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Research Article

FORMULATION AND EVALUATION OF MICROEMULSION CONTAINING DESLORATADINE FOR INTRANASAL DELIVERY

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ABSTRACT

In this study, novel Desloratadine o/w microemulsion systems were prepared to attain enhanced solubility and fast release through intranasal delivery. Desloratadine saturated solubility was determined in different oils, surfactants and cosurfactants. Triacetin and Tween 80 were selected as oily phase and surfactant respectively. Regarding the cosurfactant, Transcutol and Propylene Glycol were used separately in two comparative systems. Pseudoternary phase diagrams were constructed to identify the microemulsion regions. Visual inspection, pH, viscosity, drug content, morphology, particle size, percentage transmittance and *in-vitro* release were characterized for the selected Desloratadine loaded microemulsion formulations. The pharmacological evaluation of the selected formulae was carried through experimental induction of allergy using palm grains in white albino female rats and Lorafast® syrup was used for comparison. Plasma histamine and plasma eosinophil peroxidase concentrations were evaluated as well as histopathological examination of rat nasal mucosa. An increase in the microemulsion region in pseudoternary phase diagrams was observed when using Transcutol compared to Propylene Glycol. However, Desloratadine microemulsion formulation containing (5% Triacetin, 15% Tween 80, 30% Propylene Glycol and 50% Distilled Water) displayed highest rate of drug release (100.77±0.90% within 60 minutes) and smallest particle size (16.43±1.80nm). The chosen Desloratadine microemulsion formulations succeeded to reduce significantly the plasma histamine and eosinophil peroxidase levels. The results revealed that the developed microemulsion has great potential for intranasal delivery of Desloratadine.

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INTRODUCTION

Today, one of the most prevalent inflammatory disorders of upper respiratory tract is allergic rhinitis (AR), which is characterized by a specific Immunoglobin E-mediated hypersensitivity reaction (1). Sneezing, nasal obstruc-

tion, nasal itching, post-nasal drip and smell disorders are the most common symptoms of allergic rhinitis. Though several different mediators are involved in the pathophysiology of allergic diseases, histamine remains the principal one and thus, antihistamines represent the first line of treatment for allergic rhinitis (2,3). Desloratadine (DL) is one of the second-generation antihistaminics, which had proven its efficacy and safety in the treatment of AR. Desloratadine is the major active metabolite of the parent drug Loratadine (4-6). It acts by inhibiting the release of pro-inflammatory mediators from human mast cells/basophil (7). On the other hand, DL is characterized by its slight aqueous solubility, subsequently its availability is limited to oral administration.

Microemulsions (MEs) are defined as clear, isotropic systems of oil and water stabilized by surfactant, usually with a cosurfactant (8-10). Microemulsions are considered potential alternative carrier systems for wide variety of drugs through many routes and are of pharmaceutical importance because of their high solubilization capacity, transparency, ease of preparation, thermodynamic stability and high diffusion and absorption rates (11). In the last decade, numerous studies have highlighted that the intranasal (IN) administration provides a simple, practical and cost effective with high patient compliance route of drug delivery (12). Intra nasal antihistamines offer the advantage that relatively lower doses are effective when administered locally compared to the oral therapy. Thereby, reduced sedation or impairment of psychomotor function, which are common side effects upon oral dosing which requires much larger dose. Such factors make IN delivery an attractive and preferred route of administration, particularly if rapid symptom relief is required (13). However, it is well known that the nasal administration volume is very limited (150-200µl), which means that solubility enhancement of poorly or slightly water soluble drugs is necessary for intranasal delivery (14). Therefore, the aim of the present study was to develop the most suitable formulae for intranasal application of Desloratadine with high degree of solubility and fast rate of drug release and to evaluate the physicochemical properties in addition to the anti-allergic activity of the selected formulae.

MATERIALS AND METHODS

Desloratadine was gifted from Eva Pharm pharmaceutical company (October, Egypt). Isopropyl Myristate (IPM) was purchased from Acros Organics (Geel, Belgium).Transcutol (Diethylene glycol monoethyl ether) was kindly donated by Gattefossé (Saint-Priest, France).Triacetin (Triglyceryl acetate) was purchased from Alfa Aesar (Karlsruhe, Germany). Propylene glycol, Tween 20, 60, 80 and Isopropyl Alcohol were purchased from El-Nasr Pharm. Chem. Company (Cairo, Egypt). All other chemicals were of analytical grade and used without further purification. Water was deionized and distilled in the laboratory.

Solubility Studies

The solubility of DL in distilled water, different oils (IPM and Triacetin), surfactants (Tween 80, Tween 60 and Tween 20) and cosurfactants (Transcutol and Propylene Glycol) was determined by adding an excess amount of the drug to 1 ml of the selected vehicle in a centrifugal tube, followed by mixing at 100 rpm in a shaker water bath (JSSR-30T, Korea) at 25°C for 24 hours. Excess DL was removed by centrifugation at 10,000 rpm (Heraeus Megafuge 16R Centrifuge, USA) for 10 min, after which the concentration of DL in the supernatant was measured spectrophotometrically at λ_{max} 240 nm (Spectro UV-1800 Shimadzu, Japan) after appropriate dilution with isopropyl alcohol (15).

