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Recent Advances in Lipid Nano-Carrier Systems for the Management of Inflammatory Diseases: A Comprehensive Review

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ABSTRACT

Background: In the past two decades, extensive research has focused on lipid nanocarriers for targeted drug delivery to treat various diseases. Among these, inflammatory conditions pose a formidable challenge in modern healthcare, encompassing a diverse spectrum from autoimmune disorders to chronic inflammation. Effective therapeutic interventions necessitate the development of targeted and efficient delivery systems to address the complexities associated with drug administration.

Purpose: This review highlights different approaches of lipid-based nanocarriers to target various inflammatory diseases, such as rheumatoid arthritis, inflammatory bowel disease (IBD), psoriasis, asthma, and chronic obstructive pulmonary disease (COPD). It focuses on the advancements made in Lipid Nano-Carriers (LNC) with a special emphasis on their inherent safety, lower stability costs, and enhanced encapsulation efficiency.

Methods: Recent literature has been surveyed from PUBMED, GOOGLE SCHOLAR, etc., like search engines, for summarising detailed ongoing developments in the field of lipid nanocarriers for inflammatory diseases, which could prove to be a novel carrier for efficient drug delivery with special emphasis on surface modifications, formulations, pharmacokinetics, and efficacy.

Conclusion: This review emphasizes recent researches in the field of lipid-based nano formulations for managing inflammatory disease, as well as extensive discussion on their limitations and future prospective.

1. Introduction

Inflammation is a multistep biological response of the immune system, which acts as a defense mechanism to protect the human body from harmful stimulis' and when this inbuilt mechanism is downregulated, it leads to the pathogenesis of a group of diseases, ranging from autoimmune disorder to cardiovascular complication (Roe, 2021; Sharma *et al.,* 2023). For management of these conditions, conventional therapies like the use of non-steroidal anti-inflammatory drugs (NSAIDs-Naproxen, ibuprofen, and diclofenac) and immunosuppressive (Azathioprine, Tacrolimus, methotrexate, and corticosteroids-Prednisone), have long been the drug of choice (Chen *et al.,* 2018). However, when these drugs are administered to patients, it leads to off-target effects and results in an imbalance between therapeutic efficacy and adverse reactions. Corticosteroids such as dexamethasone and prednisone modulate the immune responses and inhibit the production of inflammatory mediators; however, they can produce harmful side effects, including immunosuppression, osteoporosis, and metabolic disturbances (Nyandoro *et al.,* 2023). Prolonged use of these agents can cause drug resistance and decreased efficacy over time (Ferrara *et al.,* 2019). They preferably act by inhibiting COX (Cyclooxygenase) enzymes and reducing the molecular synthesis of pro-inflammatory prostaglandins. These drugs are effective in mitigating pain and swelling symptoms but their regular administration can precipitate gastrointestinal complications, cardiovascular risks, and renal failures. One of the main reasons for these side effects is the non-selective nature of COX inhibition, which ultimately necessitates the development of targeted approaches in therapeutic treatment for chronic inflammatory conditions (Raj & Unsworth, 2023; Rathi *et al.,* 2024).

Thus, traditional therapeutic approaches often face limitations in precisely targeting the inflamed tissues and various inflammatory conditions. The emergence of

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nanotechnology has explored the emergence of targeted DDS (drug delivery systems) to treat inflammatory complications, which enhances drug efficacy, site absorption, and half-life (Rizvi & Saleh, 2018; Kaur *et al.,* 2023). Recently among various nanocarriers, lipid-based nanocarriers (LNC) have emerged as a promising approach, which shows potential to overcome the shortcomings of conventional treatments. Lipid nanocarriers including niosomes, liposomes, self-micro-emulsifying DDS (SMEDDS), solid lipid nanoparticles (SLN), nano lipid carrier (NLC), nanoemulsions, etc., offer several advantages, such as enhanced drug solubility, sustained release and improved bioavailability (Ghasemiyeh & Mohammadi-Samani, 2018). Various nanoparticles including polymeric nanoparticles, gold nanoparticles, carbon nanotubes, silica, etc., offer advantages like minimal organic solvent use, enhanced in-vivo stability, and diverse applications. Nano Lipid Carriers, the 2nd generation of lipid nanoparticles can address the limitations of SLNs by utilizing biodegradable lipid components, and emulsifiers for improved drug entrapment and can entrap both hydrophobic and hydrophilic drugs (Doktorovova *et al.,* 2016; Tetyczka *et al.,* 2021). They can be administered through a variety of routes e.g., orally, topically ocular, pulmonary, transdermal and parenteral for targeted delivery to inflamed tissues. In this article, the therapeutic potential of lipid nanocarriers in the treatment of different inflammatory diseases, including rheumatoid arthritis (RA), inflammatory bowel disease (IBD), psoriasis, asthma, and chronic obstructive pulmonary disease (COPD) with an extensive overview of scientific research studies stabilising their role in treating these conditions have been explained as shown in table 1.

Table 1: Overview of recent studies conducted in the field of lipid nano-carriers with a focus on their application in managing inflammatory diseases

S.no	Title of the Study	Disease	Route of Administration	Application	Reference
1	Mometasone Furoate Hydrogel	Psoriasis	Topical	Sustained drug delivery with a promising carrier system	(Kaur *et al.,* 2018)
2	NLC Co-delivering Tacrolimus and TNF	Psoriasis	Topical	Controlled drug release, promising skin permeation, low toxicity, and in vivo experiments showed a 7-fold reduction in TNF-α expression.	(Viegas *et al.,* 2020)
3	Methotrexate-loaded NLC Gel	Psoriasis	Topical	Enhanced therapeutic response, reduced local side effects, and significant anti-psoriatic efficacy	(Agrawal *et al.,* 2020)
4	Curcumin-loaded NLC for Topical Delivery	Psoriasis	Topical	Extended-release, improved skin permeation, and enhanced cell uptake	(Rapalli *et al.,* 2020)
5	Aceclofenac Lipid Carrier Hydrogel	Rheumatoid Arthritis	Transdermal	Provides an improved method for administering ACE and may be applied in the treatment of RA	(Garg *et al.,* 2021)
6	Berberine Chitosan-coated SLN	COPD	Intragastric	Versatile nanocarrier platform with improved bioavailability	(Liu *et al.,* 2022)
7	Celecoxib Lipid-Based Nanocarriers	IBD	Oral	Improved drug efficacy and localized treatment option	(Mishra *et al.,* 2020)
8	SLN of Rhynchophylline	Asthma	Intraperitoneal	Rhy-SLNs effectively reduced airway inflammation and oxidative stress	(Lv *et al.,* 2021)
9	Dexamethasone Cholesteryl Butyrate-Solid Lipid Nanoparticles	IBD	Oral	DxCb-SLN given orally was effective in reducing disease symptoms in a mouse model of DSS-induced colitis.	(Dianzani *et al.,* 2017)
10	pH-sensitive Liposomes of Mesalazine with Curcumin	IBD	Oral	pH-sensitive MZ-CM co-loaded liposomes demonstrated greater effectiveness than a single drug solution	(Aib *et al.,* 2022)

11	Lactoferrin-modified Patchouli-loaded Liposomes	IBD	Oral	LF-lipo demonstrated enhanced drug efficacy in a DSS-induced colitis murine model by reducing the disease activity index and improving colon function.	(Zhao *et al.,* 2020)
12	Budesonide Liposomes	Asthma	Intraperitoneal Injection	BUD-LNP reduced bronchial hyper -responsiveness, inflammatory factors in alveolar lavage fluid, and inflammatory cells in tissue sections, with significant reduction in airway mucus secretion.	(Zuo *et al.,* 2024)
13	Thiocolchicoside Niosomal Gel	RA	Topical	Controlled drug release, enhanced topical retention time, and reduced dosing frequency and side effects.	(Paradkar & Vaghela, 2018)
14	Rosmarinic Acid-Loaded Nanovesicles	Acute Colitis (IBD)	Oral	RA-loaded nanovesicles decreased activity index, increased mucus production, and decreased myeloperoxidase activity.	(Marinho *et al.,* 2021)
15	Niosomal Myrtenol	Asthma	Nebulization	Niosomal myrtenol displayed greater potency than budesonide in alleviating disease parameters and reduced inflammation, oxidative stress, and tissue remodeling.	(Rajizadeh *et al.,* 2023)
16	Curcumin (CUR) and Emodin (EMO) Nanoemulsion	IBD	Oral	Improved the colon inflammatory microenvironment by downregulating TNF-α and IL-6 expression.	(Lei *et al.,* 2023)
17	Curcumin Nanoemulsion	Psoriasis	Topical	Earlier and quicker healing in psoriatic mice compared to curcumin alone and betamethasone-17-valerate gel (B-17 V-gel).	(Algahtani *et al.,* 2020)
18	Salbutamol Sulfate Liposome	Asthma	Dry Powder for Inhalation (DPI)	Optimized liposomal formulation resulted in sustained in-vitro drug release of over 90% for up to 14 hours.	(Honmane *et al.,* 2019)

2. Various Lipid Nanocarriers

2.1. Liposomes

Liposomes are phospholipid-based vesicles with a size range of 50 to 500 nm in diameter that can encapsulate therapeutic agents in their aqueous core or lipid bilayer. In inflammatory conditions, liposomes have shown efficacy in delivering therapeutic drugs at the site of inflammation. Their unique phospholipid composition allows easy integration with the cell membranes, which facilitates easy drug uptake by the cells at the inflammatory sites (Nsairat *et al.,* 2022). Surface modification can also be enabled in these structures such as ligands and antibodies for targeted delivery and PEGylation of drugs that ensure prolonged circulation by evading the immune system. They can encapsulate both hydrophobic and hydrophilic drugs, which can enhance the permeability and retention effect (Olival *et al.,* 2022; Sercombe *et al.,* 2015).

