INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com

ISSN 2230 – 8407

Research Article

FORMULATION AND EVALUATION OF SIMVASTATIN LOADED MICROEMULSION BASED GEL: IN VITRO CHARACTERIZATION

Maria Saifee *[1], Pragati Bhaske [1], Reshma Toshniwal [2]

[1] Department of Pharmaceutics, Dr. Rafiq Zakaria Campus, Y. B. Chavan College of Pharmacy, Aurangabad, Maharashtra, India

[2] Reshma Toshniwal, Department of Pharmacognosy, Dr. Rafiq Zakaria Campus, Y. B. Chavan College of Pharmacy, Aurangabad, Maharashtra, India

*Corresponding Author Email: saifeemaria @gmail.com

Article Received on: 15/06/21 Approved for publication: 26/07/21

DOI: 10.7897/2230-8407.1207149

ABSTRACT

The Simvastatin loaded microemulsion based gel was formulated and in-vitro evaluation was done for the treatment of diabetic wound healing. Simvastatin is BCS class II drug which promotes wound healing by increasing the production of vascular endothelial growth factor (VEGF). Microemulsions (MEs) are oil and water colloidal system stabilized by the mixture of surfactant and co-surfactant offering enhance skin permeability for both hydrophobic and hydrophilic drugs. At first, microemulsion (ME) was prepared by water titration method and the existence of ME region was determined using pseudo-ternary phase diagram. Formulations were prepared using oil (oleic acid), Tween 80 and PEG 400 as surfactant and co-surfactant. Optimization of formulation was done using 3^2 factorial designs. Carbopol 940 was used as gelling agent for preparing microemulsion gel. The formulations were evaluated for physical appearance globule size, polydispersity index, zeta potential, percent transmittance, thermodynamic stability, dilution test, drug content, and in vitro drug release. The optimized formulation of ME showed average globule size of 151 nm and the optimized ME gel had a homogeneous texture, showed good spreadability and in vitro drug release. The present study indicates the simvastatin loaded microemulsion gel could act as promising vehicle for topical drug delivery of drug for diabetic wound healing.

KEYWORDS: Diabetic wound; 3^3 factorial design; gel; Microemulsion; Simvastatin; topical drug delivery.

INTRODUCTION

Diabetic wound is most common complication for diabetic patient during their life time[1]. Diabetic wound is classified under the class of chronic type of open wound. Wound is a loss or breaking of cellular and functional continuity in the epithelial integrity of the living tissues. Healing is very complex process start immediately after occurrence of injury. There are four stages involved in wound healing namely haemorrhage, inflammatory and proliferation phase and maturation phase[2]. Wound healing impairment in diabetic patient is due to both the impaired glucose metabolism and neurovascular complication[3].

Literature suggests that beside lipid lowering effect statin shows wound healing action in diabetic mice[4]. Besides having lipid lowering effect simvastatin promotes vascular endothelial growth factor (VEGF) production thus stimulating angiogenesis, reduce oxidative stress, improve micro vascular function and improve endothelial function, thus improving efficiency of wound healing[5,6]. It can enhance epithelialization and restore the normal skin epidermal barrier via reducing isoprenylation downstream targets of mevalonate and farnesyl pyrophosphate (FPP), decreasing FPP level can promote keratinocyte migration in vitro and epithelialization and wound closure in an ex vivo human culture wound healing model[7].

ME is thermodynamically more stable as compared to emulsion and nanoemulsion. It is isotropically clear dispersion of oil and water, stabilized by surfactant and co-surfactant. ME has emerged as potential drug delivery system for topical delivery because of its unique solubilisation capacity of both hydrophilic and lipophilic drug[8]. Due to presence of both hydrophilic and lipophilic domain penetration of drug through skin is better with ME[9]. ME based gel is less greasy and easily spreadable as compared to cream and ointment and offer solubilisation of lipophilic drug and increases its topical availability [10,11].

Simvastatin is a drug with low solubility, high permeability and classified as BCS class II drug[12] to optimize ME based gel and to study the effect of concentration of excipients such as oil and Smix on globule size and drug release. The aim of the study was to prepare and evaluate ME based gel of simvastatin to increase its solubility and availability at the site of diabetic wound.

