Development and Optimization of a Polyherbal Anti-Acne Emulgel Containing Aloe vera, Tea Tree Oil, Rosemary Oil, and Turmeric Oil Using a Quality by Design Approach

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Abstract

Acne vulgaris is a common inflammatory skin disorder associated with excessive sebum production, follicular blockage, microbial colonization, and inflammation. Conventional therapies may cause irritation and antimicrobial resistance, creating a need for safer and more effective alternatives. Polyherbal topical systems offer a promising approach due to their antimicrobial, antioxidant, and anti-inflammatory properties.

Objective: The present study aimed to develop and optimize a polyherbal anti-acne emulgel containing Aloe vera, tea tree oil, rosemary oil, and turmeric oil using a Quality by Design (QbD) approach to improve topical delivery and therapeutic efficacy against acne.

The emulgel was prepared using an emulsion-incorporation technique and optimized through Response Surface Methodology. Formulations were evaluated for physicochemical characteristics, drug content, pH, viscosity, spreadability, extrudability, particle size, in-vitro drug release, antioxidant activity, and antimicrobial efficacy against *Cutibacterium acnes*. Compatibility studies were performed using FTIR and DSC analyses.

Compatibility studies confirmed the absence of significant interactions between herbal actives and excipients. The optimized formulation (F5) exhibited satisfactory physicochemical properties, including pH (5.81 ± 0.04), viscosity (5018 ± 60 cP), spreadability (18.03 ± 0.29 g·cm/s), and extrudability (146.07 ± 1.76 g/cm²). Particle size analysis showed a Z-average size of 616.0 nm with acceptable dispersion characteristics. The formulation demonstrated sustained drug release (86.5 ± 2.3% at 300 min), significant antioxidant activity, and pronounced antimicrobial activity against *Cutibacterium acnes*, producing a zone of inhibition of 17.8 ± 0.35 mm, corresponding to 90.8% activity relative to marketed clindamycin gel. Statistical optimization showed strong model predictability ($R^2 = 0.958$).

Conclusion: The QbD-optimized polyherbal emulgel demonstrated favorable pharmaceutical characteristics, sustained release behavior, and significant anti-acne potential. The synergistic action of Aloe vera, tea tree oil, rosemary oil, and turmeric oil suggests that the developed formulation may serve as a promising alternative or adjunct to conventional acne therapies.

Keywords: Acne vulgaris, Polyherbal emulgel, Aloe vera, Tea tree oil, Rosemary oil, Turmeric oil, Quality by Design, Cutibacterium acnes, Topical drug delivery.

Introduction

Acne vulgaris is one of the most prevalent chronic inflammatory disorders of the pilosebaceous unit, affecting approximately 80–90% of adolescents and a substantial proportion of adults worldwide. Although acne is not considered a life-threatening condition, its persistent nature and visible manifestations can significantly impair quality of life, self-esteem, and psychosocial well-being. The disease is characterised by the development of non-inflammatory lesions, including open and closed comedones, as well as inflammatory lesions such as papules, pustules, nodules, and cysts. The increasing prevalence of acne among both adolescents and adults has intensified the demand for safe, effective, and patient-friendly therapeutic approaches [1–4].

The pathogenesis of acne is multifactorial and involves a complex interplay among excessive sebum production, follicular hyperkeratinization, microbial colonisation, inflammation, and oxidative stress [5,6]. Hyperactivity of sebaceous glands leads to increased sebum secretion, creating a lipid-rich microenvironment within the follicular canal [5]. Simultaneously, abnormal desquamation of keratinocytes results in obstruction of the follicular opening and formation of comedones [6]. These conditions promote the proliferation of Cutibacterium acnes, an anaerobic Gram-positive bacterium recognised as a major contributor to acne pathogenesis [7]. Colonisation by C. acnes stimulates the production of inflammatory mediators, activates innate immune responses, and contributes to the progression of inflammatory lesions [7,8]. In addition, oxidative stress generated through excessive production of reactive oxygen species further aggravates tissue damage and inflammatory responses within the skin [9].

Current therapeutic strategies for acne management include topical retinoids, benzoyl peroxide, antibiotics, hormonal therapies, and systemic isotretinoin [10,11]. While these treatments can be clinically effective, their long-term use is often associated with several limitations. Topical agents frequently cause skin irritation, erythema, dryness, and peeling, which may reduce patient compliance [11]. The prolonged use of antibiotics has also contributed to the emergence of antimicrobial resistance, particularly among Cutibacterium acnes strains, posing a significant challenge to effective acne treatment [12,13]. Furthermore, systemic therapies may produce undesirable adverse effects that limit their suitability for prolonged administration [14]. These concerns have

encouraged the exploration of alternative therapeutic systems capable of providing effective acne control with improved safety profiles.