2.2. Solid Lipid Nanoparticles (SLNs)

Solid Lipid Nanoparticles (SLNs) are a category of lipid nanocarriers, comprising a solid lipid matrix, that can enhance the therapeutic efficacy of anti-inflammatory drugs and offer advantages such as controlled drug release, stability, and biocompatibility with body tissues. It provides protection to the encapsulated therapeutic agents to prevent its premature release and on-site molecular degradation (Bayón-Cordero *et al.,* 2019). At room temperature, these nanospheres have a solid structure with a particle size ranging from 40 to 1000 nm. The composition of SLNs involves the use of solid lipids (0.1–30%), prepared from fatty acids, mono-/di-/triglycerides and glyceride mixtures, as a matrix material for drug encapsulation (Müller *et al.,* 2011). Lipophilic nature is crucial for loading lipophilic drugs topically, such as curcumin. They form a single layer on the skin surface which creates an occlusion effect to prevent water loss (transepidermal). Due to their small particle size of SLNs, they possess close interaction with the inflamed cells of the stratum corneum to increase drug permeation (DP) and drug accumulation (DA) in the epidermis/dermis region (Gordillo-Galeano *et al.,* 2018).

2.3. Niosomes

Niosomes are microscopic vesicles, which incorporate cholesterol as an excipient, containing non-ionic surfactant

in a modified composition. They are prepared by various methods like, reverse phase evaporation, micro-fluidization, trans-membrane pH gradient method etc. Structurally, they are very similar to liposomes as they both consist of a lipid bilayer compartment in their structure. They are different as they lack any charge, making it more compatible and stable and can reduce haemolysis (Ge *et al.,* 2019). These vesicles can be categorized based on their vesicles sizes as MLV (Multilamellar Vesicles, 100 to 1000 nm), LUVs (Large Unilamellar Vesicles- 100-250) & SUVs (Small Unilamellar Vesicles, 10–100 nm) (Abdelkader *et al.,* 2014). They are used to target directly the inflamed cells by recognising and binding to the receptors overexpressed on inflamed tissues and provide sustained release that ultimately delays the clearance from circulation (Kazi *et al.,* 2010). They are beneficial in combination therapy to address multiple inflammatory pathways simultaneously by encapsulating multiple drugs within a single niosomal formulation, thereby enhancing therapeutic efficacy. They are widely used in gene delivery, topical drug delivery systems, antineoplastic treatment, and cosmetics (Rinaldi *et al.,* 2017).

2.4. Nano-emulsions

Nano-emulsions (10 to1000 nm) are colloidal particulate dispersion systems of nanosize droplets of oil in water (o/w) or water in oil (w/o), simultaneously stabilized by surfactants (10 to 100 nm), acting as a carrier for drug molecules. It represents solid spheres containing immiscible liquids (Souto *et al.,* 2022). Nano-emulsions possess advantages such as increased drug loading, reproducible plasma drug profiles, sustained and targeted drug delivery, with their stability ranging from ultra-low interfacial tension (IFT) and a large interfacial area (LIA) (Preeti *et al.,* 2023). They share characteristics with micro-emulsions, including high kinetic stability, and optical transparency and find applications in various dosage forms such as creams, liquids, sprays, and foams. In inflammatory disorders, nano-emulsion offers a versatile platform for delivering lipophilic and hydrophilic drugs (Hussein *et al.,* 2022).

3. Application of Lipid Nano-Carrier Systems in various Inflammatory Diseases

3.1. Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is a chronic autoimmune disorder mainly affecting the joints, causing inflammation, pain, stiffness, and progressive damage. Unlike osteoarthritis, which is caused by gradual wear and tear of the joints (knee, hip, shoulder, etc.), rheumatoid arthritis (RA) occurs when the body is itself attacked by the immune system, thereby targeting the synovium and the linings of the membrane that surround the joints. It causes chronic inflammation and synovitis, which results in bone erosion and joint deformity (Guo *et al.,* 2018). There is a need for novel treatments in RA due to several limitations of current therapies, which mainly focus on treating symptoms rather than targeting the main cause of the disease. Even several approaches in pharmacotherapy regarding dose optimization and multiple drug combinations, RA patients experience incomplete relief from the symptoms and are at a high risk of long-term joint damage (Cho *et al.,* 2019). The use of lipid nanocarriers (LNC) as drug delivery systems for RA has sprung as a novel target. This can be achieved by encapsulating drugs within lipid-based nanoparticles, such as liposomes, niosomes or lipid nanoparticles, to enhance stability, solubility, and tissue penetration, thereby maximizing their therapeutic potential while minimizing adverse effects (Garg *et al.,* 2016).

A study was conducted to enhance the lymphatic delivery of leflunomide (to avoid 1st pass metabolism) with NLC for rheumatoid arthritis treatment; it focused on the formation of chylomicron to improve bioavailability and reduced systemic toxicity. It was prepared by melt emulsification ultra-sonication method (MEUS) with varying surfactant and lipid concentrations. The optimized formulation showed high (EE) entrapment efficiency (93.96 ± 0.47%), sustained drug release (90.35% at 48 hrs.), superior efficacy in reducing knee inflammation, enhanced intestinal lymphatic uptake, and healthy cartilage formation (Krishnan *et al.,* 2018). NLCs loaded with methotrexate (MTX) for transdermal delivery (TD) using a lipid mixture and chemical permeation enhancer (CPE) based hydrogel was developed. The prepared NLCs showed optimization criteria, including a particle size of less than 200 nm, poly-disparity index (PDI) of less than 0.2 and an entrapment efficiency of 85%. Methotrexate (MTX) loaded NLCs for transdermal delivery (TD) have been developed using a lipid mixture and CPE (Chemical Permeation Enhancer). This hydrogel showed different optimization criteria (particle size less than 200 nm). It showed a PDI Index (poly-disparity index) of less than 0.2 and drug entrapment efficiency of 85%. These gel based NLCs have the advantage of desired rheological behavior and texture profile that ensures an exceptional spreadability of drug at the inflammatory site. During In Vitro examination, it exhibits a rapid release of less than 50% of drug within 8 hours and sustained release up to 85% during 48 hours release time (Garg *et al.,* 2016). Pro-inflammatory markers like Interleukin-6 **(**IL-6**),** Interleukin-1 beta **(**IL-1β**),** Tumour necrosis factor-alpha (TNF-α), ESR (erythrocyte sedimentation rate) and C-reactive protein (CRP) were decreased (Pal *et al.,* 2023).

A novel ethosomal capsaicin for arthritis treatment in rats was developed, which showed a reduction in paw edema and provided strong antinociceptive effects. No adverse effects, such as skin irritation, swelling, burning, etc., were observed, which suggests the safety of the ethosomal capsaicin formulation (Kumar Sarwa *et al.,* 2015). In the early 1990s, SLNs were introduced, containing a variety of lipids like monoglycerides, diglycerides, and triglycerides, which can entrap drugs in their lipid matrix. Piperine-loaded SLNs were prepared and found to exhibit anti-arthritic properties when administered orally or topically to rats. It concluded a reduction in TNF-α levels attributed to the disease-modifying anti-rheumatic effects of piperine. Various biological markers, such as reduced blood leukocyte count, decreased oxidative stress, lowered levels of TNF-α, C-reactive protein and antibodies were observed (Janakiraman *et al.,* 2018). A polymeric gel of curcumin (CUR-NLC) was developed intra-articular administration using hot homogenization melt ultra-sonication method, containing Captex 200, cetylpalmitate, Labrafac PG, Labrasol & Tween 80. This smart gel was characterized to exhibit 165.12 nm particle size, 72.15% entrapment efficiency, and -21.67 mV zeta potential. Optimization was done to check the sol-gel transition at 33.21°C with 94.32% drug release over 84 hours, which explains its transition at body temperature, facilitating easy application and sustained drug release. It also possess favorable characteristics, such as appropriate particle size and high drug entrapment efficiency (Shinde *et al.,* 2021). (Figure 1)

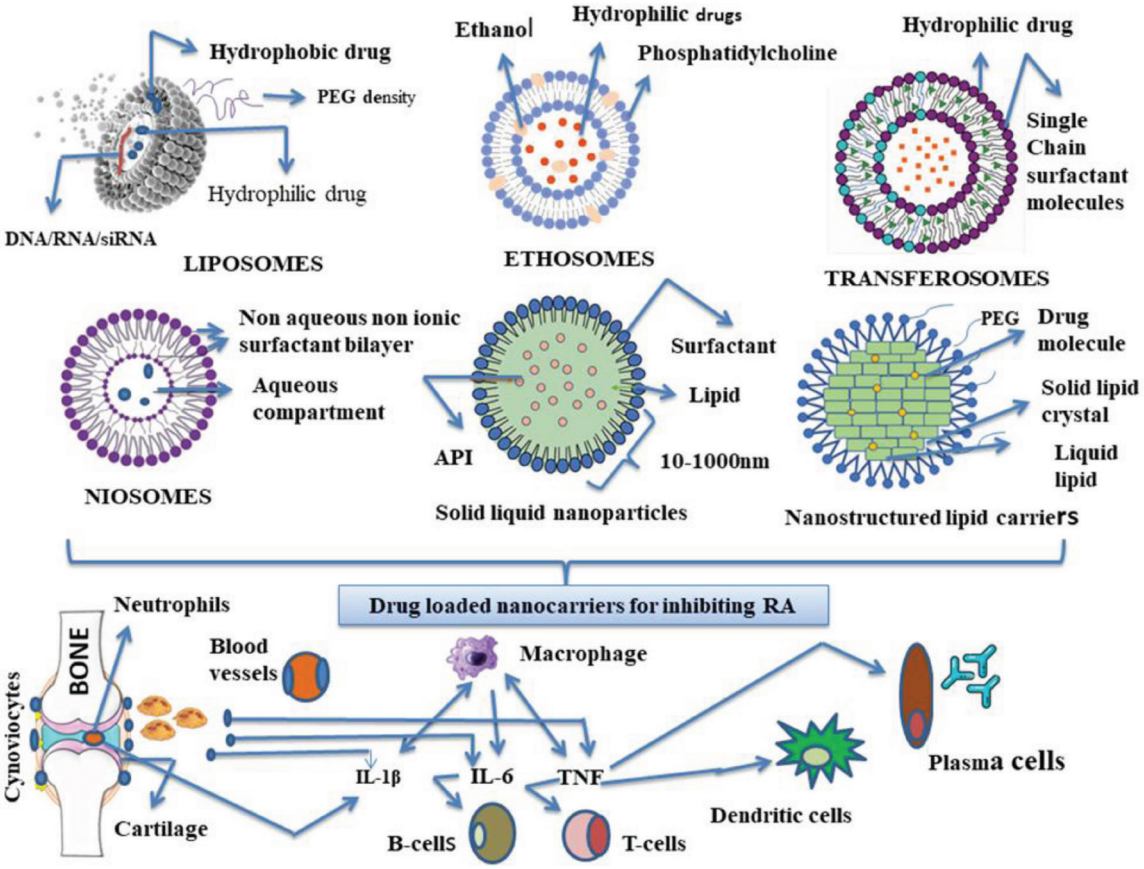

Figure 1: Various lipid nanocarrier systems used for the treatment of rheumatoid arthritis disease

