E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.605

Research Article

Development and Characterization of Sucralfate-Loaded Liposomes for Topical Delivery: Physicochemical Characterization, Sustained Release and In-Vitro Antibacterial Evaluation

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Received: 17.07.26, Revised: 22.08.26, Accepted: 25.09.26

ABSTRACT
Background: Sucralfate is widely used for its protective and therapeutic effects; however, its physicochemical properties can present challenges for formulation development. Liposomal drug delivery provides an approach for incorporating therapeutic agents into vesicular carriers and modifying their release and delivery characteristics.
Objective: The present study aimed to develop and characterize Sucralfate-loaded liposomes and to evaluate the optimized formulation for physicochemical properties, entrapment efficiency, in-vitro drug release, topical cream characteristics, and antibacterial activity.
Methods: Sucralfate was subjected to preformulation studies including organoleptic evaluation, solubility analysis, pH determination, melting-point analysis, UV spectrophotometric analysis and Fourier-transform infrared spectroscopy (FTIR). Five liposomal formulations (F1-F5) containing different ratios of soya lecithin and cholesterol were prepared by the thin-film hydration method. The formulations were evaluated for physical appearance, particle size, zeta potential and entrapment efficiency. The optimized formulation was further examined by scanning electron microscopy (SEM), incorporated into a topical cream base, and evaluated for appearance, viscosity, pH and spreadability. In-vitro drug release was investigated using a Franz diffusion cell, and the release data were fitted to different kinetic models. Antibacterial activity was assessed by the agar well-diffusion method against *Escherichia coli*.
Results: Sucralfate appeared as a white to off-white, odourless fine powder and showed poor solubility in water and phosphate buffer pH 7.4. The observed melting point was 220.17°C and the λmax was 288 nm. The calibration curve over 2-12 µg/mL demonstrated a linear relationship, with an R^2 value of 0.9998. Among the five formulations, F1 exhibited the smallest particle size (290.6 nm), highest negative zeta potential (-41.4 mV), and highest entrapment efficiency (93.48%). SEM examination demonstrated predominantly spherical nanosized vesicular structures. The optimized liposomal cream showed a smooth and homogeneous appearance, viscosity of 1694 cps, pH 6.5 and spreadability of 17.45 g·cm/s. The formulation exhibited progressive drug release, reaching 90.63% at 12 h. Among the evaluated kinetic models, the present work data reported the highest correlation for the zero-order model (R^2 = 0.980). In the antibacterial study, F1 produced a zone of inhibition of 11.23 mm against E. coli, compared with 5.61 mm for free Sucralfate and 0 mm for the control.

Keywords: Sucralfate, Liposomes, Lipid-Based Drug Delivery, Thin-Film Hydration, Entrapment Efficiency, Sustained Release, Antibacterial Activity, Escherichia Coli.

INTRODUCTION

Lipid-based drug delivery systems have attracted considerable interest because of their ability to modify drug disposition, protect encapsulated compounds and influence drug-release characteristics. Among these systems, liposomes are vesicular carriers composed principally of phospholipid bilayers and can accommodate therapeutic agents within their aqueous core or lipid bilayer depending on the physicochemical properties of the incorporated compound. The composition of the lipid bilayer can influence vesicle size, membrane rigidity, surface charge, stability and drug entrapment [1-5].

Liposomes have been investigated for the delivery of both hydrophilic and lipophilic compounds because of their biocompatibility, biodegradability and ability to modify drug release. Their characteristics can be controlled

through lipid composition and preparation conditions, making them useful carriers for pharmaceutical and topical applications [6-11]. Sucralfate is a therapeutic agent whose physicochemical characteristics present formulation considerations, particularly its poor solubility in aqueous media. In the present work, Sucralfate showed poor solubility in water and phosphate buffer pH 7.4, while showing better solubility in DMSO. This physicochemical profile provided the rationale for investigating a lipid-based vesicular system for its formulation [12-16].

