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Original Research Article

Formulation Development and Evaluation of Acyclovir Bigel Containing Lemongrass Oil

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Abstract: The present study was undertaken to formulate and evaluate a topical bigel drug delivery system of acyclovir using lemongrass oil as a natural penetration enhancer, with the aim of improving drug release and suitability for topical antiviral therapy. Acyclovir, a widely used antiviral agent for the treatment of herpes simplex virus (HSV) infections, exhibits limited topical efficacy due to poor skin permeation, thereby necessitating the development of an advanced delivery system. Bigel formulations were prepared by combining a hydrogel phase based on Carbopol 934 and an organogel phase composed of olive oil and beeswax. Five formulations (TBG1–TBG5) were developed by varying the concentration of the hydrophilic polymer while maintaining a constant drug load and organogel composition. Lemongrass oil was incorporated to enhance skin permeation, and triethanolamine was used to adjust the pH of the formulations to a skin-compatible range. Preformulation studies, including melting point determination, solubility analysis, partition coefficient determination, and Fourier transform infrared (FTIR) spectroscopy, confirmed the purity, stability, and compatibility of acyclovir with the selected excipients. The formulated bigels were evaluated for organoleptic properties, pH, viscosity, spreadability, drug content, and in vitro drug release. All formulations exhibited satisfactory homogeneity, appropriate pH values suitable for topical application, and acceptable rheological properties. In vitro drug release studies demonstrated a controlled and sustained release pattern for all formulations over the study period. Among the formulations, TBG1 showed superior performance, exhibiting the highest drug content and cumulative drug release, indicating optimal polymer concentration and effective penetration enhancement. The results of this study suggest that the developed acyclovir bigel formulation represents a promising and patient-friendly topical delivery system. The incorporation of lemongrass oil highlights the potential of natural penetration enhancers in improving topical drug delivery. Overall, this work supports the suitability of bigels as an effective carrier system for the topical administration of acyclovir in the management of HSV infections.

Keywords: Acyclovir, Bigel, Lemongrass oil, Topical drug delivery, Penetration enhancer, Antiviral therapy.

INTRODUCTION

1.1.1 Topical drug delivery

Topical drug delivery is a very important route of administration, and the innovation has continued to grow steadily in the last decade. The traditional creams and ointments are still widely used, although the development of nanocarriers, microneedles, bigels, and transdermal patches has provided more clinical and therapeutic opportunities. Topical systems can bypass first-pass metabolism and achieve local therapy to improve patient adherence, but there are still challenges associated with surmounting the barrier properties of the skin and attaining dose control (Qu M et al., 2022 [30]; Zhao et al., 2024 [60]). Recent reviews highlight the fact that personalised and precision topical drug delivery with the use of optimised penetration enhancers, smart nanocarriers, and microneedle systems will dominate the next generation of formulations (Chen et al., 2022 [5]; Donnelly et al., 2021 [8]). The permeation boosting

and therapeutic effect dual property of essential oils, natural enhancers, and hybrid systems such as bigels has also grown (Francavilla et al., 2023 [11]).

Table 1.1a: Comparison of Conventional vs. Advanced Topical Drug Delivery Systems

System	Examples	Advantages	Limitations	References
Conventional Semisolids	Creams, ointments, gels	Easy to use, low cost, patient accepted	Limited penetration, frequent dosing	**Bagmar et al., 2024 [2]**
Transdermal Patches	Nicotine, fentanyl, contraceptive patches	Sustained systemic release, bypasses liver	Only for potent/lipophilic drugs, skin irritation	**Qu et al., 2022 [30]**
Nanocarriers	Transferosomes, liposomes, nanoemulsions	Increased penetration, stability, targeted delivery	Scale-up difficulty, cost, storage	**Gupta et al., 2022 [13]; Zhao et al., 2024 [60]**
Bigels	Curcumin, antifungal drugs	Combines hydrogel + organogel, controlled release, good spreadability	Phase separation risk, formulation complexity	**Rocha-Guzmán et al., 2025 [35]; Francavilla et al., 2023 [11]**
Microneedles	Insulin, vaccines, dermatological drugs	Bypasses stratum corneum, painless, good for biologics	Costly, sterility issues, regulatory barriers	**Chen et al., 2022 [5]; Donnelly et al., 2021 [8]**

Table 1.1.b: Selected Experimental and Clinical Findings

Study/System	Active Agent(s)	Model	Main Outcome	Reference
Transferosomal bigel with thyme oil	Fluconazole	Ex vivo porcine skin & antifungal assays	Better permeation + antifungal efficacy than conventional gel	**Das et al., 2023 [7]**
Bigels for curcumin	Curcumin	Synthetic Strat-M membrane	Controlled release; permeation ↑ with organogel ratio	**Rocha-Guzmán et al., 2025 [35]**
Microneedle delivery	Multiple dermatological drugs	Preclinical & clinical	Safe, effective in psoriasis, warts, hyperpigmentation	**Chen et al., 2022 [5]**
Personalized topical therapy	Various APIs	Review of clinical & lab data	Enhanced safety & dosing consistency via barrier modulation	**Zhao et al., 2024 [60]**

1.1.2 Advantages of using topical drug delivery

Topical drug delivery has a number of therapeutic and patient benefits over traditional oral and parenteral routes. The main advantage is the possibility of offering a localized effect, which involves high drug concentrations at the point of application, e.g. skin infections or inflammation, and reduced exposure to the system (Bagmar et al., 2024 [2]). Moreover, topical formulae do not have hepatic first-pass metabolism, and therefore, increase the systemic bioavailability of some drugs that would otherwise be heavily degraded in the gastrointestinal tract (Zhao et al., 2024 [60]).

Topical preparations have a higher chance of patient compliance, as they are non-invasive, painless, and easy to apply, and thus especially chronic (Alam et al., 2013 [1e]). Sustained drug release can be achieved by a variety of modern formulations such as transdermal patches or nano-based carriers that may help to reduce the frequency of dosing and enhance therapeutic results (Gupta et al., 2022 [12]). Moreover, topical administration is beneficial when it comes to indications like dermatological processes, musculoskeletal issues and mucosal administration, where an immediate targeting of drugs is beneficial (Lopes et al., 2022 [21]). The second significant benefit is the decrease in

the gastrointestinal side effects, as topical administration of drugs bypasses the stomach and the intestines, avoiding irritation, nausea, or ulceration that may cause oral therapy (Jain et al., 2021 [14]). Moreover, in cases of drugs that are supposed to produce local effect, e.g., topical anesthetics, the action starts rather quickly, and the syndrome is controlled in the short term (Chen et al., 2022 [5]).

1.1.3 Disadvantages of Topical Drug Delivery

Topical and transdermal drug delivery systems have significant limitations in spite of these benefits. The largest obstacle is the skin barrier, especially the stratum corneum that limits the penetration of hydrophilic substances and molecules with a size higher than 500 Da (Zhao et al., 2024 [60]). Consequently, the drugs possessing proper lipophilicity, molecular weight and potency only can be delivered effectively through this route. The second disadvantage is the possibility of local irritation or allergenic reactions to active drugs, excipients, or penetration enhancers, which can result in dermatitis or sensitization when used over a long period of time (Francavilla et al., 2023 [11]). Absorption variance is also an issue, as age, hydration, disease condition, ethnicity, and location of administration can cause a considerable change in permeation rates and treatment efficiency (Lopes et al., 2022 [21]). Furthermore, not all diseases can be treated topically (particularly, systemic diseases or infections), unless special carriers such as nanoparticles or microneedles are used to enhance penetration (Ranade et al., 1991 [31]). The other weakness is that the semi-solid formulations are challenging to precisely dose, and this may result in inconsistency in the dose delivered as well as in the exposure to the drug (Bagmar et al., 2024 [2]). Lastly, topical medications have the risk of unintended movement to clothes, bedding, or even other people, thus losing their efficiency and may be unsafe (Chen et al., 2022 [5]).

