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RESEARCH

In vitro evaluation of emulgel formulation for topical application of diclofenac potassium

Diklofenak potasyumun topikal uygulaması için emulgel formülasyonunun in vitro değerlendirilmesi

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Abstract

Purpose: For superficial pain, nonsteroidal anti-inflammatory medications (NSAIDs) offer sufficient analgesia, particularly in cases of mild to severe dull pain. Diclofenac potassium is one of the most preferred drugs in this group, but its low water solubility and high permeability due to its BCS II class classification makes it a challenging active substance in the formulation process. The aim of this study was to develop and evaluate in vitro of emulgel formulations containing diclofenac potassium.

Materials and Methods: All substances used in the formulation development process were substances in conformity with pharmacope specifications. Emulgel formulations containing diclofenac potassium were prepared and evaluated in terms of pH, conductivity, rheological properties, viscosity, drug release rate and stability.

Results: The method developed and validated for the determination of the active ingredient resulted in a good linear relationship that was established between the peak areas and the concentrations (2.5-40 µg /mL) of diclofenac potassium with the determination coefficient (R2) which equals to 0.9999. F1, F2, F3 and F4 formulations were found to be stable at the end of the 1st and 3rd month when evaluated with the amount of active substance, pH and rheological properties at different temperatures and conditions. Formulations F2 and F4 are more viscous than other formulations F1 and F3. The initial pH values of all prepared formulations were found to be compatible with the skin. When the reological properties of the formulations were studied, they were determined by examining the calculated R2 values of the Herschel-Bulkley reological type (R2 values of F1, F2, F3 and F4 formulations respectively were 0.999045, 0.999301, 0.999650, 0.999631). In the drug release rate studies, the

Öz

Amaç: Yüzeysel ağrılar için nonsteroid antienflamatuvar ilaçlar (NSAİİ), özellikle hafif ve şiddetli donuk ağrı durumlarında yeterli analjezi sağlamaktadır. Diklofenak potasyum bu grupta en çok tercih edilen ilaçlardan biridir, ancak BCS II sınıfı olması nedeniyle düşük suda çözünürlüğü ve yüksek geçirgenliği onu formülasyon sürecinde zorlu bir etken madde haline getirmektedir. Bu çalışmanın amacı diklofenak potasyum içeren emüljel formülasyonları geliştirmek ve bunları in vitro olarak değerlendirmektir.

Gereç ve Yöntem: Formülasyon geliştirme sürecinde kullanılan tüm maddeler farmakope spesifikasyonlarına uygun özellikde maddelerdir. Diklofenak potasyum içeren emülgel formülasyonları pH, iletkenlik, reolojik özellikler, viskozite, salım hızı ve stabilite açısından hazırlanarak değerlendirilmiştir.

Bulgular: Etkin maddenin tayini için geliştirilen ve valide edilen yöntem, pik alanları ile diklofenak potasyumunun konsantrasyonları (2.5-40 µg/mL) arasında iyi bir lineer ilişki sağladığı 0.9999 olarak bulunan tanımlayıcılık katsayısı (R2) ile ortaya konmuştur. F1, F2, F3 ve F4 formülasyonları, etkin madde miktarı, pH ve reolojik özellikleri ile farklı sıcaklıklarda ve koşullarda değerlendirildiğinde 1. ve 3. ayın sonunda stabil olduğu tespit edilmiştir. Formülasyonlardan F2 ve F4 diğerlerinden daha viskozdir. Hazırlanan tüm formülasyonların başlangıç pH değerleri deri ile uyumludur. Formülasyonların reolojik özellikleri incelendiğinde, Herschel-Bulkley tipi sergilediği R2 değerleri incelenerek belirlenmiştir. (R2 değerleri F1, F2, F3 and F4 formülasyonları için sırasıyla 0.999045, 0.999301, 0.999650, 0.999631 olarak bulunmuştur). İlaç salım hızı çalışmaları sırasında, F2 ve F4 formülasyonlarından etkin madde salımı 6. saate kadar artarak devam etmiş ve plato değerlerine ulaşmıştır.

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release of active substance from F2 and F4 formulations continued until the 6th hour and reached plateau values.
Conclusion: Diclofenac potassium emulgel can be used as an antiinflammatory analgesic agent for topical drug delivery.
Keywords:. Diclofenac potassium, emulgel, topical nonsteroidal anti-inflammatory drug

Sonuç: Diklofenak potasyum emüljel, topikal ilaç dağıtımı için antienflamatuar analjezik bir ajan olarak kullanılabilir..