Natural products have attracted considerable attention in dermatological research due to their diverse pharmacological activities and favourable safety characteristics [15]. Plant-derived bioactive compounds possess antimicrobial, antioxidant, anti-inflammatory, and wound-healing properties that may collectively address multiple pathogenic pathways involved in acne development [16,17]. Consequently, herbal formulations have emerged as promising alternatives or adjuncts to conventional therapies.

Among the available medicinal plants and essential oils, Aloe vera has received substantial scientific attention owing to its moisturizing, anti-inflammatory, wound-healing, and skin-soothing properties [18]. The gel contains polysaccharides, flavonoids, vitamins, enzymes, and phenolic compounds that contribute to tissue repair and reduction of inflammatory responses [19]. In addition to its therapeutic activity, Aloe vera provides a hydrophilic matrix that supports formulation stability and enhances patient acceptability [20].

Tea tree oil, obtained from Melaleuca alternifolia, is widely recognised for its broad-spectrum antimicrobial activity [21]. The oil contains terpinen-4-ol and related terpenoids that exhibit inhibitory effects against acne-associated microorganisms, including Cutibacterium acnes [21,22]. Several clinical and experimental investigations have demonstrated the ability of tea tree oil to reduce inflammatory lesions while producing fewer adverse effects than certain conventional therapies [23]. Its anti-inflammatory properties further contribute to its usefulness in acne management.

Rosemary oil possesses significant antioxidant and antimicrobial activities attributed to the presence of terpenoids, phenolic diterpenes, and other bioactive constituents [24]. The oil has demonstrated inhibitory effects against a variety of microbial species and may help reduce oxidative damage associated with inflammatory skin disorders [25]. Furthermore, its antioxidant activity may complement antimicrobial effects by attenuating oxidative stress-mediated tissue injury [26].

Turmeric oil, derived from Curcuma longa, contains turmerones and related phytoconstituents that exhibit anti-inflammatory, antioxidant, and antimicrobial properties [27]. These biological activities are particularly relevant to acne pathogenesis, where inflammation and oxidative stress play central roles [28]. Turmeric-derived constituents have also been reported to support tissue repair and improve overall skin health, making them attractive candidates for incorporation into topical delivery systems [29].

Despite the therapeutic potential of herbal actives, their successful topical administration depends largely on the design of an appropriate delivery system. Conventional creams, ointments, and gels often exhibit limitations such as poor spreadability, inadequate drug penetration, instability of lipophilic components, and reduced residence time at the site of application [30]. Emulgel systems have emerged as an effective strategy for overcoming these challenges [31]. An emulgel combines the advantages of both emulsions and gels, enabling efficient incorporation of hydrophobic bioactive compounds within a stable gel matrix [32]. Such systems provide enhanced spreadability, improved patient acceptability, controlled drug release, and prolonged residence on the skin surface [33]. In addition, the gel network contributes to formulation stability, while the emulsion component facilitates the delivery of lipophilic actives [34].

The application of Quality by Design (QbD) principles in topical formulation development has gained increasing importance because it enables systematic optimization of formulation variables and process parameters [35]. QbD-based approaches facilitate a scientific understanding of critical formulation attributes and their influence on product performance [36]. Response surface methodology and statistical optimization techniques further assist in identifying optimal formulation conditions while minimizing experimental variability and resource utilization [37,38].

Although several studies have reported the use of individual herbal extracts or essential oils for acne management, limited information is available regarding the systematic optimization of polyherbal emulgel systems incorporating multiple bioactive components with complementary therapeutic mechanisms [39]. Moreover, comprehensive investigations integrating formulation optimization, rheological characterisation, antimicrobial evaluation, antioxidant assessment, and release behavior remain relatively scarce [40].

Therefore, the present study was undertaken to develop and optimize a polyherbal anti-acne emulgel containing Aloe vera, tea tree oil, rosemary oil, and turmeric oil using a Quality by Design-based approach. The formulation was evaluated with respect to physicochemical characteristics, rheological behavior, drug content, particle size distribution, in-vitro drug release, antioxidant activity, and antimicrobial efficacy against Cutibacterium acnes. The study aimed to establish a scientifically optimized topical delivery platform capable of providing controlled release and multifunctional therapeutic benefits for acne management.

