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Formulation of Emulgel for Treatment of Vitiligo

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Abstract : This study aimed to develop an Emulgel for SUFL obtained from Safoof-e-Bars used in Unani system for the treatment of vitiligo. Safoof-e-Bars (SB) is a powdered dosage form used widely to treat vitiligo, internally as zulal and local application of sufl as recommended by Hakeems. But clinically it is observed that application of sufl is not followed by most of the patients, due to side effects associated with its application on skin. Thus, present study is designed to convert Safoof-e-Bars into a more convenient and appealing newly evolved dosage form 'emulgel' so that it can be used by the patients easily without any side effects.

***Keywords*- Vitiligo, Emulgel, Safoof-e-Bars**

I. INTRODUCTION [7, 9]

Safoof-e-Bars, which is very much beneficial in vitiligo. Safoof (powder) is a dry medicament or a mixture of several medicinal ingredients which is ground or triturated and sieved. Bars was selected which is mentioned in Unani Pharmacopoeia of India and National Formulary of Unani Medicine. The ingredients of S.B are Babchi [P. corylifolia Linn. (Seeds)], Chaksu [Cassia absus Linn. (Seeds)], Panwar [C. tora Linn. (Seeds)] and Anjeer-khushk [Ficus carica Linn. (Fruits)] in equal quantity.
Safoof-e-Bars is used both internally as a ZULAL (Infusion) and externally as a SUFL (Sediment remained after decanting the soaked drug) in the form of Zimad (Paste).
10 gm of Safoof-e-Bars is soaked in 50 ml of water overnight. In the morning, the infusion (Zulal) is decanted and administered orally. The sufl is mixed with Sirka Naishkar (Vinegar) to prepare a paste and applied on the affected parts and then the affected part is exposed to Sunrays at Noon
Babchi is the main ingredient of Safoof-e-Bars and psoralen is therapeutically active compound of babchi, which might be more responsible for its therapeutic value along with other ingredients. Since psoralen is very slightly soluble/insoluble in water, therefore it does not come in the zulal, rather remains in the sediment that is in the sufl.
It is observed in number of the patients who apply the sufl that there is itching, dryness, erythema, and blister formation associated with it. These undesirable effects due to the application of sufl cause non-compliance with the medication. This may result in under treatment that hampers cure. Moreover, pre-application procedure is tedious. It needs to be formulated into paste by mixing sufl with suitable vehicle like sirka naishkar (vinegar).
In view of the above-mentioned problems, and to overcome all these problems related to traditional dosage form, present study has been designed to convert Safoof-e-Bars into a new dosage form emulgel. Gels are however limited to deliver hydrophobic drugs. So an emulsion based gels (emulgel) can be used to deliver poorly water-soluble drugs. Bioavailability and dissolution rate of emulgels are good Therefore, emulgels may serve as better option for topical delivery of poorly water-soluble drug.

INTRODUCTION TO EMULGEL [3]

Emulgel

Emulgel is known as an emulsion that has been gelled by using a gelling agent. They can be made either o/w or w/o type. Emulgel is a stable and superior system that incorporates poor water-soluble drugs. In brief, emulgel is a combination of emulsion and gel. Despite the numerous advantages of gels, one significant disadvantage is the delivery of hydrophobic medications. As a result, an emulsion-based solution is being used to overcome this limitation, allowing even hydrophobic therapeutic moieties to benefit from the unique properties of the gel.

