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FORMULATION AND EVALUATION OF CURCUMIN NANOPARTICLES FOR BRAIN CELLS

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ABSTRACT

Curcuma longa is a hydrophobic polyphenol that is produced from its rhizome. Asians often use curcumin as a spice in food and topical medicine to relieve inflammatory ailments. Its potent anti-inflammatory and neuroprotective qualities allow it to pass through the blood-brain barrier as well. Because of its wide range of pharmacological effects, curcumin has been suggested as a potential treatment for a number of neurological disorders. Curcumin has pleiotropic properties, but its rapid elimination, low stability, and poor solubility have limited its therapeutic applications. Recent advances in nanotechnology-based drug delivery systems have led to notable improvements in curcumin's bioavailability and water solubility. The benefits of employing curcumin nanoparticles and the noteworthy developments in this area of medicine are also covered. There are numerous central nervous system (CNS) illnesses. There is evidence linking curcumin nanoparticle effects and potential mechanisms of action to a number of central nervous system (CNS) diseases, such as Parkinson's, Alzheimer's, Huntington's, multiple sclerosis, epilepsy, and amyotrophic lateral sclerosis.

Keywords: *Curcumin, Nanoparticles, Bioavailability, Solubility, Stability, Blood Brain Barrier (BBB)*

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INTRODUCTION

Curcuma Longa Linn's (Zingiberaceae) rhizome is the source of the polyphenol chemical curcumin.In Indian cooking culture, it is also referred to as turmeric. Approximately 75–80% of the curcumin that is readily available is composed of curcumin, 15-20% desmethoxycurcumin, and 3-5% bis-desmethoxycurcumin.[1] It has therapeutic applications across several biomedical fields. Additional therapeutic benefits of curcumin include its anti-inflammatory, antibacterial, antioxidant, anti-tumor, anti-diabetic, and chemotherapy-preventive qualities.[2] Another benefit of curcumin is that it is safe at greater dosages, and does not produce any toxicity.[3] Curcumin is easily soluble in organic solvents such alcohols, ketones, esters, and organic acids, but it is nearly insoluble in aqueous solutions. Three primary curcuminoid compounds, curcumin, desmethoxycurcumin, and bismethoxycurcumin.[4]

Thus, curcumin's hydrophobic nature demonstrates its pharmacokinetic limits, which include low oral bioavailability, quick metabolism, and quick elimination.[5] The application of nanotechnology to medicine is a means of developing new medications or repurposing existing ones while also increasing their potency, low risk of toxicity, reduction of side effects, and acceptance of the use of reactive substances.[6] Nanoparticles also enhance the permeability and solubility. Along with developing regulated drug release and drug targeting, it also results in prolonged circulation durations and shields the molecule from partial breakdown.[7] Nanoparticles are huge, specialized entities with an average size between 20 and 500 nm. These particles are used in medical technologies.[8]

In Africa and Southwest India, this is a commonly grown crop. In South and Asian countries, it is widely used as a spice due to its flavor and yellow color. [9] Although it dissolves readily in organic solvents like acids, alcohols, ketone bodies, and esters, mini curcumin remains predominantly insoluble in aqueous solutions.[10] Curcumin also has the advantages of having few side effects, being safe at higher dosages, and not producing any toxicity.[11] This is used to treat a wide range of illnesses, including rheumatism, skin conditions, aches and pains, liver issues, inflammation, and asthma, and has been used for thousands of years in the traditional Chinese and Indian medical system known as Ayurveda.[12] The food industry uses it today as a coloring, flavoring, and preservative.

Curcumin has demonstrated some potential in the management of mood disorders.[13] It has beneficial benefits on the brain that include lowering inflammation, promoting brain plasticity, and increasing the neurotransmitters dopamine and serotonin.[14] This implies that the plant might work well as an antidepressant. Because of its quick development, nanotechnology is one of the most stable areas in element techniques.[15] Scientists are capable of discovering and manipulating materials in atomic and molecular distribution throughout a wide range of fields depending on nanotechnology.[16] Designers of nanomaterials come from several processes that are heavily regulated, employing criteria based on chemical and physical qualities, and creating distinct features that serve their objectives.[17]