1.1.4 Essential Elements of Topical Drug Delivery System.

Topical drug formulations are complicated systems that should contain the active drug along with suitable excipients to provide the required stability, penetration, and patient acceptance. All the elements of the formulation contribute to the effect of releasing, absorbing, and therapeutic effects of the drug (Sharma et al., 2021 [42]). Natural penetration enhancers, biocompatible polymers, and multifunctional excipients have also been developed recently, encouraging efficacy and safety (Lopes et al., 2022 [21]; Francavilla et al., 2023 [11]).

Table 1.2: Basic Components of Topical Drug Delivery Systems (with Explanations & Recent Examples)

Component	Function	Examples	Recent Insights	References
Active Pharmaceutical Ingredient (API)	Provides the therapeutic effect	NSAIDs (diclofenac), antifungals (ketoconazole), corticosteroids	Choice of API depends on lipophilicity, potency, and molecular weight (<500 Da preferred for skin delivery)	**Jain et al., 2021 [14]; Zhao et al., 2024 [60]**
Base / Vehicle	Carries the drug; affects release and penetration	Ointment bases (petrolatum), gels (carbopol), creams (emulsion bases)	Hydrogel/organogel hybrid bases (bigels) provide dual solubility and stability	**Francavilla et al., 2023 [11]; Rocha-Guzmán et al., 2025 [35]**
Penetration Enhancers	Increase skin permeability by disrupting lipids or proteins	Propylene glycol, oleic acid, terpenes, essential oils	Recent studies explore natural oils (tea tree, jojoba, thyme) and nanocarrier-based enhancers	**Das et al., 2023 [7]; Lopes et al., 2022 [21]**
Emulsifiers	Facilitate oil–water mixing in creams/lotions	Lecithin, polysorbates (Tween), Span series	Use of phospholipid-based and biodegradable surfactants for safer delivery	**Gupta et al., 2022 [12]**
Humectants	Retain moisture, improve drug solubility	Glycerin, sorbitol, hyaluronic acid	Hyaluronic acid also acts as penetration enhancer and skin conditioner	**Bagmar et al., 2024 [2]**
Preservatives	Prevent microbial growth, prolong shelf life	Parabens, benzyl alcohol, phenoxyethanol	Shift toward "green" preservatives (plant-based antimicrobials) due to safety concerns	**Sharma et al., 2021 [42]**

Stabilizers / Antioxidants	Maintain chemical & physical stability	BHT, vitamin E (tocopherol)	Antioxidants reduce oxidative degradation and improve cosmetic acceptability	**Francavilla et al., 2023 [11]**
Thickeners / Gelling Agents	Control viscosity and spreadability	Carbopol, xanthan gum, cellulose derivatives	Smart polymers with temperature/pH responsiveness for controlled release	**Zhao et al., 2024 [60]**
Fragrances / Colorants	Improve patient acceptability	Essential oils, natural extracts	Increasing caution: many can cause irritation or allergies, so limited in medicated products	**Lopes et al., 2022 [21]**

The API is the focal ingredient, but its effectiveness highly depends on the base/vehicle selected that either makes the formulation act as an ointment, cream, gel, or patch. Bigel systems have been of interest in recent years because of their ability to combine the solubility benefits of hydrophilic (through the use of hydrogels) and lipophilic (through the use of organogels) drugs (Rocha-Guzmán et al., 2025 [35]). Penetration enhancers play an important role in the penetration of the stratum corneum barrier. But traditional enhancers, e.g. oleic acid and propylene glycol are still popular, yet more recent studies emphasize the use of essential oils and nanocarrier-based systems to enhance skin penetration in a safer way than previously used drug (Das et al., 2023 [7]). The use of supportive excipients like humectants, emulsifiers, thickeners, and stabilizers provides stability of formulations, cosmetic acceptability and controlled release profiles. In the meantime, preservatives and antioxidants ensure microbial safety and degradation prevention, but the tendency is moving toward the use of natural or biocompatible excipients in the topical formulations of the day (Sharma et al., 2021 [42]; Francavilla et al., 2023 [11]).

1.1.5 Bigels: An Overview

Bigels consist of a hydrophilic hydrogel, and a lipophilic organogel biphasic semisolid combination to create a stable and homogeneous matrix. This amphiphilic property enables the concomitant entrapment of hydrophilic and lipophilic drugs, increasing the controlled release, biocompatibility, and spreadability (Samui et al., 2021 [37]). Bigels are drawing interest in anti-inflammatory, antifungal, antimicrobial agent delivery and are better tolerated by patients than more conventional creams or ointments (Shakouri et al., 2023 [41]).

1.1.6 Preparation of Bigels

The overall process consists of three major steps:

1. Hydrogel Preparation Disperse a natural or synthetic polymer (e.g., carbopol, HPMC, chitosan) in water, swell, neutralize or cross-link.
2. Preparation of the Organogel: Dissolve in an oil phase the organogelator (fatty acid, wax, lecithin, sorbitan ester) heating it above the melting point and allowing it to solidify to a gel network.
3. Preparation of the Bigel: Add both phases in a certain proportion (typically 70:30 or 50:50 hydrogel:organogel) and stir it carefully to keep it unseparated in phase (Sreekumar et al., 2020 [53]).

Table 1.6— Preparation Methods and Key Conditions for Bigel Components

Type	Typical Components	Procedure	Critical Parameters	References
Organogel (Oleogel)	Oil phase (e.g., vegetable oil) + organogelator (fatty acids, lecithin, waxes)	Heat oil > melting point of gelator → dissolve → cool to 25 °C for gelation	Heating temperature and controlled cooling rate	**(Samui et al., 2021 [38])**
Hydrogel	Water + hydrogelator (gelatin, carbopol, chitosan)	Disperse polymer in water → stir → neutralize or crosslink → cool	pH adjustment, polymer concentration, crosslinking	**(Shakouri et al., 2023 [41])**
Bigel	Prepared organogel + prepared hydrogel	Mix in optimized ratio under gentle stirring → allow to set	Phase ratio control, viscosity balance for stability	**(Sreekumar et al., 2020 [52])**

Table 1.7 - Recent Studies on Bigel-Based Topical Formulations (2014 – 2024)

S.No.	Drug Class	Drug Name	Composition Highlights	Experimental Model / Observation	Year	Reference
1	NSAID	Flurbiprofen	Pluronic F127, lecithin, HPMC	Ex-vivo permeation & in-vitro release; sustained delivery profile	2018	**(Charyulu RN et al., 2018 [4])**
2	Antifungal	Ketoconazole	DMSO, propylene glycol, carbopol/HPMC/guar gum	Controlled and prolonged drug release in-vitro	2024	**(Das et al., 2021 [6])**
3	Antifungal	Amphotericin-B	Span-60, coconut & almond oils, propylene glycol	Controlled release and enhanced stability	2024	**(Das et al., 2021 [6])**
4	NSAID	Ketoprofen	HPMC K4M, Pluronic F127, soy lecithin	Ex-vivo permeation, gel-sol transition studies	2020	**(Sreekumar M et al., 2020 [53])**
5	Antimicrobial	Metronidazole	Sorbitan monostearate–sesame oil organogel + carbopol 934 hydrogel	Strong activity against *E. coli*	2014	**(Singh VK et al., 2014 [50])**
6	Antifungal	Ciclopirox olamine + Terbinafine HCl	Polyethylene–liquid paraffin oleogel + poloxamer 407 hydrogel	Significant inhibition of *Microsporum canis*	2017	**(Piotrowska et al., 2017 [27])**
7	Corticosteroid	Mometasone Furoate	HPMC K100M, carbopol 934/940, cottonseed oil	pH, viscosity, spreadability optimized	2022	**(Pastore et al, 2015 [25])**
8	Retinoid	Isotretinoin	Tea tree & jojoba oils, Span 60, carbopol	Ex-vivo permeation and in-vitro release profile	2020	**(Kanoujia et al., 2020 [16])**
9	Antibiotic	Doxycycline	Carbopol 940, Span-60, olive oil	Improved drug release and anti-acne activity (in vivo rabbit ear model)	2021	**(Gupta et al., 2021 [12])**