Anahtar kelimeler: Diklofenak potasyum, emüljel, topikal nonsteroidal antienflamatuvar ilaç

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) provide adequate analgesia for superficial pain, especially when the pain is mild to moderate and dull. They are used for headache, myalgia, arthralgia, toothache, and other types of pain usually caused by local inflammatory reactions[1]. Their anti-inflammatory activity is weaker than that of glucocorticoids, the most powerful anti-inflammatory drugs, synthetic or natural have analgesic activity weaker than that of narcotic analgesics, which are powerful anesthetics but have no anti-inflammatory effect. However, they are preferred in most painful conditions because they are non-addictive and do not induce a state of narcosis characterized by drowsiness and confusion. Most of the drugs in this group have an antipyretic effect in addition to their analgesic effect. Due to their anti-inflammatory effects, they can relieve local reactions such as pain, edema, redness and increase in temperature, which are the four cardinal symptoms of inflammation. According to international statistics, almost half of the patients with a prevalence of 10-20% in osteoarthritis and 1-2% rheumatoid arthritis, which are common arthritides, use NSAIDs. The rate of use of community NSAIDs was found to be 5% in the community[2, 3]. In cases where long-term use of NSAIDs is mandatory, it is important to determine the risk factors of the patients and to modify the treatment process according to these factors in order to prevent gastrointestinal side effects. Diclofenac potassium is a non-steroidal anti-inflammatory drug that is commonly used for controlling pain and inflammation in patients with conditions such as arthritis, menstrual cramps, and musculoskeletal disorders. In addition, diclofenac potassium has been found effective in reducing the severity of symptoms in patients with rheumatoid arthritis. It can be administered orally as tablets or capsules, and it is also available in topical forms such as gels or ointments for localized pain relief. It can be applied topically in the form of an emulgel, which provides targeted relief to the affected area. The emulgel formulation allows for better absorption of the diclofenac potassium into the skin, making it an effective option for localized treatment. Furthermore, the use of emulgel as a delivery system for diclofenac potassium has shown to have stable properties under normal storage conditions. The combination of diclofenac potassium and emulgel formulation offers a convenient and efficient way to deliver the drug directly to the affected area, providing localized relief and promoting healing.

The chemical name of diclofenac potassium is Potassium [2-[(2,6-dichlorophenyl) amino]phenyl] acetate. Diclofenac potassium is slightly soluble in water, freely soluble in methanol and slightly soluble in acetone and is in Class II according to the Biopharmaceutical Classification System (BCS Class II). Drugs in this group have low solubility and high permeability. This active substance, a phenylacetic acid derivative non-selective cyclooxygenase (COX) inhibitor, was found to be as effective as aspirin and indomethacin against rheumatoid arthritis and as effective as indomethacin against osteoarthritis[4-6]. Formulations of hydrophilic and hydrophobic active substances can be prepared by using emulgels as drug carrier systems. By using oil-in-water type emulsion systems, lipophilic active substances can be loaded into the oil phase, which is the internal phase. A controlled drug release can be achieved by diffusion of the active substance from there to the external phase which facilitates penetration into the skin.

Emulgels have advantages such as enhanced drug release, improved drug loading capacity, ease of production and applicability, improved stability, controlled release and patient compliance. Emulgels, which have the advantages of both emulsions and gels, are formulations with high patient compliance that can be easily applied to the skin since they are not dense, oily in structure and do not have the difficulty of removal from the application area compared to topical formulations such as cream ointment. Bacause of their many advantages in topical use, successful formulations can be obtained by combining gels with emulsions, assisting

application of hydrophobic drugs. This improves the stability and penetration ability of emulsion formulations and enables controlled release. The presence of the gel phase prevents the system from becoming oily and prolongs the contact time on the skin[7, 8]. In this way, emulgel formulations for topical use of various hydrophobic drugs (ketoconazole, acyclovir and calcipotriol) have been reported in the literature in recent years[9, 10].

A topical emulsion formulation of mefenamic acid, a non-steroidal anti-inflammatory drug, was developed. The aim was to increase skin penetration with the preparation of emulgel formulation of a hydrophobic active substance. The formulations were evaluated in terms of rheology, spreadability, bioadhesive properties, skin irritation, in-vitro and ex-vivo release, anti-inflammatory and analgesic activity. The developed formulation was proven to show increased analgesic and anti-inflammatory activity when compared to the market preparation gel formulation[11]. Emulsion formulations containing ofloxacin with broad spectrum antibacterial activity have been developed. Ofloxacin is a BCS Class II fluoroquinolone derivative drug with low solubility and high permeability. By developing emulsion formulations, it was aimed to increase patient compliance during use by eliminating the first pass effect of this active substance, which is especially used orally, through the liver. As a result of the study, a controlled and improved drug release was obtained according to the results of in-vitro experiments[12].

