

Curcumin extraction from turmeric plant using magnetic Fe₃O₄ nanoparticles

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ABSTRACT

Objectives: In this study, it was aimed to obtain curcumin from the extracts of the turmeric plant by using a simple and fast magnetic separation method, unlike other standard methods.

Materials and methods: Magnetic iron oxide nanoparticles (IONPs) were prepared by chemical co-precipitation of Fe³⁺ and Fe²⁺ ions. Magnetic nanoparticles were used to extract curcumin from turmeric. In addition, curcumin was characterized and compared with commercial curcumin. Curcumin was recovered by purifying it from extracts of the turmeric plant.

Results: Fe₃O₄ nanoparticles were characterized using transmission electron microscopy, X-ray diffraction (XRD), Fourier-transform infrared spectroscopy, and Ultraviolet (UV)-visible spectra. Transmission electron microscopy analysis was used to describe the particle size and surface morphology of Fe₃O₄ nanoparticles, and the XRD device was used to explain X-ray diffraction. Curcumin was extracted from turmeric plant extracts purified with Fe₃O₄ nanoparticles. Fourier-transform infrared spectroscopy was used to determine the functional groups in the structure of turmeric, Fe₃O₄ nanoparticles, Fe₃O₄ turmeric complex, commercial curcumin, and curcumin. The UV spectrum of commercial curcumin and curcumin was also examined using the Shimadzu UV-1700 Pharma spectrophotometer. It has been established that it is recovered with a purification yield of 1.5 percent following purification.

Conclusion: These results suggest that curcumin, which has research potential in the field of health, may also be beneficial in terms of creating different scientific and economic expansions and producing new studies.

Keywords: Curcumin, iron oxide nanoparticles, magnetic nanoparticles, turmeric.

Turmeric is a perennial and tuberous herbaceous plant that belongs to the ginger family, with yellow flowers and large leaves. It is also called turmeric, saffron root, yellow dye, castor, and saffron. It is widely grown in China, India and Southeast Asia.^[1] Turmeric has an important place in Indian medicine since it is used especially in cold, cough, sinusitis, rheumatic diseases, cardiovascular diseases,

and skin diseases.^[2-4] Curcumin substance is obtained from the turmeric plant.^[5-7] It is known to have many pharmacological activities such as antioxidant, anti-inflammatory, anti-aging, analgesic, antiprotease activity, anticancer.^[5,8-10] Curcumin is an antioxidant that suppresses lipid peroxidation and reduces the formation of inflammatory compounds by scavenging reactive oxygen species.^[11,12] Curcumin has the ability to prevent protein accumulation that causes diseases such as Alzheimer's and Parkinson's diseases.^[10,13,14]

Isolation of biomolecules is generally carried out using different electrophoretic, chromatographic, ultrafiltration or precipitation and solvent extraction methods.^[15] All of these methods present considerable disadvantages when used on an industrial scale, such as expensive

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instrumentations, time-consuming processes, or large amounts of organic solvent waste.^[16] Methods such as thin-layer chromatography,^[17-19] high-performance liquid chromatography,^[20-24] electrochemical method,^[25, 26] spectrofluorometry^[27-29] and Ultraviolet-visible (UV-Vis) spectrophotometry^[10,24,30-33] have been utilized to determine curcumin in a diversity of matrices like *Curcuma longa*, foodstuffs, and biological materials.

With the rapid advancement of nanotechnology, interest in magnetic nanoparticles is increasing day by day. Recently, magnetic nanoparticles have been prepared in various ways, such as sol-gel self-propagation,^[34] chemical co-precipitation,^[35-37] and in the tiny pools of the water-in-oil microemulsion.^[38]

The prepared magnetic nanoparticles have been widely used in bionanotechnology such as magnetic resonance imaging, bioseparation, diagnostic agents, tumor hyperthermia and biomolecule immobilization.^[39-51] These magnetic nanoparticles have attracted the attention of researchers with their small size, low toxicity, superparamagnetism and most importantly their specific applications.^[36,51-55] In this study, curcumin, which is the miracle of nature, was obtained by purifying it quickly and easily with magnetic iron oxide nanoparticles (IONPs) without the use of expensive instruments.

MATERIALS AND METHODS

Materials

Curcumin was supplied from Alfa aesar. Iron(II)chloride tetrahydrate (FeCl₂.4H₂O), and iron(III)chloride hexahydrate (FeCl₃.6H₂O), were supplied from Merck. Turmeric and all other chemicals used were obtained from various commercial sources.