MATERIAL AND METHODS

List of Chemicals: The drugs and excipients used for the purpose of research includes following:

1.1 List of chemicals used

Table 4.1 Chemical used

S.No.	Chemicals used	Manufacturer

1.	Acyclovir	Mangalam Drugs & Organics Ltd.
2.	Olive oil	-
3.	Beewax	Research Lab fine Chem Industries, Mumbai
4.	Lemon grass oil	-
5.	Carbopol 934	Central Drug House Ltd., New Delhi
6.	Triethanolamine	Central Drug House Ltd., New Delhi
7.	Propylene glycol	Central Drug House Ltd., New Delhi
8.	Preservatives	Research Lab fine Chem Industries, Mumbai

1.2 List of Equipments and instruments:

The instruments and Equipments used are:

Table 4.2 List of Equipment's and instruments used

S. No.	Name of instrument/Equipment	Name of maker, Place	Model No.
1	UV Spectrophotometer	Shimadzu, Japan	UV-1800240V
2	FTIR spectrophotometer	Shimadzu, Japan	IR affinity-1
3	Magnetic stirrer	Remi, India	1-MLH
4	Electronic balance	Citizen, India	CX220
5	Oven	HICON, India	-
6	Homogenizer	HICON, India	-
7	Brookfield viscometer	BROOKFIELD	LDVDE

1.3 PROFILE OF EXCIPIENTS

1.3.1 Olive oil

Table 4.3 Details of Olive oil

Botanical Source	*Olea europaea* (fruit)
Appearance	Pale yellow to greenish-yellow oily liquid
Odor/Taste	Mild, characteristic odor and flavour
Solubility	Soluble in organic solvents, Insoluble in water
Melting point	−6 to −2 °C

1.3.2 Beeswax

Table 4.4 Details of Beeswax

Pharmaceutical Name	*Cera alba* (white beeswax), *Cera flava* (yellow beeswax)
Source	Secreted by honeybees (*Apis mellifera*) to build honeycombs
Odor	Characteristic honey-like odor
Taste	Bland, slightly honey-like
Solubility	Insoluble in water,Soluble in hot alcohol, chloroform, ether, and fixed oils
Melting Point	61–65°C (Cera flava), 62–67°C (Cera alba)

1.3.3 Carbopol 934

Table 4.5 Details of Carbopol 934

Chemical Formula	[–CH2–CH(COOH)–]n (cross-linked)
Trade Name	Carbopol® 934
Generic Name	Carbomer 934
Chemical Class	synthetic high-molecular-weight cross-linked polyacrylic acid polymer
Appearance	White, fluffy, hygroscopic powder
Odor/Taste	Odourless and tasteless
Solubility	Swells in water and alcohol to form a colloidal dispersion; not soluble in oils

1.3.4 Lemongrass oil

Table 4.6 Details of Lemongrass oil

Botanical Source	*Cymbopogon flexuosus* (East Indian lemongrass) or *Cymbopogon citratus* (West Indian lemongrass)
Family	Poaceae (Gramineae)
Used	Fresh or dried leaves (via steam distillation)
Appearance	Yellow to amber-colored volatile oil
Odor	Strong lemon-like scent due to high citral content
Chemical Composition	volatile monoterpenes and aldehydes, with citral
Boiling Point	~230–240°C
Solubility	Soluble in oils, alcohol, and organic solvents; Insoluble in water

1.4 Preformulation studies

Prior to starting pre-formulation studies, it is important to have a solid understanding of the drug's properties, dose, potency in comparison to dosage form. We should also conduct a literature search for information on stability and degradation, the suggested route of administration, formulation strategies, and the bioavailability and pharmacokinetics of drugs that are chemically related. By ascertaining the kinetic rate profile, compatibility with other ingredients, and physicochemical properties, a pre-formulation study seeks to develop a stable, elegant, safe, and effective dosage form.

The following pre-formulation studies were carried out on-

1. Organoleptic properties
2. Melting point
3. Partition coefficient
4. TLC
5. Solubility
6. Preparation of standard curve
7. Preparation of calibration curve
8. pH
9. FTIR

1.4.1 Organoleptic properties

The drug was observed for its appearance, color and odour.

1.4.2 Melting point

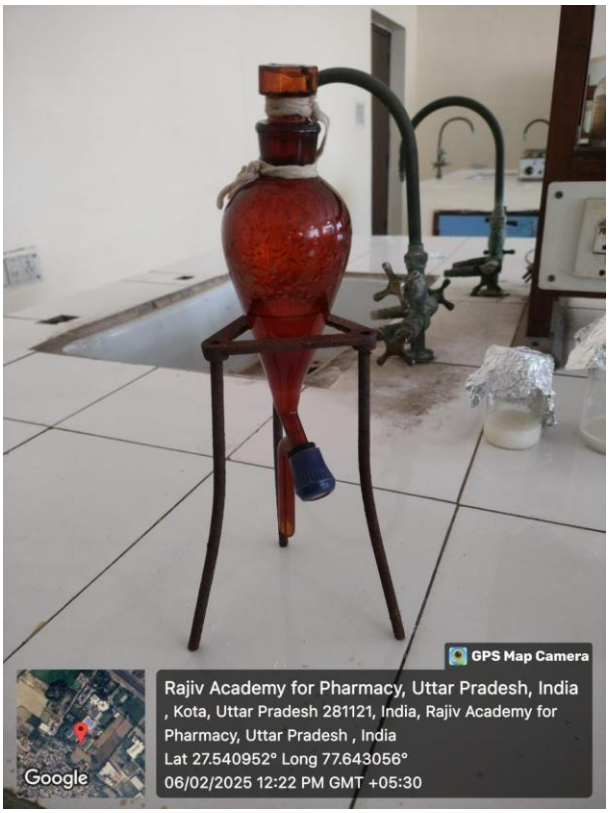
By using the open capillary method and the melting point apparatus, the melting point of acyclovir drug was determined.

1.4.3 Partition Coefficient Determination in Octanol-Water

To determine partition coefficient, 50 mg of drug was dissolved in 20 ml solvent (10 ml n-octanol and 10 ml water). Then the flasks were shaken vigorously, and the two phases were allowed to separate. The two phases were collected separately and solutions were filtered, diluted and were analyzed using UV spectrophotometer.

$P_{o/w} = C_o / C_w$

Where Co = concentration of drug in n-octanol, Cw = concentration of drug in water



Thin layer chromatography

According to British Pharmacopeia, TLC is a separation method that may be used to separate and identify various substances or components in a combination.