MATERIALS AND METHODS

Simvastatin was purchased from Swapnroop Pharmaceutical Pvt. Ltd. India. Carbopol 940 was a gift sample from Wockhardt Pvt. Ltd. Oleic acid, Tween 80, PEG 400, Triethanolamine were procured from Loba chemicals Pvt. Ltd. Mumbai, India. All other ingredients used were of analytical grade.

Preparation of Simvastatin microemulsion

Selection of oil, surfactant and co-surfactant

The solubility study of simvastatin in various oil, surfactant and co-surfactant was done to screen suitable combination. Different

oils, surfactant and co-surfactant used for screening were almond oil, olive oil, isopropyl myristate, oleic acid, tween 80, tween 20, span 60, span 20, PEG 400, Capmul MCM C8 EP, Labrafil M1944CS. In brief, an excess of simvastatin was added in 2 ml of selected oil, surfactant, and co-surfactant separately in 10 mL capacity stoppered vials[13]. The vials were stirred for 48 h on magnetic stirrer at 200rpm and then the suspension was centrifuged at 10000 rpm for 15 min. Clear supernatant liquid was separated and diluted with methanol. Solubility of simvastatin was determined by UV-spectrophotometer at ʎmax of simvastatin i.e. 238nm.

Pseudoternary phase diagram construction

To obtain concentration range of components for preparation of ME, construction of pseudo ternary phase diagram was done by water titration method. Based on solubility study of Simvastatin oleic acid was used as oil. Two different Smix (surfactant: co surfactant mixture) i.e. tween 80: span 20 and tween 80: PEG 400 where used for construction of pseudo ternary phase diagram. Both Smix where mixed in different ratio (1:1, 2:1, 3:1). The Smix was mixed with oil in the ratio of 9:1, 8:2, 7:3, 6:4, 5:5, 4:6, 3:7, 2:8, 1:9. Addition of water was done drop wise to each mixture under continuous stirring on magnetic stirrer and end point was determined [13,14]. Chemix School software was used to draw pseudo ternary plot diagram.

Formulation and optimization of Simvastatin loaded Microemulsion

Simvastatin loaded MEs were formulated using spontaneous emulsification method. Drug was added in oil, to this mixture of surfactant and co-surfactant was added and mixed properly by magnetic stirrer. Water phase was added in drop wise manner with continuous stirring on magnetic stirrer until clear MEs was formed. MEs were stored at room temperature for 24 hours for equilibration [15,16]. The composition of preliminary trials of ME formulations are shown in table 1. Based on preliminary trials, optimization of oil, surfactant and co–surfactant mixture was done. The optimization was done using 3^2 full factorial designs. The amount of oleic acid i.e. oil (X_1) and surfactant and co–surfactant mixture (X_2) were selected as independent variables and were evaluated at three levels. Nine trial batches were run and all formulations were mixed with carbopol base in 1:1 ratio and evaluated for various parameters. The variables and their levels are listed in table 2 and the composition of factorial batches are listed in table 3.

Table 1: Composition of Preliminary Batch

Batch code	Ingredient		
	Oil (mL)	Smix* (mL)	Water (mL)
1	1	6	3
2	1	5	4
3	2	6	2
4	2	5	3
5	3	6	9
6	4	5	1

Table 2: Variables and Their Levels

Coded value		-1	0	+1
X_1	Oil	0.5	1	1.5
X_2	Smix	5	6	7

Table 3: Composition of Factorial batches

Batch code	X_1	X_2	Simvastatin (mg)	Oil(X_1) mL	Smix(X_2) mL	Water mL
F_1	+1	-1	100	1.5	5	3.5
F_2	0	0	100	1	6	3
F_3	-1	0	100	0.5	6	3.5
F_4	+1	+1	100	1.5	7	1.5
F_5	0	-1	100	1	5	4
F_6	+1	0	100	1.5	6	2.5
F_7	-1	+1	100	0.5	7	2.5
F_8	-1	-1	100	0.5	5	4.5
F_9	0	+1	100	1	7	2

Formulation of microemulsion gel

The gel base was prepared by adding carbopol 940 in distilled water under stirring using magnetic stirrer. The dispersion was left for 24 hrs for swelling. The gel base formed was then mixed with ME in 1:1 ratio with constant and uniform stirring to get homogeneous ME gel. The pH of gel was adjusted between 6 and 7 with help of triethanolamine [17].

Evaluation parameter of microemulsion

The formulated ME was evaluated for zeta potential, globule size and polydispersity index using zeta sizer [18]. The percent transmittance was determined using UV-Visible spectrophotometer against water at 650nm. Drug content of ME was determined spectrophotometrically using methanol as solvent at wavelength of 238 nm [19].

