RESEARCH ARTICLE

Design and Development of Emulgel Preparation Containing Diclofenac Potassium

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Abstract

Aim: This study aims to explore the potential of emulgel in enhancing the topical delivery of diclofenac potassium. **Materials and Methods:** Emulgel formulations of diclofenac potassium were prepared using different concentrations of gelling agent's Carbopol-940. Tween-20 and span-20 were used as emulsifiers, and propylene glycol as a humectant in gel was selected for the preparation of emulgel. The effect of concentration of gelling agent on the drug release from the prepared emulgel was investigated. The compatibility study was conducted using fourier-transform infrared (FTIR) and differential scanning calorimetry (DSC). The formulated emulgel was characterized for their physical appearance, pH determination, viscosity, spreadability, swelling index, drug content, skin irritation test, microbial test, and *in vitro* diffusion study. **Result and Discussion:** FTIR and DSC study proved that the drug and excipients are compatible with each other. All the prepared formulations showed acceptable physical properties, homogeneity, consistency, spreadability, viscosity, and pH value. After 6 h of drug diffusion study, the formulation EG4 showed consistent release of the drug form emulgel with 89.72%. It might be due to the higher concentration of the emulsifying agents and the 2% concentration of the gelling agent. **Conclusion:** The study was concluded that the preparation was more stable than single emulsion and also improved desired properties for transdermal application. The emulgel preparation is the best choice for the water-insoluble drug.

Key words: Diclofenac potassium, emulgel, permeability, poorly water-soluble drug, topical drug delivery system

INTRODUCTION

The main advantage of topical delivery systems is to bypass first-pass metabolism. Avoidance of the risks and inconvenience of intravenous therapy and of the varied conditions of absorption such as pH changes, presence of enzymes, and gastric emptying time is other advantages of topical preparations. These are applying a wide spectrum of preparations for both cosmetic and dermatological, to their healthy or diseased skin. Dermatological products are diverse in formulation and range in consistency from liquid to powder, but the most popular products are semisolid preparation.[1,2] In spite of many advantages of gels, a major limitation is their inability to the delivery of hydrophobic drugs. To overcome this problem, an emulsion based approach is being used so that a hydrophobic therapeutic moiety can be fruitfully incorporated and delivered through gels. When gels and emulsions are used in united form, the dosage forms are referred as emulgels.[3] Emulgel is emulsions, either of the oil-in-water or water-in-oil type, which is gelled by mixing with a gelling agent. Both oil-in-water and water-in-oil emulsions are extensively used for their therapeutic properties and as vehicles to deliver various drugs to the skin.[4] Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin. In addition, the formulator can control the viscosity, appearance, and degree of greasiness of cosmetic or dermatological emulsions. Oil-in-water emulsions are most useful as water-washable drug bases and for general cosmetic purposes, while water-in-oil emulsions are most useful as water-washable drug

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bases and for general cosmetic purposes, while water-in-oil emulsions are employed more widely for the treatment of dry skin and emollient applications.[5-8] Diclofenac potassium is used to relieve pain and swelling or inflammation from various mild-to-moderate painful conditions. It is responsible for the anti-inflammatory, analgesic, and antipyretic activity is through restricting prostaglandin synthesis by inhibiting cyclooxygenase. It is well absorbed following oral administration. It undergoes first-pass metabolism only 50–60% dose reaches systemic circulation as unchanged drug. Absorbed into systemic circulation following topical administration as gel or transdermal system, plasma concentration generally very low compared with oral administration.[9] The aim of present work is to develop emulgel preparation containing water-insoluble diclofenac potassium.

MATERIALS AND METHODS

Diclofenac potassium was received as a gift sample from Zydus Pharmaceuticals. Carbopol-940, propylene glycol, methylparaben, and propylparaben were generous gift from Glenmark Pharmaceuticals, Mumbai.

