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RESEARCH ARTICLE

Preparation and characterization of herbal emulsion formulations

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ABSTRACT

St John's wort extract (*Hypericum perforatum L.* aerial part extract), marigold extract (*Calendula officinalis L.* flower extract), wheat germ oil (*Triticum vulgare* Vill. germ oil) and rose oil (*Rosa damascena* Mill. volatile oil) have anti-inflammatory, antimicrobial and wound healing properties. In this study, it is aimed to prepare and characterize herbal topical emulsion formulations for skin disorders with these herbal extracts and oils. Initially the compatibility of herbal ingredients was evaluated and the design of formulation as an emulsion was studied. Then decided cream formulations were prepared as o/w type emulsions. The formulations characterized via several parameters such as; macroscopic and microscopic observations, pH, electrical conductivity and rheological measurements. The characterization of prepared three formulations revealed acceptable properties while one of them had better applicability, maintained its macroscopic stability in room conditions for 6 months, had appropriate pH and electrical conductivity values and had pseudoplastic flow properties. As conclusion, a topical emulsion formulation was prepared with appropriate properties.

Keywords: Topical delivery; herbal formulations; emulsion; St John's wort extract; marigold extract.

1. INTRODUCTION

The appropriate vehicle for topical delivery has to be chosen to obtain optimum effectiveness from active ingredients. During the recent decades various topical systems have been investigated as suitable pharmaceutical vehicles for successful dermal and transdermal delivery of active substances. Emulsion has several advantages such as enhanced drug solubility, ease of manufacturing and enhancement effect on transdermal delivery over conventional formulation such as gel and ointments. An emulsion system consists of oil phase, water phase and surfactant or surfactants mixture. In this study, emulsion formulations were prepared with oil mixtures that have synergistic effect on skin disorders.

Topical application of St John's wort (*Hypericum perforatum L.*) extract [1], marigold (*Calendula officinalis L.*) extract [2, 3], wheat (*Triticum vulgare L.*) germ oil [4] and rose (*Rosa damascena L.*) oil [5] for various topical treatment approaches due to anti-inflammatory, antimicrobial and healing effects indicated in scientific literatures. In this direction, combination of above mentioned herbal ingredients together in a formulation, which is cosmetically acceptable, stable, easily prepared and applicable, will be useful for the skin

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disorders. In case of topical application of herbal substances, emulsions have offer formulation advantages due to their structure available as both aqueous and oily substances and being cosmetically acceptable [5-10].

The aim of this study was to design new emulsion formulations with herbal oils and extract for treatment of skin disorders. The formulations were characterized via several parameters such as; macroscopic and microscopic observations, pH, electrical conductivity and rheological measurements.

2. MATERIALS AND METHODS

2.1. Materials

Hypericum perforatum L. aerial part extract, *Calendula officinalis L.* flower extract, *Rosa damascena* Mill. volatile oil (Muğla Sıtkı Koçman University, Muğla, Turkey), *Triticum vulgare* Vill. germ oil (Bezmialem Vakıf University, Bezmialem center of Education, Practice and Research in Phytotherapy, İstanbul, Turkey), liquid paraffin, cetyl alcohol, Tween 80® (Merck KGaA, Darmstadt, Germany), Span 80® (Fluka, Buchs, Germany), Carbopol 974® (Corel Pharma Chem., Gujarat, India), hydroxypropyl methylcellulose (Colorcon, Dartford, UK), ascorbyl palmitate (Sigma-Aldrich Chemie GmbH, Germany), phenoxyethanol caprylyl glycol (Kale Kimya A.Ş., Kocaeli, Turkey), and de-ionized (DI) water was obtained from ultrapure water system (Model-Arium 611) of Sartorius AG (Goettingen, Germany).