Thermodynamic stability studies [20,21,22]

The ME was subjected to centrifugation for 30 min at 3500 rpm and analysed for phase separation. The formulation was subjected to heating-cooling and freeze thaw cycles. The ME samples were subjected to six cooling–heating cycles between 4˚C and 45˚C and stored at each temperature for 48 h. Sample was than analysed for precipitation or phase separation.

Evaluation parameter of microemulsion based gel

The prepared ME based gel was inspected visually for its colour, homogeneity, consistency, pH, drug content and spreadibility. Modified spreadibility apparatus consisting of wooden block with pulley at one end was used. One glass slide was fixed on wooden block and another glass having same dimension was attached to the pulley. The prepared microemulsion gel (2g) was sandwiched between lower and upper glass plate.500 g weight was placed on the top of plates for 5min to get uniform gel and excess of gel was scrapped off. Upper plate was subjected to pull of 50g. Time required by upper plate to cover a distance 10cm was noted. Spreadability (g.cm/sec) was calculated by using following formula [22, 23].

$$Spreadability = \frac{M \times L}{t}$$

Where, M=Weight tied to upper slide; L=Length of glass slide; t=Time taken for plate to slide the entire length (sec).

In vitro drug release study

In-vitro drug release study was performed by using Franz diffusion cell with effective diffusion area 4.90cm^2 and having capacity of 22mL by using cellophane membrane. ME gel containing equivalent dose of simvastatin i.e. 5mg was placed on donor compartment. The cell was placed on magnetic stirrer at 100 rpm for 10h. Sink condition was maintained using pH 6.8 phosphate buffer. At predetermined time aliquots were withdrawn and dissolution media was replenished with the equal volume of phosphate buffer and absorbance was measured at 238 nm [24, 25].

Design of Experiment: Data analysis

Design Expert 9.0.3.1 Stat-Ease Minneapollis USA trial version was used to analyse the responses. All responses were fitted to linear, interaction or quadratic models and analysed statistically by means of analysis of variance (ANOVA) and those having p-value<0.05 was included in the analysis. 3-D response surface methodology was used to study the interaction of independent variables and their effect on dependent variables. Thus from the DOE data the design space was constructed.

Table 4: Evaluation of 3^2 Factorial Batches of Microemulsion

Batch Code	Globule size (nm)	PDI*	% Transmittance	% Drug Content
F1	357	0.343	97.26 ±1.20	92.48±1.33
F2	215	0.366	99.54±0.49	88.64±1.11
F3	154	0.364	99.08±1.52	91.20±1.74
F4	256	0.356	99.31±1.23	99.52±0.21
F5	229	0.322	98.85±2.29	91.02±0.0
F6	314	0.307	98.47±4.32	89.92±3.21
F7	144	0.343	99.26±0.10	96.00±2.10
F8	204	0.362	98.91± 3.21	93.76±0.2
F9	210	0.361	98.26 ±1.20	96.32±0.21

*Poly dispersibility index

Table 5: Evaluation of 3^2 Factorial Batches of Microemulsion Based Gel

Batch Code	Physical Appearance	pH	Spreadability (gm.cm/s)	Drug Content (n=3)
F1	Faint Yellow color, Homogeneous	6.2	14.00	96.00± 3.12
F2	Faint Yellow color, Homogeneous	6.7	19.54	92.00±1.64
F3	Faint Yellow color, Homogeneous	6.0	16.41	99.20±0.78
F4	Faint Yellow color, Homogeneous	6.8	21.10	90.56±3.14
F5	Faint Yellow color, Homogeneous	6.5	18.00	100.0±1.20
F6	Faint Yellow color, Homogeneous	6.3	15.20	95.36±1.0
F7	Faint Yellow color, Homogeneous	6.8	22.00	97.17±1.44
F8	Faint Yellow color, Homogeneous	6.4	20.83	96.32±1.54
F9	Faint Yellow color, Homogeneous	6.3	16.91	99.19±1.21

Table 6: Check Point Analysis of Microemulsion

Response variable	Predicted Value	Experimental value	% Predicted error
Globule size	150.77 nm	151 nm	0.1532
% drug release	84.51	85.32	0.9493