3.2. Psoriasis

Psoriasis is an inflammatory skin disorder caused by a variety of factors like genetic variation, age, and environmental factors like microbial infections (Bacteria- Staphylococcus aureus, Propionibacterium acnes, Streptococcus pneumonia & Streptococcus pyogenes, viruses- endogenous retroviruses, herpes simplex virus (HSV), hepatitis c virus (HCV) & human papillomavirus, fungi- dermatophytes, candida species (Candida albicans & Malassezia). Along with this, medications also affect about 2% of the population with differences based on skin types. It does not only affect the skin but also

impacts the joints and other organs, suggesting a systemic nature (Campanati *et al.,* 2021). Patients suffering from Psoriasis exhibit increased risks of hyperlipidemia, hypertension (HPT), coronary artery disease (CAD), type-2 diabetes and obesity, with a higher occurrence of many metabolic syndromes in the body. It is highly associated with gastrointestinal, chronic kidney diseases, liver diseases, and inflammatory bowel conditions like Crohn's disease. Dendritic cells, which can potentiate disease initiation, may activate through recognition of antimicrobial peptides overexpressed in psoriatic skin, including LL37, β-defensins, and S100 proteins (Capon *et al.,* 2012). Treatment includes traditional medications like Methotrexate and Cyclosporine-A, along with modern targeted biological drugs based on the severity, from topical agents for mild cases to systemic therapies for moderate to severe psoriasis (Armstrong *et al.,* 2020). Cationic liposomes loaded cyclosporine gel has been formulated for the topical treatment of psoriasis. This gel can enhance the drug retention on the affected skin area and improve the drug bioavailability which can more effectively inhibit the calcineurin on T-cells. It has shown enhanced stability and reduced psoriatic scaling compared to using cyclosporine alone (Walunj *et al.,* 2020).

Food and Drug Administration (FDA) has approved PUVA therapy for severe psoriasis, which combines psoralen with UV-A radiation. Psoralen is a naturally derived furacoumarin, specifically found in the seeds of Psoralea corylifolia. It has a photosensitizing activity that is why it is used for the treatment of psoriasis. Psoralen interacts with DNA and forms monoadducts upon UV-A exposure which leads to apoptosis. This conventional treatment with psoralen suffers from low skin deposition and poor tissue permeability, along with the sensation of burning and tissue pigmentation, which ultimately hinders PUVA's effectiveness and safety. Due to this, a study was conducted to enhance the effectiveness and safety of topical PUVA therapy for severe psoriasis by formulating psoralen-loaded liposomal nanocarriers. In this study skin penetration and permeation studies demonstrated significant enhancement with liposomal carriers compared to the normal solution (Doppalapudi *et al*., 2017). Nano lipid carrier containing dithranol encapsulated in a gel has been developed to assess its effectiveness against psoriasis compared to traditional ointments. In this, the hot melt homogenization method was employed to prepare dithranol-loaded NLCs. Various characterizations were performed to analyze them with respect to particle size and entrapment efficiency. This gel was applied to the imiquimod (IMQ)-induced psoriatic plaque model, and it showed a significant reduction in psoriasis symptoms, as confirmed by both Psoriasis Area Severity Index (PASI) scoring and enzyme-linked immunosorbent assay (ELISA) analysis of cytokines such as Interleukins-17, 22, 23, and Tumor Necrosis Factor-α (TNF-α) (Sathe *et al*., 2019). Recently a liposomal gel containing a dual loaded trans-retinoic acid (TRA) and betamethasone (BT) has been developed to treat psoriasis. It exhibited superior skin permeation and retention compared to free drugs. This dual-loaded liposomal gel effectively reduces epidermal thickness and cytokine levels (TNF-α & IL-6) upon topical application (Li *et al*., 2022).

It was found that in 20% of the population, skin irritation was a prominent side effect when patients were treated with calcipotriol (CAL), which is a synthetic form of vitamin D. Later on, CAL was combined with multiple combinations of drugs to see whether these side effects were seen or not. A formulation incorporating calcipotriol and methotrexate (MTX) within nanostructured lipid carriers (CAL-MTX-NLCs) was formulated for psoriasis management. It was observed that incorporating MTX resulted in decreased release and permeation of CAL as compared to MTX. Along with that, MTX displayed enhanced release efficiency and 2.4–4.4 times higher permeation, when incorporated into NLCs compared to the control group (Lin *et al*., 2010). Similarly, a derivative of vitamin- A known as acitretin (ACT) was administered orally to address persistent psoriasis in adults. However, its use has been reduced due to various systemic side effects and increased risk of birth defects. When it is administered topically, it possesses a few challenges, such as low water solubility, skin irritation, and environmental instability, which ultimately impact patient acceptance. These challenges were addressed by developing a nanostructured lipid carrier of acitretin for psoriasis, combining ACT-NLCs into a 1% w/w carbopol 934 P gel, and tests on human cadaver skin (HCS) were conducted to assess in vitro skin deposition. Study revealed comparatively higher drug deposition, with 81.38% from the ACT-NLC gel compared to 47.28% from plain ACT gel (Agrawal *et al.*, 2010). Another approach for the treatment of psoriasis was to optimize niosomes through customized formulations exploring their versatility, enabling tailored drug release and skin permeation. In this a niosomes loaded with cyclosporine and pentoxifylline were studied and based on box-behnken design, it was successfully formulated with favorable characteristics. Drug permeation, predominant retention in the skin layer, and marked improvement in histopathology were successfully confirmed in In Vitro & In Vivo studies. Benefits associated with the niosomes as effective carriers for co-delivery were confirmed, offering enhanced therapeutic outcomes for psoriasis while potentially mitigating cyclosporine's systemic side effects (Bhardwaj *et al.*, 2022). (Figure 2)

