

Article

Exploring the Potential of Transdermal Nanobilosomal Gel for Magnified Anti-Inflammatory Efficacy of Thymol for Managing Rheumatoid Arthritis

Deepti Tripathi ^{1,2}, Ranjit Singh ¹, Parveen Kumar ^{3,*}, Preeti Kush ^{1,*} and Gul Naz Fatima ²

- ¹ Adarsh Vijendra Institute of Pharmaceutical Sciences, Shobhit University, Gangoh, Saharanpur 247341, Uttar Pradesh, India; tri.dt91@gmail.com (D.T.); ranjitsps@gmail.com (R.S.)
- ² Faculty of Pharmacy, Babu Banarasi Das Northern India Institute of Technology, Lucknow 226028, Uttar Pradesh, India; gul08fatima@gmail.com
- ³ Anant Materials Pvt Ltd., Sonipat 131001, Haryana, India
- * Correspondence: parveenkaushik7@gmail.com (P.K.); preetikush85@gmail.com (P.K.)

Abstract

This research aims to develop a chitosan-coated, TH-loaded nanobilosomal gel (CH-TH-BG) to magnify the transdermal delivery and anti-inflammatory efficacy of thymol (TH) for the management of rheumatoid arthritis (RA). Initially, chitosan-coated, TH-loaded bilosomes (CH-TH-BLs) were prepared and optimized by Box–Behnken design. The optimized CH-TH-BLs exhibited enhanced entrapment efficiency (83.52%) and a positive zeta potential (+36.3 mV). Further, the optimized lyophilized CH-TH-BLs were incorporated into the carbopol gel (CH-TH-BG) and characterized thoroughly. The CH-TH-BG exhibited superior pharmaceutical properties, including high drug content ($98.65 \pm 1.43\%$), optimal viscosity ($10,400 \pm 12.6$ cps), excellent spreadability (5.33 ± 0.15 cm), extrudability, and a slightly acidic pH (5.40 ± 0.10), which resembles the pH of human skin. In vitro drug release revealed that the developed gel exhibited a biphasic release pattern, with a rapid release followed by sustained release. Notably, ex vivo results revealed a ~2.0-fold increase in permeation flux and a ~2.8-fold increase in skin retention compared to the TH solution. In vivo results confirmed a significant reduction in paw edema and pro-inflammatory biomarkers (TNF- α and IL-6), alongside recovery of body weight and ankle joints. In conclusion, the CH-TH-BG is a transformative transdermal platform for effective management of RA.

Keywords: rheumatoid arthritis; bilosomes; thymol; bilosomal gel; chitosan; transdermal delivery



Academic Editors: Huihua Yuan and Hongyun Xuan

Received: 31 December 2025

Revised: 5 February 2026

Accepted: 9 February 2026

Published: 10 February 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\) license](https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Rheumatoid arthritis (RA) is a systemic and chronic autoimmune inflammatory disease that has a significant global impact (0.5–1%) and is more common in Western countries. Moreover, it predominantly affects women (~three times higher), especially those over 60, due to hormonal variations [1]. RA is characterized by joint inflammation, synovial hyperplasia, immune cell infiltration, and pannus formation [2]. Additionally, patients can face a higher fatality rate due to various extra-articular complications caused by RA that affect the lungs, skin, and heart [3]. The pathogenesis of RA is complex and not fully understood. However, some studies suggest that its development is associated with an abnormal immune response, leading to the production of RA autoantibodies and the activation of various immune cells, including dendritic cells, T and B cells, neutrophils,