FORMULATION AND CHARACTERIZATION OF CLYNDAMYCIN NANOEMULSIONS

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Introduction

Clindamycin (as phosphate) is the commonly prescribed topical antibiotics for acne vulgaris with anti-inflammatory properties [1]. Resistance of this drug could happen due to the low and variable concentrations of the drug achieved in the pilo-sebaceous ducts [2]. To overcome this problems, clyndamycin nanoemulsions were developed. Reliable drug delivery systems providing better drug penetration can result in better efficacy and also help in the prevention of development of resistance.

Methods

Construction of ternary phase diagrams

Ternary phase diagrams were constructed using aquoeus titration method. Sigma plot 11 software (Systat Software, Inc., CA, USA)was applied for providing ternary phase diagrams. In this study, vitamin E acetate was used as oil while Labrasol® and Plurol oleic® were utilized as surfactant and co-surfactant, respectively, in the weight ratio of3:1. The oil phase and the surfactant phase were together mixed at the weight ratios of 1:9, 2:8, 3:7, 4:6, 5:6, 6:4, 7:3, 8:2, and 9:1. After mixing, the mixture was titrated with an aliquot of water. When clear and transparent liquid formulations were appeared, the samples were marked as points on the phase diagrams. The area covered by these points was classified as microemulsion region. These samples were chosen for further addition of the drug.

Preparation of clyndamycin loaded nanoemulsions

Table 1. Formulation compositions of the developed nanoemulsions of clyndamycin

Formulation	Vitamin E Acetate	Labrasol® and Plurol Oleique®	Water	Clyndamycin
B1-w/o	19%	73%	8%	0,64 mg/g
B1-o/w	14%	56%	30%	0,64 mg/g
B2-o/w	14%	56%	30%	2,4 mg/g

Evaluation of physical properties of prepared clyndamycin nanoemulsions

All of the prepared clyndamycin nanoemulsions were subjected to the following evaluation tests: measurements of droplet size, size distribution, zeta potential, pH measurement, and transmission electron microscopy (TEM).

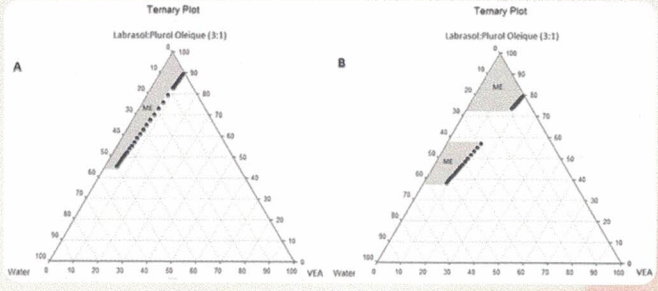

Figure 1. Ternary phase diagrams of the nanoemulsions systems (gray areas) containing different weight ratios of vitamin E acetate (VEA) and Labrasol®/Plurol Oleique® (3:1) including 1:9 (A) and 2:8 (B).

Table 2. Physical characteristics of the developed nanoemulsions of clyndamycin

Formulation	Size (nm)	Polydispersity Index	Zeta Potential (mV)	pH
B1-w/o	73,89 ± 2,76	0,212 ± 0,012	-8,78 ± 0,34	5,88 ± 0,07
B1-o/w	57,52 ± 0,74	0,173 ± 0,013	-9,93 ± 0,94	5,16 ± 0,09
B2-o/w	59,20 ± 5,42	0,250 ± 0,015	-9,00 ± 1,25	5,17 ± 0,15

Figure 2. Physical appearance of clyndamycin formulated as w/o nanoemulsion B1-w/o (left), and o/w nanoemulsions B1-o/w (centre), B2-o/w (right)

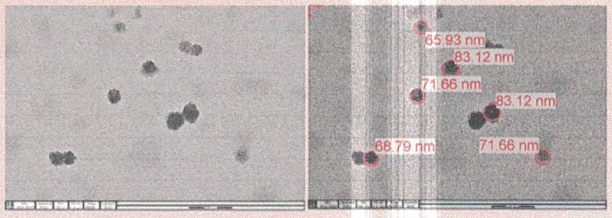

Figure 3. Transmission electron microscopy (TEM) images of B1-w/o nanoemulsion of clyndamycin at a magnification of 40.000x. The bar is 200 nm.

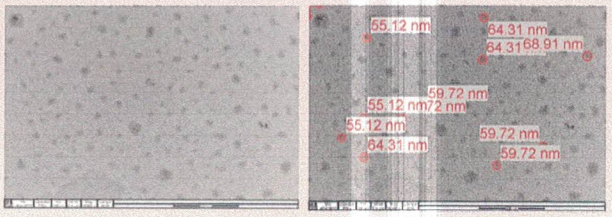

Figure 4. Transmission electron microscopy (TEM) images of B2-o/w nanoemulsion of clyndamycin at a magnification of 25.000x. The bar is 500 nm.

Based on the equal drug loading, o/w nanoemulsion presented the smaller droplet size (57.52 ± 0.74 nm) than w/o nanoemulsion (73.89 ± 2.76 nm) (Table 2). The developed o/w nanoemulsions also have higher incorporation efficiency, better polydispersity index (indicating homogenous formulation or uniform particle size distribution) and better zeta potential value (indicating the degree of stability) than w/o nanoemulsions (Table 2). Moreover, all the nanoemulsion formulations demonstrated pH around 5 that is compatible to the skin (Table 2).The morphology of the nanoemulsions was spherical shape and in the same range with the sizes measured from photon correlation spectroscopy (Figure 4). All these data indicated the successful formation of clydamycin nanoemulsions. From the finding, it also concluded that the developed o/w nanoemulsion has superiority than w/o nanoemulsion.

Conclusions

The data from this study can be concluded that both types of the developed nanoemulsions have good physical characteristics. However, the w/o nanoemulsions showed better characteristics than o/w nanoemulsions. In vitro penetration tests are required to further confirm these results.

References:

1. Del Rosso, J.Q., Schmidt, N.F., 2010. A review of the anti-inflammatory properties of clindamycin in the treatment of acne vulgaris, Cutis. 85: 15-24.
2. Kubba, R., Bajaj, A., Thappa, D.M., Sharma, R., Vedamurthy, M., Dhar, S., 2009, Antibiotic resistance in acne, Indian J. Dermatol. Venereol. Leprol. 75:37-38.

CERTIFICATE

THIS CERTIFICATE ACKNOWLEDGES THAT

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AS PRESENTER

at Second International Seminar on Pharmaceutical Sciences and Technology (2nd ISPST 2016)

Bandung, November 24th - 25th 2016

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