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Formulation and Development of Diclofenac Topical Emulgels

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ABSTRACT:

Introduction: Topical drug delivery system has been the most appropriate and convenient approach over the past two decades. Many conventional semisolid dosage forms such as creams, gels, and lotions found to have problems such as sticky in nature, lesser spreading coefficient, and stability issues.[1] To overcome such issues, a novel, stable topical drug delivery approach can be used to formulate successful drug delivery for hydrophobic drugs. In recent years, the concept of emulgel has gained significant interest in the topical drug delivery system.[2] An emulgel is a combination of emulsion and gel system, which is formulated by mixing emulsion either o/w or w/o with a gelling agent.[3] Emulgel provides several benefits such as better loading capacity, stability, controlled release, improved patient compliance, avoids first pass metabolism, and gastric complications.[4,5] In the present investigation, a model anti-inflammatory drug

Objectives: The present research work was aimed to develop a novel emulgel for Diclofenac to enhance the drug absorption by the topical application, which overcomes the demerits of oral dosage form and conventional gel system of Diclofenac.

Methods: Methodology Preparation of Diclofenac emulgel The gel phase and emulsion phase were prepared separately. First, the gel phase was prepared by dispersing the different concentrations of carbopol 934 in distilled water and mixed by a mechanical stirrer. The emulsion phases were prepared by the addition of varying amounts of span 20 in varying quantities of liquid paraffin followed by mechanical stirring. The aqueous phase of emulgel was prepared by incorporating tween 20 in distilled water with continuous stirring, then methyl and propylparaben were added in propylene glycol, and Diclofenac (0.5 g) was dissolved in ethanol, and both the solutions were mixed with water phase of the emulsion. Both the water and oil phases were heated at 70–80°C for 20 min. Later, the oily phase was added to the aqueous phase by gentle stirring and allowed to cool. Finally, the prepared emulsion was mixed with gel base in a 1:1 ratio by manual stirring to get a clear emulgel of Diclofenac.

Results: All the Diclofenac emulgels formulations were found to be homogenous and showed no clogging and lumps which indicate good texture of system. All formulation batches were found to be homogenous yellowish milky emulsions previously while emulgels were found to be whitish viscous creamy preparation. The pH of all the formulations was ranging in between 6.1-6.5 which is comparable to the human skin pH which is around. Emulgel is considered to be good if it takes minimum time to spread on the surface. Among the various gels studied F3 emulgel has better spreadability. The values of spreadability indicate that the gel is easily spreadable by small amount of shear.

Conclusions: In this study emulgels were prepared by using two different gel forming polymers in which the gel formulation with Carbomer 934 showed better clarity and stability for longer period of time. In the study it was observed that the concentration of tween80 and linseed oil have shown effect on viscosity, spreadability and in-vitro drug permeability.In terms of pH the observed

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value of all the formulations were comparable to human skin pH. All the formulation were found to be easily spreadable. In drug permeation study and drug release data showed that F6 formulation showed better drug release data compared to other formulations. So it is considered as the optimized batch. Hence, Diclofenac emulgel was successfully prepared and evaluated.