The thin-film hydration method is a conventional approach for liposome preparation in which lipid components are dissolved in an organic solvent, the solvent is removed under reduced pressure to form a thin lipid film, and the resulting film is subsequently hydrated with an aqueous phase. The present work employed varying quantities of soya lecithin and cholesterol to investigate their influence on the characteristics of Sucralfate-loaded liposomes [17-21].

Therefore, the present study was designed to prepare Sucralfate-loaded liposomes, characterize the resulting vesicular systems, identify an optimized formulation, incorporate the optimized liposomes into a topical cream, evaluate in-vitro drug release, and compare the antibacterial activity of the optimized liposomal formulation with free Sucralfate against *E. coli* [21-23].

MATERIALS AND METHODS

Materials

Sucralfate was used as the active pharmaceutical ingredient. Soya lecithin and cholesterol were used as the principal lipid components for liposome preparation. Chloroform, methanol, phosphate buffer, DMSO and other analytical-grade reagents were used during formulation and evaluation. Beeswax, liquid paraffin, methyl paraben, borax and lavender oil were used for preparation of the liposomal cream.

Preformulation Studies

Organoleptic Evaluation

Sucralfate was evaluated visually for colour, odour, physical state and appearance. The drug was observed as a white to off-white, odourless fine powder.

Solubility Study

The solubility of Sucralfate was qualitatively assessed in water, phosphate buffer pH 7.4, acetone, ethanol, methanol, chloroform and DMSO. A fixed quantity of drug was introduced into each solvent and the extent of dissolution was observed after shaking at room temperature.

Melting Point and PH

The melting point of Sucralfate was determined using a digital melting-point apparatus. The pH was measured using a calibrated digital pH meter. The observed melting point was 220.17°C and the measured pH was 3.56.

UV Spectrophotometric Analysis

A Sucralfate stock solution was prepared in DMSO and scanned over the wavelength range of 200-400 nm. The maximum absorption wavelength was found to be 288 nm. A calibration curve was prepared using concentrations ranging from 2-12 µg/mL.

FTIR Analysis

FTIR analysis was performed over the range of 4000-400 cm^{-1} using a KBr pellet technique. Characteristic absorption bands were recorded and compared with reference assignments to assess the identity and chemical integrity of Sucralfate.

Preparation of Sucralfate-Loaded Liposomes

Five liposomal formulations were prepared using the thin-film hydration method. Soya lecithin and cholesterol were used in different ratios while maintaining the drug quantity at 1 g as shown in table 1. The lipid components and drug were dissolved in chloroform: methanol (1:1). The organic solvent was removed under reduced pressure using a rotary evaporator to form a thin lipid film.

The lipid film was subsequently hydrated using phosphate buffer pH 7.4. The hydrated dispersion was vortexed for 30 min and sonicated for 60 min to obtain the liposomal formulations.

Table 1. Composition of Sucralfate-loaded liposomal formulations

Ingredient	F1	F2	F3	F4	F5
Soya lecithin (mg)	50	100	150	200	250
Cholesterol (mg)	250	200	150	100	50
Sucralfate (g)	1	1	1	1	1

Chloroform: methanol (1:1) (mL)	10	10	10	10	10
Phosphate buffer pH 7.4 (mL)	10	10	10	10	10
Sonication time (min)	60	60	60	60	60

Characterization of liposomes

The prepared formulations were evaluated for physical appearance, particle size, zeta potential, entrapment efficiency and surface morphology.

Particle size was determined using a Malvern Zeta-sizer based on dynamic light scattering. Zeta potential was measured using the same instrument after suitable dilution of the formulation.

Entrapment efficiency was determined after separation of free drug from the vesicular fraction by centrifugation. The drug content in the supernatant was estimated spectrophotometrically at 288 nm. Entrapment efficiency was calculated as:

EE (%) = [(Total drug - Free drug) / Total drug] × 100

SEM was used to examine the morphology of the optimized formulation.

Preparation of Sucralfate liposomal Cream

The optimized liposomal dispersion was incorporated into a cream base containing beeswax, liquid paraffin, methyl paraben, borax and lavender oil. The oil phase was heated and the aqueous phase was separately prepared. The aqueous phase was incorporated into the oil phase with continuous mixing, followed by incorporation of the optimized liposomes as shown in table 2.

