Sveučilište u Zagrebu

FAKULTET KEMIJSKOG INŽENJERSTVA I TEHNOLOGIJE

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KONTROLIRANO OTPUŠTANJE FLAVONOIDA IZ MAGNETSKIH NANONOSAČA VANJSKIM MAGNETSKIM POLJIMA

DOKTORSKI RAD

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DOCTORAL THESIS

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SAŽETAK

KONTROLIRANO OTPUŠTANJE FLAVONOIDA IZ MAGNETSKIH NANONOSAČA VANJSKIM MAGNETSKIM POLJIMA

Flavonoidi su prirodni antioksidansi polifenolne strukture koji pokazuju terapeutski potencijal zbog svojih protuupalnih, antikancerogenih, antimikrobnih i antioksidativnih svojstava. Međutim, ograničena bioraspoloživost i apsorpcija u organizmu, slaba topljivost u vodi i nestabilnost u fiziološkim uvjetima smanjuju njihovu učinkovitost kao biološki aktivnih tvari. Učinkovita strategija za prevladavanje tih ograničenja je ugradnja u mezoporozne nanonosače. Izniman kandidat za dostavu flavonoida su nanočestice magnetita zbog svoje biorazgradivosti, fizikalno-kemijskih svojstava i superparamagnetičnosti. Funkcionalizacija nanočestica magnetita poli(etilen-glikolom) poboljšava učinkovitost flavonoida smanjenjem imunološke reakcije organizma. U okviru ovog doktorskog rada, solvotermalnom metodom sintetizirane su funkcionalizirane nanočestice magnetita. Provedena je strukturna, morfološka, termička i magnetska karakterizacija nanočestica različitim eksperimentalnim tehnikama te je ispitana stabilnost nanočestica u fosfatnom puferu. Mezoporozna struktura nanočestica magnetita potvrđena je Brunauer-Emmett-Tellerovom analizom. Ugradnja flavonoida: kvercetina, miricetina i miricitrina provedena je metodom adsorpcije, a efikasnost ugradnje kvantificirana je UV-Vis spektroskopijom. Strukturnom, morfološkom i termičkom karakterizacijom potvrđena je ugradnja flavonoida u mezoporozne nanočestice magnetita. Kinetika otpuštanja flavonoida iz istraživanih nanonosača *in vitro* kontrolirana je primjenom vanjskog permanentnog i oscilirajućeg magnetskog polja i kvantificirana UV-Vis spektroskopijom. Rezultati ovog doktorskog rada ukazuju na to da je razvijen nanosustav za efikasnu ugradnju flavonoida radi prevladavanja njihove slabe topljivosti i nestabilnosti u fiziološkim uvjetima. Ujedno su pronađeni optimalni uvjeti za kontrolirano otpuštanje flavonoida iz nanočestica magnetita pomoću vanjskog oscilirajućeg i permanentnog magnetskog polja.

Ključne riječi: nanočestice magnetita, nanonosači, kvercetin, miricetin, miricitrin, otpuštanje lijekova, magnetsko polje

ABSTRACT

THE CONTROLLED RELEASE OF FLAVONOIDS FROM MAGNETIC NANOCARRIERS BY EXTERNAL MAGNETIC FIELDS

Flavonoids are natural antioxidants with a polyphenolic structure that exhibit therapeutic potential due to their anti-inflammatory, anti-cancer, antimicrobial and antioxidant properties. However, limited bioavailability and absorption in the body, poor solubility in water and instability in physiological conditions reduce their effectiveness as biologically active substances. An effective strategy to overcome these limitations is encapsulation into nanocarriers. An exceptional candidate for flavonoid delivery are mesoporous magnetite nanoparticles due to their biodegradability, physicochemical properties and superparamagnetic nature. Functionalization of nanoparticles with poly(ethylene glycol) further improves the effectivness of flavonoids by reducing the body's immune response. In the framework of this doctoral thesis, magnetite nanoparticles functionalized with poly(ethylene glycol) were synthesized by the solvothermal method. Structural, morphological, thermal and magnetic characterization of nanoparticles was carried out using different experimental techniques, and the stability of nanoparticles was tested in phosphate buffer. The mesoporous structure of magnetite nanoparticles was confirmed by Brunauer-Emmett-Teller analysis. Encapsulation of flavonoids: quercetin, myricetin and myricitrin was carried out by the adsorption method, and the efficiency of encapsulation was determined by UV-Vis spectroscopy. Structural, thermal and morphological characterization confirmed the encapsulation of flavonoids into magnetite nanoparticles. *In vitro* kinetics of flavonoid release from magnetic nanocarriers was controlled by combination of external permanent and oscillating magnetic fields and quantified by UV-Vis spectroscopy. The results of this doctoral dissertation indicate that a nanosystem has been developed for the efficient encapsulation of flavonoids in order to overcome their low solubility and instability in physiological conditions. At the same time, optimal conditions were found for the controlled release of flavonoids from magnetite nanocarriers using an external oscillating and permanent magnetic field.

Key words: magnetite nanoparticles, nanocarriers, quercetin, myricetin, myricitrin, drug release, magnetic field