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FORMULATION AND CHARACTERIZATION OF ANTIEPILEPTIC TRANSDERMAL GEL

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ABSTRACT

The oral route is generally preferred for patient compliance; however, it is significantly affected by hepatic first-pass metabolism, often requiring higher drug doses. To overcome these limitations, transdermal emulgels offer improved drug localization and distribution through adequate percutaneous absorption, enhancing both local and systemic therapeutic effects. The present study focuses on formulating a primidone-loaded emulgel designed to provide enhanced permeability, controlled release, and effective localized delivery via the topical route. As skin is one of the most accessible organs and a major site for topical drug administration, it supports various localized applications, including ophthalmic, vaginal, rectal, and dermal routes. In this work, primidone was quantified using a validated UV spectrophotometric method at 257 nm in phosphate buffer (pH 7.4), demonstrating linear, precise, and reproducible calibration curves. Preformulation studies confirmed that the drug was light yellow and odorless, with no detectable interactions between formulation components. Prepared emulgels were evaluated for sensory feel, color, pH, consistency, and extrudability. Among all formulations, PTEG4—containing Carbopol 940 (2 g), PVP, nutmeg oil, and mentha oil—exhibited superior performance. In-vitro release studies and kinetic modeling indicated that all formulations (PTEG1–PTEG4) followed a mechanism combining Fickian diffusion and super case-II transport ($n > 0.5$). PTEG4 demonstrated prolonged drug release with a t50% exceeding 15 hours, confirming its potential as a controlled-release transdermal drug delivery system for primidone.

KEYWORDS: Primidone; Transdermal emulgel; Controlled release; Percutaneous absorption; Carbopol 940; Drug release kinetics; Fickian diffusion; Super case-II transport; Topical delivery.

1. INTRODUCTION

The administration of drugs through the oral route is widely regarded as the most convenient and patient-friendly method due to its simplicity, accessibility, and compliance **(Samuel and Ekpan 2023).** However, many therapeutically important drugs, including antiepileptic agents, undergo extensive hepatic first-pass metabolism, significantly reducing their bioavailability and often necessitating higher or more frequent dosing. This limitation has encouraged researchers to explore alternative, non-invasive drug delivery systems that can bypass hepatic metabolism while maintaining stable plasma concentrations **(Anselmo *et al.*, 2019).**

Transdermal drug delivery has emerged as an effective approach for achieving controlled, sustained, and site-specific drug administration. The skin, being the largest and one of the most easily accessible organs of the human body, serves as a valuable route for systemic as well as localized delivery **(Chen *et al.*, 2019).** It offers several advantages, such as avoidance of gastrointestinal degradation, reduced dosing frequency, improved patient compliance, and the ability to maintain constant therapeutic levels over an extended period. These benefits are particularly valuable for chronic conditions like epilepsy, where maintaining stable drug concentrations is essential for therapeutic efficacy and minimizing adverse effects **(Patsalos *et al.*, 2018).** Among various transdermal delivery systems, emulgels

have gained increasing attention due to their superior spreadability, stability, and capacity to incorporate both hydrophilic and lipophilic drugs. Emulgels are formed by integrating an emulsion into a gel base, resulting in a formulation that enhances drug permeation through the skin while offering ease of application and better patient acceptability. The gel matrix reduces the greasiness commonly associated with ointments and enhances the drug's residence time on the skin, making it suitable for controlled drug delivery applications **(Ganju *et al.*, 2024).** Primidone, a well-known antiepileptic drug, suffers from limitations such as variable absorption and pronounced first-pass metabolism when administered orally. These drawbacks make it a suitable candidate for transdermal delivery, where the drug can directly enter systemic circulation without metabolic degradation **(Mandrioli and Mercolini 2017).** Developing a primidone-based transdermal emulgel can potentially enhance its therapeutic action by offering sustained release, steady plasma levels, and improved patient adherence— especially crucial for long-term epilepsy management. Another significant drawback of oral primidone therapy is its extensive first-pass metabolism in the liver **(Shakya *et al.*, 2018).** After ingestion, a large portion of the drug is metabolized before it reaches systemic circulation, reducing its overall bioavailability. This necessitates higher doses or more frequent dosing schedules to maintain adequate therapeutic concentrations, which can further contribute to side effects, decreased patient compliance, and long-term toxicity concerns **(Ilan, 2020).**

Formulating primidone into a transdermal emulgel offers additional benefits. Emulgels combine the advantages of emulsions and gels, providing a non-greasy, easily spreadable, and stable system that enhances drug penetration through the skin **(Jain *et al.*, 2025).** The gel matrix can sustain drug release over an extended period, helping to maintain steady plasma levels and minimizing the peaks and troughs commonly associated with oral dosing. Such controlled and prolonged release is especially valuable in epilepsy management, where maintaining consistent drug concentrations is essential to prevent breakthrough seizures **(Waris *et al.*, 2024).**

This study focuses on the formulation and characterization of a primidone-loaded transdermal emulgel with desirable physical properties, optimized drug release, improved permeability, and controlled delivery behavior. Comprehensive preformulation, physicochemical evaluation, in-vitro release studies, and kinetic modelling were performed to determine the suitability of the developed formulation. Through these investigations, the work aims to establish an efficient, patient-friendly, and therapeutically effective transdermal gel system for antiepileptic therapy.