2.2. Preparation of Formulations

Compatibility of herbal contents is evaluated by pre-formulation studies in the light of related articles. The effect of parameters such as the content of surfactant, oil, herbal extracts, HLB number of surfactant blend and additive content on emulsion stability was studied by trial and error method [9-11]. Formulations with selected herbal ingredients were prepared by the emulsion method to obtain o/w emulsion formulations. St John's wort extract, marigold extract, wheat germ oil, rose oil, ascorbyl palmitate, cetyl alcohol, liquid paraffin were used as oil phase [9]. Span 80® was used as hyrophobic surfactant and mixed with oil phase with a magnetic stirrer (RH basic, IKA, Staufen, Germany). Distilled water that mixed Tween 80® (hydrolic surfactant) and phenoxyethanol caprylyl glycol (preservative) was used as water phase of emulsions. Formulations were prepared by adding water phase to oil phase while mixing by mechanic stirrer (IKA RW 20, Staufen, Germany) at 1000 rpm for 30 min at room temperature. The emulsion was mixed for 30 min more to obtain stable formulations. Carbopol 974® or hydroxypropyl methylcellulose (HPMC) was added to the water phase for F1 and F2 formulations, respectively. F3 formulation was prepared without any gelling agent. Formulations with their contents are presented below in Table 1.

The HLB of emulsion formulation blend of tween 80 (HLB=15) and span 80 (HLB=4.3) was calculated according equation. Wa and Wb are weights of Tween 80 and Span 80 in the formulation, respectively.

$$HLBmix = \frac{(W\,a \times HLBa) + (Wb + HLBb)}{Wa + Wb}$$

Table 1. Contents with their amounts as gram for three emulsion formulations coded as F1, F2 and F3 are presented.

Contents	F1	F2	F3
Liquid paraffin	12.5	12.5	12.5
Cetyl alcohol	10	-	5
Tween 80®	0.64	0.44	0.64
Span 80®	0.36	0.36	0.34
Carbopol 974®	0.25	-	-
HPMC	-	0.5	-
Distilled water	15	15.95	15.75
Phenoxyethanol caprylyl glycol	0.25	0.25	0.25
Hypericum perforatum *L.* extract	3.5	7.5	5.5
Calendula officinalis *L.*extract	3.5	7.5	5
Rosa damascena L. oil	1	1	1
Triticum vulgare *L.*oil	1.5	2	2
Ascorbyl palmitate	1.5	2	2
Total amount	**50**	**50**	**50**

2.3. In vitro Characterization Studies

Characterization studies were performed with the macroscopic and microscopic observations, measurement of pH, and determination of rheological behavior, electrical conductivity and stability of the formulations. Stability observations were performed under room conditions (25±1 ºC) for 6 months in terms of macroscopic observations.

Microscopic observation

The microscopic observation of the formulations was examined and photographed by using an optical microscope (Olympus CH40) to show particular structure of emulsion systems. The type of formulation (o/w or w/o) could be

observed by this method. Methylene blue could dissolve in water and the solution of methylene blue was used to dye water phase of emulsions. All slides were dyed and then covered by glass. The microscope samples were examined at room temperature under x10 magnification.

Measurement of pH

The pH values of the formulations were determined by using a pH meter (Jenway 3040 Ion Analyzer, U.K.) at 25±1 °C. All experiments were replicated three times.

Measurement of electrical conductivity

The electrical conductivity (σ) of formulations was measured by using a conductivity meter (Jenway, 4071, U.K.) at 25±1 °C. All experiments were replicated three times.

Rheological measurements

The rheological analysis of the formulations was performed at 25±0.1°C using an AR 2000 controlled stress/controlled rate rheometer (Haake MARS, platte PP35 Ti, plate cover MPC35, Karlsruhe, Germany). In continuous shear analysis, the upward and downward flow curves for each formulation were measured over shear rates ranging from 10 to 900 s^{-1}. All experiments were replicated at three times.

