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Elastic Liposome Gel Scheme for Delivery of Polymixin Bacterium Sulphate in Deep Skin Infection

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ABSTRACT:
Prehospital treatment that is provided on-site is essential for reducing the severity of injuries resulting from acute Skin infection, particularly those that are second and third degree. Skin infection usually cover a substantial portion of the body and have uneven forms and depths. It's always appropriate to use typical sheet-like wound dressings because of the severity and intricacy of infection injuries. As an alternative, large-scale, rapid, and convenient dressing changes can be achieved with sprayable dressings. Depending on the reagent composition, they can also stop secondary damage and infection. In addition to acting as a therapeutic barrier to relieve pain and provide moisturization, sprayable skin infection dressings also absorb extrudates, guard against bacterial infections, and transport tiny molecules and medications. The latest advancements in sprayable hydrogel-based wound dressings are covered in this study. A summary of the many types of burn wounds, the best burn dressing designs and attributes, and the state of commercial spray-on burn dressings are provided. Researchers are actively concentrating on altering the solution viscosities, propellant systems, and pump nozzle designs for spray formulations in order to attain the best healing capabilities employing sprayable wound dressings. Lastly, the topic of replacing skin transplant procedures with hydrogel-based dressings for tissue regeneration is covered.

1. Introduction

The largest organ of the body is 'skin'. Skin provides protections against homeostasis also provides protection against UV light, physical and chemical pollutants, toxicity on skin can be manifested and it produces lots of skin disorders like skin cancer and melanogenesis. Now a day, skin cancer is the most serious illness. When expose to harmful UV lights the abnormal growth of cell is formed. It is mostly occurring in population of fair-skinned people. In India, these types of problems are also increased. Themortality rate and morbidity rate are also increases. UV-light damages skin cells, over time these lesions grow into actinic Keratoses (orange) and if ignored, may progress to squamous cell carcinoma. The first stage of cancer is initiation, second one is promotion and third one is progression. These stages are mediatory for biochemical and molecular changes.

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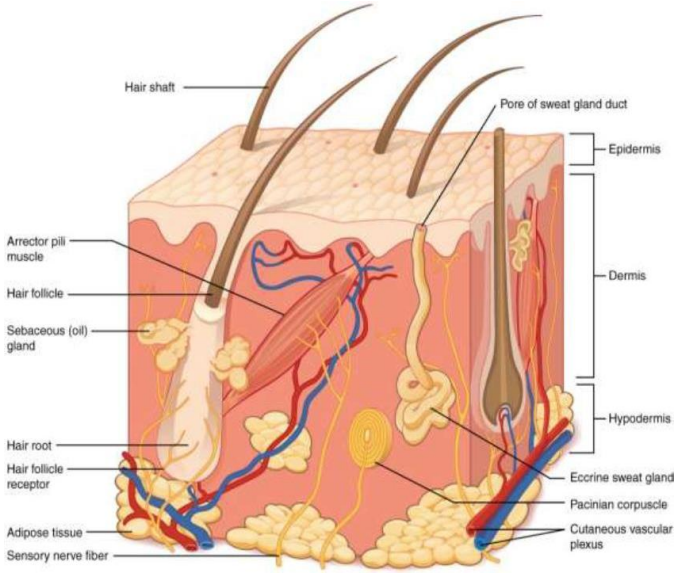

Figure 01 structure of skin

Topical Drug Delivery System

There are various types of routes of administration of drugs. Topical drug delivery systemis one of them. This route is used for the management of pain, incontinence of urination and contraception. This formulation is also used for the treatment of cutaneous disorders like acne, psoriasis. This may penetrate the skin layer or mucous membrane. It gives therapeutic action on application site. These preparations maybe used in the form ointments, gels, creams, lotions, spray solution, eye drop, nasal drop. These formulations must have physical and chemical stability and produces sufficient amount of therapeutic profile. Formulation was releasing the medicaments and deliver to the site of action.

