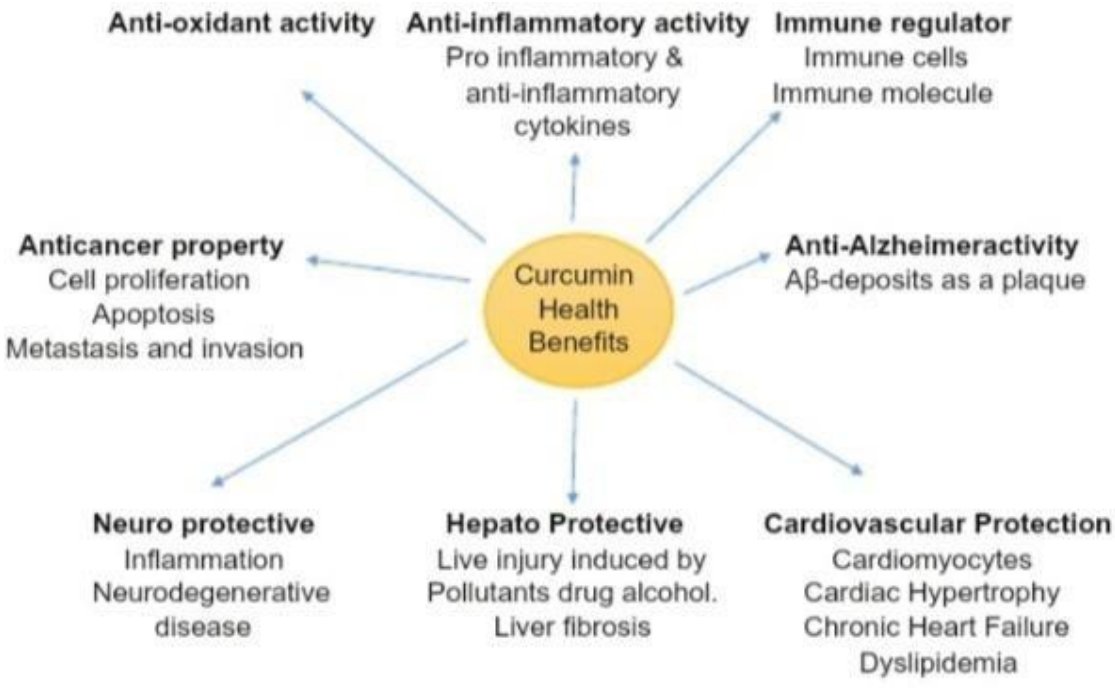

Fig4: -Representation of curcumin health benefits

Source of curcumin:

1. High solubility High permeability Class
2. Low solubility High permeability Class
3. High solubility Low permeability Class
4. Low solubility Low permeability Class

Curcumin against covid-19 included inflammation:

During COVID-19 people face different health issues, some of them face respiration issues, hyper inammation, condition and many more. After their study it observes, it's all because of cytokine blast which is the main reason behind this hyperactive condition. Now during this pandemic, we focus on managing this life-threatening infection with natural sources and this time we show our trust on curcumin because of its list of benefits with low side effects. Here, different dosage forms of curcumin are formulated and used but nanocurcumin produces remarkable responses. Curcumin affects productivity of interleukin cytokines and also works on mRNA expression.On further studies researchers observe that on modulation by curcumin, also reduces the level , and granulocyte-macrophage colony-stimulating factor, that is, mediated factors.

Preparation of curcumin niosomes:

Curcumin niosomes are another advancement in curcumin formulation to improve the effectiveness of this poor solubility and permeability drug. Curcumin niosomes are prepared by a thin-lm hydration method; they contain nonionic surfactant and cholesterol. The nonionic surfactant and cholesterol were mixed with 20mL chloroform in a rotatory evaporator and immersed in a water bath at 60°C after that curcumin drug was added into it with solvent. Now evaporate the solvent and a thin lm form which is further dissolved in 20mL of phosphate buffer, then placed in a water bath at 60°C and rotated at 120rpm to hydrate the layers.

Preparation of curcumin-loaded self-emulsifying drug delivery system:

Preparation of Curcumin-loaded LiposomesIn the present study, liposomes were used as a drug delivery system to improve the stability, bioavailability and anticancer activity of lipophilic Cur. So far, a number of liposomal formulations of Cur have been reported by other groups. Curcumin loaded liposomes is a novel advancement in medical science. Curcumin liposomes were formulated using the extrusion technique. In this method, lipids and curcumin were dissolved in chloroform to get stock solutions. Then curcumin was mixed with 40mg of lipid and ActivationCDK Representation of curcumin response against apoptosis Curcumin Novel drug delivery systemAsian Pacific Journal of Health Sciences chloroform was removed from the samples through the evaporation process, so a thin lipid was obtained. That lm further dissolved in a mixture of cyclohexane and methanol and freeze-dried for 8 hours at low pressure. Now the lms were hydrated by addition of 1.5ml of NaCl at 64°C, in a water bath, with gentle mixing. Finally, sonicated liposomal suspensions for 8minutes at 64°C and extruded 10 times through Nucleopore polycarbonate filters with pore sizes of 400 and 100 nm and we get curcumin loaded liposomes.

