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NANOEMULSION-BASED GEL FORMULATION OF LAMIVUDINE FOR TRANSDERMAL DELIVERY

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ABSTRACT

Lamivudine is a anti-viral drug. The main purpose of the study is to develop nanoemulgel formulalation for transdermal delivery of Lamivudine using aloeveragel. The nanoemulsion can be prepared by using olive oil as oil phase and Tween-80 as surfactant and PEG 400 as co-surfactant were used in different ratio to determined by pseudoternary phase diagram. Four nanoemulsion were developed and coded as ON1, ON2, ON3, ON4 and the optimized formulation ON4 was converted into correponding gel by using Aloevera gel. The Lamivudine loded nanoemulsion were characterized by drug entrapment efficiency, pH, viscocity, transmittance and drug release, stability studies. Further, nanoemulgel formulation were evaluated by drug entrapment efficiency, pH, viscosity, drug release, stability studies. The nanoemulgel showed better release control and used for transdermal delivery of Lamivudine.

KEYWORDS: Nanoemulgel, Lamivudine, transdermal delivery sytem.

INTRODUCTION

Nanoemulgel has dual control release and emerged as one of the important transdermal delivery system. Nanemulgel has nanorange in the range of 10-100µm, can penetrate rapildly and delivered active substances quicker and deeper. By reducing interfacial tension gelling agent promoted good stability for nanoemulsion. Nanoemulgel has better adhesion on the surface of the skin and has increasing solubilising capacity which leads to more concentration gradient towards skin and increase better skin penetration.[1]

For poorly permeable liphophilic drugs, nanoemulsion can be used as excellent vehicles in pharmaceutical field for parentral, oral and ocular and transdermal delivery. Nanoemulsion obtained by low energy emulsification or high energy emulsification methods. High energy methods requires high shear mixing, ultrasonication or high-presure homogenization. The low energy emulsification used the advantages of physicochemical properties of the system that willexploits phase transition to obtain nanoemulsion.[2]

Transdermal drug delivery system (TDDS) are the discrete dosage form and self contained, when they applied to the skin for delivery drugs to the systemic circulation. By transdermal drug delivery sytem the drawback can be overcome.[3] Transdermal drug delivery system is a novel drug delivery system, main purpose is to avoid the side effects of the drugs and to achive a constant delivery of the drugs when applied to the skin.[4]

Lamivudine widely used in the treatment for HIV infected patients and it is an antiretroviral drug. They must be administerd for the life span of the patients most of the anteretroviral including lamivudine are virustatic in nature. To suit various drug molecules novel drug carriers such as transdermal are versatile. Controlled dug delivery system preffered to full fill the long term treatment with anti- HIV agents. Lamivudine requires frequent administration for prolonged period of time and having short biological half life. To achive constant plasm levels for prolonged period of time transdermal route is choosen, Which could be advantageous because of less dosing regimens.[5] The purpuse of this study is to formulate nanoemulsion based emulgel formulation by using gelling agent aloevera gel to overcome the problem associated with lamivudine. Hence, in the present study, nanoemulsion was prepared by spontaneous emulsification method and pseudoternary diagram were constructed to find out nanoemulsion region. Finally the nanoemulgel was obtained by incorporating nanoemulsion in Aloeveragel.

EXPERIMENTAL

MATERIALS

Olive oil were purchased from sigma-Aldrich (St Louis, MA, USA), Tween-80 and polyethylene glycol

purchased from SDFCL, Mumbai. Aloevera pulp was obtained from cultivated aloevera.