Methodology

Fourier-transform infrared (FTIR) study

Drug and excipients compatibility study was conducted using FTIR study. The IR spectrum of diclofenac potassium, Carbopol in separate, and combined form was determined in the range of 4000 cm^{-1}–400 cm^{-1} by preparing dispersion in drug potassium bromide under the same operating conditions.[10]

Differential scanning calorimetry study (DSC)

DSC finds many applications in characterizing materials. A quantitative application includes the determination of heat of fusion, and qualitative application is the determination of melting point. It is an important tool in establishing the purity of various preparations. The instrument was calibrated using indium as standard. The sample (2–10 mg) was weighed accurately in aluminum pan and sealed hermetically using a crimper. Thermograms were obtained by heating the encapsulated samples at a constant heating rate of 5°C/min with chart speed of 5 mm/min under an atmosphere of nitrogen. The exact peak temperatures, melting point, and heat of fusion were determined. The temperature range for the scan was 30°C–300°C for all the samples.[11]

Formulation of emulgel

For the preparation of the emulgel at first the gel bases with the different concentrations of the gelling agent were prepared, and the diclofenac potassium emulsions were prepared with different concentrations of the liquid paraffin, emulsifiers individually. For the preparation of the emulgel, prepared emulsion was mixed with the gel base with the constant stirring in 1:1 proportion Table 1.

Evaluation of emulgel

Emulgel preparations containing diclofenac potassium were subjected to various evaluation parameters such as drug content, pH, spreadability, swelling index, and viscosity.[12]

Skin irritation test

Skin irritation test for emulgel formulation was conducted over skin of human volunteers. The study was conducted by taking volunteers consent. Healthy eight human volunteers were selected for the skin irritation test. The prepared emulgel formulation was applied on the skin of hand and observed for any type of undesirable effect.[13]

Microbial test

Antibacterial activity of the prepared emulgel formulations was checked by disc diffusion method. The formulations were tested against the Gram-positive as well as Gram-negative bacteria. The discs were soaked into the formulation to be tested for some time. These discs were placed into the Petri dishes containing agar media, and then, these plates incubated at 37°C for 24 h. After 24 h, dishes were observed for the growth of the microorganisms/bacteria.[14]

In vitro drug diffusion studies

The *in vitro* drug released studies were conducted using a modified Franz diffusion cell (FD). The formulations were applied on dialysis membrane of 0.45 µm pore size which was placed between donor and receptor compartment of the FD cell. Phosphate buffer pH 5.5 was used as a dissolution media. The temperature of the cell was maintained at 37°C by circulating hot water through jacket. This whole assembly was kept on a platform having magnetic induction point and the solution was stirred continuously using a magnetic bead. Samples were analyzed spectrophotometrically at 278.8 nm and the percent drug released was calculated.[15]

Optimization of emulgel formulation

As per the tests performed for the evaluation of the prepared gel, emulsion and the mixture of both, i.e., emulgel, one batch of the prepared emulgel was optimized on the basis of diffusion study.

RESULT AND DISCUSSION

FTIR spectrum of diclofenac potassium, Carbopol-940, and combination of diclofenac potassium and Carbopol-940 is shown in Figure 1. FTIR spectroscopy shows various vibrations between the functional groups at different bond. All the characteristic peaks showed clear stretching vibration due to varying functional groups and indicating no overlapping found over the peaks. Hence, the excipient and drug are compatible with each other. DSC thermograms of diclofenac

potassium, Carbopol-940, and combination of diclofenac potassium and Carbopol-940 were depicted in Figure 2. It indicated that thermogram of diclofenac potassium do not show any characteristic sharp peak hence considered as amorphous nature with melting point near to standard value. Thermogram of Carbopol-940 indicated that endothermic peak at 106°C near to its melting point 116°C. Combined thermogram of diclofenac potassium and Carbopol-940 indicated that the Carbopol-940 showed sharp melting point and indicated that Carbopol-940 was completely melt with diclofenac potassium at higher temperature. It was also observed that no characteristic endothermic and exothermic peak was found. Hence, diclofenac potassium and Carbopol-940 were physically stable with each other.

