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FORMULATION AND EVALUATION OF NYSTATINNIOSOMAL GEL DRUG DELIVERY SYSTEM

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ABSTRACT

Purpose: Niosomes are becoming more essential in medication administration due to their potential to minimize toxicity and alter pharmacokinetics and bioavailability. Topically applied Niosomes may prolong drug residence duration in the stratum Corneum and epidermis while lowering drug absorption in the blood stream. It can serve as drug storage and delivery systems. The drug release rate and affinity for the drug can be adjusted by changing the vesicular composition or surface features. Desired location Nystatin with a broad spectrum of action that can be used to treat both superficial and systemic infections. Infections caused by fungi. **Materials and Procedures**: In order to increase low skin penetration while reducing negative Effects Nystatin Niosomes were generated using a Ether injection method in conjunction with topically conventional drug administration. Using a way A Ether injection Method approachwas used to make Nystatin Niosomes utilizing varies ratios of non-ionic surfactant (Span 60) and cholesterol. Size- Spherical shape-Unilamellar, entrapment efficiency, and Drug Content, Viscosity and pH range Antifungal activity test were all examined in the Following Formulations. Were discovered for the Nystatin Niosomes formulations. The size range was discovered to the spherical. Niosomes of Nystatin synthesized with Span 60 at a ratio were found to be promising. Carbopol was added in different concentrations. The prepared gels were tested for a variety of physicochemical properties. **Results:** The formulations were screened for Physical appearance The gel prepared by test clarity, cooler, homogeneity and present of Evaluation pH- pH after 0^{th} days-6.0,5.9,7.0, pH after 15^{th} days-6.8,6.9,7.0 pH after th days 6.7,6.9,7.0 Rheology test - RPM 0.1-FS-54888 FL-44091 Vesicles size Diameter-2.52-3.42 µm FS 60FL 100 Drug Content- Formulation Code % Drug content-FS-1 94.64,FS-2 93.41,FL-1 95.22,FL-2 91.73

Medicine Entrapment Efficiency- FS 98.70 FL 99.02 Stability Study Entrapment efficiency(%) 5°C refrigeration temperature 52.4,50.1,49.6,49,3- (%) 50°C room Temperature-98.13, 94.94, 92.8,91.8 Anti fungal test Diameter Zone of Inhibition (mm) ***Aspergillus Niger*** 26.8,- 36.0, 27.5, 35.1 20.5.

KEYWORD: Span 60, Cholesterol, Stearic acid, Diethyl ether Triethanolamine.

INTRODUCTION

Even the oral route is the convenient route for delivery of drugs, it has some limitation in the treatment of skin diseases. The topical delivery system has better percutaneous absorption than the semi solid preparations. Recently niosomes are becoming popular in the field of topical drug delivery due to its outstanding characteristics like enhancing the penetration of drugs, providing a sustained pattern of drug release and ability to carry both hydrophilic and lipophilic drugs. Topically applied Niosomes can increase residence time of drug in the stratum corneum and epidermis. Topical applicability of niosomes was further enhanced by developing niosomal gel formulation using carbopals. The release from the niosomal gelwas highly prolonged when compare to conventional gel formulation. As well as the presence of other ingredients that act as skin permeation co-enhancers

Fungal Infection

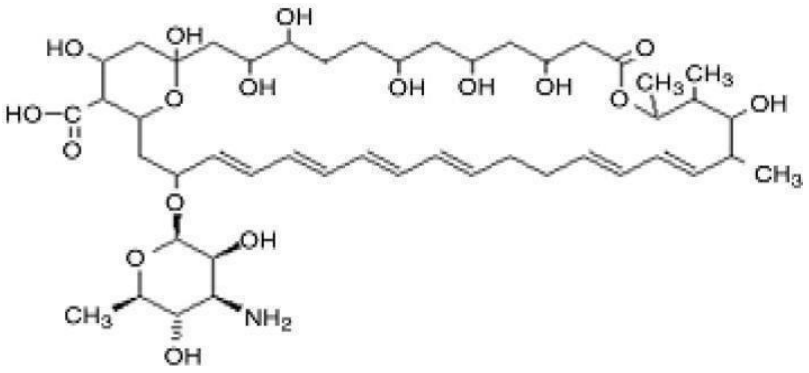
Dermatophyte is a sort of parasite that contaminate top layer of skin. Organisms had been perceived as causitaive specialist of human infection sooner than microorganisms. Parasites causing favus (Trichophytons chonleinii) and thrush (Candida albicans) had been portrayed as soon as in 1839. Organism contaminations anyway are incredibly normal and some of them are not kidding and, surprisingly, lethal. "With the control of most bacterial contaminations in the created nations, parasite disease accepted more noteworthy significance. Organisms are eukaryotic protista that contrast from microorganisms and different prokaryotes in numerous ways." They have inflexible cell dividers containing chitin, manna and different polysaccharides

