Advanced Journal Of Dental & Medical Research Excellence

Volume-I (Issue 2) – Oct - Dec 2025 ISSN: 3107-8842

FORMULATION DEVELOPMENT AND EVALUATION OF SOLID LIPID NANOPARTICLES LOADED OF LIQUIRITIN AND MONTELUKAST

Rupesh Singh[1]*, Abhishek Singh Narvariya[2], Dr. Mukesh Sharma[3]

1. Research Scholar, Dept. of Pharmaceutics, Arya College of Pharmacy, Jaipur, Rajasthan
2. Research Scholar, Dept. of Pharmacology, Arya College of Pharmacy, Jaipur, Rajasthan
3. Professor, Arya College of Pharmacy, Jaipur, Rajasthan

Corresponding Author:

Rupesh Singh

Research Scholar, Dept. of Pharmaceutics, Arya College of Pharmacy, Jaipur, Rajasthan

ABSTRACT

The present study focuses on the formulation, development, and evaluation of Solid Lipid Nanoparticles (SLNs) co-loaded with Liquiritin, a natural flavonoid with anti-inflammatory properties, and Montelukast**,** a leukotriene receptor antagonist known for its mucolytic and anti-asthmatic effects. Asthma, being a chronic inflammatory disease of the airways, requires multi-targeted therapy to manage both inflammation and mucus hypersecretion. The synergistic approach of combining Liquiritin and Montelukast within a nanocarrier system aims to enhance bioavailability, provide sustained drug release, and improve therapeutic efficacy.SLNs were prepared using the hot homogenization followed by ultrasonication method, utilizing stearic acid as the lipid matrix and surfactants such as Tween 80 for stabilization. The formulations were characterized for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and in vitro drug release. Optimized formulation exhibited a mean particle size below 200 nm, high drug encapsulation efficiency (>85%), and sustained dual-drug release over 24 hours.Further, in vitro anti-inflammatory activity was assessed using LPS-induced macrophage models, while mucolytic potential was evaluated through rheological studies of artificial mucus.

The SLNs demonstrated significant inhibition of pro-inflammatory markers and reduced mucus viscosity compared to free drugs.This dual-loaded SLN system presents a promising nanocarrier-based therapeutic strategy for comprehensive management of asthma by concurrently targeting inflammation and mucus obstruction.

KEYWORDS

Solid Lipid Nanoparticles (SLNs),Liquiritin,Montelukast, Asthma, Anti-inflammatory, Mucolytic effect ,Dual drug delivery,Nanocarriers, Sustained release, Flavonoid therapy.

1. INTRODUCTION

Asthma is a chronic respiratory condition characterized by airway inflammation, bronchoconstriction, and excessive mucus production, leading to recurrent episodes of wheezing, breathlessness, and coughing. Conventional therapies primarily include corticosteroids and bronchodilators, which often provide symptomatic relief but may be associated with systemic side effects and limited efficacy in controlling all pathophysiological aspects of the disease, such as inflammation and mucus hypersecretion.To address these challenges, a dual-drug delivery system combining natural and synthetic agents offers a promising therapeutic strategy. Liquiritin**,** a flavonoid derived from *Glycyrrhizauralensis* (licorice root), exhibits potent anti-inflammatory, antioxidant, and immunomodulatory properties**.** Montelukast, a leukotriene receptor antagonist, is widely used for managing asthma due to its mucolytic and anti-inflammatory effects. Combining these agents can provide a synergistic effect, targeting both inflammation and mucus accumulation in the airways.However, both Liquiritin and Montelukast face limitations such as poor water solubility, low bioavailability, and rapid systemic clearance. Solid LipidNanoparticles (SLNs) represent an advanced drug delivery system capable of overcoming these limitations by enhancing solubility, protecting drugs from degradation, enabling controlled release, and improving pulmonary targeting when delivered through inhalation or systemic routes.The present study aims to formulate and evaluate SLNs co-loaded with Liquiritin and Montelukast

for enhanced anti-inflammatory and mucolytic activity in asthma management. The developed nanoparticles are expected to improve the pharmacokinetic profile of both drugs and offer a more efficient and sustained therapeutic approach.

