Elucidating the role of transferosomes for the management of gout: A comprehensive review

Jasveer kaur [1], Harpreet kaur [1], Aakriti [2], Om silakari [1], Bharti sapra[1]*

[1]Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, 147002, India

[2]General Physician, Chopra Nursing Home, Ludhiana, Punjab, 141104, India

Email: bhartijatin2000@yahoo.co.in

Abstract

Millions of people throughout the world suffer from gout, a chronic inflammatory disease. It is predominantly brought on by uric acid crystals building up in the joints, which causes excruciating pain and swelling. Conventional therapies are accessible, but their efficacy and safety are frequently limited, highlighting the need for more sophisticated and dependable therapy alternatives. Nanotechnology has become a viable option for improving drugs delivery method in recent years. Strategies utilizing liposomes, polymeric nanoparticles, metal and non-metal oxide nanoparticles, and liquid crystalline nanoparticles have demonstrated promise in enhancing bioavailability and more precisely addressing inflammatory regions. Transferosomes, a unique class of ultra-deformable, lipid-based vesicles, have drawn a lot of interest as an innovative drug delivery system for the treatment of gout. A growing amount of data from preclinical and clinical research demonstrates that transferosome-based formulations are safe and effective, and they can address many of the drawbacks of conventional gout treatments.

Keywords: Transferosomes, joint inflammation, skin permeation.

1. Introduction

Gout is a painful and chronic inflammatory condition which is accompanied by the abnormal formation of uric acid crystals in the joints, characterized by intense pain and considerable swelling. The condition can persist for years, often affecting a person's quality of life. The underlying cause of gout is the formation of monosodium urate (MSU) crystals, which can deposit in various tissues throughout the body. The

formation of uric acid crystals requires serum uric acid (SUA) levels to rise above a certain threshold. Hyperuricemia is the primary factor in the development of gout as a pathogenic defect However, many persons who are diagnosed with hyperuricemia do not suffer from gout and even formation of UA crystals do not take place in them. Gout only develops in 5 percent of patients who have hyperuricemia levels that are higher than 9 mg/dL. Accordingly, it is hypothesized that the occurrence of gout is also influenced by other variables, such as a hereditary susceptibility (1). Figure 1 depicts the pathophysiology of gout and provides a clearer understanding of the disease.

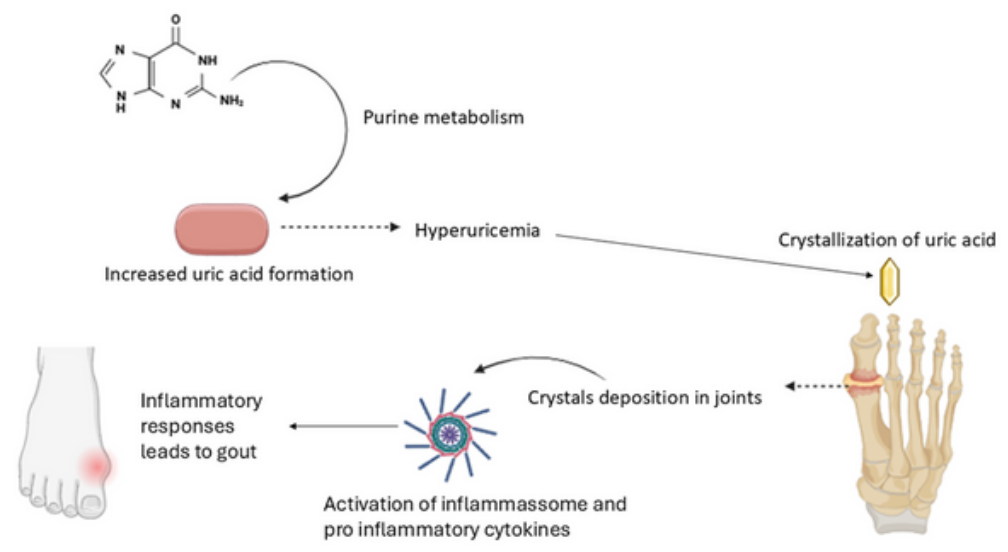

Figure 1. Pathophysiology of gout

In 2020, gout affected approximately 55.8 million people worldwide, with a 22.5% increase in age-standardized prevalence since 1990. Men were over three times more likely to have gout than women, and prevalence rose with age. By 2050, gout cases are projected to reach 95.8 million, primarily due to population growth. The age-standardized prevalence in 2050 is expected to be around 667 per 100,000 people (2). It can cause discomfort and may lead to several health complications. However, traditional therapies for gout have several drawbacks, including ineffective medication distribution to the affected tissues and the risk of adverse effects. Recent advancements in nanotechnology have given rise to a new medication delivery mechanism called transferosomes. This article explores the potential of transferosomes to revolutionize gout treatment by enhancing medication delivery efficacy while minimizing adverse effects. Future research must focus on the development and testing of therapeutic interventions for the prevention and treatment of gouty arthritis. Combining clinical and epidemiological evidence and animal experiments could significantly benefit this field (3).