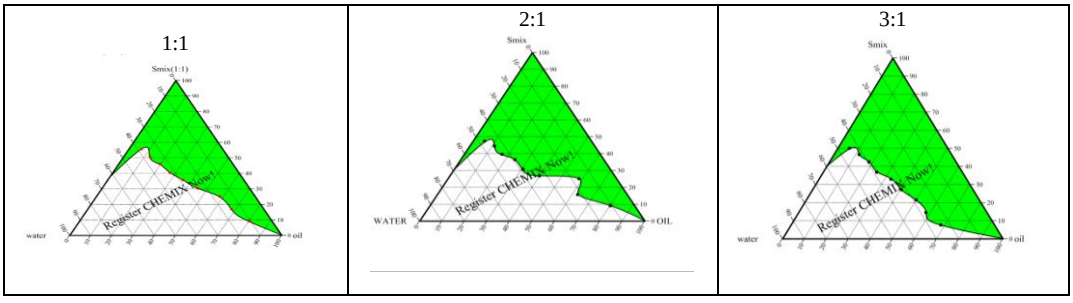

Figure 1: Pseudo Ternary Phase Diagram of Different ratios of Tween 80:PEG 400

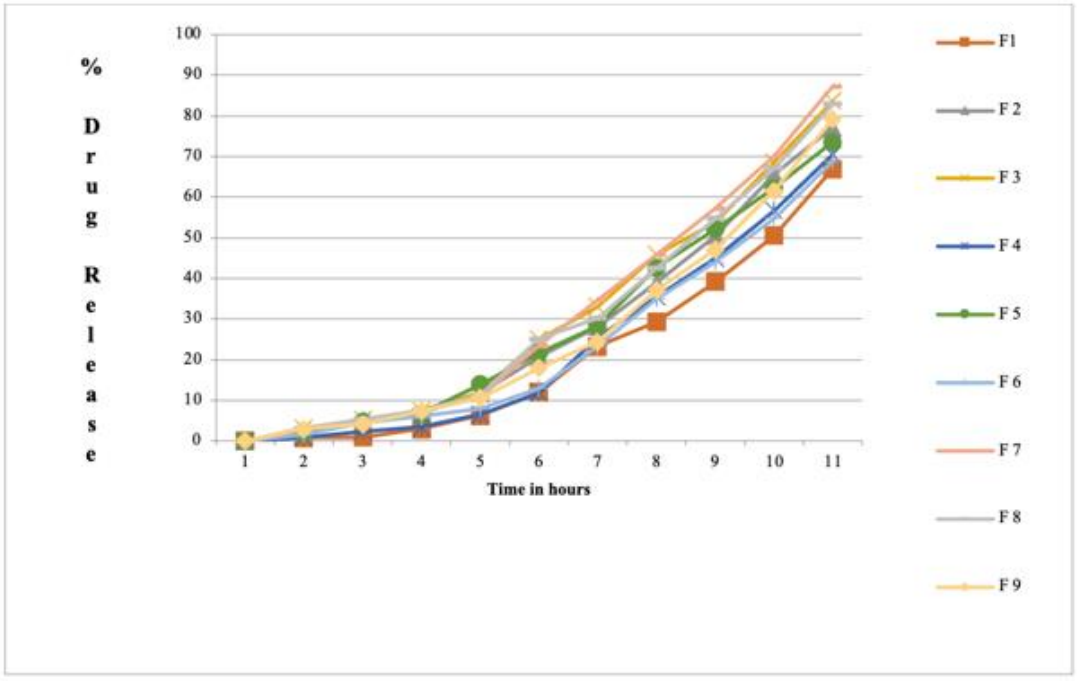

Figure 2: In vitro drug release of factorial batches of microemulsion based gels

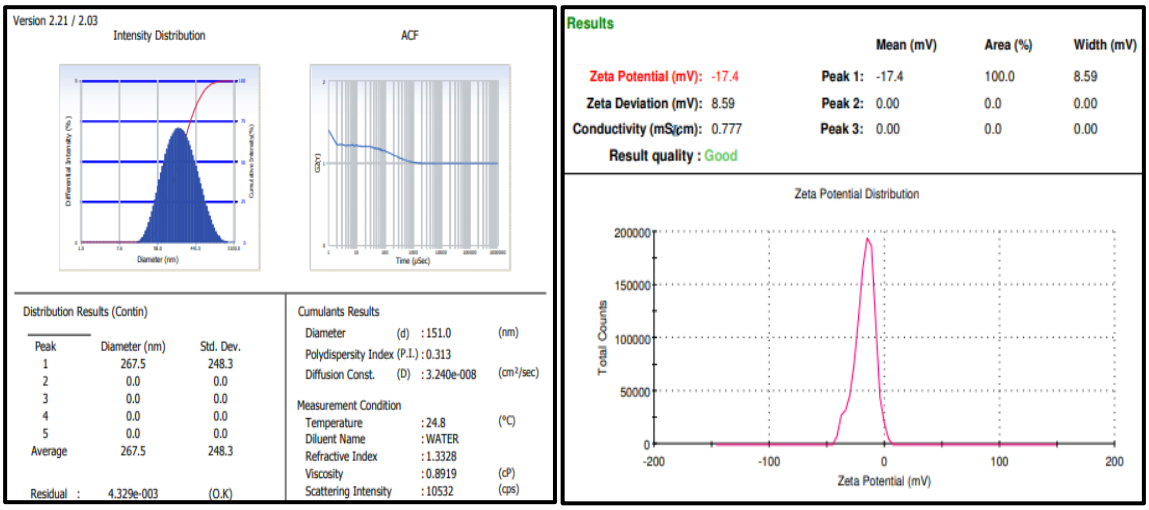

Figure 3: Globule size and Zeta potential of Optimized Microemulsion gel Based Formulation

RESULT AND DISCUSSION

Solubility of Simvastatin in different solvents was studied. Solubility was found highest in oleic acid (104.042 mg/mL), tween 80 (236.22 mg/mL) and polyethylene glycol (124.16 mg/mL) followed by isopropyl myristate (74.50 mg/mL), span 60 (226.22 mg/mL) and labrofill M1944 CS (97.46 mg/mL). Based on solubility studies oleic acid, tween 80, PEG 400 was used for further studies of miscibility.

The ME region, concentration of component to be mixed for preparation of ME was determined using pseudo ternary phase diagram. From ternary phase diagram (Figure 1), it was observed that Tween 80: Span 20 Smix showed less region of ME as compared to that of Tween 80 : PEG 400 Smix. Tween 80: PEG 400 in ratio of 2:1 showed highest region of ME among the other phase diagram, and was used for further studies.

Evaluation of preliminary batches

The preliminary batches were evaluated for various evaluation parameters and based on the results formulation having batch code 1 was selected further for optimization using 3^2 full factorial designs.

Evaluation of formulated microemulsion based gel by 3^2 factorial design

Evaluation of microemulsion

The globule size of ME was determined and was found in the range between 144nm to 357nm. PDI of all 9 batches was found to be low and ranges from 0.307- 0.366. Result of globule size and PDI is presented in table 4.The transparency of the system is determined by percentage transmittance. It was found in range of 99 to 97.26% (Table 4). Percentage transmittance determines the