Gels are straight to darken semisolids that have a significant amount of vehicle to polymer, i.e., the central individual that is gelling. Colloidal association was formed using a polymeric or consistency modifier added to an appropriate vehicle. By immobilising and obtaining the soluble particles, colloidal association limits the flow of fluid. Skin drug conveyance arrangement of skin contaminations utilizes different measurements structures like strong,

semisolid and fluid definition. Non ionic surfactant scattering gives discharge design in supported manner however created gel definition work on effective appropriateness. Different measurements structures are accessible in semisolid structure, containing unmistakable properties

- **Chemical Name:** 2-(4-isobutyl-phenyl) propionic acid
- **Molecular weight:** 926.13
- **Structural Formula:**
- **Melting Point:(°C): 153-155**
- **Solibility:** Insoluble in water Soluble In Diethyl ether and Chloroform Methonol, ethanol.

- **Structural Formula**



MATERIALS AND METHODS

Materials

Nystatin was gifted by Alkem Pharmaceuticals, Mumbai. Span 40, Span 60, Tween 60 was purchased from SD Fine Chemicals Ltd., Mumbai. CHO was purchased from Loba Chemie Pvt Ltd., Mumbai. Carbopol 934 was purchased from Himedia, Mumbai. Disodium hydrogen orthophosphate and Potassium dihydrogen orthophosphate were purchased from SD Fine Chemicals Ltd., Mumbai. Chloroform, Methanol, Glycerol and Triethanolamine were purchased from SD Fine Chemicals Ltd., Mumbai. All other materials were of analytical grade.

Pre formulation StudiesCompatibility Studies

- Drug and excipients interaction study is carried out by FTIR technique.
- Drug Compatibility Studies Instrument of Difference scanning calorimeter

Preparation of Nystatin NiosomesEther injection method

Drug span60 and cholesterol are dissolved in equal quantity in 5ml diethyl ether. Beaker is dissolved. The solution is loaded with the help of injection phosphate buffer is taken whose pH 7.4 taken in a 500 ml beaker in Placed on a magnetic stringer, operated at a temperature of 55 to 60 at 200 rpm, then operated for 30 minutes at a room temperature for 30 minutes, the solution is injected drop by drop, after which Niosomes are formed.

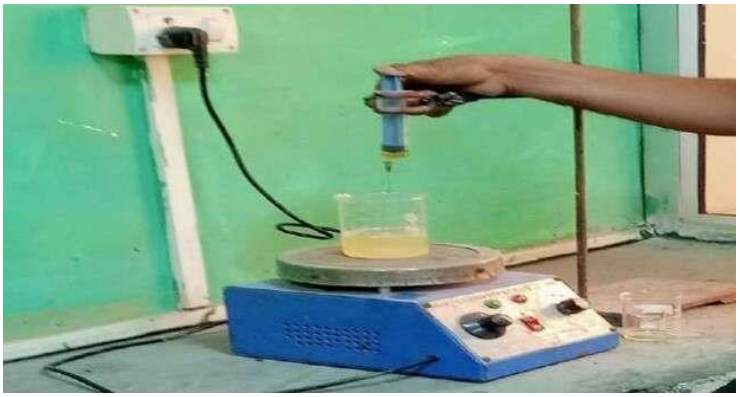


Figure: Ether injection method.

Table of Composition of Nystatin Niosomes Suspension.

S.N	Ingredients	FS-1	FS-2
1	Nystatin	150mg	250mg
2	Span60	15 gm	20 gm
3	Cholesterol	10 gm	10 gm
4	Steric acid	5 ml	10ml
5	Diethyl either	q.s	q.s
6	Buffer solution pH 7.4	200 ml	250 ml

Formulation of Nystatin Niosomal GelProcedure

1. Weighed amount of Carbopol 940 was soaking for one day in 200ml distilliled water
2. Carbopol 940 was homogenized in homogenizer.
3. Mix other ingredients [Nystatin Niosomal suspension Glycerin,] properly in another beaker.
4. Then add the above mixture in homogenized Carbopol 940.
5. Then add required amount of Triethanolamine.
6. Then homogenize the above mixture, add orange oil and formation of gel.

