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A Review on the preparation methods of Curcumin Nanoparticles

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ABSTRACT

Design and development of herbal nanoparticles has become a frontier research in the nanoformulation arena. Curcumin is the main bioactive component contained in Curcuma longa, largely employed in traditional medicine. Recently, beneficial properties, useful for prevention and treatment of several disorders, have been discovered for this compound. Although curcumin has shown therapeutic efficacy against many human ailments, one of the major problems with curcumin is its poor bioavailability, which appears to be primarily due to poor absorption, rapid metabolism, and rapid systemic elimination. Therefore introduction of nanotechnology provides a solution towards increased bioavailability of curcumin. In this review, the various methods of preparation of curcumin nanoparticles are briefly discussed.

Keywords: curcumin, preparation methods, nanoparticles.

METHOD OF PREPARATION:-

· ·Coacervation techniques

Nanoprecipitation method

Spray drying method

· Single emulsion method

· Solvent evaporation method

· Microemulsion

· Wet milling method

· Thin film hydration method

· Solid dispersion method

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- Emulsion polymerization method
- Fessi method
- Ionic gelation method
- Ultrasonication
- Antisolvent precipitation method

1. Single Emulsion Solvent Evaporation Technique

Curcumin loaded nanoparticles were prepared by using single emulsion solvent evaporation technique.

In glass tube, to take 100-200 mg of PLGA polymer was dissolved in 5 ml of dichloromethane (DCM), then 10 or 20 mg curcumin powder dissolved in solvent mixture and intermittent vortex for 30 min. The mixture of drug/polymer was added in glass tube containing 10 ml of aqueous PVA solution. After, adding the drug/polymer mixture in PVA solution then vortex for more 10 sec at high speed. This polymer mixture was emulsified in ice water bath for 7 min at 40 % amplitude by using probe sonicator. This emulsified mixture was poured into 30 ml of 0.5% aqueous solution under magnetic stirring.

Dichloromethane was evaporated under high magnetic stirring at 800 rpm for 3 hrs. The nanoparticles were collected by using centrifugation at 20,000 rpm for 15 min and washed for 3 times with distilled water. Then supernatants were collected, pellets of the nanoparticles was resuspended in 5 ml distilled water. Schematic diagram for preparation of curcumin nanoparticle by single emulsion solvent evaporation technique shown in figure 1. [3]

Coacervation techniques: In this method of synthesis, the polymer is dissolved in organic solvent (e.g. dichloromethane, ethyl acetate, or acetonitrile) and herbal drug (curcumin) is suspended directly in polymeric solution and it is allowed to homogenize properly. Nanoparticles are collected by centrifugation. It is inexpensive method. The main drawback of this method is that it requires large amount of solvent. Chirio *et al.*, 2011 formulated curcumin loaded nanoparticles by using this technique.

Nanoprecipitation method: Nanoprecipitation method is also known as Solvent displacement method. In this method, desired polymer is suspended in the suitable solvent to form polymeric solution and herbal drug (curcumin) is added into it. After that this drug- polymer solution is added into water under continuous stirring which results in precipitation. After that the solvent is allowed to evaporate by hot air flow. Spray drying resulted in the formation of drugs in the amorphous state, which may get partially crystallized during processing. In this method of synthesis, curcumin and polymer are dissolved in same solvent or mixture of solvents. Chin *et al*., 2014 prepared starch nanoparticles for controlled release of curcumin.

Spray drying method: Curcumin nano-crystals can be formulated by spray drying method. For that Curcumin nano-suspensions, having a drug concentration of 10% (w/w), are dried with a Mini Spray-dryer. The spray-dried Curcumin nanocrystals are directly collected after the process. Yallapu *et al*., 2010 fabricated curcumin encapsulated PLGA nanoparticles.