Construction of phase diagram

Using titration technique, pseudoternary phase diagrm were contstructed. olive oil used as oily phase and Tween-80 were taken as surfactants and PEG-400 were taken as co-surfactants. Three weight ratio were optimized to determine the optimum ratio which can result in maximum nanoemulsion existence areas 3:1(85%), 3:1(90%). The olive oil ratio to surafactant and co-surfactant were varied to 2:1 (85%), 2:1 (90%), 3:1(85%), 3:1(90%). By using micro syringe the above mixtures were titrated using water by dropwise manner. For the determination of end point composition of the titrated sample were calculated and plotted on the pseudoternary phase diagram by using Chemix software.[7]

Preperation of nanoemulsion

Nanaoemuosion were prepared by mixing accuarate quantity of surfactant and co-surfactant to that mixture oily phase added, at room temperature mix the formulation until it get complete dispersion. Then for the above mixture drug added and vortexed the formulation until transparent solution obtained. Selected nanoemulsion formulation composition were given in the table no 1.[8]

Preperation of nanoemulgel

Nanaoemulgel can be prepared by mixing the obtained nanoemulsion with the aloegel base in the ratio 1:1 by gentle stirring. By measuring the pH, nanoemulgel can be characterized visually and chemically.[9]

Table 1: Formulation of Lamivudine nanoemulgel with selected oil,surfactant, co-surfactnat and water from pseudoternary phase diagram.

Formulation code	Smix ratio	Surfactants	oil	Oil% (w/w)	Smix% (w/w)	Water% (w/w)	Drug(gm)
ON1	2:1 (85%)	Tween-80	Soyabean oil	20	70	10	0.5gm
ON2	2:1 (90%)			10	79	11	0.5gm
ON3	3:1 85%			11	83	6	0.5gm
ON4	3:1 (90%)			14	79	7	0.5gm

RESULT

Determination of drug –excipient compatability studies

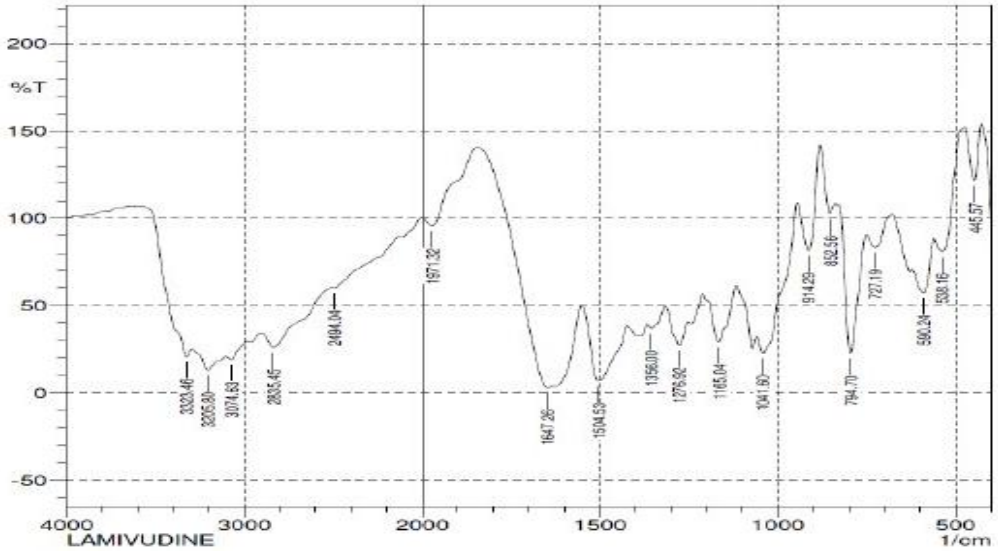


Figure 1: FTIR spectra of pure drug Lamivudine.