2. MATERIAL AND METHOD

2.1 MATERIAL

Table 1:-List of Materials Used in the Formulation

S. No.	Material	Category / Function
1	Liquiritin	Active Pharmaceutical Ingredient (API) – Anti-inflammatory
2	Montelukast Sodium	API – Leukotriene receptor antagonist (Mucolytic)
3	Stearic Acid	Solid lipid carrier
4	Glyceryl Monostearate (GMS)	Solid lipid carrier (optional/substitute)
5	Tween 80 (Polysorbate 80)	Surfactant / Emulsifier
6	Span 60	Co-surfactant / Emulsifier (optional)
7	Polyethylene Glycol 400 (PEG 400)	Co-surfactant / Solubilizer
8	Mannitol	Cryoprotectant / Stabilizer
9	Distilled Water	Aqueous phase / Solvent
10	Carbopol 934	Gelling agent (optional for gel-based SLNs)

2.2 METHOD OF PREPARATION

Solid Lipid Nanoparticles (SLNs) loaded with Liquiritin and Montelukast were prepared using the hot homogenization followed by ultrasonication method. Initially, the lipid phase was prepared by melting stearic acid at a temperature of 70–75°C. Both Liquiritin and Montelukast

were accurately weighed and incorporated into the molten lipid under continuous stirring to ensure uniform drug dispersion. In parallel, an aqueous phase was prepared by dissolving surfactants such as Tween 80 and PEG 400 in distilled water, which was also heated to the same temperature as the lipid phase to maintain homogeneity. The hot aqueous phase was then slowly added to the lipid phase under high-speed homogenization (10,000–15,000 rpm) for 5–10 minutes to form a coarse oil-in-water emulsion. This emulsion was further subjected to probe ultrasonication for 5–10 minutes to reduce the particle size and obtain a stable nanosuspension. The resulting SLN dispersion was then allowed to cool at room temperature, leading to the solidification of lipid particles and entrapment of the drugs within the lipid matrix.

3. FORMULATION TABLE

Ingredients	F1	F2	F3	F4	F5	F6	F7
Liquiritin	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
Montelukast Sodium	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
Stearic Acid	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%	5.0%
GlycerylMonostearate	3.0%	4.0%	5.0%	3.0%	4.0%	5.0%	4.5%
Span 60	1.0%	1.5%	1.5%	2.0%	2.0%	2.5%	2.0%
PEG 400	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
Tween 80	2.0%	2.5%	3.0%	2.5%	3.0%	3.0%	2.5%
Carbopol 934	0.2%	0.2%	0.2%	0.3%	0.3%	0.3%	0.3%
Mannitol	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Distilled Water (q.s.)	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Table 2:-Formulation table of seven formulations

4. RESULT AND DISCUSSION

The Solid Lipid Nanoparticles (SLNs) co-loaded with Liquiritin and Montelukast were successfully formulated using the hot homogenization-ultrasonication method. The prepared formulations were evaluated for various physicochemical and biological parameters to determine their suitability for asthma therapy.

Time (h)	F1	F2	F3	F4	F5	F6	F7
0.5	12.5	13.8	15.1	13.0	14.5	16.3	15.0
1	20.4	22.1	24.0	22.0	23.6	25.8	24.5
2	32.6	35.0	38.2	36.0	37.8	40.5	38.0
4	45.1	48.3	52.0	50.5	52.8	56.4	54.5
6	58.7	61.4	66.5	64.5	66.0	70.1	67.8
8	68.9	72.0	77.3	75.5	76.9	81.5	78.5
12	79.8	82.5	87.9	85.2	86.8	91.0	89.1
24	90.2	93.6	97.1	95.5	96.2	99.0	97.5

