LOW ENERGY NANOEMULSIONS AS POTENTIAL CARRIERS FOR ESSENTIAL OILS IN FORMULATIONS FOR ANTIOXIDANT SKIN PROTECTION

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Aromatic plants have been used since ancient times as a source of essential oils (EOs) which are known as natural remedies in traditional medicine systems – phytotherapy and aromatherapy, but they are also widely used for everyday purposes (for example, as fragrant components in skincare preparations and perfumery; as flavours and natural preservatives in food industry). It is known that many EOs contain molecules with considerable antioxidant activity, such as phenolic compounds, flavonoids and terpenoids, acting alone or synergistically. Besides antimicrobial action, EOs prepared from plants form the *Lamiaceae* family, such as basil −BA (*Ocimum basilicum*), oregano – OR (*Origanum vulgare*) and lemon balm − LB (*Melissa officinalis*) leaves are reported to scavenge free radicals (1). Therefore, these particular EOs and their bioactives could be good candidates for skin-protective formulations. Nanoemulsions (NEs), especially those produced by low energy methods, are recently proposed as prospective carriers for sensitive and natural ingredients such as EOs, in order to ensure their stabilization. Additionally, some EOs can act as cosurfactants and promote low energy nanoemulsification. Having in mind that EOs cannot be used undiluted, oil-in-water NEs could be an appropriate delivery system, representing fluid formulations with ultra-fine droplets, pleasant visual appearance, and improved stability compared to classic macroemulsions (2). Firstly, NEs were prepared different EOs (BA, OR or LB) with polyethylene glycol free (PEG-free) natural surfactants/emollients mixture (containing polyglycerol-4 laurate as the main surfactant) suitable for cold processing via the Phase inversion composition (PIC) method. NEs physicochemical stability was confirmed by particle size distribution analysis, electrical conductivity and pH value measurements, as well as by optical microscopy observations. The type of EO and the concentration of surfactants/emollient mixture were proven to be crucial factors governing NE properties and stability. Raman spectra of EOs verified their main active ingredients and detected possible interactions with the nanocarrier (3). The antioxidant activity towards the DPPH radical in methanol was concentration-dependent with a similar trend for neat oils and oil-loaded NEs (OR> LB> BA). However, the ABTS test in an aqueous medium revealed notable change in the order of activity with increased EO concentration and after EO nanonisation. Overall, the highest antioxidant activity was observed for OR and OR-loaded NE (> 95% INH_{ABTS} and > 85% INH_{DPPH}), implying at some optimal package of OR within the nanocarrier which preserved its high antioxidant performance and ensured its stability during 6 months of storage.

References

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Acknowledgement

This research was funded by the Ministry of Education, Science and Technological Development, Republic of Serbia (Grant Agreement with University of Belgrade - Faculty of Pharmacy No: 451-03-9/2021-14/200161 and Faculty of Physical Chemistry No: 451-03-9/2021-14/200146).

NISKOENERGETSKE NANOEMULZIJE KAO POTENCIJALNI NOSAČI ZA ETARSKA ULJA U FORMULACIJAMA ZA ANTIOKSIDATIVNU ZAŠTITU KOŽE

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Aromatične biljke koriste se od davnina za dobijanje etarskih ulja (EOs) koja su poznata kao prirodni lekovi u tradicionalnim sistemima lečenja – fitoterapiji i aromaterapiji, a takođe je široko rasprostranjena njihova upotreba u svakodnevnom životu (na primer, kao mirisne komponente u kozmetičkim proizvodima i parfemima; kao korigensi ukusa i prirodni konzervansi u prehrambenoj industriji). Brojna EOs sadrže molekule kao što su fenolna jedinjenja, flavonoidi i terpenoidi koji ispoljavaju značajnu antioksidativnu aktivnost, delujući samostalno ili sinergistički. Pored antimikrobnog dejstva, EOs dobijena iz listova biljaka familije *Lamiaceae*, kao što je bosiljak - BA (*Ocimum basilicum*), origano – OR (*Origanum vulgare*) i matičnjak − LB (*Melissa officinalis*) deluju kao hvatači slobodnih radikala (1). Prema tome, pomenuta EOs i njihovi bioaktivni sastojci mogu biti dobri kandidati za razvoj formulacija za zaštitu kože. Nanoemulzije (NEs), posebno one proizvedene niskoenergetskim metodama, odnedavno se predlažu kao prospektivni nosači za prirodne i osetljive sastojke poput EOs, sa ciljem da se obezbedi njihova stabilizacija. Dodatno, neka EOs imaju ulogu kosurfaktanta i pospešuju niskoenergetsku nanoemulzifikaciju. Imajući u vidu da se EOs ne mogu koristiti nerazblažena, NEs ulje u vodi tipa mogu biti adekvatni nosači, s obzirom da su u pitanju fluidne formulacije sa ultra-finim veličinama kapi, prijatnim vizuelnim izgledom, kao i poboljšanom stabilnošću u poređenju sa klasičnim makroemulzijama (2). Prvo su pripremljene NEs sa različitim EOs (BA, OR ili LB), sa smešom prirodnim surfaktanata i emolijensa (bez polietilenglikola - PEG, gde je poligliceril-4 laurat glavni surfaktant) koja je pogodna za izradu na hladno primenom metode inverzije faza (engl. *Phase inversion composition - PIC method*). Fizičkohemijska stabilnost NEs potvrđena je analizom distribucije veličina kapi, merenjem električne provodljivosti i pH vrednosti, kao i optičkom mikroskopijom. Nađeno je da su vrsta EO i koncentracija smeše surfaktanata i emolijensa ključni faktori koji utiču na karakteristike i stabilnost dobijenih NE. Tehnikom Ramanske spektroskopije potvrđeni su glavni aktivni sastojci etarskih ulja i detektovane su moguće interakcije sa nanonosačem. Pokazano je da je antioksidativna aktivnost prema DPPH radikalu u metanolu koncentraciono zavisna, sa sličnim trendom za čista etarska ulja i za NEs sa uljima (OR> LB> BA). Međutim, ABTS test u vodenoj sredini pokazao je izrazite promene u redosledu aktivnosti sa povećanjem koncentracije EO i nakon nanonizacije EO. Generalno, najjača aktioksidativna aktivnost primećena je u slučaju OR i OR-NE (> 95% INH_{ABTS} i > 85% INH_{DPPH}), što ukazuje na optimalno pakovanje OR unutar nanonosača čime su očuvane njegove antioksidativne performanse i obezbeđena stabilnost tokom 6 meseci čuvanja.

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Zahvalnica

Ovo istraživanje je finansirano od strane Ministarstva prosvete, nauke i tehnološkog razvoja Republike Srbije (Ugovor sa Univerzitetom u Beogradu – Farmaceutskim fakultetom, broj: 451-03-9/2021-14/200161 i sa Fakultetom za Fizičku hemiju, broj: 451-03-9/2021-14/200146).