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DEVELOPMENT AND CHARACTERIZATION OF TOPICAL DRUG DELIVERY SYSTEM CONTAINING NIOSOMES

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ABSTRACT

Niosomes are vesicular drug delivery system; it acts as a carrier and protects the drug from the internal environment. It has been also used because of its higher diffusivity in skin for promoting dermal delivery of drug which has to act topically. The aim of present study is to developed and characterise topical drug delivery system containing niosome by using antifungal agent. The antifungal agent widely used for the treatment of infection due to fungal species like *Trichophyton rubum, Trichophyton mentagrophyts, Malassezia furfur* etc. most of the antifungal drug are poorly water soluble. Sustained release of Niosomes can be applied to drugs with low water solubility since those could be maintained in the circulation via niosomal encapsulation. Niosomes were formulated by rotary evaporation hydration method by using phospholipids, cholesterol and Non ionic surfactant such as span and Tween. Primary placebo batches of niosome were prepared and evaluated for particle size and shape. Then octopirox loaded batches of niosome were prepared and evaluated for size, shape and Entrapment efficiency. For the delivery of niosome through skin topical dosage form i.e. cream was prepared. Evaluation of cream containing niosome was carried out for viscosity, measurement of pH, spreadability etc. the results obtained are shown in the present work. From the results it can be concluded that the formulation evaluated for the drug release of the optimized batch i.e. V- using o/w cream base, it was concluded that the drug release rate increases with its increasing concentration.

KEYWORD: Niosome, Octopirox.

OBJECTIVE

To prepare Niosomal cream for Topical Drug Delivery System.

INTRODUCTION[1-5]

Novel drug delivery attempts to either sustain drug action at a predetermined rate, or by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects. Different types of pharmaceutical carriers such as particulate, polymeric, macromolecular and cellular are present. Particulate type carrier also known as colloidal carrier system includes lipid particles (low and high density lipoprotein-LDL and HDL, respectively), microspheres, nanoparticles, polymeric micelles and vesicular like liposomes, sphingosome, niosomes, transferosomes, pharmacosomes, virosomes.[6,7] Niosomes are non-ionic surfactant vesicles having a bilayer structure formed by selfassembly of hydrated surfactant monomers. The bilayer is multilamellar or unilamellar which enclose aqueous solution of solutes and lipophilic components are in the bilayer itself. Niosomes are formed by hydration of non-ionic surfactant dried film resulting in imbibing or encapsulating the hydrating solution. Major component of niosomes is non-ionic surfactant which give it an advantage of being more stable when compared to liposomes thus overcoming the problems associated with liposomes i.e. susceptibility to oxidation, high price and the difficulty in procuring high purity levels which influence size, shape and stability . Niosomes can entrap both hydrophilic and lipophilic drugs in aqueous layer and vesicular membrane respectively. The bilayers of niosomes have both inner and outer surfaces to be hydrophilic with sandwiched lipophilic area in between. Thus a large number of drugs and other materials can be delivered using Niosomes.

MATERIALS AND METHODS

Octopirox was obtained as a gift sample Clariant, Mumbai. Soya lecithin (granular phosphatidylcholine 90H) was obtained as a gift sample from phospholipid GmbH Nattermannallee, Germany. Span 20,40,60,80 and Tween 20,40,60,80 were made available from the laboratory.

Evaluation of raw materials

Identification and standardization of drug and other excipients were carried out as per the official procedures mentioned in respective monographs.

Preparation of Niosome.[8, 9]

The niosome were formulated by rotary evaporation hydration method. The octopirox concentration was varied from 0.5 to 2%.

The soya lecithin, cholesterol, surfactant and drug was dissolve in chloroform and methanol in a concentration 7:3 and evaporated using rotary flash evaporator under reduce pressure. The flask containing mixture was kept for 1hour under vacuumed pressure to remove solvent residue. The dried film was hydrated with 10% calcium chloride solution for overnight to disperse the film in the form of niosome and these are evaluated for particle size, vesicular shape and entrapment efficiency.