Characterization

Transmission electron microscopy (TEM) was used to examine the particle size and surface morphology of Fe₃O₄ nanoparticles. X-ray diffraction (XRD) of the nanoparticles was determined with the Bruker™ D8 Advance device (Bruker BioSciences Espanola, S.A. Madrid, Spain). Fourier transform infrared spectroscopy (FTIR) was used to determine the functional groups in the structure of turmeric,

Fe₃O₄ nanoparticles, Fe₃O₄ turmeric complex, commercial curcumin, and curcumin. The UV spectrum of commercial curcumin and curcumin was measured using the Shimadzu UV-1700 Pharma spectrophotometer (UV-1700 Pharma Spec, Shimadzu, Kyoto, Japan).

Synthesis of Fe₃O₄ nanoparticles

Magnetic Fe₃O₄ nanoparticles have been prepared by the co-precipitation method according to previous literature.^[54] 50 mL 1.0 M FeCl₂.4H₂O and 1.75 M FeCl₃.6H₂O solutions were prepared with deionized water in two different beakers. Then this solution transferred to a 250 mL three-necked flask and stirred under a nitrogen atmosphere. It was observed that the color of the solution turned dark brown immediately after addition. This color indicated that IONPs were formed.

The resulting solution was heated to 80°C for 1 hour. The precipitates were isolated from the solvent by magnetic filtration and washed several times with deionized water until neutral pH. They were dried under vacuum at 50°C for 10 hours.

Curcumin extraction using magnetic nanoparticles

0.5 g Fe₃O₄ nanoparticles and 1 g turmeric were mixed in the sonicator in a 1:1 ethanol/water mixture for 6 hours. Then magnetic nanoparticles were separated from the Fe₃O₄-curcumin composite by magnetic decantation. The resulting composite structure was dried, and ethanol and water were added in a ratio of 1:1 and remixed in the sonicator for 1 hour. The mixture was adjusted to pH 5-6. Magnetic nanoparticles were separated from the curcumin mixture by magnetic separation with a permanent magnet. The insoluble curcumin mixture was separated and the soluble part was evaporated in the evaporator and dried in a vacuum oven at 50°C.

RESULTS

Fe₃O₄ nanoparticles were obtained according to the co-precipitation method of Fe²⁺ and Fe³⁺ ions.^[54]

Characterization of Fe₃O₄ nanoparticles and Fe₃O₄-turmeric complexes

Transmission electron microscopy analysis was performed to see the particle size and

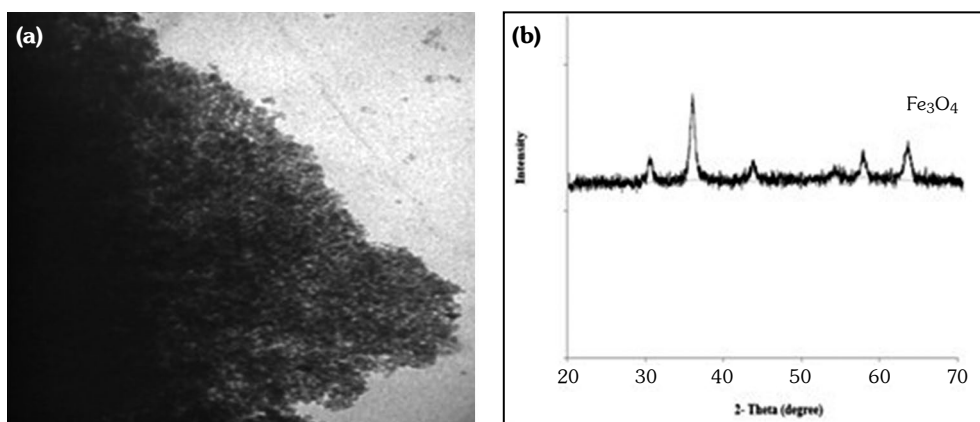


Figure 1. Transmission electron microscopy (a) and X-ray diffraction (b) result of Fe_3O_4 nanoparticles.

morphology of synthesized Fe_3O_4 nanoparticles (Figure 1a). The dense aggregates were exhibited due to the lack of any repulsive force between Fe_3O_4 nanoparticles.

Figure 1b shows XRD patterns of synthesized Fe_3O_4 nanoparticles. The characteristic peaks of the Fe_3O_4 crystal were seen at $2\theta = 30.3^\circ, 35.5^\circ, 43.0^\circ, 53.0^\circ, 57.4^\circ,$ and 63.5° , respectively.

The properties of the Fe_3O_4 nanoparticles surface, due to the presence of under-coordinated iron (Fe) (III) sites, confer high specificity to select iron-chelating molecules from complex matrices.^[17] Presenting a keto-enol functionality, curcumin tended to bind very well towards the surface of the magnetic nanoparticles.

