

A Review on Different Methods of Preparation and Therapeutic Applications of Curcumin Nanoparticles

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ABSTRACT: Curcumin (diferuloylmethane) is one of the most potent, non-toxic, and critical bioactive components of Turmeric. The primary disadvantages of Curcumin include low absorption and poor bioavailability. This study addresses strategies for producing and using curcumin nanoparticles in the treatment of cancer and injury infections. Curcumin nanoparticles offer excellent antibacterial, antiviral and antiprotozoal effects. Nano-gel-loaded Curcumin, microemulsion, and nano-cream nanoparticles can therefore be used for medication delivery. Curcumin is a bioactive and main phenolic turmeric component derived from Curcuma longa rhizome Linn. Curcumin has proven excellent therapeutic advantages over generations in several illnesses. Curcumin has a significant positive and pleiotropic regulatory role various diseases. including for cancer. diseases. cardiovascular Alzheimer's disease, inflammatory conditions, neurological disorders, etc.

Despite these fantastic improvements in therapeutic applications, the clinical consequences of natural Curcumin are undermined by low solubility, chemical-physical instability, poor bioavailability, rapid metabolism, and pharmacokinetics. However, an efficient delivery method can overcome these limitations. Pharmacokinetic Curcumin, systemic bioavailability, and biological activity were introduced in 2005 to promote active scientific investigation through encapsulation or loading into nanoforms of Curcumin (nanoformulations). Once clinical and human studies are finished, a significant percentage of nanoformulations can be converted to medicinal use. This research provides an overview of an efficient curcumin nanoformulation for alternative therapy of several human illnesses. One of the most exciting areas of modern scientific inquiry is nanotechnology. In medicine, the nanotechnology-based medication

delivery system is an innovative way of treating dreadful diseases. In recent years, plant-based medicines have played a significant role in healthcare. Biological nanoparticles have no unwanted side effects. The bio-active component derived from a rhizome called Curcumin. Curcumin-(1,7-Bis-(4-hydroxy-3-methoxyphenyl), hepta-1, 6-diene-3, 5-dione) that shows diverse pharmacologic activities. However, the medical usage of Curcumin is limited due to its poor water solubility and bioavailability. However, clinical trials have indicated that nanoparticles of Curcumin are more soluble and bioavailable. The therapeutic efficacy of curcumin nanoparticles increases with the usage of medicine in different nanoforms. The study explored the medical applications of curcumin nanoparticles against cancer, microbial inflammation, acquired immunodeficiency syndrome, malaria, Alzheimer's, and inflammatory disease.

KEYWORDS: Nanoparticles, Curcumin, Nanoformulation, Cancer

I. INTRODUCTION

A rapidly rising field is nanotechnology, its application in science and technology to produce novel nano-level materials. It is an interdisciplinary field that uses approaches from many areas. Nanoparticles have particular features such as enormous surfaces, a quantum effect, and the capacity to bind and contain such substances as drugs. Nanoparticles depend on their size, shape, and morphologic texture on their physical, chemical, optical, and electrical properties. Two primary methodologies for synthesizing nanoparticles were used: bottom-up and top-down. Nanoparticles have been produced from molecular components, which are chemically built by recognizing comparable molecules in the bottomup process. In the top-down method, nanoparticles



were also made from la larger entities. Bottom-up was often used to produce chemical and biological nanoparticles.

Nanoparticles for their application in medicines, such as drug transport, DNA structure testing, protein identification, tissue engineering, infection detection, cell killing, and phagokinetic investigations, have been thoroughly reviewed and used. The primary use of nanotechnology in medicine was the invention of nanoparticles as drug delivery devices. Nanoparticles are broad, controlled particle size, site-specific targeting, bioavailability, stability, biological degradation, and controlled release. Metallic nanoparticles. including silver, gold, platinum, copper, etc., were produced for clinical use. These metal nanoparticles can be kept and maintained in the body that can have dangerous side effects. These limits can be overcome using biological sources for the creation of nanoparticles. Nanomaterials are not found in the body and are harmless.