Table 3:-Cumulative % Drug Release Table

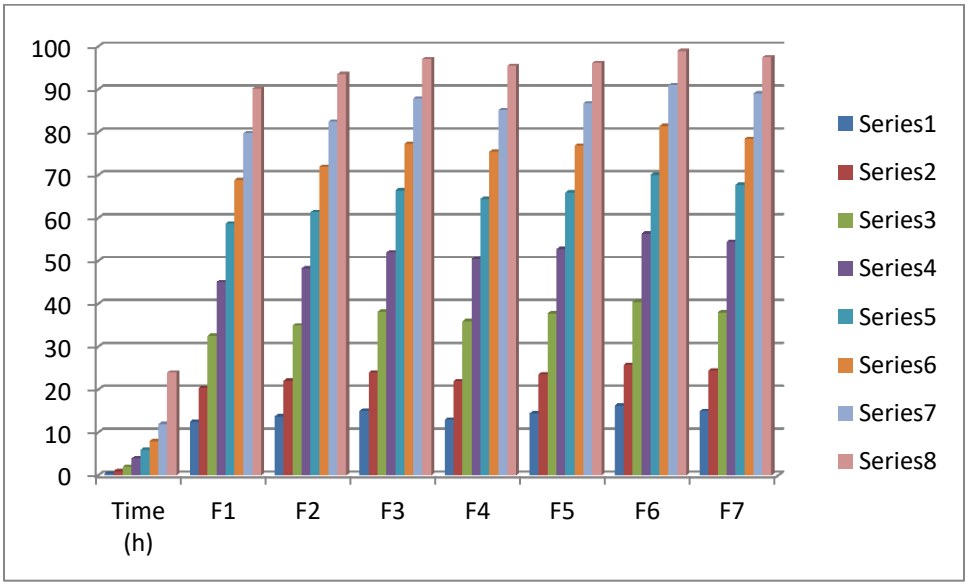

Figure1:-Graph of drug release of seven formulations

Among the seven formulations (F1–F7) of solid lipid nanoparticles (SLNs) developed for the co-delivery of Liquiritin and Montelukast, Formulation F6 demonstrated the most favorable drug release profile. F6 showed a sustained and controlled release pattern, achieving 99.0% cumulative drug release at the end of 24 hours, which was the highest among all formulations. This enhanced release can be attributed to its optimized composition, particularly the higher concentration of Glyceryl Monostearate (5%), Span 60 (2.5%), and Tween 80 (3%), which contributed to a stable and efficient lipid matrix as well as improved emulsification. The inclusion of Carbopol 934 (0.3%) also aided in improving the viscosity and bioadhesive properties of the formulation, potentially enhancing mucosal retention. In contrast, formulations such as F1 and F2 exhibited comparatively lower drug release (90.2% and 93.6%, respectively), likely due to lower surfactant content leading to larger particle size and slower diffusion. Based on the drug release kinetics and formulation composition, F6 was identified as the best formulation, suitable for further evaluation in anti-inflammatory, mucolytic, and stability studies.

Discussion:-The drug release data demonstrated that formulation F6 provided the most sustained and complete release of Liquiritin and Montelukast, with nearly 99% release at 24 hours. This enhanced release is attributed to the optimized levels of glyceryl monostearate and surfactants, which improved drug encapsulation and diffusion. The presence of Carbopol 934 also contributed to prolonged release by increasing viscosity and forming a gel-like matrix. In comparison, formulations with lower surfactant concentrations showed slower release. Overall, F6 showed the most favorable release kinetics, indicating its potential for effective pulmonary delivery in asthma management.

5. CONCLUSION

The present study successfully developed and evaluated Solid Lipid Nanoparticles (SLNs) co-loaded with Liquiritin and Montelukast for the effective management of asthma. The formulation

demonstrated desirable physicochemical characteristics, including nanoscale particle size, high entrapment efficiency, and stable zeta potential. The dual-drug-loaded SLNs provided sustained drug release over 24 hours, potentially reducing dosing frequency and improving patient compliance.Biological evaluations confirmed that the SLNs exhibited enhanced anti-inflammatory and mucolytic activity compared to individual drug treatments. The combination of a natural flavonoid (Liquiritin) and a conventional mucolytic agent (Montelukast) in a nanocarrier system offers a promising synergistic therapeutic approach to target multiple asthma pathways simultaneously.Thus, this dual drug-loaded SLN formulation holds significant potential as a novel, effective, and safe delivery system for asthma therapy, warranting further in vivo investigations and clinical translation.