Construction of Pseudoternary Phase Diagrams

To investigate concentration range of components for the existing boundary of MEs, pseudo-ternary phase diagrams were constructed using the water titration method (16). Based on the results of the solubility studies, the oil and surfactant employed in the present study

were Triacetin and Tween 80 respectively. Transcutol and propylene glycol were used as cosurfactants in two comparative systems. The mixtures of oil, surfactant and cosurfactant at certain weight ratios were weighed into glass vials and were shaken to ensure complete mixing. Phase diagrams were constructed by titrating these mixtures with aliquots of distilled water in 10% increments in the range from 10-50% w/w. following each water addition; the mixtures in vials were vortexed for 2-3 minutes before the next addition of water (17).

Preparation of DL Loaded Microemulsions

In order to prepare the drug loaded MEs, the appropriate oil, surfactant and cosurfactant weight ratios were weighed in glass vials. The aqueous phase was titrated to the above mixture at ambient temperature and vortexed. Then, 0.5 % w/w of DL was accurately weighed, added to the mixture and vortexed. The resultant MEs were stored for 24 hours at room temperature for equilibrium before further investigation (18, 19). For pH adjustment 0.1% w/w citric acid of the final weight was dissolved in the distilled water. A constant point at 50% w/w water was selected for all formulation for minimizing the nasal irritation with such high water content.

Evaluation of DL Loaded Microemulsions

Visual Inspection

The prepared formulae were examined for clarity, fluidity, homogeneity and phase separation (20).

pH Measurement

The pH of 10% w/w aqueous solution was measured by pH meter (Jenway, UK). The solutions were prepared by dissolving 1 g of each microemulsion formulae in 9 g of distilled water (21).

Viscosity Measurements

The viscosity of microemulsions was measured at room temperature (DV-E Brookfield Viscometer, USA) using spindle no. 40 with speed started at 5 rpm and gradually increased until reached 100 rpm at constant time interval of 30 seconds (22).

Assay of Drug Content

Amount of 1 g of the prepared Desloratadine ME was weighted in a 100 ml volumetric flask and dissolved in isopropyl alcohol. This solution was vortexed for 5 minutes to ensure complete dissolving of the drug and filtered through filter syringe 0.45 µm. 1 ml of the filtered solution was diluted appropriately with isopropyl alcohol and DL content was analyzed spectrophotometrically at 240 nm (23).

Morphology

The morphology and structure of the prepared Desloratadine microemulsion were studied using transmission electron microscopy (TEM) (JEOL, Japan). The TEM observation was performed after diluting the microemulsion with distilled water (1:10). A drop of the diluted microemulsion was deposited on a carbon-coated grid. The coated grid was dried, then taken on a slide and covered with a cover slip and observed under the microscope (24).

Particle Size Determination

The determination of the particle size is done for ME formulations containing DL using TEM, as it is capable of point-to-point resolution (25).

Percentage Transmittance

Transparency of ME formulations was determined by measuring percentage transmittance through UV Spectrophotometer. The ME formulations were diluted with distilled water in ratio of (1:10). Percentage transmittance of samples was measured at 760 nm with distilled water taken as blank (26).

***In-Vitro* Drug Release**

Drug release studies were carried out in USP dissolution apparatus II (rotating paddle) using 500 ml of phosphate buffer of pH 6.5 as dissolution medium at 50 rpm and 37±0.2°C. One gram of each selected DL ME formulation (equivalent to 5 mg DL) was placed in ready-to-use dialysis bag made up of cellulose nitrate semi-permeable membrane. The bags were attached to the paddle by thread (27). At predetermined time intervals (5,10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110 and 120 minutes), 3

ml of samples were withdrawn from the dissolution media at each time and replaced by equal amount of drug free phosphate buffer (pH 6.5). The samples were analyzed for DL concentration spectrophotometrically at 240 nm. Control samples with the same composition of oil, surfactant and cosurfactant were used in order to eliminate the effect of microemulsion components on the UV absorption of DL.

Mathematical Comparison for Release Data

In this study, the release data of DL from different ME formulations and the pure drug was compared through calculating the mean dissolution time (MDT) and percentage of dissolution efficiency (%DE) (28). DD solver Excel software was used to compute both MDT and % DE.

Zeta Potential Measurements

Zeta potential measurements of the chosen formulations were determined by (Zetasizer, UK equipped with the Malvern PCS software version 1.27) (29). Samples were placed in clear disposable zeta cells and results were recorded (30).

***In Vivo* Evaluation of the Selected Formulae**

All animal procedures were performed in accordance with protocols reviewed and approved by The Scientific Research Ethics Committee of Faculty of Pharmacy, Al-Azhar University, Egypt.