3. RESULTS and DISCUSSION

3.1. Preparation of Formulations

After pre-formulation study three formulations were prepared successfully. The HLB values of formulations were found 11.148, 10.185 and 11.287 for F1, F2 and F3 formulations, respectively. The HLB system is particularly useful to identify surfactants for oil and water emulsification. There are two basic emulsion types. One is water-in-oil (w/o) that water is dispersed in oil phase and other is oil-in-water (o/w) that oil is dispersed in aqueous phase. Water-in-oil emulsions (w/o) require low HLB surfactants. Oil-in-water (o/w) emulsions often require higher HLB surfactants that are more than ten [12]. Our results were showed that the type of formulations is oil in water. But the values are at limit which confirms the formulations are not so oily or water base.

The macroscopic observation results showed that all the formulations were uniform, had light pink color, and did not present any incompatibility in terms of herbal ingredients. The main stability problems of emulsions are creaming, sedimentation, flocculation, phase inversion and coalescence [13]. To use herbal oil blend as oil phase is main difficulty of preparing stabilized emulsion formulation. Stability observations did not demonstrate any significant change for 6 months during the macroscopic characterization of formulations. It was concluded that the herbal oil blend could use to prepare emulsion type formulations.

3.2. Measurement of pH

The pHs of formulations were 3.94, 4.64 and 4.94 for F1, F2 and F3, respectively. High oil content of formulations could affect the pH of formulations due to acidic compositions of oils. The pH of topical formulations for dermal delivery should be around five [14]. The pH values of all formulations were compatible with the skin pH value. But as it was seen, F1 and F2 have low values than F3 that is more compatible for skin.

3.3. Measurement of electrical conductivity

The electrical conductivity of formulations is measured to show if the formulations are w/o or o/w. For w/o emulsion system, the electrical conductivity cannot be measured. Because, oil phase could inhibits conductivity. Desirable electrical conductivity results were obtained from formulation depends on their composition and conductivity values, which were found as 51.2, 55.9 and 9.1 μS/cm for F1, F2 and F3, respectively. All results are acceptable for skin application. The electrical conductivity measurements showed that all formulations were o/w systems as confirmed also with HLB calculation results.

3.4. Microscopic observation

The results of microscopic observations, which are presented in Figure 1 confirmed that the emulsion systems were performed and F3 formulation was more uniform than F1 and F2 formulations. Blue external phase showed that all the systems are oil in water system. Low polydispersity of F3 confirmed high long term stability of formulation.

The polymeric substances could use to increase stability of emulsion formulations [15]. These substances could increase the viscosity of emulsion and decrease coalescences of emulsion droplets. In this study, F3 formulation was prepared without polymeric substance while F1 was prepared with carbopol and F2 was prepared with hydroxylpropylmethyl cellulose. The microscopic images of F1 and F2 are cloudy due to polymeric structure of formulations.