Emulgel can deliver both hydrophilic and lipophilic drugs due to the presence of both aqueous and non-aqueous phases. In recent years, they have been used as a control release formulation. These are biphasic systems that have better drug loading capacity and better stability. Emulgel has several good properties, such as good spread ability, greaseless, thixotropic, good shelf life, odourless, and a pleasant appearance over the conventional topical formulation. Emulgel has both gel and emulsion properties and functions as a dual control release system

Advantages of Emulgel

1. Using water/oil/water emulsions, hydrophobic drugs can be quickly implemented into the gel base.
2. Improved stability and load capacity.
3. Easy for production and a low-cost mechanism.
4. The first metabolism is avoided.
5. Avoid gastrointestinal incompatibility.
6. Target drug delivery on the body.
7. Improved patient compliance.
8. Improved patient acceptability and suitability for self-medication.
9. Ability to easily terminate medication

The rationale of Emulgel as topical drug delivery

Various semisolids and other preparations are available on the market for restoring the skin's fundamental role or pharmacologically altering an operation to the underline tissue. The formulations, such as lotions, ointments and creams have several drawbacks, including being sticky, having a low spreading coefficient, and having stability issues. Only transparent gels have exposure in pharmaceutical and cosmetic preparations due to overall limitations within the semisolid preparations

As a result, an emulsion-based solution is used to address this limitation. Hence, the hydrophobic moiety of the drug should be incorporated and provided through gels. Drug/oil/water emulsions may be used to integrate hydrophobic drugs into emulgel. Since solubility acts as a barrier, most drugs cannot be inserted directly into gel bases, causing problems during drug release. The emulgel system helps to incorporate a hydrophobic drug into the oil phase, after which oily globules are easily dispersed into the aqueous phase, resulting in an oil/water emulsion. The emulsion can be mixed into the gel base. This may result in enhanced drug stability and release over simply incorporating the drug into the gel base.

II. MATERIALS AND METHODS:

2.1 Raw material Collection: The botanical powders, including Babchi, Chaksu, Panwar, Anjeer-khushk were procured from a local Ayurvedic store.

2.2 Preparation of Extract:

All the coarsely powdered drug was taken in equal proportion mixed together then extract was taken in 1:1 of water & ethanol. Drug and water was taken in the ratio as of Zulal (1:5). Same amount of Ethanol was added in water. The extract was filtered and then subjected to rotatory shaker for 24 hrs at 100 rpm.

III. FORMULATION STUDIES [2]

3.1. Selection of Oily Phase

Weigh about 1gm of each oil into vials and a suitable volume of the hydroalcoholic extract is added to each oil sample. Mixing each oil-extract solution is heated and thoroughly mixed using cyclomixer to ensure uniform distribution of the hydroalcoholic extract within the oil phase until a homogeneous mixture is achieved. The solubility of the hydroalcoholic extract in each oil was evaluated by visual inspection for any signs of precipitation or separation.

3.2. Selection of Surfactant

About 300 mg of each surfactant and 300 mg oil taken in a vial. This mixture heated and cyclomixed. From this mixture, take 150 mg and add to 50 ml distilled water. The ease of emulsion formulation was monitored by noting the number flask inversion required to produce clear and uniform emulsion. Various combinations were evaluated for % transmittance at 638.2 nm by UV visible spectrometer using distilled water as blank.

3.3. Selection of Co-surfactant

The surfactant mixture was prepared by mixing 200 mg of Tween 80 surfactant and 100 mg of cosurfactant with 300 mg of clove oil in given in table to assess relative efficiency of the cosurfactant to improve the emulsification ability of selected surfactant and to check number of flask inversion. The oil-S-mix mixture at each ratio was slowly titrated with distilled water. The addition of distilled water was carried out with at room temperature until a micro emulsion was formed.

3.4. Optimization of micro emulsion [10]

The microemulsion existence region was determined by constructing pseudo-ternary phase diagram. Titration method was employed for its determination. On the basis of the solubility study of extract, oils, surfactants, co-surfactants and aqueous phase were used for construction of phase diagram. The pseudo ternary phase diagrams of surfactant and co-surfactant mixture (S-mix), oil and doubled distilled water were plotted by the water titration method. The surfactant used was tween-80, and the co-surfactant used was PEG 400. The ratio of surfactant (S) to co-surfactant (CoS) was fixed at different ratios of 1:1, 2:1, and 1:2 on the weight basis for each phase diagram. The oil phase was mixed with the surfactant and co-surfactant mixture at the ratios (volume basis) of 1:9, 1:8, 1:7, 2:12, 2:10, 2:8, 2:7, 2:6, 2:1, 3:7, 3:6, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1(w/w). The oil and S-mix phases at each ratio were weighed separately, mixed, and stirred using a magnetic stirrer at a speed of 500 rpm until homogeneous mixtures were achieved. The oil-S-mix mixture at each ratio was slowly titrated with distilled water. The addition of distilled water was carried out with a constant stirring speed, and the final mixture was stirred with a constant stirring speed for 15 minutes at room temperature until a microemulsion (ME) was formed.