Animal Modeling

Thirty female white albino rats weighting 250 ± 50 g were selected for the evaluation of anti-allergic activity. Animals were housed six per cage and were kept under constant temperature 25°C ± 1°C and 12 hours light/dark cycles. Animals were allowed free access to standard food pellets and water. All the animals were acclimatized in the animal facility for at least 2 weeks prior the experiment (31). The animals were divided into five groups, each consisting of six animals. Group 1 (negative control) was intranasally administered normal saline. Group 2 (positive control group) was intranasally challenged using palm grains. While Group 3 and 4 were treated intranasally with Desloratadine ME F5 and F9 respectively after intranasal challenge. Finally, group 5 was treated orally with commercial Desloratadine syrup (Lorafast®) after intranasal challenge.

Intranasal Challenge

According to Kato et al, protocol with some modifications, all groups except group 1 (negative control) were intranasally challenged by instillation of 1 mg of palm grains suspension in 20 µl of phosphate buffer saline (pH 6.5) by the aid of micropipette for 10 consecutive days. While, the negative control group received 20 µl of intranasal phosphate buffer saline alone (32).

Treatment

After 10 days of intranasal challenge, blood samples were withdrawn from the negative and positive control groups (1&2) before sacrification. However, the other three groups started receiving Desloratadine treatment once daily for 7 days at a dose of (1mg/kg). Group (3) and (4) received intranasal instillation of Desloratadine microemulsions. While, the last group received oral treatment with commercial Desloratadine syrup (Lorafast®) at same dose (1mg/kg). Finally, the three remaining groups were sacrificed after 7 days of treatment.

Determination of Plasma Histamine Concentration and Eosinophil Peroxidase Concentration

Before sacrification of rats, blood samples were withdrawn from the orbital sinus. Blood samples were allowed to clot for two hours at room temperature. Then, centrifugation for 20 minutes at approximately 1,000 rpm was done. The supernatant was separated in EDTA-filled tubes and stored at -20°C. Plasma histamine concentration and plasma eosinophil peroxidase concentration were assayed using ELISA kits.

Statistical Analysis

Statistical analysis and correlations were performed using SPSS program version 14. Student “t” test and one-way ANOVA followed by Bonferroni’s post hoc analysis were used for

comparisons between groups. The level of statistical significance was set at probability $P < 0.05$.

Histopathological Study

Autopsy samples were taken from the nose of rats in different groups and fixed in 10 % formal saline for 24 hours. After washing with distilled water, dehydration was done using different serial dilutions of alcohol (methyl, ethyl and absolute ethyl). Specimens were cleared in xylene and embedded in paraffin at 56 degree in hot air oven for 24 hrs. Tissue blocks made up from paraffin bees wax were prepared for sectioning at 4 microns thickness by sledge microtome. The obtained tissue sections were collected on glass slides, deparaffinizedand finally stained by hematoxylin& eosin stain for examination by means of light electric microscope (Nikon 120V, Japan equipped with Nikon camera)(33).

RESULTS AND DISCUSSION

Solubility Studies

Solubility of the drug in the vehicle is one of the most important attributes in the successfulness of ME, as it would help to maintain the drug in the solubilized form (34,35). The solubility of DL in various vehicles is presented in table (I). Triacetin showed higher solubilization capacity compared to IPM. The solubility of Desloratadine in Tween 80 was found to be the best among all the investigated surfactants. DL was more soluble in Transcutol than in propylene glycol. Transcutol is commonly used as a cosurfactant in the preparation of ME since it proved its higher solubilizing effect than other cosurfactants (36).

Construction of Pseudo ternary Phase Diagrams

Construction of pseudoternary diagrams was performed to determine the region of microemulsion. The surfactant and cosurfactants mass ratio had been found to be a key factor influencing the phase properties (37). Low concentrations of surfactants failed to form microemulsion systems especially with high concentrations of oil. While, regarding the influence of the cosurfactant type on the ME region, it was displayed that Transcutol gave larger ME existence area when compared to propylene glycol which is obvious in figures (1&2).

The prepared microemulsions were visually inspected before and after the addition of DL. Clear homogenous systems were revealed with no phase separation. It was previously reported that to minimize irritation, pH of the nasal formulation should be adjusted between 4.5 and 6.5 units (38). The addition of DL to the plain MEs caused significant increase in the pH, which was alkaline. For this reason, 0.1% w/w of citric acid was added to the aqueous phase for pH adjustment. Citric acid addition positively modified the pH of the prepared ME to fit the nasal physiological pH. The pH values of 10% (w/w) aqueous solutions of the microemulsion systems were found to be in the range of 5.13±0.21 and 5.90±0.20 units as shown in table (III). Therefore, the pH of all the prepared formulas was within the required range and was considered to be safe for intranasal administration. The viscosity of a microemulsion can be affected by the component ratio and concentrations of oil, water and surfactant (39). Consequently, the viscosity of microemulsions was calculated from the slope of shear stress versus shear rate plots (40). It has been reported that the viscosity of intranasal formulations can influence drug absorption across the nasal mucosa (41). Viscous formulations would tend to stay longer in the nasal cavity and increase the mean residence time. However, increasing the viscosity can decrease the drug penetration rate across the mucus layer and lead to a delay in the drug's reaching the cellular surface (42). Lesser the viscosity, better the administration of the formulation, since less viscous formulations have a better flow property than the high viscous formulations (43). As displayed in table (III), F1 with lowest concentration of tween 80 (5% w/w) possessed the lowest viscosity (5.28±1.11cp). Whereas, F2 with the highest tween 80 (25% w/w) concentration showed the highest viscosity which indicates a direct relationship between tween 80 concentration and the value of viscosity (23.80±1.12cp). Concerning the drug content, the percentage of DL in different ME formulae was between 100.90±0.89% and 103.81±0.48%. DL microemulsion appeared as dark spherical droplets with brighter surrounding as shown in figure (3). The particle size of all formulations was