Since prehistoric times people have employed natural botanical components for various purposes. As a natural defense tactic, plants have generated thousands of secondary metabolites. Most of these metabolites have a pharmacological effect and drug design. In recent years, plantderived medicines have played an important role in healthcare. Turmeric, a perennial herb of the Zingiberaceae family, is a traditional Asian medicinal product. Curcuminoids are characteristic of the yellow turmeric color. Curcuminoids are three primary constituents of polyphenols: Curcumin (77%), desmethoxycurcumin (17%), and bisdemethoxycurcumin (3 percent). Curcumin is the most bioactive component, of these (1,7-Bis-(4hydroxy-3-methoxyphenyl)-hepta-1, 6-diene-3, 5dione). Due to its broad bio-active and pharmacological action, such as antioxidants, antiinflammatory agents, and antioxidants. However, owing to its poor water solubility, volatility, and low absorption, Curcumin was restricted to therapeutical utilization. Low absorption, quick metabolism, and fast systemic removal are the main causes of Curcumin's limited bioavailability. Drug delivery techniques based on nanoparticles were used to enhance their solubility, stability, and bioavailability. Curcumin has been developed in recent years in numerous nanoforms such as nanosuspension, nanoemulsion, solid nanoparticles of the lipid, hydrogel nanoparticles, and more. Several studies demonstrated that curcumin nanoparticles are a therapeutic agent for a wide spectrum of illnesses.



Fig 1: Chemical Structure of Curcuminoids

II. METHODS OF PREPARATION



Fig 2: Methods of Curcumin nanoparticles synthesis

1. Coacervation techniques

In this process of curcumin synthesization, the polymer is dissolved into an organic solvent (e.g., dichloromethane, ethyl acetate, acetonitrile) and hydrophobic medicinal cure immediately suspended in the polymeric solution and can be suitably combined and whisked. Nanoparticles are collected via centrifugation. It is an economical method, and no hazardous solvents are used. The fundamental disadvantage of the technique of coercion is that many solvents are needed. Using this method, Chirio et al. created nanoparticles laden with Curcumin.





Fig 3: Coacervation technique

2. Nanoprecipitation method

The nanoprecipitation procedure is also known as the solvent displacement method. This technique was used to suspend the polymer required in a solvent and add Curcumin to the solution. This polymer solution is then continuously agitated and was precipitated into the water.



Fig 4: Nanoprecipitation method

3. Spray drying method

In this production procedure, Curcumin and polymer are combined in the same solvent or solvent mix. Then the solvent can be evaporated using heated airflow. Spray drying has led to the development of amorphous medications, which can be partially solidified during treatment. The spray drying procedure permits curcumin nanocrystals to be created.



Fig 5: Spray drying method

4. Single emulsion method

The standard synthesis method for curcumin-nanoparticles is the single emulsion approach. Curcumin nanoparticles were created via solvent dispersion and high-speed homogenization or ultrasonic in this synthesis technique. Another solvent was evaporated by continuous magnetic stirring at ambient temperature or low pressure. The solidified nanoparticles are ultrasonically collected and cleansed to eliminate impurities, then contained in distilled water and frozen to produce the nanoparticles. Curcumin-powered poly (lacticco-glycolic acid) can also be created using nanoparticles (PLGA).

5. Solvent evaporation method

The procedure of solvent evaporation consists of two principal processes. The solution consists of curcumin polymer and drug-like I and solvent evaporation dissolving for curcumin resolution. It leads to solid growth. The emulsion created is subsequently converted by solvent evaporation into a suspension of nanoparticles. The advantage of this technology is that low temperatures were required for solvent evaporation and that heat deposition is prevented. The drawbacks are the relative cost of the reagents used in the technique, selecting the correct solvent is tricky, and organic solvent evaporation is a timeconsuming task. This method was utilized to create nanoparticles loaded with PLGA curcumin.

6. Microemulsion method

A microemulsion is perfect for the production of nanoparticles. Water-hydrophobic in nature and oil hydrophilic in nature are the surfactants used in this process. The microemulsion is generated by removing a small quantity of surfactant and adding Curcumin, oil, and water. It forms a turbid solution, frequently resembling tiny droplets. This microemulsion technique synthesizes



curcumin nanoparticles to boost Curcumin's biological activity.

Various types of surfactants are used to increase the surface stability of nanoparticles. The method is simple and can efficiently be utilized to supply medicines with decreased energy costs. The microemulsion process is affected by certain conditions, such as variations in temperature and pH.