3.5. Stability to Freeze thaw Cycle [2]

In order to assess the thermodynamic stability of microemulsion they were subjected to freeze-thaw cycles. Formulation was stored at room temperature for 24 hours followed by 24 hours at 5˚C in refrigerator, thus completing one such freeze thaw cycle. Likewise, three alternate freeze thaw cycles were carried out and the formulations were visually observed for any sign of phase separation and/or precipitation.

3.6. Study of %T, Globule size

The formulation batches which strongly withstand the freeze-thaw cycles were further subjected for flask inversion, %T, globule size, zeta potential and polydispersity index was determined by Horiba Nanopartica SZ100 Particle Size Analyzer. Prior to analysis the formulation 50 mg was diluted to 50 ml with double distilled water. These micro emulsions were tested for % T measured at 638.2nm, counting the number of flask inversions required for formation of clear emulsion, globule size, polydispersity index, zeta potential.

3.7. Method of preparation of Emulgel [5]

The gel bases were prepared by dispersing carbopol-934 in purified water (80°C) with constant stirring at 200 Revolution per Minutes (RPM). The oil phase of the emulsion was prepared by dissolving hydroalcoholic extract in clove oil while the aqueous phase was prepared by dissolving Tween 80 and methyl paraben in purified water. Propyl paraben was dissolved in PEG 400, and were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70° to 80°C; then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature. The obtained emulsion was mixed with the gel in 1:1 ratio with gentle stirring to obtain the emulgel.

3.8. Optimization of Emulgel

Optimization of Emulgel were performed by changing the amount of gelling agent, whereas preparation of emulsion was same in all the formulations

Table 1: optimization of emulgel

Sr. No.	Ingredients and properties (%w/w)	F1	F2	F3	F4
1	Extract (active ingredient)	23.5	23.5	23.5	23.5
2	Carbopol-934 (gelling agent)	0.5	1	1.5	2
3	Clove oil (oily vehicle)	8	8	8	8
4	Tween 80 (emulsifying agent)	2	42	4	4
5	PEG 400 (emulsifying agent)	4	4	4	4
6	Propylene glycol (humectants)	5	5	5	5
7	Methylparaben (preservative)	0.03	0.03	0.03	0.03
8	Propylparaben (preservative)	0.01	0.01	0.01	0.01
9	Purified water (aqueous vehicle)	Q.S	Q.S	Q.S	Q.S

3.9. Evaluation of Emulgel [6]

Appearance: Emulgel was tested visually for appearance to identify the presence of any aggregates.

Colour: colour of the Emulgel was observed visually

Odor: odor was observed by smelling the Emulgel directly.

Consistency: consistency was checked visually.

Homogeneity: Emulgel was checked visually to identify any non-homogeneity.

Oily feel: oily feel was checked by spreading on skin surface and by washing with tap water.

Stickiness: stickiness was also checked by spreading on skin surface.

Grittiness: Emulgel was checked for grittiness by spreading on skin surface.

Phase separation: Emulgel was observed visually for phase separation.

Determination of viscosity: Viscosity of Emulgel was determined by using a Brookfield viscometer

Spreadability study: Spreadability denotes the extent of area to which the emulgel readily spreads on application to skin or the affected part. The bioavailability efficiency of an emulgel formulation also depends on its spreading value. The Spreadability was expressed in terms of time in seconds taken by two slides to slip off from the emulgel which was placed in between the slides, under certain load. Lesser the time taken for separation of the two slides, better the Spreadability.

