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Abstract

Development and *In Vitro* Characterization of Diacerein Loaded Chitosan–Chondroitin Sulfate Nanoemulgel for Osteoarthritis †

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Abstract: The proficient functions of diacerein and anti-inflammatory polymers have been utilized to develop sustained release transdermal diacerein nanoemulgel for long-term osteoarthritis treatment by overcoming the deleterious outcomes of drugs associated with the oral route. Natural anti-inflammatory and biodegradable polymers like Chitosan (CHS) and chondroitin sulfate (CS) were used to formulate diacerein nanoparticles (DCR-NPs) through the ionic gelation method. Design Expert software was used for preparation of optimized preparation by investigating the impact of polymers and surfactant concentrations on particle size, PDI and entrapment efficiency employing Response Surface Methodology (RSM). DCR-NPs formulated using CHS, CS and Tween 80 in optimized concentrations depicted spherical nanoparticles with particle size of 320.0 ± 3 nm having PDI, zeta potential and entrapment efficiency of 0.3 ± 0.07, 40 ± 0.3 mV and 82 ± 4.16%, respectively. DCR-NPs were further analyzed for confirmation of electrostatic interactions between polymers and drug through Fourier transform-infrared spectroscopy (FTIR). In vitro studies show 95% release of DCR in 72 h exhibiting the Korsmeyer–Peppas model. For transdermal delivery, the nanoemulgel of optimized DCR-NPs was formulated utilizing argan oil as a permeation enhancer with intrinsic anti-inflammatory properties, providing a synergistic effect to the formulation. Nanoemulgel was characterized in terms of visual appearance, spreadability, drug content and rheological behavior providing sustained release of drug up to 4 days following Higuchi model with improved *ex vivo* permeation, confirmed by fluorescent microscopy. Concisely, DCR-nanoemulgel sustained the release of drug with good penetration and enhanced therapeutic properties owing to the presence of CHS, CS and argan oil possessing anti-inflammatory attributes.

Keywords: diacerein; nanoparticles; emulgel; transdermal route; delayed effect

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