Fig 6: Single emulsion method



Fig 7: Microemulsion method

7. Wet milling method

Wet milling is the method of synthesis used in Curcumin for nanoparticles. The medicinal hydrophobic Curcumin was suspended in appropriate solvent curcumin. With the ultrasonic process, the solution obtained is further agitated. Distilled water is also required for the creation of curcumin nanoparticles. The resultant solution can then be centrifuged, and this method produces nanoparticles. Researchers report the production of nanoparticles of Curcumin using this technique.



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Fig 8: Wet milling method

8. Thin-film hydration method

Curcumin and surfactants can be combined with organic solvents in this approach under sonic conditions. The solvent is allowed to evaporate under specific pressure, and distilled water is then put into the sound and centrifuged to produce nanoparticles curcuminoids with nanosuspension. Curcumin nanoparticles are making piperin along with Curcumin by this synthesis process.

9. Solid dispersion method

Thus, matrix and hydrophobic medicinal products like Curcumin. The matrix might be crystalline or amorphous. This method is utilized to dissolve the insoluble hydrophobic drug.

10. Emulsion polymerization method

It is a fast and easy-to-use approach for curcumin nanoparticles to synthesize. Organic and continuous phases are two types of emulsion techniques that can generate nanoparticles from Curcumin. Ultrasound dissolves the surfactant in pure water, transforms the Curcumin into an organic solvent, and adds the surfactant solution. Moorthi and colleagues have revealed that they are adopting this technology to create curcumin nanoparticles, using piperine and Curcumin to increase the biological activities of manufactured curcumin nanoparticles.

11. Fessi method

Curcumin is dissolved in the suitable sonic solvent in this production method. The solution was added with a unique surfactant with a continuous mixture of pure water. This method can spontaneously produce nanoparticles of Curcumin. Moorthi and associates employed this method to produce curcumin nanoparticles.

12. Ionic gelation method

This is important and easy for nanoparticles to synthesized. The excellent solvent dilutes a hydrophobic medicine such as Curcumin, exhibiting 100% solubility of Curcumin. This solvent was then added to the polymer solution under the constant stirring condition. This technique depends on the linkages between the polymer and the drug, such as Curcumin. Chabab and colleagues have reported the production and use of chitosan as a curcumin nanoparticles polymer. This polymer enhanced the solubility and stability of nanoparticles in Curcumin.

13. Ultrasonication method

This method is frequently employed in less water-soluble drugs. Curcumin is initially dissolved into an organic solvent for synthesis applications using this method. For many intervals, the resulting solution in ultra-sonic settings were added to the polyelectrolyte solution.

14. Antisolvent precipitation method

The strategy of manufacturing a slightly water-soluble medicine is precipitation against solvents. In this technique, Curcumin was dissolved in an organic solvent, and with continuous agitation, this solution is added to the deionized water. This method can therefore manufacture nanoparticles of Curcumin. Kakar and coworkers took this strategy to make curcumin nanoparticles. The advantage of this synthesis approach is to synthesize the low solubility of curcumin nanoparticles with suitable technology. Ionic gelation is both practical and superior and the antisolvent precipitating method for the manufacture of curcumin nanoparticles. In both treatments, there are some or other deficiencies suitable for drugs such as Curcumin.

Given that Curcumin is poorly soluble, various synthesis strategies improve nanoparticles' solubility and stability. The ionic gelation process depends on the combination of polymer and drugs. Synthesis in antisolvent precipitation depends on the stirring speed, time, and temperature. If nanoparticles of Curcumin be used for medicines, the technique of microemulsion is appropriate. For further investigation in the formulation of curcumin nanoparticles, research on the unique method of curcumin nanoparticles production is essential.





Fig 9: Antisolvent precipitation method

III. THERAPEUTIC APPLICATIONS 1. Anticancer activity

Cancer is the most common devastating disease in the world. Conventional therapies such as chemotherapy, radiation, and surgery have considerable adverse effects. It is therefore essential to develop a safer and alternative treatment strategy for this malignant illness. To produce novel medicines, natural sources such as plants are currently used. Plants were believed to contain many life-saving, non-toxic pharmacological compounds that can be used to cure various malignancies. Curcumin is a herbal medication utilized for many malignancies such as pancreas, oral, breasts, prostate, skin, ovary, etc. Numerous important cell signaling mechanisms mediate these effects. Curcumin nanoformulation was recently used as a cancer therapy, improving absorption, solubility, and targeting malignant cells.