The aim of this study was to develop and evaluate emulgel formulations of diclofenac potassium, a BCS Class II drug, prepared using Carbomer and penetration enhancing excipients. In vitro characterization of the formulations included physical evaluation, pH, conductivity analysis, rheological studies and in vitro release studies. Diclofenac potassium emulgel is not available on the Turkish market yet. Herein, for the first time, this study tested the in vitro characterization of various diclofenac potassium emulgel formulations.

MATERIALS AND METHODS

Materials

Diclofenac potassium, isopropyl alcohol, propylene glycol, carbomer 980, liquid paraffin, Tween 20, Span 20, PEG 400 and glycerine were obtained from Sigma Aldrich. HPLC-grade acetonitrile and methanol were purchased from Merck (Germany). The water was purified by Direct-Q® 3 UV water purification system (Millipore, USA). All other chemicals used were of analytical grade and were used without any further chemical modification.

Analytical procedure for determination of diclofenac potassium

The High Performance Liquid Chromatography (HPLC) system utilized was a Shimadzu Nexera 2 (Japan) system that has an injection valve, solvent pump, and diode-array detector (PDA/DAD) installed. The chemical was successfully separated using a C18 column (4,6 x 250 mm, 5 µm, GL Sciences). A combination of 50 mM potassium dihydrogen phosphate (KH2PO4) buffer (pH:2,5) and 30:70, v/v metanol was used as the mobile phase. This was supplied at a flow rate of 1 mL/min, which produced the best resolution within an acceptable analysis time and column back pressure. There was a 10 µL injection volume. At 280 nm, the UV detector was in operation. The active ingredient's stock solution (100 µg/mL) was made in methanol. To generate standard solutions within the concentration range of 2.5-40 µg/mL, the stock solution was diluted using pH 6.8 phosphate buffer[13, 14]. A full validation of the HPLC method was carried out in accordance with the ICH guidance for Bioanalytical Method Validation[15]. The developed HPLC method was validated in terms of selectivity, linearity, precision, sensitivity, and accuracy.

Preparation and optimization of emulgel formulations

Preparation of emulsion formulations was carried out in three steps. First, the emulsion phase was prepared, then the gel phase was prepared and as the last step, these two phases were combined to obtain homogeneous formulations. Carbomer 980 was used as a gel-forming agent and left to swell for 24 hours with a certain amount of water, stirring continuously at constant speed[16, 17].

Then pH was adjusted to 6.0-6.5 with the addition of triethanolamine. The aqueous and oily phases were heated to 70–80 °C individually. Then, the oily phase was introduced to the aqueous phase and stirred continuously until it cooled to room temperature. To create the emulgel, the emulsion was combined with the gel in a 1:1 ratio while being gently stirred[18, 19]. Table 3 provides a discussion of the various formulations' makeup.

In vitro characterization of emulgel formulations

Evaluation of physical appearance

This was done by examining the overall appearance of the prepared emulgel formulations, whether there were physical stability problems such as phase separation, and properties such as color and odor.

pH and conductivity measurements

The pH values of formulations F1, F2, F3 and F4 were determined at room temperature using a pH meter (Thermo Scientific-Orion 5 Star pH Meter). Conductivity measurements were performed with an Eutech Instruments PC 2700 conductometer. Measurements were repeated 3 times at room temperature and evaluated by calculating arithmetic mean and SD values.

Rheology analysis

Rheology measurements were performed with a TA Instruments Discovery HR-1 Hybrid Rheometer. Rheology analyses of F1, F2, F3 and F4 formulations were performed in three replicates 24 hours after gel preparation. As a result of the analyses, shear stress and viscosity values were obtained for each formulation against varying shear rate values. Shear rate-shear stress and shear rate-viscosity graphs were created and R^2 values of these graphs were calculated. Flow properties of the formulations according to the graphs were evaluated[20, 21]. The viscosity of the formulations was measured at 25±1ºC using a Brookfield viscometer (spindle no:40). Measurements were taken in triplicates.