Figure: formulation.

Table of Composion of Nystain Niosomal gel.

S.N	Ingredients	Quntity
1	Nystatin Niosomal suspension	200 ml
2	Carbopol 940	10gm
3	Glycerine	20 ml
4	Tri-ethonalamine	10 ml
5	Purified Water	q.s

Evaluation of Nystatin Niosomal gel

- **Physical appearance**

The gel prepared by test clarity, cooler, homogeneity and present of evaluation

- **pH**

The pH of clear definition was checked with computerized pH meter.

- **Rheology test**

Viscosity Test Study by Brookfield viscometer

- **Drug content**

Drug content in the niosomal gel equivalent to 1ml was determined by lysing the Niosomes gel. 100ml using n-propanol. 1ml of the lysed Niosomal solution was then diluted up to 10ml using 7.4 phosphate buffers. The absorbance of the dilution was then calculated spectrophotometrically at 325nm.

- **Entrapment Efficiency**

To test the entrapment efficiency of the formulations, 1 ml of the suspension was combined with 10 ml distilled water and Centrifugation at 15,000 rpm for 60 minutes at 4°C in a high-speed cooling centrifuge to separate Niosomes from unentrapped medicine. The legal drug content in the supernatant was measured to use a UV- Visible Spectrophotometer at 306 nm after suitable dilution. The fraction of drugs entrapment in Niosomes was calculated using the formula below.

Figure of uv visible spectroscopy.

Stability study

Vesicle stability with respect to drug leakage and drug degradation upon storage was studied at refrigeration (4 0C), room temperature (25 0C) and high temperature (50 0C) for a period of one month on niosomal suspension and gel samples containing a known amount of Nystatin contained in light resistant containers. Samples were withdrawn at weekly intervals, and entrapment efficiency was determined.

Antifungal activity test

Antifungal effectiveness experiments were conducted to determine the biological functions of Niosomal formulation in comparison to other antifungal formulations. Nystatin gel, both simple and commercially available gel Aspergillus niger gel as a test microorganisms. The agar diffusion test is used to determine this. Using the 'Cup plate' approach Potato dextrose layer The test organisms were planted on agar media (20 ml).In petric dishes, allow to solidify. Cups were created on the spot. agar layer solidified with the help of a sterile borer (5 mm).1 g of medication is included in 5ml of Niosomal gel solution. one cup (hole) inscribed with the letter '5 ml and ml of The second container is filled with commercialized gel

solution (1 g of medication).

RESULTS AND DISCUSSION

Calibration curve of Nystatin

Table Calibration curve of Nystatin.

Conc.(µg/ml)	Absorbance
0	0
5	0.21
10	0.416
15	0.601
20	0.753
25	0.904
30	1.076

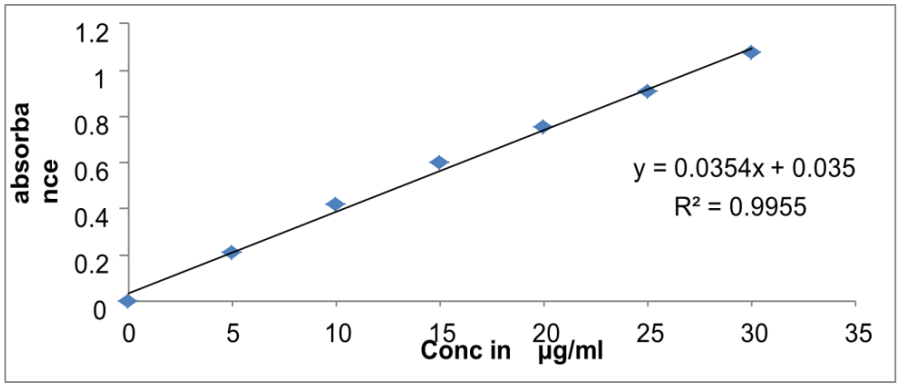


Figure U.V: Visual Spectroscopy graph.

Table of Drug Nystatin powder Physical test.

Parameter	Specifications	Results
Appearance	Yellowish crystalline powder	Yellowish crystalline powder
Solubility	Very slightly soluble in water,	slightly soluble inmethanol
	Insoluble in chloroform, ether	Insoluble in chloroform, ether
Identification	U.V Spectroscopy: at 305nm	Absorbance 0.67
pH (3%)	Between 6-8	6.5
Loss on drying	Not more than 5%	4.5%
Melting point	153-155 ^{0}C	153.6 ^{0}C
Particle size	Not less than 98.0% <80	74

Fourier Transmission Infra Red (FTIR) Analysis Table of Solubility Studies of Nystatin

SOLVENT	SOLIBILITY
Water	Highly soluble in water
Diethyl ether	Highly soluble in water
Chloroform	Freely soluble in water
Methanol	Freely soluble in water
Ethanol	soluble in water
Tri-ethanolamine	Sparingly soluble inAcetonitrile

Drug Excipients Compatibility Study

Table of FT-IR Spectrum of Nystatin pure drug.