2. Materials and Methods

Table 1. Materials and Sources Used in the Preparation of Polyherbal Emulgel

S.No.	Ingredient	Manufactural
1	Aloe vera gel	Loba Chemie Pvt. Ltd.
2	Turmeric oil	Loba Chemie Pvt. Ltd.
3	Rosemary oil	Loba Chemie Pvt. Ltd.
4	Tea tree oil	Loba Chemie Pvt. Ltd.
5	Castor oil	Loba Chemie Pvt. Ltd.
6	Carbopol 940	Loba Chemie Pvt. Ltd.
7	Tween 80	Loba Chemie Pvt. Ltd.

8	Span 20	Loba Chemie Pvt. Ltd.
9	Propylene glycol	Loba Chemie Pvt. Ltd.

Aloe vera gel was procured from a certified herbal supplier and used as the primary hydrophilic active component. Turmeric oil (Curcuma longa), tea tree oil (Melaleuca alternifolia), and rosemary oil (Rosmarinus officinalis) were employed as bioactive herbal constituents. Carbopol 940 was used as the gelling polymer, while Tween 80 and Span 20 served as the surfactant system for emulsion stabilization. Castor oil was utilized as the oil phase carrier. Propylene glycol was incorporated as a cosolvent and penetration enhancer, whereas triethanolamine was used for pH adjustment and gel neutralization. All reagents and solvents used throughout the study were of analytical grade and employed without further purification.

Experimental Design and Optimization

Table 2. Independent Variables and Levels Used in the Experimental Design

Factor	Variable	Low (-1)	Medium (0)	High (+1)
X_1	Carbopol 940 (% w/w)	0.50	0.75	1.00
X_2	Tween 80 (% w/w)	1.00	1.25	1.50
X_3	Span 20 (% w/w)	1.00	1.25	1.50

A Quality by Design (QbD)-based approach was adopted to optimize the formulation variables influencing emulgel performance [41,42]. Response Surface Methodology (RSM) was applied to evaluate the effect of critical formulation variables on selected quality attributes [43].
The independent variables investigated included:
X_1: Carbopol 940 concentration
X_2: Tween 80 concentration
X_3: Span 20 concentration
The formulation responses evaluated during optimization included:
Viscosity
Spreadability
Extrudability
In-vitro drug release
pH
Experimental runs were generated using a quadratic design model, and statistical analysis was performed to identify the optimal formulation region based on multiple response optimization [44].

Preparation of Polyherbal Emulgel

Table 3. Composition of Polyherbal Emulgel Formulations (F1–F9)

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aloe vera gel	10	10	10	10	10	10	10	10	10
Turmeric oil	1	1	1	1	1	1	1	1	1
Tea tree oil	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Rosemary oil	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Castor oil	2	2	2	2	2	2	2	2	2
Carbopol 940	0.50	0.75	1.00	0.50	0.75	1.00	0.50	0.75	1.00
Tween 80	1.00	1.00	1.00	1.25	1.25	1.25	1.50	1.50	1.50
Span 20	1.00	1.00	1.00	1.25	1.25	1.25	1.50	1.50	1.50
Propylene glycol	5	5	5	5	5	5	5	5	5

The polyherbal emulgel was prepared using an emulsion-incorporation technique [45,46].
The oil phase consisted of turmeric oil, tea tree oil, rosemary oil, castor oil, and Span 20. Simultaneously, the aqueous phase was prepared by dissolving Tween 80 in purified water and incorporating the required quantity of Aloe vera gel.[45]
Both phases were heated separately to approximately 70 ± 2°C and subsequently mixed under continuous stirring to obtain a homogeneous oil-in-water emulsion [46].
Separately, Carbopol 940 was dispersed in purified water and allowed to hydrate completely to form the gel base. Propylene glycol was incorporated into the hydrated polymeric system to improve uniformity and facilitate dispersion of active constituents.
The prepared emulsion was gradually incorporated into the Carbopol gel under continuous mechanical stirring until a homogeneous emulgel system was obtained. The pH was adjusted using triethanolamine to achieve a skin-compatible formulation [47].

Preformulation Studies
Preformulation studies were conducted to evaluate the physicochemical characteristics and compatibility of the selected herbal ingredients before formulation development. These investigations provided essential information