For the production of parenteral emulsions, a high-pressure homogenizer is used. This technology is well established and very well accepted for the large-scale productions of Nanoparticles. Lipid Nanoparticles have been prepared by high pressure homogenization techniques. Two type of homogenization is used cold andhot for the preparation of Nanoparticles. The Lipid is been melted in both the process and the active compound is been dissolved and dispersed in high pressure homogenization. Through a narrow gap high pressure of liquid is been pushed (100-2000 bar). The forming particles may be disrupting by high shear stress and cavitation forces which may down the submicron range. This technique is used forthe production of lipid nanoparticles. This technique is also used for the manufacture of parenteral lipid emulsion for long period. Other available technique may produce the problems. In curtained conditions, the high energy may affect the temperature and pressure of the system.

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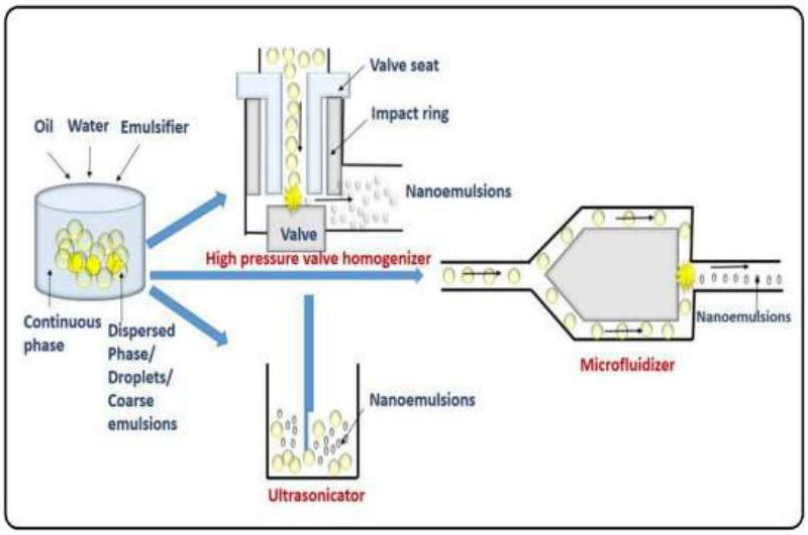

Figure 02 mechanism of tropical gel

Identification of Drug

One of the major preliminary tests to be done for verification and assuring the purity of the drug sample prior to formulation creation is identification of the procured medication. As a Compendial test, an identification test is included to assist in establishing the identity of goods as purported. The appearance, solubility, and melting point of the drug sample were used to identify it in the current study, and this was confirmed by Fourier-transform infrared (FT-IR) spectroscopy assessment of distinct functional groups.

Appearance

The procured drug sample was visually observed for its color and was compared with the reported appearance of the drug.

Solubility of drug

As a purity test, quantitative solubility tests are used. The drug's solubility in water and buffer solutions of various pH levels was tested. In a clean dry test tube, 10 mg of sample was placed, and buffer solution was gradually added in 0.1 ml aliquots with continuous shaking until it dissolved completely. The amount of solvent required to dissolve the medication powder was recorded, and the solubility was compared to previously published values[115].

Melting Point

The melting point is one of the methods for determining the purity of a medicine. As a result,the melting point apparatus was used to determine it for the sample using the capillary method (VMP-D, Veego). A small amount of the material was inserted in the melting point equipment in a capillary tube (closed at one end). The temperature at which the substance began to turn into a liquid and the temperature at which the solid vanished completely wereboth recorded.