Peak	Group
3360	Aliphatic primary amine
3187,2937	CH Stretching
1675	O=C-NH2
703.89,636	Out of plane N-H Wagging

FT-IR Spectrum of Nystatin pure drug

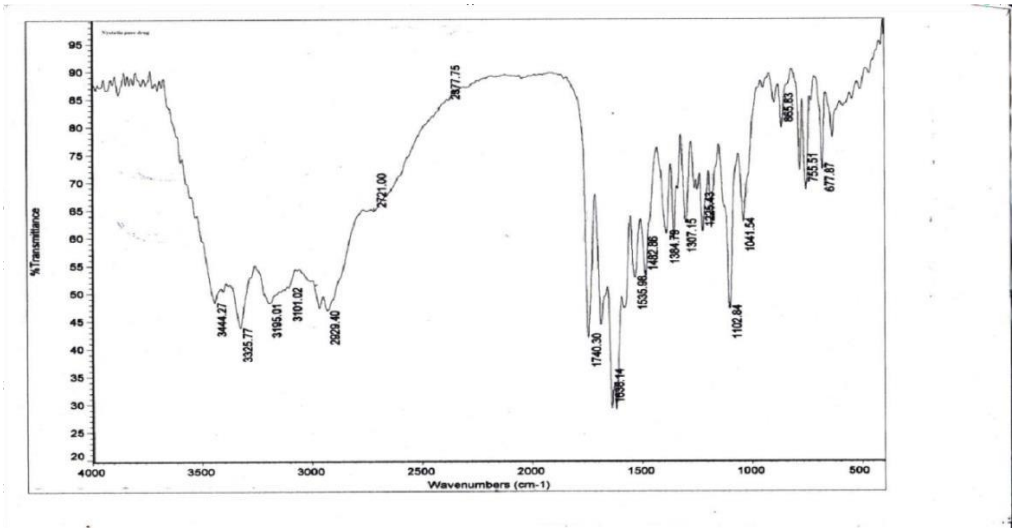


Figure: FTIR Graph of Nystatin.

Table: FT-IR Spectrum of Drug+Cholesterol+Span60.

Peak	Group
3366	Aliphatic primary amine
2917,2849	CH Stretching vibration
1735	O=C Stretching vibration
1654	O=C-NH2 Group

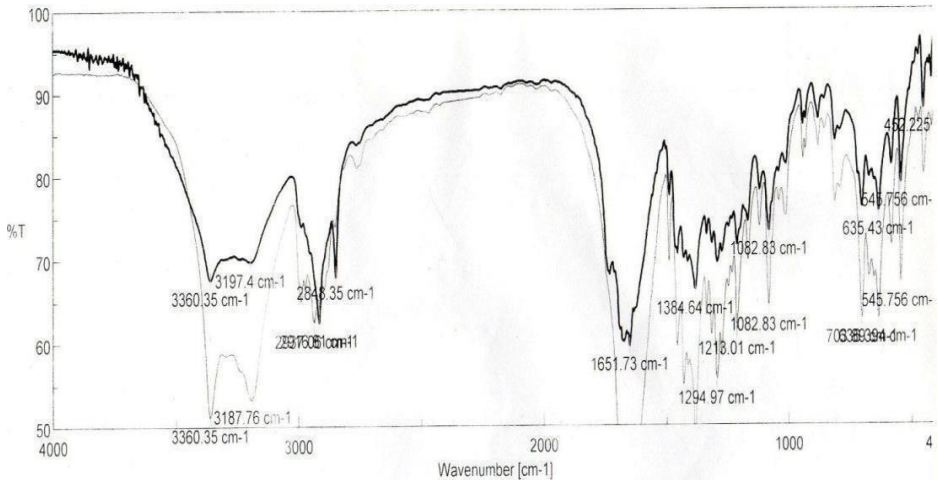


Figure: Drug+Cholesterol+Span60.