Breast cancer

Breast cancer is a widespread condition that primarily affects women worldwide. Curcumin micelles in vitro studies show that triple-negative breast cancer (TNBC) has improved absorption, cytotoxicity, and extended half-life. TNBC is a highly malignant, chemotherapy-resistant tumor with no estrogen receptor, progesterone, or human factor 2 epidermis. Magnetic nanoparticles with a curcuminoid power showed an effective anticancer action with imaging and magnetic cell targeting features in TNBC (MDA-MB-231 cell line). The growth of cell-reactive oxygen species has been accelerated, and the potential of mitochondrial membranes has been lost. The combination of curcumin-encapsulated nanoparticles and the electroporation process MCF-7 demonstrated enhanced activity in human breast cancer cells.

Ovarian cancer

Depending on the cells they develop, ovarian cancer comprises many cancers. The main interruption in the treatment of advanced ovarian cancer is chemoradiation resistance. Yallapu et al. produced a monoclonal nanoparticles antibody to improve site-specificity and sensitivity to ovarian chemoradiotherapy for cell resistance. A2780CP, cisplatin-resistant, reduced cell proliferation and boosted apoptosis when treatment with nanoparticle conjugate in ovarian cancer cells. Curcumin-encapsulated nanoemulsion and paclitaxel showed anticancer efficiency in human ovarian cell adenocarcinoma, which improves the apoptotic response to medication-resistant SKOV3 SKOV3 (taxol-resistant). Nanoemulsion and hindered the activity of the Kappa B nuclear factor (NF5-0B) and decreased P-glycoprotein expression.

Pancreatic cancer

co-polymer-loaded The curcumin nanoparticles are N-isopropyl acrylamide, N-vinyland 2-pyrrolidone poly (ethylene glycol) monoacrylate. It acts as a possible inhibitor of tumor growth in xenograft models for human pancreatic cancer. Nanocurcumin was further stopped in combination with gemcitabine, tumor development with induction of apoptosis, activation of NFSB reduced, and MMP-9 and cyclin D1 expression. The therapeutic effectiveness of nano curcumin has been demonstrated by cell viability clonogenic studies. Curcumin-powered and magnetic nanoparticles significantly stopped the



multiplication of human pancreas cancer cells (HPAF-II and Panic-1) in the xenograft mice model. This formula has demonstrated more good stability with improved absorption and biodistribution compared to normal Curcumin.

Prostate cancer

Prostate cancer is a disease that occurs in the prostate gland of the male reproductive system. It can progressively spread to other parts of the body, like bones and lymph nodes. Lactic coacid is curcumin-loaded (PLGA) glycolic nanoparticles created with the anticancer potential of curcumin nanoparticles against prostate cancer. PLGA-curcumin nanoparticles released bioactive Curcumin into the cytoplasm after integration into the cancer cells. The expression of nuclear and androgen receptors (STAT3 and AKT) was eliminated, and the primary anti-apoptotic proteins that contribute to apoptosis were suppressed. In vitro studies in prostate cancer cell lines with curcumin loaded PLGA nanospheres have revealed long-term continuing curcumin delivery and increased intracellular absorption the of nanospheres.

2. Antimicrobial activity

Microorganisms cause many human infections. Many chemicals have been used for the destruction of bacteria, fungi, protozoa, and viruses. Traditionally, Turmeric was utilized as an antibacterial agent. As curcumin nanoparticles are more antimicrobial than ordinary Curcumin, they are used. The wet-milling technique of nanocurcumin has revealed antibacterial and antifungal activities. Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Penicillium notatum, or Aspergillus niger, without surfactants and highly active in Staphylococcus aureus, were water dispersible. The nanoparticles penetrated the infected cells, damaging the cell wall and ultimately causing cells to die. Nanocurcumin was more Gram-positive than Gram-negative bacteria reactive. In a different study, curcumin enclosure and increased injury cure activities in the Vivo mice model have inhibited the growth of methicillin-resistant S. aureus and P. aeruginosa. Likewise, nanoparticles of curcumin-loaded tripolyphosphate in vitro mouse skin studies have reduced the growth of S. aureus and P. aeruginosa.