'Mobile phase – n butanol : glacial acetic acid : water - 15 ml : 9ml : 6 ml
Stationary phase – silica gel
RF value -0.50-0.62

$$Rf = \frac{\text{Distance travelled by the compound (spot)}}{\text{Distance travelled by the solvent front}}$$

Procedure –
We prepare a solution of mobile phase
Then take TLC plates and prepare silica gel in motar pestle
After preparation, we spread silica gel on TLC plate and keep it 24 hrs
Next day take tween chamber and marked TLC plate upto 2 cm and spoting drug on TLC and keep on chamber for 75 min

After 75 min we perform on uv chamber to observe

Figure 4.1 TLC plate of Acyclovir

Solubility

Take excess amount of drug and cleaned culture tube contain 10 ml of various solvent ethanol, phosphate buffer (6.8), water, and DMSO add 100 mg drug .tube securely sealed and shaken for 24 hours at room temperature on a water bath shaker set 25˚c then after shaking each sample was centrifuged at 15000 rpm for 24 hours to separate supernatant was carefully removed and filtered appropriately dilute and concentration using spectrophotometry to determine solubility of drug in each solvent Identification of drug by UV spectrophotometry Preparation of standard curve Preparation of stock solution 100mg of drug was weighed and dissolved in 100ml distilled water. From the above solution, 1000µg/ml solution was prepared by taking 1ml from above solution and diluting up to 10ml with distilled water. The resultant solution was scanned in the UV region (400nm) using UV spectrophotometer (Shimadzu, UV-1800240.

Standard curve of acyclovir in water

To make standard dilutions of 2, 4, 6, 8, 10, 12, 14, and 20 µg/ml from 1000 µg/ml solution, aliquots of 0.2, 0.4, 0.6, 0.8, 0.10, 0.12, 0.14, and 1 ml were transferred into 10 ml volumetric flasks, and the volume was adjusted to the mark. After measuring the absorbance, a graph was created that showed the absorbance against concentration.

Figure 4.2 UV spectrum of acyclovir in water with λmax 253nm

Calibration curve of acyclovir in phosphate buffer 7.4

For 250 ml – 6.8045 gm KH_2PO_4 are dissolved in distilled water and dilute 250ml distilled water For 250 ml – 2gm NaOH are dissolved in distilled water and diluted 250 ml From 1000µg/ml solution, standard dilutions of 2, 4, 6, 8,10,12,14 and 20 µg/ml were prepared by transferring aliquots of 0.2, 0.4, 0.6, 0.8,0.10,0.12,0.14 and 1ml in 10ml volumetric flasks and volume was made up to mark. The absorbance was measured and graph was plotted between and concentration and absorbance.

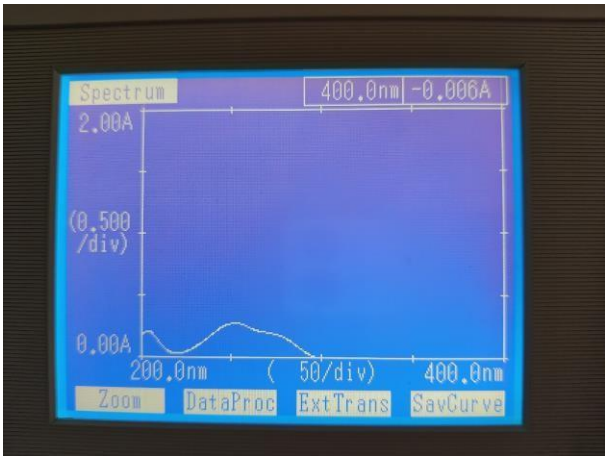


Figure 4.3 UV spectrum of acyclovir in phosphate buffer 7.4 with λmax 253nm

1.4.7 pH

The pH of drug solution in water was measured using a digital pH meter.

1.4.8 Fourier Transform Infrared Spectroscopy of acyclovir

In a glass mortar and pestle, the medication and potassium bromide were combined separately and then triturated. Using an infrared spectrophotometer (Shimadzu, IR affinity-1), the triturated mixture was compressed and then processed for FTIR spectra by scanning in the 4000-400 cm-1 range. The spectra offer comprehensive details on the

structural configurations of molecular compounds since FTIR is associated with covalent or hydrogen bonds. FTIR is used to verify the drug's functional identification and identify any interactions it may have with excipients.

1.5 Formulation Development

1.5.1 Screening of hydrophilic polymer for hydrogel

Separately, Carbopol 934, HPMC K100M, and Carbopol 940 were soaked in distilled water for 24 hours at varying concentrations (1%, 1.5%, and 2%). Viscosity, spreadability, and visual examination were used to screen the hydrogel.

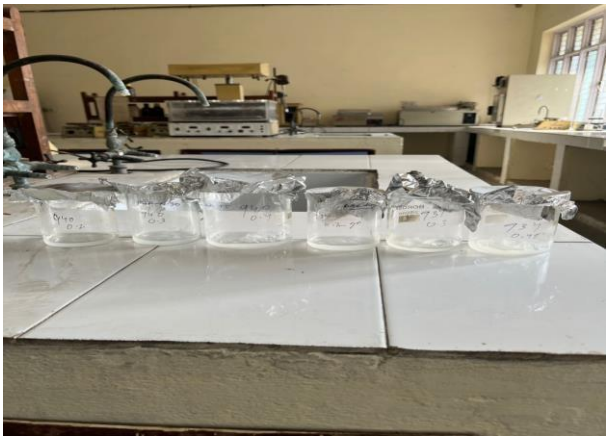


Figure 4.4 Different compositions of hydrogels

1.5.2 Screening of oils for organogel

Based on the drug's solubility in oils, a variety of oils were evaluated. The drug's solubility in lemon, peppermint, olive, eucalyptus, and sesame oils was examined. Acyclovir's solubility in oil served as the basis for the selection. For seventy-two hours, excess acyclovir was poured to each capped glass vial that held five milliliters of oils on a motorized mixer. For ten minutes, the resultant dispersion was centrifuged at 15,000 rpm. Filtrates were tested after being suitably diluted. Using the same medium as the blank, the absorbance of solutions was measured at 253 nm using a double beam UV spectrophotometer.

1.5.3 Screening of thickening agent for organogel

The thickening ingredient was chosen based on the organogel's appearance, viscosity, and spreadability. Different types of beeswax, span 60 (sorbitan monostearate), stearic acid, and olive oil in varying concentrations (5%, 10%, and 15%) were used to create organogels.

1.5.4 Screening of ratio of hydrogel and organogel for bigel formulation

Hydrogel and Organogel swere screened according to their appearance, viscosity, and spreadability. Different ratios of hydrogel and organogel (50:50, 60:40, 70:30, 80:20, and 90:10) were used to create the bigel. In hydrogel, the medication (%) was distributed.

Figure 4.5 Different compositions of Organogels

1.6 Preparation of acyclovir loaded bigel containing lemongrass grass oil

Step 1 – Preparation of Hydrogel

Firstly, we prepared a hydrogel, take a weighed quantity of ingredients, drug and essential oil. Then Acyclovir drug was dissolved in water and stir for few minutes after that hydrophilic polymer Carbopol 934, propylene glycol was added and keep it aside for few minutes then added lemongrass oil and triethanolamine dropwise in hydrogel at room temperature.

Step 2 – Preparation of Organogel

Take olive oil for organogel and add thickening agen beeswax and heat the solution at 50 to 70˚c with continuous stirring.

Step 3 – Preparation of Bigel

After making hydrogel and organogel separately, we slowly added organogel in hydrogel dropwise with continuous stirring.

Table 4.7 Composition of Bigel

Contents	TBG1	TBG2	TBG3	TBG4	TBG5
Acyclovir (g)	5.00	5.00	5.00	5.00	5.00
Carbopol 934 (g)	0.5	1	1.5	2	2.5
Propylene glycol (ml)	5	5	5	5	5
Beewax (gm)	7.5	7.5	7.5	7.5	7.5
Olive oil(ml)	41.4	41.4	41.4	41.4	41.4
Lemongrass oil (ml)	2-3 drops	2-3drops	2-3drops	2-3drops	2-3drops
Purified water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Triethanolamine (q.s)	To adjust pH 6-7				

1.7 Evaluation of bigel

- **Viscosity**

Using spindle number 63, the Brookfield viscometer was used to evaluate the viscosity of the formulated bigel. For every bigel, the process was carried out three times. The angular velocity was maintained at 50 rpm for the test,

which was carried out at room temperature.