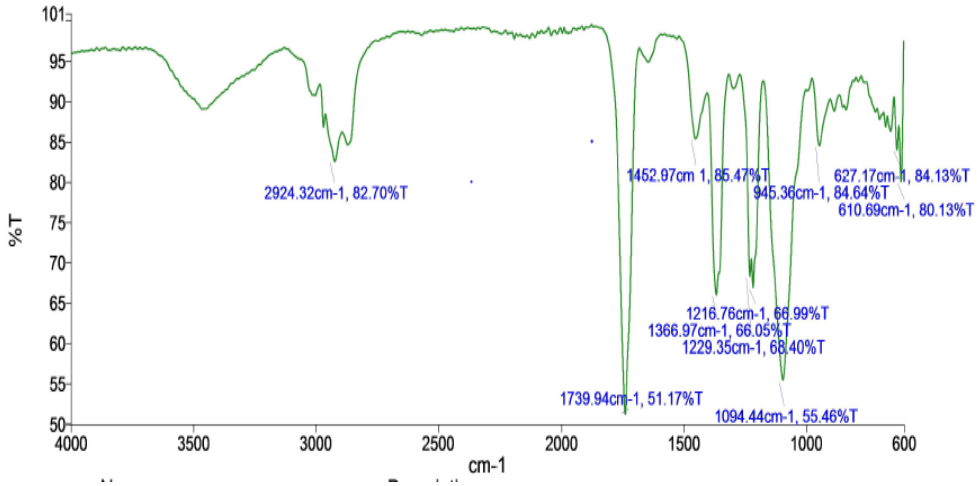


Fig 2: FTIR of nanoemulsion formulation.

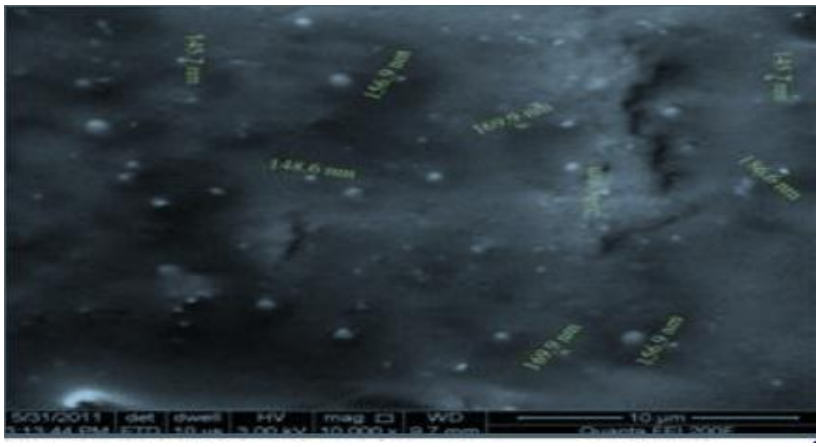
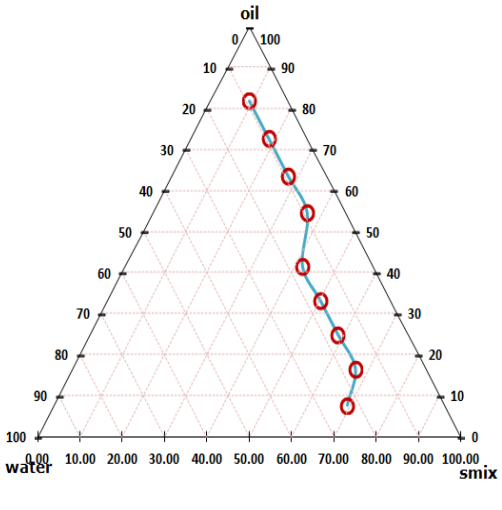
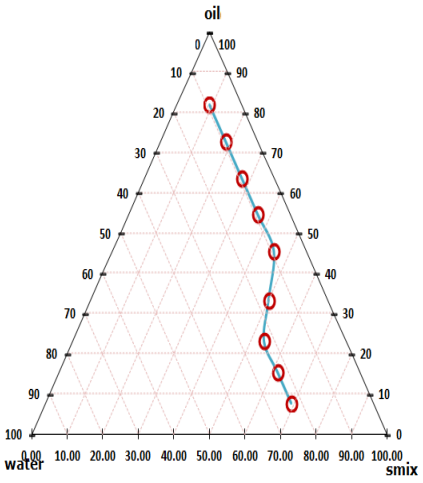