For this reason, a lot of nano formulation-based techniques have been tried in the last few years to enhance the pre-clinical, in vitro, and in vivo properties of curcumin.[18] Adjuvants that stabilizing agents, conjugates/polymer a combination, lipid/liposomes, hydro/micro/nano gel-like substances, micelles, and nanoparticles (NPs) are used in nano formulation-based techniques.[19]

Advantages of curcumin Nanoparticles

Enhanced Bioavailability

Curcumin's absorption and distribution in the brain can be enhanced by nanoparticles, resulting in a more effective administration of the drug's therapeutic effects.[20]

Targeted Delivery

Curcumin's therapeutic benefits can be enhanced by using nanoparticles that are specifically made to target brain cells, hence reducing off-target effects.[21]

Greater Stability

Curcumin nanoparticles have a longer half-life of activity than free curcumin, which breaks down fast in the body.[22]

Neuroprotective Effects

Curcumin's anti-inflammatory and antioxidant qualities can help shield brain tissue from harm and promote general brain health. By raising the concentration of curcumin in the brain, nanoparticles can intensify these benefits.[23]

Potential for Disease Treatment

Curcumin nanoparticles appear to have potential for treating neurological conditions including Parkinson's and Alzheimer's.[24]

Route of administration for curcumin Nanoparticles

Intranasal Administration

Using the trigeminal and olfactory nerve pathways, releasing nanoparticles through the nostrils allows them to pass through the blood-brain barrier and reach brain cells directly. Absorption is happening quickly.[25]

Intracerebral Administration

Using methods like convection-enhanced delivery or stereotactic injection, nanoparticles can be injected directly into particular brain areas and can be precisely targeted. [26]

Intrathecal Administration

By injecting nanoparticles via intrathecal lumbar puncture into the cerebrospinal fluid (CSF), it is possible to distribute them throughout the brain and spinal cord and the entire central nervous system.[27]

Intravenous Administration

Administered intravenously, nanoparticles have the ability to cross the blood-brain barrier (BBB) and move throughout the body, eventually arriving at brain cells.[28]

Methodology

Extraction of herbal drug

Preparation of Raw Material

Clean and cut the turmeric rhizomes into small pieces to increase the surface area for extraction.

Drying

Dry the turmeric pieces to reduce moisture content, as water can interfere with the extraction process.

Grinding

Grind the dried turmeric into a fine powder to enhance the efficiency of extraction.

Solvent Extraction

Use a suitable solvent like ethanol or ethyl acetate to extract curcuminoids from the turmeric powder. This can be done through techniques such as maceration or percolation.

Filtration

After extraction, filter the solution to remove solid particles and impurities, obtaining a crude extract.

Concentration

Concentrate the crude extract to increase the curcumin content. This can be achieved through evaporation or other concentration methods.

Purification

Purify the concentrated extract through techniques like column chromatography to isolate curcumin from other compounds.

Drying

Dry the purified curcumin to remove any remaining solvent, resulting in a solid curcumin extract.[29]

Figure No.1: Curcumin Powder

METHOD OF PREPARATION

Method of Single Emulsion-Solvent Evaporation.
Method of Thin Film Hydration.
Technique of Micro Emulsion.
Method of Desolation
Agitation and Sonication Method.
Cross Linking Method.
Freeze Dried Anti Solvent Crystallization and High-Pressure Homogenizer Method.
Co-Precipitation Method
Electro spraying Method [30]

Preparation of Curcumin Nanoparticles

Single Emulsion Solvent Evaporation Technique

Curcumin-loaded nanoparticles were produced utilizing a single emulsion solvent evaporation process. In a hollow glass container, dissolve 100-200 mg of calcium stearate polymer in 5 ml of dichloromethane (DCM), then add 10 or 20 mg of curcumin powder and vortex for 30 minutes. The drug/polymer mixture was introduced into a glass tube containing 10 mL of aqueous PVA solution. After integrating the drug and polymer in PVA solution, a vortex for at least 10 seconds at high speed.