- **Spreadability**

To assess spreadability, excess bigel was sandwiched between two glass slides and crushed to a uniform thickness by holding a weight (in grams) for five minutes. The pan was filled with weight (in grams). Spreadability may be measured by measuring the amount of time needed to separate the two slides, which is the time for the upper glass slide to move across the bottom plate. For every bigel, the process was carried out three times.
S= (m×l)/t
"S= Spreadability
l=Length moved on upper glass slide
m=Weight tied to upper slide.
t=Time taken"

- **pH of bigel**

The precisely weighed bigel was dissolved in 10 milliliters of pure water, and the pH of the resulting mixture was then measured at 25 °C using a digital pH meter. For every formulated bigel, the process was carried out three times.

- **Drug content**

A 'UV visible double beam spectrophotometer' was used to measure the filtered material at 253 nm after 1g of the bigel was dissolved in 25 ml of phosphate buffer pH 5.5 and the proper dilutions were prepared using the same buffer solution.

- **In vitro drug release**

A modified in vitro permeation equipment and an egg membrane was used to perform in vitro drug release. The study's dissolving media was phosphate buffer, which has a pH of 7.4. The study's egg membrane was immersed in phosphate buffer throughout the whole night. After precisely weighing two grams, the bigel was put over the middle section of the egg membrane, which was then secured to one of the opening ends of the hollow glass cylinder. The glass cylinder was then attached to the iron shaft and dipped until the membrane just touched the 50 milliliters of phosphate buffer. Throughout the investigation, a magnetic stirrer set at 50 rpm was used to keep the dissolving medium at 37 +/- 0.5 °C. This temperature was maintained until the experiment's conclusion. Five milliliter aliquots of the receptor medium sample were taken out and filtered within a predetermined time frame. After diluting each filtered sample, the absorbance at 253 nm was determined using a UV spectrometer (Elias, 2019 [9]).

1.2 Rationale of the work

Present work deals with acyclovir drug bigel system for the treatment of herpes simplex virus so as to gain various advantages such as improved bioavailability, patient-compliance, sustained and controlled delivery of drugs.

The vast family of herpesviruses includes the Herpes simplex virus types 1 (HSV-1) and 2 (HSV-2). Together with varicella-zoster, they are further classified in the Alpha herpes virinae subfamily. These viruses can establish latency within sensory ganglia, have a brief reproductive cycle, and destroy the host cell quickly. HSV-1 is widely known for producing encephalitis and orofacial lesions in both adults and children, albeit these conditions are not exclusive. Aseptic meningitis, genital herpes, and severe infections in newborns are all brought on by HSV-2. The diagnosis and treatment of many illnesses have advanced significantly (Singh et al., 2024 [49]).

Acyclovir is a widely used antiviral drug, primarily indicated for the treatment of herpes simplex virus (HSV) infections, including genital herpes, cold sores, and varicella zoster virus (VZV) infections. While oral administration of acyclovir is common, it is associated with systemic side effects, and for topical treatments, the drug's limited skin permeation significantly reduces its therapeutic efficacy. Achieving an effective topical concentration of acyclovir at the site of infection is a key challenge in the development of dermatological formulations (Klysik et al., 2020 [18]). To enhance the transdermal delivery of acyclovir, a topical drug delivery system that can overcome the stratum corneum barrier (the outermost layer of the skin) is essential. One promising approach is the formulation of bigels, which combine the benefits of hydrogels and oleogels. Bigels are known for their superior skin penetration, controlled release, and high bioavailability of active ingredients due to their dual-phase structure. The oleophilic (oil) and hydrophilic (water) components in the bigel matrix facilitate the release and absorption of drugs, especially those with both hydrophilic and lipophilic properties.

However, even with bigels, penetration enhancement remains a key challenge in transdermal drug delivery. Lemongrass oil (Cymbopogon citratus) has garnered attention for its ability to enhance the permeability of the skin. Rich in citral, lemongrass oil is known to disrupt the skin's lipid barrier and increase drug diffusion across the epidermis, making it a suitable candidate for use as a penetration enhancer in topical formulations. Unlike synthetic

enhancers, lemongrass oil is biocompatible, non-toxic, and naturally derived, aligning with the increasing demand for green pharmaceutical formulations.

Incorporating lemongrass oil into a bigel formulation for acyclovir could significantly improve the drug's permeability and bioavailability at the site of action, thus enhancing its therapeutic efficacy for topical antiviral treatment. Despite the potential of combining bigels and lemongrass oil, limited research has been conducted on their synergistic effects, particularly in the case of acyclovir.

RESULTS AND DISCUSSION

2.1 Organoleptic properties

Table 5.1 Organoleptic properties of Acyclovir

Appearance	White powder
Color	White
Odour	Odourless

2.2 Determination of melting point (MP)

Capillary fusion method was used to determine the melting point of acyclovir using capillary tube melting point apparatus. Firstly, small amount of sample was filled in the capillary tube. After that, the capillary was placed in capillary holder and thermometer was kept in another holder and temperature was measured. The melting point of drug was fount between 254-256˚c.

Table 5.2 M.P. of Acyclovir

Name of drug	MP (˚C)	Average melting point (˚C)
Acyclovir	254˚C	255˚C
	256˚C	
	255˚C	

2.2 Determination of melting point (MP)

Capillary fusion method was used to determine the melting point of acyclovir using capillary tube melting point apparatus. Firstly, small amount of sample was filled in the capillary tube. After that, the capillary was placed in capillary holder and thermometer was kept in another holder and temperature was measured. The melting point of drug was fount between 254-256˚c.

Table 5.2 M.P. of Acyclovir

S. No	Partition coeffiecient	Average
1.	0.86	0.84
2.	0.84	
3.	0.82	

2.4 Thin layer chromatography

Retention factor was calculated with the help of formula that is distance travelled by the sample divided by distance travelled by solvent and value found to similar or quite equal to literature value that indicate identity and purity of the drug.RF value reported was 0.66 as mention below Calculation = RF value = 10/15=0.66

2.5 Determination of solubility

Table 5.4 Solubility of Acyclovir

S.no	Solvent	Solubility
1	Ethanol	Very slightly soluble
2	Water	Slightly soluble

3	DMSO	Highly soluble
4	Phosphate buffer ph 6.8	Slightly soluble

2.6 Preparation of standard curve in Distilled water

Concentration (µg/ml)	Absorbances
2	0.076
4	0.142
6	0.214
8	0.276
10	0.328
12	0.389
14	0.440

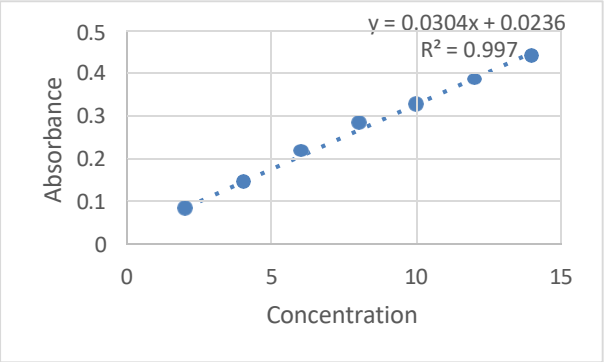


Figure 5.1 standard curve of Acyclovir in Distelled water

2.7 Calibration curve in phosphate buffer 7.4

Concentration (µg/ml)	Absorbances
2	0.073
4	0.152
6	0.212
8	0.284
10	0.325
12	0.396
14	0.457

