Development and in vitro characterization of diacerein loaded chitosan-chondroitin sulfate nanoemulgel for osteoarthritis

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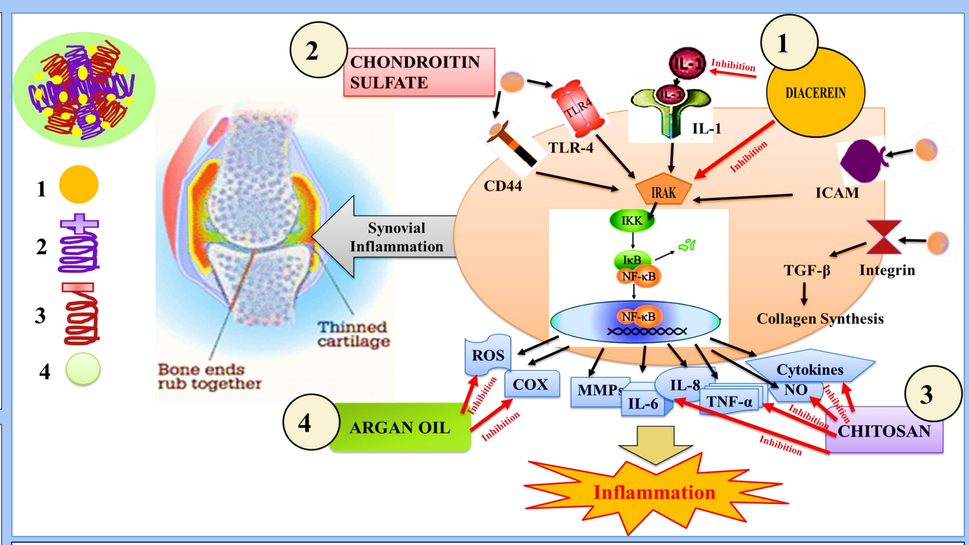
Introduction

Osteoarthritis (OA), an intricate degenerative joint disease is considered as one of the most prevalent disabling condition among the elderly population [1]. Diacerein (DCR) has gained much attention due to its improved disease modifying anti-catabolic, anti-inflammatory and pro-anabolic actions on cartilage of joints by producing inhibitory action on interleukin-1β [2]. Clinical acceptance of DCR was limited owing to the presence of gastrointestinal adverse effects. Transdermal delivery of DCR is aimed to reduce the side effect profile associated with the oral route with provision of sustained drug delivery. Chitosan (CHS) and Chondroitin Sulfate (CS) were employed as natural anti-inflammatory and biodegradable polymers to formulate diacerein through ionic gelation method. Argan oil being used in formulating emulgel has proven its permeation enhancing effect together with anti-inflammatory properties [3].



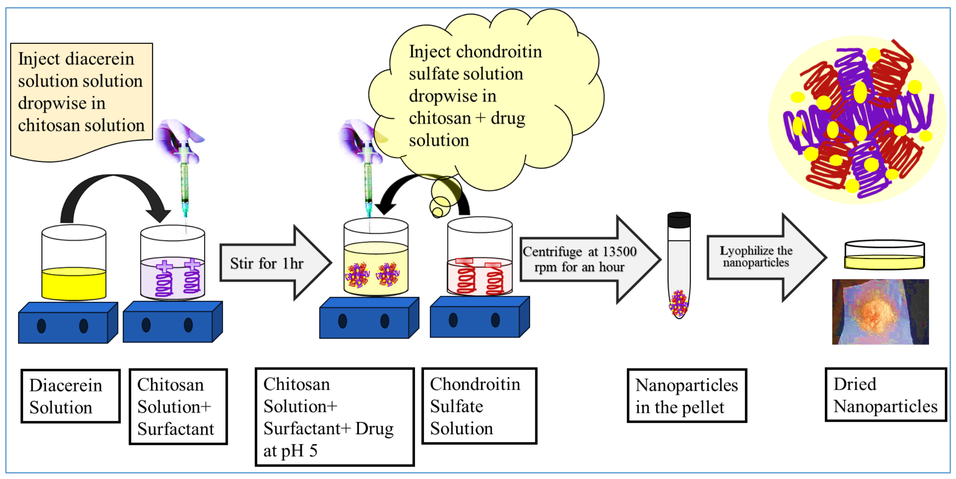
Four in one formulation (Mechanism of action of DCR, CS, CHS and Argan Oil)