2. MATERIAL AND METHODS

2.1 Analytical methods: The drug samples will be studied for determination of absorption maxima (λmax) in phosphate buffer pH 7.4

2.1.1 Determination of absorption maxima (λmax)

The absorption maxima of drug (Primidone) will be determined by scanning drug solution in double beam ultraviolet spectrophotometer between 200 to 400 nm wavelengths at dissolution medium (phosphate buffer pH 7.4) solution. Accurately weighed required quantity of drug 50 mg (Primidone) was dissolved in 50 ml of dissolution medium containing Phosphate buffer pH 7.4 in 50 ml volumetric flask with the help of sonication in bath sonicator for 20 min to obtain 1000 µg/ml solution. From resulting solution take 1 ml and was diluted up to 100 ml with Phosphate buffer pH 7.4 solvent separately with sonication for 20 min to get 10 µg / ml solution with the help of methanol in 10 ml volumetric flasks **(Yadav *et al.*, 2024).**

2.1.2 Preparation of calibration curve of Primidone

Accurately weighed required quantity of drug 50 mg (Primidone) was dissolved in 50 ml of dissolution medium containing Phosphate buffer pH 7.4 in 50 ml volumetric flask with the help of sonication in bath sonicator for 20 min to obtain 1000 µg/ml solution. From resulting solution take 10 ml and was diluted up to 100 ml with Phosphate buffer pH 7.4 solvent separately with sonication for 20 min to get 100 µg / ml solution. From above prepared resulting solution of 100 µg / ml, withdrawn 0.5 ml, 1.0 ml, 1.5 ml upto 4.0 ml aliquots and diluted up to 10 ml with respective solvent (Phosphate buffer pH 7.4) in 10 ml volumetric flasks to get concentration of 5 µg / ml, 10 µg / ml, 15 µg / ml, upto 40 µg / ml respectively. The absorbance of each solution was measured separately at 305 nm for Phosphate buffer pH 7.4. The absorbance was measured and standard curve was plotted between absorbance vs concentration **(Unde and Kurup 2021).**

2.2 Preformulation studies of drug sample

Preformulation studies may carried out to standardize a spectrophotometric method of estimation for drug and to investigate any possible drug polymer interaction. Melting point determination, Determination of distribution coefficient, Drug polymer interaction was studied by carrying out Fourier Transform Infrared (FTIR) spectral studies etc **(Thakore *et al.*, 2021).**

2.2.1 Organoleptic properties*:* The organoleptic properties of drug such as color, odor and taste noted visually.

2.2.2 Microscopic examination: The microscopic examination of the drug sample was done to identify the nature / texture of the powder. The required amount of powder will spread on a glass slide and examine under phase contrast microscope and drug powder was crystalline in nature **(Alamgir, 2017).**

2.2.3 Physical Characteristics

- **Density:** The drug powder will be weighed accurately and kept through a glass funnel into graduated cylinder. During this experiment the volume will note and bulk density will be determined. The tapped density will determine using tapped density apparatus. Bulk and tapped densities of Primidone was to be 0.881 gm / cm^3 and 0.921gm / cm^3 **(Randhawa, 2021).**
- **Particle size:** The average particle size (davg) of drug will be determined by means of optical microscope fitted with ocular micrometer and stage micrometer. The particle size of unmilled Primidone was to be 29.7 µm **(Kalam *et al.*, 2022).**
- **Flow properties:** The flow properties of drug powder were characterized in terms of carr's index, hausner's ratio and angle of repose **(Salim *et al.*, 2023).** The Carr's index ((IC)) and Hausner's ratio (HR) of drug powders were calculating according to following equation:

Carr's Index (IC) = ρTapped - ρBulk / ρTapped

Hausner's ratio (HR) = ρTapped / ρBulk

The angle of repose (θ) was measured by fixed height method. This was calculated by following equation:

Angle of repose (θ) = $\tan^{-1}$ 2 H / D

Where H is the surface area of the free standing height of the powder pile and D is diameter of pile that formed after powder flow from the glass funnel.