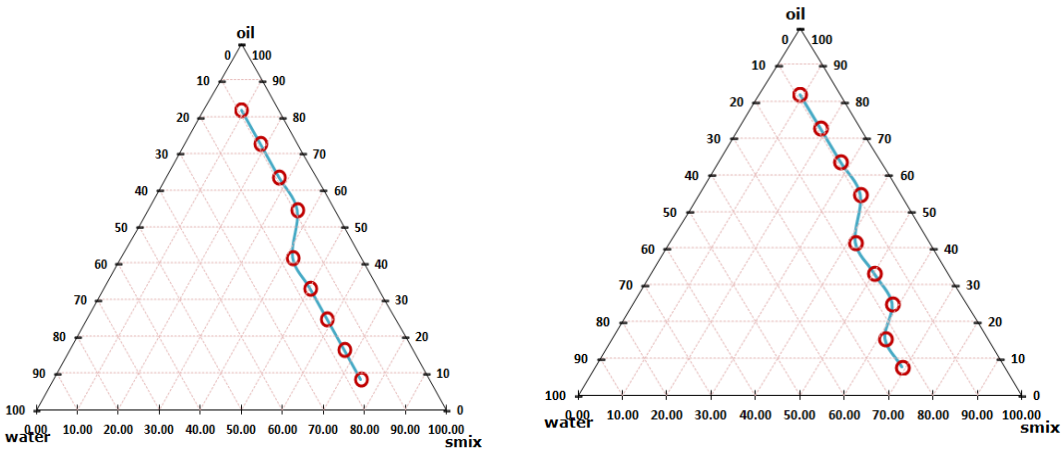
Fig 3: SEM image of nanoemulsion formulation.



2:1(85%)



2:1(90%)



3:1(85%) **3:1(90%)**

Fig 4: Pseudoternary phase diagram using Olive oil as oil phase, Tween 80 as surfactant, PEG 400 as cosurfactant and water (Tween 80: PEG 400 = 2:1 85%, 2:1 90% and 3:1 85% 3:1 90%).

Table 2: Transmittance,Viscosity(ps), pH, Drug entrapment efficiency (Nanoemulsion)

Formulationcode	Transmittance	Viscosity (ps)	pH	Drug entrapment efficiency
ON1	96.56 ± 0.728	0.836±0.002	6.74± 0.015	93.16± 0.045
ON2	98.79 ± 0.014	0.853±0.002	6.75± 0.030	98.23± 0.040
ON3	99.43 ± 0.014	0.863±0.002	7.32± 0.015	98.66± 0.030
ON4	99.67 ± 0.021	0.874±0.002	7.41 ± 0.005	98.88± 0.045