It showed that curcumin is a good ligand for the surface of Fe_3O_4 nanoparticles. This confirms the literature that curcumin has an important ability to form stable complexes with Fe (III).^[16,56] Figure 2 shows the structure of the Fe_3O_4 -turmeric complex.

The FTIR spectrum of the turmeric, Fe_3O_4 , and Fe_3O_4 -turmeric complexes, respectively, was given in Figure 3. The FTIR bands at low wavenumbers ($<700\text{ cm}^{-1}$) come from vibrations from the Fe-O bonds. The FTIR bands around 604 and 534 cm^{-1} belong to the stretching vibration mode of Fe-O bonds in magnetite nanoparticles. It was observed that the stretching vibration modes of the turmeric, C-O bands,

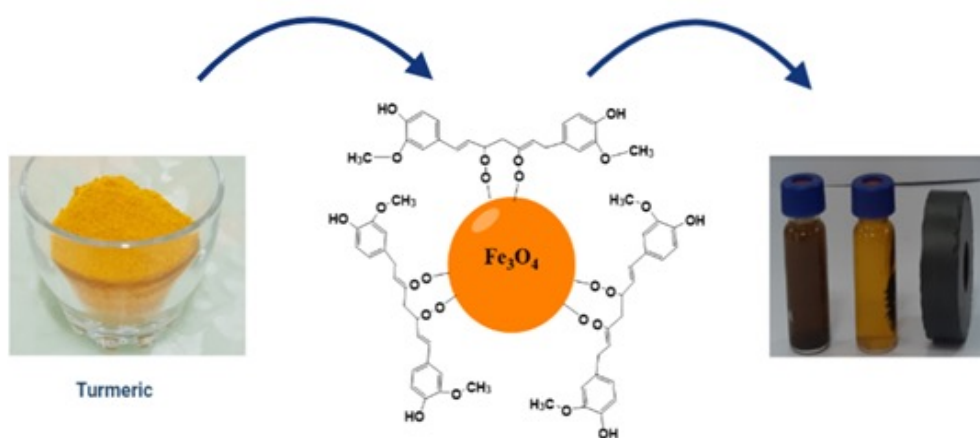


Figure 2. Fe_3O_4 -turmeric complex.

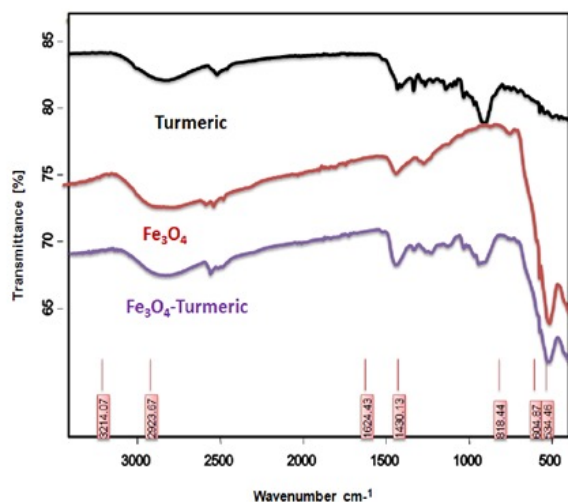


Figure 3. Fourier transform infrared spectroscopy spectrum of turmeric, Fe₃O₄ nanoparticles and Fe₃O₄-turmeric.

C=O bands, and C=C bands were at 994 cm⁻¹, 1511 cm⁻¹, and 1626 cm⁻¹, respectively. The formation of the Fe₃O₄-turmeric was assigned by the disappearance of the characteristic band at about 994 cm⁻¹ and the appearance of a C=C at 1624 cm⁻¹.

Characterization of curcumin and commercial curcumin

Fourier-transform infrared spectra of curcumin obtained with commercial curcumin were compared. The FTIR spectrum of commercial curcumin of O-H, C-H, C=O and C=C bands were observed at 3508 cm⁻¹, 1626 cm⁻¹, 1506 cm⁻¹, 1426 cm⁻¹, 1203 cm⁻¹, 1024 cm⁻¹, respectively. Similarly, the isolated curcumin bands were observed at 3271 cm⁻¹, 1600 cm⁻¹, 1508 cm⁻¹, 1203 cm⁻¹, 1024 cm⁻¹, respectively (Figure 4).