2.2.4 Solubility determination

Saturation solubility of drug API (Primidone) was determined by incremental method analysis method in various solvents. The exact quantity of drug 50 mg was placed on the conical flask and the various solvents i.e. distilled water, 0.1 N HCl, Phosphate buffer pH 6.8 and pH 7.4 phosphate buffers separately filled in burette. The solvent was slowly added into drug containing conical flask until the drug was solubilized and stirred constantly overnight at 37±0.5ºC. The samples were filtered by using whatmann filter paper (0.45µm pore size). The solubility assessment of drug was determined by calculation of concentration µg/ml unit **(Plöger *et al.*, 2018).**

2.2.5 Partition coefficient

The partition coefficient of drug samples was observed in mixed solvent of 100 ml containing n-octanol: phosphate buffer pH 7.4. 100 mg of drug was added into 50 ml each of an noctanol and buffer phase in a separating funnel. The mixture was shaken for 24 h until equilibrium reached. Both medium were divided and collected individually, filtered. The quantity of API dissolved in aqueous medium was diluted and determined by UV spectrophotometric method. The partition coefficient of API was calculated from the proportion between the concentrations of drug in organic and buffer solution quantity using following equation **(Asare-Addo and Conway 2017).**

Log P (oct / pH 7.4) = Log (C noct – C pH7.4) equilibrium

2.2.6 Melting point

The melting point of drug samples were obtained by pinch of drug material sample filled in capillary tube by manually. Capillary tube sealed from one end with a bunsen flame burner individually. The filled capillary tube was kept in melting point apparatus and identified the temperature at which the drug was starting to melt **(Tian *et al.*, 2025). 2.2.7 Drug excipient compatibility study: Infrared spectroscopy of drugs.**

The functional group determination of drug samples was identified by IR spectroscopy. Infra- red spectroscopy was carried out by using Shimadzu IR Spectra photometer as method given below. The characteristic peaks were reported as wave number. The FTIR spectra of dried drug samples (Primidone) independently were obtain by FTIR spectrophotometer by means of the potassium bromide disc method. The drug sample was pulverized and thoroughly mixed with a dried powder of IR grade potassium bromide material with weight ratio of 3:1 (i.e 9 mg of KBr in 1 mg of drug). The mixture of materials was pressed using a hydrostatic press at a pressure of 10 tons for 5 min at room temperature with required humidity. The disc of sample was placed in the sample holder for measuring the spectrum and the spectra were recorded as the wave number ranges 4000-400/cm at a resolution of 4/cm. The compatibility i.e. drug-excipients interaction studies are helpful for dosage form design. For compatibility studies drug / excipients ratio are selected and investigated based on the reasonable drug / excipient ratio in the final product. Drug and other Excipients were weighed as 1:1 ratio and passed through sieve # 40, mixed well. The blend was filled in amber color glass vials and stopped with grey rubber stoppers followed by aluminium seal **(Rojek *et al.*, 2024).**

2.3 Preparation of transdermal emulgel

The transdermal emulgel with drug in different combinations prepared by the high-speed homogenization method. Emulgel with drug in different combinations prepared by the highspeed homogenization method. The various formulations were prepared using varying amount of gelling agent and penetration enhancers. The composition of the formulation was prepared with nutmeg oil as a carrier, surfactant Tween 20 and glycerin in purified water by high-speed homogenization. The gel base was prepared by dispersing Carbopol 940 in distilled water with constant stirring at a moderate speed using mechanical shaker, then the pH was adjusted to 6–6.5. The oil phase of the emulsion was prepared by dissolving span 20 in nutmeg oil. The aqueous phase was prepared by dissolving tween 20 in distilled water and required weighed quantity of drug was dissolved in ethanol. Now all prepared both solutions were mixed with the aqueous phase. Both the oily and aqueous phases were separately heated to 70–80°C, then the oily phase was added to the aqueous phase with continuous stirring until it got cooled to room temperature. The obtained emulsion was mixed with the

gel base in 1:1 ratio with gentle stirring to obtain the emulgel **(Ansari *et al.*, 2025).**

Table 1: A variety of composition of different transdermal emulgel formulations.