Extrudability test: The Emulgel formulation was filled into collapsible aluminium tube and sealed by crimping the end. The tubes were pressed to extrude the material and the extrudability of the emulgel was checked.

Microbiological contamination: Microbiological analysis of emulgel was carried out as per the methodology described in USP.

Determination of pH: Five gram of emulgel was dissolved in 45 mL of distilled water and then the pH was determined by using digital pH meter

IV. RESULT AND DECISION:

4.1. Selection of Oily Phase

The solubility of extract was checked in various oils such as rose oil, olive oil, Jojoba oil, clove oil, coconut oil, anise oil, sunflower oil. Out of 7 oils tested, clove oil has shown no sign of precipitation with maximum solubility of hydroalcoholic extract also clove oil act as a skin penetration enhancer thus clove oil selected as oily phase.

4.2 Selection of Surfactant

The Surfactant were compared for ease of emulsification of the selected oily phase. i.e clove oil. Selection of surfactant primarily based on their efficiency to spontaneously emulsify the selected oil. Surfactant such as Tween 20, Tween 60, Tween 80, Span 20 were tested it was observed out of 5 surfactants tested, Tween 80 have shown better emulsification ability with 97.3% Transmittance requiring 0 flask inversion for ease of emulsification. Thus Tween 80 selected as surfactant.

4.3 Selection of Co-surfactant

Addition of a cosurfactant to the surfactant containing formulation lowers the interfacial tension fluidizes the hydrocarbon region of the interfacial film, and decreases the bending stress of interface which improves the dispersibility and drug absorption from the formulation. Various cosurfactant such as PEG 400, Span 20, Ethylene glycol was tested Out of 3 co- surfactant tested, PEG 400 have shown better emulsification ability with 98.2% Transmittance requiring 1 flask inversion for ease of emulsification.

4.4. Optimization of micro emulsion

For the microemulsion base, this study used the surfactant tween-80 and the co-surfactant PEG 400 because previous studies have proven that the combination of both is the right choice to produce microemulsion preparations with good physical characteristics and stability. The ratio of oil, surfactant, and co-surfactant in the microemulsion region was determined using cosurfactant using a pseudo-ternary phase diagram. If the ratio of surfactant to co-surfactant changes, where the former continuously increases, the interfacial tension will become better and more optimal, producing a good microemulsion. However, if the amount of co-surfactant is elevated beyond the surfactant, a reduction in emulsification will occur, therefore, it is better to use more surfactant than co-surfactant. The results of this study show microemulsion preparations with precise characteristics and good stability for seven days with a tween 80: PEG 400 ratio of 2:1 thus S-mix of the 2:1 ratio had a wider microemulsion area. A decrease in the oil level can lead to an increase in the microemulsion formation area. Non formation of microemulsion may be attributed to the surfactant concentration. The lower the surfactant concentration, the less micellar formation that plays a role in bringing together the oil and water phases in the microemulsion. Surfactants and co-surfactants are adsorbed at the interface, reducing the interfacial energy, and providing a mechanical barrier to prevent coalescence. The added cosurfactant can create and fill the gaps in the surfactant molecule. The co-surfactant addition can cause greater penetration of the oil phase in the

hydrophobic region of the surfactant monomer, thereby lowering the interfacial tension. The S-mix of the ratio of 2:1 showed a greater area than that S-mixes of other ratios.

4.5 Stability to Freeze thaw cycle

After subjecting the various formulated microemulsion to freeze thaw cycle microemulsion having oil: Smix 2:1 ratio and surfactant and co-surfactant in the ratio of 2:1 have shown neither separation and nor color change. Thus oil: Smix ratio 2:1 and surfactant and co-surfactant in the ratio of 2:1 considered as optimized ratio for microemulsion formulation.