The UV spectrum of commercial curcumin and curcumin was measured. The strong interaction between IONPs attached to the surface and phenolics in the compounds was demonstrated by UV-Vis spectrophotometry. The absorption spectrum of commercial curcumin and curcumin showed a maximum wide band at approximately 423 nm in Figure 5.^[16,55-58]

Many researchers have studied the amount of curcumin in turmeric. Priyadarsini^[59] reported that turmeric contains 2-9% curcuminoids, depending on the origin and the soil conditions in which it was grown. Lal reported that it is found in different amounts according to the production regions in India. It has reported that it is found at

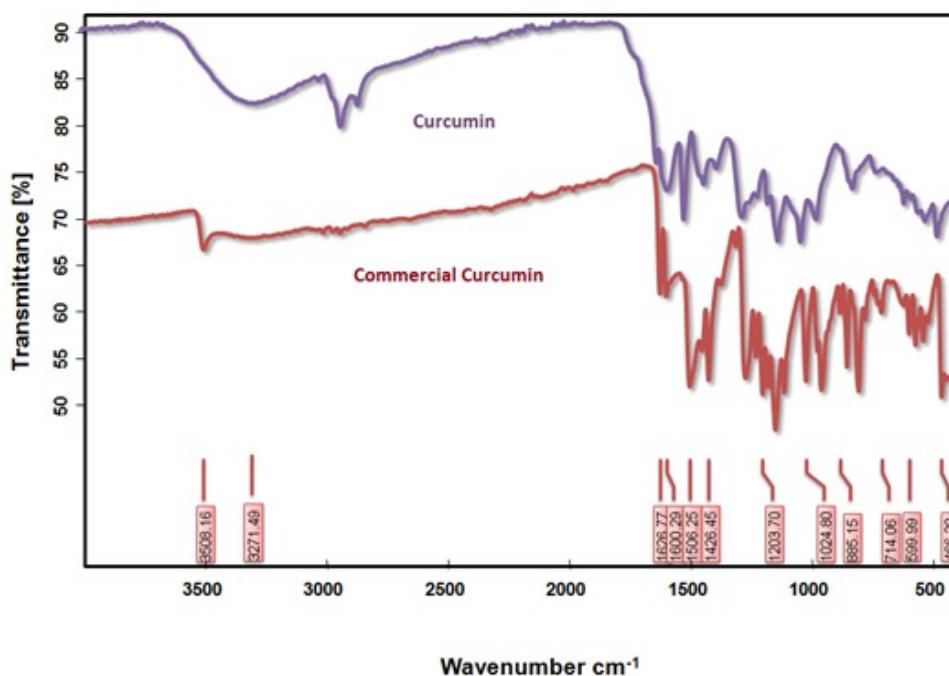


Figure 4. Fourier transform infrared spectroscopy spectrum of curcumin and commercial curcumin.

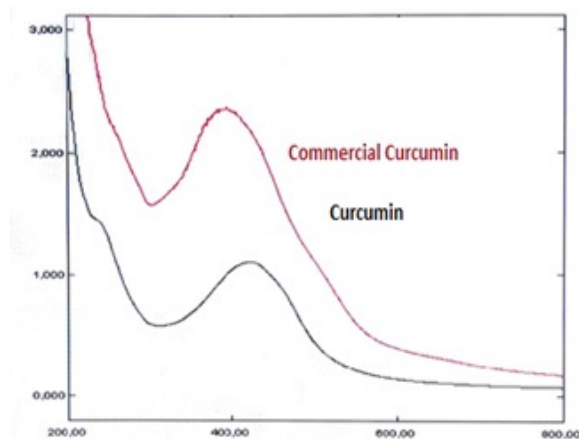


Figure 5. Ultraviolet spectrum of curcumin and commercial curcumin.

a rate of 2% in Madras and 4-7% in Alleppey.^[60] In another study, Paultre et al.^[61] explained that the amount of curcumin is 3-10%. From the standard curcumin calibration graph, the curcumin concentration was found to be 0.0275 mM at 423 nm. The amount of curcumin was calculated as 15 mg by using the concentration. Curcumin was recovered from the extracts of the turmeric plant by magnetic purification with an amount of 1.5%.

DISCUSSION

There is a need for alternative treatment methods in the treatment of cancer and many diseases. The therapeutic uses of medicinal plants have attracted considerable attention in recent years.

Curcumin is a natural flavonoid. It has many important properties such as anticancer, antioxidant, and antibacterial effects. Different techniques such as chromatographic, electrophoretic are used to isolate biomolecules. These methods are both time-consuming and expensive. Therefore, simpler and more economical techniques are needed for isolation.