Table 1: formulation plan for Niosome

Surfactant	Batch code	Conc. of cholesterol and soya lecithin (mg) (1:1)	Amt. of surfactant (mg)	Amt. of drug (mg)
Span 80	V-1	500:500	600	50
	V-2	500:500	600	100
	V-3	500:500	600	150
	V-4	500:500	600	200
Tween 80	V-5	500:500	700	50
	V-6	500:500	700	100
	V-7	500:500	700	150
	V-8	500:500	700	200

Preparation of O/W Cream

Accurately weighed quantity of ingredient in oil phase such as stearic acid and lanoline were taken in one beaker and melt at 75^0 C. In another beaker glycerin and triethanolamine containing water was mixed and heated at 70^0C and slowly this phase was incorporated in oil phase with continuous stirring and simultaneously preservative were added to it. Stirring was continued till the temperature comes down to 40^0C-45^0C and cream base was formed.

Preparation of W/O Cream

Accurately weighed quantity of ingredient in oil phase such as petroleum jelly, paraffin oil, span 80, and lanoline were taken in one beaker and aqueous phase ingredient such as sorbitol solution (70%) was taken in another beaker containing adequate water and both this beaker containing different phases were heated on water bath till 75^0 C temp and at this temperature point, the oily phases was added to aqueous phase with constant stirring. Stirring was continued till room temperature is attained and cream base was formed.

Preparation of Niosomal Cream

Niosome containing drug was mixed into cream base by using glass rod with concentration of niosome in cream base being 0.5 to 2%.

Evaluation of Niosome[10-15]

Size and its distribution

Niosome assume spherical shape, its diameter can be determining using.

Light Microscopy

Light microscopy has been utilized to examine the gross size distribution of large vesicles. The size of the noisome can be characterized with stage micrometer and eye piece micrometer. The eye piece micrometer is calibrated stage micrometer. The sizes around 100 particles were measured and their average particle size determine.

Drug entrapped efficiency

Niosome entrapped Octopirox was estimated by centrifugation-UV absorbance method. The prepared Niosome were placed in centrifugation tube and centrifuged at 6000 rpm for 90 minute. The supernatant formulation was separated and volume is measured. From that supernatant formulation 2ml is withdrawn and The unentrapped Octopirox was determined by UV spectrophotometer at 307 nm. The samples from the supernatant were diluted 50 times before going for absorbance measurement. The free Octopirox in the supernatant gives us the total amount of unentrapped drug. Encapsulation efficiency is expressed as the percent of drug entrapped. For determining Entrapment efficiency reverse calculation is done. [72]

Further, using the Value of unentrapped drug calculated the entrappment efficiency.

Entrapment efficiency= (Amount of entrapped drug / Total amount added) × 100

Evaluation of Niosomal Cream

Measurement of pH

The pH of various cream formulations was determined by using digital pH meter. 1 gm of cream was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values are calculated and mentioned in table.

Spredability

Spreadability is a term expressed to denote the extent of area to which the cream readily spreads to skin or affected part. A special apparatus has been designed. Spreadability is expressed in terms of time in seconds taken by two slides to slip off from cream, placed between, under the application of a certain load. Lesser the time taken for the separation of two slides, resultant better the spreadability. Spredability was calculating by using formula.

Spredability = $\frac{m \times l}{t}$

Where,

S = Spredability (gm/sec)

m = weight tide to the upper slide (20gm)

t = time taken in seconds

Drug content

lgm of niosomal loaded cream taken and dissolved in methanol and filtered using Watman filter paper and from the filtrate dilution of concentration 10µg/ml were prepared and analyzed at ʎmax 307 nm by UV spectrophotometer absorbance method. From observed absorbance value and the concentration value in 1 ml the drug present in formulation is calculated. This **value was** compared with the actual amount of drug was to be taken for the formulation. And the drug content was calculated. Finding is reported.