Evaluation of emulgel

Evaluation data of the prepared emulgels such as pH, spreadability, viscosity, drug content, and swelling index are as depicted as in Table 2. pH of the prepared emulgel formulation was found in the range of 5.5–6.8 which is acceptable range for the topical preparations. EG1 formulation do not show results for some of the evaluation parameters. EG1 formulation failed to show gelling property, might be due to 0.5% of the Carbopol-940. Spreadability of the formulation was found in the range of 23.80–55.55 g.cm/s. After studying the spreadability of the formulation, it was found that as the concentration of the gelling agent increases spreadability decreases [Figure 3]. Viscosity of the emulgel was found in the range of 12500–21100 Cps. EG5 and EG6 do not show the readings on Brookfield viscometer for the viscosity, it might be due to the higher concentration of the gelling agent and high consistency. After determining the drug content in the prepared formulation of the emulgel, it was found that 94.31%–98.80% of drug was present in the formulation. Swelling index was found in the range of 3.38%–26.98%. After studying the swelling index of the formulation, it was found that as the concentration of gelling agent increases the swelling index increases [Figure 4]. After evaluating the emulgel formulation for the skin irritation test on eight healthy human volunteers, no irritation occurred on the skin and any other undesirable effects were not found on the skin of volunteers where the emulgel formulation was applied.

Table 1: Formulation of gel and emulsion

Ingredients (%)	GF1	GF2	GF3	GF4	GF5	GF6
Formulation of gel						
Carbopol 940	0.5	1.0	1.5	2.0	2.5	3.0
Propylene glycol	2	2	2	2	2	2
Methylparaben	0.1	0.1	0.1	0.1	0.1	0.1
Ingredients (%)	**EF1**	**EF2**	**EF3**	**EF4**	**EF5**	**EF6**
Formulation of emulsion						
Diclofenac potassium	1	1	1	1	1	1
Span 20	2	6	2	6	2	6
Liquid paraffin	5	5	10	10	20	20
Tween 20	2	6	2	6	2	6
Propylene glycol	10	10	10	10	10	10
Methylparaben	0.2	0.2	0.2	0.2	0.2	0.2
Propylparaben	0.3	0.3	0.3	0.3	0.3	0.3
Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Ethanol	2	2	2	2	2	2

Microbial test

Microbial test of all the prepared emulgel formulation was performed and the results of the microbial test are mentioned in Table 3. The microbial test was performed by taking gentamicin as a standard preparation, and the zone inhabited

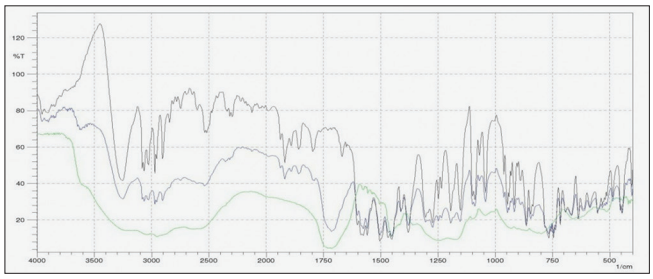

Figure 1: Fourier-transform infrared spectra of diclofenac potassium, Carbopol-940, and mixture

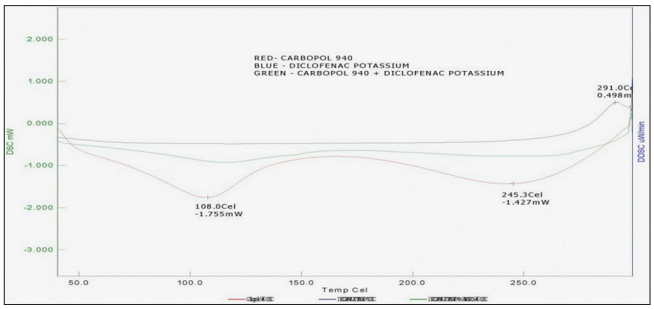

Figure 2: Differential scanning calorimetry thermogram of diclofenac potassium, Carbopol-940, and mixture