Aim of Study

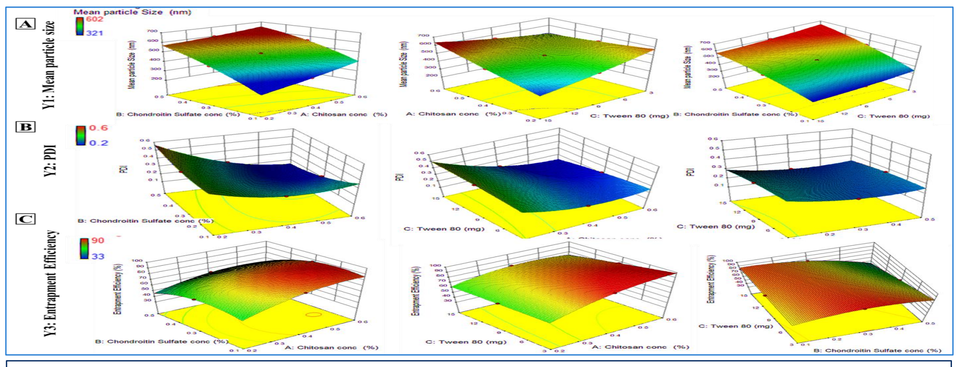
To develop and characterize DCR-nanoemulgel for transdermal application utilizing biomimetic polymers and natural penetration enhancer possessing anti-inflammatory activities that will help to design a formulation which may provide multiple benefits, *i.e.*, enhanced therapeutic effect, improve targetability and decrease off-target effects.

Methodology

Step 1: Preparation of drug loaded nanoparticles

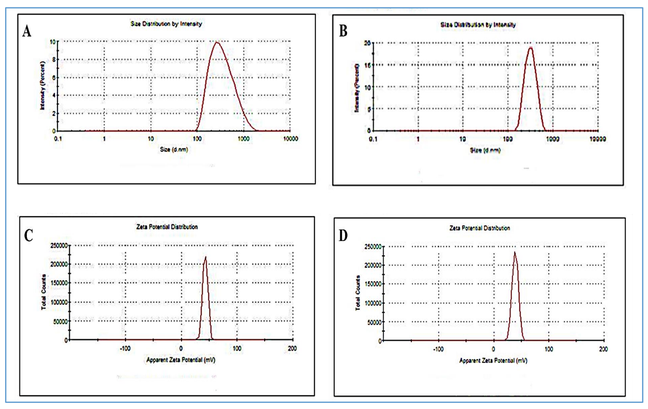


Optimization of nanoparticles using Design Expert Software

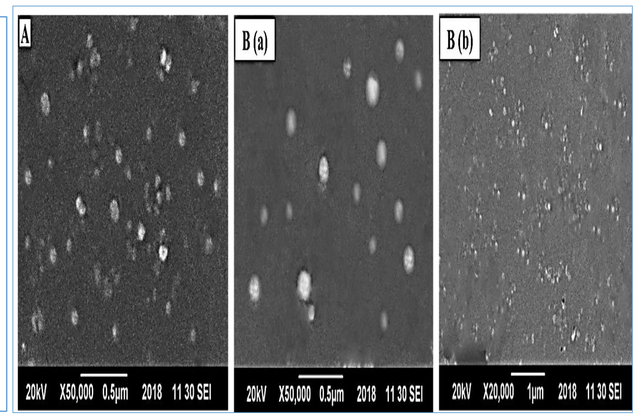


Three-dimensional response surface plot demonstrating effect of CHS, CS and Tween 80 on (A) mean particle size, (B) PDI and (C) Entrapment Efficiency of DCR-NPs

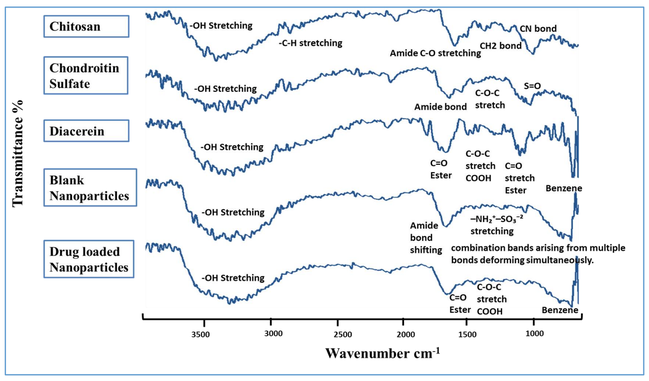
Results and Discussion



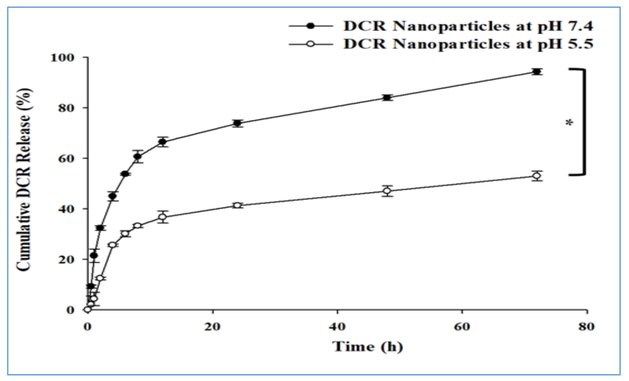
(A) Particle size of blank formulation (B) DCR loaded formulation (C) Zeta potential of blank formulation (D) DCR loaded formulation