In Vitro release study

In vitro release studies were performed using modified diffusion cell. Dialysis membrane (Hi Media molecular weight 12000- 14000) was placed between receptor and donor compartments. Octopirox niosomal cream was place in the donor compartment. The receptor compartment was filled with phosphate buffer pH 7.4 (20ml). The temperature of diffusion cell was maintained at 37±0.5^{0}C. Receptor compartment fluid was stirred at 60 rpm using small magnetic bid. At fix time interval, (after 60 minute) 1ml aliquot was withdrawn from receptor compartment through side tube and equal amount of fresh buffer was added in the receptor compartment. The sample was analyzed by UV – visible spectrophotometer at 307 nm. Results are shown in table.

RESULT AND DISCUSSIONS

Particle size analysis

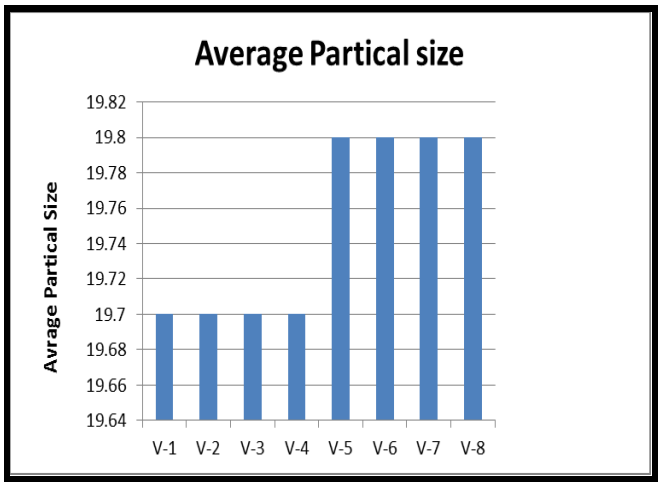
Average particle size of niosome as determine by optical microscopy by using stage micrometer and ocular micrometer are shown in table and in figure.

Drug entrapment Efficiency

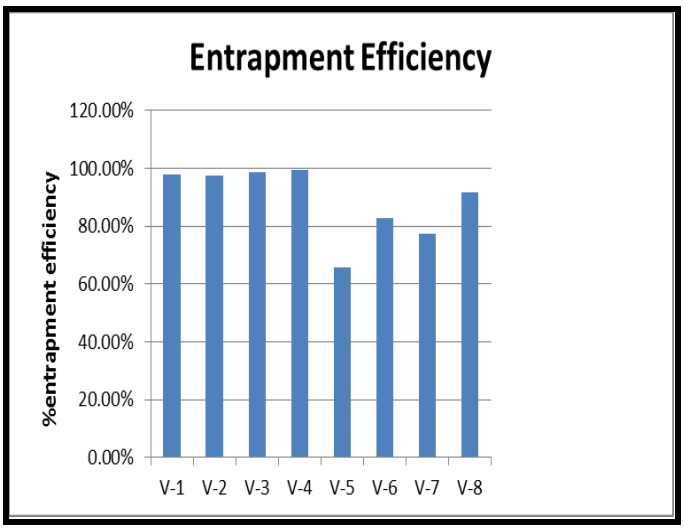
The result of % drug entrapment efficiency are shown in table the formulation V-5 shows the least entrapment about 65.81 % and higher drug entrapment was shown by formulation. Figure shows the comparison of % entrapment efficiency of formulation V-1 to V-8.

Table 2: Result of average particle size and drug entrapment efficiency

Surfactant	Batch code	Average particle size in µm	% Drug Entrapment
Span 80	V-1	19.7	97.86 %
	V-2	19.7	97.62 %
	V-3	19.7	98.40 %
	V-4	19.7	99.36 %
Tween 80	V-5	19.8	65.81 %
	V-6	19.8	82.90 %
	V-7	19.8	77.20 %
	V-8	19.8	91.45 %



Graph 1- Comparison of average particle size of batch V1 –V8



Graph-2 Comparison of % entrapment efficiency of batch V1 –V8

Evaluation of cream Niosomal Cream

pH, Drug content and Speradability

The pH value, Drug content, and speradability of selected batch of niosomal cream are mentioned bellow.