2. Limitations of current treatment

Suboptimal gout care is caused by a variety of variables, including clinicians who don't adhere to established procedures, patients who don't adhere to their medicines, and communication gaps between doctors and their patients. Patients need to be reminded of the need of adhering to long-term treatment and other elements of sickness diagnosis and care. Low medication adherence may also be caused by a lack of motivation and an inability to purchase the prescription. Around one in a hundred people taking allopurinol may develop a usually mild skin rash, though in rare cases it can signal a serious allergic reaction. Renal issue is another risk with the treatment line (4).

3. Transferosomes®

Transferosomes® are novel lipid-based vesicles that are the modified form of liposomes and have also gained a lot of interest for the transdermal delivery of drugs. They are small, with a diameter of approximately 100 nm, and are referred to as transferosomes. The name comes from the words "transfere" in Latin and "soma" in Greek, which mean "to carry across" and "body," respectively. These tiny carriers

have properties like prosomes, which are cells involved in exocytosis. With this delivery carrier, drugs can be delivered to bodily tissues non-invasive. IDEA AG, a German company, has registered Transferosome as a trademark to refer to its technology for delivering drugs. Membrane-enclosed transferosomes with an activator on the outer edge; because of the edge activator, the lipid layer is ultra-deformable and flexible. Because of their ability to deform and squeeze through minute holes and constrictions in the skin, these vesicles permeate easily (5). Transferosomes offer a significant advantage over ordinary liposomes i.e. exceptional stability. Moreover, transferosomes are considerably enhanced by edge activators (anionic surfactants), which significantly boost their performance compared to liposomes. Numerous studies indicate that transferosomes can carry bioactive compounds and hydrophilic and lipophilic molecules with a molecular weight ranging from 200 to 10^6. They have a transport efficiency of over 50% when applied to human skin. The transferosomes are amphiphilic vesicular systems (6). Figure 2. Shows how the vesicles penetrate through the skin's layers, starting from the outer stratum corneum, moving into the epidermis and dermis. They carry the drug safely across these barriers without degradation. Once they reach the systemic circulation, the vesicles release the drug gradually for effective absorption.

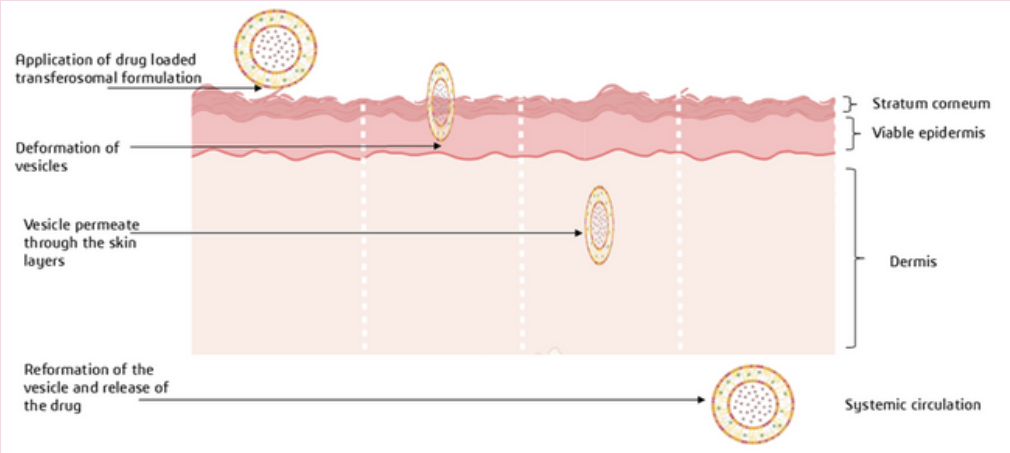

Figure 2. The mechanism of drug release and transferosome trafficking via the skin

4. Therapeutic applications of transferosomes

Transferosomes are novel vesicular drug carriers that improve transdermal drug absorption by getting past the limits of the epidermal barrier (7). These elastic vesicles, which are made of water, phospholipids, and surfactants, can distort to enter skin pores, increasing medication absorption and lowering toxicity (8). Transdermal vaccination, insulin delivery, and the injection of NSAIDs and steroidal hormones are merely a few of their many medical applications. Preparation techniques include reverse phase evaporation, modified hand shaking, and thin film hydration method (9). Transferosomes are intriguing possibilities for skin cancer treatment and other dermal and transdermal applications due to their adaptability and flexibility; multiple products are undergoing advanced clinical testing (10).