FTIR Spectrum of Cholesterol

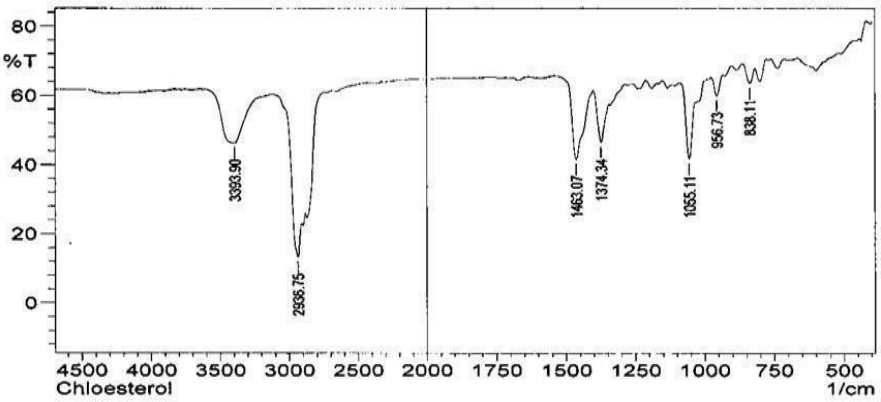


Figure: Cholesterol.

FTIR Spectrum of Carbopol

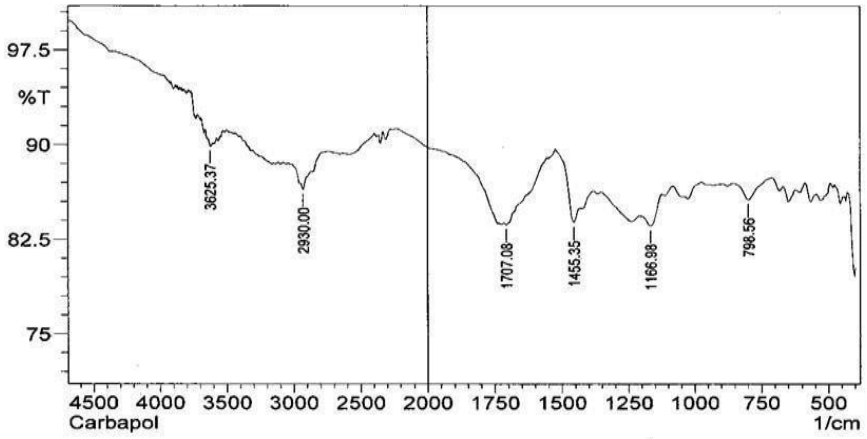


Figure: - Carbopol.

Differential Scanning Calorimetry (DSC) AnalysisDSC of Nystatin pure drug

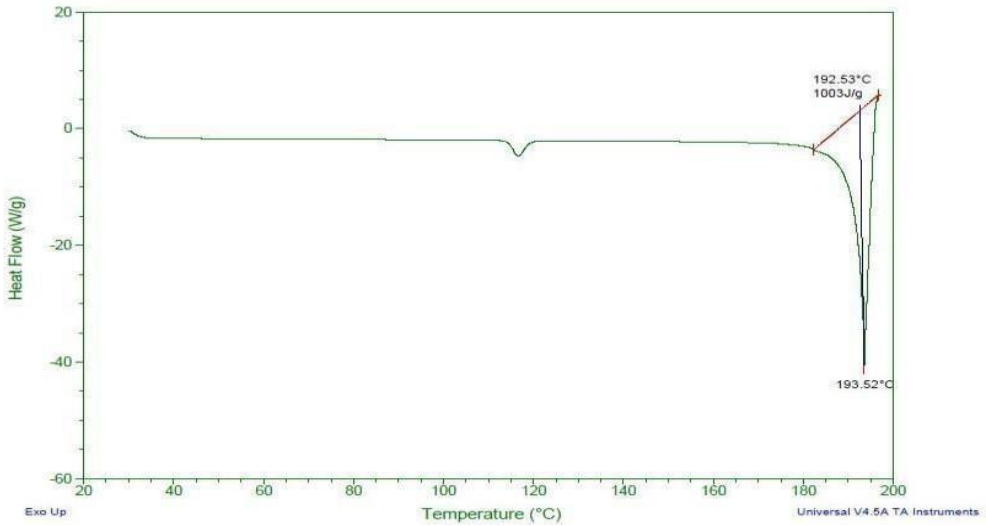


Figure: DSC of Nystatin pure drug.