Table 3: pH, Drug content and Speradability

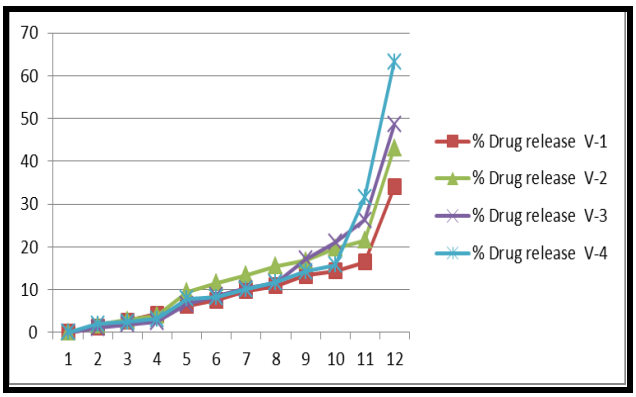
	Batch	pH	%Drug content	Spreadability (gm/sec)
O/W Cream	V-1	6.83	70.94	8.0
	V-2	6.72	82.05	9.2
	V-3	6.83	90.59	10.9
	V-4	6.83	94.01	8.5
	V-5	6.84	78.63	10.0
	V-6	6.74	87.17	9.2
	V-7	6.74	93.16	9.2
	V-8	6.80	98.29	10.9
W/O cream	V-1	6.59	67.52	8
	V-2	6.74	76.06	7
	V-3	6.04	84.61	7.5
	V-4	6.50	91.45	8.5
	V-5	6.52	72.64	8.5
	V-6	6.71	76.90	6.6
	V-7	6.80	82.90	7
	V-8	6.66	95.72	5.7

In vitro drug diffusion study

In vitro release study for batch V-1 to V-4 using O/W cream

Table 4: comparative study of time Vs % drug release for batch V-1 to V-4

Time (hour)	% Drug release V-1	% Drug release V-2	% Drug release V-3	% Drug release V-4
1	1.15	1.79	1.13	2.05
2	2.73	2.99	1.93	2.47
3	4.27	4.01	2.45	3.11
4	6.32	9.57	6.60	7.90
5	7.60	11.62	8.54	8.29
6	9.74	13.50	10.37	10.08
7	10.94	15.55	11.62	11.70
8	13.33	16.75	17.20	14.27
9	14.35	19.75	21.08	15.81
10	16.40	21.55	26.32	31.62
24	34.00	43.16	48.60	63.24

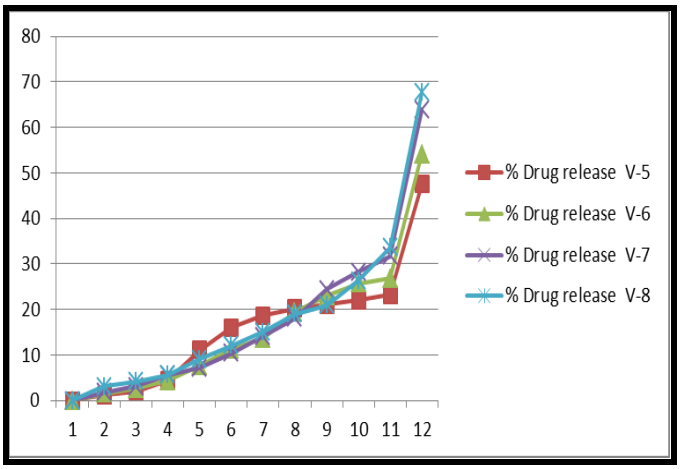


Graph 3-comparative study of time Vs % drug release for batch V-1 to V-4

In vitro release study of batch V-5 to V-8 using O/W cream

Table 5: comparative study of time Vs % drug release for batch V-5 to V- 8

Time (hour)	% Drug release V-5	% Drug release V-6	% Drug release V-7	% Drug release V-8
1	1.19	1.5	1.83	3.07
2	2.05	2.64	3.13	4.2
3	4.44	4.35	5.58	5.59
4	11.11	7.70	7.17	9.1
5	16.06	11.28	10.37	12.13
6	18.63	13.58	14.13	15.04
7	20.17	19.40	18.11	18.97
8	21.11	22.99	24.44	20.89
9	22.05	25.72	28.26	26.28
10	23.24	26.83	31.68	33.68
24	47.52	54.10	63.81	67.69

