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DEVELOPMENT AND ASSESSMENT OF AN EMULGEL FOR ANTI-INFLAMMATORY EFFECTS

Kunal Deore*[*1], Shivangni Rathore[2], Revathi A Gupta[3]

[1] Student, Institute of Pharmacy, Dr. APJ Abdul Kalam University, Indore (M.P.)
[2] Assist, Professor, Institute of Pharmacy, Dr. APJ Abdul Kalam University, Indore (M.P.)
[3] Principal, Institute of Pharmacy, Dr. APJ Abdul Kalam University, Indore (M.P.)

A B S T R A C T :

Emulgels have emerged as one of the most promising drug delivery methods for hydrophobic drugs in recent years. Emulgels have become popular in medicinal and cosmetic formulations. Emulgel is the term used to describe the combination of gel and emulsion. By mixing an emulsion with gelling chemicals, an emulgel can be created. Despite their many advantages, gels have serious disadvantages when it comes to the administration of hydrophobic medications. Therefore, the emulsion-based approach is being used to overcome this limitation. Emulgel's dual-release control release makes it an intriguing topical medication delivery device. such as emulsion and gel. The goal of this research project is to create a stable emulgel of the hydrophobic medication piperine for the treatment of inflammatory diseases. Since piperine, a BCS Class II medication, has a high permeability and low solubility, an emulgel was created to improve the drug's solubility while simultaneously guaranteeing patient compliance.

Creation of a better product than the one that is presently on the market, with improved penetration and, eventually, efficacy as compared to the marketed product. developing pharmaceutical formulations by utilising the Quality by Design (QbD) principle. The quality of the final pharmaceutical formulation is checked. Instead of evaluating the final formulation's quality, the QbD approach enables us to improve formulation quality and test formulation.

Keywords: Emulgel, , *in vitro* diffusion, quality by design, BCS class II medicine, Piperine, anti inflametry gel.

Introduction

As emulsions, emulgels may be defined as either an oil phase dispersed within a continuous aqueous phase or an aqueous phase dispersed within a continuous oil phase. When appropriate polymers are added, the mixture changes into a gel. Emulgels are thought to be a very useful method of administering hydrophobic medications. In essence, an emulgel blends the qualities of gels and emulsions. Two immiscible liquids combine to generate emulsions, which are dispersion systems in which one liquid is dissolved in the other. By nature, this biphasic system causes emulsions to be more unstable. The emulsion's stability is increased with the application of emulsifiers or surfactants. Emulsions typically consist of an oil phase, which may comprise various oils and/or waxes, and an aqueous phase, which may include water or solvents like propylene glycol, glycerin, and polymethylene glycol.

An oil-in-water (o/w) emulsion is created when oil droplets are uniformly dispersed throughout the aqueous phase. On the other hand, the distribution of the aqueous phase throughout the oil phase is what defines a water-in-oil (w/o) emulsion.

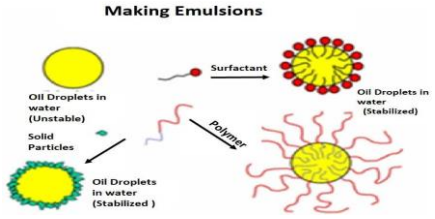

Figure 1 : Formation of emulsion

Theories of emulsification:

The function of emulsifying agents, sometimes known as surfactants, in producing physically stable emulsions is the subject of the emulsification hypothesis. The interface between the oil and aqueous phases is where this phenomena takes place. At this interface, surfactants play a critical role in determining the emulsion's stability. To explain how surfactants and emulsifiers behave while creating stable emulsions, a number of theories have

been put forth. However, not all theories apply to all emulsifiers or surfactants since the two phases' concentrations and the system's pH might affect how successful a certain hypothesis is. Some of the most well-known ideas of emulsions include the orientated wedge theory, surface tension theory, and interfacial film theory.

Surface tension theory

- The Oriented wedge theory
- The Interfacial film theory

Material and Methods

Apparatus and chemicals: Piperine by M/s Drug India Hydrabad., Trancutol P by Dr. Reddy's Laboratories, Hyderabad, Twin 20, Span 20, Isopropyl Alcohol by Ranchem Ltd.., India, Mineral oil by Loba Chemie, Mumbai.

Methods: Preparation of emulsion with RHLB emulsifier blend ratio

The emulsions were made for concentrations of 1%, 1.5%, and 2% using the emulsifier blend ratio that was previously acquired. The emulsions were then tested for stability, and one concentration was selected for the further batches of formulation.

Table 1 provided the compositions of every formulation.