Preparation of curcumin nanospinges :

Nanosponges are the newest technology which facilitate targeted drug delivery for extended periods of time for those drugs which have low solubility and permeability problems.

Nanosponges are nano size particles having a tiny sponge-like structure. This system of delivery belongs to the BCS second class of drug which also improves the bioavailability related factors.The curcumin loaded nanosponge were formulated by emulsion solvent diffusion method. The nanosponge preparation contains varying concentrations of Eudragit L-100 with polyvinyl alcohol DCM also. First, Eudragit L-100 was taken and dissolved in dichloromethane. This mixture was added into aqueous solution of polyvinyl alcohol and with constant stirring at 1200rpm for 2 h and added curcumin. Now alter the product and dry it in an oven at 40°C for 24h. Then nally dried curcumin loaded nanosponges were obtained.

Preparation of microspheres :

Microspheres are one of the multiparticulate delivery systems which are prepared to produce prolonged or controlled drug delivery, as well as to improve bioavailability and stability and to achieve target drug delivery. Curcumin microspheres were formulated by solvent evaporation technique, where Eudragit S 100 was dissolved in a mixture of Propan-1-ol and Chloroform (1:2) at 28°C, that is, room temperature and with constant stirring add curcumin. Then pour 100ml of water containing 0.02% of sodium lauryl sulfate at 1000rpm for 90min.

Finally collect, alter, and wash the mixture. Then washed microspheres dried at room temperature to make them rigid.

Discussion:

The present review is based on the advancement of curcumin in the eld of pharmaceutics that includes various parameters and techniques which have glorious research in future here we compare various properties of curcumin with each other and studded its application in managing life threatening diseases by the ability of high loading capacity of drug in the novel formulation.

Conclusion

Curcumin has received worldwide attention because of its multiple health benefits. Many researchers suggest that curcumin can help in the management of many health issues such as cancer, inflammation, diabetes, oxidative stress, Alzheimer's disease, obesity, and many more. However, curcumin belonging to the BCS ClassIV category means having low solubility and low permeability to overcome this issue when curcumin is combined with piperine bioavailability of curcumin increases.

Reference:

1. Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: An age-old spice with modern targets. Trends Pharmacol Sci 2009;30:85-94
2. Araújo CC, Leon LL. Biological activities of Curcuma longa L. Mem Inst Oswaldo Cruz 2001;96:723-8.
3. Tirkey N, Kaur G, Vij G, Chopra K. Curcumin, a diferuloylmethane, attenuates cyclosporine-induced renal dysfunction and oxidative stress in rat kidneys. BMC Pharmacol 2005;5:15.

4. Sharma RA, Steward WP, Gescher AJ. Pharmacokinetics and pharmacodynamics of curcumin. Adv Exp Med Biol 2007;595:453-70.
5. Lazaro ML. Anticancer and Carcinogenic properties of curcumin: Considerations for Its clinical development as a cancer chemo preventive and chemotherapeutic agent. Mol Nutr Food Res 2008;52Suppl1:S103-27.
6. Deepika S, Rizwana K, Sharma B. A review on proniosomes drug delivery: An innovative approach. World J Pharm Res 2020;9:1322-33.
7. Walve JR, Rane BR, Gujrathi NA. Proniosomes: A surrogate carrier for improved transdermal drug delivery system. Int J Res Ayurveda Pharm 2011;2:743-50
8. Bharat AB, Indra BD, Ichikawa H, Ahn KS, Sethi G, Sandur SK, et al. Curcumin Biological and Medicinal Properties. 2006. p.297-368.
9. Yin S, Zheng X, Yao X, et al. Synthesis and Anticancer Activity of Mono Carbonyl Analogues of Curcumin.Journal of Cancer Therapy;2013:4,113
10. Parize AL, Stulzer KH. Evaluation of chitosan microsphere contains curcumin cross linked with sodium tripolyphosphate. Quim Nova 2012;35:1127-1132.
11. Bagchi A. Extraction of curcumin. IOSR J Environ Sci Toxicol Food Technol 2012;1:1-16.
12. Xiao-Yu Xu, Meng X, Li S, et al. A Review Article: Bioactivity, Health Benefits, and Related Molecular Mechanisms of Curcumin: Current Progress, Challenges, and Perspectives.Nutrients;2018:10,1553.
13. CFR Code of Federal Regulations Title 21. Available from: https:// www.accessdata.fda.gov
14. Ahmed S, Anuntiyo J, Malemud CJ, Haqqi TM. Biological basis for the use of botanicals in osteoarthritis and rheumatoid arthritis. eCAM 2005;2:301-8.
15. Pan MH, Huang TM, Lin JK. Biotransformation of curcumin through reduction .