Table 2. Composition of liposomal cream

Ingredient	Quantity	Function
Sucralfate liposomes	10 mL	Active ingredient
Beeswax	4.0 g	Emulsifier/thickener
Liquid paraffin	15 mL	Moisturizing/skin-softening agent
Methyl paraben	0.03 g	Preservative
Lavender oil	3-4 drops	Fragrance
Borax	0.4 g	Buffering/preservative component

Evaluation of Liposomal Cream

The prepared cream was evaluated for physical appearance, homogeneity, viscosity, pH and spreadability. Viscosity was determined using a Brookfield viscometer. The pH was measured after dispersing the cream in distilled water. Spreadability was determined using the horizontal-slide method.

In-Vitro Drug Release

In-vitro release was studied using a Franz diffusion cell. Phosphate buffer pH 6.8 was used as the receptor medium, maintained at 37 ± 0.5°C with continuous stirring. Samples were withdrawn at predetermined intervals and replaced with an equal volume of fresh receptor medium. Drug concentration was determined spectrophotometrically. The release data were fitted to zero-order, first-order, Higuchi and Korsmeyer-Peppas models.

Antibacterial Activity

The antibacterial activity of free Sucralfate and the optimized liposomal formulation was evaluated by the agar well-diffusion method against *Escherichia coli*. Nutrient agar plates were inoculated with the bacterial suspension. Wells were prepared and loaded with control, free Sucralfate solution (1 mg/mL) or Sucralfate-loaded liposomes (1 mg/mL). The plates were incubated at 37°C for 24 h and the zones of inhibition were measured.

RESULTS AND DISCUSSION

Preformulation Characteristics

Sucralfate was obtained as a white to off-white, odourless fine powder. The drug was poorly soluble in water and phosphate buffer pH 7.4, sparingly soluble in ethanol and methanol, practically insoluble in acetone, insoluble in chloroform and soluble in DMSO. The observed pH was 3.56 and the melting point was 220.17°C.

The UV spectrum showed a maximum absorption at 288 nm. The calibration curve demonstrated a concentration-dependent increase in absorbance over the investigated range of 2-12 µg/mL and produced an R^2 value of 0.9998 as shown in figure 1.

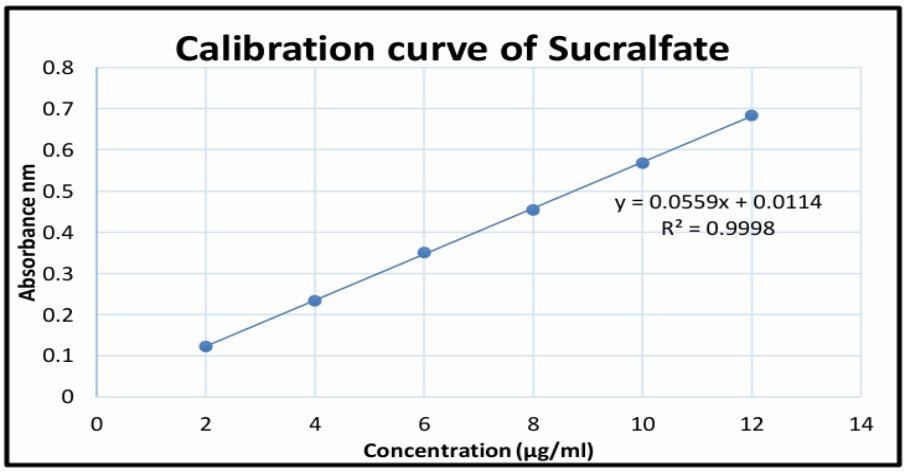


Figure 1 Calibration curve of Sucralfate

FTIR analysis demonstrated characteristic bands at 3465.74, 1662.46, 1265.35, 1151.17 and 1055.19 cm^{-1}, corresponding in the present work to N-H stretching, C=N stretching, C-O stretching, S=O stretching of sulfone and S=O stretching of sulfoxide groups, respectively. These observations supported the identity of the drug sample as shown in figure 2.

