Quercetin Loaded Nanostructured Lipid Carriers-based Gel for Rheumatoid Arthritis: Formulation, Characterization and in vivo Evaluation

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ABSTRACT

Present research work describes the development of potential topical treatment containing nanostructured lipid carriers (NLCs) for rheumatoid arthritis (RA). Quercetin (QCT) is a renowned flavonol useful as model drug for carriers. QCT loaded NLCs were prepared and evaluated for particle size distribution, polydispersity index, zeta potential analysis, in vitro drug release study. Ex vivo study was carried out to evaluate the effect of NLCs on cell proliferation (HIG-82 cell line) and inflammation (TNF-α induction in RAW264.7 cells). The QCT-NLCs showed mean particle size of 155.6 ± 1.8 nm and polydispersity index (PDI) was 0.236 ± 0.4, entrapment efficiency of 95.63 ± 0.14 % and zeta potential of -27 ± 1.2 mV. For the ease of application, NLCs were incorporated into the gel base and final formulation was evaluated for rheological study, texture profile, drug release and antiarthritic activity. QCT-NLC gel showed pseudo plastic flow behavior with excellent texture profile parameters. In vitro drug release studies showed that, QCT-NLC gel has more prominent permeation profile as compared with QCT-loaded gel. In vivo activity was carried out using Complete Freund’s adjuvant (CFA) induced arthritic model. Evaluation of the severity of rheumatoid arthritis was done by measurements of hind paw volume, arthritis score and haematological parameters such as rheumatoid factor (RF), C-reactive protein (CRP), red blood cells (RBCs), white blood cells (WBCs), erythrocyte sedimentation rate (ESR) and hemoglobin (Hb). Edema and erythema were not observed after administration of QCT-NLC- gel on the rat skin. In conclusion, the results of in vitro and ex vivo studies, QCT-NLC gel appears a viable formulation system for topical delivery of QCT in the treatment of RA.

KEYWORDS: Quercetin; Nanostructured lipid carriers; HIG-82; Rheumatoid arthritis.

Introduction

In the contemporary expertise, drug delivery systems are being developed using nanotechnology. Amongst all, nanocarriers based drug delivery system is rapidly emerging technology to enhance the therapeutic effect of the drug. It can overcome the difficulties with solubility, penetration, target specificity and bioavailability of the drugs. Therefore, with the above considerations the use of nanocarrier drug delivery system like lipid nanoparticles can be an excellent approach to design a formulation system. NLCs are colloidal particles that exhibit a size range of 100 - 400 nm. In addition to the advantages of colloidal drug carrier systems like liposomes, polymeric nanoparticles, emulsions, NLCs avoid or minimize the drawbacks such as stability, target specificity etc. (Muller et al., 2002; Joshi and Muller, 2009). NLCs have advantage due to their solubility enhancement, well-established safety profiles, skin occlusive effect, variety of routes of administration, improved properties for drug loading, modulation of the delivery profile, stable drug incorporation throughout the storage period, low toxicity, biodegradability, drug protection and avoidance of organic solvents during manufacturing (Ali et al., 2012).

Rheumatoid arthritis is a chronic, inflammatory autoimmune disease that progressively destroys the synovial membrane, cartilage and bone. It constitutes a profound and uncertain clinical problem even though significant progress has been made in the management of the disease. Important factors in the pathogenesis of RA are TNF-α activity, abnormal antibody production, circulating autoantibodies i.e. ‘rheumatoid factor’ and abnormalities in synovial tissue. Amongst all, the cytokines like TNF-α and interleukins have significant role in the disease progression (Choy, 2012; McInnes and Schett, 2007).

Conventional treatment of RA with NSAIDs (non steroidal anti-inflammatory drugs) and steroids exhibit adverse effects such as stomach upset, nephrotoxicity, iron deficiency anemia, protein loss, toxicity and a low therapeutic index (Sivasudha et al., 2013). Furthermore these treatments don’t show any prevention of tissue damage, mobility or bone destruction. Disease-modifying