less than 100 nm, which is an important criterion in microemulsion preparation. All of them are found to fall in the range between 16.43±1.80nm and 40.85±1.82nm. Transparency is an important characterization of the successfulness of the microemulsion. The prepared DL microemulsion formulations showed percentage transmittance within the range of 100.08±1.11 to 100.96±1.29, which indicated clear and transparent systems.

In vitro Release

As illustrated in figures (4&5) the rate of DL release from all the prepared ME formulations was significantly higher than that from the pure drug. The release properties of the prepared DL MEs depend on the oil type and concentration used in their preparation. It was found that increasing the oil concentration lead to decreased rate of drug release compared to corresponding formulations prepared with lower oil concentration. The ratio of 1:2 between tween 80 and either Transcutol (F5) or propylene glycol (F9) gave the highest rate of DL release, which was 100.72±0.36% within 70 minutes and 100.77±0.90% within 60 minutes respectively. By comparing S1 formulations with S2 ones, it was found that DL ME formulations prepared with propylene glycol have higher rates of drug release than formulations prepared with Transcutol. This phenomenon might be attributed to the difference in the solubility of DL in the cosurfactants. S1 possessed higher solubility in transcutol when compared to system containing PG (S2). This could be explained on the basis that the high solubility of the drug in the vehicle might have restrained the release of the drug into the medium (44). F9 showed the lowest MDT and the highest % DE (21.60 min and 82.63%) respectively, which indicate fastest rate of drug release among the other formulations as shown in (table IV).

Desloratadine microemulsion formulations composed of 5/15/30/50 %w/w of triacetin/tween80/transcutol/water (F5) from (S1) and of 5/15/30/50 %w/w of triacetin/tween80/propylene glycol/water (F9) from (S2) with the highest rates of drug release, smallest particle sizes and optimal physical parameters for intranasal application were selected for further investigations (zeta potential measurements and *in vivo* evaluation).

Zeta Potential Measurements

Zeta potential results of the chosen Desloratadine microemulsion F5 & F9 were found to be -13.54±1.51mV and -15.67±1.08mV respectively as shown in table (V). This indicates the stability of the formulation. This may be because slightly negative charge of the droplets resulted into neither strong aggregation nor repulsion of the globules (45).

In vivo Evaluation of the Selected Formulae

F5 and F9 were selected to study their anti-allergic and anti-inflammatory activities compared to the commercial Lorafast® syrup. As demonstrated in table (VI) and figures (6&7), it was found that F9 showed significantly reduced plasma histamine concentration compared to the positive control and F5. However, no significant difference was found between F9 and Lorafast® syrup. F9 showed significantly reduced plasma eosinophil peroxidase concentration compared to the positive control, F5 and Lorafast® syrup.

Histopathological Examination

Concerning the histopathological findings as displayed in figure(8), the nasal mucosa of the induced group showed severe congestion in the blood vessels, inflammatory cells infiltration in addition to stratification of mucosal epithelium.

Examination of the histopathology of nasal mucosa of the rats treated with F5 revealed fewer focal inflammatory cells infiltration and congested blood vessels when compared to the positive control group. While, rats treated with F9 displayed neither inflammatory cells infiltration nor stratification of mucosal epithelium. Only, reduced blood vessels congestion compared to the positive control group. Regarding the group treated with Lorafast® syrup, minor blood congestion and inflammatory cells infiltration with no stratification of mucosal epithelium was observed. F9 succeeded to reduce the allergic chemical mediators and to normalize the nasal mucosa more than F5 and Lorafast® syrup.