In vitro dissolution studies

In vitro release studies were performed on a horizontal shaker in an incubator operating at a speed of 100 rpm and a constant temperature of 37 ° C. Molecular weight of 500-1000 Da dialysis membranes were kept in distilled water for 15 minutes. Dialysis membranes were filled with 1 gram each of emulgel formulations containing active substance and closed on both sides. The release study was performed in 3 parallels. Dissolution experiment was performed for 24 hours in release medium containing 100 mL pH 6.8 phosphate buffer. At 15, 30, 45, 90, 120, 180, 240, 300, 360, 420 and 480 minutes, 1 mL of the release medium was sampled and replaced with the same amount of buffer solution[22, 23]. Quantification analysis of the dissolution samples was performed by HPLC method.

Table 3. Composition of different formulation batches

Ingredient	F1 (mg/g)	F2 (mg/g)	F3 (mg/g)	F4 (mg/g)
Diclofenac potassium	10.00	10.00	10.00	10.00
Isopropyl alcohol	50.00	50.00	50.00	50.00
Propylene glycol	25.00	25.00	-	50.00
Carbomer 980	10.00	10.00	10.00	10.00
Liquid paraffin	25.00	25.00	25.00	25.00
Tween 20	0.03	0.03	0.03	0.03
Span 20	0.03	0.03	0.03	0.03
PEG 400	-	25.00	25.00	-
Glycerine	25.00	-	25.00	-
Distilled Water	qs	qs	qs	qs

Stability studies

Accelerated stability studies of F1, F2, F3 and F4 formulations were carried out at +4ºC in a refrigerator and also in a stability cabinet (Nüve TK 252) at +25ºC temperature and 60% relative humidity, +40ºC temperature and 75% relative humidity conditions for 3 months. The formulations were evaluated for physical properties, pH and rheology at the end of the first and third months[24, 25].

Statistical analysis

All experimental methods were carefully carried out in triplicate to guarantee data reproducibility and reliability. The mean value obtained from these three independent repetitions was then used to present the experiment's results. The data was expressed as mean ± standard deviation (SD), which gives a clear picture of how the data were distributed around the mean. This allowed for the expression of variability and

dispersion within the data. The SPSS program, version 11.0 (SPSS Inc.) was used, which is renowned for its powerful statistical capabilities and intuitive interface, for statistical analysis. Significance was considered if *p*-value < 0.05. One-way ANOVA was used to determine whether there are any statistically significant differences between the means of two or more independent (unrelated) groups.

RESULTS

The linearity of the method was evaluated within the range of diclofenac potassium concentrations of 2.5-40 µg/mL. The calibration curve obtained by plotting the peak areas (mAu) versus the concentrations of diclofenac potassium (ng/mL) is shown in Figure 2. The calibration curve equation calculated using linear regression analysis was y=19429.2x-5246.95 (Figure 2). A good linear relationship was established between the peak areas and the concentrations (2.5-40 µg /mL) of diclofenac potassium with the determination coefficient (R^2)=0.9999. Figure 3 shows the HPLC chromatograms of the active substance prepared at different concentrations.

The amount of Carbomer 980 used at 1% in the study was decided by pre-formulation experiments. Four different formulations were prepared with varying concentrations of propylene glycol, PEG 400 and glycerin and the formulations were evaluated primarily for their viscosity and rheological properties. Since an emulsion formation will be achieved in the formulation, the preparation of liquid paraffin as the oil phase and Tween 20 and Span 20 as surfactants by adding them to the appropriate phases was found appropriate in the preliminary evaluations. Due to the poor solubility of the active substance, it was planned to add propylene glycol, ethanol and PEG 400 as cosurfactants in the formulation. Although excipients are registered in the pharmacopoeia and are frequently used in topical formulations, whether there is any incompatibility between the active substance and excipients will be evaluated with the planned stability studies.