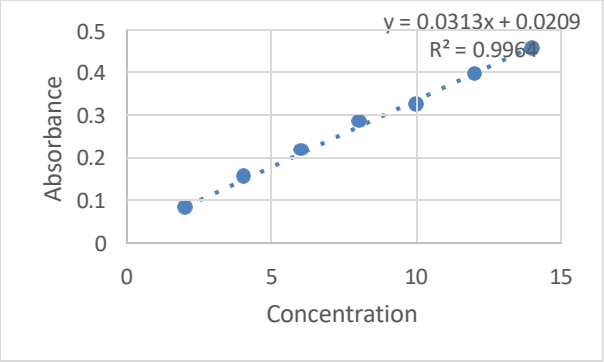


Figure 5.2 Calibration curve of Acyclovir in phosphate buffer

2.8 Fourier Transform Infrared Spectroscopy of acyclovir

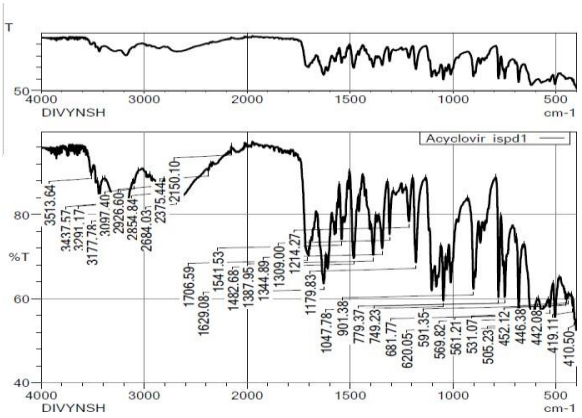


Figure 5.3 FTIR of Acyclovir

Table 5.5 Interpretation of FTIR of Acyclovir

Wavenumber (cm^{-1})	Functional Group / Vibration	Interpretation / Assignment
3513.64	O–H/N–H stretching	Strong broad peak indicates hydrogen bonding (alcohols or amines)
3443.77	N–H stretching	Primary or secondary amine group
3177.17	C–H (aromatic) stretching	Aromatic ring presence
3097	C=C (alkene) stretching	Alkene groups present
2926.60, 2854.84	C–H (alkane) stretching	Methylene/methyl groups (aliphatic chains)
1629.08	C=C / C=N stretching	Conjugated system in purine ring
1541.53	N–H bending (amide II band)	Amide functional group
1482.95, 1387.99	C–H bending (CH_3, CH_2)	Aliphatic side chains
1344.89	C–N stretching	Amine or amide group
1214.27, 1179.83	C=O ring vibrations	Possible ether linkage
1047.78, 1014.71	C–N stretching	Possible nitrogen linkage

Drug–Excipient compatibility studies

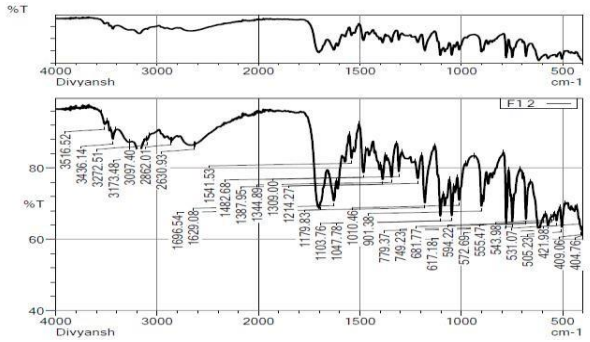


Figure 5.4 FTIR of mixture of acyclovir and carbopol 934

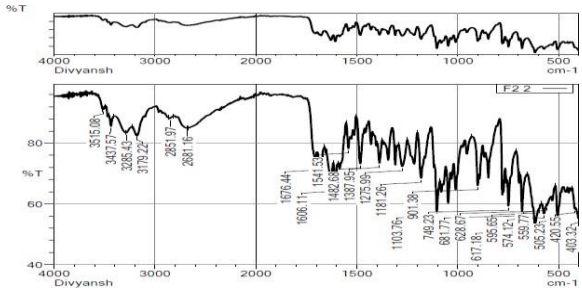


Figure 5.5 FTIR of mixture of acyclovir and methyl paraben

Verifying that the medicine and the polymer to be used are compatible and that the drug is not reacting with the polymer is essential when creating a formulation for the creation of the final dosage form. Fourier Transform Infrared Spectroscopy, or FTIR, can be used to ascertain it.

2.10 Screening of hydrophilic polymer for hydrogel

By screen out different hydrophilic polymer like HPMC K 100 M, Carbopol 934, Carbopol 940 we find out that 1% Carbopol 934 shows better appearance, spreadibilty and texture.

Table 5.6 Composition of hydrogels

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
HPMC K 100 M (%)	1	1.5	2	-	-	-	-	-	-
Carbopol 934 (%)	-	-	-	1	1.5	2	-	-	-
Carbopol 940 (%)	-	-	-	-	-	-	1	1.5	2
Distilled water (q.s) Ml	100	100	100	100	100	100	100	100	100

2.11 Screening of thickening agent for organogel

By screenout different organogelators like beeswax, stearic acid, span 60 we find out that 15% beeswax shows better appearance, spreadibilty and texture.

Table 5.7 Composition of organogel

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bees wax (%)	5	10	15	-	-	-	-	-	-
Stearic acid (%)	-	-	-	5	10	15	-	-	-
Span 60(%)	-	-	-	-	-	-	5	10	15
Olive oil (ml)	100	100	100	100	100	100	100	100	100

2.12 Screening of ratio of hydrogel and organogel for bigel formulation

We carried out screening of ratio of hydrogel and oraganogel by mixing in different proportion with the help of literature survey. We found 50:50 ratio is more suitable for further formulation based on their appearance, spreadability, texture.

Table 5.8 Ratio of different composition of hydrogel and organogel

Hydrogel (g)	50	60	70	80	90
Organogel (g)	50	40	30	20	10
Triethanolamine q.s (ml)	Q.S	Q.S	Q.S	Q.S	Q.S

2.13 Evaluation of bigel

- **Organoleptic properties**

All the formulations are evaluated on the basis of color, texture and homogeneity etc. all the formulation shown satisfactory results, that are mentioned in the given table 5.9.

Table 5.9 Organoleptic properties of Formulated Bigel

Formulation code	colour	Texture	Stability after (48 hours)
TBG1	White	Smooth	Stable
TBG2	White	Smooth	Stable
TBG3	White	Soft	Stable
TBG4	White	Soft	Stable
TBG5	yellowish	Rough	Stable

Viscosity

Amoung all the formulation TBG4 show lower while TBG3 show the highest across different rpm rang as shown in the table 5.10.

Table 5.10 Viscosity of formulated Bigel

Formulation code	Viscosity(cps)
TBG1	11570
TBG2	11550
TBG3	11590
TBG4	11545
TBG5	11565

Spreadability

Amoung all the formulation TBG5 show lower while TBG4 show the highest spreadability value as mentioned in given table 5.11.

Table 5.11 Spreadability of formulated Bigel

Formulation code	Spreadabilty (mm)
TBG1	18.29
TBG2	15.86
TBG3	16.70
TBG4	20.55
TBG5	12.35

pH of bigel

The pH of the formulation should be ranged between 5 to 7. The pH of the Prepared formulation found between 5 to 7 as mentioned in given table 5.12.

Table 5.12 pH for formulated Bigel

S.No	Formulation code	pH
1	TBG1	5.54

2	TBG2	6.0
3	TBG3	6.2
4	TBG4	6.3
5	TBG5	5.50

Drug content

The range of 74.32-94.55 was determined to contain the medication concentration of formulations TBG1 through TBG5.

Table 5.13 Drug content of formulated Bigel

Formulation code	%Drug content
TBG1	94.55±0.42
TBG2	78.20±0.55
TBG3	86.88±0.24
TBG4	90.15±0.45
TBG5	74.32±0.9
Values are expressed as mean ±S.D.	