Magnetic Fe₃O₄ nanoparticles, with their low toxicity, biocompatibility, and easy separation with the help of magnets, have attracted a lot of attention in recent years, especially in applications such as targeted drug therapy, cancer therapy, enzyme immobilization, hyperthermia, and magnetic resonance imaging. Biocatalytic

applications are also used in different fields such as biomedicine, biomedical, and bioengineering. A suitable magnetic field is created by adding biomolecules or organic substances to these magnetic nanoparticles, and the separation of substances can be performed quickly and easily by using magnets.^[42,51]

For the isolation of curcumin, unlike other purification techniques, the use of magnetic nanoparticles was preferred considering the advantage of a simple and fast separation technique with the help of magnets. In the study, Fe₃O₄ nanoparticles were synthesized and their structure was confirmed by characterization techniques.^[37,55,56,59,63-68]

In Figure 1a, the morphology and particle size of Fe₃O₄ nanoparticles was examined by TEM analysis. The formation of nanoparticles was confirmed.^[5,62,63] In addition, characteristic peaks of the synthesized Fe₃O₄ crystals were analyzed (Figure 1b). These peaks were seen by XRD analysis at 2θ = 30.3°, 35.5°, 43.0°, 53.0°, 57.4° and 63.5°, respectively.^[37,56-58,62] Turmeric, Fe₃O₄, and Fe₃O₄-turmeric compound FTIR spectra were also studied (Figure 3). The stretching vibrations of Fe₃O₄, Fe-O bonds, the stretching vibrations of in the turmeric structure C-O bands, C=O bands, and C=C bands were confirmed.^[37,58,61-64] Curcumin was obtained from the extracts of the turmeric plant by using the obtained nanoparticles. It was determined that curcumin from the extracts of the turmeric plant was recovered with a purification efficiency of 1.5%.

The FTIR and UV spectra of commercial curcumin and curcumin were examined and compared. Figure 5 showed a significant interaction between surface-bound IONPs and phenolics in the compounds. The absorption spectra of both commercial curcumin and obtained curcumin showed a broad band maximum at 423 nm.^[16,59,65]

It is thought that this study can be beneficial in terms of the fact that curcumin, which has the potential to research in the field of health, can create different expansions both scientifically and economically and produce new studies.

In conclusion, Fe₃O₄ magnetic nanoparticles were synthesized and used to obtain curcumin from turmeric. The synthesized Fe₃O₄ magnetic

nanoparticles were characterized by FTIR, XRD and TEM. The resulting curcumin compound was purified quickly and easily in the presence of magnetic IONPs without using expensive devices. Then, it was compared to commercial curcumin. Curcumin from extracts of the turmeric plant was recovered with a purification yield of 1.5%. With this method, it is predicted that biomolecules that can be easily transported from the laboratory to the industrial level can be easily purified by using an economical and environmentally friendly method, without the need for expensive devices.

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Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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REFERENCES