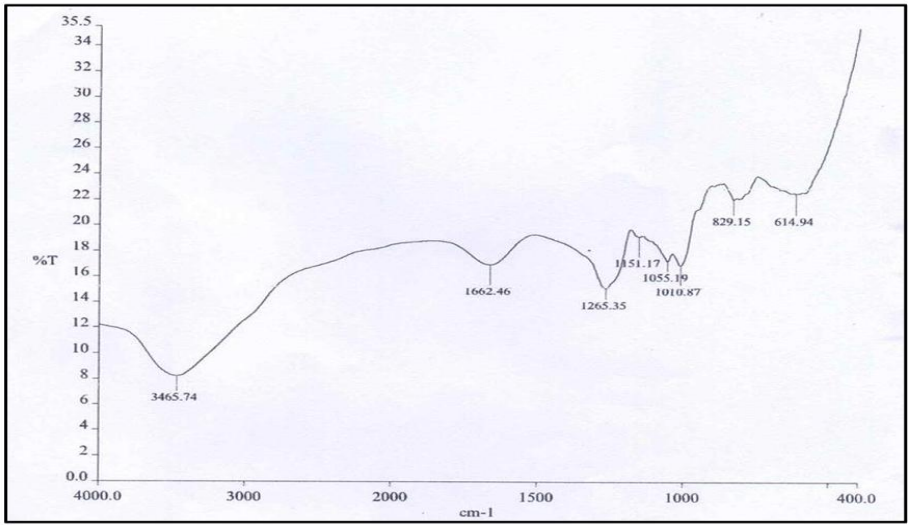


Figure 2: FTIR study of Sucralfate

Physical Characteristics of Liposomes

All prepared liposomal formulations exhibited acceptable physical characteristics. The optimized formulation was described as an off-white/creamy, odorless and homogeneous smooth dispersion, with no visible phase separation.

Particle Size

Particle size varied considerably among the formulations. F1 exhibited a particle size of 290.6 nm, while F4 showed a comparable size of 294.2 nm. F2 and F3 showed substantially larger particle sizes of 805.5 and 724.0 nm, respectively, whereas F5 showed an intermediate value of 516.4 nm as presented in table 3. The observed variation indicates that the lecithin-to-cholesterol ratio influenced vesicle size.

Table 3. Particle size of Sucralfate-loaded liposomes

Formulation	Particle size (nm)
F1	290.6
F2	805.5
F3	724.0

F4	294.2
F5	516.4

Zeta Potential

F1 demonstrated the highest absolute zeta potential (-41.4 mV). F2, F4 and F5 also showed absolute zeta-potential values above 30 mV, whereas F3 exhibited a lower absolute value of -19.7 mV. The comparatively high absolute surface charge of F1 suggests greater electrostatic repulsion between vesicles under the measurement conditions as represented in table 4.

Table 4. Zeta potential of Sucralfate-loaded liposomes

Formulation	Zeta potential (mV)
F1	-41.4
F2	-37.1
F3	-19.7
F4	-34.4
F5	-36.4

Entrapment Efficiency

F1 exhibited the highest entrapment efficiency of 93.48%, followed by F2 (86.34%), F3 (81.57%), F4 (79.68%) and F5 (73.43%). The higher entrapment observed with F1 indicates that its lipid composition was favourable for incorporation of Sucralfate into the vesicular system as shown in table 5. Considering particle size, zeta potential and entrapment efficiency together, F1 was selected as the optimized formulation.

Table 5. Entrapment efficiency

Formulation	Entrapment efficiency (%)
F1	93.48
F2	86.34
F3	81.57
F4	79.68
F5	73.43

SEM Analysis

SEM examination of F1 showed predominantly spherical vesicular structures with reported particle diameters ranging from approximately 90.48 to 165.9 nm in the micrographs. The observed morphology was generally smooth and spherical, with some aggregation attributed in the present work to sample-preparation effects as shown in figure 3.

