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RESEARCH ARTICLE

Urate crystal degradation for treatment of gout: a nanoparticulate combination therapy approach

Sanjay Tiwari · Harinath Dwivedi · Koshy M. Kymonil · Shubhini A. Saraf

Abstract The objective of the present work was to develop polymeric nanoparticles of uricase and aceclofenac (NSAID) and to incorporate them into gel, for delivering drugs to synovial joints, for effective treatment of Gout. Nanoparticles containing uricase and aceclofenac were prepared by double emulsion solvent evaporation method and emulsion solvent evaporation, using PLGA (50:50) as carrier, respectively. Process parameters were optimized using Taguchi L4 orthogonal array and L9 array, respectively. The formulations were characterized for particle size, entrapment efficiency, surface charge, in vitro drug release, ex vivo drug permeation, and urate crystal degradation activity. The particle size and entrapment efficiency for optimized batch was found to be 228.8 nm and 81.26 % for uricase nanoparticles and 288.5 nm and 85.36 % for aceclofenac nanoparticles, respectively. The developed nanoparticles formulations displayed zero order and Higuchi release kinetics with non-Fickian diffusion, respectively. The in vivo studies were performed in rabbit model. Topical application of gel containing polymeric uricase nanoparticles alone and a combination of both, uricase nanoparticles and aceclofenac nanoparticles in rabbit model test groups, provided complete removal of urate crystals and inflammation within 40 and 25 days of treatment, respectively. The combination treatment therapy resulted in effective treatment of gout due to degradation of crystals and anti-inflammatory response.

Keywords PLGA · In vivo · Synovial joint · Crystals · Anti-inflammatory

S. Tiwari · H. Dwivedi · K. M. Kymonil
Babu Banarasi Das National Institute of Technology and Management, Lucknow, U.P., India 227105

S. A. Saraf (✉)
Department of Pharmaceutical Sciences, Babasaheb Bhimrao Ambedkar University (A Central University), VidyaVihar, Rae Bareli Road, Lucknow, Uttar Pradesh, India 226025
e-mail: shubhini.saraf@gmail.com

Introduction

Gout is a common systemic rheumatic disease. Most frequently, it causes recurrent attacks of acute arthritis and can sometimes lead to chronic arthropathy, tophi depositions, and renal diseases. This metabolic disorder develops due to excessive production of uric acid in the body due to metabolism of purines which get deposited into the joints in the form of monosodium urate crystals. Initial symptoms of gout usually consist of intense episodes of painful swelling in a single joint, most often in the feet especially the big toe. It can affect the insteps, ankles, heels, knee, wrists, fingers, elbows, etc. causing pain, swelling, redness, heat, and stiffness in joints [1].

Gout can be treated by xanthine oxidase inhibitors, drugs that increase the renal elimination of urate. Drugs that decrease inflammation which is caused by deposition of urate crystals are NSAIDs, colchicines, corticosteroids, etc. Polyethylene glycol (PEG)–uricase is another potentially powerful agent for treating refractory gout in those cases where other treatments are not possible. PEG–uricase is effective in dissolving tophi and could have a role in "debulking" tophi in advanced gout before switching to another agent for maintenance treatment [2].

Uricase is normally found in animals but has disappeared in the course of evolution in human beings [1]. It catalyzes the oxidation of less water-soluble uric acid (7 mg/dl at 37 °C) into allantoin, which is nearly ten times more water soluble,

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