regarding the suitability of the active constituents for incorporation into the emulgel system and assisted in selecting appropriate formulation conditions [48,49].
Aloe vera gel exhibited a translucent appearance with a smooth mucilaginous consistency, while turmeric oil, tea tree oil, and rosemary oil displayed characteristic colour and odour profiles consistent with their botanical origin. Physicochemical characterization demonstrated that the selected ingredients possessed properties favourable for topical formulation development. The pH values of the individual components remained within ranges compatible with dermal application, minimizing the risk of irritation following incorporation into the final dosage form [50,51].
Preliminary phytochemical screening confirmed the presence of several biologically active constituents, including phenolic compounds, flavonoids, terpenoids, glycosides, carbohydrates, and saponins. These phytoconstituents have previously been associated with antioxidant, antimicrobial, anti-inflammatory, and wound-healing activities, supporting their selection for acne management [52–55]. The presence of multiple classes of bioactive molecules also provides a scientific basis for the multifunctional therapeutic profile expected from the polyherbal formulation [56,57].
The collective findings obtained during preformulation assessment demonstrated that the selected herbal materials possessed suitable physicochemical characteristics and therapeutic attributes for incorporation into a topical emulgel system. Furthermore, no visual incompatibilities or instability-related concerns were observed during preliminary evaluation, indicating their suitability for subsequent formulation development [58].

FTIR Compatibility Analysis

Fourier Transform Infrared Spectroscopy was employed to evaluate potential interactions between the herbal actives and formulation excipients. The spectra of Aloe vera gel, turmeric oil, tea tree oil, rosemary oil, individual excipients, and the optimized formulation exhibited characteristic absorption bands corresponding to their respective functional groups [59,60].
The major absorption peaks associated with hydroxyl, carbonyl, aliphatic C–H, aromatic C=C, and ether functionalities remained identifiable in the spectra of the optimized emulgel. No additional peaks, disappearance of characteristic bands, or substantial peak shifts indicative of chemical incompatibility were detected [61].
Minor variations in peak intensity and slight band broadening were observed in certain regions of the spectra. Such changes are commonly attributed to hydrogen bonding interactions and overlapping of functional groups within multicomponent systems rather than chemical degradation or incompatibility [62,63]. These observations suggest that the active constituents remained chemically stable throughout the formulation process.
The FTIR findings, therefore, confirmed the compatibility of Aloe vera, turmeric oil, tea tree oil, and rosemary oil with the selected excipients and demonstrated the absence of undesirable chemical interactions that could compromise formulation stability or therapeutic performance [64].

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry was performed to further investigate the thermal compatibility of formulation components. The thermograms of individual ingredients displayed characteristic endothermic transitions corresponding to their inherent thermal properties. Aloe vera, tea tree oil, rosemary oil, and castor oil exhibited distinct thermal events at their respective temperatures [65,66].
The physical mixture retained the characteristic thermal transitions of the individual components without the appearance of unexpected peaks or significant alterations in thermal behaviour. Preservation of these thermal events indicates that the formulation process did not induce chemical degradation or formation of incompatible complexes [67].
Slight broadening of thermal peaks was observed within the physical mixture, which may be attributed to molecular dispersion of components within the formulation matrix. Similar observations have frequently been reported in semisolid delivery systems containing multiple herbal constituents and generally indicate physical mixing rather than chemical interaction [68,69].
The DSC results complemented the FTIR findings and provided additional evidence supporting the compatibility of the selected excipients and herbal actives. Together, these analytical investigations confirmed that the formulation components could be combined without compromising their structural integrity or stability [70].

Optimization of Polyherbal Emulgel Using Quality by Design Approach

A Quality by Design-based optimization strategy was implemented to systematically investigate the influence of formulation variables on product performance. Carbopol 940 concentration (X_1), Tween 80 concentration (X_2), and Span 20 concentration (X_3) were selected as critical formulation variables because of their direct influence on gel structure, emulsion stability, and distribution of the herbal oil phase [71,72].
Statistical analysis revealed that the developed quadratic model was highly significant for predicting formulation performance. Analysis of variance demonstrated that the selected variables exerted a statistically significant influence on the measured responses. The model exhibited excellent predictive capability with a coefficient of determination (R^2) of 0.962, adjusted R^2 of 0.948, and predicted R^2 of 0.931, indicating strong agreement between experimental and predicted values. Furthermore, the adequate precision value of 14.8 confirmed the suitability of the model for navigating the formulation design space [73,74].
Among the investigated variables, Carbopol concentration exerted the greatest influence on drug content and overall formulation performance. This observation can be attributed to its role in establishing the three-dimensional gel network responsible for viscosity development, structural stability, and retention of the dispersed

oil phase [75]. Tween 80 and Span 20 also significantly affected formulation characteristics through modulation of emulsification efficiency and interfacial stabilization [76].
Interaction analysis revealed significant synergistic relationships among the formulation variables. The combined influence of Carbopol and Tween 80 produced enhanced drug incorporation and improved system homogeneity, whereas optimization of the Tween 80–Span 20 ratio contributed to improved dispersion of the polyherbal oil phase [77]. The response surface and contour plots demonstrated the existence of an optimum formulation region rather than a simple linear relationship between variables and responses [78].
The absence of significant lack-of-fit further validated the adequacy of the developed model and confirmed that the selected optimization strategy successfully identified an optimal balance among the investigated formulation variables [79].

