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Formulation and Characterization of Curcumin Emulgel for Topical Delivery

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ABSTRACT

Emulgels have shown as a promising drug delivery system for the delivery of hydrophobic medications. The aim of the study was to prepare emulgel of curcumin, a NSAID, using Carbapol 940 as a gelling agent. Mentha oil and clove oil were used as penetration enhancers. Emulgels, with their dual release control system of gel and emulsion, have become one of the most remarkable topical delivery systems. Emulgel is the term for the dosage form that is used when gel and emulsion are combined. Emulgel has multiple advantageous properties for dermatological use like that being thixotropic, easily spreadable, greaseless, easily removable, nonstaining, emollient, long shelf life, transparent and pleasing appearance. Emulgel is more effective than ordinary gel in terms of healing aspects and deeper drug penetration because it can also provide a local concentration of medication in the affected area. Emulgels are thermodynamically stable systems that possess various characteristics, including improved permeability, extended drug release, emulsion stability, and strong thermodynamic stability. The patient adherence to topical formulations is significant in relation to chronic skin diseases, like fungal infections, acne, psoriasis. The formulations were evaluated for rheological studies, spreading coefficient studies, swelling index, determination of pH, globule size and its distribution in emulgel, drug content determination, in vitro release, stability study.

INTRODUCTION

Topically administered medication is a controlled method of delivering medication through the skin, vaginal, ophthalmic, and rectal routes to any part of the body. The ability to avoid first pass metabolism is the primary benefit of topical delivery systems. [2] A topical drug delivery system is a formulation that is applied topically to treat skin conditions directly, such as acne, psoriasis, or localized skin infections like fungal infections, with the goal of delivering a drug's pharmacological or other effects to the skin's surface or inside the skin. They are applying a broad range of dermatological and cosmetic preparations to their healthy or sick skin. [1]

Emulgels are emulsions mixed into gels, either of the water in oil or oil in water type. Because they have the benefits of both gels and emulsions such as being thixotropic, greaseless, spreadable, washable, non-staining, and compatible with a variety of excipients they are acceptable to patients. [7], [11] the development of emulgel formulations is necessary because formulations such as creams and ointments have issues with being greasy, being difficult to remove from the skin, and leaving stains. [5]

The goal of this work was to create an emulgel formulation of the hydrophobic medication curcumin using two types of penetration enhancers, namely clove oil and mentha oil, along with carbopol 940 as a gelling agent. Investigations were conducted into the effects of penetration enhancers and gelling agents. [7]

Classification of topical drug delivery system

Classification of topical drug delivery systems: [2], [3]

1. Solid: Plasters, Powders, Ointments.

2. Semi solid: Creams, Pastes, Poultices, Gels.

3. Liquid: Emulsions, Liniment, Lotions, solution, tinctures, Suspensions, Paints.

4. Miscellaneous: Transdermal drug delivery systems, Tapes and Gauzes, Rubbing alcohols.

ADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM [2], [1], [5]

- Improved patient acceptability.
- Avoidance of gastrointestinal incongruity.
- More selective to a specific site.
- Improve bioavailability and low doses can be more effective than other traditional semi-solid preparation techniques.
- Hydrophobic drug can be easily combined in emulgel form by using emulsion as the drug barrier, which is finally dispersed in to gel.
- Easy to use and easy to apply.
- Their hydrophilic and hydrophobic natures facilitate better skin penetration.

DISADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM [3], [1]

- Skin irritation on contact dermatitis.
- Poor permeability of some drug through skin.
- Larger particle size drugs are not easy to absorb through the skin.

Emulgel

Since the middle of the 1980s, emulsion-gels have become more and more significant in topical semisolid dosage forms for pharmaceuticals. Emulgels are emulsions, either water-in-oil or oil-in-water, that are gelled through mixing with a gelling agent.[1] Transparent gels are one of the major groups of semisolid preparations whose use has grown tremendously in both pharmaceutical and cosmetic preparations. According to USP, gel is a semisolid system made up of liquid wrapping and penetrating either large organic molecules or dispersions of small inorganic particles. [1] Emulgel is being used so that a hydrophobic therapeutic moiety is successfully incorporated and enjoy the unique property of gels. Further, Emulgel for dermatological use have several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaining, water-soluble, greater shelf life, bio-friendly, clear & pleasant appearance.[2], [11]

ADVANTAGES OF EMULGEL [2], [1]

- The incorporation of hydrophobic drugs.
- Producing feasibility and low preparation cost.
- When compared to other traditional semi-solid preparations, improve bioavailability and low doses can be effective.
- No intensive sonication.
- Improve Patient Compliance.
- Easy to formulate and cost-effective preparation.
- Better stability.