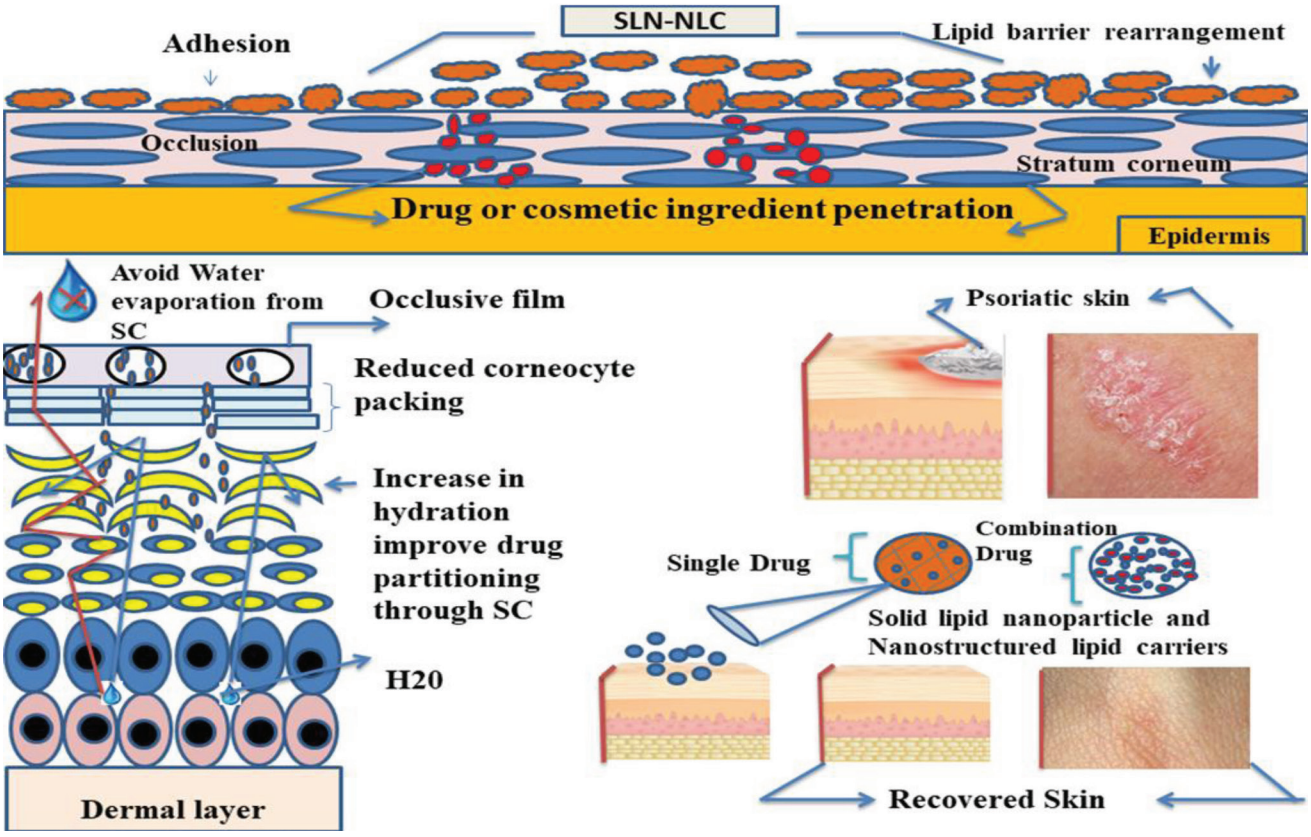

Figure 2: Permeation of LCs through psoriatic skin and recovery

3.3. Inflammatory bowel disease (IBD)

Inflammatory bowel diseases (IBD) are a group of chronic inflammatory conditions affecting the digestive tract, including Crohn's disease (any part of GI tract-mouth to anus) and ulcerative colitis (colon & rectum). These diseases are characterized by unpredictable flare-ups, causing symptoms such as abdominal pain, diarrhoea, fatigue, and weight loss (Bruner *et al.,* 2023). After several advances in conventional treatments like immunosuppressants and anti-inflammatory drugs, many patients still experience inadequate symptom control and uncontrolled side effects (Day & Lemberg, 2020). Recently, lipid nanocarriers have emerged as a promising treatment for the management of acute or chronic IBD. These nanocarriers consist of lipids, which are the natural components of the cell membranes. They possess better tissue compatibility and are well tolerated by the body. A small size range helps for targeted delivery to the tainted arrears of the gut (Yasmin *et al.,* 2022). In these lipid compartments, various drugs can be entrapped including anti-inflammatory agents, immunomodulatory, peptides, and antibiotics. They are released when triggered by environmental stimuli, such as pH, enzymes, in the inflamed gut. Clinical studies have shown significant results with lipid nanocarriers in IBD management, which results in an improved disease activity scores, reduced inflammation and enhanced patient quality of life (Yang & Merlin, 2019).

Curcumin (CC) loaded lipid based nanocarriers have been prepared to access its therapeutic potential in inflammatory bowel disease. The study was aimed to assess the efficacy of 3 distinct lipid-based nanocarriers: self-nanoemulsifying drug delivery systems (SNEDDS), nanostructured lipid carriers (NLC), and lipid core-shell protamine nanocapsules (NC), all containing CC as an anti-inflammatory agent. During the In Vitro assessment, permeability of CC across the monolayer were compared which indicates a 30–fold higher permeability of CC compared to SNEDDS, indicating superior transport across the intestinal barrier. CC-SNEDDS and CC-NLC exhibited a reduction in TNF-α secretion by lipopolysaccharide-activated macrophages (J774 cells), expressing their potential anti-inflammatory effects (Beloqui *et al.,* 2016). USFDA has recently approved GRAS (generally regarded as safe) material to develop lipid nanocarriers encapsulating

cortisone (CRT). These NLCs were evaluated for their therapeutic efficacy against Dextran Sulphate Sodium (DSS) induced colitis in mice. It supports favourable physicochemical properties with a hydrodynamic diameter of 182 nm and high encapsulation efficacy. Therapeutic treatment with CRT-loaded NLCs regulates various disease activity index, weight variation and histological parameters in colitic mice. Besides this, they remarkably reduced the inflammation by inhibiting pro-inflammatory cytokines and down-regulation of the expression of inflammatory enzymes, such as cyclo-oxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS). From this, it was concluded that CRT-encapsulated NLCs efficiently manage the severity of colitis induced by DSS, focusing their potential as a promising therapeutic approach for inflammatory bowel diseases (Mishra *et al.,* 2023).

Recently, to target the inflamed tissues of the colon, the antioxidant and anti-inflammatory compound oleuropein (OLE) was encapsulated in the lipid compartments. This NLC-OLE formulation evinces enhanced efficacy in reducing TNF-α (Tumour Necrosis Factor alpha) secretion and intracellular reactive oxygen species (ROS) in activated macrophages compared to conventional OLE. It manifests superior anti-inflammatory effects, including reduction in the levels of TNF-α and IL-6, decreased neutrophil infiltration and improved colon histopathology (Huguet-Casquero *et al.,* 2020). Another approach to treat IBD is by designing α-tocopherol nanoemulsion (NE) stabilized by ascorbyl-2, 6-dipalmitate (ADP) for smart drug delivery of curcumin (CC) to the intestinal epithelium. A notable difference in the intracellular retention was expressed, which was characterized by their small size, negative surface charge, stability in gastrointestinal conditions and non-toxicity in Caco-2 cell models. A major reduction in the intracellular reactive oxygen species (ROS) levels reported its effective therapeutic potential for IBD treatment (Plaza-Oliver *et al.,* 2020). The Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) formulation which are thermodynamically and kinetically stable systems contain budesonide, they are prepared by mild agitation followed by successive aqueous media dilution, have shown ability in reducing inflammation correlated with IBD. SNEDDS consist of various amalgamated blend of lipids and surface-coating emulsions. Proficient drug permeability across biological membranes, facilitating rapid emulsion formation in the gastrointestinal tract (GIT) was shown by these lipid-based nanoparticles. This helps in maintaining the drug in a soluble state and due to their smaller droplet size, it easily expedites the drug transport through membranes, ultimately improving the oral bioavailability of drugs (Subramaniam *et al.,* 2023). (Figure 3)

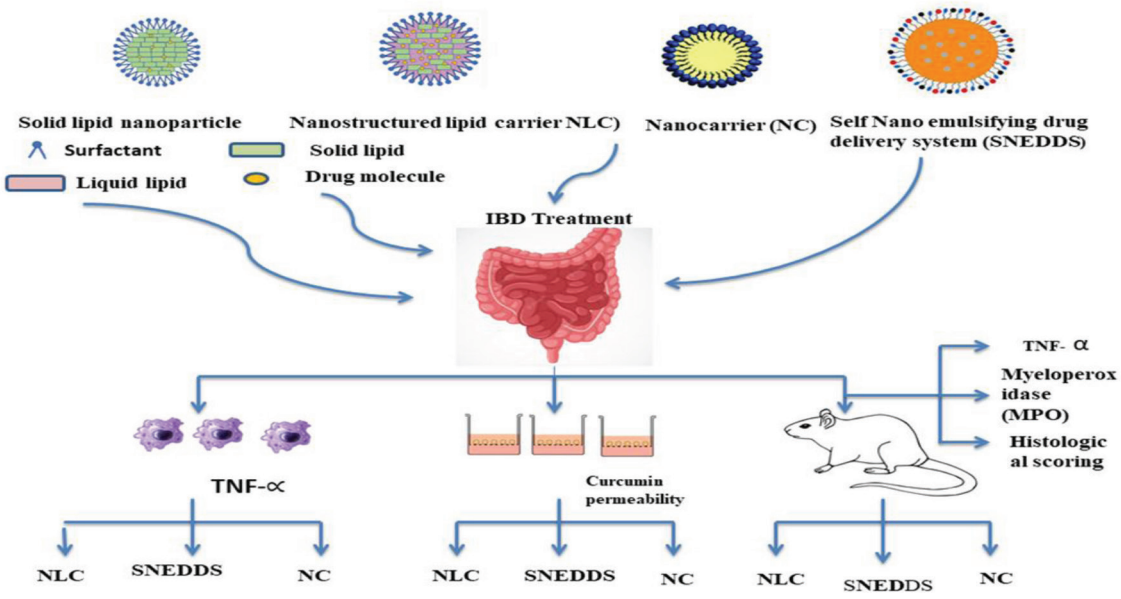

Figure 3: Various lipid-based nanocarriers in the treatment of IBD

3.4. Inflammation-mediated Respiratory Diseases

The lungs interfere directly with the outside world via air passages, comprising of two main sections, first being conducting zone encompassing the nasal passage (sinuses), trachea, bronchi and bronchioles and the second being the respiratory zone (RZ), the alveoli. Prevalent pulmonary diseases globally are tuberculosis, lung cancer, respiratory

infections, asthma, and COPD, collectively exhibiting severity and fatality risks (Cukic *et al.,* 2012). Asthma impacts approximately 262 million individuals worldwide and stands as a pervasive obstructive respiratory condition, while COPD is characterized by airflow obstruction, which ranks as the third leading cause of global mortality (Knight, 2020). Bronchodilators are commonly employed to alleviate constricted bronchial passages and treat the underlying diseases. It includes both long-acting and short-acting beta-2 agonists (LABAs and SABAs), which act upon β-2 receptors to relax airway smooth muscles (Li *et al.,* 2022). Presently the high use of corticosteroids like budesonide, fluticasone propionate, and cislesonide play a crucial role in reducing airway inflammation. Inhaled corticosteroids have proved more effective in asthma treatment but their application in COPD maintenance remains doubtful. Inhalation through open mouth method remains the primary route for administering single or combination of drugs through inhalers either metered or dry powders, which ensures enhanced local drug delivery and minimized systemic concentrations (Kahnert *et al.,* 2023). Despite the notable triumph of local drug delivery, overcoming biological barriers and robust clearance mechanisms poses a formidable challenge for researchers. Factors such as the mucus layer and ciliary clearance mechanisms in the airways restrict drug retention in the lungs. Therefore there is a growing interest in developing nanoparticle-encapsulated drug technologies to strive enhancing drug stability and retention at targeted airway sites (Leong & Ge, 2022).