The difference between the SEM-observed dimensions and the DLS-derived hydrodynamic diameter should be recognized because these techniques measure particle dimensions under different

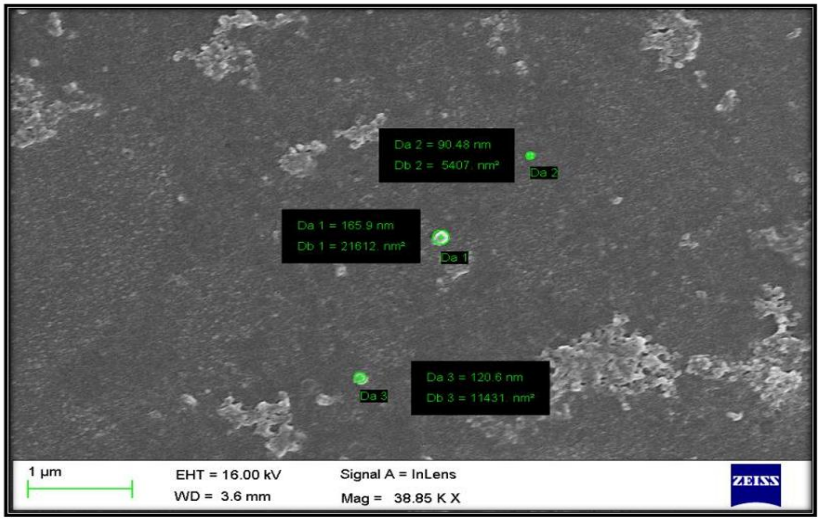


Figure 3: Scanning electron microscope (SEM)

In Vitro Drug Release

The in-vitro drug release investigation of the liposomal formulation showed a progressive and sustained drug release over the course of 12hr. The cumulative % drug release grew gradually from 0% at 0 hour to 90.63% at 12 hours which confirms the successful controlled release characteristic of the formulation as shown in figure 4. This sustained-release feature is desired because it assists in preserving therapeutic levels of the medicine for a longer time.

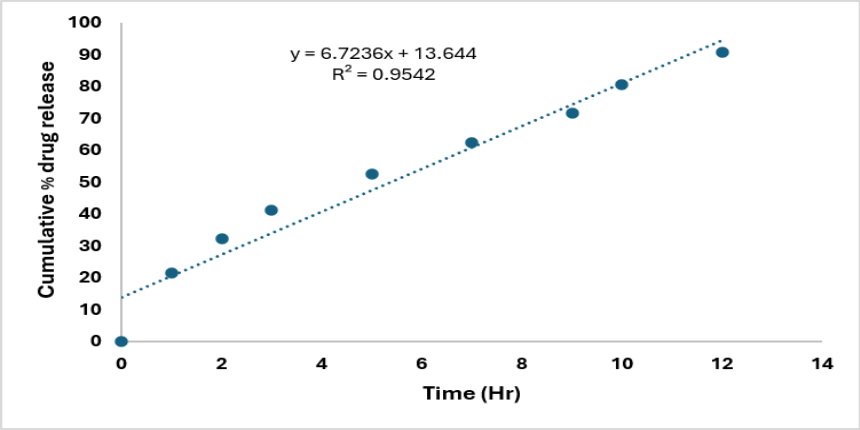


Figure 4: Drug release study

Antibacterial Activity

The antibacterial activity of the liposomal F1 formulation was assessed against E. coli and compared with the plain medication and control. The control group showed no zone of inhibition (0 mm) but the plain Sucralfate (1 mg/mL) demonstrated a minimal antibacterial activity with zone of inhibition of 5.61 mm. In contrast, the Liposome F1 formulation (1 mg/mL) revealed a substantially greater zone of inhibition of 11.23 mm as shown in figure 5 and table 6. These results show that the antibacterial activity of the liposomal formulation is significantly increased compared to the standard drug solution. The improved effect may be due to improved drug encapsulation, improved contact with bacterial cells and sustained release property of the liposomal system which together boost the availability and efficacy of the medicine at the target site.