- **In vitro drug release**

The in-vitro drug release profile of the five bigel formulations (TBG1 to TBG5) demonstrates a sustained and progressively increasing release pattern over a 180-minute period. Among the formulations, TBG1 exhibited the highest cumulative drug release (%CDR) at each time point, reaching 70.85% at 180 minutes, indicating the most efficient release. This was closely followed by TBG2 (68.88%), TBG3 (66.84%), TBG4 (66.08%), and TBG5 (64.61%). The drug release rate gradually increased for all formulations, with TBG5 consistently showing the lowest %CDR, suggesting that variations in the hydrogel and organogel composition directly influence the release kinetics. Overall, the formulations showed controlled and sustained drug release, ideal for topical therapeutic applications. Overall, the results suggest that TBG1 is the most promising formulation in terms of drug release efficiency, likely due to its optimal balance of hydrogel and organogel phases and better integration of the penetration enhancer (lemongrass oil). These findings support its selection for further development and evaluation in topical delivery applications.

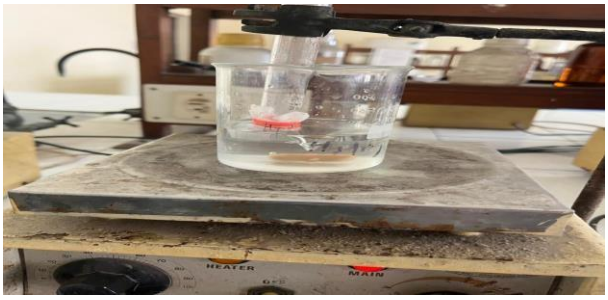


Figure 5.6 In-vitro drug release testing of formulated Bigel

TBG1

Table 5.14 In-vitro release kinectis of TBG1

Time (minutes)	Absorbance	Conc. (µg/ml)	Drug in 5ml (µg)	Drug in 20ml (µg)	Drug in 5ml (mg)	Drug in 20ml (mg)	CDR (µg)	%CDR
30	0.680	0.3269	1.6345	32.69	0.001635	0.03269	32.69	4.67
60	1.087	0.5226	2.6130	52.26	0.002613	0.05226	84.95	12.14

90	1.582	0.7606	3.8030	76.06	0.003803	0.07606	161.01	23.00
120	1.987	0.9543	4.7715	95.43	0.004772	0.09543	256.44	36.63
150	2.295	1.1024	5.5120	110.24	0.005512	0.11024	366.68	52.38
180	2.690	1.2928	6.4640	129.28	0.006464	0.12928	495.96	70.85

TBG2

Table 5.15 In-vitro release kinetics of TBG2

Time (minutes)	Absorbance	Conc. (µg/ml)	Drug in 5ml (µg)	Drug in 20ml (µg)	Drug in 5ml (mg)	Drug in 20ml (mg)	CDR (µg)	%CDR
30	0.645	0.3101	1.5505	31.01	0.001551	0.03101	31.01	4.43
60	1.052	0.5058	2.5290	50.58	0.002529	0.05058	81.59	11.65
90	1.498	0.7202	3.6010	72.02	0.003601	0.07202	153.61	21.94
120	1.915	0.9207	4.6035	92.07	0.004604	0.09207	245.68	35.10
150	2.268	1.0904	5.4520	109.04	0.005452	0.10904	354.72	50.67
180	2.651	1.2745	6.3725	127.45	0.006373	0.12745	482.17	68.88

TBG3

Table 5.16 In-vitro release kinetics of TBG3

Time (minutes)	Absorbance	Conc. (µg/ml)	Drug in 5ml (µg)	Drug in 20ml (µg)	Drug in 5ml (mg)	Drug in 20ml (mg)	CDR (µg)	%CDR
30	0.615	0.2957	1.4785	29.57	0.001479	0.02957	29.57	4.22
60	1.020	0.4904	2.4520	49.04	0.002452	0.04904	78.61	11.23
90	1.423	0.6832	3.4160	68.32	0.003416	0.06832	146.93	20.99
120	1.842	0.8856	4.4280	88.56	0.004428	0.08856	235.49	33.64
150	2.233	1.0736	5.3680	107.36	0.005368	0.10736	342.85	48.98
180	2.600	1.2500	6.2500	125.00	0.006250	0.12500	467.85	66.84

TBG4

Table 5.17 In-vitro release kinetics of TBG4

Time (minutes)	Absorbance	Conc. (µg/ml)	Drug in 5ml (µg)	Drug in 20ml (µg)	Drug in 5ml (mg)	Drug in 20ml (mg)	CDR (µg)	%CDR
30	0.598	0.2875	1.4375	28.75	0.001438	0.02875	28.75	4.11
60	1.010	0.4856	2.4280	48.56	0.002428	0.04856	77.31	11.04
90	1.400	0.6731	3.3655	67.31	0.003366	0.06731	144.62	20.66
120	1.805	0.8678	4.3390	86.78	0.004339	0.08678	231.40	33.06
150	2.220	1.0673	5.3365	106.73	0.005337	0.10673	338.13	48.30

180	2.590	1.2442	6.2210	124.42	0.006221	0.12442	462.55	66.08

TBG5

Table 5.18 In-vitro release kinetics of TBG5

Time (minutes)	Absorbance	Conc. (µg/ml)	Drug in 5ml (µg)	Drug in 20ml (µg)	Drug in 5ml (mg)	Drug in 20ml (mg)	CDR (µg)	%CDR
30	0.570	0.2740	1.3700	27.40	0.001370	0.02740	27.40	3.91
60	0.980	0.4711	2.3555	47.11	0.002356	0.04711	74.51	10.64
90	1.355	0.6514	3.2570	65.14	0.003257	0.06514	139.65	19.95
120	1.775	0.8524	4.2620	85.24	0.004262	0.08524	224.89	32.13
150	2.180	1.0481	5.2405	104.81	0.005241	0.10481	329.70	47.10
180	2.550	1.2259	6.1295	122.59	0.006130	0.12259	452.29	64.61

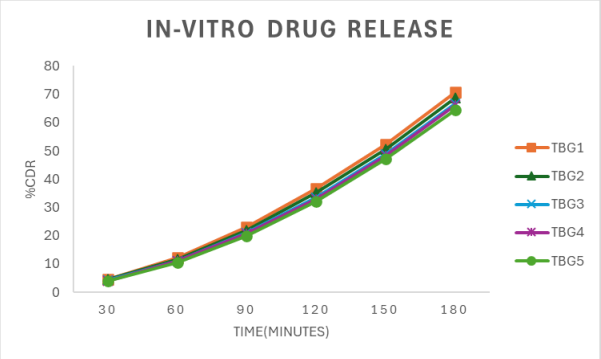


Figure 5.7 In-vitro drug release graph for the five bigel formulations (TBG1 to TBG5)

Release kinetic modelling

To find the acyclovir release profile from the formulated bigel, kinetic model was applied to the optimal formulation, TBG1. Based on the findings, it was discovered that the formulation TBG1 had sustained pharmacological action, exhibited zero order kinetics, had a higher R2 value of 0.988 and released the drug slowly.