The material itself mixture was emulsified in a cold bath for seven minutes at 40% amplitude with a probe sonicator. This emulsified liquid was placed in 30 milliliters of 0.5% aqueous solution and magnetically stirred. Dichloromethane evaporated for three hours using strong magnetic stirring at 800 rpm. The nanoparticles were gathered through centrifuging at 20,000 rpm for 15 minutes and washed on three separate occasions with distilled water. The nanoparticle pellets were subsequently revived in 5 milliliters of distilled water.[31][32]

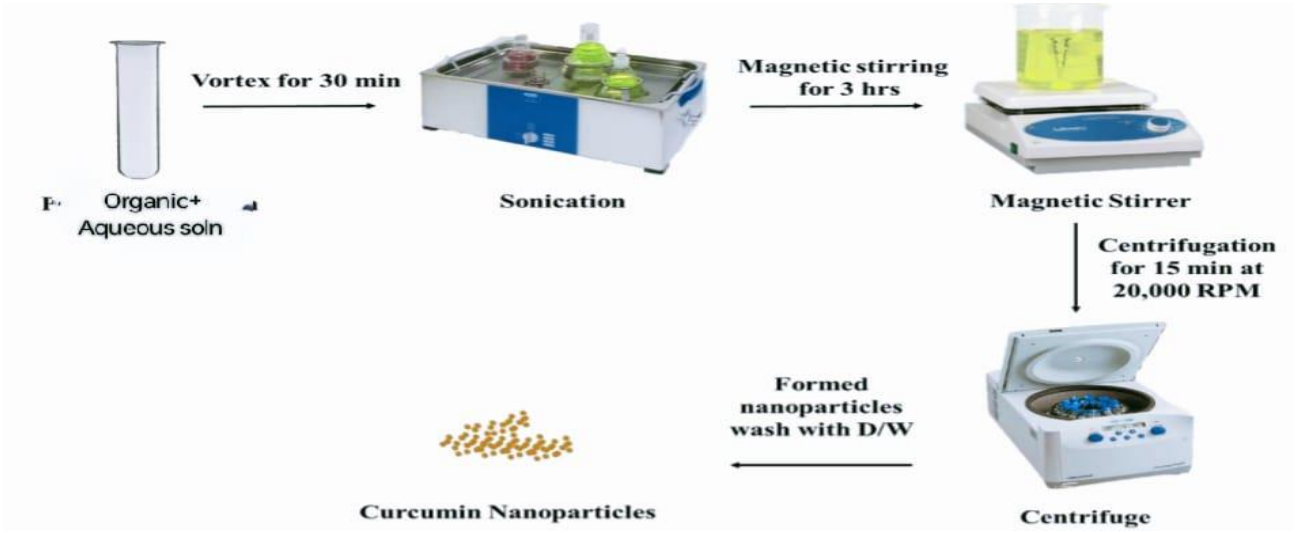


Figure No.2: Single emulsion solvent evaporation technique

Formulation Table

Sr No.	Ingredients	Quantity	Role
1	Calcium stearate	100-200 mg	stabilizing qualities, potential to increase bioavailability, and ability to change release profiles
2	Curcumin	10-20 mg	Anti-inflammatory, antibacterial, antioxidant, anti-tumor, chemotherapy-preventive
3	Dichloromethane (DCM)	5 ml	It has the ability to dissolve a wide range of organic compounds, volatility, and low toxicity.
4	Polyvinyl Alcohol (PVA)	10 ml	stabilizer or surfactant, also improve the biocompatibility
5	Distilled water	5 ml	Solvent

Table No. 1: Formulation

Evaluation Test

Physical Evaluation

Size

The nanoparticle size plays an important role in their long circulation, biodistribution, and clearance.

Color

Curcumin Nanoparticles mostly present in Orange -Yellow colour

Shape

Nanoparticles including helices, zigzags, belts, spherical, oval, cubic, prismatic, and pillar morphologies. [33]