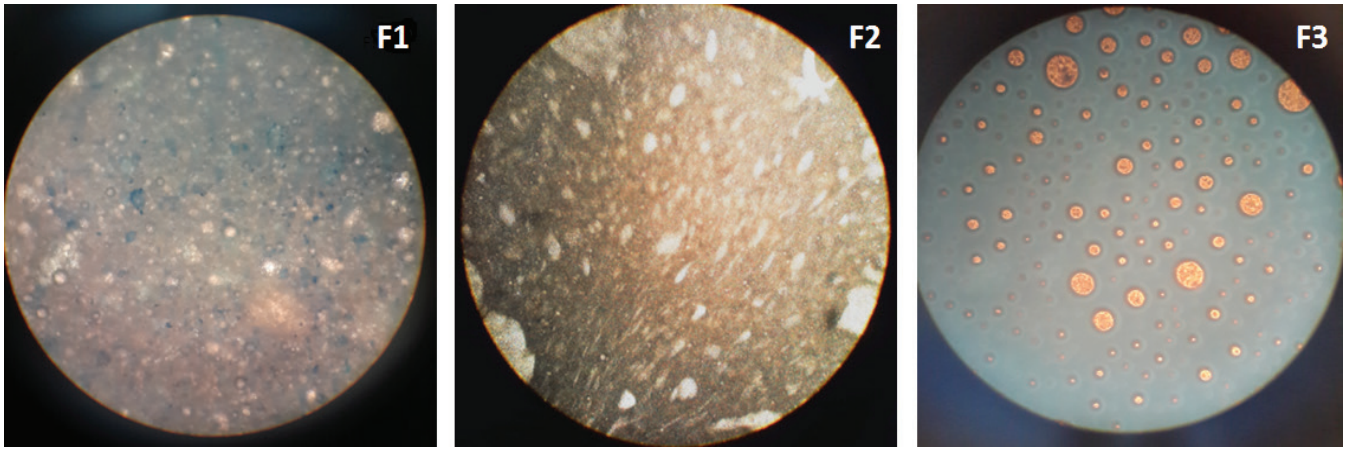

Figure 1. The microscopic images of F1, F2 and F3 formulations.

3.5 Rheological measurements

Rheological studies carried out in order to test the viscosity and flow properties of formulations. The rheological properties of topical formulations affect both the ease of application and spreadability on skin surface. As shown in Figure 1, viscosity decreases with increasing shear rate, as expected from pseudoplastic fluids. And also, the shear stress changes upon shear rates have been used to determine whether the rheological behavior of the formulation is Newtonian or non-Newtonian [16]. It was shown that all the formulations exhibited pseudoplastic flow property at 25°C (Figure 2 and Figure 3). When the starting point of viscosity values compared it was seen that F1 formulation has higher viscosity than F2 and F3. But F3 formulation, without polymer, has higher viscosity than F2. It was thought that cetyl alcohol, a solid lipid, affected viscosity of formulations. Because F1 formulation was prepared with 20 %, F3 was prepared with 5 % and F2 was prepared without cetyl alcohol. The flow behavior of formulations are close each other due to similar formulation composition. By the way, the greatest degree of pseudoplasticity was exhibited with F1 formulation.