Table 1: Preparation of emulsion

Ingredients	1%	1.50%	2%
Piperine	0.2	0.2	0.2
Transcutol P	5	5	5
Mineral oil	35	35	35
Isopropyle myristate	15	15	15
tween 20	0.7	1	1.4
Span 20	0.3	5	0.6
BHT	0.1	0.1	0.1
water	qs	qs	qs
Total weight	490	490	490

Table 2 Formulation batches containing Carbomer 980

Ingredients	C1	C2	C3	C4	C5	C6
Piperine	0.2	0.2	0.2	0.2	0.2	0.2
Transcutol P	5	5	5	5	5	5
Mineral oil	35	35	35	35	35	35
Isopropyle myristate	15	15	15	15	15	15
tween 20	0.7	1	1.4	0.7	1	1.4
Span 20	0.3	5	0.6	0.3	5	0.6
BHT	0.1	0.1	0.1	0.1	0.1	0.1
Carbopol	0.25	0.25	0.25	0.5	0.5	0.5
Sodium benzoate	0.15	0.15	0.15	0.15	0.15	0.15
water	qs	qs	qs	qs	qs	qs

Method:

- **Drug Phase:** The drug was dissolved in Transcutol P while being stirred until a clear solution formed.
- **Oil Phase:** BHT was slowly stirred while dissolving in isopropyl myristate. Span 80 and mineral oil were added while swirling slowly and thoroughly mixing. For ten minutes, the drug phase was introduced to the oil phase while being stirred.
- **Aqueous Phase:** Tween 20 and filtered water were combined, and Carbopol 980 was stirred while being distributed.

- **Emulsification:** After adding the aqueous phase to the oil phase, the mixture was homogenised for 30 minutes at a speed of 3000–4000 RPM.
  Sodium Benzoate was added after being dissolved in purified water. Following the addition of the resultant solution, the emulsified bulk was homogenised for 30 minutes at a speed of 3000–4000 RPM.

Experimental work

3.1 Preformulation Studies

The study of a medical ingredient's physical and chemical properties, both alone and in conjunction with excipients, is known as preformulation. Preformulation studies aim to identify the physicochemical properties and excipients that may affect the manufacturing process, formulation design, and pharmacokinetic-biopharmaceutical aspects of the final product.

3.2 Determination of Solubility

Solubility was tested in various media including ethanol, methanol, absolute ethanol, acetone, chloroform, ether, water, 10% v/v HCl and 10% w/v sodium hydroxide.

3*.3 UV and FTIR Spectroscopy*

The wavelength of maximum absorbance was then found by scanning the solution containing 10µg/ml between 200 and 400 nm.
The reference standard FT-IR spectra of piperine and the acquired FT-IR spectrum of piperine were compared.

1. Result and discussion

4.1 Preformulation Study

- **4.1.1 Description**
- Piperine is light yellow crystalline solid
- 4.1.2 Result of Solubility
- Insoluble in water, piperine is soluble in ethanol, diethylene glycol monoethyl ether, dimethyl sulfoxide, and chloroform.

4.2 Result of Melting Point

The medicine's melting point was determined to be comparable to the stated value, confirming that the drug samples that were received met the stated specifications. The melting point of a particular pharmacological ingredient will vary depending on any impurities that may be present. Curcumin has a reported melting point of 131°C. When the capillary technique was used to determine the medication's melting point, the substance began to melt at 128°C and melted fully at 130°C. The aforementioned test revealed that the sample medication satisfies the Piperine standard test.

4.3 UV Spectroscopy

A peak with an absorbance of 0.5650 was seen at 342 nm in a solution of 10µg/ml in methanol. The identity of the piperine molecule is confirmed by the absorbance maxima at 342 nm, which is one of its hallmarks.

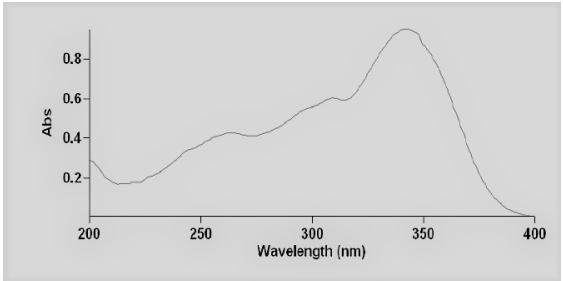

Fig 2. Lambda max determination of Piperine

4.3.1 FT-IR Spectroscopy

The drug's infrared spectrum was found to be comparable to piperine's normal infrared spectrum, indicating that the sample was pure. This validates the piperine identity.