3. Anti-HIV activity

A human immunodeficiency virus (HIV) attacks the immune system by killing CD4+T cells. The steady disintegration of immunity leads to immunodeficiency syndrome (AIDS). CD4+ T cells are a type of white blood cell that defends the body from disease. Antiretroviral therapy decreases the infection but has not yet been removed. An alternative medication must thus be established to cure this devastating condition and stated that nanoparticles made with curcumin-loaded apo transferrin utilizing sol-oil technology are powerful in stopping the reproduction of HIV-1 by transfermediated endocytose. In HIV-infected cells, transferrin receptors are generally expressed. Curcumin-loaded apo-transferrin nanoparticles, in particular, involve the receptor and transfer the drug to the infected cell. The drug is released gradually, and the viral cDNA synthesis blocks the termination of replication by HIV-1.

4. Antimalarial activity

Malaria is caused by parasites and worn by female Anopheles mosquitoes. In vivo studies of curcumin-laden nanoparticles exhibited antimalarial effectiveness. Toxicity studies have proven the oral and cytotoxic effects of nanoformulations. Curcuminous chitosan nanoparticles heal infected Plasmodium yoelii mice by reducing the development of hemozoin.

5. Anti-inflammatory activity

Turmeric was used in ancient Indian medicine as an anti-inflammatory medicine. The inhibitory effect of 50 mg/kg was equivalent to average Curcumin 400 mg/kg of ordinary Curcumin. The anti-inflammatory effect of nano curcumin was increased. The potential of curcumin-encapsulated exosomes in the lipopolysaccharide-generated septic shock mice was explored. This study showed more outstanding stability, targeted selectivity, and high blood concentrations of exosome-produced Curcumin.

6. Traditional therapeutic activity Cardiovascular disease

The proliferation and migration of smooth vascular muscle cells (VSMCs) are exhibited during vascular development due to vascular injury and atherogenesis. The vascular injury usually occurs following angioplasty, organ stent transplantation, or implantation. Cardiovascular such as statins, treatment, effectively reduces VSMC migration. We have constructed a self-assembled amphiphilic hexanol chitosan nano matrix that contains Curcumin which manipulates the proliferation and migration of CBMD by cells and low-dosage fatal effects. The Chemotherapy first line of is doxorubicin



hydrochloride (DOX), although it is closely associated with severe cardiotoxicity. The coadministered formulation of pluronic nano curcumin may mitigate this unfavorable effect by reducing apoptosis and reactive oxygen radicals (ROS). It has been proven further that a DOX formulation created in vivo oxidative stress can overcome multidrug resistance in cancer cells and facilitate cardiomyopathy linked with doxorubicin by reducing overall glutathione and glutathione peroxidase activity in the cardiovascular tissue. Angiogenesis has become a significant health issue in atherosclerosis and other cardiovascular disorders. The successfully inhibited angiogenesis of curcumin nanoparticles in poly (ester amine) in the zebrafish model, a new antiangiogenesis treatment.

Alzheimer's, Neurodegenerative and Brain Diseases

Many human illnesses evolve in the central nervous system (CNS), brain, or spinal cord. Curcumin distribution to these locations needs overcoming of the complicated blood-brain barrier (BBB). The promising method is synthesizing nanoparticles of peptides derived from apolipoprotein E (ApoE) (residues 141-150).

With the deposition of β -amyloid peptide $(A\beta)$, Alzheimer's (AD), which is toxic to monomeric and fibrillary species and typical AD lesions, develops in senile plaques. Curcumin is a pathological amyloid molecule that has received considerable attention and hence has the diagnostic potential of introducing Curcumin. Biodegradable PLGA – Nanoformulation is non-toxic, and human SK-N-SH neuroblastoma cells increase proteins H2O2-induced ROS. In the presence of H2O2, this formulation may suppress the expression of the redox-sensitive transcription factor Nrf2, a suggested method commonly shown in DA for neuronal protection. Cumin formulations contain biotin poly (ethylene glycol), biodegradables poly(halcianocyanoacrylates), liposomal PEG, antitransferred in, lipid conjugate lysosome, nanoliposome, co-poliposome PEG-polylactic acid block, and Clic-chemistry-based nanoliposomes was also shown to be the inhibition of $A\beta$ aggregation and toxicity recycle of AB. Another critical study employing NanoCurcTM formulation found that the low H2O2 levels, greater glutathione levels, and reduced three-and-seven caspase activity in athymic mice suggest a favorable intracellular redox medium that deserves this AD treatment. In addition, PBCA polymers in combination with Curcumin in ApoE3

provide an essential advantage in the treatment of $A\beta$ -induced cytotoxicity in AD. Curcumin Gold functional nanoparticles efficiently bind to amyloid protein/peptide and concurrently prevent the fibrillation of amyloids and dissolve them as artificial molecular chaperones.