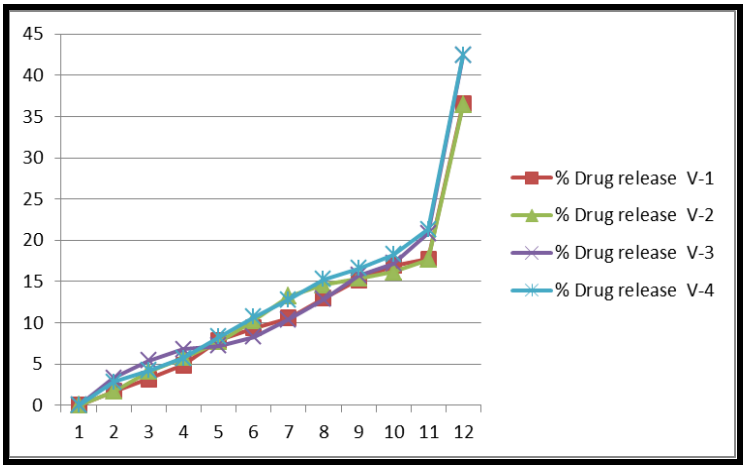


Graph 4-comparative study of time Vs % drug release for batch V-5 to V-8

In vitro release study of batch V-1 to V-4 using W/O cream

Table 6: comparative study of time Vs % drug release for batch V-1 to V-4

Time (hour)	% Drug release V-1	% Drug release V-2	% Drug release V-3	% Drug release V-4
1	1.7	1.7	3.3	2.8
2	3.2	4.1	5.4	4.2
3	4.9	5.8	6.8	5.7
4	7.9	7.7	7.2	8.3
5	9.4	10.25	8.3	10.7
6	10.59	13.24	10.37	12.82
7	12.99	14.61	12.87	15.25
8	15.21	15.38	15.72	16.58
9	16.92	16.15	17.20	18.29
10	17.70	17.69	20.85	21.32
24	36.58	36.41	42.39	42.47

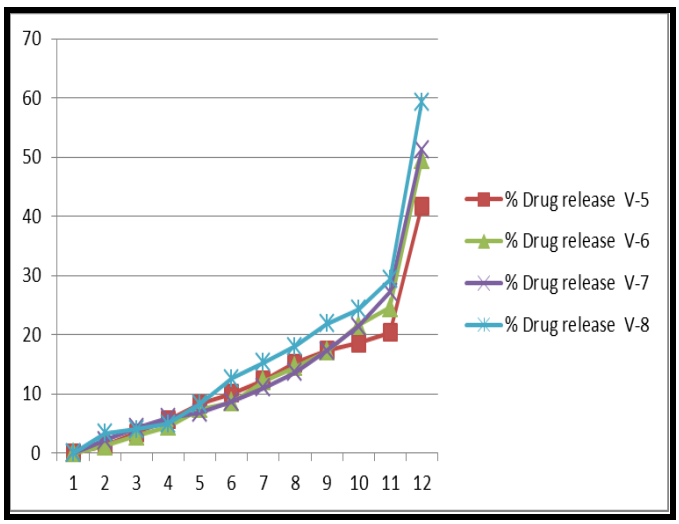


Graph 5-comparative study of time Vs % drug release for batch V-1 to V-4

In vitro release study of batch V-5 to V-8 using W/O cream

Table 7: comparative study of time Vs % drug release for batch V-5 to V-8

Time (hour)	% Drug release V-5	% Drug release V-6	% Drug release V-7	% Drug release V-8
1	1.36	1.2	2.2	3.4
2	3.5	2.9	4.3	4.0
3	5.6	4.52	6.0	5.0
4	8.3	7.52	6.8	8.37
5	10.08	8.63	8.7	12.64
6	12.30	12.13	11.05	15.29
7	15.21	14.61	13.61	18.08
8	17.43	17.17	17.32	21.88
9	18.63	21.62	21.42	24.27
10	20.34	24.61	27.23	29.35
24	41.70	49.91	51.22	59.23



Graph 6-Comparative study of time Vs % drug release for batch V-5 to V-8

CONCLUSION

The aim of this study was to formulate and evaluate niosome of octopirox. From the result obtained from executed experiment it can be conclude that.The drug and excipients were evaluated for confirmation. The entrapment efficiency results help to conclude that the V-16 batch having higher entrapment efficiency. The optimized batch also showed better drug entrapment. When niosomal cream evaluate for spreadability, pH, shown well consistency. When evaluated for the drug release of the optimized batch i.e. V-32 using o/w cream base, it was concluded that the drug release rate increases with its increasing concentration. The niosomal cream was evaluated for stability study; it was found there was no significant change in pH and Drug content.