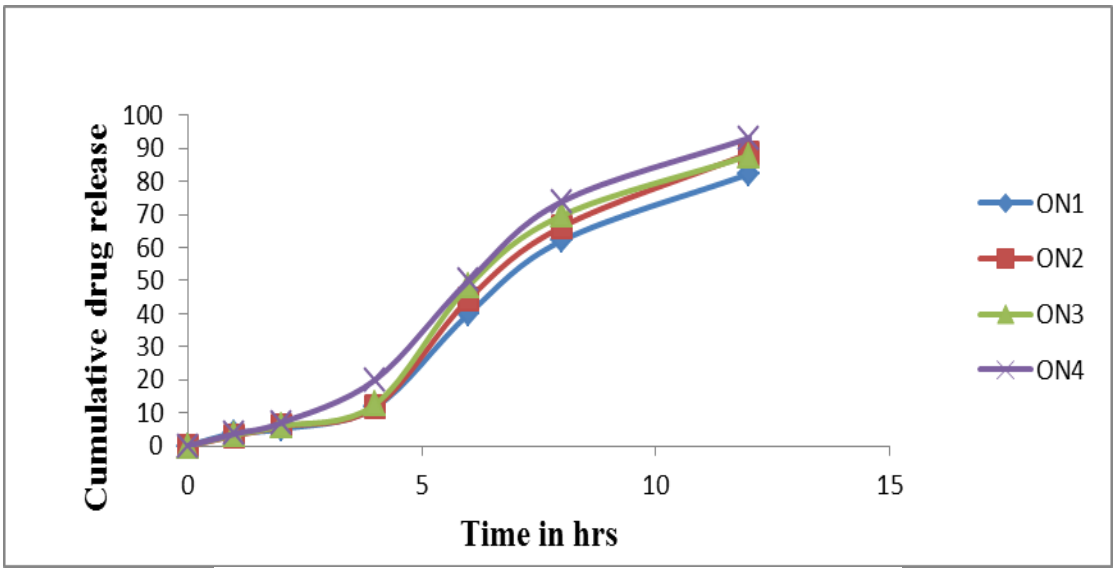


Fig 5: % Cumulative drug release of formulation ON1-ON4.

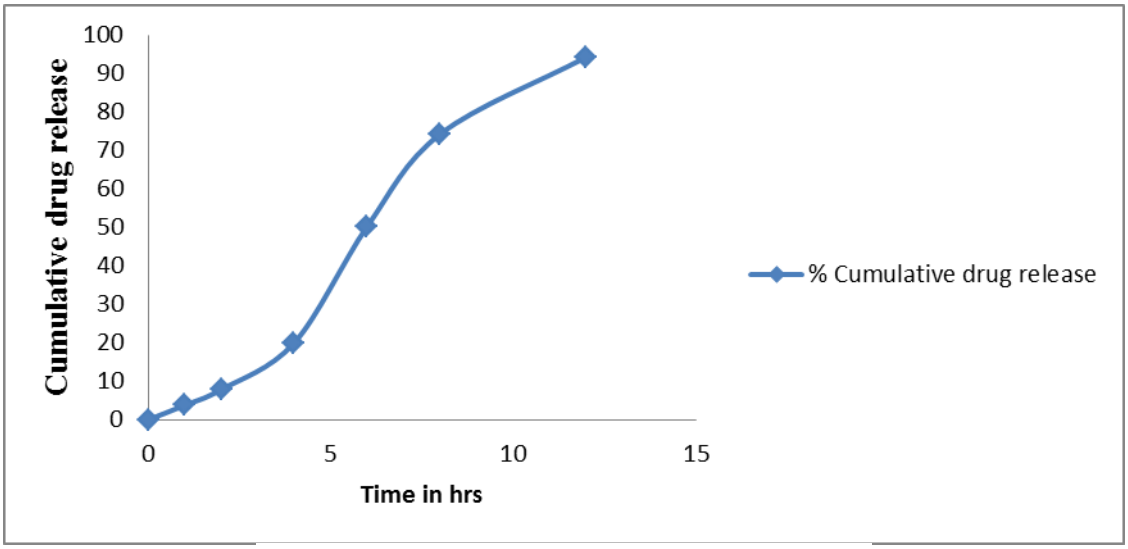


Fig 6: Cumulative drug release of ON4(Nanoemulgel).

Table 3: Intermediate stability studies for optimized Nanoemulsion at 30^0 C± 2^0 C 75 ± 5% RH.

Parameter	Duration in months		
	0	3	6
	ON4		
Drug entrapment content	98.88	95.39	91.87
Cumulative drug release	93.21	91.56	88.23

Table 4: Intermediate stability studies for optimized Nanoemulgel at 30^0 C± 2^0 C 75 ± 5% RH.