In male Lacca mice, the Aluminum adverse effect was entirely restored by oral lipid nanoformulation (AlCl3), resulting in 97% recovery of membrane lipids and 73% mending acetylcholinesterase. Likewise, neurotoxicity produced by acrolein may be reversed by PLGA-based curcumin nanoformulation. This inversion was achieved by restoring synthase, ROS, and reactive nitrogen levels of μ g-glutamylcysteine, but not glutathione neuroprotection.

A new superparamagnetic iron oxide technique paired with Curcumin has shown that amyloid plaques can be demonstrated ex vivo in Tg2576 mice brains (MRI). In comparison, in the nontransgenic muse, no plaque was found. Significant accumulation and co-location of nanoparticles with amyloid plaques have been found in immunohistochemical exams of mouse This formulation, therefore, has a brains. considerable potential to use MRI for noninvasive AD diagnostic scans using positron tomography (PET). The gasoline/magnetic nanoparticles are suitable for early diagnostic, effective targeting, and cerebrovascular amyloid therapy agents, combined with anti-amyloid antibodies loaded with curcumin/dexamethasone (s).

Mitochondrial malfunction causes various human disorders, including Huntington's disease. The alleviation of mitochondrial defects could produce a therapeutic effect. Significant cytosolic and mitochondrial fractions in cells are indicated as mitochondrial chemotherapeutic targets in the Vitro assessment of the curcumin nanoformulation PLGA-b-PEG-triphenyl-phosphonium library (PLGA-b-PEG-TPP). polymer Another nanoformulation of solid lipid-based Curcumin attenuates Huntington's three-nitro propionic acid illness in rats by increasing the complex II activities, restoring glutathione and superoxide dismutase. Reduction of mitochondrial swelling, lipid peroxidation, protein carbonyl, and reactive oxygen in mitochondrial dysfunctions in HD was also enhanced.

Stroke

Stroke causes irreversible deterioration of the CNS by blood, oxygen, and nourishment. Curcumin may limit stroke risk by decreasing cholesterol, clogging the arteries, and acting as



blood dilute agent. Concept evidence for balb/c mice reveals three times - 1555 times more bioavailability, three to four times stronger pharmacodynamics, and 8,135 times higher brain targeting when Curcumin is used to treat stroke as solid lipid nanoparticle treatments. The use of liquid chromatography paired with the tandem mass spectrometry to simultaneously identify Curcumin can be checked using a sensitive technique using salbutamol in mouse and brain tissue as an internal standard. Solid lipids are recommended for effective brain dispersion of Curcumin for the oral Nanoformulation of Ntrimethvl chitosan. Presented Curcumin (Nisopropyl acrvlamide) Nanoformulation demonstrated improved neurobehavioral activity in the brain's center, which was cytokine-generated blockage produced brain ischemia (TNF-α and IL-1β). This formula can also prevent brain injury caused by oxidative stress after blocking the middle cerebral artery of rats. The strength of grip, motor activity, and biochemical brain research have been evaluated for the efficiency of this composition. A recent study showed the participation of Curcumin encapsulated as a brain stroke epigenetic agent in 200 nm exosomes. Other efficient solid lipid nanoparticle curcumin alleviates overwhelming oxidative and nitrogen stress, acetylcholinesterase, complex mitochondrial enzymes, and cerebral ischemic-reperfusion physiological parameters in rats show their involvement of protected against cerebral ischemic insult.