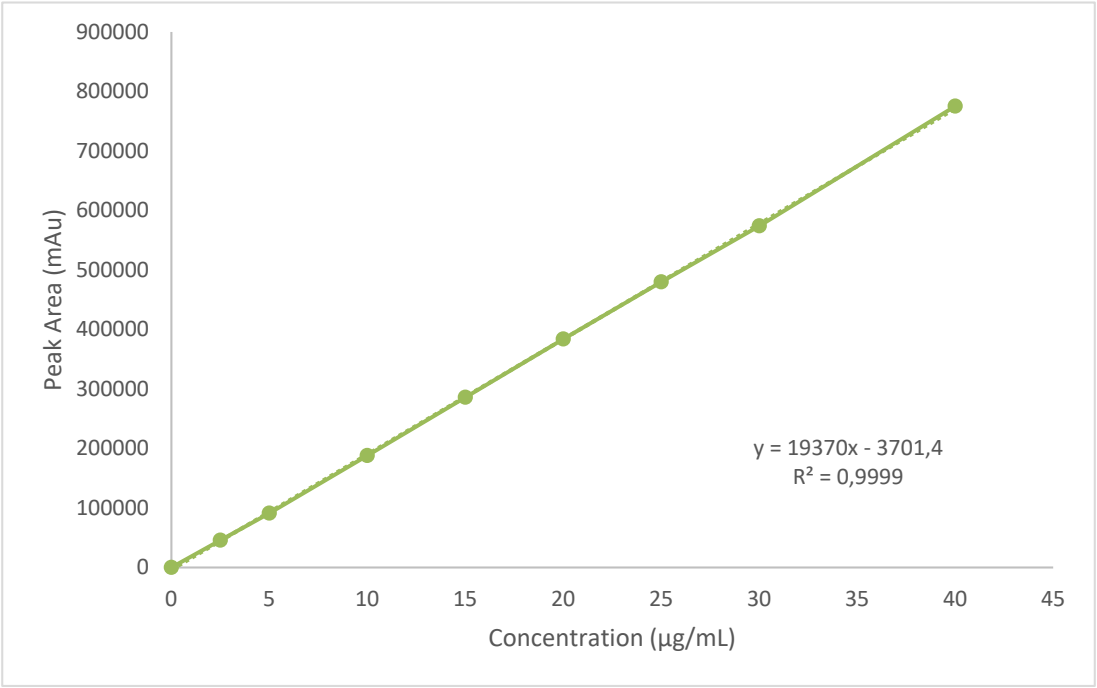

Figure 2. Calibration curve of diclofenac potassium

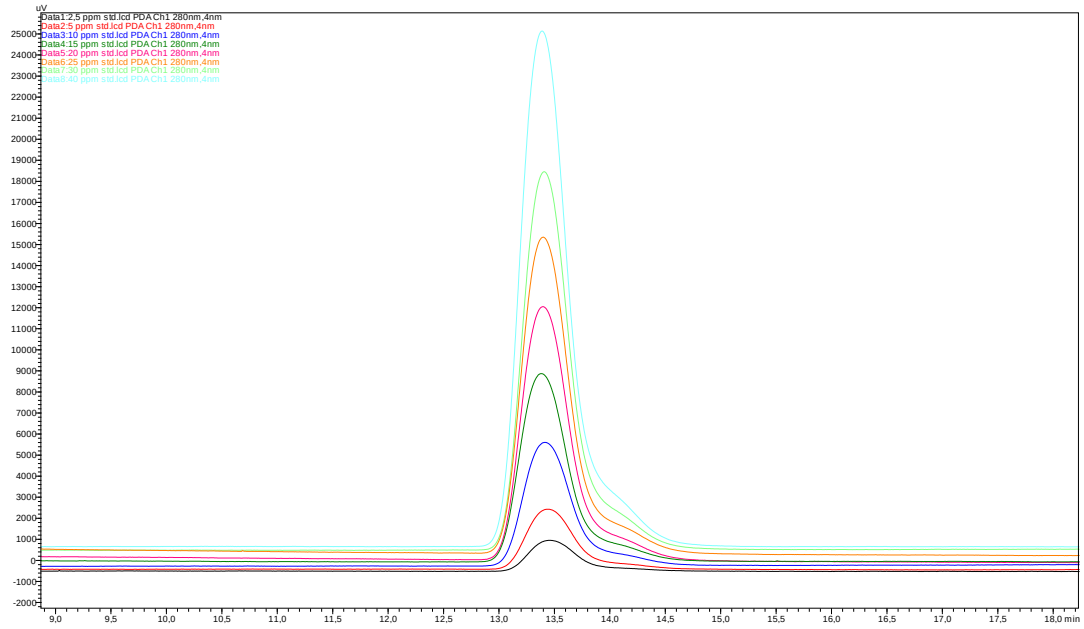

Figure 3. HPLC chromatograms of diclofenac potassium (2.5-40 µg/mL)

Emulgel formulations were yellowish white viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Results have been discussed in Table 4.

The results of pH and conductivity measurements are given in Table 5.

Graphs created in Trios software program as a result of rheology analysis of F1, F2, F3 and F4 formulations were evaluated as program output. Shear rate-shear stress and shear rate-viscosity graphs were created and R^2 values were determined[26]. R^2 values for the graphs and different reological types are given in the Table 6.