Single emulsion method: Single emulsion method is the conventional method for the synthesis of curcumin nanoparticles. In this method, curcumin nanoparticles are prepared by dispersing it in a suitable solvent, followed by high speed homogenization or ultrasonication to form the emulsion. Further the solvent from the emulsion is evaporated by continuous magnetic stirring at room temperature or under reduced pressure. The solidified nanoparticles are ultrasonicated and collected, followed by washing with distilled water to remove additives and lyophilized to get nanoparticles. Curcumin loaded poly (lactic-co-glycolic acid) (PLGA) nanoparticles can also be prepared. Sari *et al*., 2013 produced curcumin nanoparticles by this method.

Solvent evaporation method: Solvent evaporation method includes two major steps: (i) preparation of drug-polymeric solution (ii) evaporation of dispersing solvent used for dissolving curcumin. It results in the formation of solid mass. The emulsion formed is then converted into nanoparticles suspension by evaporation of the solvent. Advantage of this method is that low temperature required for evaporation of solvent and thermal deposition can be prevented. Disadvantages are: (i) the reagents used in this method are quite expensive (ii) selection of proper solvent is somehow difficult and evaporation of organic solvent is time consuming process. PLGA (Poly (lactic

acid-co-glycolic acid) loaded curcumin nanoparticles are synthesized by this technique. Liemann *et al*., 2013 formulated PHBV nanoparticles by solvent evaporation method.

Microemulsion: Microemulsion is considered as an ideal method for nanoparticles fabrication. The surfactants used in this method are hydrophobic in nature for water soluble drugs and hydrophilic in nature for oil soluble drugs. Microemulsion is formed when a small amount of surfactant is stirred and curcumin is added in it along with oil and water. It results in the formation of turbid solution which generally appears like small droplets. Various typof surfactants are used to increase the surface stabilization of curcumin nanoparticles. This method is easy and can be effectively used for drug delivery with less energy expenditure. Microemulsion technique is affected by certain parameters like temperature and pH variation. Lin *et al*., 2009 formulated phospholipid-based curcumin-encapsulated microemulsions.

Wet milling method: Curcumin nanoparticles can be synthesized from wet-milling method. Curcumin is suspended in an appropriate dispersing solvent. The obtained solution is further agitated under ultrasonication method. Distilled water is used for the synthesis of curcumin nanoparticles. The obtained solution is then allowed to centrifuge and the formed nanoparticles are collected. Giat *et al*., 2014 fabricated nanocurcumin by wet milling method.

Thin film hydration method: In this method of synthesis, herbal drug (curcumin) and surfactants are allowed to mix in a suitable organic solvent under sonication condition. Solvent is allowed to evaporate under certain pressure. After that distilled water is added in sonication condition and the obtained nanosuspension is then centrifuged to obtain curcumin nanoparticles. Moorthi *et al*., 2012 demonstrated curcumin nanoparticles synthesis by this method of synthesis.

Solid dispersion method: In this method, the matrix and hydrophobic drugs like curcumin are mixed. Matrix can be in the amorphous or in crystalline form. This method can be used to dissolve the insoluble hydrophobic drug. This is fast and readily scalable method used for curcumin nanoparticles synthesis. Moorthi *et al*., 2012 synthesized curcumin nanoparticles by solid dispesion method.

Emulsion polymerization method: Organic and continuous phase are two types of emulsion techniques which can be used for the synthesis of curcumin nanoparticles. By this method, the surfactant is dissolved in pure water by ultrasonication, then curcumin is dissolved in an organic solvent and finally the solution is added to the surfactant. Moorthi *et al*., 2012 have reported synthesis of curcumin nanoparticles by using this method and piperine was used along with curcumin to increase the biological activity of synthesized curcumin nanoparticles.

Fessi method: In this method of synthesis, curcumin is dissolved in suitable solvent under sonication condition. The solution thus obtained is further added in pure water along with certain surfactant with constant stirring. Curcumin nanoparticles can be spontaneously synthesized by this method. Moorthi *et al*., 2012 have used this method for fabrication of curcumin nanoparticles. This is easy and simple method of nanoparticles synthesis.