transparency of the system. The high value of % transmittance indicated that the system was optically clear which is pre-requisite for ME formulation. Drug content of all factorial batches of ME was found in the range of 88.64 to 99.52% as shown in table 4.

Thermodynamic stability

All prepared batches of ME were subjected to different thermodynamic stability tests. After centrifugation, it was observed that all nine formulations did not show any sign of phase separation, thus passing the test. The ME samples were subjected to six cooling–heating cycles as mentioned in procedure. All nine formulations did not show any precipitation and phase separation.

Dilution test

All prepared batches were inspected visually for appearance and it was noted that all formulation showed no sign of phase separation on dilution. The dilution test indicated that formulated ME was o/w type and on dilution with water it remain stable with no phase separation [26, 28].

Evaluation of microemulsion based gel

All prepared ME based gels was found to be in faint yellow colour, with smooth homogeneous texture. The pH of the formulations was found between pH 6 to 6.9 measured by digital pH meter. The ME was incorporated in carbopol gel and spreadibility was studied. Spreadability of formulations was found to be 12.05g.cm/s to 19.85g.cm/s. The results indicated that all formulations had good spreadibility indicating comfortable application to skin which is a prerequisite property of topical formulation from patient compliance point of view. Drug content of based gels was found to be in range of 92 to 100% which indicates better drug loading capacity of all formulations (Table 5).