FT-IR Analysis of Pure Drug

For the solid-state characterization of pharmaceutical materials, Fourier Transform Infrared (FT-IR) is an important supplementary method. The substance was identified utilising an Alpha Bruker FTIR spectrophotometer and infrared spectroscopy. The disc method was used to prepare the sample. In a mortar-pestle, the medication was triturated with potassium bromide (about 5 mg sample with 100 mg dry potassium bromide) to obtain a fine and

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homogenous mixture. The pellets were made by compressing the powder with a potassium bromide press at 20 psi for 10 minutes. The sample disc was prepared and inserted in the sample compartment. In the range of 4000-400 cm-1, the sample was scanned in transmission mode. The acquired IR spectra were compared to a pure drug's standard spectrum[16].

Preparation of standard and sample solutions

Following the preparation of a 500 g/mL stock standard solution in water, dilutions were carried out to create eight standard solutions (0.1, 0.5, 1.0, 2.0, 4.0, 6.0, 8.0, and 10 g/L). Similarly, the limit of detection (LOD) and limit of quantitation (LOQ) for this approach were determined by serial dilutions of a 5-FU standard solution (1.0 g/mL) with water (50.0, 75.0, 100.0, 125.0, 150.0, and 200.0 g/mL). The samples were diluted in water to the proper concentration. Prior to injection, the standards and samples were filtered using a 0.22 m pore size filter (Millipore, Bedford, USA).

2. Method Validation

The developed analytical method was validated for various parameters like system suitability, Specificity, linearity, Precision, accuracy and LOD & LOQ as per ICH guidelines and data obtained were statistically analysed.

System Suitability

A system suitability test was performed for the validation of the analytical procedure. For SST selection some parameter was used like Percent relative standard deviation (% RSD) of the area, RSD of Retention Time (RT), USP tailing factor, theoretical plates, and resolution were used. For the determination of these parameters, standard solutions were pushed or injected by 6 times.

Physical parameters of drug

Before moving forward with formulation development, it is necessary to identify the purchased drug sample and ensure its purity.

Specificity

This method is used for the determination and establishment of SLNs dispersion for lipids and surfactants. It did not interfere into the quantification of drugs. This method was evaluated by comparing the chromatograms of 5 Fluorouracil extracted from the SLNs and the blank nano-particle for the peak determination.

Linearity

For the determination of linearity, stock solution of 10 concentrations between 50 to 200 µg/ml was injected in triplicate. Calibration curve of 5 Fluorouracil was plotted by peak area versus percentage of drug concentration. If the intercept is < 1% then the linearity was confirmed.

3. Results and Discussion

Collection of drug

Polymixin bacterium sulphate was obtained as a gift sample from Encube Ethical Pvt. Ltd. Goa. Span 60, Cholesterol and carbopol 934 were purchased from Loba Chemicals, Mumbai. Lecithin was purchased from Research lab Mumbai. All other ingredients were of analytical grade.

Table 6 summarises the identification tests and inferences for the drug sample based on its appearance, solubility, and melting point determination.

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Table 1: Identification Test for Drug

Parameters	Observations	Reported	Inferences
Appearance	White powder	White to almost white powder	Complies
Melting Point	280-285 ^{0}C	282 283 ^{0}C	Complies
Solubility	solubility of 5-Fluorouracil is 12.1 mg/ml in water	solubility of 5-Fluorouracil is 12.2 mg/ml in water	Complies

Drug Solubility Determination

The drug dissolution period was found to be 10 to 12 hours to reaches the equilibrium solubility. It did not generate excessive degradants. In short periods these may show insufficient dissolution and long period show unwanted degradants. For phase solubility studies the experimental optimum time is provided. Various pH is been determined by the saturation solubility of Polymixin b sulphate.