1. Introduction

Topical drug delivery system has been the most appropriate and convenient approach over the past two decades. Many conventional semisolid dosage forms such as creams, gels, and lotions found to have problems such as sticky in nature, lesser spreading coefficient, and stability issues.[1] To overcome such issues, a novel, stable topical drug delivery approach can be used to formulate successful drug delivery for hydrophobic drugs. In recent years, the concept of emulgel has gained significant interest in the topical drug delivery system.[2] An emulgel is a combination of emulsion and gel system, which is formulated by mixing emulsion either o/w or w/o with a gelling agent.[3] Emulgel provides several benefits such as better loading capacity, stability, controlled release, improved patient compliance, avoids first pass metabolism, and gastric complications.[4,5] In the present investigation, a model anti-inflammatory drug Diclofenac was chosen since its oral dosage form has demerits such as first pass metabolism, gastric ulcerogenic effects, and metabolic degradation.[6] Diclofenac even though available in conventional gel form since it is a hydrophobic drug formulating it in emulgel makes it more fruitful way to deliver through the skin. .[7] Percutaneous absorption of drugs from topical formulation involves the release of the drug from the formulation and permeation through skin to reach the target tissue. The release of the drug from topical preparations depends on the physicochemical properties of the vehicle and the drug employed. In order to enhance drug and skin permeation, methods such as the selection of suitable vehicle, co-administration of a chemical enhancer have been studied. Use of topical agents requires an appreciation of the factors that influence percutaneous absorption. Molecules can penetrate the skin by three routes, through intact stratum corneum, through sweat glands, or through the sebaceous follicle. The surface of the stratum corneum presents more than 99% of the total skin surface available for percutaneous drug absorption1. Passage through this outermost layer is the rate –limiting step for percutaneous absorption. The major steps involved in percutaneous absorption include the establishment of a concentration gradient ,which provides the driving force for drug movement a across the skin ,release of drug from the vehicle (penetration co-efficient);and drug diffusion across the layers of the skin(diffusion co-efficient).preferable characteristic of topical drugs include low molecular mass (600 Daltons),with adequate solubility in oil & water ,and have high partition co-efficient for the topical formulation. Gels are a relatively newer class of dosage form created by entrapment of large amounts of aqueous or hydro alcoholic liquid in a network of colloidal solid particles.gel formulations generally provide faster drug release compared with ointments and creams. Major drawback of topical dosage form diffusion of drug in the delivery of hydrophobic drugs, and permeation through stratum corneum is for hydrophilic drugs. Therefore, to overcome this limitation emulgels are prepared.

2. Objectives

Aim: The present research work was aimed to develop a novel emulgel for Diclofenac to enhance the drug absorption by the topical application, which overcomes the demerits of oral dosage form and conventional gel system of Diclofenac.

3. Methods

Methodology Preparation of Diclofenac emulgel The gel phase and emulsion phase were prepared separately. First, the gel phase was prepared by dispersing the different concentrations of carbopol 934 in distilled water and mixed by a mechanical stirrer. The emulsion phases were prepared by the addition of varying amounts of span 20 in varying quantities of liquid paraffin followed by mechanical stirring. The aqueous phase of emulgel was prepared by incorporating tween 20 in distilled water with continuous stirring, then methyl and propylparaben were added in propylene glycol, and Diclofenac (0.5 g) was dissolved in ethanol, and both the solutions were mixed with water phase of the emulsion. Both the water and oil phases were heated at 70–80°C for 20 min. Later, the oily phase was added to the aqueous

Journal of Chemical Health Risks

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phase by gentle stirring and allowed to cool. Finally, the prepared emulsion was mixed with gel base in a 1:1 ratio by manual stirring to get a clear emulgel of Diclofenac. The pH of all the prepared emulgels was adjusted by dropwise addition of Triethanolamine.[8-10] A quantity of 100 g of Diclofenac was prepared for all the six formulations and the formulation composition of Diclofenac emulgels is shown in Table . Evaluation of emulgels Drug-polymer compatibility by Fourier transforms infrared (FTIR) study This study was carried out by FTIR spectroscopy to verify whether the drug and polymer are compatible with one another or not. It was evaluated by obtaining the IR spectral data of Diclofenac and physical mixture of Diclofenac with carbopol 934 using ATR-Bruker FTIR spectrophotometer. The interaction study was concluded from the interpretation of IR spectra.