Table I. Solubility of Desloratadine in various vehicles at 25°C*

Type	Vehicle	Solubility (mg/ml)
Aqueous Solubility	Distilled Water	0.11 ± 0.05
Medium Chain Triglyceride	Isopropyl Myristate	7.49 ± 0.30
Short Chain Triglyceride	Triacetin	12.77 ± 0.10
Surfactant	Tween 80	30.13± 0.25
Surfactant	Tween 20	22.60 ± 0.60
Surfactant	Tween 60	15.00 ± 0.40
Cosurfactant	Transcutol	211.08 ± 1.75
Cosurfactant	Propylene Glycol	67.34 ± 0.90

* Each value represents mean ± SD (n=3)

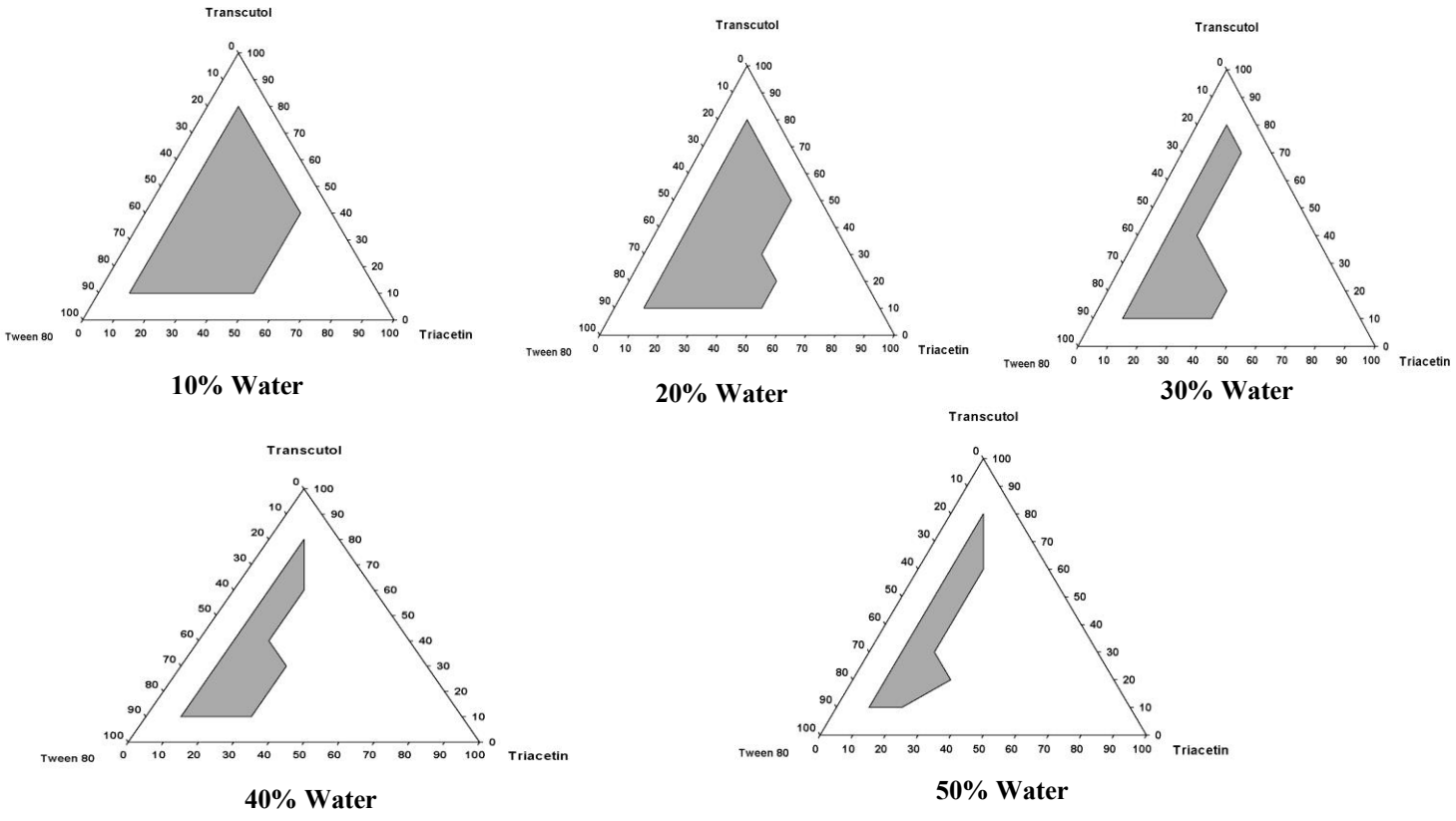

Figure 1: Pseudoternary Phase Diagrams of ME of S1 Containing Triacetin /Tween 80 /Transcutol /Water (from 10% to 50% in five Steps) (The gray areas representing microemulsion regions)