Parameter	Duration in months		
	0	3	6
	G-ON4		
Drug entrapment content	98.29	95.39	92.55
Cumulative drug release	94.29	91.78	86.23

RESULTS AND DISCUSSION

After screening olive oil were choosen as oily phase, Tween-80 and PEG-400 were choosen as surfactant and co-surfactant, so many ratio Smix were their but only four ratios were taken 2:1(85%), 2:1(90%), 3:1(85%), 3:1(90%) as shown in the figure no 4. The nanoemulsion were prepared by mixixng the accuarate quantity of surfactant and co-surfactant then to that olive oil added, then vertexed the above mixture, finally transperant nanoemulsion obtained. Then nanoemulgel can be prepared by mixing nanoemulsion and gel with same quantity 1 to 1 ratio by gentle mixing, Finally aloevera gel added to the nanoemulsion and nanoemulgel were prepared. For each surfactant and co-surfactant ratio pseudoternary phase diagram were constructed.so that nanoemulsion formulation can be optimized for 3:1(90%), were formulated as nanoemulgel.

FTIR spectra of the pure drug and the formulation showed that there is no incompatibility between the drug and the component used (fig 4, Pseudoternary phase diagrm were contstructed to find the nanoemulsion region as shown in Fig. Among the formulation the ON4 nanoemulsion showed highest entrapment efficiency of 98.88± 0.045%. Viscosity of nanoemulsion formulation were recorded by Brookefield viscometer and found that in the range of 0.836±0.002 ps0.853±0.002 ps, 0.863±0.002 ps, 0.874±0.002 ps for the formulation ON1, ON2. ON3, ON4 respectively. The pH of all the formulation were found to be in the range 6.74± 0.015 to 7.41 ± 0.005 and By using colorimeter the percentage of transmittance of nanoemulsion were measured and found that maximum transmittance for ON4 ie 99.67 ± 0.021%. The results of pH, %EE, viscocity and transmittance were depicted in Table no 2. The SEM image of the optimized formulation confirmed the formation of nanosized emulsion and observed smooth surface on the vesicles as shown in Fig 3.

By using franz diffusion cell (FD) the in-vitro drug released studies were determined. The formulation were applied on to the dialysis membrane using 0.45µm pore size and the formulation placed in the donar and receptor compartment of the FD cell. Phosphate buffer used as dissoliution medium. By circulating hot water through jacket temperature of the cell maintained at 37^0C. By using magnetic induction point the whole assembly was kept on a platform continuously stirred by using magnetic bead. The percent drug released were calculated by using spectrophotometrically at 278.8nm samples were analyzed. % Cumulative drug release of formulation ON1-ON4 were shown in Fig 5 and found

that nanoemulsion formulation offer controlled release of the drug over a period of 12 hrs. The various formulation of nanomulgel shows clear liquid in appearance.

And the nanoemulgel shows clear gel in appearance, the pH of the nanoemulgel were found to be pH 7.41, permitting to use the nanoemulgel formulation on the skin and found that non –irritating nature of the formulation. The viscosity for nanoemulgel was found to be 1.324 ps. with these results it showed that it can removed rapidly from the site of applicayion and provide good spreadability for the formulation. Drug entrapment efficiency were found to be 98.92%, the result showed that the drug were uniformly entrapped through the formulation while formulating nanoemulgel. By using Franz diffusion cell in-vitro drug release can be determined. using the dialysis which offer controlled release of the formulation as shown in Fig 6.

CONCLUSION

To better patient compliance in coming years transdermal drug delivery will used extensively. Nanoemulgel helpful in enhancing spreadability, adhesion, viscosity and adhesion and extrusion, this novel drug delivery become popular. For long term stability they become solution for loading hydrophobic drugs in water soluble gel base. In this preparation nanoemulgel of Lamivudine were prepared and evaluated for physicochemical characterstics. Liike pH, viscosity, transmittance, drug entrapment efficiency and *in-vitro* drug release. Nanoemulgel formulation performed *in-vitro* drug release to determine the drug release from nanoemulgel. In-vitro drug release of nanoemulgel(ON4) showed maximum drug release of 94.29%. Finally concluded that the nanoemulsion based emulgel has good potential for transdemal drug delivery system.

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