Ionic gelation method: Hydrophobic drug such as curcumin is dissolved in proper solvent which showed complete solubility of curcumin in it and then this solvent is added in polymeric solution under constant stirring condition. This method depends on the cross linking of polymer along with drug such as curcumin. Chabib *et al*., 2012 reported synthesis of curcumin nanoparticles and used chitosan as a polymer. This polymer improved the solubility and stability of curcumin nanoparticles.

Ultrasonication: This method is generally employed for the drugs which are less water soluble. By this technique, curcumin is first dissolved in an organic solvent and the resulting solution is then added into the polyelectrolye solution under ultrasonication condition for several intervals of time and the formed curcumin nanoparticles are collected. Zhang *et al*., 2011 have synthesized curcumin nanoparticles by using this technique of ultrasonication.

Antisolvent precipitation: Antisolvent precipitation is the method of synthesis of the poorly water soluble drug. In this method of synthesis, curcumin is dissolved in an organic solvent followed by the addition of this solution into the deionized water under constant stirring. Hence, curcumin nanoparticles can be synthesized by this method. Yadav *et al*., 2014 used this method for synthesis of curcumin nanoparticles.

Advantage of this method of synthesis is that it is suitable technique for synthesis of poorly soluble curcumin nanoparticles.

REFERENCES

1. Zhang H, Zhang L, Yuan P, Wang C (2011); Preparation and in vitro release characteristics of curcumin in nanosuspensions; Zhongguo Zhong Yao Za Zhi, Chinese; 36(2); 132-135. 1. 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. 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.
4. 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 Polymer Science ; 8.
5. 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.
6. 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
7. Leimann F.V, Cardozo L, Sayer C, & Araújo P.H (2013); Poly(3-hydroxybutyrate-co-3- hydroxyvalerate) nanoparticles prepared by a miniemulsion/solvent evaporation technique. Effect of PHBV molar mass and concentration, Brazilian Journal of Chemical Engineering; 30(2); 369-377.
8. Li L, Braiteh F.S, Kurzrock R. (2005); Liposome-encapsulated curcumin: in vitro and in vivo effects on proliferation, apoptosis, signaling, and angiogenesis;

Cancer; 104(6); 1322–1331.

9. Lin C.C (2009); Stability and characterization of phospholipid-based curcumin-encapsulated microemulsions, Food Chem; 116(4); 923–928.
10. Liu A, Lou H, Zhao L, Fan P. (2006); Validated LC/MS/MS assay for curcumin and tetrahydrocurcumin in at plasma and application to pharmacokinetic study of phospholipid complex of curcumin; J Pharm Biomed Anal.; 40(3); 720–727.
11. Masuda T, Isobe J, Jitoe A and Nakatani N. (1992); Antioxidative curcuminoids from rhizomes of Curcuma xanthorrhiza. Phytochemistry; 31(10); 3645-3647.
12. Moorthi C, Kiran Krishnan, Manavalan R (2012); Preparation and characterization of curcumin-piperine dual drug loaded nanoparticles, Asian Pacific Journal of Tropical Biomedicine; 2(11); 841-848.
13. Ohori H, Yamakoshi H, Tomizawa M (2006); Synthesis and biological analysis of new curcumin analogues bearing an enhanced potential for the medicinal treatment of cancer; Mol Cancer Ther.; 5(10); 2563–2571.
14. 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); 1053–1064.
15. Preetha A, Banerjee R, Huilgol N, (2007); Tensiometric profiles and their modulation by cholesterol: implications in cervical cancer. Cancer Invest.; 25(3); 172–181.
16. Sari T.P, Mann B, Sharma R, Kumar R, Vikrant N (2013); Process Optimization for the Production of Nanoencapsulated Curcumin and Analysis for Physicochemical Characteristics and Antioxidant Mechanism; Int. J.