DISADVANTAGES OF EMULGEL [2], [1]

- The possibility of allergenic reaction.
- Drug of large particle size not easy to absorb through the skin.
- Entrapment of air bubble during formulation.
- The poor permeability of some drug through the skin.

IDEAL PROPERTIES OF DRUG CANDIDATE TO FORMULATE AS EMULGEL [1], [10]

- Drug dose should be low i.e. less than 10 mg.
- Molecular weight of drug should be 400 Dalton or less
- Half-life of drug 10 hr or less
- Oral bioavailability and therapeutic index should be low.
- A medication that is less polarity and does not cause irritation or sensitization is ideal.

METHODS OF FORMULATION OF EMULGEL

Emulgel is formulated by following steps: [8], [2]

1. Selection of components

2. Preparation of emulsion

3. Preparation of emulgel

1. Selection of components

Drug Solubility was assessed in variety oils by excess addition of drug followed by vigorously stirred for 72 hours to achieve equilibrium. After that samples centrifuged and supernatant was taken and solubility was determined by appropriate analytical techniques. Then, excipients in each category with the highest solubility of drug are selected for additional research.

2. Preparation of emulsion

Following the drug's solubilization in oil, the oil is combined with a mixture of surfactant and co-surfactant, which is subsequently diluted with water to create an emulsion of the known drug.

3. Preparation of emulgel [1], [10]

Emulgel preparation includes three Steps:

Step 1: Gel base formulation- The pH was brought to 6-6.5 using triethanolamine or NaOH, and the polymer was dissolved in the purified water with continuous mixing at a moderate pace using a mechanical shaker to create the gel phase.

Step 2: In the formulation of an o/w or w/o emulsion: an emulsifier (such as span) is dissolved in an oil vehicle (such as liquid paraffin) to create the oil phase, and a hydrophilic emulsifier (such as tween) is dissolved in purified water to create the water phase. Both the dissolved drug and methyl and propyl parabens are combined with ethanol to form a watery phase, which is then blended together. Humectants such as propylene glycol are used to dissolve the parabens. After the aqueous and oily phases have been freely heated to between

70°C and 80°C, the oily phase is continuously blended into the aqueous phase. To form an emulsion, this mixture is allowed to cool to room temperature.

Step 3: Emulsion is added to gel base gradually while blending: to create emulgel, a 1:1 ratio of gel to emulsion is mixed together. [1]

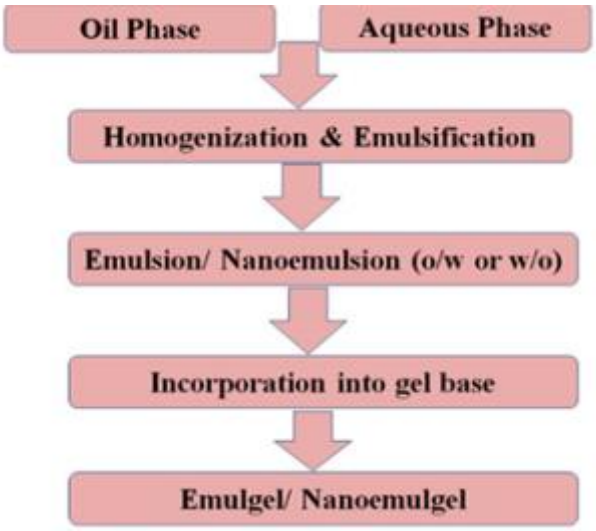

Fig 1: basic steps in preparation of emulgel [10]

CHARACTERIZATION OF EMULGEL

1. Physical examination [1], [4]

The optimized emulgel formulations were examined visually for their colour, homogeneity and consistency.

Table 1: physical parameters of formulation batches

Formulation	Color	Homogeneity	Consistency	Phase separation
F1	Yellow	Excellent	Excellent	None
F2	Yellow	Excellent	Excellent	None
F3	Yellow	Excellent	Excellent	None
F4	Yellow	Excellent	Excellent	None

2. Determination of pH

The pH of emulgel formulations were determined by digital pH meter. 1g of gel was disintegrated in 10 ml of distilled water. The measurement of pH of each formulation was executed in triplicates. The pH range of many topical formulations, as determined by a pH meter, is between **6 to 6.5**. [2], [11]

3. Determination of Rheological properties [8]

A Brookfield viscometer with Spindle number S64 was used to measure the viscosity of 20g of prepared emulgel placed in a 25ml beaker.