For the treatment of asthma, lipid nanocapsules as a carrier for inhaled fluticasone propionate (FP) have been prepared, which show an encapsulation rate of up to 97%. Various factors like drug solubility in oil and water (O&W) and the oil/water (O/W) partition coefficient were studied and were found crucial for optimizing encapsulation behaviour. Nebulization is a critical step in inhalation therapy and these lipid nanocapsules didn't compromise FP retention within LNCs, and no phase separation occurred post-nebulization. After nebulizing the formulation, it didn't leak from the nanocapsules and stayed stable during treatment without separating into layers (Umerska *et al.,* 2015). It was found that those nanocapsules that were 100 nm wide, with less surfactant and more oil, held more of the medication and stayed stable better during nebulization than smaller ones. For COPD treatment, the therapeutic efficacy of berberine (Ber) encapsulated SLNs with chitosan was prepared. This system addressed a few limitations of berberine, which possesses low solubility and bioavailability. Various characterisations were performed, which confirmed the nano-sized particles with higher stability and controlled drug release properties. Further study was carried out to find the efficacy and compare the anti-inflammatory activity of Ber-loaded SLN chitosan nanoparticles and pure berberine in a cigarette smoke-induced COPD rat model. Based on Histopathological evaluation, it showed reduction in inflammation and decreased inflammatory cell counts and cytokine levels in (BALF) broncho-alveolar lavage fluid in lung tissues (Liu *et al.,* 2022). (Figure 4)

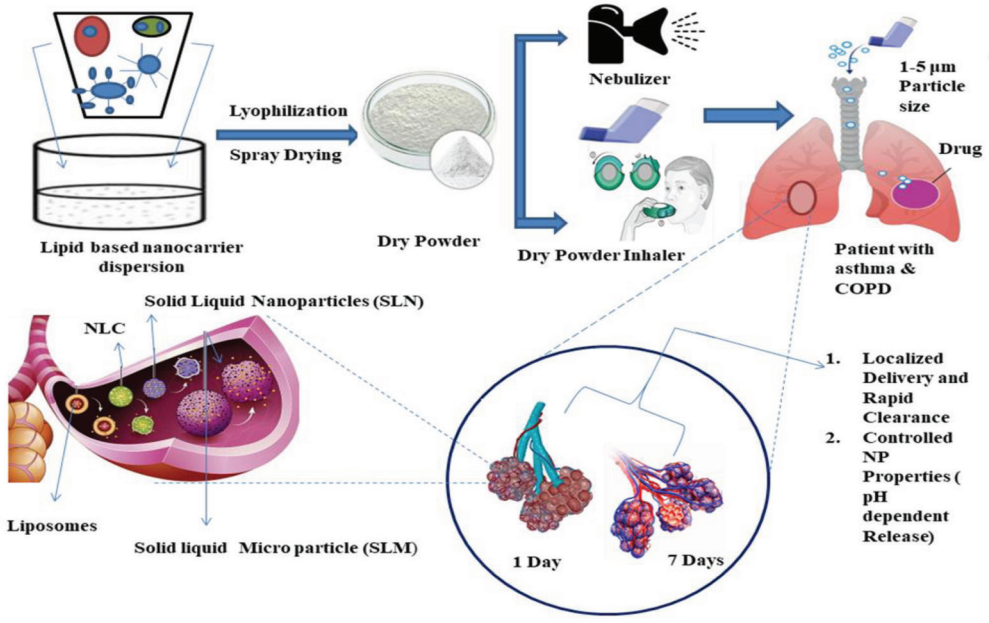

Figure 4: Lipid nanocarriers system for drug delivery in asthma and COPD

Inhalation is a favorable route of administration for pulmonary disorders due to its ability to directly target the affected areas of the lungs for sustained and targeted delivery at the site of inflammation. Myrtle is a traditional medicine, which contains myrtenol as a potent compound known for its antimicrobial, antioxidant, and healing properties (Alipour *et al.,* 2014). Niosomes possess a few advantages such as enhanced stability and the ability to target specific cells (goblet & basal cells), which is attributed to their unique design. PEGylation is the attachment of polyethylene glycol (PEG) to the surface of niosomes, that evade the immune system and play a crucial role in prolonging their circulation time in the bloodstream (Witika *et al.,* 2022). Myrtenol-loaded niosomes have been synthesized and tested in rats with allergic asthma, focusing on their anti-inflammatory, anti-oxidative, and anti-remodeling effects. Here the animals were exposed daily (for 1 week) to inhalation of drug/vehicle, following ovalbumin-induced asthma induction. It was observed that myrtenol-loaded niosomes exhibited favourable physicochemical properties. It caused reductions in nitric oxide (NO), interleukin-17 (IL-17), and malondialdehyde (MDA) levels, while increasing IL-10 and total antioxidant capacity (TAC) levels in tissue and/or BALF compared to control and other treatment groups (Rajizadeh *et al.,* 2019).

4. Limitations

Lipid nanocarriers face a few of the challenges that complicate their effective use in drug delivery, particularly in the context of chronic inflammatory conditions. One significant hurdle lies in achieving optimal drug loading and controlled release, especially for drugs with low lipid solubility, crucial for maintaining sustained therapeutic effects (Plaza-Oliver *et al.,* 2021). Stability is also an issue during storage and circulation, such as lipid oxidation, particle aggregation, and drug leakage (John *et al.,* 2024). It precisely targets the specific sites within inflamed tissues or cells within inflammatory lesions, but the mechanism is complex due to the dynamic and heterogeneous nature of these environments. Moreover, the mucosal barrier in the gastrointestinal tract can impede the effective penetration of nanolipid carriers, which ultimately hinders the drug delivery to inflamed tissues, which in response may trigger immune responses in the gastrointestinal tract, potentially exacerbating inflammation in patients with inflammatory bowel disease (Rossi *et al.,* 2021). With the diverse characteristics of lung cells and the influence of airway structure on particle deposition, it has become crucial to overcome physiological and membrane barriers in the lungs for inhaled lipid nanoparticle formulations. Particle size and design considerations in aerosol delivery systems are essential for the effective targeting of respiratory areas affected by various diseases (Leong & Ge, 2022). To achieve targeted delivery to inflamed joints in rheumatoid arthritis, it could be challenging due to the factors like bio-distribution influenced by particle size and surface charge. The immune system recognises and clears the nanoparticles as foreign particles that may lead to immune responses, reducing therapy efficacy (Wen *et al.,* 2023; Pham, 2011). Due to their limited ability to penetrate thickened skin layers, there is variability in drug release kinetics and immunogenicity (Akombaetwa *et al.,* 2023). To address these challenges, it requires innovative approaches and careful consideration of various factors to optimize lipid nanocarrier based drug delivery systems for inflammatory conditions.

5. Conclusion

Inflammation is the body's natural mechanism to defend itself from harmful stimuli within the body or entering from the environment. However effective management of these conditions is required to prevent the onset of chronic inflammatory diseases. Due to the shortfall of conventional therapies that fail to address the underlying causes and may potentiate severe adverse effects (ulcer, bleeding, perforation of the GI tract, liver and renal toxicity, loss of appetite), there is a need to develop more precise and site targeted therapy (directly to the inflamed tissues) for such a condition that reaches the site of infection and cure. Nanotechnology, mainly second-generation lipid nanoparticles like SLNs, liposomes, Niosomes and NLCs, have transformed the drug delivery systems. They possess advantages such as improved drug solubility, controlled release, and targeted delivery to inflamed tissues. They have shown their efficacy in targeting a range of inflammatory diseases. In this review various lipid nanocarriers have been discussed that showed efficacy in the management of inflammatory diseases, along with the recent formulation, research findings, and application.

6. Future perspective

Lipid nanoparticle studies have demonstrated substantial potential, yet there are a few challenges to overcome before claiming clinical success. Despite extensive exploration into fabrication, modification, storage, and toxicity, challenges remain, particularly to scale up the production to ensure long-term stability and toxicity concerns. Solid lipid nanocarriers (SLNs) and nano-structure lipid carriers (NLCs) are the most effective lipid nanoparticles, that have undergone successful clinical trials conducted in the past five years and over 2000 patents filed globally. Lipid nanotechnology holds great promise in the fields of biomedical science, vaccine development, biomimetics, and therapeutics, particularly in

managing chronic inflammatory diseases. Future research aims to develop new lipid nanocarriers for targeted drug delivery, reducing inflammation and improving therapeutic outcomes. These efforts have to be focused on enhancing biocompatibility, optimizing formulations, and exploring novel applications to tackle the complexities of inflammatory disorders effectively.

Abbreviations

LNC: Lipid Nano Carriers; **IBD**: Inflammatory Bowel Disease; **COPD**: Chronic Obstructive Pulmonary Disease; **NSAIDs**: Non-Steroidal Anti-Inflammatory Drugs; **COX**: Cyclooxygenase; **SLN**: Solid Lipid Nanoparticles; **NLC**: Nano-Structured Lipid Carriers; **UA**: Ursolic Acid; **VL**: Visceral Leishmaniasis; **TNF**: Tumour Necrosis Factor; **MTX-NLCs**: Methotrexate-loaded Nanostructured Lipid Carriers; **MTX**: Methotrexate; **MRSA**: Methicillin-Resistant Staphylococcus Aureus; **ACE**: Aceclofenac; **Rhy**: Rhynchophylline; **MLVs**: Multilamellar Vesicles; **LUVs**: Large Unilamellar Vesicles; **SUVs**: Small Unilamellar Vesicles; **RA**: Rheumatoid Arthritis; **LNLC**: Leflunomide Nanostructured Lipid Carriers; **TQ-NLCs**: Tamanu Oil-Stabilized Nanostructured Lipid Carriers; **TNF-α**: Tumour Necrosis Factor Alpha; **CUR-NLC**: Curcumin Nanostructured Lipid Carriers; **PUVA**: Psoralen with UV-A; **FDA**: Food and Drug Administration; **PASI**: Psoriasis Area Severity Index; **ELISA**: Enzyme-Linked Immunosorbent Assay; **TRA**: Trans Retinoic Acid; **BT**: Betamethasone; **CAL**: Calcipotriol; **ACT**: Acitretin; **HCS**: Human Cadaver Skin; **CC**: Curcumin; **SNEDDS**: Self-Nanoemulsifying Drug Delivery Systems; **GRAS**: Generally Regarded as Safe; **USFDA**: United States Food and Drug Administration; **CRT**: Cortisone; **DSS**: Dextran Sulphate Sodium; **COX-2**: Cyclo-Oxygenase-2; **iNOS**: Inducible Nitric Oxide Synthase; **OLE**: Oleuropein; **ROS**: Reactive Oxygen Species; **NE**: Nanoemulsion; **ADP**: Ascorbyl-2,6-Dipalmitate; **GIT**: Gastrointestinal Tract; **LABAs**: Long-Acting Beta-2 Agonists; **SABAs**: Short-Acting Beta-2 Agonists; **FP**: Fluticasone Propionate; **LNCs**: Lipid Nanocapsules; **BALF**: Broncho-Alveolar Lavage Fluid; **PEG**: Polyethylene Glycol; **NO**: Nitric Oxide; **IL-17**: Interleukin-17; **MDA**: Malondialdehyde; **TAC**: Total Antioxidant Capacity.