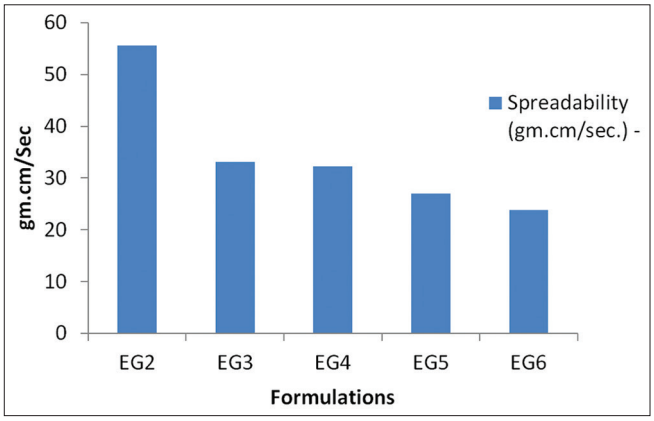

Figure 3: Spreadability of emulgel preparation

by the discs of emulgel formulations was compared with the zone inhabited by the discs of the gentamicin. All emulgel formulations showed a satisfactory zone of inhibition in comparison with gentamicin. EG4 showed the maximum zone of inhibition with gentamicin.

In vitro diffusion studies

The *in vitro* release profile of diclofenac potassium from its various emulgel formulations was depicted in Figure 5. At the 1st h of the diffusion study, EG4 formulation showed the maximum drug release with 31.46% and lowest concentration of drug release was shown by the EG6. At the 2nd h of diffusion study, formulation EG4 again showed the maximum release of drug with 32.89% and lowest drug release was observed in the EG5 with 22.57%. After 6 h of drug diffusion study, the formulation EG4 showed consistent release of the drug form emulgel with 89.72%. It might be due to the higher concentration of the emulsifying agents and the 2% concentration of the gelling agent.

Optimization of emulgel formulation

On the basis of the all evaluation tests performed for the emulgel formulation, the EG4 formulation with 2% of gelling agent, 6% of emulsifying agents, and 10% concentration of oil phase showed good results among all formulations. Hence, EG4 formulation was considered as the optimized emulgel formulations.

CONCLUSION

Emulgel formulations were developed and evaluated successfully with conclusion that Carbopol-940 with 2% concentration showed excellent gelling property. 10% liquid paraffin in emulsion showed good dispersion property in gel formulation. Hence, at last, it was concluded that emulgel preparation is the only choice for water-insoluble drugs like diclofenac potassium with promising effect in drug release as transdermal drug delivery system.