4. Globule size and its distribution in emulgel [8]

To calculate this parameter 1.0 gm of product was disintegrated in water and stirred to become dispersion and then sample was put into the photocell of Malvern zetasizer.

5. Swelling index [3], [5], [1]

To establish the swelling index of prepared topical emulgel, 1 g of gel is acquired on porous aluminium foil and then put in individually in a 50 ml beaker containing 10 ml 0.1 N NaOH. Then, samples were removed from beakers at varying time intervals and put it on a dry place for Sometimes after it reweighed. Swelling index is estimated as follows:

$$\text{Swelling index (SW) \%} = [(Wt - Wo)/Wo] \times 100$$

Where, (SW) % = Equilibrium percent swelling,

Wt = Weight of swollen Emulgel after time t,

Wo = Original weight of Emulgel at zero time

6. Spreading coefficient [8],[1]

It can be determined by using Slip and Drag technique, as suggested by Mutimer, for this Consider 2gm of emulgel and applied on lower side slide which is elevated with wooden block and sandwiched is prepared by using other glass slide having same size which is connect with hook having 500mg weight placed. After 5 min extra weight was placed on pan

which connected with second slide. Time to cover 5cm distance for upper slide was noted and used to calculate spreadability by using following formula:

$$S=M.L/T$$

Where, S= Spreadability,

M= Weight bounded to upper slide,

L= Length of glass slides

T= Time taken to detach the slides

7. Drug content determination [1], [3]

1 g of prepared emulgel is mixed with 25 ml of ethanol. The resultant solution is sonicated for 30 min. Determine its absorbance using ultraviolet UV spectrophotometer. Standard plot of the drug is prepared in the same solvent. Concentration and drug content can be determined using the same standard plot by putting the value of absorbance.

Drug content = (Concentration × Dilution factor × Volume taken) × (Conversion factor)

Table 2: absorbance of curcumin in ethanol

Drug Content Determination by UV Visible spectroscopy	
Concentration in mcg/ml	**Absorbance**
2	0.2675
4	0.4128
6	0.6296
8	0.8452
10	1.0325
12	1.2959
14	1.4695

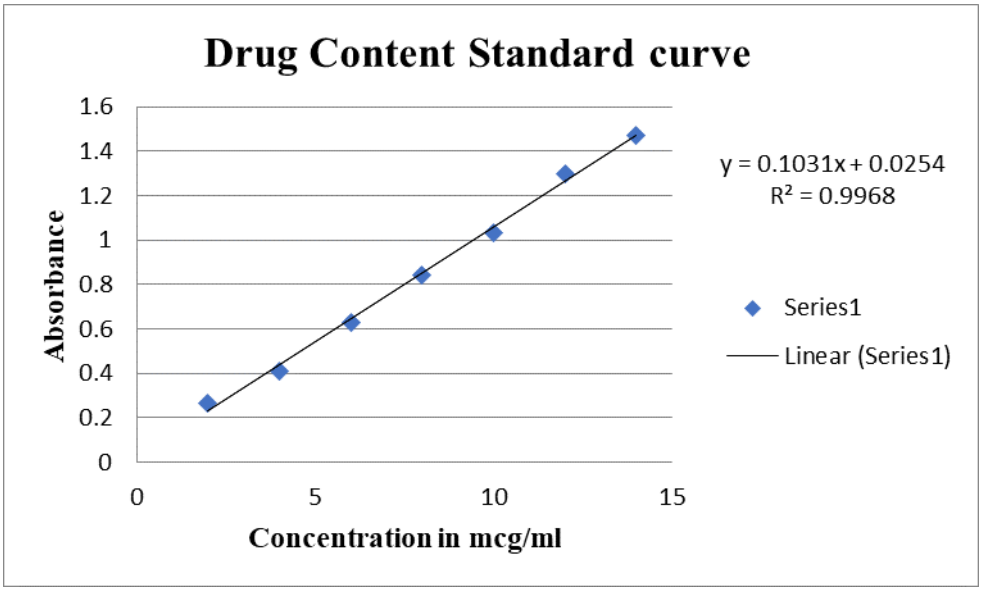

Fig 2: standard curve of curcumin for drug content determination

8. In-vitro Diffusion studies [7]

A Franz diffusion cell is used in the in vitro drug release investigations. The dialysis membrane, which is fixed between the donor and receptor compartments of the Franze Diffusion cell, is coated with the prepared emulgel formulation. A recently made pH 7.4 phosphate buffer solution is used as the dissolution medium and poured into the receptor compartment to solubilize the medication. The Franze Diffusion cell's water jacket circulates to keep the temperature at 37°C. For continuous stirring, the assembly is maintained on a magnetic stirrer. To keep the sink condition, a 5 ml sample is taken out at appropriate intervals and replaced with an equivalent volume of new dissolving medium. The cumulative percentage of drug release is computed as a function of time after the aliquots are collected and examined at a specific wavelength using a UV-Vis Spectrophotometer.