Inflammatory diseases

Inflammation is the body's biological protective response to injuries or illnesses. There are over a dozen inflammatory illnesses. Monocytegenerated myeloid cells help fight inflammatory Antiviral, antioxidant, diseases. and neuroprotective has been shown to be Curcumin. The nanotech curcumin mixture successfully decreases lipopolysaccharide inflammation in rats (LPS). At the same time, blood and brain concentrations of lactic acid, kidney function, and neuronal apoptosis do not cause adverse effects. Another nanoformulation based on PLGA-Eudragit S100 significantly reduced the production of TNF- α with macrophages stimulated by LPS (J774 cells). Neutrophil infiltration and TNF- α dumps in the mouse dextran sulfate colitis model were similarly decreased in vivo tests. I showed that inflammatory bowel disease treatment is a suitable technique (IBD). Curcumin nanoemulsion revealed a reduction in neutrophil migration, lowered TNF- α levels, and oxidation stress in rats causing LPS-

induced lung and liver-associated damage. Exosome-mediated Curcumin can stimulate in vivo myeloid cells (Lipopolysaccharide septic shock animal (LPS) model) efficiently.

A new nanoformulation transdermal nanocarrier gel is designed to prevent inflammation and is not irritating (skin irritation rating of 0.49) and is suitable for human ingestion. This can be created for localized inflammation as a therapy Curcumin-polluted solid strategy. lipid nanoparticles reduced adequate levels of IL-1ß expression and lower serum, proinflammatory cytokines, anti-inflammatory cytokines, cytokine IL-10. A synergistic impact of the combination of celecoxib and curcumin nanoformulation drugs was achieved in the ulcerative colitis model of rats. Furthermore, solid curcumin-coated nanoparticles investigated for hepatoprotection. The were examination has confirmed this: the extent of liver damage and repairs, (ii) the levels of alanine aminotransferase and aspartate aminotransferase, (iii) oxidative stress markers (malondialdehyde, superoxide dismutase, and reduced glutathione), and (iv) TNF- α in the model of carbon tetrachloride for hepatic damage.

Rheumatoid Arthritis is a persistent inflammatory disorder in joints and cartilages. The entire Freund arthritic rat adjuvant experiment created effective solid lipid solid nanoparticles coated with Curcumin. Arthritic rat model results have shown a considerable increase in blood leucocyte counts, (ii) oxidative-necrotic stress, (iii) TNF- α and C-reactive protein, (iv) cyclic citrullinated antibody levels of peptide, and (v) radiological abnormalities that improve arthritis protectiveness.

Diabetes

Diabetes is a sign of excessive blood glucose in humans. Curcumin was beneficial against disorders related to cardiac, renal, and liver disease. Curcumin can therefore be predicted to boost the therapeutic effect of nanoparticles and lipid/liposomes. The self-emulsifying therapeutic delivery device for diabetic neuropathy was studied in male Sprague - Dawley rats. The data validated higher neurosensory function, including nerve function and the inflammatory protein (NF-µB, IKK- β , COX-2, INOS, TNF- α , and IL-6), including the nerve function. Diabetes is also linked to high free radicals and systemic proinflammatory cytokines that may impact lipid profiles. In PLGA - curcumin nanoformulation in Streptozotocininduced diabetic rats, the study showed reduced Creactive protein, IL 6, and TNF levels, significantly



reducing plasma triglyceride total and an increase in high-density lipoprotein cholesterol. In a leptindeficient paradigm for mice resistance, liposomal nanoparticles have suppressed the proinflammatory pathway in liver tumor necrosis factors, inducible nitric oxide producing dendritic cells, and macrophages of adipose tissue (ATM) that may restore resistance to insulin.

REFERENCES

- Anand P, Kunnumakkara A.B, Newman R.A, Aggarwal B.B. (2007); Bioavailability of curcumin: problems and promises. Mol Pharm. 4(6);807–18.
- [2]. Anand P, Thomas S.G, Kunnumakkara A.B, Sundaram C, Harikumar K.B, Sung B, Tharakan S.T, Misra K, Priyadarsini I.K, Rajasekharan K.N, Aggarwal B.B. (2008); Biological activities of curcumin and its analogues (Congeners) made by man and Mother Nature. Biochem Pharmacol.76(11);1590–611.
- [3]. Ganta S, Amiji M. Mol Pharm 2009; 6(3): 928-939.
- [4]. Chabib L, Martien R, Ismail H, (2012), Formulation of nanocurcumin using low viscosity chitosan polymer and its cellular uptake study into T47D cells. Indonesian J. Pharm. 23(1):27–35.
- [5]. Chin S.F, Akmar Mohd Yazid S.N, and Pang S.C. (2014), Preparation and Characterization of Starch Nanoparticles for Controlled Release of Curcumin., Int. J. of PolymerScience;8.
- [6]. Chirio D, Gallarate M, Peira E, Battaglia L, Serpe L, Trotta M; (2011), Formulation of curcumin-loaded solid lipid nanoparticles produced by fatty acids coacervation technique. J. Microencapsul.28(6),537-48.
- [7]. Giat L, Sinh D.T, Toan T.P, (2014); High concentration Nanacurcumin fabrication by wet milling method curcumin with glassball, International Journal of Scientific & Technology research, 3(8); 345-348
- [8]. Leimann F.V, Cardozo L, Sayer C, & Araújo P.H, (2013); Poly (3hydroxybutyrate-co-3hydroxyvalerate) nanoparticles prepared by а miniemulsion/solvent evaporation technique. Effect of PHBV molar mass and concentration, Brazilian Journal of Chemical Engineering, 30(2), 369-377.