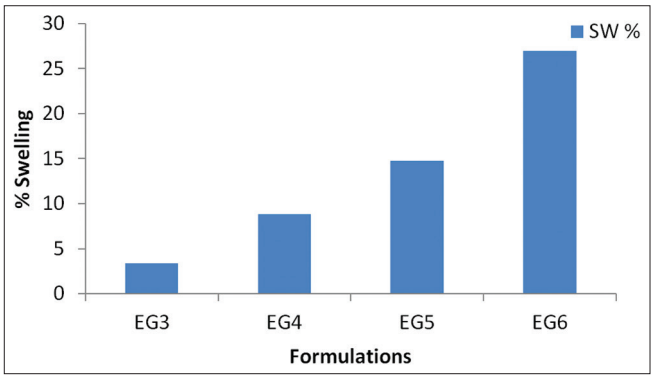

Figure 4: Swelling index of emulgel preparation

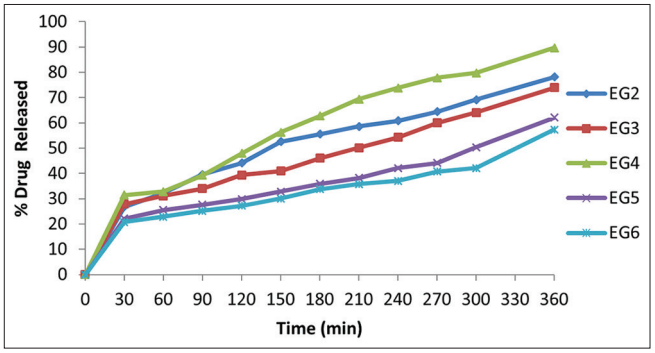

Figure 5: *In vitro* drug release from emulgel formulation

Table 2: Evaluation parameters of emulgel preparations

Batch		EG1	EG2	EG3	EG4	EG5	EG6
pH		6.8	5.8	6.4	6.2	5.5	6.0
Spreadability (g.cm/s)		-	55.55	33.11	32.25	27.02	23.80
Viscosity (cps)	Speed at 12 rpm	12500	15750	20750	21100	-	-
Drug content (%)		97.64	98.22	98.57	98.80	97.64	94.31
Swelling index (%)		-	-	3.38	8.84	14.78	26.98
Skin irritation		No	No	No	No	No	No

Table 3: Zone inhibited by discs of emulgel formulation and gentamicin

Formulation	Gentamicin mm	*S. Aureus* mm	Gentamicin mm	*E. coli* mm
EG1	18	14	16	12
EG2	14	12	21	12
EG3	25	10	17	10
EG4	16	15	15	14
EG5	14	12	20	10
EG6	16	12	18	16

S. aureus: Staphylococcus aureus, Escherichia coli: Escherichia coli

REFERENCES

1. Mohammad KP, Mohanta PG, Nayar C. Emulgel: An Advanced Review. J Pharm Sci Res 2013;5:254-8.
2. Sonam V, Charu S, Easwari TS, Shukla VK. Emulgel based gel technique: Novel approach for enhancing topical drug delivery of hydrophobic drugs. Int J Pharm Res Sch 2014;3:1-2.
3. Kapoor D, Vyas RB, Lad C, Patel M, Lal B, Parmar R. Formulation characterization of emulgel of NSAID. Pharm Chem J 2014;1:9-16.
4. Howard C, Nicholas G. In: Allen LV, Popovich NG, Ansel HC, editors. Ointments, Creams and Gels in Pharmaceutical Dosage Form and Drug Delivery Systems. 7th ed. New Delhi: Lippin Cott Willians and Wilkins; 2000. p. 244-50.
5. Singla V, Saini S, Joshi B, Rana AC. Emulgel: A new platform for topical drug delivery. Int J Pharm Biosci 2012;3:485-98.
6. Panwar AS, Upadhyay N. Emulgel: A review. Asian J Pharm Life Sci 2011;1:333-41.
7. Joshi B, Singh G, Rana A. Emulgel: A comprehensive review on the recent topical drug delivery. Int Res J Pharm 2011;2:66-70.
8. Khunt DM, Mishra DA. Formulation design and development of piroxicam emulgel. Int J PharmTech Res 2012;4:1332-44.
9. Available from: https://en.wikipedia.org/wiki/Diclofenac.
10. Fan M, Dai D, Huang B. In: Fourier transform infrared spectroscopy for natural fibre. Salih SM, editor. Materials Science Fourier Transform-Materials Analysis. Ch. 3. Intech. 2012. p. 45-68.
11. Kodre KV, Attarde SR, Yedhe PP, Patil RY, Borge VU. Differential scanning calorimetry: A review. Res Rev J Pharm Anal Differ Scanning Colorimetry 2014;3:11-22.
12. Dhas A, Deshmukh G. Formulation and evaluation of topical adalapalene emulgel. Am J Pharm Technol Res 2016;6:530-6.
13. Shah M, Modi D, Shah H. A future approach in novel drug delivery system through micro-emulgel: Review. World J Pharm Pharm Sci 2016;5:243-59.
14. Panwar S, Mukhopadhyay S, Kothiyal P. Formulation and evaluation of triconazole emulgel for topical drug delivery. Am J Pharm Technol Res 2015;5:478-91.
15. Vanna S, Al Essandra T, Mario P. Effect of vehicle on diclofenac sodium permeation from new topical formulation: *In-vitro* and *in-vivo* studies. Curr Drug Deliv 2009;6:93-100.

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