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ORIGINAL ARTICLE

Downregulation of pro-inflammatory markers IL-6 and TNF-α in rheumatoid arthritis using nano-lipidic carriers of a quinone-based phenolic: an in vitro and in vivo study

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Abstract

Rheumatoid arthritis (RA) is a joint ailment with multi-factorial immune-mediated degenerative pathogenesis, including genetic and environmental defects. Resistance to disease-modifying anti-rheumatic drugs (DMARDs) happens due to excessive drug efflux over time, rendering the concentration insufficient to elicit a response. Thymoquinone (TQ) is a quinone-based phenolic compound with antioxidant and anti-inflammatory activities that downregulate numerous pro-inflammatory cytokines. However, its pharmaceutical importance and therapeutic utility are underexplored due to intrinsic physicochemical characteristics such as inadequate biological stability, short half-life, low hydrophilicity, and less systemic availability. Tamanu oil-stabilised nanostructured lipid carriers (TQ-NLCs) were prepared and optimised using Box-Behnken design (BBD) with the size of 153.9 ± 0.52 nm and surface charge of −30.71 mV. The % entrapment efficiency and drug content were found to be 84.6 ± 0.50% and 14.75 ± 0.52%, respectively. Furthermore, the TQ-loaded NLCs (TQ-NLCs) assayed for skin permeation for transdermal delivery which significantly ($p < 0.05$) increased skin enhancement ratio 14.6 times compared to the aqueous solution of TQ. Tamanu oil displayed the synergistic anti-inflammatory potential with TQ in comparison to pure TQ, as evidenced against carrageenan (CRG)-induced paw oedema model and Freund's adjuvant-induced arthritic model. The arthritic and X-ray scores significantly ($p < 0.05$) reduced in TQ-NLCs and standard formulation-treated groups. Moreover, serum pro-inflammatory marker TNF-α and IL-6 levels were also significantly ($p < 0.05$) reduced in TQ-NLCs gel-treated group compared to the arthritic control group.

Keywords Thymoquinone · Transdermal · Synovial delivery · Lipid-based drug delivery · Pro-inflammatory cytokines

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