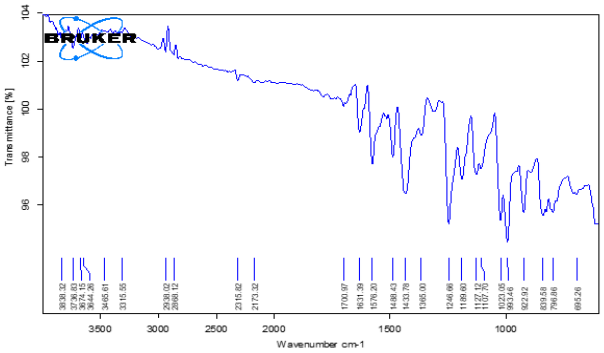

Fig 3. FT-IR of Piperine

4.4 Drug - Excipients Compatibility Study

FT-IR Spectroscopy

The drug and excipients were found to be compatible after FTIR analysis of the physical mixes of the drug and excipients in a 1:1 ratio that had been stored in vials for 24 hours.

When the IR spectra of piperine, excipients, and their combination are compared, all of the piperine's distinctive bands are discovered to be intact.

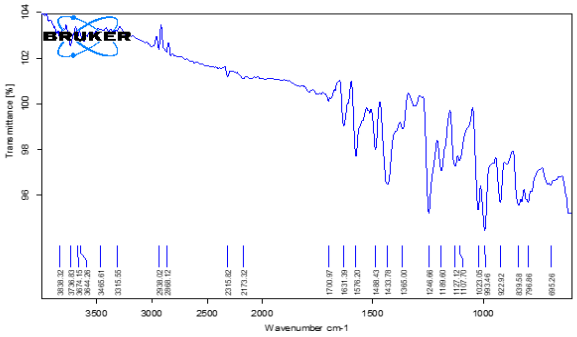

Figure 3 FT-IR Spectra of *Blend*

4.5 Evaluation of Emulgel

4.5.1 Physical Properties

Every formulation that was created had a white look. Oil and aqueous phases separated from one another in non-homogenous formulations C1, C4, H1, H2, H3, H4, H5, and H6. After a few days, formulas C1, C2, C3, C4, C5, H1, H2, H3, H4, H5, and H6 exhibit separation. Among these formulations, C6, S1, S2, S3, S4, S5, and S6, there is no indication of separation.

4.5.2 Rheological Studies

Viscosity in carbomer-based formulations is concentration dependent. The formulation becomes more viscous as the carbomer content rises. The viscosity also affects the formulation's physical stability. Phase separation and non-homogenous formulation can result from low viscosity.

When the formulation is physically stable, HPMC also exhibits concentration-dependent viscosity. As the concentration of HPMC Polymer in the formulations increases, so does their viscosity.

Formulations S1 through S6 also demonstrate the concentration-dependent viscosity of the Polymer Sepineo P600 while the emulsifier concentration remains constant.

4.5.3 pH

It was discovered that all of the formulations had pH values between 4.2 and 6.4. It was determined that the pH range was suitable for preventing skin irritation. Skin irritation may result from formulations with higher or lower pH values.

4.5.4 Spreadability by Texture analyzer

The extent to which the final mixture spreads when applied topically to the skin or other body parts that are impacted. The formulation's medicinal effectiveness is impacted by its spreadability. The formulation's rheological characteristics have a direct impact on its spreadability. The formulation's viscosity, which in turn influences its spreadability, is directly impacted by the gelling agent concentration.

The formulation's firmness value has varied between 30.12 and 41.23 g. The formulation's spreadability will decrease as its hardness value increases. The polymer has demonstrated a concentration-dependent impact on the formulation's hardness or spreadability.

4.5.**5 Extrudability**

Extrudability is good for formulations C1, C5, H1, H6, and S4, and outstanding for formulations C2, C3, C6, S3, S5, and S6. Excellent extrudability shows how easily emulgel may be applied and withdrawn from the tube. The degree to which a semisolid formulation is extruded out of the tube is determined by its extrudability. The consistency and viscosity of the formulation determine the extrudability. The degree of extrusion of the formulation increases with decreasing viscosity.

4.5.**6 Drug Content Determination**

All of the piperine formulations' % drug content was calculated, and the results are shown in the table above. The range of the drug content was 96.2 to 9.9%. The robust procedure of adding and mixing the medication in bulk may be the reason why the drug content in each formulation is almost the same.

4.5.7 **In-vitro release of study**

Table 3 displays the emulgel formulations' cumulative drug release percentage, which is visually shown in picture 3.

At the conclusion of eight hours, the total drug release percentage for all created emulgel formulations varied from 85.16 to 97.87%. After eight hours, the formulations C6 and S2 showed the highest drug release. Formulation C6 exhibits a greater drug release from the formulation because of a lower gelling agent concentration and a more uniform formulation with improved penetration thanks to a penetration enhancer. Because Formulation S2 has more penetration enhancers and less gelling agent, it provides a greater drug release.