DSC of Cholesterol

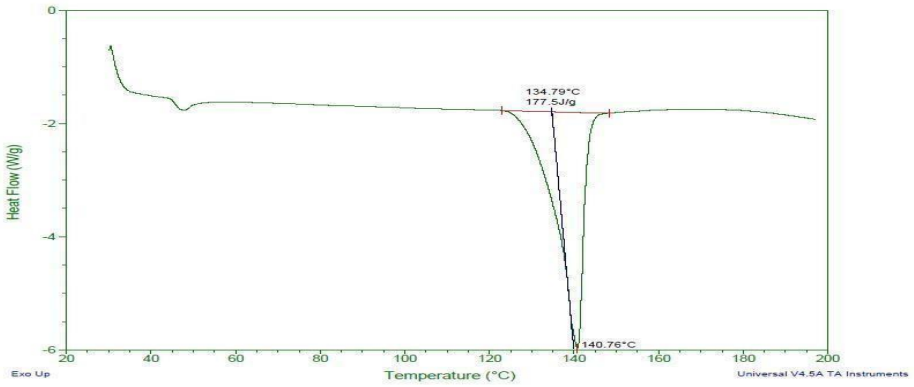


Figure: - DSC of Cholesterol.

DSC of Drug+ Cholesterol+Span60

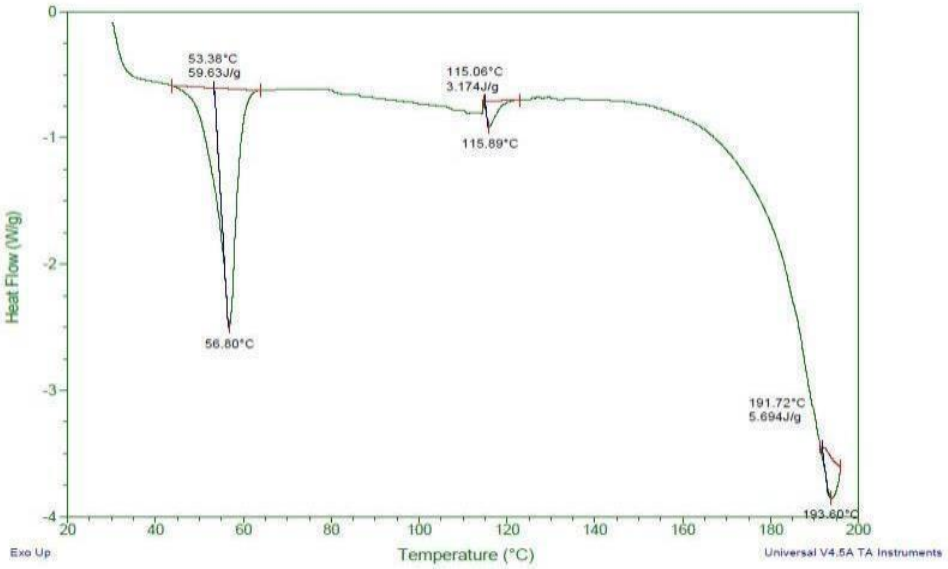


Figure: DSC of Drug+ Cholesterol+Span60.

Formulation of Nystatin Niosomal

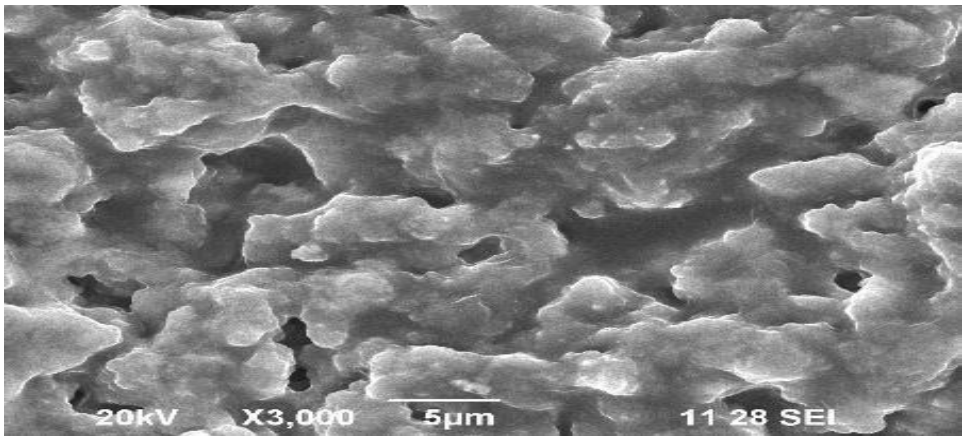


Figure: Formulation of Nystatin Niosomal.