Table 4. Physical parameters of formulations

Formulation	Color	Homogeneity	Consistency	Phase separation
F1	White	Excellent	Excellent	None
F2	White	Excellent	Excellent	None
F3	Pale yellow	Excellent	Excellent	None
F4	White	Excellent	Excellent	None

Table 5. pH and conductivity measurements of formulations

Formulation	pH (Mean±SD)	Conductivity (Mean±SD)
F1	6.41±0.01	180.72±1.23
F2	6.45±0.02	155.90±2.76
F3	6.50±0.01	172.21±1.21
F4	6.48±0.02	160.34±2.71

Table 6. Shear rate-shear stress graphs and R^2 for different flow types values

Reological Type	R^2 (1)	R^2 (2)	R^2 (3)	Mean
	F1			
Newtonian	-0.841389	-0.823698	-0.823665	
Bingham	0.920000	0.921300	0.921100	
Casson	0.970666	0.975643	0.975076	
Power Law	0.998100	0.998110	0.998000	
Herschel-Bulkley	0.999111	0.999012	0.999013	0.999045
	F2			
Newtonian	-0.594352	-0.583353	-0.589351	
Bingham	0.920120	0.921000	0.920230	
Casson	0.960566	0.969666	0.971462	
Power Law	0.987100	0.988122	0.989110	
Herschel-Bulkley	0.999031	0.999654	0.999234	0.999301
	F3			
Newtonian	-0.568949	-0.579949	-0.469897	
Bingham	0.929870	0.917765	0.923872	
Casson	0.956766	0.963456	0.957482	
Power Law	0.977666	0.978776	0.978346	
Herschel-Bulkley	0.999098	0.999987	0.999875	0.999650
	F4			
Newtonian	-0.623451	-0.558435	-0.634352	
Bingham	0.912356	0.909876	0.912378	
Casson	0.943476	0.946763	0.926996	
Power Law	0.967623	0.967534	0.961290	
Herschel-Bulkley	0.999000	0.999908	0.999987	0.999631

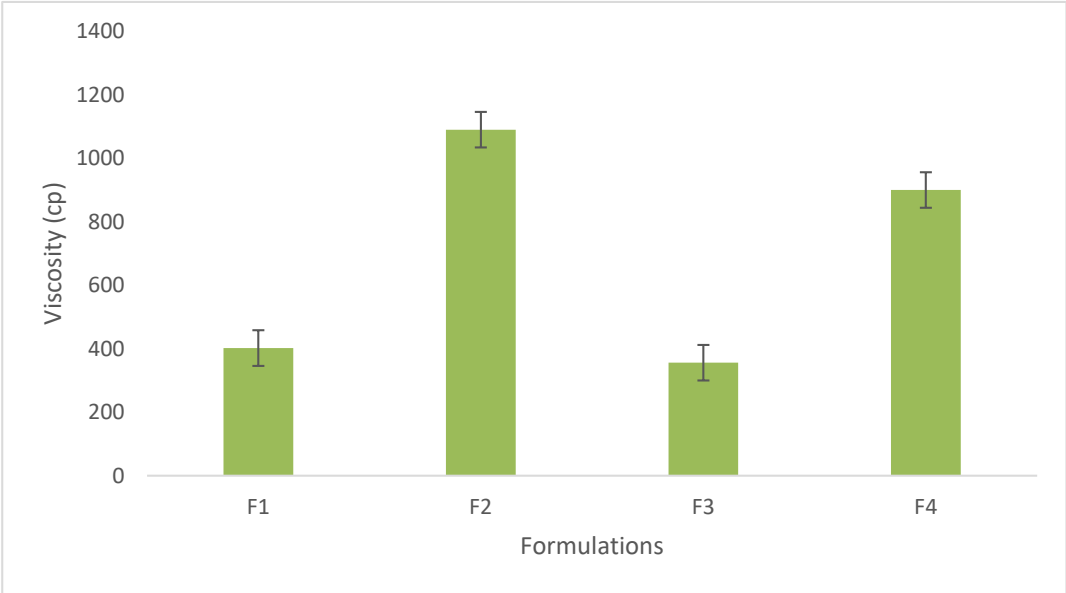

Figure 4. Viscosity of the formulations F1–F4 (mean ± SD).