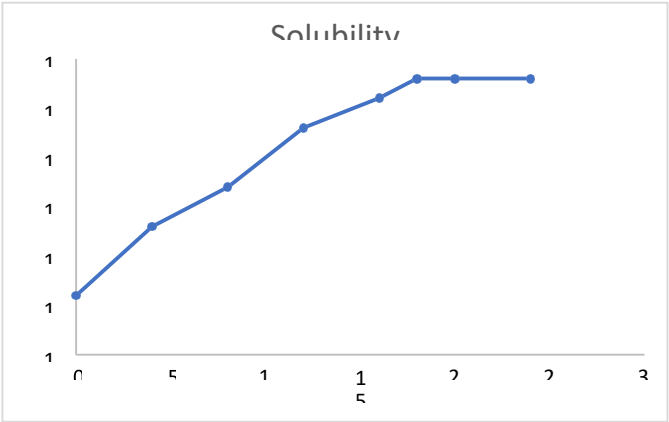

Figure 32: Solubility Curve of Polymixin b sulphate

Table 7: Solubility of Polymixin b sulphate in various pH Buffer Solutions

Buffer Solvents with Different Ph	Solubility of Drug (mg/ml ± SD)
pH 2.5	**121.25 ± 0.85**
pH 3.5	**121.19 ± 0.75**
pH 4.5	**129.45 ± 0.49**
pH 5.5	**131.51 ± 0.78**
pH 6.5	**135.48 ± 0.95**
pH 7.5	**135.15 ± 0.78**
pH 8.5	**135.47 ± 0.74**
pH 9.5	**145.42 ± 0.79**
pH 10.5	**131.15 ± 0.69**
Water 7.0	**131.45 ± 0.85**

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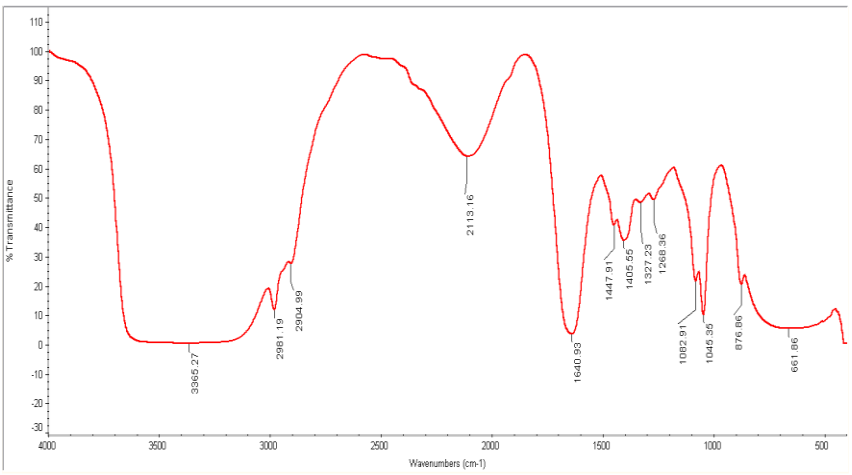
FTIR Study

The sample is confirmed to be of the medication Polymixin b sulphate based on the observations' conformance to the given criteria. Fourier-transform infrared (FT-IR) spectroscopy was used to determine the various functional groups present in the powder drug sample, which were then compared to the standard spectra of Polymixin b sulphate for confirmation.



Peak	Reference (cm^{-1})	Observed (cm^{-1})
N-H stretching	3291	3365.27, 2981.19, 2904.99
C=O stretching	1692	1640.93,1447.91,1405.55
stretching of the C-O-C bridge	1028	1082.91,1045.35

4. Conclusion

In Pre formulation study, the drug samples of polymixin bacterium sulphate were characterized for the physiochemical properties and found to be within specified limit. Partition coefficient for polymixin bacterium sulphate was found to be 0.998. Physical Interaction of Drug and Excipients study was conducted. The observation showed no physical interaction between drug and excipients

Drug Excipients Compatibility study was carried out by FTIR. FTIR of drug and excipients showed unchanged peaks of polymixin bacterium sulphate. The result indicated that there is no chemical interaction between polymixin bacterium sulphate, lipids and excipients mixtures.

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Conflict of interest: Nill

References

[1] Dodds A, Chia A, Shumack S. Actinic keratosis: rationale and management. Dermatology and therapy. 2014 Jun;4(1):11-31.