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References

Abdelkader, H., Alani, A. W., & Alany, R. G. (2014). Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. *Drug delivery*, *21*(2), 87–100. https://doi.org/10.3109/10717544.2013.838077

Agrawal, Y. O., Mahajan, U. B., Mahajan, H. S., & Ojha, S. (2020). Methotrexate-Loaded Nanostructured Lipid Carrier Gel Alleviates Imiquimod-Induced Psoriasis by Moderating Inflammation: Formulation, Optimization, Characterization, In-Vitro and In-Vivo Studies. *International journal of nanomedicine*, *15*, 4763–4778. https://doi.org/10.2147/IJN.S247007

Agrawal, Y., Petkar, K. C., & Sawant, K. K. (2010). Development, evaluation and clinical studies of Acitretin loaded nanostructured lipid carriers for topical treatment of psoriasis. *International journal of pharmaceutics*, *401*(1-2), 93–102. https://doi.org/10.1016/j.ijpharm.2010.09.007

Aib, S., Iqbal, K., Khan, N., Khalid, S., Adnan, M., Umair, S. M., & Dar, M. J. (2022). pH-sensitive liposomes for colonic co-delivery of mesalazine and curcumin for the treatment of ulcerative colitis. *Journal of Drug Delivery Science and Technology*, *72*, 103335. https://doi.org/10.1016/j.jddst.2022.103335

Akombaetwa, N., Ilangala, A. B., Thom, L., Memvanga, P. B., Witika, B. A., & Buya, A. B. (2023). Current Advances in Lipid Nanosystems Intended for Topical and Transdermal Drug Delivery Applications. *Pharmaceutics*, *15*(2), 656. https://doi.org/10.3390/pharmaceutics15020656

Algahtani, M. S., Ahmad, M. Z., & Ahmad, J. (2020). Nanoemulsion loaded polymeric hydrogel for topical delivery of curcumin in psoriasis. *Journal of Drug Delivery Science and Technology*, *59*, 101847. https://doi.org/10.1016/j.jddst.2020.101847

Alipour, G., Dashti, S., & Hosseinzadeh, H. (2014). Review of pharmacological effects of Myrtuscommunis L. and its active constituents. *Phytotherapy research: PTR*, *28*(8), 1125–1136. https://doi.org/10.1002/ptr.5122

Armstrong, A. W., & Read, C. (2020). Pathophysiology, clinical presentation, and treatment of psoriasis: a review. *Jama*, *323*(19), 1945-1960. https://doi.org/10.1001/jama.2020.4006

Bayón-Cordero, L., Alkorta, I., & Arana, L. (2019). Application of Solid Lipid Nanoparticles to Improve the Efficiency of Anticancer Drugs. *Nanomaterials (Basel, Switzerland)*, *9*(3), 474. https://doi.org/10.3390/nano9030474

Beloqui, A., Memvanga, P. B., Coco, R., Reimondez-Troitiño, S., Alhouayek, M., Muccioli, G. G., Alonso, M. J., Csaba, N., de la Fuente, M., & Préat, V. (2016). A comparative study of curcumin-loaded lipid-based nanocarriers in the treatment of inflammatory bowel disease. *Colloids and surfaces. B, Biointerfaces*, *143*, 327–335. https://doi.org/10.1016/j.colsurfb.2016.03.038

Bhardwaj, P., Tripathi, P., Pandey, S., Gupta, R., & Patil, P. R. (2022). Cyclosporine and pentoxifylline laden tailored niosomes for the effective management of psoriasis: in-vitro optimization, ex-vivo and animal study. *International Journal of Pharmaceutics*, *626*, 122143. https://doi.org/10.1016/j.ijpharm.2022.122143

Bruner, L. P., White, A. M., & Proksell, S. (2023). Inflammatory Bowel Disease. *Primary care*, *50*(3), 411–427. https://doi.org/10.1016/j.pop.2023.03.009

Campanati, A., Marani, A., Martina, E., Diotallevi, F., Radi, G., & Offidani, A. (2021). Psoriasis as an Immune-Mediated and Inflammatory Systemic Disease: From Pathophysiology to Novel Therapeutic Approaches. *Biomedicines*, *9*(11), 1511. https://doi.org/10.3390/biomedicines9111511

Capon, F., Burden, A. D., Trembath, R. C., & Barker, J. N. (2012). Psoriasis and other complex trait dermatoses: from Loci to functional pathways. *Journal of investigative dermatology*, *132*(3), 915-922. https://doi.org/10.1038/jid.2011.395

Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., ... & Zhao, L. (2018). Inflammatory responses and inflammation-associated diseases in organs. *Oncotarget*, *9*(6), 7204. https://doi.org/10.18632/oncotarget.23208

Cho, S. K., Kim, D., Won, S., Lee, J., Choi, C. B., Choe, J. Y., Hong, S. J., Jun, J. B., Kim, T. H., Koh, E., Lee, H. S., Lee, J., Yoo, D. H., Yoon, B. Y., Bae, S. C., & Sung, Y. K. (2019). Factors associated with time to diagnosis from symptom onset in patients with early rheumatoid arthritis. *The Korean journal of internal medicine*, *34*(4), 910–916. https://doi.org/10.3904/kjim.2017.113

Cukic, V., Lovre, V., Dragisic, D., & Ustamujic, A. (2012). Asthma and Chronic Obstructive Pulmonary Disease (COPD) - Differences and Similarities. *Materia socio-medica*, *24*(2), 100–105. https://doi.org/10.5455/msm.2012.24.100-105

Das, S., Ghosh, S., De, A. K., & Bera, T. (2017). Oral delivery of ursolic acid-loaded nanostructured lipid carrier coated with chitosan oligosaccharides: Development, characterization, in vitro and in vivo assessment for the therapy of leishmaniasis. *International journal of biological macromolecules*, *102*, 996–1008. https://doi.org/10.1016/j.ijbiomac.2017.04.098

Day, A. S., & Lemberg, D. A. (2020). Identification and diagnosis of Crohn disease and ulcerative colitis in children. *Journal of paediatrics and child health*, *56*(11), 1731–1734. https://doi.org/10.1111/jpc.14925

Dianzani, C., Foglietta, F., Ferrara, B., Rosa, A. C., Muntoni, E., Gasco, P., ... & Serpe, L. (2017). Solid lipid nanoparticles delivering anti-inflammatory drugs to treat inflammatory bowel disease: Effects in an in vivo model. *World journal of gastroenterology*, *23*(23), 4200. https://doi.org/10.3748/wjg.v23.i23.4200

Doktorovova, S., Kovačević, A. B., Garcia, M. L., & Souto, E. B. (2016). Preclinical safety of solid lipid nanoparticles and nanostructured lipid carriers: Current evidence from in vitro and in vivo evaluation. *European Journal of Pharmaceutics and Biopharmaceutics*, *108*, 235-252. https://doi.org/10.1016/j.ejpb.2016.08.001

Doppalapudi, S., Jain, A., Chopra, D. K., & Khan, W. (2017). Psoralen loaded liposomal nanocarriers for improved skin penetration and efficacy of topical PUVA in psoriasis. *European journal of pharmaceutical sciences: official journal of the European Federation for Pharmaceutical Sciences*, *96*, 515–529. https://doi.org/10.1016/j.ejps.2016.10.025

Ferrara, G., Petrillo, M. G., Giani, T., Marrani, E., Filippeschi, C., Oranges, T., Simonini, G., & Cimaz, R. (2019). Clinical Use and Molecular Action of Corticosteroids in the Pediatric Age. *International journal of molecular sciences*, *20*(2), 444. https://doi.org/10.3390/ijms20020444

Garg, N. K., Tandel, N., Bhadada, S. K., & Tyagi, R. K. (2021). Nanostructured Lipid Carrier-Mediated Transdermal Delivery of Aceclofenac Hydrogel Present

an Effective Therapeutic Approach for Inflammatory Diseases. *Frontiers in pharmacology*, *12*, 713616. https://doi.org/10.3389/fphar.2021.713616

Garg, N. K., Tyagi, R. K., Singh, B., Sharma, G., Nirbhavane, P., Kushwah, V., ... & Katare, O. P. (2016). Nanostructured lipid carrier mediates effective delivery of methotrexate to induce apoptosis of rheumatoid arthritis via NF-κB and FOXO1. *International journal of pharmaceutics*, *499*(1-2), 301-320. https://doi.org/10.1016/j.ijpharm.2015.12.061

Ge, X., Wei, M., He, S., & Yuan, W. E. (2019).Advances of Non-Ionic Surfactant Vesicles (Niosomes) and Their Application in Drug Delivery. *Pharmaceutics*, *11*(2), 55. https://doi.org/10.3390/pharmaceutics11020055

Ghasemiyeh, P., & Mohammadi-Samani, S. (2018). Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages. *Research in pharmaceutical sciences*, *13*(4), 288–303. https://doi.org/10.4103/1735-5362.235156

Gordillo-Galeano, A., & Mora-Huertas, C. E. (2018). Solid lipid nanoparticles and nanostructured lipid carriers: A review emphasizing on particle structure and drug release. *European Journal of Pharmaceutics and Biopharmaceutics*, *133*, 285-308. https://doi.org/10.1016/j.ejpb.2018.10.017

Guo, Q., Wang, Y., Xu, D., Nossent, J., Pavlos, N. J., & Xu, J. (2018). Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. *Bone research*, *6*, 15. https://doi.org/10.1038/s41413-018-0016-9