Ingredient	LTEG1	LTEG2	LTEG3	LTEG4	LTEG5	LTEG6	LTEG7	LTEG8
Primidone (mg)	100	100	100	100	100	100	100	100
Carbopol 934 (g)	0.5	1	1.5	2	0.5	1	1.5	2
Liquid paraffin (ml)	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Clove oil (ml)	4	6	8	10	0	0	0	0
Mentha Oil	0	0	0	0	4	6	8	10
Tween 20 (ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Polyvinyl pyrrolidone (mg)	50	50	50	50	50	50	50	50
Ethanol (ml)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Water (ml)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

2.4 Characterization of transdermal emulgel

The preparing systems evaluated with various parameters such as Organoleptic evaluation, physical evaluation of gel, determination of pH, spread ability, tube extrudability, viscosity, in Vitro diffusion studies, skin irritation study, drug release kinetic data analysis: The release data was fitted to various mathematical models **(Sharma *et al.*, 2022).**

2.4.1 Physical examination: The prepared emulgel formulations were inspected visually for their color, appearance and consistency. The prepared emulgel formulations were inspected visually for their feeling after application on skin, color intensity, pH determination, consistency and extrudability determination **(Burki *et al.*, 2020).**

2.4.2 Particler size and polydispersity index (PDI): GS and PDI were determination by mean droplet size and polydispersity index of the emulsions was determined by zetasizer by sending samples of formulation to centre **(Yue *et al.*, 2022).**

2.4.3 Viscosity determination: The viscosity of the formulated batches was determined by using a brook field viscometer.

2.4.4 Spreadability: Spreadability was determined by principle involved in this spreadability method is 'slip' and 'drag'. Thus, a ground glass slide is fixed onto the wooden block, while another upper glass slide having the same dimensions as that of the fixed ground slide is provided with a hook and placed on the ground slide. 2 g of emulgel were placed in between the glass slides and a weight of 1 kg was applied on the upper slide for 5 min to form a uniform film of the formulation between the slides. Excess of the formulation was scrapped off from the edges. The top plate was then subjected to a fixed weight of 100 g with the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7 cm was noted. A shorter interval indicates better spreadability **(Alexander and Krasnyuk 2022).** Spreading coefficient is determined by using the formula.

$$S + m * l / t$$

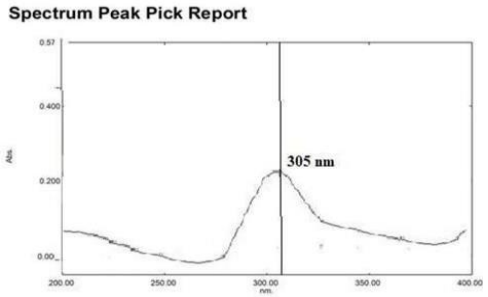
where, S = Spreadability, m = Weight tied to upper slide, l = Length of glass slides, t = Time taken to separate the slides completely from each other.

2.4.5 Drug content determination: One gram each of emulgel was taken and dissolved in methanol and sonicated for 1 h respectively. The resulting solutions were filtered with 0.45 µm filter to obtain clear solutions. The drug content was analyzed using a UV spectrophotometer method at 234 nm **(Gaikwad and Jadhav 2018).**

2.4.6 In-vitro permeation studies: In-vitro permeation studies of the developed gels were carried out using Franz-diffusion cell. The dialysis membrane (Himedia, thickness 0.025 mm) was cut into equal pieces (6 cm×2.5 cm) and soaked into distilled water for 12 h before use. The drug release studies of the ECB emulgel was carried out in 10 ml of phosphate buffer pH 6.8 saline maintained at 37±2° with a magnetic stirrer with constant heating equipment. A sample of 2 ml of ECB emulgel was placed in receptor compartment. Aliquot samples of 1 ml were withdrawn at the regular interval and replaced with same volume of fresh buffer. The aliquots were diluted with fresh media, if necessary. Amount of drug diffused through the membrane was measured by using U.V. spectrophotometer at the wavelength 234 nm against phosphate buffer (pH 6.8 saline) as the blank **(Donthi *et al.*, 2023).**

3. RESULT AND DISCUSSION

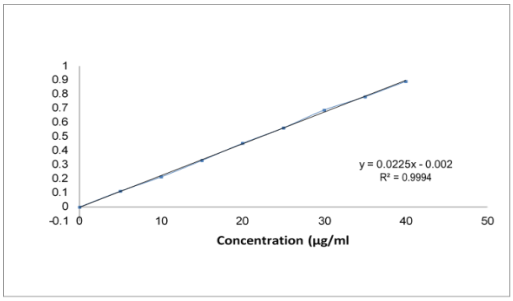
3.1 Analytical methods: The absorption maxima of drug (Primidone) determined by scanning drug solution in double beam ultraviolet spectrophotometer between 200 to 400 nm wavelengths at dissolution medium (phosphate buffer pH 7.4) solution. The spectrums of Primidone absorption maxima (λmax). The absorbance was measured and standard curve was plotted between absorbance vs. concentration.



Graph 1: Absorption maxima (λ-max) of Primidone in phosphate buffer pH 7.4 solution (10 µg/ml).

Table 2: Standard curve of Primidone in phosphate buffer pH 7.4 (257 nm).

