Development of a submicron emulsion-based delivery system to improve the anti-inflammatory activity of urolithin A

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Rok wydania

2025

Czasopismo

Journal of Pharmacy and Pharmaceutical Sciences

Numer woluminu

28

Strony

15553/1-15553/15

DOI

10.3389/jpps.2025.15553

Kolekcja

Naukowa

Streszczenie

Objective:

Despite the antioxidant, anti-inflammatory, and anti-cellular-aging activities of urolithin A (UroA), a naturally occurring postbiotic, its high lipophilicity hampers its pharmaceutical application. To overcome this limitation improving its stability and bioavailability, submicron emulsions (S-EMs) were designed.

Methods:

Nineteen formulations (S-EM 1/S-EM 19) were prepared by two different methodologies. S-EMs were characterized evaluating macroscopical appearance and size distribution by photon correlation spectroscopy (PCS). One selected S-EM was loaded with UroA and characterized by PCS, transmission electron microscopy (TEM), small angle x-ray scattering (SAXS) and Fourier-transform infrared spectroscopy (FT-IR). Z potential, pH and syringeability were evaluated. UroA entrapment was studied efficiency by ultrafiltration and HPLC, while *in vitro* release by dialysis. Cytotoxicity was evaluated by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) (MTT) viability test on primary dermal human fibroblasts. The anti-inflammatory activity of S-EM-UroA was evaluated at 3, 6, and 24 h post-injection using the carrageenan-induced paw edema model in male C57BL/6 mice, and compared with UroA suspension and unloaded S-EM.

Results:

Język

Angielski

Typ publikacji

Artykuł

The preformulative study enabled to select method and composition for S-EM preparation. S-EM 18 was selected for UroA loading (SEM-UroA), due to mean diameter, zeta potential, pH and syringeability suitable for intraperitoneal administration. The loading of UroA (0.2 mg/mL) did not influence S-EM physicochemical features, while maintaining technological properties for 3 months. *In vitro* drug release showed a biphasic profile, 2.35-fold faster in the case of SEM-UroA compared to the drug suspension. *In vitro* studies revealed absence of cytotoxicity at concentrations up to 5 µM. *In vivo* studies, conducted as a first step in assessing the potential of S-EM-UroA, demonstrated a dose-dependent anti-inflammatory effect. Specifically, S-EM-UroA at 2 mg/kg reduced paw edema at 24 h ($p < 00.5$; One-Way ANOVA followed by Tukey's test), and at 4 mg/kg significantly reduced edema at all time points ($p < 0.01$), whereas the UroA suspension or S-EM had no effect on carrageenan-induced paw edema at any time point.

Conclusion:

These findings underscore the potential of UroA loaded S-EM as an effective delivery system, demonstrating its superiority over simple UroA suspensions in enhancing the systemic anti-inflammatory effects of the postbiotic.

Słowa kluczowe

urolithin-A, ellagic acid, submicron emulsion, dialysis, carrageenan-induced paw edema model

Adres publiczny

http://dx.doi.org/10.3389/jpps.2025.15553