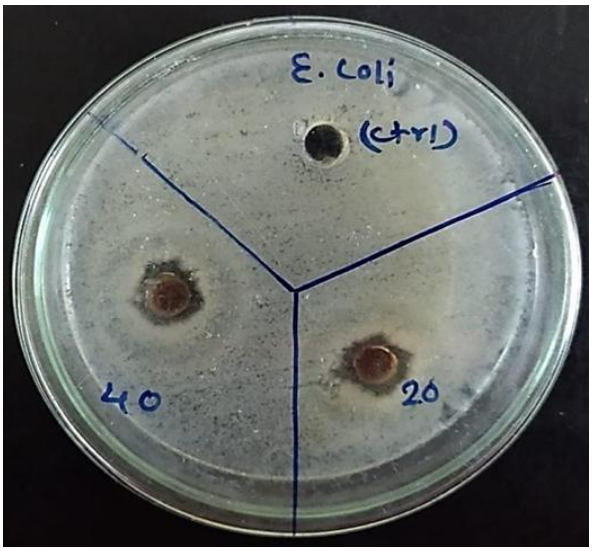


Figure 5: Antimicrobial activity

Table 6: Antimicrobial activity of Formulation against Escherichia coli

S. No.	Sample Name	Zone of Inhibition (mm)
1.	Control	0 mm
2.	Sucralfate drug 1 mg/mL	5.61 mm

3.	Liposome F1 formulation 1 mg/mL	11.23 mm

CONCLUSION

The present study effectively generated and analyzed Sucralfate loaded liposomes by thin-film hydration process and formulation F1 was recognized as optimum formulation based on its physicochemical features. Among the examined formulations, F1 formulation exhibited a particle size of 290.6 nm, zeta potential of -41.4 mV and greatest entrapment effectiveness of 93.48% showing successful incorporation of Sucralfate into the liposomal vesicles. SEM investigation also revealed mainly spherical vesicular structures.

The optimized liposomal formulation was successfully combined into a topical cream with a smooth and homogenous appearance, acceptable pH (6.5), viscosity (1694 cps) and spreadability (17.45 g·cm/s). The in-vitro release analysis showed a sustained and progressive release of Sucralfate and the release data showed the best fit to the zero-order model (R^2=0.980) with 90.63% released after 12 h. Furthermore, antibacterial examination against Escherichia coli showed the improved zone of inhibition of Liposome F1 (11.23 mm) compared to free Sucralfate (5.61 mm) and control (0 mm).

To summarize, the data suggest that Sucralfate-loaded liposomes may provide a viable topical delivery strategy to improve drug entrapment, provide prolonged drug release and improve the observed in-vitro antibacterial activity of Sucralfate. Further investigations especially stability, skin permeability, ex-vivo/in-vivo evaluation and comprehensive microbiological examination would be needed to show its potential for practical topical application.

REFERENCES

1. Caritá AC, Eloy JO, Chorilli M, Lee RJ, Leonardi GR. Recent advances and perspectives in liposomes for cutaneous drug delivery. Curr Med Chem. 2018;25(5):606-635. doi:10.2174/092986732466617100912015 4.
2. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon. 2022;8(5):e09394. doi:10.1016/j.heliyon.2022.e09394.
3. Lombardo D, Kiselev MA. Methods of liposomes preparation: formation and control factors of versatile nanocarriers for biomedical and nanomedicine application. Pharmaceutics. 2022;14(3):543. doi:10.3390/pharmaceutics14030543.
4. Torres-Flores G, Gonzalez-Horta A, Vega-Cantu YI, Rodriguez C, Rodriguez-Garcia A. Preparation and characterization of liposomal everolimus by thin-film hydration technique. Adv Polym Technol. 2020;2020:5462949. doi:10.1155/2020/5462949.
5. Elsayed MMA, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: reviewing three decades of research. Int J Pharm. 2007;332(1-2):1-16. doi:10.1016/j.ijpharm.2006.12.005.
6. Carita AC, Eloy JO, Chorilli M, Lee RJ, Leonardi GR. Recent advances and perspectives in liposomes for cutaneous drug delivery. Curr Med Chem. 2018;25(5):606-635. doi:10.2174/092986732466617100912015 4.
7. Mezei M, Gulasekharam V. Liposomes—a selective drug delivery system for the topical route of administration: lotion dosage form. Life Sci. 1980;26(18):1473-1477. doi:10.1016/0024-3205(80)90087-2.
8. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes—novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. J Control Release. 2000;65(3):403-418. doi:10.1016/S0168-3659(99)00222-9.
9. Touitou E, Godin B. Ethosomes for skin delivery. J Drug Deliv Sci Technol. 2007;17(5):303-308. doi:10.1016/S1773-2247(07)50046-8.
10. Carita AC, Eloy JO, Chorilli M, Lee RJ, Leonardi GR. Recent advances and perspectives in liposomes for cutaneous drug delivery. Curr Med Chem. 2018;25(5):606-635. doi:10.2174/092986732466617100912015 4.
11. Antimisiaris SG, Marazioti A, Kannavou M, Natsaridis E, Gkartziou F, Kogkos G, et al. Overcoming barriers by local drug delivery with liposomes. Adv Drug Deliv Rev. 2021;174:53-86. doi:10.1016/j.addr.2021.01.019.
12. Sapkota R, Dash AK. Liposomes and transferosomes: a breakthrough in topical and transdermal delivery. Ther Deliv.