Table 3: Evaluation of Emulgel

S. No.	Batch no.	Discription	Homogeinity	Phase seperation	viscocity Ps	pH	Spreadability	Extrudability	Drug Content
1	C1	White smooth non uniform emulgel	No	Yes	1.22	4.52	30.56	++	97.2
2	C2	White smooth non uniform emulgel	Yes	Yes	2.01	4.6	31.05	+++	96.7
3	C3	White smooth uniform emulgel	Yes	Yes	1.74	4.65	30.44	+++	98.8
4	C4	White smooth non uniform emulgel	No	Yes	1.89	4.27	33.24	+	99.1
5	C5	White smooth non uniform emulgel	Yes	Yes	1.65	4.32	31.85	++	98.9
6	C6	White smooth uniform emulgel	Yes	No	1.88	4.4	36.88	+++	99.2
7	H1	White smooth non uniform emulgel	No	Yes	1.52	5.6	30.12	+	96.2
8	H2	White smooth non uniform emulgel	No	Yes	1.68	5.5	30.56	+	97.2
9	H3	White smooth uniform emulgel	No	Yes	1.72	5.2	31.06	++	96.2
10	H4	White smooth uniform emulgel	No	Yes	1.48	5.5	32.64	+	96.8
11	H5	White smooth non uniform emulgel	No	Yes	1.46	5.1	33.56	+	97.2
12	H6	White smooth uniform emulgel	No	Yes	1.52	5.2	34.78	++	98.3
13	S1	White smooth uniform emulgel	Yes	No	4.52	5.3	41.23	+	99.5
14	S2	White smooth uniform emulgel	Yes	No	3.88	5.2	39.66	++	99.9
15	S3	White smooth uniform emulgel	Yes	No	2.22	5.5	39.45	+++	99.7
16	S4	White smooth uniform emulgel	Yes	No	3.31	5.8	39.23	++	98.9
17	S5	White smooth uniform emulgel	Yes	No	1.88	6.2	38.45	+++	99.9
18	S6	White smooth uniform emulgel	Yes	No	2.42	6.4	38.33	+++	98.9

In-Vitro Drug release study of selected formulation of emulgel

Table 4: In-Vitro Drug release study of selected formulation of emulgel

Time(hr)	Selected Formulations								
	C4	C6	H5	S1	S2	S3	S4	S5	S6
15min	17.45	20.12	16.56	18.35	22.12	21.16	16.54	23.32	22.06
30min	24.12	27.94	21.22	22.46	29.45	29.54	21.16	28.24	27.81
45min	41.56	32.44	26.79	27.56	33.56	33.54	26.42	34.12	34.51
1hr	45.88	55.23	31.44	33.34	56.77	42.85	32.34	46.64	39.91
2hr	66.11	67.84	37.68	41.12	69.48	51.15	39.48	59.24	44.67
3hr	69.24	75.36	42.56	47.23	76.63	67.76	48.53	65.32	48.06
4hr	71.25	79.41	51.75	55.47	82.14	74.95	56.27	75.27	55.41
5hr	79.56	86.24	59.35	63.36	89.42	85.46	63.38	79.02	61.37
6hr	82.33	91.43	71.22	70.25	93.43	92.34	74.23	83.58	65.52
7hr	85.12	96.24	76.28	78.56	97.42	95.23	79.25	89.37	70.54

4.6 Stability Studies of best formulation C6

Table 5: Stability study of selected formulation of emulgel

Stability study of optimized batch C6 for 1 month			
Parameters	25°C /RH 60%	30°C/ RH 65%	40°C/ RH 75%
Colour& appearance	White smooth Cream	White smooth Cream	White smooth Cream
Homogeneity	Good	Good	Good
Phase Separation	No	No	No
pH	4.44	4.56	4.52
Spreadability(g/s)	36.88	37.11	37.22
Extrudability	+++	+++	+++
Viscosity	1.88	1.92	2.1
Drug content (%)	99.2	99.04	98.98
In-vitro release (%)	96.89	96.56	96.12

Conclusion

An effort was made in this work to create an Emulgel formulation of piperine for topical administration. It may be inferred from the experimental results that: They were compatible since there was no contact between the polymer and the medication, according to the physical stability research and infrared spectra of piperine and piperine and excipient combinations. The HLB technique was used to produce the emulsion for the combination of two emulsifiers, and its stability was assessed. Emulgel is made using polymers such carbomer, hydroxypropyl methyl cellulose, and Sepineo P 600.

The Emulgel formulations satisfy the requirements for assessment criteria such in-vitro release studies, drug content determination, rheological characteristics, spreadability, extrudability, and physical qualities. The formulation emulgel C6 and S2 had the highest drug release, according to results from in-vitro release experiments. After three months of stability testing at 25°C± 2°C/60% RH± 5% RH, 30°C± 2°C/65% RH± 5% RH, and 40°C± 2°C/75% RH± 5% RH, it was determined that there was no discernible difference between optimised batches C6 and S2.

In order to improve patient compliance, piperine was shown to be a good option for creating an emulgel for topical administration.

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