REFERENCE

1. Debjit Bhowmik, Harish Gopinath, B. Pragati Kumar, S.Duraivel1, K.P.Sampath Kumarv, Recent Advances In Novel Topical Drug Delivery system, The Pharma Innovation, *2012*; 1(9): 12-31.
2. Kalpesh Chhotalal Ashara, Jalpa S. Paun, M.M Soniwala, J.R.Chavda, S. V. Nathvani, Nitin M. Mori and Vishal P. Mendapara Vesicular Drug Delivery System: A Novel Approach Mintage journal of Pharmaceutical & Medical Sciences, *2014;* 3(1): 1-14.
3. Anchal Sankhyan and Pravin Pawar, Recent Trends in Niosome as Vesicular Drug Delivery System, Journal of Applied Pharmaceutical Science; 2012; 02(06): 20-32.
4. Seema M. Jadhav, Pournima Morey, Mrs. Manisha Karpe, Vilasrao Kadam Novel Vesicular System: An Overviwe Journal of Applied Pharmaceutical Science, *2012;* 2(1): 193-202.
5. Biju S.S., Talegaonkar S., Mishra P.R., Khar R.K. Vesicular systems: An overview. Ind. J. Pharma. Sci. *2006*; 68(2): 141-153.
6. Goldberg E.P.Eds., In; Targeted Drugs, 2nd edn, Wiley, Newyork, pp 312, *1983*.
7. Kalpesh Chhotalal Ashara, Jalpa S. Paun, M.M Soniwala, J.R.Chavda, S. V. Nathvani, Nitin M. Mori and Vishal P. Mendapara Vesicular Drug Delivery System: A Novel Approach Mintage journal of Pharmaceutical & Medical Sciences, *2014;* 3(1): 1-14.
8. Todd, J.A., Modest, E. J., Rossow, P. W. and Tokes, Z. A.,, Biochem. Pharmacol; *1982;* 34(2): 541.
9. Egbaria et al, "Liposome as a drug delivery system," Advance drug delivery reviews *1990;* 5(1): 287- 300.

10. Jain SK, Jain NK, Controlled and Novel Drug Delivery, New Delhi: CBS Publisher, pp-199, *1997*.
11. Aly A. Abdelbary , Mohamed H.H. Abou Ghaly, Design and optimization of topical methotrexate loaded niosomes for enhanced management of psoriasis: Application of Box–Behnken design, in-vitro evaluation and in-vivo skin deposition study, International Journal of Pharmaceutics, *2015*; 48(5): 235–243.
12. Trailokya Das, Jiban Debath, Bipul Nath, Suvakanta Dash, Formulation And Evaluation of An Herbal Cream For Wound Healing Activity, International Journal of Pharmacy and Pharmaceutical Sciences, *2014:* 6(2): 693-697.
13. Rokade Vishal Suresh and Kadu Promod Kerunath, Formulation And Evaluation of Novel Antibacterial Ciprofloxacin Loaded Niosomal Cream, International Research Journal of Pharmacy, *2015*; 6(8): 519-527.
14. Mahaptra Annad Prasad, Mishra Dipak Kumar, Panda Prabhudutta, Formulation and Evaluationof Cream Prepared From Croton Sparsiflorus Morong And Healing Activity,International Journal of Research In, *2012;* 3(6): 803-807.
15. Singla Kapil, Rao Rekha, Saini Vipin, Formulation and Evaluation of Lornoxicam Niosomal Gel, International Research Journal of Pharmacy, *2012;* 3(4): 379- 389.