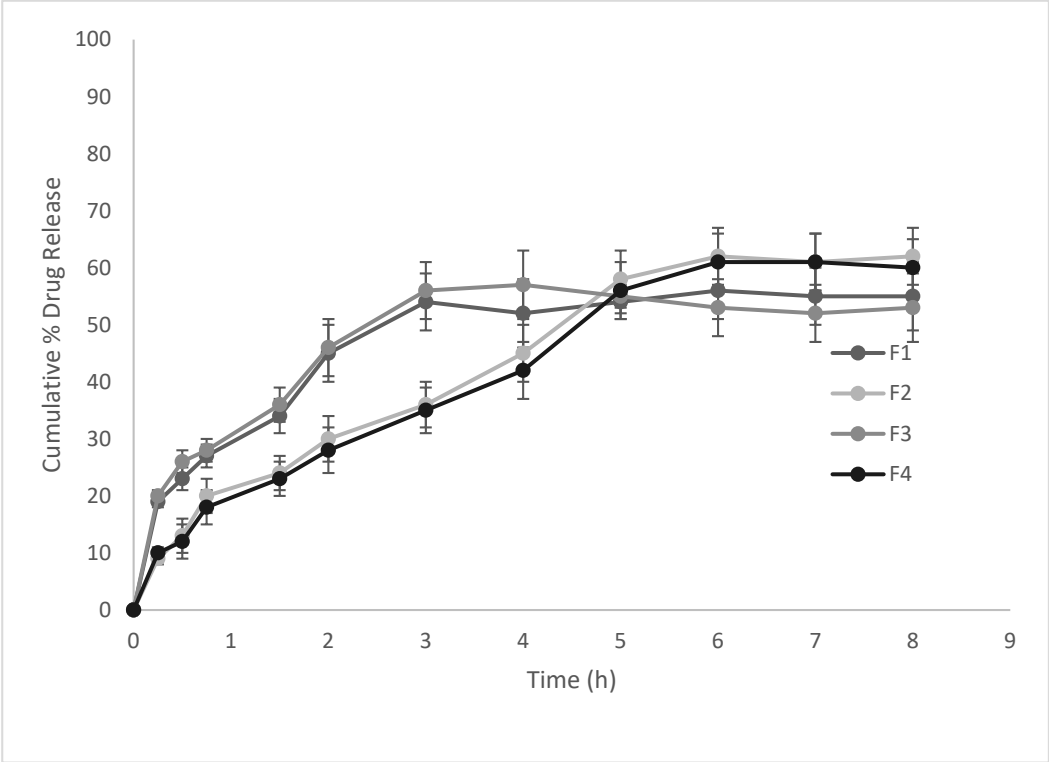

Figure 5. In vitro cumulative drug release of formulation F1–F4 formulations.

In viscosity measurements, F2 and F4 formulations were found to be more viscous than F1 and F3 formulations (Figure 4).

In vitro dissolution profiles of formulations F1, F2, F3 and F4 are given in Figure 5.

For the physical properties of the formulations, color, homogeneity, consistency and phase separation as given in Table 1 no change was observed in the first and third months at varying temperatures and humidity rates. When the amount of active substance present in the formulation was evaluated at the end of the 1st and 3rd months compared to the baseline, it did not deviate more than ±5% and remained within the acceptance limits. The pH values of F1, F2, F3 and F4 formulations kept at certain temperature and humidity in stability cabinets were measured at the end of the 1st and 3rd months and are given in Table 7. Also in the Table 8 the change of R^2 values of shear rate-shear stress graphs obtained from rheology measurements of F1, F2, F3 and F4 formulations in stability studies are presented. In stability studies, pH values and R^2 values of shear rate-shear stress graphs of the formulations were evaluated by comparing them with the initial values determined as optimum in the formulation studies.

Table 7. pH values of F1, F2, F3 and F4 formulations at the end of 1st and 3rd months

	pH						
	Initial	1st month			3rd month		
		+4°C	+25°C	+40°C	+4°C	+25°C	+40°C
F1	6.41±0.01	6.40±0.01	6.39±0.01	6.38±0.01	6.40±0.01	6.38±0.01	6.38±0.01
F2	6.45±0.02	6.44±0.01	6.45±0.02	6.44±0.02	6.44±0.02	6.44±0.02	6.42±0.02
F3	6.50±0.01	6.49±0.01	6.51±0.01	6.48±0.02	6.49±0.02	6.52±0.01	6.48±0.02
F4	6.48±0.02	6.46±0.01	6.47±0.02	6.46±0.02	6.47±0.02	6.47±0.02	6.46±0.03

Table 8. R^2 values of shear rate-shear stress graphs obtained at the end of 1st and 3rd months