4. Results

The gel section and emulsion section had been prepared one by one. First, the gel section turned into prepared by means of dispersing the one-of-a-kind concentrations of carbopol 934 in distilled water and mixed by a mechanical stirrer. The emulsion stages were prepared by using the addition of various amounts of span 20 in various quantities of liquid paraffin followed by mechanical stirring. The aqueous segment of emulgel was organized by incorporating tween 20 in distilled water with non-stop stirring, then methyl and propylparaben have been introduced in propylene glycol, and Diclofenac (0.five g) become dissolved in ethanol, and both the solutions had been blended with water section of the emulsion. each the water and oil phases had been heated at 70–80°C for 20 min. Later, the oily section become introduced to the aqueous segment by means of gentle stirring and allowed to chill. finally, the prepared emulsion was mixed with gel base in a 1:1 ratio by means of guide stirring to get a clean emulgel of Diclofenac. The pH of all the prepared emulgels became adjusted by using dropwise addition of Triethanolamine.[8-10] A quantity of one hundred g of Diclofenac become prepared for all the six formulations and the formulation composition of Diclofenac emulgels is proven in desk.

evaluation of emulgels Drug-polymer compatibility by means of Fourier transforms infrared (FTIR) take a look at This take a look at turned into achieved through FTIR spectroscopy to affirm whether or not the drug and polymer are compatible with each other or not. It changed into evaluated by obtaining the IR spectral information of Diclofenac and physical mixture of Diclofenac with carbopol 934 using ATR-Bruker FTIR spectrophotometer. The interplay examine became concluded from the translation of IR spectra.

Appearance :

All the formulated Diclofenac emulgels were visually inspected for color, clarity, and homogeneity.

Ph:

The pH of all the formulated emulgels was measured by digital pH meter.

Rheological study :

The viscosity of the emulgels was measured by Brookfield viscometer with “T” bar spindle at 5 rpm at a temperature of 25±2°C and the viscosity was recorded in cps.

Spreadability:

An ideal topical gel should possess a sufficient spreading coefficient when applied or rubbed on the skin surface. This was evaluated by placing about 1 g of formulation on a glass slide. Another glass slide of the same length was placed above that, and a mass of 500 g was put on the glass slide so that the gel gets sandwiched between the two glass slides and spreads at a certain distance.[15] The time taken for the gel to travel the distance from the place of its position was noted down. Spreadability was determined by the following formula.

Where, S-Spreadability, g.cm/s
M-Weight put on the upper glass
L-Length of glass slide
T-Time for spreading gel in sec

Swelling index :

It was measured by placing 1 g of formulation in a porous aluminum foil and was placed in a 50 ml beaker containing 10 ml of 0.1 N sodium hydroxide. The samples were removed from beakers at different time intervals and put on the dry place for some time and reweighed.The swelling index of emulgels was calculated using the following formula. .

5. Discussion

The future of pharmaceutical products will be rush up with topical delivery products because of drawbacks in oral, parenteral and other routes and more patient

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compliance.Loading of hydrophobic drug in hydrophilic gel matrix was found a solution by emulgel. Emulgel possess excellent bioadhesion, viscosity and long term stability which will increase compliance. In this study emulgels were prepared by using two differentGel forming polymers in which the gel formulation with Carbomer 934 showed better clarity and stability for longer period of time.

Ingredients	**Formulation code**					
	AG-1	**AG-2**	**AG-3**	**AG-4**	**AG-5**	**AG-6**
Diclofenac	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g	0.5 g
Carbopol 934	0.50%	1%	1.50%	2%	2.50%	3%
Liquid Paraffin	5 ml	5 ml	8 ml	8 ml	10 ml	10 ml
Span 20	0.20%	0.50%	0.20%	0.50%	0.20%	0.50%
Tween 20	0.20%	0.50%	0.20%	0.50%	0.20%	0.50%
Methylparaben	0.20%	0.20%	0.20%	0.20%	0.20%	0.20%
Propylparaben	0.20%	0.20%	0.20%	0.20%	0.20%	0.20%
Ethanol	5 ml	5 ml	5 ml	5 ml	5 ml	5 ml
Distilled water	q.s	q.s	q.s	q.s	q.s	q.s
Triethanolamine	q.s to adjust pH	q.s to adjust pH	q.s to adjust pH	q.s to adjust pH	q.s to adjust pH	q.s to adjust Ph

Table 1: Formulation design of Diclofenac emulgels

Swelling index (SW) % = [(Wt-Wo)]/Wo × 100
Where, (SW) % = Equilibrium percent swelling
Wt = Weight of swollen emulgel after time t,
Wo = Weight of emulgel before swelling at zero time, t.