1. Arlı M, Çelik H. The biological importance of curcumin. *EASJ* 2020;6:21-34.
2. Chumroenphat T, Somboonwatthanakul I, Saensouk S, Siriamornpun S. Changes in curcuminoids and chemical components of turmeric (*Curcuma longa* L.) under freeze-drying and low-temperature drying methods. *Food Chem* 2021;339:128121.
3. Ammon HP, Anazodo MI, Safayhi H, Dhawan BN, Srimal RC. Curcumin: A potent inhibitor of leukotriene B₄ formation in rat peritoneal polymorphonuclear neutrophils (PMNL). *Planta Med* 1992;58:226.
4. Miquel J, Bernd A, Sempere JM, Díaz-Alperi J, Ramírez A. The curcuma antioxidants: Pharmacological effects and prospects for future clinical use. A review. *Arch Gerontol Geriatr* 2002;34:37-46.
5. Peng S, Li Z, Zou L, Liu W, Liu C, McClements DJ. Enhancement of curcumin bioavailability by encapsulation in sophorolipid-coated nanoparticles: An in vitro and in vivo study. *J Agric Food Chem* 2018;66:1488-97.
6. Basol N, Savas AY, Meral A, Erbas O. The valuable effects of potent antioxidant curcumin in cisplatin induced liver and kidney injury. *Cumhuriyet Med J* 2018;40:9-18.
7. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: Problems and promises. *Mol Pharm* 2007;4:807-18.
8. Meng R, Wu Z, Xie QT, Cheng JS, Zhang B. Preparation and characterization of zein/carboxymethyl dextrin nanoparticles to encapsulate curcumin: Physicochemical stability, antioxidant activity and controlled release properties. *Food Chem* 2021;340:127893.
9. Aggarwal BB, Sundaram C, Malani N, Ichikawa H. Curcumin: The indian solid gold. In: Aggarwal, BB, Surh, YJ, Shishodia, S, editors. *The Molecular Targets and Therapeutic Uses of Curcumin in Health and Disease*. New York; Springer Publications; 2007. p. 1-76.
10. Anand P, Thomas SG, Kunnumakkara AB, Sundaram C, Harikumar KB, Sung B, et al. Biological activities of curcumin and its analogues (Congeners) made by man and Mother Nature. *Biochem Pharmacol* 2008;76:1590-611.
11. Pérez-Garrido A, Helguera AM, Ruiz JM, Rentero PZ. Topological sub-structural molecular design approach: Radical scavenging activity. *Eur J Med Chem* 2012;49:86-94.
12. Wang YJ, Pan MH, Cheng AL, Lin LI, Ho YS, Hsieh CY, et al. Stability of curcumin in buffer solutions and characterization of its degradation products. *J Pharm Biomed Anal* 1997;15:1867-76.
13. Yan JW, Li YP, Ye WJ, Chen SB, Hou JQ, Tan JH, et al. Design, synthesis and evaluation of isaindigotone derivatives as dual inhibitors for acetylcholinesterase and amyloid beta aggregation. *Bioorg Med Chem* 2012;20:2527-34.
14. Masuda M, Suzuki N, Taniguchi S, Oikawa T, Nonaka T, Iwatsubo T, et al. Small molecule inhibitors of alpha-synuclein filament assembly. *Biochemistry* 2006;45:6085-94.
15. Kitts DD, Weiler K. Bioactive proteins and peptides from food sources. Applications of bioprocesses used in isolation and recovery. *Curr Pharm Des* 2003;9:1309-23.
16. Magro M, Campos R, Baratella D, Ferreira MI, Bonaiuto E, Corraducci V, et al. Magnetic purification of curcumin from *Curcuma longa* rhizome by novel naked maghemite nanoparticles. *J Agric Food Chem* 2015;63:912-20.
17. Horák D, Babic M, Macková H, Benes MJ. Preparation and properties of magnetic nano- and micro-sized particles for biological and environmental separations. *J Sep Sci* 2007;30:1751-72.
18. Safarik I, Safarikova M. Magnetic techniques for the isolation and purification of proteins and peptides. *Biomagn Res Technol* 2004;2:7.
19. Lyon JL, Fleming DA, Stone MB, Schiffer P, Williams ME. Synthesis of Fe oxide Core/Au shell nanoparticles by iterative hydroxylamine seeding. *Nano Letters* 2004;4:719-23.