- [9]. Prasad S, Gupta S.C, Tyagi A.K, Aggarwal B.B. (2014); Curcumin, a component of golden spice: from bedside to bench and back. Biotechnol Adv. 32(6); 1053–64.
- [10]. Lin W, Cooper C, Camarillo I. The effectiveness of electroporation-based nanocurcumin and curcumin treatments on human breast cancer cells. In: Proceedings of ESA annual meeting on electrostatics; 2014 June 17-19; University of Notre Dame, Notre Dame, Indiana. USA: Electrostatics Society of America; p. 1-7.
- [11]. Rocha BA, Gonçalves OH, Leimann FV, Rebecca ESW, Silva-Buzanello RA, Filho LC, Araújo PHH, Cuman RKN, Bersani-Amado CA. Adv Med Plant Res 2014; 2(4): 62-73.
- [12]. Bisht S, Mizuma M, Feldmann G, Ottenhof N, Hong SM, Pramanik D, Chenna V, Karikari C, Sharma R, Goggins MG, Rudek MA, Ravi R, Maitra A, Maitra A. Mol Cancer Ther 2010; 9(8): 2255-2264.
- [13]. Yallapu MM, Ebeling MC, Khan S, Sundram V, Chauhan N, Gupta BK, Puumala SE, Jaggi M, Chauhan SC. Mol Cancer Ther 2013; 12(8): 1471-1480.
- [14]. Ruddon RW. Cancer biology, 4th ed. Oxford University Press, Oxford, 2007, pp. 223.
- [15]. Yallapu MM, Khan S, Maher DM, Ebeling MC, Sundram V, Chauhan N, Ganju A, Balakrishna S, Gupta BK, Zafar N, Jaggi M, Chauhan SC. Biomaterials 2014; 35(30): 8635-8648.
- [16]. Mukerjee A, Vishwanatha JK. Anticancer Res 2009; 29(10): 3867-3876.
- [17]. Bhawana, Basniwal RK, Buttar HS, Jain VK, Jain N. J Agric Food Chem 2011; 59(5): 2056-2061.
- [18]. Krausz AE, Adler BL, Cabral V, Navati M, Doerner J, Charafeddine RA, Chandra D, Liang H, Gunther L, Clendaniel A, Harper S, Friedman JM, Nosanchuk JD, Friedman AJ. Nanomedicine 2015; 11(1): 195-206.
- [19]. Mirnejad R, Jahromi MAM, Al-Musawi S, Pirestani M, Ramandi MF, Ahmadi K, Rajayi H, Hassan ZM, Kamali M. Iran J Biotech 2014; 12(3): e1012.
- [20]. Gandapu U, Chaitanya RK, Kishore G, Reddy RC, Kondapi AK. PLoS One 2011; 6(8): e23388.



- [21]. Dandekar PP, Jain R, Patil S, Dhumal R, Tiwari D, Sharma S, Vanage G, Patravale V. J Pharm Sci 2010; 99(12): 4992-5010.
- [22]. Akhtar F, Rizvi MM, Kar SK. Biotechnol Adv 2012; 30(1): 310-320.
- [23]. Sun D, Zhuang X, Xiang X, Liu Y, Zhang S, Liu C, Barnes S, Grizzle W, Miller D, Zhang HG. Mol Ther 2010; 18(9): 1606-1614.
- [24]. Yallapu MM, Maher DM, Sundram V, Bell MC, Jaggi M, Chauhan SC. J Ovarian Res 2010; 3:11.