Projection microscope

Figure: Nystatin loaded Niosomes.

Rheology test

Viscosity Test Study by Brookfield viscometer different rpm and Formulation FS and FL Evaluate.

S.N		***Viscosity CPS***	
	RPM	***FS***	***Fl***
1	*0.1*	*54888*	*44091*
2	*0.5*	*11937*	*9178*
3	*1.0*	*5699*	*4499*
4	*5.0*	*1188*	*935*
5	*10.0*	*666*	*542*
6	*20.0*	*415*	*325*
7	*50.0*	*202*	*172*
8	*100*	*132*	*114*

Vesicle size Diameter

Projection microscope the mean vesicle size of medication stacked Niosomes of the various clusters as indicated by the went between 2.52 - 3.42 µm. was in the scope of 0.370 - 0.420 for drug stacked Niosomes which demonstrates a restricted vesicle size.

Vesicle Size diameter of Niosomes

S.No	Type of formulation	Size (µm)
1	FS	50
2	FL	200

Drug content

The drug content various formulation result discussion and analysis data various formulation code % of drug content

S,N	Formulation Code	% Drug content
1	FS-1	94.64
2	FS-2	93.41
3	FL-1	95.22
4	FL-2	91.73

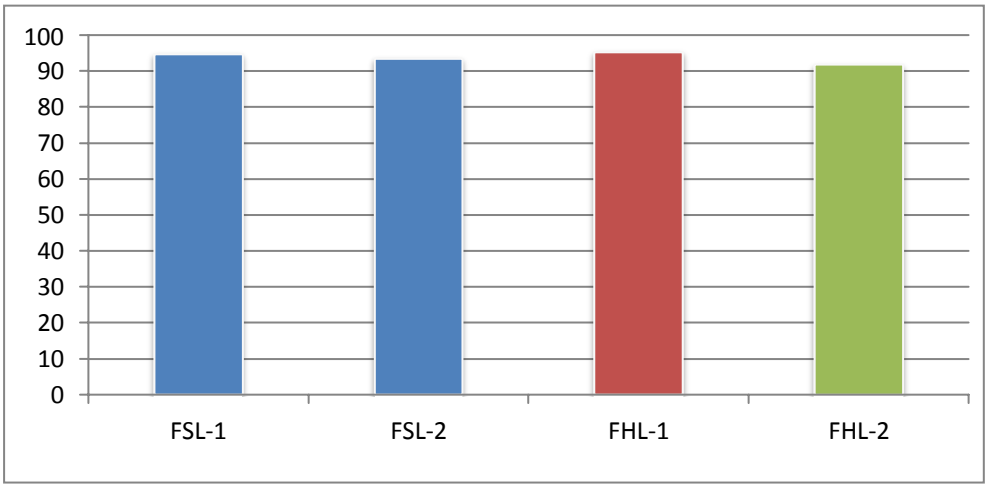


Figure: - Drug content.

Drug Entrapment Efficiency

Table of Drug Entrapments Efficiency

S.N	Formulation	Drug EntrapmentEfficiency
1	FSL	98.70
2	FHL	99.02
3	Plain gel	98.88

Flow Chart of Drug Entrapments Efficiency

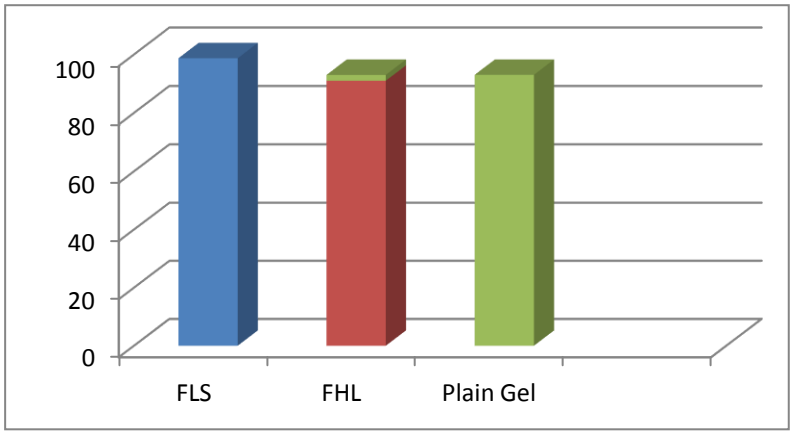


Figure:- Flow Chart of Drug Entrapments Efficiency.