SEM images of optimized blank and (B) DCR-NPs at different resolutions

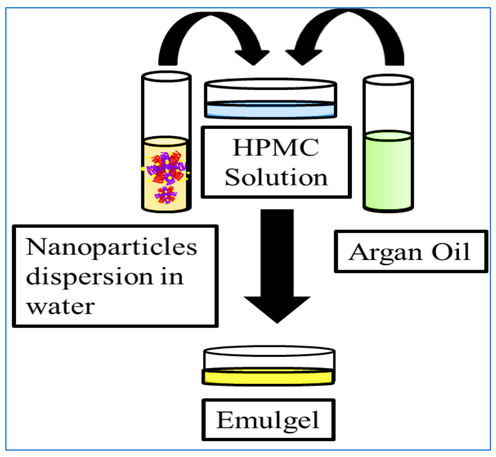


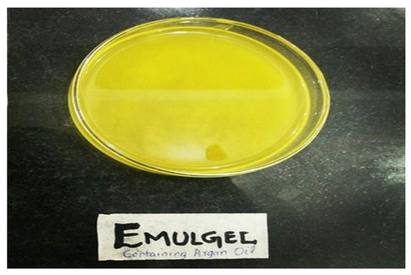
FTIR spectrum of CHS, CS, DCR, Blank NPs and DCR-NPs



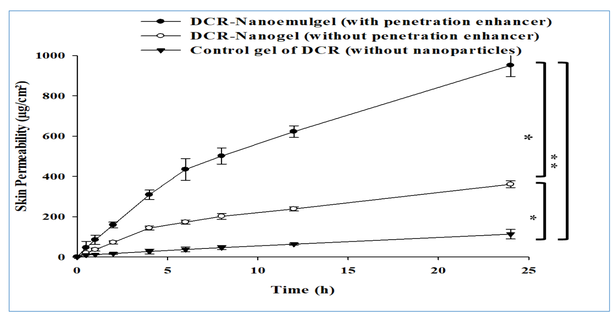
In vitro release profile of DCR-NPs at pH 7.4 and 5.5

Step 2: Preparation of drug loaded nanoemulgel

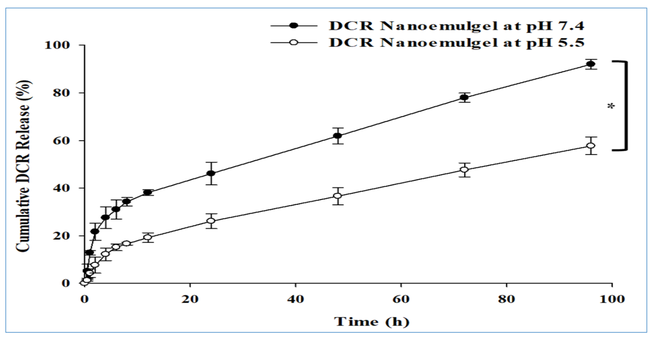




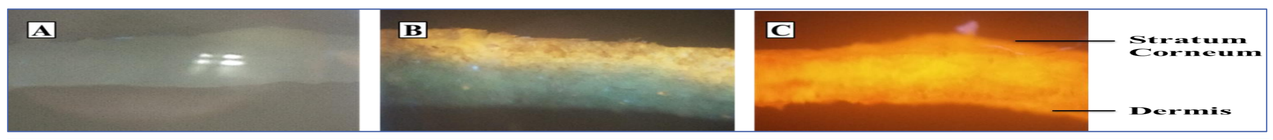
Fluorescent nanoparticles are prepared in a similar fashion by addition of Rhodamine dye in chitosan solution



Skin permeation studies of DCR-Nanoemulgel, DCR-Nanogel and Control gel



In vitro release profile of DCR-Nanoemulgel at pH 7.4 and 5.5



Fluorescence images of vertical sliced rat skin after Rhodamine loaded nanoparticles permeation. (A) Normal Skin without fluorescence (B) Fluorescence imaging after 10 min (C) Fluorescence imaging after 45 min. Note: Stratum corneum at upside; Dermis at lower side

Conclusions

DCR-nanoemulgel represents novel nanocarrier system with enhanced therapeutic efficacy, better penetration properties and sustained release profile upto 96 hours. DCR-nanoemulgel developed in this work is 4 in 1 formulation containing DCR, natural biopolymers (CHS, CS) and penetration enhancer (Argan oil) possessing anti-inflammatory properties and better targetability at desired site (due to CS) which might lead to greater therapeutic value and restorative ability to the formulation.

References

1. J.-R. Kim, J.J. Yoo, H.A. Kim, (2018).Therapeutics in osteoarthritis based on an understanding of its molecular pathogenesis, Int J Mol Sci. 19 ,674-689.
2. Pavelka K, Bruyere O, Cooper C, Kanis JA, Leeb BF, Maheu E, Martel-Pelletier J, Monfort J, Pelletier J-P & Rizzoli R (2016). Diacerein: Benefits, risks and place in the management of osteoarthritis. An opinion-based report from the ESCEO. Drugs & aging, 33(2): 75-85.
3. Gul R, Ahmed N, Ullah N, Khan MI & Elaissari A (2018). Biodegradable Ingredient-Based Emulgel Loaded with Ketoprofen Nanoparticles. AAPS PharmSciTech, 1-13.