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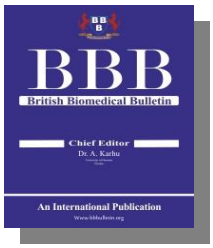

Original

Emulgel: A no Refuseable Formulation to Improve Solubility, Penetration and Percentage of Aceclofenac Release for Suppressing Prostaglandins E_2 Synthesis

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A R T I C L E I N F O

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A B S T R A C T

Aim and Objective: Formulation, development and evaluation of Aceclofenac emulgel.
Method: simple way aceclofenac dissolve in oil base then add this oil base into previously prepared gel lead to provide aceclofenac emulgel.
Result and Discussion: Aceclofenac have better therapeutic action than diclofenac diethyl amine but is water insoluble. While ointment and gel like formulations are not preferred by patient as have greasiness, less effective, less shelf-life etc. To overcome these problems aceclofenac emulgel was formulated which improves solubility, permeability and finely bioavailability of aceclofenac which render it more use as topically as analgesic than diclofenac diethyl amine. This research was shown by researchers in terms of various parameters in this article.

Introduction

Aceclofenac is NSAID used for the treatment of rheumatoid arthritis and osteoarthritis which reduces levels of prostaglandin E_2 in the synovial fluid and suppresses its production by blood polymorph nuclear leukocytes or mononuclear cells. Oral administration of aceclofenac causes gastrointestinal ulcers and gastrointestinal bleeding with chronic use. Topical use may reduce these side effects.[1] Topical preparation was used for the localized effect at the site of their application by virtue of drug penetration into the underlying layer of skin or mucous membrane.[2,3] Within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can enjoy the unique properties of gels. When gels and emulsions are used in combined form the dosage forms are referred as Emulgel.[4] As the name suggest they are the combination of emulsion and gel. In recent years, there has been great interest in the use of novel polymers with complex functions as emulsifiers and thickeners because the gelling capacity of these compounds allows the formulation of stable emulsions and creams by decreasing surface and interfacial tension and at the same time increasing the viscosity of the aqueous phase. In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Emulgel for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water-soluble, longer shelf life, bio-friendly, transparent & pleasing appearance.[5] Aceclofenac is the NSAID used as pain remover. It is the hydrophobic moiety so emulgel formulation is well suited for such drug. Emulgel can be easily washable with better Spreadability so it is more advantageous then conventional ointment, gel or paste.[6]

Some advantages of emulgel are as follow:

- Avoidance of first pass metabolism.
- Medication can be self-applied.
- Improve patient compliance.
- Medication can be terminated when needed.
- Suitable for drug with short half-life and potent drug.
- Site specific drug delivery.[7]

There are some disadvantages of emulgel which are as follow: Drug of large particle size not easy to absorb through the skin. Poor permeability of some drugs through skin. Skin irritation or allergic reaction on contact dermatitis. Occurrence of bubble during formation of emulgel. So many formulations is applied to the skin or mucous membrane that either improves or repairs a fundamental function of skin or pharmacologically alters an action in the underlined tissues. Such products are referred as topical or dermatological products. Many widely used topical agents like ointments, creams lotions have many Disadvantages. They have very sticky causing uneasiness to the patient when applied. Moreover they also have lesser spreading coefficient and need to apply with rubbing And they exhibit the problem of stability also. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has Expanded both in cosmetics and in pharmaceutical preparations. A gel is colloid that is typically 99% wt. liquid, which is immobilized by surface tension between it and a macromolecular

network of fibers built from a small amount of a gelatin substance present. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels.[8,9]

Material and Method

Material

Aceclofenac was purchased from ACS laboratory, Ahmedabad, Gujarat, India. Carbomer 934 P was purchased from S.D. Fine, Chemical ltd, Mumbai, India. Methyl salicylate and liquid paraffin were purchased from suvidhinath Lab. Mumbai, India. Tween-80 was purchased from molychem lab, Mumbai, India.

Method

1. Preparation of gel (See table 1.)
2. Preparation of oil phase (See table 2.)
3. Preparation of aqueous phase (See table 3.)