Concentration (µg/ml)	Absorbance
0	0
5	0.113
10	0.214
15	0.331
20	0.453
25	0.562
30	0.689
35	0.783
40	0.892



Graph 2: Standard curve of Primidone in phosphate buffer pH 7.4 (257 nm).

3.2 Preformulation studies of drug sample

Preformulation studies may carried out to standardize a spectrophotometric method of estimation for drug and to investigate any possible drug polymer interaction. Melting point determination, Determination of distribution coefficient, Drug polymer interaction was studied by carrying out Fourier Transform Infrared (FTIR) spectral studies etc. The organoleptic properties of drug such as color, odor and taste noted visually and results. The microscopic examination of the drug sample was done to identify the nature / texture of the powder and drug powder was crystalline in nature. The solubility assessment of drug was determined by calculation of concentration µg/ml unit. The solubility of Primidone at different pH medium. The partition coefficient of Primidone was found to be 1.91. The results are shown in triplicate manner**.** The results are shown in triplicate manner and it was 181°C ± 0.12. The FTIR spectrum for Primidone (recorded from a KBr pellet) is illustrated in Figure 7.3 and 7.4. Characteristic infrared (IR) absorption bands due to amine N - H stretching (3450, 3314, 3212 cm^{-1}), aromatic (C = C) stretching (1619cm^{-1}), and orthodistributed aryl C - Cl stretching (1052cm^{-1}) were observed.

Table 3: Organoleptic characteristics of drug (Primidone).

Drug	Color	Odor	Taste
Primidone (PMD)	Pale cream-colored	Odorless	Slightly bitter

Table 4: Flow properties of drug (Primidone) (n = 3).

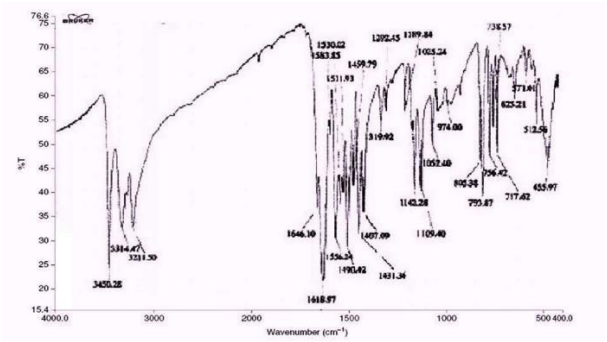
Drug	Carr's index (%)	Hausner's ratio	Angle of repose θ
Primidone	26.01±0.61	1.13±0.012	24.2±0.16

Table 5: The solubility of Primidone at different pH medium (n=3).

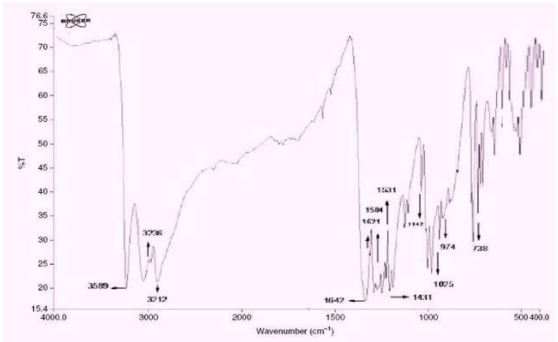
Solubility medium	Solubility (µg / ml)
Water	241.5±9.21
0.1 N HCl	1089.0±27.91
Phosphate buffer pH 6.8	331.8±8.32
Phosphate buffer pH 7.4	302.2±7.87

Table 6: Partition coefficient of drug samples.

S. No	Drug Samples	Partition coefficient (mean ± SD)
1	Primidone	1.91±0.021
Mean ± S.D, n=3		



Graph 3: The I. R. Spectrum of Primidone sample (S1)



Graph 4: The I. R. Spectrum of Primidone drug and all excipient (S2)

3.3 Characterization of transdermal emulgel formulation

The prepared transdermal emulgel formulations were examined visually for their feeling after application on skin, color intensity, pH determination, consistency and extrudability determination. The emulgels were tested for homogeneity by visual inspection prior to the gels being filled into containers. The Formulation PTEG4 was best formulations among all the prepared formulations. The globule size and polydispersity index (PDI), viscosity, spreadability and drug content of prepared formulations also examined. This formulation PTEG4 was prepared emulgel Carbopol 940 (2g), PVP, castor oil and mentha oil for base.

Table 7: Physical characterization of various transdermal emulgel.