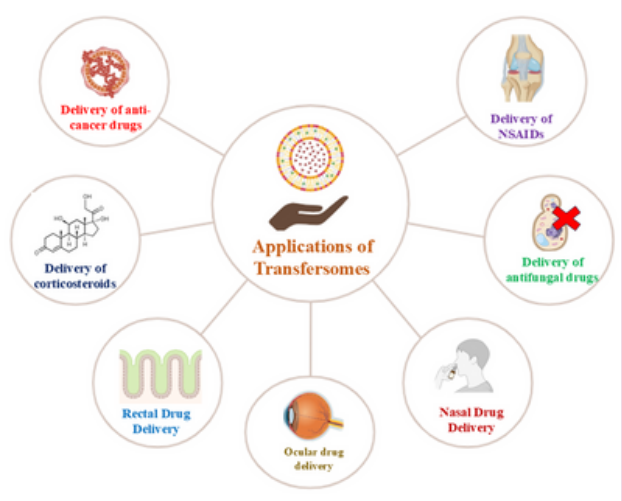

Figure 3. Different transferosome uses for delivering different agents using different delivery mechanisms

5. Key studies on transferosomes in gout treatment

Studies have shown that transferosomes can be used in the treatment of gout. These studies are key to understanding the effectiveness of transferosomes in treating this condition. Transferosomes have the potential to revolutionize drug delivery and improve treatment outcomes for a variety of conditions like arthritis, osteoarthritis, etc. Table 1 lists the potential therapeutic agents that can be delivered using transferosomes for the treatment of gout.

Table 1. Potential therapeutic agents delivered topically by ultra-deformable system for Gout

Nanocarrier system	Drug	Method of Preparation	Result	Ref
Transferosome	Allopurinol	Thin film hydration method	Selected formulation demonstrated a drug permeation of 79.84%, with a flux of 13.06 µg/cm²/hr, indicates a significant enhancement in permeation compared to the standard allopurinol formulation, which exhibited a flux of only 7.05 µg/cm²/hr.	(6)
Transferosome	Indomethacin	Rotary evaporation sonication method	The Indomethacin-Hyaluronan transferosomal gel showed approximately 3.04-fold higher drug permeation than conventional Indomethacin gel and 1.73-fold higher than indomethacin-transferosomal gel. It also exhibited a 3.31-fold increase in flux over Indomethacin Gel and 1.85-fold over Indomethacin Gel,confirming its superior transdermal delivery performance.	(11)
Transethosome	Colchicine	Cold method	Colchicine-transethosomes exhibited high biocompatibility, high permeation, sustained delivery and lesser toxic effects as compared to 40% ethanol solution.	(12)
Transferosome	Dexibuprofen	Thin film hydration method	The selected formulation, Dexibuprofen transferosomal gel, followed sustained release by releasing the drug 38.1% in 4 hours.	(13)

6. Conclusion and future prospects

Conventional oral therapies for gout often face significant limitations due to patient comorbidities, poor drug tolerance, and systemic side effects. In recent years, nanotechnology-based drug delivery systems such as liposomes, niosomes, ethosomes, and particularly transferosomes have emerged as promising alternatives, offering more targeted and effective approaches to gout management. Among these, transferosomes stand out due to their ultra-deformable lipid bilayers, which enable deep transdermal penetration and localized drug delivery directly to inflamed joints. This unique capability not only enhances drug bioavailability and prolongs release but also significantly reduces systemic toxicity, thereby improving anti-inflammatory and antigout effectsTransferosomes reduce systemic exposure, increase therapy effectiveness, and encourage improved patient adherence by precisely delivering therapeutic chemicals to the site of injury. Numerous commercially available transferosomal formulations, including Flexiseq, TDT-067, Transfersulin, Triamcinolone acetonide, and Diractin, have already shown improved targeted delivery and skin penetration. These pharmaceuticals have demonstrated clinical effectiveness in treating inflammatory disorders, diabetes, fungal infections, and osteoarthritis, highlighting the therapeutic usefulness and adaptability of transferosome-based administration. These achievements pave the path for additional research into using transferosomes as a vehicle to deliver a greater variety of medications. This system's versatility presents a great deal of promise for transdermal treatment of both acute and chronic diseases.

Furthermore, transferosome development's incorporation of Computer-Aided Drug Design (CADD) is expected to spur innovation in this area. In order to maximize skin penetration, CADD helps select for appropriate lipids and edge activators and predicts drug-excipient interactions, vesicle stability, and entrapment efficiency. With further study and technical development, transferosomes have the potential to revolutionize future treatment approaches and establish themselves as a key component of personalized, non-invasive drug delivery systems.

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