Table 2: pH of the formulations

Formulations	**Ph**			**Mean(n=3)**
F1	6.3	6.5	6.0	6.2
F2	6.7	6.1	6.4	6.4
F3	6.1	6.3	5.9	6.1
F4	6.5	5.9	6.2	6.2
F5	6.4	6.7	6.1	6.4
F6	6.8	6.3	6.4	6.5
F7	6.6	6.1	6.3	6.3
F8	6.6	6.0	6.4	6.2

Journal of Chemical Health Risks

www.jchr.org

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Table 3: Spreadability of the Formulations

Formulations	Time (sec.)		Mean(n=3)	
F1	12	13	15	13
F2	14	12	11	12
F3	10	11	13	11
F4	11	13	12	12
F5	16	14	15	15
F6	15	17	13	15
F7	13	16	15	14
F8	18	16	15	16

Table 4: Extrudability study of formulations

Formulations	Time (sec.)		Mean(n=3)	
F1	14	18	17	16
F2	13	15	16	14
F3	13	12	15	13
F4	18	16	19	17
F5	15	19	18	17
F6	16	20	19	18
F7	18	17	21	18
F8	16	15	19	16

Table 5: Rheological study of formulations

Formulations	Viscosity (cPs)		Mean(n=3)	
F1	1252	1089	1467	1269
F2	1029	1287	1445	1253
F3	955	1189	1076	1073
F4	1023	1187	1654	1288
F5	1286	1837	1342	1488
F6	1314	1764	1456	1511
F7	1048	1421	983	1150
F8	1363	1678	1710	1583

Table 6: % Drug diffusion of formulations

Formulations	% Drug diffusion
F1	94.3
F2	87.6
F3	96.9
F4	93.3
F5	97.4
F6	98.5

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 2274-2280 | ISSN:2251-6727

F7	95.1
F8	91.3

Table 7: Drug release kinetics of different formulations

Time (hrs.)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	5.17	4.1	5.56	5.76	3.94	8.8	4.1	5.18
2	12.02	7.25	13.61	7.51	6.15	16.51	7.25	7.93
3	16.54	10.93	21.25	11.05	9.37	29.72	10.93	12.45
4	25.16	12.28	32.13	16.54	11.2	38.64	12.28	17.62
5	33.47	23.68	39.58	25.93	22.46	47.38	23.68	26.01
6	41.31	28.41	46.4	30.24	25.34	55.13	28.41	32.85
7	49.67	33.06	51.79	38.85	29.81	63.02	33.06	42.65
8	58.46	37.12	62.83	40.69	34.65	70.61	37.12	46.42
9	60.02	42.62	68.32	45.65	40.65	83.45	42.62	49.83
10	68.32	49.53	74.82	52.25	46.74	77.54	49.53	52.64
11	74.6	53.62	81.25	55.48	50.15	90.05	53.62	57.45
12	76.77	60.31	89.53	63.42	58.09	98.86	60.31	62.06

Conclusion:

In this study emulgels were prepared by using two different gel forming polymers in which the gel formulation with Carbomer 934 showed better clarity and stability for longer period of time. In the study it was observed that the concentration of tween80 and linseed oil have shown effect on viscosity, spreadability and in-vitro drug permeability.In terms of pH the observed value of all the formulations were comparable to human skin pH. All the formulation were found to be easily spreadable. In drug permeation study and drug release data showed that F6 formulation showed better drug release data compared to other formulations. So it is considered as the optimized batch. Hence, Diclofenac emulgel was successfully prepared and evaluated.

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