UV Spectroscopic Evaluation

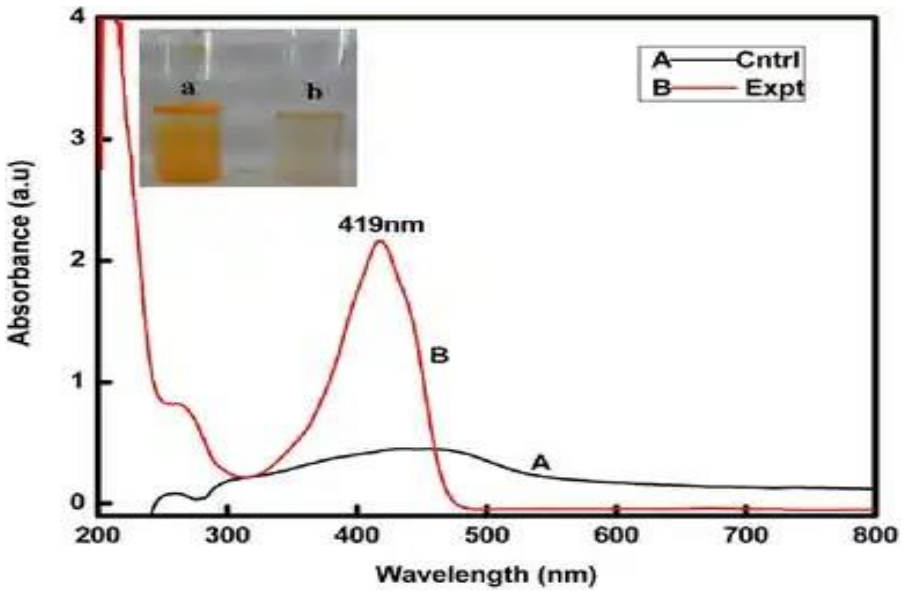
The UV range for curcumin nanoparticles intended for brain cells wavelength is around 420 to 450 nanometers. The quantity of curcumin existing in the nanoparticles can be determined by measuring using UV spectroscopy.[34]

Testing for Solubility

Dissolve curcumin nanoparticles in a range of solvents or media.

pH Testing

Use a pH meter or pH indicator strips used to determine the curcumin nanoparticles pH. Make sure the pH is between 7.2 and 7.4, which is the physiological range that is appropriate for brain cells.[35]



Graph No.1: UV Spectra Range

RESULT

The curcumin nanoparticles for brain cells are formulated, evaluated and showing the result as following:

Sr. No.	Test	Result
1	Physical Evaluation	Color: Orange Shape: Cluster
2	UV Spectroscopic Evaluation	Absorbance: 429 nm
3	Testing For Solubility	Insoluble: Aqueous Solution Soluble: Organic Solvent
4	PH Testing	Acidic: Yellow color (Ph-4) Neutral: Dark Yellow (Ph - 7.9) Basic: Red color Curcumin (Ph-11)

Table No. 2: Result and Discussion

DISCUSSION

Formulating curcumin nanoparticles involves careful consideration of the preparation method, characterization, and evaluation test. The goal is to enhance the therapeutic potential of curcumin for treating brain-related conditions by improving its solubility, stability, and delivery to brain cells.

CONCLUSION

Because of nanoparticles' enhanced functionality, stability, and pharmacokinetic and pharmacodynamic qualities, nanotechnology presents a promising drug delivery method. A polyphenolic hydrophobic molecule with antimicrobial, antiseptic, anticancer, and anti-inflammatory properties is curcumin. Due to its low solubility and bioavailability, curcumin has a limited clinical applicability. Several systems, such as liposomes, nanoparticles, micelles, and phospholipid complexes, can improve the solubility, stability, bioavailability, and resistance to degradation of curcumin. Curcumin is one old phytochemical whose health benefits have been proven, as well as new applications that significantly improve terminal illnesses. Curcumin research is among the few examples of broad applications backed by dependable procedures and methodological tenets.The new technological ideas for this molecule's biological administration have recently had the most effects. Specifically, improvements at the brain level have been demonstrated thanks to the use of nanoparticles, which may even transform medicine. To guarantee the security of all clinical trials, it is practical to highlight toxicity concerns, nevertheless, as with any chemical agent.