Table 5.19 Release kinetic data for model fitting

Time (min)	√t	log t	%CDR	% Drug Remaining	log %CDR	log % Drug Remaining
30	5.48	1.477	4.67	95.33	0.670	1.979
60	7.75	1.778	12.14	87.86	1.084	1.944
90	9.49	1.954	23.00	77.00	1.362	1.886
120	10.95	2.079	36.63	63.37	1.564	1.802
150	12.25	2.176	52.38	47.62	1.719	1.678
180	13.42	2.255	70.85	29.15	1.850	1.464

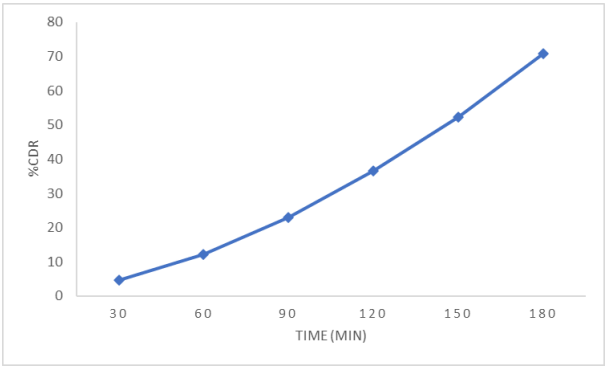


Figure 5.8 Zero order release of formulation TBG1

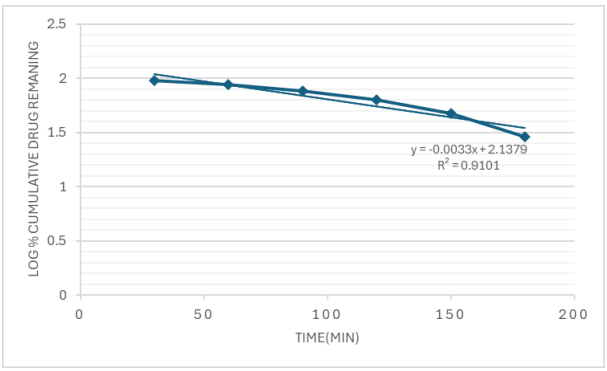


Figure 5.9 First order release of formulation TBG1

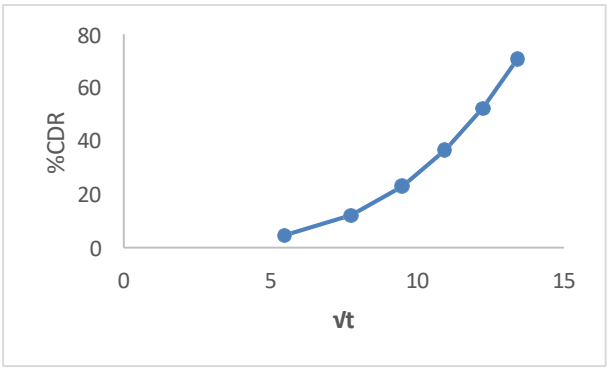


Figure 5.10 Higuchi model

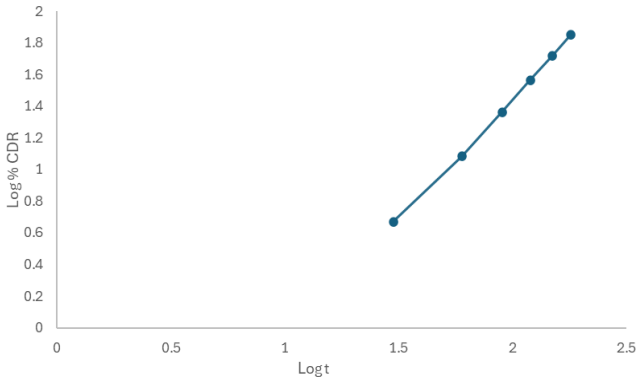


Figure 5.11 Korsmeyaer-Peppas model

Table 5.20 R2 numbers for several kinetic release models used in the TBG1 formulation

Formulation code	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyer-Peppas R^2	Model fitting

TBG1	0.982	0.910	0.988	0.963	Higuchi model

DISCUSSION

The current research was done to prepare and evaluate a topical delivery system of acyclovir using a bigel as the base and integrate lemongrass oil, a natural penetration enhancer, so as to enhance drug release and penetration and retain appropriate physicochemical properties to be used topically. Biphasic systems composed of hydrogel and organogel networks (Bigels) combine the advantages of lipophilic systems and hydrophilic systems and are particularly successful with topical delivery of drugs with low skin penetration such as acyclovir.

Pre formulation studies validated the identity, purity and physicochemical suitability of acyclovir to be used as a topical formulation. The melting point of Acyclovir (254-256˚C) was observed to be very consistent with the values provided in the literature implying stability of the drug and purity. The studies of the partition coefficient revealed moderate lipophilicity, which means that intrinsic skin penetration cannot be performed easily and that a penetration-enhancing delivery system is needed. The necessity of a bigel system together with penetration enhancers to enhance the topical bioavailability can also be justified by the solubility studies that demonstrated that acyclovir is highly soluble in DMSO and only slightly soluble in water and buffer. Acyclovir's FTIR analysis verified the existence of distinctive functional groups, and drug-excipient compatibility tests revealed no appreciable changes or disappearance of peaks, indicating absence of chemical interaction between acyclovir and formulation excipients such as Carbopol 934 and preservatives. This confirms the chemical stability of the drug within the bigel matrix.

Assessment of Bigel Formulations

There were no indications of phase separation or grittiness, and all of the bigels that were created were found to be smooth, homogeneous, and physically stable. All of the formulations' pH values fell between 5.5 and 6.3, which is within the acceptable range for topical application and is not likely to irritate the skin. Measurements of viscosity showed that an increase in Carbopol concentration led to an increase in viscosity, which is consistent with densification of the polymer network. Viscosity and spreadability values were inversely correlated; formulations with moderate viscosity were more spreadable. For topical formulations to guarantee patient compliance and ease of application, this balance is essential.

Although TBG1 had the highest drug content, indicating better drug distribution within the matrix at lower polymer, drug content analysis showed acceptable uniformity across all formulations.

In Vitro Drug Release Studies

The in vitro drug release experiments showed that all bigel preparations had a controlled and sustained release profile in 180 minutes. TBG1 showed the best cumulative drug release as compared to TBG2, TBG3, TBG4, and TBG5. This decreasing release rate with increasing polymer concentration can be explained by the fact that the higher the concentration of polymer, the higher the viscosity and the polymeric networks the slow diffusion of drugs.

This increase in the drug release could be attributed to a good balance between the hydrogel and organogel phases, reduced polymer density, and efficient penetration enhancement with lemongrass oil in TBG1. The occurrence of the organogel phase may have enabled the better partitioning of acyclovir into the lipid domain whereas the existence of the hydrogel phase ensured the hydration of stratum corneum, which along with the above-mentioned feature enhanced the diffusion of the drug.

The kinetic analysis of release indicated that the release of the drug was based on the diffusion-controlled action, which is characteristic of semi-solid polymeric system. The following system of bigel was, therefore, effective in giving sustained release and keeping the drug level sufficient at the point of application.

The results obtained in this research paper show clearly that bigels can be used as a promising topical delivery system of acyclovir. The use of lemongrass oil as a natural penetration enhancer played a significant role towards increased performance of the drug release. Compared to all formulations, TBG1 was the optimized formulation with good physicochemical properties, maximum drug content, and good in vitro drug release.

The study helps to justify the effectiveness of partnership between natural bioactive product and modern drug delivery methods to promote effectual therapy with preserving formulation safety and patient tolerance.

The kinetic analysis of release indicated that the release of the drug was based on the diffusion-controlled action, which is characteristic of semi-solid polymeric system. The following system of bigel was, therefore, effective in giving sustained release and keeping the drug level sufficient at the point of application.

Conclusion

Among the various formulations developed, TBG1 emerged as the most effective based on its superior

drug release profile and good physicochemical stability. Characterization studies revealed that TBG1 possessed desirable rheological properties, homogeneity, and compatibility between the phases, making it a promising carrier for acyclovir. The inclusion of lemongrass oil not only contributed to the improved penetration of the drug through the skin but also offered additional antimicrobial and soothing properties, supporting its use in dermatological applications.

This research supports the potential of bigel systems, especially those incorporating natural bioenhancers, as efficient and sustainable alternatives to conventional topical therapies. The findings contribute valuable insights to the growing field of novel drug delivery systems and pave the way for future studies focusing on clinical validation and broader therapeutic applications.

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