20. Zhang Y, Kohler N, Zhang M. Surface modification of superparamagnetic magnetite nanoparticles and their intracellular uptake. *Biomaterials* 2002;23:1553-61.
21. Lu Y, Yin Y, Mayers BT, Xia Y. Modifying the surface properties of superparamagnetic iron oxide nanoparticles through a sol-gel approach. *Nano Letters* 2002;2:183-6.
22. Urbanova V, Magro M, Gedanken A, Baratella D, Vianello F, Zboril R. Nanocrystalline iron oxides, composites, and related materials as a platform for electrochemical, magnetic, and chemical biosensors. *Chem Mater* 2014;26:6653-73.
23. Mackay ME, Tuteja A, Duxbury PM, Hawker CJ, Van Horn B, Guan Z, et al. General strategies for nanoparticle dispersion. *Science* 2006;311:1740-3.
24. Magro M, Faralli A, Baratella D, Bertipaglia I, Giannetti S, Salviulo G, et al. Avidin functionalized maghemite nanoparticles and their application for recombinant human biotinyl-SERCA purification. *Langmuir* 2012;28:15392-401.
25. Magro M, Sinigaglia G, Nodari L, Tucek J, Polakova K, Marusak Z, et al. Charge binding of rhodamine derivative to OH- stabilized nanomaghemite: Universal nanocarrier for construction of magnetofluorescent biosensors. *Acta Biomater* 2012;8:2068-76.
26. Sinigaglia G, Magro M, Miotto G, Cardillo S, Agostinelli E, Zboril R, et al. Catalytically active bovine serum amine oxidase bound to fluorescent and magnetically drivable nanoparticles. *Int J Nanomedicine* 2012;7:2249-59.
27. Magro M, Valle G, Russo U, Nodari L, Vianello F. Maghemite Nanoparticles and Method for Preparing Thereof. 2012; World Patent WO/2012/010200.
28. Venerando R, Miotto G, Magro M, Dallan M, Baratella D, Bonaiuto E, et al. Magnetic nanoparticles with covalently bound self-assembled protein corona for advanced biomedical applications. *J Phys Chem C* 2013;117:20320-31.
29. Magro M, Campos R, Baratella D, Lima G, Holà K, Divoky C, et al. A magnetically drivable nanovehicle for curcumin with antioxidant capacity and MRI relaxation properties. *Chemistry* 2014;20:11913-20.
30. Nagpal M, Sood S. Role of curcumin in systemic and oral health: An overview. *J Nat Sci Biol Med* 2013;4:3-7.
31. Liu D, Chen Z. The effect of curcumin on breast cancer cells. *J Breast Cancer* 2013;16:133-7.
32. Yallapu MM, Jaggi M, Chauhan SC. beta-Cyclodextrin-curcumin self-assembly enhances curcumin delivery in prostate cancer cells. *Colloids Surf B Biointerfaces* 2010;79:113-25.
33. Maheshwari RK, Singh AK, Gaddipati J, Srimal RC. Multiple biological activities of curcumin: A short review. *Life Sci* 2006;78:2081-7.
34. Yang X, Li Q, Zhao J, Li B, Wang Y. ChemInform abstract: Preparation and magnetic properties of controllable-morphologies Nano-SrFe 12 O 19 particles prepared by sol-gel self-propagation synthesis. *Journal of Alloys and Compounds* 2009;475:312-5.
35. Wang X, Zhao C, Zhao P, Dou P, Ding Y, Xu P. Gellan gel beads containing magnetic nanoparticles: An effective biosorbent for the removal of heavy metals from aqueous system. *Bioresour Technol* 2009;100:2301-4.
36. Wu Y, Wang Y, Luo G, Dai Y. In situ preparation of magnetic Fe₃O₄-chitosan nanoparticles for lipase immobilization by cross-linking and oxidation in aqueous solution. *Bioresour Technol* 2009;100:3459-64.
37. Ozyilmaz E, Asciglu S, Yilmaz M. Calix[4]arene tetracarboxylic acid-treated lipase immobilized onto metal-organic framework: Biocatalyst for ester hydrolysis and kinetic resolution. *Int J Biol Macromol* 2021;175:79-86.
38. Wang Y, Wang X, Luo G, Dai Y. Adsorption of bovin serum albumin (BSA) onto the magnetic chitosan nanoparticles prepared by a microemulsion system. *Bioresour Technol* 2008;99:3881-4.
39. Sayin S, Yilmaz E, Yilmaz M. Improvement of catalytic properties of *Candida rugosa* lipase by sol-gel encapsulation in the presence of magnetic calix[4]arene nanoparticles. *Org Biomol Chem* 2011;9:4021-4.
40. Yilmaz E. Enantioselective enzymatic hydrolysis of racemic drugs by encapsulation in sol-gel magnetic sporopollenin. *Bioprocess Biosyst Eng* 2012;35:493-502.
41. Gupta AK, Gupta M. Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. *Biomaterials* 2005;26:3995-4021.
42. Ozyilmaz E, Alhiali A, Caglar O, Yilmaz M. Preparation of regenerable magnetic nanoparticles for cellulase immobilization: Improvement of enzymatic activity and stability. *Biotechnol Prog* 2021;37:e3145.
43. Krízová J, Spanová A, Rittich B, Horák D. Magnetic hydrophilic methacrylate-based polymer microspheres for genomic DNA isolation. *J Chromatogr A* 2005;1064:247-53.
44. Ito A, Shinkai M, Honda H, Kobayashi T. Medical application of functionalized magnetic nanoparticles. *J Biosci Bioeng* 2005;100:1-11.
45. Mornet S, Vasseur S, Grasset F, Veverka P, Goglio G, Demourgues A, et al. Magnetic nanoparticle design for medical applications. *Progress in Solid State Chemistry* 2006;34:237-47.
46. Neuberger T, Schöpf B, Hofmann H, Hofmann M, von Rechenberg B. Superparamagnetic nanoparticles for biomedical applications: Possibilities and limitations of a new drug delivery system. *Journal of Magnetism and Magnetic Materials* 2005;293:483-96.
47. del Campo A, Sen T, Lellouche JP, Bruce IJ. Multifunctional magnetite and silica- magnetite nanoparticles: Synthesis, surface activation and applications in life sciences. *Journal of Magnetism and Magnetic Materials* 2005;293:33-40.