REFERENCE

1. Anand P., Kunnumakkara A.B., Newman R.A., Aggarwal B.B. Bioavailability of curcumin: problems and promises. Mol Pharm. 2007;4(6):807–18.
2. Ohori H., Yamakoshi H., Tomizawa M.Synthesis and biological analysis of new curcumin analogues bearing an enhanced potential for the medicinal treatment of cancer. Mol Cancer Ther. 2006;5(10):2563.
3. Aarti B. Shinde, Vidhya M. Danole, Anita V. Waghmode, Yogesh B. Raut, Sanjay K. Bais. IJPHT Journal Current Scenario Of Herbal Medicine And Future Prospects. 2024;2(2):1622-1633.
4. Benameur T., Giacomucci G., Panaro M.A., Ruggiero M., Trotta T., Monda V., Pizzolorusso I., Lofrumento D.D., Porro C., Messina G. New promising therapeutic avenues of curcumin in brain diseases. Molecules. 2021;27(1):236.
5. Salehi B., Calina D., Docea A.O., Koirala N., Aryal S., Lombardo D., Pasqua L., Taheri Y., Marina Salgado Castillo, Martorell M., Martins N. Curcumin's nanomedicine formulations for therapeutic application in neurological diseases. Journal of Clinical Medicine. 2020; 9(2):430.
6. Del Prado-Audelo, M.L., Caballero-Florán I.H., Meza-Toledo J.A., Mendoza-Muñoz N., González-Torres M., Florán B., Cortés H. and Leyva-Gómez. Formulations of curcumin nanoparticles for brain diseases. Biomolecules. 2019;9(2):56.
7. Pore A.V., Bais S.K., Kale T.H., Quality Aspects of Herbal Drugs and its Formulation. International Journal of Advanced Research in Science, Communication and Technology (IJARSCT). 2023;3(2):326.
8. Yavarpour-Bali H., Ghasemi-Kasman M. and Pirzadeh M., Curcumin-loaded nanoparticles: A novel therapeutic strategy in treatment of central nervous system disorders. International journal of nanomedicine. 2019;4(2):4449-4460.
9. Tsai Y.M., Chien C.F., Lin L.C. and Tsai T.H., Curcumin and its nano-formulation: the kinetics of tissue distribution and blood–brain barrier penetration. International journal of pharmaceutics. 2019;416(1):331-338.
10. Cheng K.K., Yeung C.F., S.W.Chow and S.F.Chow. Highly stabilized curcumin nanoparticles tested in an in vitro blood–brain barrier model and in Alzheimer's disease Tg2576 mice. The AAPS journal. 2013;15(1):324-336.
11. S. D. Sonawane, S. K. Bais, S. A. More, Novel Drug Design International Journal of Advanced Research in Science Communication and Technology. 2023;3(1): 528.
12. Lim K.J., Bisht S., Bar E.E., Maitra A. and Eberhart C.G. A polymeric nanoparticle formulation of curcumin inhibits growth, clonogenicity and stem-like fraction in malignant brain tumors. Cancer biology & therapy. 2011;11(5):464-473.
13. Sadegh Malvajerd, Azadi A., Izadi Z., Kurd M., Dara T., Dibaei M., Sharif Zadeh, Akbari Javar and Hamidi M. Brain delivery of curcumin using solid lipid nanoparticles and nanostructured lipid carriers: Preparation, optimization, and pharmacokinetic evaluation. ACS chemical neuroscience. 2018;10(1):728-739.
14. Dhivya S. and Rajalakshmi A., Review on the preparation methods of Curcumin Nanoparticles. Pharma Tutor. 2018;6(9):6-10.
15. Yallapu M.M., Nagesh P.K., Jaggi M., Chauhan S.C. Therapeutic applications of curcumin nanoformulations. The AAPS journal. 2015;17(1):1341.