Parameters	Formulations			
	LTEG1	LTEG2	LTEG3	LTEG4
Feel of application Skin	Smooth	Smooth	Smooth	Smooth
Consistency	Poor	Good	Good	Excellent uniform
Extrudibility	Good	Good	Excellent	Excellent
Globule (Particle) size nm	151.11	147.14	137.17	134.11
Polydispersity index (PDI)	0.221	0.213	0.201	0.198
Viscosity (cps)	1434	1523	1579	1635
pH	6.22	7.21	7.13	7.11
Spreadability (g.cm/sec)	8.1	9.43	10.02	11.08
Drug Content (%)	98.31	98.11	98.19	99.32

Table 8: Physical characterization of various transdermal emulgel.

Parameters	Formulations			
	PTEG5	PTEG6	PTEG7	PTEG8
Feel of application Skin	Smooth	Smooth	Smooth	Smooth
Consistency	Good	Good	Good	Uniform
Extrudibility	Good	Good	Good	Average
Particle size (nm)	141.84	131.04	117.08	104.27
Polydispersity index (PDI)	0.231	0.233	0.221	0.208
Viscosity (cps)	1634	1602	1589	1504
pH	7.02	7.11	7.73	7.01
Spreadability (g.cm/sec)	9.1	10.03	11.12	13.18
Drug Content (%)	99.01	99.21	99.27	99.03

Table 9: Dissolution data of transdermal emulgel (LTEG1 to PTEG8).

Time (h)	PTEG 1	PTEG 2	PTEG 3	PTEG 4	PTEG 5	PTEG 6	PTEG 7	PTEG 8
0	0	0	0	0	0	0	0	0
2	0.545	0.531	0.421	0.211	0.645	0.502	0.411	0.321
4	1.743	1.134	0.976	0.911	1.843	1.024	1.234	0.876
6	5.01	3.6	2.54	1.341	4.01	2.87	2.6	1.54
8	9.34	7.89	6.32	5.34	8.34	7.02	8.89	5.32
10	19.11	16.34	13.23	11.98	18.11	15.67	15.34	14.23
12	39.23	33.12	26.43	22.21	37.23	29.1	32.12	28.43

14	54.67	48.23	40.41	33.67	53.67	41.69	47.23	41.41
16	72.76	62.23	53.31	47.32	70.76	58.79	61.23	54.31
18	82.11	76.21	70.31	62.34	81.98	66.56	84.21	69.31
20	93.13	92.23	83.21	74.21	91.21	79.02	91.23	87.21
22	98.21	98.12	96.23	86.25	97.24	88.35	98.98	98.23
24	99.92	99.89	99.11	98.13	99.88	99.67	99.89	99.68

Table 10: In-vitro dissolution data of transdermal emulgel (PTEG1).

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.164	0.545	-0.264	99.46	1.998
4	2.000	0.602	0.523	1.743	0.241	98.26	1.992
6	2.449	0.778	1.503	5.01	0.700	94.99	1.978
8	2.828	0.903	2.802	9.34	0.970	90.66	1.957
10	3.162	1.000	5.733	19.11	1.281	80.89	1.908
12	3.464	1.079	11.769	39.23	1.594	60.77	1.784
14	3.742	1.146	16.401	54.67	1.738	45.33	1.656
16	4.000	1.204	21.828	72.76	1.862	27.24	1.435
18	4.243	1.255	24.633	82.11	1.914	17.89	1.253
20	4.472	1.301	27.939	93.13	1.969	6.87	0.837
22	4.690	1.342	29.463	98.21	1.992	1.79	0.253
24	4.899	1.380	29.976	99.92	2.000	0.08	-1.097

Table 11: In-vitro dissolution data of transdermal emulgel (PTEG2).

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.159	0.531	-0.275	99.47	1.998
4	2.000	0.602	0.340	1.134	0.055	98.87	1.995
6	2.449	0.778	1.080	3.6	0.556	96.40	1.984
8	2.828	0.903	2.367	7.89	0.897	92.11	1.964
10	3.162	1.000	4.902	16.34	1.213	83.66	1.923
12	3.464	1.079	9.936	33.12	1.520	66.88	1.825
14	3.742	1.146	14.469	48.23	1.683	51.77	1.714
16	4.000	1.204	18.669	62.23	1.794	37.77	1.577
18	4.243	1.255	22.863	76.21	1.882	23.79	1.376
20	4.472	1.301	27.669	92.23	1.965	7.77	0.890
22	4.690	1.342	29.436	98.12	1.992	1.88	0.274
24	4.899	1.380	29.967	99.89	2.000	0.11	-0.959

Table 12: In-vitro dissolution data of transdermal emulgel (PTEG3)

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.126	0.421	-0.376	99.58	1.998
4	2.000	0.602	0.293	0.976	-0.011	99.02	1.996
6	2.449	0.778	0.762	2.54	0.405	97.46	1.989
8	2.828	0.903	1.896	6.32	0.801	93.68	1.972
10	3.162	1.000	3.969	13.23	1.122	86.77	1.938
12	3.464	1.079	7.929	26.43	1.422	73.57	1.867
14	3.742	1.146	12.123	40.41	1.606	59.59	1.775

16	4.000	1.204	15.993	53.31	1.727	46.69	1.669
18	4.243	1.255	21.093	70.31	1.847	29.69	1.473
20	4.472	1.301	24.963	83.21	1.920	16.79	1.225
22	4.690	1.342	28.869	96.23	1.983	3.77	0.576
24	4.899	1.380	29.733	99.11	1.996	0.89	-0.051

Table 13: In-vitro dissolution data of transdermal emulgel (PTEG4).