Honmane, S., Hajare, A., More, H., Osmani, R. A. M., & Salunkhe, S. (2019). Lung delivery of nanoliposomal salbutamol sulfate dry powder inhalation for facilitated asthma therapy. *Journal of liposome research*, *29*(4), 332-342. https://doi.org/10.1080/08982104.2018.1531022

Huguet-Casquero, A., Xu, Y., Gainza, E., Pedraz, J. L., & Beloqui, A. (2020). Oral delivery of oleuropein-loaded lipid nanocarriers alleviates inflammation and oxidative stress in acute colitis. *International journal of pharmaceutics*, *586*, 119515. https://doi.org/10.1016/j.ijpharm.2020.119515

Hussein, J., El-Bana, M. A., El-kHayat, Z., El-Naggar, M. E., Farrag, A. R., & Medhat, D. (2022). Eicosapentaenoic acid loaded silica nanoemulsion attenuates hepatic inflammation through the enhancement of cell membrane components. *Biological procedures online*, *24*(1), 11. https://doi.org/10.1186/s12575-022-00173-z

Janakiraman, K., Krishnaswami, V., Rajendran, V., Natesan, S., & Kandasamy, R. (2018). Novel nano therapeutic materials for the effective treatment of rheumatoid arthritis-recent insights. *Materials today. Communications*, *17*, 200–213. https://doi.org/10.1016/j.mtcomm.2018.09.011

John, R., Monpara, J., Swaminathan, S., & Kalhapure, R. (2024). Chemistry and Art of Developing Lipid Nanoparticles for Biologics Delivery: Focus on Development and Scale-Up. *Pharmaceutics*, *16*(1), 131. https://doi.org/10.3390/pharmaceutics16010131

Kahnert, K., Jörres, R. A., Behr, J., & Welte, T. (2023). The Diagnosis and Treatment of COPD and Its Comorbidities. *DeutschesArzteblatt international*, *120*(25), 434–444. https://doi.org/10.3238/arztebl.m2023.027

Kaur, N., Sharma, K., & Bedi, N. (2018). Topical Nanostructured Lipid Carrier Based Hydrogel of Mometasone Furoate for the Treatment of Psoriasis. *Pharmaceutical nanotechnology*, *6*(2), 133–143. https://doi.org/10.2174/2211738506666180523112513

Kaur, S., Goyal, A., Rai, A., Sharma, A., Ugoeze, K.C. & Singh, I. (2023). Quercetin nanoformulations: recent advancements and therapeutic applications. *Advances in Natural Sciences: Nanoscience and Nanotechnology*, *14*(3), p.033002. https://doi.org10.1088/2043-6262/acedaa

Kazi, K. M., Mandal, A. S., Biswas, N., Guha, A., Chatterjee, S., Behera, M., & Kuotsu, K. (2010).Niosome: A future of targeted drug delivery systems. *Journal of advanced pharmaceutical technology & research*, *1*(4), 374–380. https://doi.org/10.4103/0110-5558.76435

Knight A. (2020). Managing the overlap of asthma and chronic obstructive pulmonary disease. *Australian prescriber*, *43*(1), 7–11. https://doi.org/10.18773/austprescr.2020.002

Krishnan, Y., Mukundan, S., Akhil, S., Gupta, S., & Viswanad, V. (2018). Enhanced Lymphatic Uptake of Leflunomide Loaded Nanolipid Carrier via Chylomicron Formation for the Treatment of Rheumatoid Arthritis. *Advanced pharmaceutical bulletin*, *8*(2), 257–265. https://doi.org/10.15171/apb.2018.030

Kumar Sarwa, K., Rudrapal, M., & Mazumder, B. (2015). Topical ethosomal capsaicin attenuates edema and nociception in arthritic rats. *Drug delivery*, *22*(8), 1043–1052. https://doi.org/10.3109/10717544.2013.861041

Lei, F., Zeng, F., Yu, X., Deng, Y., Zhang, Z., Xu, M., ... & Li, C. (2023). Oral hydrogel nanoemulsion co-delivery system treats inflammatory bowel disease via anti-inflammatory and promoting intestinal mucosa repair. *Journal of Nanobiotechnology*, *21*(1), 275. https://doi.org/10.1186/s12951-023-02045-4

Leong, E. W. X., & Ge, R. (2022). Lipid Nanoparticles as Delivery Vehicles for Inhaled Therapeutics. *Biomedicines*, *10*(9), 2179. https://doi.org/10.3390/biomedicines10092179

Li, N., Qin, Y., Dai, D., Wang, P., Shi, M., Gao, J., Yang, J., Xiao, W., Song, P., & Xu, R. (2022). Transdermal Delivery of Therapeutic Compounds With Nanotechnological Approaches in Psoriasis. *Frontiers in bioengineering and biotechnology*, *9*, 804415. https://doi.org/10.3389/fbioe.2021.804415

Li, Y., Ji, Z., Wang, Y., Li, X., & Xie, Y. (2022). Breathing Exercises in the Treatment of COPD: An Overview of Systematic Reviews. *International journal of chronic obstructive pulmonary disease*, *17,* 3075–3085. https://doi.org/10.2147/COPD.S385855

Liao, C. C., Yu, H. P., Yang, S. C., Alalaiwe, A., Dai, Y. S., Liu, F. C., & Fang, J. Y. (2021). Multifunctional lipid-based nanocarriers with antibacterial and anti-inflammatory activities for treating MRSA bacteremia in mice. *Journal of nanobiotechnology*, *19*(1), 48. https://doi.org/10.1186/s12951-021-00789-5

Lin, Y. K., Huang, Z. R., Zhuo, R. Z., & Fang, J. Y. (2010). Combination of calcipotriol and methotrexate in nanostructured lipid carriers for topical delivery. *International journal of nanomedicine*, *5*, 117–128. https://doi.org/10.2147/ijn.s9155

Liu, H., Li, Y., Zhang, X., Shi, M., Li, D., & Wang, Y. (2022). Chitosan-Coated Solid Lipid Nano-Encapsulation Improves the Therapeutic Antiairway Inflammation Effect of Berberine against COPD in Cigarette Smoke-Exposed Rats. *Canadian respiratory journal*, 2022, 8509396. https://doi.org/10.1155/2022/8509396

Lv, C., Li, H., Cui, H., Bi, Q., & Wang, M. (2021). Solid lipid nanoparticle delivery of rhynchophylline enhanced the efficiency of allergic asthma treatment via the upregulation of suppressor of cytokine signaling 1 by repressing the p38 signaling pathway. *Bioengineered*, *12*(1), 8635-8649. https://doi.org/10.1080/21655979.2021.1988364

Marinho, S., Illanes, M., Ávila-Román, J., Motilva, V., & Talero, E. (2021). Anti-inflammatory effects of rosmarinic acid-loaded nanovesicles in acute colitis through modulation of NLRP3 inflammasome. *Biomolecules*, 11(2), *162*. https://doi.org/10.3390/biom11020162

Mishra, R. K., Ahmad, A., Kumar, A., Ali, A., Kanika, Jori, C., Tabrez, S., Zughaibi, T. A., Almashjary, M. N., Raza, S. S., & Khan, R. (2023). Cortisone-loaded stearoyl ascorbic acid based nanostructured lipid carriers alleviate inflammatory changes in DSS-induced colitis. *Biomaterials advances*, *148*, 213383. https://doi.org/10.1016/j.bioadv.2023.213383

Mishra, R. K., Ahmad, A., Kumar, A., Vyawahare, A., Raza, S. S., & Khan, R. (2020). Lipid-based nanocarrier-mediated targeted delivery of celecoxib attenuate severity of ulcerative colitis. *Materials science & engineering. C, Materials for biological applications*, *116*, 111103. https://doi.org/10.1016/j.msec.2020.111103

Müller, R. H., Shegokar, R., & Keck, C. M. (2011). 20 years of lipid nanoparticles (SLN and NLC): present state of development and industrial applications. *Current drug discovery technologies*, *8*(3), 207–227. https://doi.org/10.2174/157016311796799062

Nsairat, H., Khater, D., Sayed, U., Odeh, F., Al Bawab, A., & Alshaer, W. (2022). Liposomes: structure, composition, types, and clinical applications. *Heliyon*, *8*(5), e09394. https://doi.org/10.1016/j.heliyon.2022.e09394

Nyandoro, V. O., Omolo, C. A., Ismail, E. A., Yong, L., & Govender, T. (2023). Inflammation-responsive drug delivery nanosystems for treatment of bacterial-induced sepsis. *International journal of pharmaceutics*, *644*, 123346. https://doi.org/10.1016/j.ijpharm.2023.123346

Olival, A., Vieira, S. F., Gonçalves, V. M. F., Cunha, C., Tiritan, M. E., Carvalho, A., Reis, R. L., Ferreira, H., & Neves, N. M. (2022). Erythrocyte-derived liposomes for the treatment of inflammatory diseases. *Journal of drug targeting*, *30*(8), 873–883. https://doi.org/10.1080/1061186X.2022.2066107

Pal, R. R., Rajpal, V., Singh, N., Singh, S., Mishra, N., Singh, P., Maurya, P., Alka, &Saraf, S. A. (2023). Downregulation of pro-inflammatory markers IL-6 and TNF-α in rheumatoid arthritis using nano-lipidic carriers of a quinone-based phenolic: an in vitro and in vivo study. *Drug delivery and translational research*, *13*(2), 627–641. https://doi.org/10.1007/s13346-022-01221-7

Paradkar, M., & Vaghela, S. (2018). Thiocolchicoside niosomal gel formulation for the pain management of rheumatoid arthritis through topical drug delivery. *Drug Delivery Letters*, *8*(2), 159-168. https://doi.org/10.2174/2210303108666180216151234

Pham, C. T. (2011). Nanotherapeutic approaches for the treatment of rheumatoid arthritis. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, *3*(6), 607-619. https://doi.org/10.1002/wnan.157