All the nine formulations of ME based gel showed in vitro drug release in range from 66.93 to 87.20% at 10 h. The drug release of all factorial batches is shown in Figure 2. Based on study of in–vitro drug release it was concluded that as concentration of oil increases from 0.5 mL to 1.5 mL, percent drug release of simvastatin decreases simultaneously. As concentration of Smix increases from 5 mL to 7 mL it was found that drug release increased due to the fact that as concentration of Smix increases, globule size decreases which result into increase surface area that leads to increase in drug release [26, 27, 28].

Design of experiment: Data Analysis

All formulations prepared using factorial design was characterized for various responses like globule size and cumulative percent drug release. The response surface methodology was used to determine the effect of independent variables i.e. concentration of oil and concentration of Smix on dependent variable i.e. globule size and cumulative % drug release.

Effect of formulation variable on globule size and % in vitro drug release

Statistical analysis of all the nine batches when studied using Statease software gave the effect of independent variables on dependent variables. The independent variables selected were concentration of oil and Smix concentration and dependent variables was globule size and cumulative % drug release. The regression equation obtained for dependent variable globule size was

$$\boldsymbol{Globule\ size = +231.44 + 70.83X1 - 30.00X2}$$
(eqn 1)

Where, X_1 and X_2 are concentration of oleic acid and Smix respectively

Equation 1 shows that factor X_1 i.e. concentration of oil has positive impact on globule size while factor X_2 i.e. concentration of Smix has negative impact on globule size. Based on equation it was concluded that as concentration of oil increases globule size of ME also increases and as concentration of Smix increases globule size decreases. The result was found in accordance with previous study of Radwan et al, Elmataeeshy et al [29,30].

Similarly the regression equation obtained for variable cumulative % drug release was

$$\%\ \boldsymbol{Drug\ release = +76.11 - 8.00X1 + 2.50X2}$$
(eqn 2)

Equation 2 shows that coefficient X_1 i.e. concentration of oil has negative impact on globule size while coefficient X_2 i.e. concentration of Smix has positive impact on % drug release. Based on equation it was concluded as concentration of oil increases % drug release of ME also decreases and as concentration of Smix increases % drug release was found to be increased. The result was found in accordance with reported result of Patel, et al, Said, et al and Balate, et al. [22,27,31].

Optimization of microemulsion based gel

The design expert software was used to optimize the ME with respect to optimum globule size and cumulative % drug release by keeping two independent variables within range and dependent variable also within range. The optimized formulation (Batch F10) was prepared as per the design space which contains 0.6 ml oil, 6.8 ml Smix and 2.6 ml water and evaluated. Based on table 6, it was observed that predicted value of response and experimental value was found to be very close to each other. % predicted error was less than 3% which also confirmed the validity of 3^2 design for optimization of ME. The optimized ME was converted into gel by mixing 1% carbopol gel base with ME in 1:1 ratio for preparation of microemulsion based gel.

Evaluation of optimized batch of microemulsion

The optimized microemulsion formulation i.e. batch F10 was evaluated for globule size, PDI, zeta potential, % transmittance, % drug content and thermodynamic stability then the microemulsion based gel was evaluated for physical appearance, spreadability, drug content, in-vitro drug release.

Globule size was measured by zeta sizer which was found to be 151nm with PDI 0.313 (Figure 3) indicating narrow particle size distribution of globules in optimized formulation**.** PDI is a measure of homogeneity of particles in formulation. PDI values of all nine formulations result varied from 0.0 to 1.0 and if value is close to 0.0, it indicates narrow size distribution [27,28].

Zeta potential of optimized ME (Figure 3) was found to be -17.4 mV which indicate stability of ME. The optimized formulation prepared based on DOE experiment also showed required globule size and PDI. The degree of the zeta potential gives the idea of the potential stability of the colloidal system. Large negative or positive zeta potential of globules will repel each other and the

globules will not coalesce. The zeta potential value obtained for optimized formulation of microemulsion indicates good stability. Drug content of optimized ME was found to be 99.50 ±1.21% which indicates better loading. Optimized formulation shown no sign of phase separation on dilution which indicates that formulation was of o/w type.

The optimized microemulsion formulation was also found to be thermodynamic stable and the centrifugation test and heating and cooling test studies showed that ME was stable with no phase separation and existed as monophasic liquid.