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.063	0.211	-0.676	99.79	1.999
4	2.000	0.602	0.273	0.911	-0.040	99.09	1.996
6	2.449	0.778	0.402	1.341	0.127	98.66	1.994
8	2.828	0.903	1.602	5.34	0.728	94.66	1.976
10	3.162	1.000	3.594	11.98	1.078	88.02	1.945
12	3.464	1.079	6.663	22.21	1.347	77.79	1.891
14	3.742	1.146	10.101	33.67	1.527	66.33	1.822
16	4.000	1.204	14.196	47.32	1.675	52.68	1.722
18	4.243	1.255	18.702	62.34	1.795	37.66	1.576
20	4.472	1.301	22.263	74.21	1.870	25.79	1.411
22	4.690	1.342	25.875	86.25	1.936	13.75	1.138
24	4.899	1.380	29.439	98.13	1.992	1.87	0.272

Table 14: In-vitro dissolution data of transdermal emulgel (PTEG5).

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.194	0.645	-0.190	99.36	1.997
4	2.000	0.602	0.553	1.843	0.266	98.16	1.992
6	2.449	0.778	1.203	4.01	0.603	95.99	1.982
8	2.828	0.903	2.502	8.34	0.921	91.66	1.962
10	3.162	1.000	5.433	18.11	1.258	81.89	1.913
12	3.464	1.079	11.169	37.23	1.571	62.77	1.798
14	3.742	1.146	16.101	53.67	1.730	46.33	1.666
16	4.000	1.204	21.228	70.76	1.850	29.24	1.466
18	4.243	1.255	24.594	81.98	1.914	18.02	1.256
20	4.472	1.301	27.363	91.21	1.960	8.79	0.944
22	4.690	1.342	29.172	97.24	1.988	2.76	0.441
24	4.899	1.380	29.964	99.88	1.999	0.12	-0.921

Table 15: in-vitro dissolution data of transdermal emulgel (PTEG6).

Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.151	0.502	-0.299	99.50	1.998
4	2.000	0.602	0.307	1.024	0.010	98.98	1.996
6	2.449	0.778	0.861	2.87	0.458	97.13	1.987
8	2.828	0.903	2.106	7.02	0.846	92.98	1.968
10	3.162	1.000	4.701	15.67	1.195	84.33	1.926
12	3.464	1.079	8.730	29.1	1.464	70.90	1.851
14	3.742	1.146	12.507	41.69	1.620	58.31	1.766

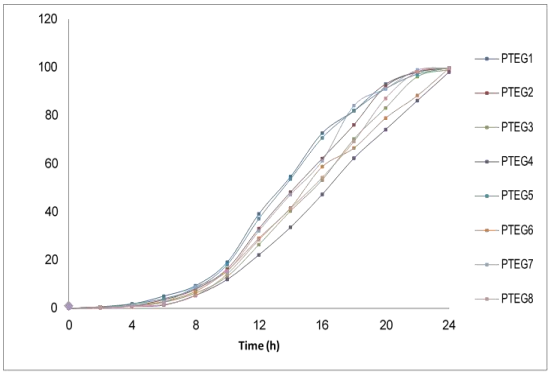
16	4.000	1.204	17.637	58.79	1.769	41.21	1.615
18	4.243	1.255	19.968	66.56	1.823	33.44	1.524
20	4.472	1.301	23.706	79.02	1.898	20.98	1.322
22	4.690	1.342	26.505	88.35	1.946	11.65	1.066
24	4.899	1.380	29.901	99.67	1.999	0.33	-0.481

Table 16: in-vitro dissolution data of transdermal emulgel (PTEG7)