Preparation of emulgel

Weigh accurately Carbomer 934P, soaked into sufficient water, and made the gel by adding tri ethanol amine in a beaker. Then, mix tween-80, PEG 400, water, and drug as an aqueous phase and made oil phase by mixing liq. Paraffin and methyl salicylate. Stir both the phase separately for a few minute. Then add oily phase into aqueous phase, so the emulsion is formed. Add this emulsion slowly into the previously formed Carbomer 934P gel with continuously stirring. Stir until homogeneous mass of emulgel was formed. Fill in to the glass jar or collapsible tube.[10]

Characterization of emulgel

Drug content analysis

Accurately weighted 1 gm of emulgel was dissolved in iso propyl alcohol, after appropriate dilution Aceclofenac content was analyzed by spectrophoto-metrically at wavelength 275 nm (shimadzu, UV 1700, japan).[11]

In-vitro drug release

USP apparatus type-II was used for *in vitro* release study. In this study, activated gelatin paper was used as semipermeable membrane. Accurately weighted 1 gm of emulgel was placed in semipermeable membrane, then adds 5 ml of phosphate buffer in it, cover with thread and put in USP apparatus. Cover it with wire helix which sinks the membrane. Phosphate buffer pH 6.8 was used as dissolution medium. Withdraw 5 ml at 15, 30, 45, 60, 120, 240, 360 and 480 min. at regular time interval and measure the UV absorbance at wavelength 274 nm.[12]

Physical appearance

The prepared emulsified gel formulations containing Aceclofenac were inspected visually for their color, homogeneity, consistency and phase separation.

Measurement of pH

The pH of various emulsified gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml Distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values are calculated.

Rheological study

The viscosity of different emulsified gel formulation was determined

at 37 ^{0} C using a brook field viscometer with spindle 6.

Fitting of results into different kinetic equation

The results of *in vitro* release profile obtained for all the formulations were plotted in models of data treatment as follows:-

- Zero - order kinetic model - % CPR Vs. time.
- First - order kinetic model - Log cumulative percent drug remaining Vs. time.
- Higuchi's model- cumulative percent drug released vs. square root of time.
- Korsmeyer / peppa's model - Log cumulative percent drug released Vs. log time
- Hixon crowel model - Cube root of % drug to be remaining Vs. Time in minute.[13]

Result and Discussion

Emulgel was prepared by taking the Aceclofenac as a model drug. When all the formulations were subjected to physical examination, the gels appeared to be translucent suggesting that the drug was completely solubilized rather dispersed/ suspended in the gel matrix. Effect of Carbomer 934P conc. was studied. Total three formulations were prepared subjected to viscosity measurement. Conc. 1.5 % was found to be optimum for its easy Spreadability, Washability as well. In 2 % conc. Too much viscosity was found so it is not easily spreadable. In 1 % conc. Viscosity is very low, so it is not applicable. *In vitro* drug release study was found to be optimum in F2 batch. Drug release was found 88 % after four hour release study. Various model for kinetic study was applied to *in vitro* release data. First order kinetic model found to be minimum value of Some of Square of Residue (SSR). Polyethylene glycol 400 was used as water soluble base, which make the Emulgel easily washable. Tween-80 used as surfactant which makes the emulsion with drug entrapment in emulsion. Various models have been studied for SSR. Aceclofenac emulgel formulation follow first order kinetics model.

Standard curve for aceclofenac

See figure 1.

First order kinetic model plot

Log % drug to be remaining vs. time (min). (See figure 2.)

Conclusion

Thus in case of gout or rheumatic pain instead of aceclofenac tablet oral or topical liniment, gel or solution, Aceclofenac emulgel provide better pain killer effect for sustained period of time. From the experiment it can be concluded that the present study on the drug Aceclofenac was carried out to optimize the concentration of Carbomer 934P which shows good rheological, *in vitro* drug release and Spreadability as well at the conc. 1.5 %. Above and below this concentration drug released was affected as rheological properties where affected.