Optimized microemulsion based gel was found to be in yellow colour, with smooth homogeneous texture. The pH of the topical formulation should be compatible with skin pH. A change in pH may causes irritation to skin. pH of the optimized ME based gel formulation was found to be 6.7 which was compatible with that of skin pH. The spreadability of optimized formulation was found to be 18.32gm.cm/s. Drug content of optimized ME based gel was found to be 98.40 ±1.64% and in-vitro drug release of optimized ME based gel was found to be 83.42 % which was found to be very close to the predicted value i.e. 84.51%. in 10 hour.

CONCLUSION

In the present work simvastatin microemulsion based gel was prepared for diabetic wound healing. Simvastatin microemulsion was prepared using oil, Smix and water. The study showed that optimized microemulsion prepared using oleic acid, Smix that is tween 80 and PEG 400 in ratio of 2:1 and water gave required globule size and predicted percent drug release. The microemulsion based gel was optimized for drug content, globule size, spreadibility, percent transmittance and percent drug release. The globule size of optimized microemulsion gel was found to be 151 nm and it showed 83.42% drug release in 10 h which was very close to the predicted values. The zeta potential value of microemulsion was found to be -17.4 mV indicating stability of formed microemuslion. Thus in conclusion a successful microemulsion based gel of simvastatin was formulated which can be tried for diabetic wound healing.

REFERENCES

1. Nasiri LYM., Adarvishi S. Literature review on the management of diabetic foot ulcer. World Journal of Diabetes. 2015; 6 (1): 37-53.
2. Mohan, H. Textbook of Pathophysiology. JAYPEE brothers medical publishers(P) Ltd. India. 2010; 6th ed.: pp:167-173.
3. Brem H, Tomic-Canic M. Cellular and molecular basis of wound healing in diabetes. The Journal of Clinical Investigation. 2007; 117 (5), 1219–1222.
4. Yasavini S., Anusa RS., Vedhahari B N., Prabhu PC., RamyaDevi, D. Topical hydrogel matrix loaded with simvastatin microparticles for enhanced wound healing activity, Material Science And Engineering C. 2017; 72, 160-167.
5. Sameh N, Aly UF, Abou-Taleb HA, Abdellatif AAH., Prospective role of simvastatin on wound healing: review of the literature, Journal of Bioequivalence and Bioavailability. 2018; 10(2), 36-42.
6. Asai J, Takenaka H, Hirakawa S, Sakabe J, Hagura A, Kishimoto S M, K, Kajiya K, Kinoshita S, Tokura Y, Katoh, N. Topical simvastatin accelerates wound healing in diabetes by enhancing nngiogenesis and lymphangiogenesis. The American Journal of Pathology. 2012 ; 181(6), 2217-2224.
7. Rohilla A, Rohilla S, Kumar A, Khan MU, Deep A .Pleiotropic effects of statins: A boulevard to cardioprotection. Arabian Journal of Chemistry. 2016; 9: S21-S27.
8. Kawakami K, Yoshikawa T, Hayashi T, Nishihara Y, Masuda K. Microemulsion formulation for enhanced absorption of poorly soluble drugs. II. In vivo study. Journal of Controlled Release. 2002; 81(1-2) 75-82.
9. Nastiti CM R R, Ponto T, Abd E, Grice J E, Benson HAE, Roberts MS. Topical Nano and Microemulsions for skin delivery. Pharmaceutics. 2017; 9(4): 37–62.
10. Ashara KC, Paun JS, Soniwala MM, Chivada JR, Mori N M. Microemulsion based gel – A novel topical drug delivery system, Asian Pacific Journal of Tropical Disease. 2014; 4 (1): S27-S32.
11. Hardenia A, Jayronia S, Jain S. Emulgel: An emergent tool in topical drug delivery, International Journal of Pharmaceutical Sciences and Research. 2014; 5(5): 1653-1660.
12. Singh V, Bushettii SS, Raju AS, Ahmad R, Singh M, Bisht A. Microemulsions as promising delivery systems: A review. Indian Journal of Pharmaceutical Education and Research. 2011; 45(4): 392-401.
13. Hajjar B, Zier KI, Khalid N, Azarmi S, Lobenberg R. Evaluation of microemulsion based gel formulation for topical drug delivery of diclofenac sodium. Journal of Pharmaceuitcal Investigation. 2018; 48: 351-362.
14. Shahzadi I, Masood M I, Chowdhary F, Anjum AA, Nawaz MA, Maqsood , Zaman M. Microemulsion formulation for topical delivery of miconazole Nitrate. International Journal of Pharmaceutical Sciences Review and Research. 2014; 24(2): 3 0-36.
15. Iradhati AH, Jufri M. Formulation and physical stability of griseofulvin microemulsion Gel. International Journal of Applied Pharmaceutics. 2017; 9: 23-27.
16. Syed HK, Peh KK. Identification of phase of various oil, surfactant/ cosurfactant and water system by ternary phase diagram. Acta Poloniae Pharmaceutica- Drug Research. 2014; 17(2):301-309.
17. Mishra R, Parbhavalkar KS, Bhatt LK. Preparation optimization and evaluation of zaltoprofen- loaded microemulsion and microemulsion–based gel of transdermal delivery. Journal of Liposome Research. 2016; 26(4): 297-306.
18. Patel MR, Patel RB, Parikh, J.R.,. Patel,B. G. Novel microemulsion-based gel formulation of tazarotene for therapy of acne. Pharmaceutical Development and Technology. 2016; 21(8): 921-932.
19. Nikumdh KV, Sevankar SG, Patil MP. Formulation development in-vitro and in-vivo evaluation of microemulsion based gel loaded with ketoprofen. Drug delivery. 2015; 22(4): 509-515.
20. Coneac, G., Vlaia, V., Olariu, L., Mut,A. M., Anghel, D.F., llie, C. et al. Development and evaluation of new microemulsion-based hydrogel formulations for topical delivery of fluconazole. AAPS PharmSciTech. 2015; 16, 889–904.
21. Rao S, Barot T, Rajesh KS, Jha LI. Formulation, optimization and evaluation of microemulsion based gel of Butenafine Hydrochloride for topical delivery by using simplex lattice mixture design, Journal of Pharmaceutical Investigation. 2015; 46(1): 1-12.
22. Patel TB, Patel TR, Suhagia BN. Preparation, characterization, and optimization of microemulsion for topical delivery of itraconazole. Journal of Drug Delivery and Therapeutics. 2018; 8 (2):136-145.
23. Urmaliya H, Gupta MK, Agrawal A, Jain NK, Dubey A. Formulation development and evaluation of microemulsion gel of ketoconazole as an antifungal agent. Pharmacia: An International Journal of Pharmaceutical Sciences. 2016; 2(3): 120-130.
24. Kamble AV, Awandekar NIB, Trivedi R V, Umekar M J. Development and evaluation of microemulsion based topical gel contaning oxiconazole nitrate. International Journal of Pharmacy and Pharmaceutical Research. Human. 2017; 11(1): 241-261.