Plaza-Oliver, M., Beloqui, A., Santander-Ortega, M. J., Castro-Vázquez, L., Rodríguez-Robledo, V., Arroyo-Jiménez, M. M., Préat, V., & Lozano, M. V. (2020). Ascorbyl-dipalmitate-stabilised nanoemulsions as a potential localised treatment of inflammatory bowel diseases. *International journal of pharmaceutics*, *586*, 119533. https://doi.org/10.1016/j.ijpharm.2020.119533

Plaza-Oliver, M., Santander-Ortega, M. J., & Lozano, M. V. (2021). Current approaches in lipid-based nanocarriers for oral drug delivery. *Drug delivery and translational research*, *11*(2), 471–497. https://doi.org/10.1007/s13346-021-00908-7

Preeti, Sambhakar, S., Malik, R., Bhatia, S., Al Harrasi, A., Rani, C., Saharan, R., Kumar, S., Geeta, & Sehrawat, R. (2023). Nanoemulsion: An Emerging Novel Technology for Improving the Bioavailability of Drugs. *Scientifica*, *2023*, 6640103. https://doi.org/10.1155/2023/6640103

Raj, S., & Unsworth, L. D. (2023). Targeting active sites of inflammation using inherent properties of tissue-resident mast cells. *Acta biomaterialia*, *159*, 21–37. https://doi.org/10.1016/j.actbio.2023.01.024

Rajizadeh, M. A., Najafipour, H., SamarehFekr, M., Rostamzadeh, F., Jafari, E., Bejeshk, M. A., & Masoumi-Ardakani, Y. (2019). Anti-Inflammatory and Anti-Oxidative Effects of Myrtenol in the Rats with Allergic Asthma. *Iranian journal of pharmaceutical research: IJPR*, *18*(3), 1488–1498. https://doi.org/10.22037/ijpr.2019.1100749

Rajizadeh, M. A., Nematollahi, M. H., Jafari, E., Bejeshk, M. A., Mehrabani, M., Razeghinia, M. S., & Najafipour, H. (2023). Niosome nanocarrier enhances the ameliorating effects of myrtenol in the lungs of rats with experimental asthma. *OpenNano*, *11*, 100129. https://doi.org/10.1016/j.onano.2023.100129

Rapalli, V. K., Kaul, V., Waghule, T., Gorantla, S., Sharma, S., Roy, A., Dubey, S. K., & Singhvi, G. (2020). Curcumin loaded nanostructured lipid carriers for enhanced skin retained topical delivery: optimization, scale-up, in-vitro characterization and assessment of ex-vivo skin deposition. *European journal of pharmaceutical sciences: official journal of the European Federation for Pharmaceutical Sciences*, *152*, 105438. https://doi.org/10.1016/j.ejps.2020.105438

Rathi, R., Kaur, S., Chopra, H., Kaur, M., Kumar, S. & Singh, I. (2024). Advancements in microsponges for the management of vaginal and colorectal diseases: A comprehensive review. *Applied Chemical Engineering*, 2334-2334. 10.59429/ace.v7i2.2334

Rinaldi, F., Del Favero, E., Rondelli, V., Pieretti, S., Bogni, A., Ponti, J., Rossi, F., Di Marzio, L., Paolino, D., Marianecci, C., & Carafa, M. (2017).pH-sensitive niosomes: Effects on cytotoxicity and on inflammation and pain in murine models. *Journal of enzyme inhibition and medicinal chemistry*, *32*(1), 538–546. https://doi.org/10.1080/14756366.2016.1268607

Rizvi, S. A. A., & Saleh, A. M. (2018).Applications of nanoparticle systems in drug delivery technology. *Saudi pharmaceutical journal: SPJ : the official publication of the Saudi Pharmaceutical Society*, *26*(1), 64–70. https://doi.org/10.1016/j.jsps.2017.10.012

Roe, K. (2021). An inflammation classification system using cytokine parameters. *Scandinavian journal of immunology*, *93*(2), e12970. https://doi.org/10.1111/sji.12970

Rossi, J. F., Lu, Z. Y., Massart, C., & Levon, K. (2021). Dynamic Immune/Inflammation Precision Medicine: The Good and the Bad Inflammation in Infection and Cancer. *Frontiers in immunology*, *12*, 595722. https://doi.org/10.3389/fimmu.2021.595722

Sathe, P., Saka, R., Kommineni, N., Raza, K., & Khan, W. (2019). Dithranol-loaded nanostructured lipid carrier-based gel ameliorate psoriasis in imiquimod-induced mice psoriatic plaque model. *Drug development and industrial pharmacy*, *45*(5), 826–838. https://doi.org/10.1080/03639045.2019.1576722

Sercombe, L., Veerati, T., Moheimani, F., Wu, S. Y., Sood, A. K., & Hua, S. (2015). Advances and Challenges of Liposome Assisted Drug Delivery. *Frontiers in pharmacology*, *6*, 286. https://doi.org/10.3389/fphar.2015.00286

Sharma, M., Rathi, R., Kaur, S., Singh, I., Abd Kadir, E., Chahardehi, A. M., & Lim, V. (2023). Antiinflammatory activity of herbal bioactive-based formulations for topical administration. In *Recent Developments in Anti-Inflammatory Therapy*, 245-277. Academic Press. https://doi.org/10.1016/B978-0-323-99988-5.00015-2

Shinde, C., Venkatesh, M. P., Pramod Kumar, T., & Pai, D. R. (2021). Nanostructured lipid carrier-based smart gel: a delivery platform for intra-articular therapeutics. *Autoimmunity*, *54*(1), 35–44. https://doi.org/10.1080/08916934.2020.1846184

Souto, E. B., Cano, A., Martins-Gomes, C., Coutinho, T. E., Zielińska, A., & Silva, A. M. (2022). Microemulsions and Nanoemulsions in Skin Drug Delivery. *Bioengineering (Basel, Switzerland)*, *9*(4), 158. https://doi.org/10.3390/bioengineering9040158

Subramaniam, S., Elz, A., Wignall, A., Kamath, S., Ariaee, A., Hunter, A., Newblack, T., Wardill, H. R., Prestidge, C. A., & Joyce, P. (2023). Self-emulsifying drug delivery systems (SEDDS) disrupt the gut microbiota and trigger an intestinal inflammatory response in rats. *International journal of pharmaceutics*, *648*, 123614. https://doi.org/10.1016/j.ijpharm.2023.123614

Tetyczka, C., Hartl, S., Jeitler, R., Absenger-Novak, M., Meindl, C., Fröhlich, E., Riedl, S., Zweytick, D., & Roblegg, E. (2021).Cytokine-Mediated Inflammation in the Oral Cavity and Its Effect

on Lipid Nanocarriers. *Nanomaterials (Basel, Switzerland)*, *11*(5), 1330. https://doi.org/10.3390/nano11051330

Umerska, A., Mouzouvi, C. R., Bigot, A., & Saulnier, P. (2015).Formulation and nebulization of fluticasone propionate-loaded lipid nanocarriers. *International journal of pharmaceutics*, *493*(1-2), 224–232. https://doi.org/10.1016/j.ijpharm.2015.07.008

Viegas, J. S. R., Praça, F. G., Caron, A. L., Suzuki, I., Silvestrini, A. V. P., Medina, W. S. G., Del Ciampo, J. O., Kravicz, M., & Bentley, M. V. L. B. (2020). Nanostructured lipid carrier co-delivering tacrolimus and TNF-α siRNA as an innovate approach to psoriasis. *Drug delivery and translational research*, *10*(3), 646–660. https://doi.org/10.1007/s13346-020-00723-6

Walunj, M., Doppalapudi, S., Bulbake, U., & Khan, W. (2020). Preparation, characterization, and *in vivo* evaluation of cyclosporine cationic liposomes for the treatment of psoriasis. *Journal of liposome research*, *30*(1), 68–79. https://doi.org/10.1080/08982104.2019.1593449

Wen, J., Li, H., Dai, H., Hua, S., Long, X., Li, H., ... & Xu, C. (2023). Intra-articular nanoparticles based therapies for osteoarthritis and rheumatoid arthritis management. *Materials Today Bio*, *19*, 100597. https://doi.org/10.1016/j.mtbio.2023.100597

Witika, B. A., Bassey, K. E., Demana, P. H., Siwe-Noundou, X., & Poka, M. S. (2022). Current Advances in Specialised Niosomal Drug Delivery: Manufacture, Characterization and Drug Delivery Applications. *International journal of molecular sciences*, *23*(17), 9668. https://doi.org/10.3390/ijms23179668

Yang, C., & Merlin, D. (2019). Nanoparticle-Mediated Drug Delivery Systems For The Treatment Of IBD: Current Perspectives. *International journal of nanomedicine*, *14*, 8875–8889. https://doi.org/10.2147/IJN.S210315

Yasmin, F., Najeeb, H., Shaikh, S., Hasanain, M., Naeem, U., Moeed, A., Koritala, T., Hasan, S., & Surani, S. (2022). Novel drug delivery systems for inflammatory bowel disease. *World journal of gastroenterology*, *28*(18), 1922–1933. https://doi.org/10.3748/wjg.v28.i18.1922

Zhao, Y., Yang, Y., Zhang, J., Wang, R., Cheng, B., Kalambhe, D., ... & Huang, Y. (2020). Lactoferrin-mediated macrophage targeting delivery and patchouli alcohol-based therapeutic strategy for inflammatory bowel diseases. *Acta Pharmaceutica Sinica B*, *10*(10), 1966-1976. https://doi.org/10.1016/j.apsb.2020.07.019

Zuo, X., Gu, Y., Guo, X., Zheng, W., Zheng, H., An, Y., ... & Wang, F. (2024). Preparation of Budesonide-Loaded Liposomal Nanoparticles for Pulmonary Delivery and Their Therapeutic Effect in OVA-Induced Asthma in Mice. *International journal of nanomedicine*, 673-688. https://doi.org/10.2147/IJN.S441345

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