2021;12(2):145-158. doi:10.4155/tde-2020-0122.
13. Umbarkar M, Thakare S, Surushe T, Giri A, Chopade V. Formulation and evaluation of liposome by thin film hydration method. J Drug Deliv Ther. 2021;11(1):64-67. doi:10.22270/jddt.v11i1.4677.
14. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963;52(12):1145-1149. doi:10.1002/jps.2600521210.
15. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. Int J Pharm. 1983;15(1):25-35. doi:10.1016/0378-5173(83)90064-9.
16. Bergmans D, Bonten M, Gaillard C, van Tiel F, van der Geest S, Stobberingh E. In vitro antibacterial activity of sucralfate. Eur J Clin Microbiol Infect Dis. 1994;13(7):615-620. doi:10.1007/BF01971318.
17. Bragman SGL, Pankhurst CL, Casewell MW. Activity of sucralfate (sucrose octa-sulphate), an anti-ulcer agent, against opportunistic Gram-negative bacilli. J Antimicrob Chemother. 1995;36(4):703-706. doi:10.1093/jac/36.4.703.
18. Tryba M, Mantey-Stiers F. Antibacterial activity of sucralfate in human gastric juice. Am J Med. 1987;83(3B):125-127. doi:10.1016/0002-9343(87)90841-2.
19. Welage L, Carver P, Welch K. Antibacterial activity of sucralfate versus aluminum chloride in simulated gastric fluid. Eur J Clin Microbiol Infect Dis. 1994;13(12):1046-1052. doi:10.1007/BF02111825.
20. Masuelli L, Tumino G, Turriziani M, Modesti A, Bei R. Topical use of sucralfate in epithelial wound healing: clinical evidences and molecular mechanisms of action. Recent Pat Inflamm Allergy Drug Discov. 2010;4(1):25-36. doi:10.2174/187221310789895649.
21. Abtahi-Naeini B, Saffaei A, Sabzghabaee AM, et al. Topical sucralfate for treatment of mucocutaneous conditions: a systematic review on clinical evidences. Dermatol Ther. 2022;35(4):e15334. doi:10.1111/dth.15334.
22. Vejdan AK, Khosravi M, Amirian Z, Daneshmand M, Babak B, Samira K, et al. Evaluation of the efficacy of topical sucralfate on healing haemorrhoidectomy incision wounds and reducing pain severity: a randomised clinical trial. Int Wound J. 2020;17(4):1047-1051. doi:10.1111/iwj.13369.
23. Rudiman R, Hanafi RV, Evan C, Halim F. The efficacy of topical sucralfate in improving pain and wound healing after haemorrhoidectomy procedure: a systematic review, meta-analysis, and meta-regression of randomised clinical trials. Int Wound J. 2023;20(2):543-553. doi:10.1111/iwj.13901.