An improved nanoemulsion formulation containing Kojic monooleate: optimization, characterization and in vitro studies

ABSTRACT

Tyrosinase inhibitors have become increasingly important targets for hyperpigmentation disease treatment. Kojic monooleate (KMO), synthesized from the esterification of kojic acid and oleic acid, has shown a better depigmenting effect than kojic acid. In this study, the process parameters include the speed of high shear, the time of high shear and the speed of the stirrer in the production of nanoemulsion containing KMO was optimized using Response Surface Methodology (RSM), as well as evaluated in terms of its physicochemical properties, safety and efficacy. The optimized condition for the formulation of KMO nanoemulsion was 8.04 min (time of high shear), 4905.42 rpm (speed of high shear), and 271.77 rpm (speed of stirrer), which resulted in a droplet size of 103.97 nm. An analysis of variance (ANOVA) showed that the fitness of the quadratic polynomial fit the experimental data with large F-values (148.79) and small p-values ($p < 0.0001$) and an insignificant lack of fit. The optimized nanoemulsion containing KMO with a pH value of 5.75, showed a high conductivity value (3.98 mS/cm), which indicated that the nanoemulsion containing KMO was identified as an oil-in-water type of nanoemulsion. The nanoemulsion remains stable (no phase separation) under a centrifugation test and displays accelerated stability during storage at 4, 25 and 45 °C over 90 days. The cytotoxicity assay showed that the optimized nanoemulsion was less toxic, with a 50% inhibition of cell viability (IC50) > 500 μg/mL, and that it can inhibit 67.12% of tyrosinase activity. This study reveals that KMO is a promising candidate for the development of a safe cosmetic agent to prevent hyperpigmentation.

Keyword: Response surface methodology; Hyperpigmentation; Nanoemulsion; Kojic monooleate; Optimization; Formulation; Cytotoxicity; Tyrosinase inhibitory activity; In vitro