[2] Costa C, Scalvenzi M, Ayala F, Fabbrocini G, Monfrecola G. How to treat actinic keratosis? An update. Journal of Dermatological Case Reports. 2015 Jun 30;9(2):29.

[3] Winton GB, Salasche SJ. Dermabrasion of the scalp as a treatment for actinic damage. Journal of the American Academy of Dermatology. 1986 Apr 1;14(4):661-8.

[4] Chia A, Lim A, Shumack S, Moreno G.

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www.jchr.org

JCHR (2024) 14 (03), 2505-2511 | ISSN: 2251-6727

Actinic keratoses. Australian family physician. 2007 Jul;36(7).

[5] Schmitt JV, Miot HA. Actinic keratosis: a clinical and epidemiological revision. Anais brasileiros de dermatologia. 2012; 87:425-34.

[6] Jansen MH, Kessels JP, Nelemans PJ, Kouloubis N, Arits AH, van Pelt HP, Quaedvlieg PJ, Essers BA, Steijlen PM, Kelleners-Smeets NW, Mosterd K. Randomized trial of four treatment approaches for actinic keratosis. New England Journal of Medicine. 2019 Mar 7;380(10):935-46.

[7] Warino L, Tusa M, Camacho F, Teuschler H, Fleischer Jr AB, Feldman SR. Frequency and cost of actinic keratosis treatment. Dermatologic surgery. 2006 Aug;32(8):1045-9.

[8] Nilsson K, Svensson S, Landberg G. Retinoblastoma protein function and p16 INK4a expression in actinic keratosis, squamous cell carcinoma in situ and invasive squamous cell carcinoma of the skin and links between p16 INK4a expression and infiltrative behavior. Modern pathology. 2004 Dec;17(12):1464-74.

[9] Gupta AK, Davey V, Mcphail H. Evaluation of the effectiveness of imiquimod and 5- fluorouracil for the treatment of actinic keratosis: Critical review and meta-analysis of efficacy studies. Journal of cutaneous medicine and surgery. 2005 Oct;9(5):209-14.

[10] Tanghetti E, Werschler P. Comparison of 5% 5-fluorouracil cream and 5% imiquimod cream in the management of actinic keratoses on the face and scalp. Journal of drugs in dermatology: JDD. 2007 Feb 1;6(2):144-7.

[11] Jeffes EW, Tang EH. Actinic keratosis. American journal of clinical dermatology. 2000 May;1(3):167-79.

[12] Pelizzo G, Avanzini MA, Icaro Cornaglia A, De Silvestri A, Mantelli M, Travaglino P, Croce S, Romano P, Avolio L, Iacob G, Dominici M. Extracellular vesicles derived from mesenchymal cells: perspective treatment for cutaneous wound healing in pediatrics. Regenerative medicine. 2018 Jun;13(4):385-94.

[13] Lippold BC. How to optimize drug penetration through the skin. Pharmaceutica ActaHelvetiae. 1992 Jan 1;67(11):294-300.

[14] Okamoto H, Yamashita F, Saito K, Hashida M. Analysis of drug penetration through the skin by the two-layer skin mode. Pharmaceutical research. 1989 Nov;6(11):931-7.

[15] Kalbitz J, Neubert R, Wohlrab W. Modulation of drug penetration in the skin. Die Pharmazie. 1996 Sep 1;51(9):619-37.

[16] Beloqui A, Solinís MÁ, Rodríguez-Gascón A, Almeida AJ, Préat V. Nanostructuredlipid carriers: promising drug delivery systems for future clinics. Nanomedicine: Nanotechnology, biology and medicine. 2016 Jan 1;12(1):143-61.Czajkowska- arriers: A

[17] potential use for skin drug delivery systems. Pharmacological Reports. 2019 Feb 1;71(1):156-66.