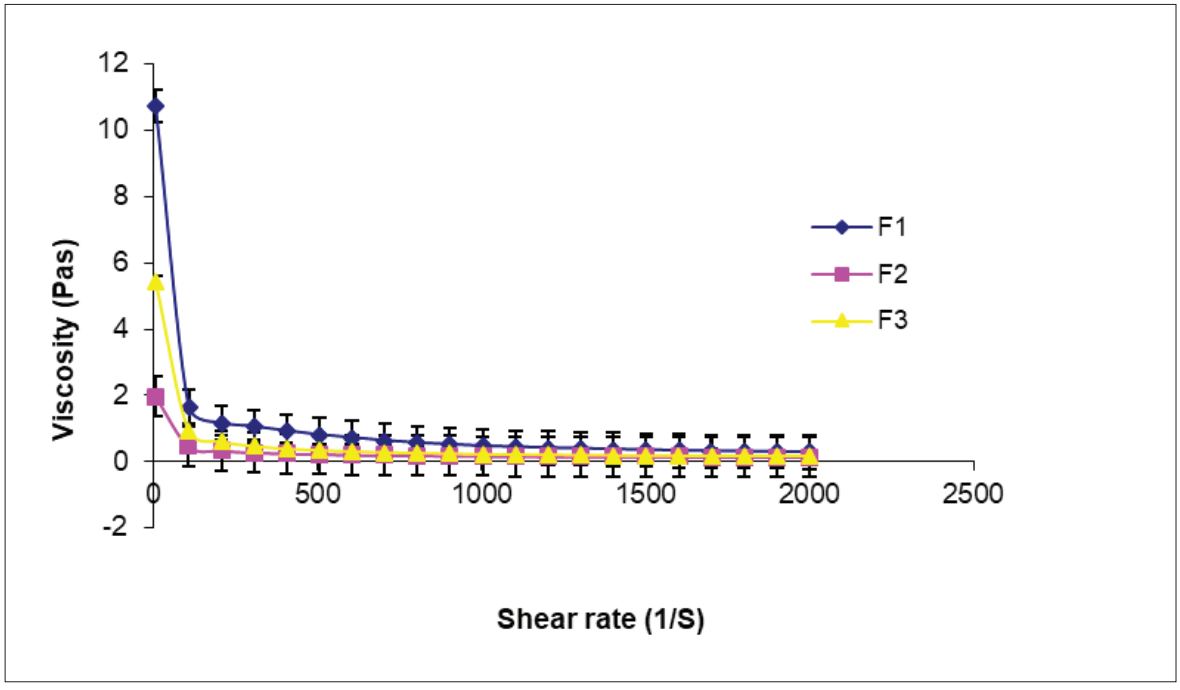

Figure 2. Viscosity versus shear rate curves of F1, F2 and F3 formulations.

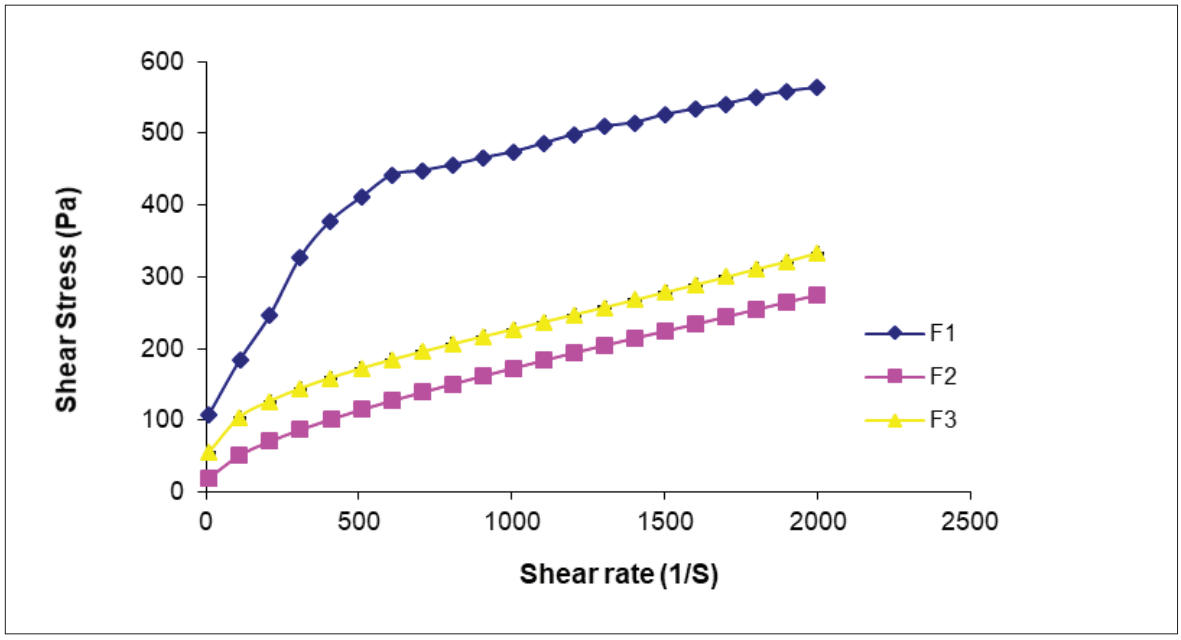

Figure 3. Flow curves of F1, F2 and F3 formulations.

The next step of this study is to perform detailed stability and dermatological tests on the final formulation after accomplishing the formulation development studies for F3.

4. CONCLUSION

Emulsion formulations have many advantages for topical application of active ingredients. In our study, emulsion formulations were prepared with herbal ingredients such as; St John's wort extract, marigold extract, wheat germ oil and rose oil. These extracts and oils are useful for skin disorders as inflammation, wounds and microbial infection. According to aim of this study, three emulsion formulations were prepared successfully. The formulations were characterized via several parameters. All the formulations have acceptable criteria for topical application of herbal substances. But, F3, formulation without polymer, were chosen for further studies due to microscopic observation and pH measurement study results. For further studies, stability studies are going on and dermatologic activity of formulations will be evaluated as clinical study.

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