Table 3: in-vitro drug release % of formulation

Sr. No.	Time (Min)	Formulation 1	Formulation 2	Formulation 3	Formulation 4
1.	**00**	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00	00.00 ± 00.00
2.	**30**	10.17 ± 1.28	11.72 ± 0.98	12.32 ± 0.75	15.65 ± 2.65
3.	**60**	16.52 ± 2.34	15.96 ± 3.94	19.32 ± 3.25	22.56 ± 3.69
4.	**90**	18.92 ± 1.96	21.49 ± 4.18	22.67 ± 3.98	33.56 ± 4.56
5.	**120**	23.64 ± 2.11	28.70 ± 6.24	30.01 ± 6.89	39.56 ± 5.26
6.	**150**	30.35 ± 2.67	35.22 ± 4.72	36.95 ± 5.37	43.85 ± 6.25
7.	**180**	34.78 ± 1.28	42.69 ± 3.21	40.53 ± 6.00	51.45 ± 4.59
8.	**210**	39.36 ± 4.62	49.74 ± 5.18	48.14 ± 5.45	60.54 ± 5.85
9.	**240**	44.69 ± 5.36	58.28 ± 4.85	52.42 ± 6.21	66.75 ± 4.62
10.	**270**	58.74 ± 2.63	65.85 ± 6.25	59.45 ± 3.89	70.52 ± 5.21
11.	**300**	67.38 ± 1.96	76.07 ± 5.66	69.56 ± 5.26	78.15 ± 6.12
12.	**330**	79.36 ± 4.25	84.11 ± 3.36	78.25 ± 4.58	86.35 ± 6.43
13.	**360**	88.58 ± 7.27	91.23 ± 2.54	89.86 ± 7.56	95.42 ± 6.75

9. Stability study [4], [11]

When the optimized formulation was stored in various storage conditions, its physicochemical characteristics and drug content were found to remain stable.

FUTURE PROSPECTIVES [7], [1]

Emulgel addresses aquaphobic behaviour in pharmaceuticals, that combines gels and emulsions to achieve dual controlled release effects. Emulgel is a better choice for class II drugs, which have poor solubility and high permeability. according to the BCS classification systems, making it more effective and profitable. Emulgel is more efficient and profitable than other topical medication delivery technologies because of all these benefits. These characteristics will be applied in the future to transfer a wider variety of topical medications, like emulgel. Emulgel has several advantages over other topical drug delivery methods, all of which increase their efficacy and profitability.

Marketed formulations of emulgel [3], [1], [2]

Table 4: the preparations of emulgel that are market commercially are listed below in table

Brand name	Active ingredient	Manufacturer
Miconaz-H-Emulgel	Miconazole nitrate, hydrocortisone	Medical union pharmaceutical
Voltaren	Diclofenac-diethyl-ammonium	Novartis pharma
Excex gel	Clindamycin, adapalene	Zee laboratories
Lupigyl gel	Metronidazole, clindamycin	Lupin pharma

CONCLUSION [4], [1], [5], [8]

After thorough literature survey, we reached into a conclusion that emulgel is a novel approach that has been shown to be the most effective, convenient, and superior delivery method available. [1], [5] In comparison to traditional topical delivery systems, it provides excellent drug release and gel-like properties due to its non-greasy nature and lack of oily bases. [8] Emulgel is useful for delivering drugs to their intended location and has a high drug loading capacity. Because of its tiny particle size, a drug's skin penetration is effective. [4] Emulgel has a dual control release effect and is created by mixing emulsion into the gel base the emulsion's stability increases and other problem such as phase separation and creaming are resolved. [1]

Similarly in the study, topical emulgels containing curcumin were prepared and subjected to physicochemical analyses, i.e. rheological studies, spreading coefficient studies, Drug content determination and in vitro release studies. [4]

In vitro release of the tests formulations was carried out to determine drug release from emulgel rate and duration of drug release. According to the in vitro studies, formulation F4 had a maximum release of 95.42 in 360 min. [4]

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