25. Shinde UA, Modani SH, Singh KH. Design and development of repaglinide microemulsion Gel for transdermal delivery, AAPS PharmSciTech. 2018; 19(1): 315-325.
26. Jagdale S, Pawar S. Gellified emulsion of ofloxacin for transdermal drug delivery system, Advanced Pharmaceutical Bulletin. 2017; 7(2): 229-239.
27. Said M, lsayed I, Aboelwafa AA, Elshafeey A.H. Transdermal agomelatine microemulsion gel: pyramidal screening, statistical optimization and invivo bioavailability, Drug Delivery. 2017; 24:1, 1159-1169.
28. Sabale V, Vora S. Formulation and evaluation of microemulsion based hydrogel for topical delivery. International Journal of Pharmaceutical Investigation. 2012; 2(3), 140-149.
29. Radwan SAA, Elmeshad AN, Shoukri RA. Microemulsion loaded hydrogel as promising vehicle for dermal delivery of the sertaconazole: design, optimization and ex-vivo evaluation, Drug Development and Industrial Pharmacy. 2017; 43(8), 1351-1365.
30. Elamataeeshy ME, Sokar MS, Bahey-El –Din M, Shaker DS. Enhanced transdermal permeability of terbinafine through novel nanoemulgel formulation: Development, in vitro and in vivo characterization. Future journal of pharmaceutical sciences. 2018; 4(1) 18-28.
31. Balata GF, Shamardl H E, lmoneim HMA, Hakami AA, Almodhwahi MA. Propolis emulgel: a natural remedy for burn and wound, Drug Development and Industrial Pharmacy. 2018; 44(11): 1797-1808.

Cite this article as:

Maria Saifee *et al*. Formulation and evaluation of simvastatin loaded microemulsion based gel: In vitro characterization. Int. Res. J. Pharm. 2021;12(7):1-7.
http://dx.doi.org/10.7897/2230-8407.1207149

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publishing quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial members.