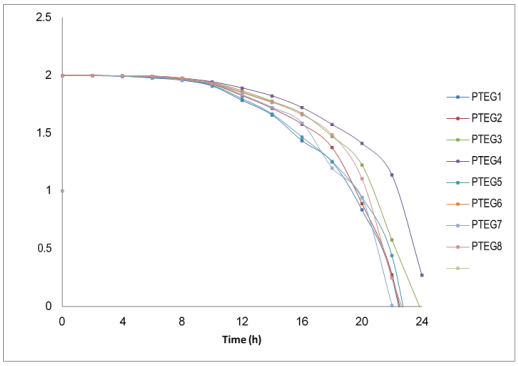
Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.123	0.411	-0.386	99.59	1.998
4	2.000	0.602	0.370	1.234	0.091	98.77	1.995
6	2.449	0.778	0.780	2.6	0.415	97.40	1.989
8	2.828	0.903	2.667	8.89	0.949	91.11	1.960
10	3.162	1.000	4.602	15.34	1.186	84.66	1.928
12	3.464	1.079	9.636	32.12	1.507	67.88	1.832
14	3.742	1.146	14.169	47.23	1.674	52.77	1.722
16	4.000	1.204	18.369	61.23	1.787	38.77	1.588
18	4.243	1.255	25.263	84.21	1.925	15.79	1.198
20	4.472	1.301	27.369	91.23	1.960	8.77	0.943
22	4.690	1.342	29.694	98.98	1.996	1.02	0.009
24	4.899	1.380	29.967	99.89	2.000	0.11	-0.959

Table 17: in-vitro dissolution data of transdermal emulgel (PTEG8).

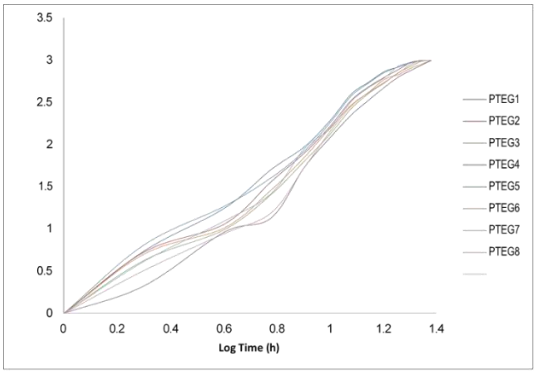
Time (h)	√Time	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
2	1.414	0.301	0.096	0.321	-0.493	99.68	1.999
4	2.000	0.602	0.263	0.876	-0.057	99.12	1.996
6	2.449	0.778	0.462	1.54	0.188	98.46	1.993
8	2.828	0.903	1.596	5.32	0.726	94.68	1.976
10	3.162	1.000	4.269	14.23	1.153	85.77	1.933
12	3.464	1.079	8.529	28.43	1.454	71.57	1.855
14	3.742	1.146	12.423	41.41	1.617	58.59	1.768
16	4.000	1.204	16.293	54.31	1.735	45.69	1.660
18	4.243	1.255	20.793	69.31	1.841	30.69	1.487
20	4.472	1.301	26.163	87.21	1.941	12.79	1.107
22	4.690	1.342	29.469	98.23	1.992	1.77	0.248
24	4.899	1.380	29.904	99.68	1.999	0.32	-0.495

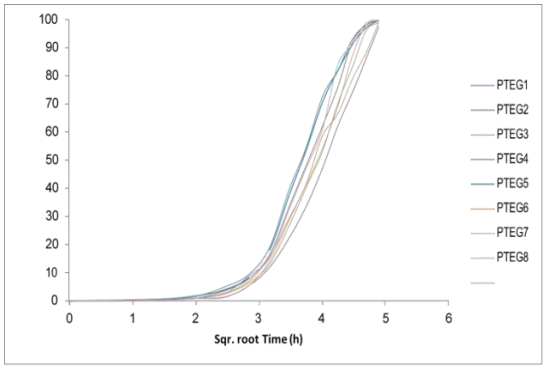


Graph 5: Zero-order plots for transdermal emulgel delivery system (PTEG1 to PTEG8)



Graph 6: First-order plots for transdermal emulgel delivery system (PTEG1 to PTEG8) emulgel delivery system (PTEG1 to PTEG8)





Graph 7: Korsmeyer's-Peppas plot for transdermal transdermal emulgel delivery system emulgel delivery system (PTEG1 to PTEG8)

Graph 8: Higuchi kinetic plot for transdermal emulgel delivery system (PTEG1 to PTEG8)

4. CONCLUSION

The study successfully developed a primidone-loaded emulgel designed for improved permeability, controlled release, and localized topical delivery. Among all formulations, PTEG4—prepared using Carbopol 940 (2 g), PVP, nutmeg oil, and mentha oil—showed the most favorable characteristics, including suitable physical properties and optimal drug-release behavior. Release kinetics indicated a combination of Fickian diffusion and super case-II transport, with PTEG4 demonstrating prolonged drug release (t50% > 15 hours), confirming its potential as an effective controlled-release topical drug delivery system.

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