	Shear rate-shear stress R^2						
	Initial	1st month			3rd month		
		+4°C	+25°C	+40°C	+4°C	+25°C	+40°C
F1	0.999045	0.999001	0.999131	0.998678	0.999029	0.999001	0.998543
F2	0.999301	0.999210	0.999100	0.998991	0.998780	0.999002	0.998906
F3	0.999650	0.999600	0.999507	0.998900	0.999599	0.999090	0.998880
F4	0.999631	0.999502	0.999445	0.998870	0.999443	0.999401	0.998670

DISCUSSION

In this study, preparation of emulgel formulations containing diclofenac potassium and evaluation of different formulation components were carried out. Numerous medicinal items that either improve or restore a basic skin function or pharmacologically change a tissue's response are applied to the skin or mucous membranes. Numerous common topical medications, such as ointments, creams, and lotions, have a number of drawbacks. They have a lower spreading coefficient when applied by rubbing, which makes them uncomfortable for the patient, and they also have stability issues. The usage of translucent gels in pharmaceutical and cosmetic preparations has increased as a result of all these aspects falling under the larger category of semisolid preparations. With the application of the emulgel formulation to the skin surface, which has the advantages of both emulsion and gel dosage forms, the transition of the active substance loaded into the inner phase of the emulsion system to the outer phase and the controlled release of the gel system, thanks to its reticulated structure, provides efficacy. In this sense, it is a preferred and promising approach for better patient compliance in the future.

Although there are more topical preparations prepared with diclofenac sodium salt in the world pharmaceutical market than those prepared with dilofenac potassium salt, studies have shown that the potassium salt is more effective in both oral and topical applications[27]. In an other study, depending on the degree of pain, disability and stiffness due to inflammation or injury, diclofenac potassium gel 6% with phonophoresis appears to be more effective and therefore more advisable than diclofenac sodium gel 6% alone or diclofenac sodium gel 6% with phonophoresis[28]. This study also recommends the application of topical analgesics delivered to deeper tissues via phonophoresis for the treatment of chronic muscle injuries and presents its advantages over manual massage.

When the shear rate-shear stress graphs obtained as a result of rheology analysis of F1, F2, F3 and F4 formulations are evaluated, it is seen that the flow curve does not pass through the starting point and the flow starts after a certain threshold shear stress value. This type of flow curve shows that emulgels exhibit plastic flow characteristics from non-Newtonian flows. After the threshold sheer stress is exceeded, shear thinning continues according to the flow curve. This means that the formulations exhibit viscoplastic flow behavior derived from plastic flows. In mathematical modeling, all emulgel formulations are derived from plastic flow models of the Herschel-Bulkley model. When rheology studies conducted with carbopols in the literature are examined, it is determined that polymer solutions exhibit shear thinning behavior and generally conform to the Herschel-Bulkley flow model. Flow graphs, flow types and flow models were found to overlap with the studies conducted with different carbopolymers[29].

In stability studies, the physical properties of F1, F2, F3 and F4 formulations were evaluated at the end of the first and third months, no change was observed in color, odor and homogeneity, and no visible microbial no growth was detected and no phase separation was observed. This indicates that the formulations at +4ºC temperature, +25ºC temperature 60% relative humidity, and at +40ºC temperature 75% relative humidity conditions for 3 months, remains physically stable for 3 months.

The solubility of the active substance in water is a very important parameter in the development of any formulation, whether topical or systemic. In emulgel formulations based on oil-in-water (O/W) type emulsions, it is possible to develop effective dosage forms by loading BCS class II drugs with low solubility and high permeability into the oil phase[30]. Since diclofenac potassium is insoluble in water, the formulation was prepared using isopropyl alcohol and PEG 400 and propylene glycol were tried in different ratios to increase solubility. Different ratios

of glycerin were added to evaluate the viscosity of the final formulation. The formulations planned and prepared in this way were evaluated for their physical appearance, pH, rheological properties, viscosity, drug release and stability tests. Therefore diclofenac potassium emulgel can be used as an antiinflammatory analgesic agent for topical drug delivery. For formulations for which in vitro characterization studies have been completed, in vivo anti-inflammatory activity studies should be performed to prove efficacy and to reveal the mechanism.

Author Contributions: Concept/Design : ED; Data acquisition: ED; Data analysis and interpretation: ED; Drafting manuscript: ED; Critical revision of manuscript: ED; Final approval and accountability: ED; Technical or material support: ED; Supervision: ED; Securing funding (if available): n/a.
Ethical Approval: Ethics Committee approval certificate is not required. This study, focused on in vitro characterization tests of developed emulgel formulations.
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