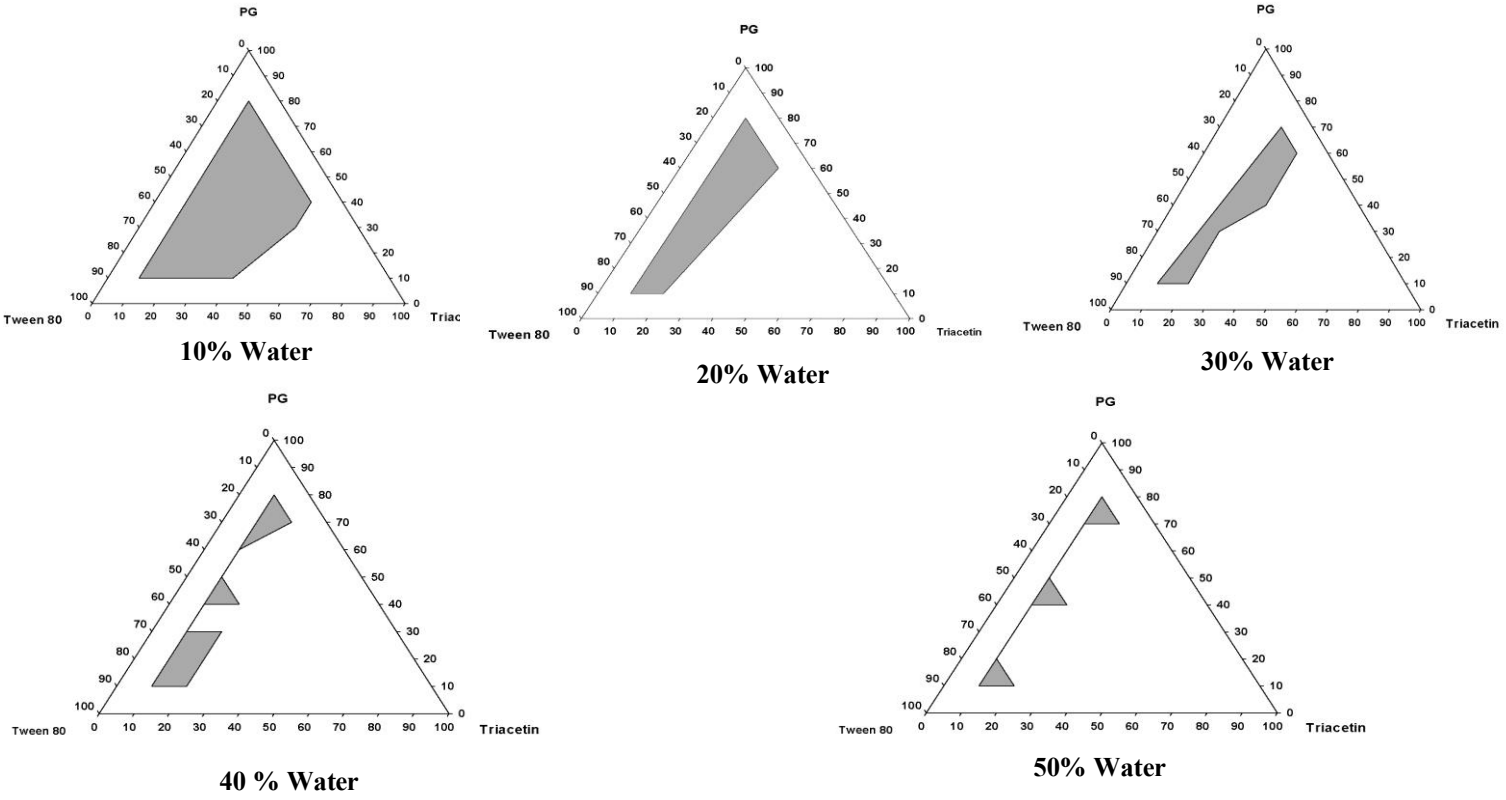

Figure 2. Pseudoternary Phase Diagrams of ME of S2 Containing Triacetin /Tween 80 /Propylene Glycol /Water (from 10% to 50% in five Steps) (The gray area representing microemulsion regions)

Table III. Evaluation parameters of the selected DL Microemulsion formulations*

System Number	Formulation Code	Visual Inspection	pH	Viscosity (cp)	Drug Content (%)	Particle Size (nm)	Transmittance (%)
S1	F1	Clear and Homogenous	5.47±0.15	5.28±1.11	101.59±0.73	25.63±1.24	100.63±1.09
S1	F2		5.27±0.12	6.02±1.22	103.65±0.63	29.87±1.10	100.08±1.11
S1	F3		5.57±0.06	7.68±1.06	103.81±0.48	34.02±1.21	100.33±0.35
S1	F4		5.13±0.21	9.48±0.89	101.27±0.73	40.85±1.82	100.52±0.64
S1	F5		5.80±0.10	14.80±1.76	101.17±0.99	18.22±0.86	100.45±0.64
S1	F6		5.90±0.20	15.70±0.80	102.70±0.99	34.87±1.55	100.20±1.56
S2	F7		5.53±0.21	4.49±1.21	101.59±0.76	25.48±2.41	100.19±0.83
S2	F8		5.43±0.06	6.36±0.66	100.90±0.89	23.45±2.35	100.72±0.37
S2	F9		5.63±0.15	11.30±0.95	101.79±0.75	16.43±1.80	100.96±1.29
S2	F10		5.67±0.21	18.60±1.21	102.06±0.71	28.94±1.99	100.41±0.92
S2	F11		5.80±0.10	20.40±1.00	102.70±0.73	35.75±1.83	100.40±1.46
S2	F12		5.57±0.12	23.80±1.12	102.54±0.69	39.37±1.02	100.77±1.12