48. Saiyed ZM, Sharma S, Godawat R, Telang SD, Ramchand CN. Activity and stability of alkaline phosphatase (ALP) immobilized onto magnetic nanoparticles (Fe₃O₄). *J Biotechnol* 2007;131:240-4.
49. Yilmaz E, Sezgin M, Yilmaz M. Immobilized copper-ion affinity adsorbent based on a cross-linked β -cyclodextrin polymer for adsorption of *Candida rugosa* lipase. *Biocatal Biotransform* 2009;27:360-6.
50. Yildiz H, Ozyilmaz E, Bhatti AA, Yilmaz M. Enantioselective resolution of racemic flurbiprofen methyl ester by lipase encapsulated mercapto calix[4]arenes capped Fe₃O₄ nanoparticles. *Bioprocess Biosyst Eng* 2017;40:1189-1196.
51. Ozyilmaz E, Sayin S. A magnetically separable biocatalyst for resolution of racemic naproxen methyl ester. *Bioprocess Biosyst Eng* 2013;36:1803-6.
52. Chen F, Luo GS, Wang YJ. Studies on adsorption properties of chemically modified chitosan resins to diuretics. *Acta Polymerica Sinica* 2005:53-9.
53. Caglar O, Ozyilmaz E, Erbas O. Superparamagnetic iron oxide nanoparticles use in the temporal lobe epilepsy model. *D J Tx Sci* 2021;6:66-72.
54. Yilmaz E, Sezgin M, Yilmaz M. Immobilization of *Candida rugosa* lipase on magnetic sol-gel composite supports for enzymatic resolution of (R,S)-Naproxen methyl ester. *Journal of Molecular Catalysis B: Enzymatic* 2011;69:35-41.
55. Saikia C, Das MK, Ramteke A, Maji TK. Effect of crosslinker on drug delivery properties of curcumin loaded starch coated iron oxide nanoparticles. *Int J Biol Macromol* 2016;93:1121-32.
56. Borsari M, Ferrari E, Grandi R, Saladini M. Curcuminoids as potential new iron-chelating agents: spectroscopic, polarographic and potentiometric study on their Fe(III) complexing ability. *Inorganica Chimica Acta* 2002;328:61-8.
57. Ozyilmaz E, Sayin S, Arslan M, Yilmaz M. Improving catalytic hydrolysis reaction efficiency of sol-gel-encapsulated *Candida rugosa* lipase with magnetic β -cyclodextrin nanoparticles. *Colloids Surf B Biointerfaces* 2014;113:182-9.
58. Hiremath CG, Heggnavar GB, Kariduraganavar MY, Hiremath MB. Co-delivery of paclitaxel and curcumin to foliate positive cancer cells using Pluronic-coated iron oxide nanoparticles. *Prog Biomater* 2019;8:155-168.
59. Priyadarsini KI. The chemistry of curcumin: From extraction to therapeutic agent. *Molecules* 2014;19:20091-112.
60. Lal J. Turmeric, curcumin and our life: A review. *Bulletin of Environment Pharmacology and Life Sciences* 2012;1:11-7.
61. Paultre K, Cade W, Hernandez D, Reynolds J, Greif D, Best TM. Therapeutic effects of turmeric or curcumin extract on pain and function for individuals with knee osteoarthritis: A systematic review. *BMJ Open Sport Exerc Med* 2021;7:e000935.
62. González-Martínez E, Pérez AG, González-Martínez DA, Águila CRD, Urbina EC, Ramírez DU, et al. Chitosan-coated magnetic nanoparticles; exploring their potentialities for DNA and Cu(II) recovery. *Inorganic and Nano-Metal Chemistry* 2021;51:1098-107.
63. Pham XN, Nguyen TP, Pham TN, Tran TTN, Tran TVT. Synthesis and characterization of chitosan-coated magnetite nanoparticles and their application in curcumin drug delivery. *Advances in Natural Sciences: Nanoscience and Nanotechnology* 2016;7:045010.
64. Ebadi M, Bullo S, Buskara K, Hussein MZ, Fakurazi S, Pastorin G. Release of a liver anticancer drug, sorafenib from its PVA/LDH- and PEG/LDH-coated iron oxide nanoparticles for drug delivery applications. *Sci Rep* 2020;10:21521.
65. Ebadi M, Saifullah B, Buskaran K, Hussein MZ, Fakurazi S. Synthesis and properties of magnetic nanotheranostics coated with polyethylene glycol/5-fluorouracil/layered double hydroxide. *Int J Nanomedicine* 2019;14:6661-78.
66. Prakash N, Sadaf M, Salomi A, Daniel EC. Cytotoxicity of functionalized iron oxide nanoparticles coated with rifampicin and tetracycline hydrochloride on *Escherichia coli* and *Staphylococcus aureus*. *Appl Nanosci* 2019;9:1353-66.
67. Mareeswaran PM, Babu E, Sathish V, Kim B, Woo S, Rajagopal S. p-Sulfonatocalix[4]arene as a carrier for curcumin. *New Journal of Chemistry* 2014;38:1336-45.
68. Barick KC, Rathee E, Gawali SL, Sarkar A, Kunwar A, Priyadarsini KI, et al. Pluronic stabilized Fe₃O₄ magnetic nanoparticles for intracellular delivery of curcumin. *RSC Advances* 2016;6:98674-81.