RESEARCH

Nanostructured Lipid Carrier (NLCs)-Based Topical Gel of Tofacitinib for IMQ- Induced Psoriasis: Design In-Vitro and In-Vivo Assessment

Devyanshi Kushwaha[1] · Shipra Tripathi[1] · Shailendra K Saraf[1] · Neelam Datt[1]

Abstract

The present study aimed to develop and characterize a nanostructured lipid carrier (NLCs)-based topical gel of Tofacitinib for the treatment of psoriasis, with both in vitro and in vivo characterization. The NLCs were prepared using the ultra-sonication and homogenization method and analyzed for particle size, polydispersity index, zeta potential, drug entrapment efficiency, drug loading, surface morphology (via SEM), thermal properties (DSC, TGA), chemical characterization (FTIR), and in vitro cytotoxicity against the A375 cell line. The optimized NLCs were incorporated into a Carbopol 940 gel and evaluated for drug content, rheological behavior, texture profile, in vitro drug release, ex vivo skin permeation, biochemical, and histopathological effects. The NLCs appeared as spherical nanostructures with a narrow size distribution, within the nanometric range. The formulations demonstrated significant skin permeation within the epidermal and dermal layers. Histopathological examination of skin samples confirmed the formulation's effectiveness in treating psoriasis. The NLC-based gel demonstrated potential as a drug delivery system, increasing the percutaneous penetration of Tofacitinib and reducing inflammation and erythema, thereby enhancing psoriasis treatment.

Keywords Nanostructured lipid carriers · Tofacitinib; factorial design · Psoriasis · Cytotoxicity

Introduction

Approximately 125 million people worldwide suffer from psoriasis, an autoimmune disorder with a global prevalence of 4.4% [1, 2]. While it can affect other organs, the skin is most frequently involved. Key features include epidermal hyperplasia and ongoing inflammation caused by abnormal, uncontrolled keratinocyte growth [3]. Psoriasis arises from dysregulated immune responses driven by the JAK-STAT pathway, which transmits signals from proinflammatory cytokines such as IL-12, IL-23, IL-17, IL-22, and IFN-γ.

This pathway leads to keratinocyte overproduction, recruitment of inflammatory cells, and the development of skin plaques by activating STAT3 and other transcription factors. Blocking JAK-STAT signaling reduces cytokine levels and tissue changes in psoriatic lesions [4, 5]. Tofacitinib is a well-studied Janus kinase (JAK) inhibitor and a clinically validated pharmaceutical agent with proven efficacy in human trials. In contrast, hesperidin, betulin, and other potential agents have been studied mainly in animal models and are not considered primary, effective treatments on their own for a complex condition like psoriasis. Tofacitinib targets the JAK-STAT pathway to alleviate psoriasis symptoms by blocking inflammatory signaling in keratinocytes and immune cells. The choice of treatment depends on the severity of the condition, the type of psoriasis, and individual factors such as age and overall health. For localized cases of psoriasis ranging from mild to severe, a wide range of treatment options is available. Topical active ingredients are often the first-line treatment for mild to moderate psoriasis, including corticosteroids, vitamin D analogs, retinoids, coal tar, dithranol, and calcineurin inhibitors [6, 7]. These therapies help penetrate the epidermal barrier, enhance absorption, and reduce the required dosage [8]. They enable

✉ Neelam Datt
  neelima12pharm@gmail.com

  Devyanshi Kushwaha
  kushwahadipti289@gmail.com

  Shipra Tripathi
  shipratripathi101@gmail.com

  Shailendra K Saraf
  dirpharmniec@gmail.com

[1] Babu Banarasi Das Northern India Institute of Technology, Lucknow, India