* Each value represents mean ± SD (n=3)

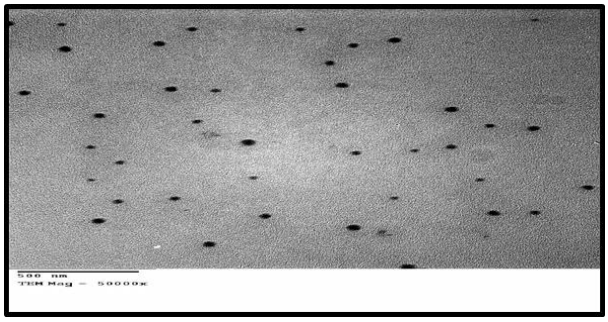

Figure 3. Transmission electron microscope image of Desloratadine loaded microemulsion

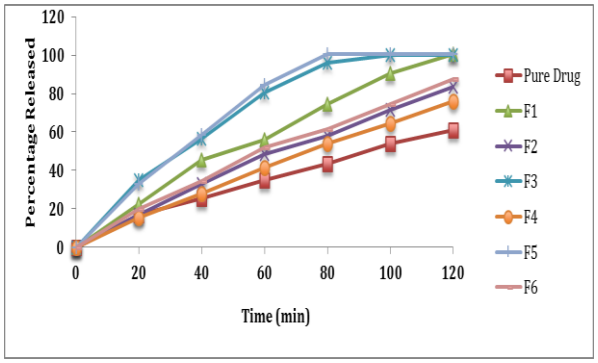

Figure 4. Release profiles of DL from the pure drug and different ME formulations of S1

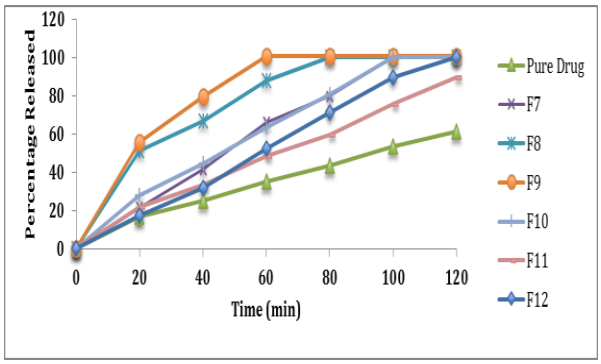

Figure 5. Release Profiles of DL from the pure drug and different ME formulations of S2

Table IV. Comparison of release profiles using MDT and % DE

System Number	Formulation Code	MDT (min)	% DE
	Pure drug	51.84	34.70
S1	F1	51.12	53.78
S1	F2	54.87	45.49
S1	F3	34.87	71.03
S1	F4	55.75	40.71
S1	F5	33.46	72.63
S1	F6	54.62	47.75
S2	F7	48.70	51.64
S2	F8	37.52	53.20
S2	F9	21.60	82.63
S2	F10	46.35	53.77
S2	F11	55.19	48.37
S2	F12	56.55	48.66

Table V. Zeta potential results of the chosen Desloratadine microemulsion*

System Number	Formulation Code	Zeta Potential (mV) ± SD
S1	F5	- 13.54±1.51
S2	F9	-15.67±1.08

* Each value represents mean ± SD (n=3)

Table VI. Plasma histamine and eosinophil peroxidase concentrations in the negative control, positive control and the treated groups*

Group	Plasma Histamine Concentration (ng/ml)	Plasma Eosinophil Peroxidase Concentration (ng/ml)
Negative Control	17.20 ±1.31	0.55±0.06
Positive Control	105.57±1.45[a]	5.62±0.66 [a]
F5	40.47±1.76 [ab]	2.33±0.14[ab]
F9	25.23±1.20 [abc]	1.04±0.07[abc]
Lorafast®	29.23±1.45 [abc]	1.55±0.06[abcd]

* Each value represents mean ± SD (n=6)

* a, b, c or d: significant difference from negative control, positive control, F5 or F9 respectively using one-way ANOVA followed by Bonferroni's post hoc analysis for multiple comparisons $P < 0.05$.