16. Mandal M., Jaiswal P., Mishra A. Role of curcumin and its nanoformulations in neurotherapeutics: A comprehensive review. Journal of biochemical and molecular toxicology. 2020;34(6):22478.
17. Panzarini E., Mariano S., Tacconi S., Carata E., Tata A.M., Dini L. Novel therapeutic delivery of nanocurcumin in central nervous system related disorders. Nanomaterials. 2020;11(1):2.
18. Nagansurkar S.B., Bais S.K., Shinde S., Some Typical Medicinal Plants And Their Active Constituents Ability For Wound Healing. International Journal of Pharmacy and Herbal Technology. 2024;2(1):389-406.
19. Heidari S., Mahdiani S., Hashemi M., Kalalinia F. Recent advances in neurogenic and neuroprotective effects of curcumin through the induction of neural stem cells. Biotechnology and Applied Biochemistry. 2020;67(3):430.
20. Shabbir U., Rubab M., Tyagi A. Curcumin and its derivatives as theranostic agents in Alzheimer's disease: The implication of nanotechnology. International Journal of Molecular Sciences. 2020;22(1):196.
21. Shome S., Talukdar A.D., Choudhury M.D., Bhattacharya M.K., Upadhyaya H. Curcumin as potential therapeutic natural product: a nano biotechnological perspective. Journal of Pharmacy and Pharmacology. 2016;68(12):1481.
22. Mohanty C., Sahoo S.K. The in vitro stability and in vivo pharmacokinetics of curcumin prepared as an aqueous nanoparticulate formulation. Biomaterials. 2010; 31(25):6597.
23. Rahimi H.R, Nedenia R., Shamloo A.S., Nike Hosts, Oskuee R.K. Novel delivery system for natural products: Nano-curcumin formulations. Avicenna journal of phytomedicine. 2016;6(4):383.
24. Mohi-Ud-Din R, Mir R.H., Wani T.U., Shah A.J., Mohi-Ud-Din I, Dar M.A., Pottoo F.H. Novel drug delivery system for curcumin: Implementation to improve therapeutic efficacy against neurological disorders. Combinatorial Chemistry & High Throughput Screening. 2022;25(4):607.
25. Sabouni N., Marzouni H.Z., Palizban S., Meidani N.S., Kesharwani P., Jamialahmadi T., Sahebkar A. Role of curcumin and its nanoformulations in the treatment of neurological diseases through the effects on stem cells. Journal of Drug Targeting. 2023;31(3):243-60.
26. J.P. Lavande, S.K.Bais, B.A.Nagane Novel Drug Delivery System International Journal of Advanced Research in Science Communication and Technology. 2023;3(1):208.
27. Ray B., Bisht S., Maitra A., Lahiri D.K. Neuroprotective and neurorescue effects of a novel polymeric nanoparticle formulation of curcumin (NanoCurc™) in the neuronal cell culture and animal model: implications for Alzheimer's disease. Journal of Alzheimer's disease. 2011;23(1):21.
28. Bhat A., Mahalakshmi A.M., Ray B., Tuladhar S., Hediyala T.A., Manthiannem E., Padamati J., Chandra R., Chidambaram S.B., Sakharkar M.K. Benefits of curcumin in brain disorders. BioFactors. 2019;45(5):666.
29. B Mythri R, M Srinivas Bharath M. Curcumin: a potential neuroprotective agent in Parkinson's disease. Current pharmaceutical design. 2012;18(1):91.
30. Ramalingam P. Enhanced oral delivery of curcumin from N-trimethyl chitosan surface-modified solid lipid nanoparticles: pharmacokinetic and brain distribution evaluations. Pharmaceutical research. 2015;(32):389-402.

31. Dolatabadi S., Karimi M., Nasirizadeh S., Hatamipour M., Mohammadzadeh S., Jaafari M.R. Preparation, characterization and in vivo pharmacokinetic evaluation of curcuminoids-loaded solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). Journal of Drug Delivery Science and Technology. 2021;2(1):62.
32. Kakkar V., Muppu S.K., Chopra K., Kaur I.P. Curcumin loaded solid lipid nanoparticles: an efficient formulation approach for cerebral ischemic reperfusion injury in rats. European Journal of Pharmaceutics and Biopharmaceutics. 2013;85(3):339-450.
33. Fang M., Jin Y., Bao W., Gao H., Xu M., Wang D., Wang X., Yao P., Liu L. In vitro characterization and in vivo evaluation of nanostructured lipid curcumin carriers for intragastric administration. International journal of nanomedicine. 2012;2(2):5395
34. Patwekar S.L., Khavane, K.B., Chainpure P.R. and Shivpuje S.A., A review on different preparation methods used for development of curcumin nanoparticles. International Journal of Creative Research Thoughts. 2021;9(1):4088-4101.
35. Pandit R.S., Gaikwad S.C., Agarkar G.A., Gade A.K., Rai M., Curcumin nanoparticles: physico-chemical fabrication and its in vitro efficacy against human pathogens. Biotech. 2015;5(1):991.