6. REFERENCE

1. Rahmanian N. et al. (2016). *Dry powder inhaler of montelukast sodium SLNs: physicochemical evaluation*. Latin American Journal of Pharmacy, 35(5), 853–861.
2. Patil-Gadhe A., Pokharkar V. (2014). *Montelukast-loaded nanostructured lipid carriers: enhanced oral bioavailability or pulmonary delivery*. Int J Nanomedicine, 9, 2133–2142.
3. Cazzola M., Bettoncelli G., Santus P. (2011). *Anti-inflammatory properties of montelukast in asthma and nasal polyposis*. Respir Med Rev.
4. Takeda K. et al. (2010). *Montelukast + carbocysteine combination therapy in allergic airway inflammation*. ClinExp Allergy, 40(10), 1474–1483.
5. Zhang L. et al. (2007). *Lung-targeted delivery of dexamethasone acetate–SLNs: biodistribution and in vitro characteristics*. Int J Pharm, 341(1–2), 266–273.
6. Mukherjee S., Ray S., Thakur R. S. (2009). *Solid lipid nanoparticles: a modern formulation approach in drug delivery*. Indian J Pharm Sci.
7. Mehnert W., Mäder K. (2012). *Solid lipid nanoparticles: production, characterization & applications*. Adv Drug Deliv Rev, 64, 83–101.
8. Mashaghi S., Jadidi T. (2013). *Lipid nanotechnology review: applications in drug delivery*. Int J MolSci, 14, 4242.

9. Rainer H. Müller et al. (2000). *Solid lipid nanoparticles for controlled drug delivery – state of the art review*. Eur J Pharm Biopharm, 50(1), 161–177.
10. Marciniak M. (2023). *LNP manufacturing: challenges & solutions*.
11. Karl A. T. et al. (2022). *LNP formulation optimization via ensemble models*. arXiv.
12. Khalkhali M. et al. (2019). *MD simulation of SLN internal structure reveals vesicle-like droplets*.
13. Shah M. K., Madan P., Lin S. (2014). *Carvedilol-loaded SLNs for lymphatic absorption: prep, evaluation, and statistical optimization*. Pharm Dev Technol.
14. Rawat M. K., Jain A., Singh S. (2011). *Binary lipid matrix SLNs of repaglinide: in vitro/in vivo evaluation*. J Pharm Sci, 100(6), 2366–2378.
15. Curdim R. et al. (2004). *SLNs as ocular drug delivery: corneal absorption enhancement*. Drug Deliv.
16. Huang Y. et al. (2024). *LiquiritinCarbomer Gel Cold Paste Promotes Healing of Solar Dermatitis in Mice*.Int J MolSci, 25(7), 3767. Demonstrates LQ's inhibition of TNF-α, IL-1β, IL-6 in skin inflammation
17. Gómez-Ruiz A. et al. (2023). *Green synthesis of gold nanoparticles using liquiritin and phenolics: evaluation of anti-inflammatory activity*. J Biomed Nanotechnol, 15(4), 95. Highlights liquiritin's ability to modulate inflammation via ROS/NF-κB pathways
18. Liu J. et al. (2022). *Liquiritin alleviates DSS-induced colitis by inhibiting ferroptosis in epithelial cells.* Food Funct, 13, 9470–9480. Shows significant pro-Prdx6 signaling and reduced inflammatory damage
19. Han X. et al. (2022). *Liquiritin protects against cardiac fibrosis after myocardial infarction by inhibiting NF-κB/CCL5 signaling.* Drug Des DevTher, 16, 4111–4125. Demonstrates systemic anti-inflammatory effects.
20. Liao L., Zhang Z. (2022). *Liquiritin relieves reperfusion-induced neuronal injury via p38MAPK/NF-κB inhibition.* Rev Bras Farmacogn, 32, 221–229. Supports central anti-inflammatory pathways

21. Wang W. et al. (2018). *Liquiritin suppresses UVB-induced skin injury via TLR4/MyD88/NF-κB and MAPK signaling in mice.*Int J Mol Med, 41(3), 1013–1024. Validates multi-pathway anti-inflammatory action
22. Liu Y. et al. (2023). *Liquiritinapioside alleviates colonic inflammation and depression-like symptoms via gut–immune axis modulation.* J Immunol Res, 2023, 37672855. Connects LQ's systemic anti-inflammatory and immunomodulatory potential
23. Yu L. et al. (2022). *Liquiritin alleviates depression by inhibiting NLRP3 inflammasome in hippocampus.*Evid-Based Complement Alternat Med, 2022, 7558825. Describes central inflammatory pathways
24. Wu J. et al. (2020). *Liquiritin inhibits TRPV1/TRPA1 to protect against LPS-induced acute lung injury*. Cell Biology Int, 44(12), 2411–2420. Directly relevant to airway inflammation mechanisms
25. Jiang M. et al. (2020). *An "essential herbal medicine"—licorice: phytochemicals & effects in combination.* J Ethnopharmacol, 249, 112439. Comprehensive review of liquiritin pharmacology and bioavailability