4.6 Study of %T, Globule size of optimized micro emulsion

Optimized micro emulsion which found stable to freeze thaw cycle were evaluated for % T and globule size it was found that 98 % transmittance were observed with zero number of flask inversion and particle size found to be 92.4 nm.

4.7 Evaluation of Emulgel:

On evaluation of Emulgel it was found that Emulgel with 2% gelling agent i.e Carbopol 934 was optimized concentration to formulate Safoof- e-bars hydro alcoholic extract into Emulgel.

Table 2: evaluation of emulgel

Sr. no	Evaluation	F1	F2	F3	F4
1	Appearance	Opaque liquid	Opaque liquid	Opaque liquid	Opaque, smooth & glossy
2	Colour	Dark brown	Dark brown	Dark brown	Dark brown
3	Odour	Pleasant	Pleasant	Pleasant	Pleasant
4	Consistency	Poor	Poor	Poor	Excellent
5	Homogeneity	0	0	0	+++
6	Oily feel	Absent	Absent	Absent	Absent
7	Grittiness	Absent	Absent	Absent	Absent
8	Phase separation	Present	Present	Present	Absent
9	Extrudability test	Poor	Poor	Poor	Excellent
10	Microbiological contamination	Present	Present	Present	Absent
11	Spreadability	+	+	+	+++
12	Determination of PH	5.24	5.106	5.34	5.55

Table 3: optimized formula of emulgel

Sr. No.	Ingredients and properties (%w/w)	F4
1	Extract (active ingredient)	23.5
2	Carbopol-934 (gelling agent)	2
3	Clove oil (oily vehicle)	8
4	Tween 80 (emulsifying agent)	4

5	PEG 400 (emulsifying agent)	4
6	Propylene glycol (humectants)	5
7	Methylparaben (preservative)	0.03
8	Propylparaben (preservative)	0.01
9	Purified water (aqueous vehicle)	Q. S

Conclusion: In this research, we have formulated Emulgel loaded with extract obtained from Safoof-e-bars, which are used in Unani system of medicines for the treatment of vitiligo. Formulation of Emulgel helps in overcoming the disadvantages associated with the external use of Safoof-e-bars such as itching, dryness, erythema and blister formation thus affecting the patience compliances to overcome the above-mentioned problems safoof-e-bars are successfully converted to Emulgel.

Reference:

1. C Srinivas, S Vanitha Sagar. Enhancing the bioavailability of simvastatin using microemulsion drug delivery system. Asian J Pharm Clin Res 2012;5:134-9.
2. Faizi Muzaffar, UK Singh, Lalit Chauhan. Review on microemulsion as futuristic drug delivery. Int J Pharm Pharm Sci 2013;5:39-53.
3. Single V, Saini S, Joshi B, Rana AC. Emulgel: a new platform for topical drug delivery. Int J Pharm Biol Sci 2012;3:485-98
4. Jain A, Deveda P, Vyas N, Chauhan J et al. Development Of Antifungal Emulsion Based Gel For Topical Fungal Infection(S). IJPRD 2011; 2(12)
5. Mohamed MI. Optimization of Chlorphenesin Emulgel Formulation. AAPS J. 2004; 6 (3).
6. Kumar V, Mahant S, Rao R, Nanda S. Emulgel based topical delivery system for loratadine. ADMET & DMPK 2014;2(4):25471
7. Department of Ayush. Physicochemical standards of Unani formulations. Part IV. New Delhi: CCRUM; 2006. p. 144. 145, 157-160.
8. Afaq SH, Tajuddin, Siddiqui MMH. Standardization of herbal drugs. Aligarh: AMU Press; 1994. p. 41-42. 143-146
9. Mohd Shadab, Shariq Shamsi, Design and Development of Unani Emulgel for Vitiligo. Journal of Ayurveda and Integrative Medicine xxx (2018) 1-10
10. Formulation and Evaluation of Herbal Emulgel Loaded with Extract of Cedrus deodara for its In-Vitro Anti-Inflammatory Activity. International Journal of Ayurvedic Medicine; Vol 13 (3), 2022; 749-753.