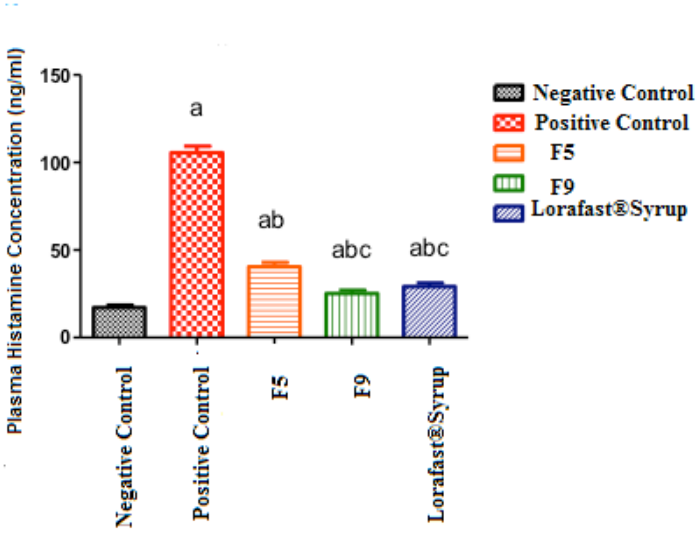

Figure 6. Comparison between the plasma histamine concentration in the negative control, positive control and the treated groups

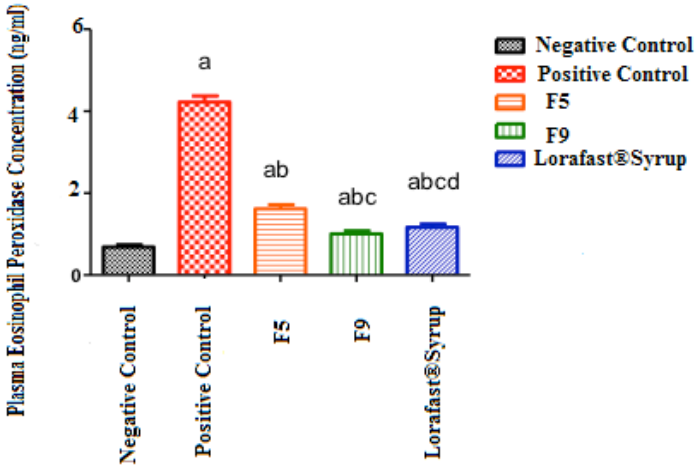

Figure 7. Comparison between the eosinophil peroxidase concentration in the negative control, positive control and the treated groups

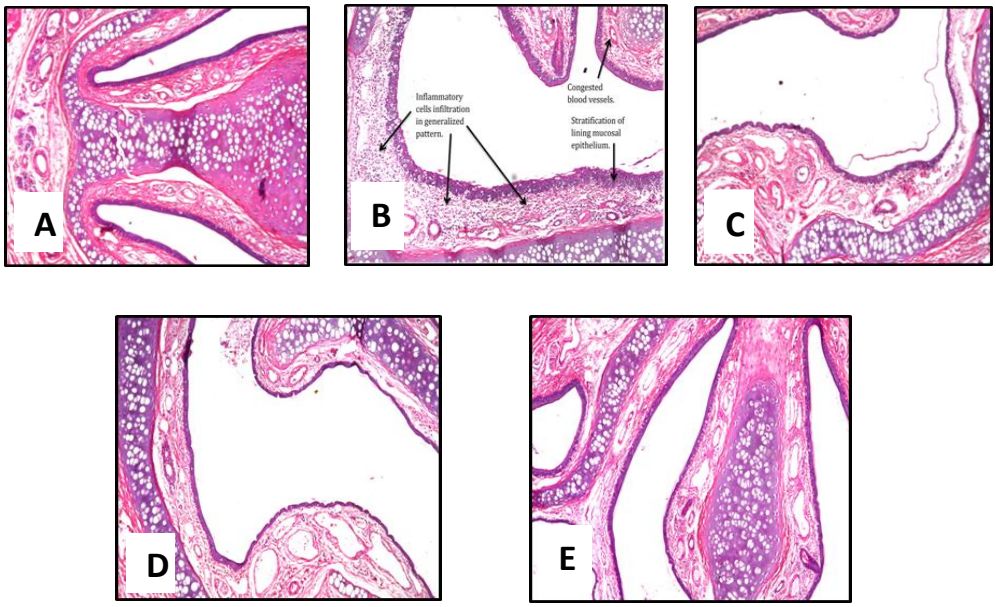

Figure 8. Photomicrograph of rat nasal mucosae (A) negative control, (B) positive control, (C) F5 treated nasal mucosa, (D) F9 treated nasal mucosa and (E) Lorafast® syrup treated nasal mucosa

CONCLUSION

According to the above-mentioned results, it was obvious that the physicochemical parameters and the *in vitro* release are highly affected by the composition and the ratios of the used oil, surfactant and cosurfactants. The most successful DL ME formulation was F9 comprising (5% w/w) Triacetin as oil phase, (15% w/w) Tween 80 as surfactant, (30% w/w) propylene Glycol as cosurfactant and (50% w/w) water, which showed the highest rate of drug release, smallest particle size and suitable viscosity for intranasal administration. Moreover, F9 was more effective than F5 in reducing the plasma histamine and eosinophil peroxidase concentrations, inflammation of nasal mucosa and the congestion of blood vessels. At the same time, F5 displayed no significant difference when compared to the commercial Lorafast® syrup. To conclude, microemulsion systems based on the studied compositions might be a promising approach for the rapid onset intranasal delivery of Desloratadine for the treatment of allergy.

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Disclosure

No conflicts of interest were reported in this work.

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