Stability Study

Vesicle stability with respect to drug leakage and drug degradation upon storage was studied

at refrigeration (4 ˚C), room temperature (30 ˚C) and high temperature (50 ˚C) for a period of one month on Niosomal suspension and gel samples containing a known amount of Nystatin , contained in light resistant containers. Samples were withdrawn at weekly intervals, and entrapment efficiency was determined.

Stability test of Refrigeration and Room Temperature

Temperature of storage		
Time of storage inday	**Entrapment efficiency (%) 4°Crefrigeration temperature**	**Drug Content (%) 50 °C room temperature**
0	52.4	98.13
15	50.1	94.94
30	49.6	92.8
45	49.3	91.8

Antifungal Activity test

The antifungal efficacy experiments compared the biological activity of Niosomal formulation to ordinary Nystatin gel and marketing Nystatin Gel ***tricoderma*** with ***Aspergillus*** Niger as the test organism. Agar diffusion tests using the 'Cup late' technique are used to determine this. In the Petric dishes, a surface of Potato dextrose agar media (20 ml) inoculated with the test microorganisms was allowed to harden. With the use of a sterile borer, cups were created on the hardened agar layer (5 mm). One cup (i.e., whole) labeled with 'F' is filled with 0.5 ml of Niosomal gel solution (1 g of drug), while the other cup (i.e., whole) marked with 'M' is filled with 0.5 ml of marketed gel solution (1 g of Similirity, the third. The plates were then incubated at 37°C for 24 hours after being kept at room temperature for 1 hour. The inhibition zones surrounding each cup were measured.

Table of Anti fungal test Zone of Inhibition.

Formulation code	**Diameter Zone of Inhibition**	
	Tricoderma	***Asperigillus Niger***
FLS-1	2.7.5	35.0
FLS-2	28.0	36.0
FLS-3	25.0	27.5
FLS-4	30.0	35.1
FLS-2	26.0	20.5
FLS-1	20.1	28.1
FLS-2	35.2	32.3
FLS-3	30.0	25.0

CONCULATION

Dermatophyte is a sort of saprophytic organism which contaminate top layer of the skin, nails

and hairs. The backbone of the executives of contagious infectivity and Dermatophyte related with skin and nail wounds has been oral and skin antifungal medication conveyance frameworks.

Polyene antifungal like Nystatin was viewed as compelling against numerous fungal contamination as well as molds disease. Moreover, contagious contamination is related with aggravation consequently consolidated treatment of antifungal and mitigating, for example, Nystatin is recommended for the successful treatment. According to BCS characterization it is Class-IV medication which has low penetrability and low dissolvability. Because of its poisonous profile it can't be figuredout into inject able definitions.

Niosomes transporter delivered the dynamic drug fixing in maintainable way and creates Niosomal conveyance framework for contagious contamination. A short time later Niosomal gel was produced for development of effective appropriateness of Niosomal scattering to restrict API at target site of activity.

Pre-formulation concentrate on gives profiles of medications and different fixings included the definition improvement. The normalization of medications and excipients is an indispensable piece of exploration work. The medication and excipients were normalized and found to conform to pharmacopoeia determinations. Subsequently, they were utilized for additional improvement of definitions.

In definition advancement of Niosomal scattering, at first clear Niosomal detailing was ready by utilizing different centralizations of Span 60 and cholesterol. The clusters werestreamlined for different handling and definition boundaries.

Streamlining of Niosomal scattering is one of the basic cycles that need thought of number of variables and fixings collaboration in definition improvement. We have taken on a approach. Amount of length 60 and cholesterol were liked as two autonomous factors and different execution pointers were contemplated to lay out the result of centralization of lipid stage on Niosomes execution. The various boundaries contemplated were vesicle size, size appropriation, exemplification effectiveness and in-vitro drug discharge from the acquired information. Niosomal scattering showed supported delivered than traditional scattering. It was affirmed by ex-vivo study by utilizing porcine skin. Along these lines stable Niosomal scattering of Nystatin and lemon grass, was created.

In definition improvement and assessment of Niosomal gel at first gels were exposed to Rheological review. Rheological characteristic of 2% Carbopol gel was better when contrasted with other gel (1%, 1.5% w/w) and subsequently, was considered for additional investigations. It was presumes that Niosomal gel showed slow arrival Medication than Conventional gel. In-vitro drug testimony concentrate on extracted porcine skin for 48 hrs showed that the Niosomal gel shows more medication affidavitthan Conventional gel.

Skin aggravation study uncovers that created Niosomal gel having essential disturbance record is zero. Therefore, definition was viewed as protected and non aggravation to the skin.

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