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Table 1. Formulation of gel

Ingredient	F1	F2	F3
Water	22 ml	22 ml	22 ml
Carbomer	1%,	1.5 %	2 %
TEA	q.s	q.s	q.s

Table 2. Formulation of oil phase

Liquid paraffin	7 ml
Methyl salicylate	8 ml

Table 3. Formulation of aqueous phase

Tween-80	5 ml
PEG 400	2.5 ml
Drug	1 %
Water	15

Table 4. Evaluation of emulgel

Parameter	F1	F2	F3
PH	7-8	7-8	7-8
Irritation	No irritation	No irritation	No irritation
Washability	Easily washable	Easily washable	Easily washable
Appearance	Off white	Off white	Off white
Viscosity	70 poise	90 poise	136 poise
	Low	Medium	High

Table 5. Kinetic model fitting in emulgel

Model name	Some of square of residue value
Zero order model	329.82
First order model	0.0048
Higuchi model	3.319
Korsmayer peppas model	3.5396
Hixon crowell model	0.075

Table 6. Data of standard curve of aceclofenac

Concentration (µ/ml)	Absorbance
0	0
5	0.129
10	0.262
15	0.377
20	0.5
25	0.687
30	0.747

Table 7. *In vitro* release data of optimized batch

TIME (min)	Absorbance	conc. (mcg\ml)	mcg\500 ml	mg\500 ml	mg \5 ml	cum/5 ml	actual release	% CPR
15	0.228	9.08	4540	4.54	0.0454	0.0454	4.5854	22.93
30	0.343	13.68	6840	6.84	0.0684	0.1138	6.9538	34.77
45	0.5	19.96	9980	9.98	0.0998	0.2136	10.1936	50.97
60	0.503	20.08	10040	10.04	0.1004	0.314	10.354	51.77
120	0.666	26.6	13300	13.3	0.133	0.447	13.747	68.74
180	0.8	31.6	15800	15.8	0.158	0.605	16.405	82.03
240	0.85	33.96	16980	16.98	0.1698	0.7748	17.7548	88.77

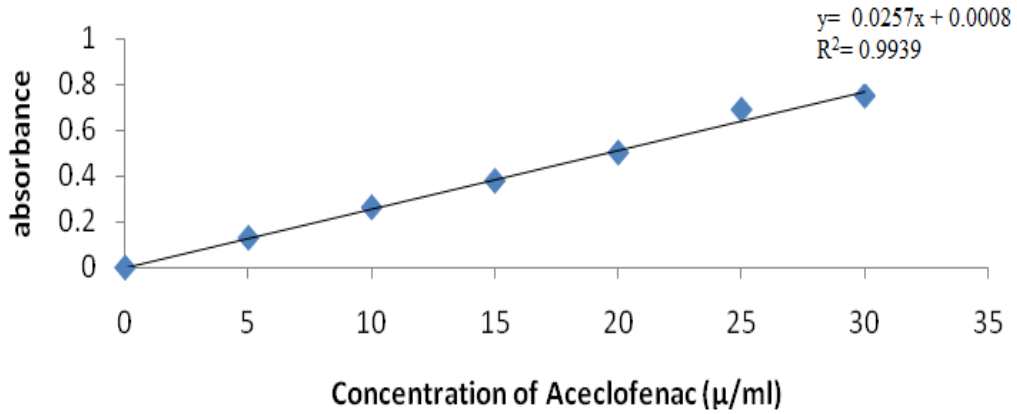

Figure 1. Standard curve of aceclofenac

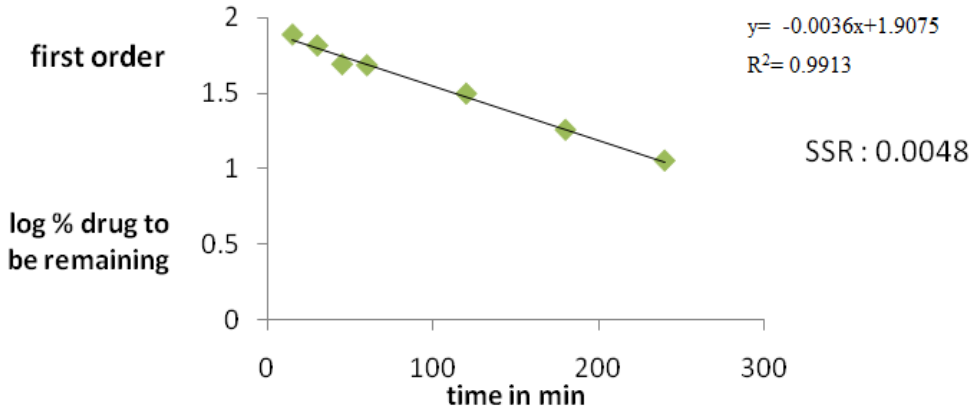

Figure 2. Oder kinetic plot of emulgel

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