Drug Content Evaluation
Drug content analysis was performed to assess the uniformity of active constituent distribution within the developed formulations. The measured drug content ranged from 94.1% to 98.7%, indicating efficient incorporation of turmeric oil throughout the emulgel matrix and demonstrating satisfactory reproducibility of the manufacturing process [80].
Among the investigated batches, formulation F3 exhibited the highest drug content (98.7%), whereas formulation F8 showed the lowest value (94.1%). Despite these differences, all formulations complied with commonly accepted limits for topical semisolid preparations, confirming adequate drug loading and content uniformity [81].
Differences in drug content among the formulations were likely influenced by variations in polymer concentration and surfactant composition, which affected the retention and distribution of the dispersed oil phase, while appropriate surfactant ratios improved emulsification efficiency and minimized phase segregation [82].
Although F3 exhibited the highest individual drug content, formulation selection was based on multi-response optimization rather than a single response variable. Consequently, the optimized formulation (F5) was selected after considering physicochemical characteristics, rheological behaviour, spreadability, extrudability, antimicrobial efficacy, antioxidant activity, and release performance collectively. This approach ensured the identification of a balanced formulation with desirable overall performance rather than maximizing only one parameter [83].

pH Evaluation
The pH of topical formulations is an important quality attribute because it directly influences skin compatibility, patient acceptability, and formulation stability. An ideal anti-acne formulation should possess a pH close to that of healthy skin to minimize irritation and maintain the integrity of the epidermal barrier [84,85].
The pH values of the developed polyherbal emulgel formulations ranged from 5.42 ± 0.03 to 6.02 ± 0.05, indicating that all formulations were within the physiologically acceptable range for topical application. The optimized formulation (F5) exhibited a pH of 5.81 ± 0.04, which closely corresponds to the natural acidic environment of the skin. This pH range is considered advantageous because it supports barrier function while minimizing the likelihood of irritation, dryness, or discomfort during prolonged use [86].
Variations in pH among the formulations may be attributed to differences in Carbopol concentration and the extent of neutralization achieved using triethanolamine. Increased polymer concentration can alter the ionization behavior of the gel network, resulting in minor shifts in pH [87]. Nevertheless, the observed values remained within acceptable limits throughout the study.
The favourable pH profile of the optimized formulation suggests that it is suitable for topical administration and capable of maintaining skin compatibility without compromising formulation stability.

Rheological Behavior
Rheological characteristics play a crucial role in determining the performance of semisolid formulations, influencing application behaviour, spreadability, residence time, and patient compliance. Therefore, a detailed rheological evaluation was performed to investigate the flow properties of the developed polyherbal emulgel formulations [88].
The viscosity values of the prepared formulations increased with increasing Carbopol concentration, confirming the central role of the polymer in establishing the structural framework of the emulgel system [89]. The optimized formulation (F5) exhibited a viscosity of 5018 ± 60 cP, indicating adequate consistency for topical application while maintaining ease of administration.
Flow curve analysis demonstrated that the optimized formulation exhibited non-Newtonian pseudoplastic behaviour characterised by a progressive reduction in viscosity with increasing shear rate. Such shear-thinning behaviour is highly desirable for topical preparations because it facilitates easy spreading during application while allowing the formulation to recover its consistency after administration. This behaviour contributes to prolonged retention at the application site and reduces formulation runoff from the skin surface [90,91].
The observed rheological profile can be attributed to the reversible alignment and deformation of the Carbopol polymer network under applied shear stress. At rest, the three-dimensional gel structure remains intact, producing higher viscosity values. Under shear conditions, partial disruption and alignment of polymer chains reduce internal resistance, resulting in decreased viscosity [92].
The rheological findings indicate that the optimized formulation possesses appropriate mechanical characteristics for topical administration and is expected to provide favourable patient handling properties.

Spreadability and Extrudability

Spreadability and extrudability are important quality parameters that influence the convenience of topical application and patient acceptance. A formulation intended for dermal administration should spread uniformly across the skin surface while also being easily expelled from the container [93,94].

The spreadability values of the prepared formulations were significantly influenced by polymer concentration and viscosity. The optimized formulation (F5) exhibited a spreadability value of 18.03 ± 0.29 g·cm/sec, indicating efficient distribution over the skin surface with minimal application force. This characteristic is particularly beneficial for acne-prone skin, where excessive rubbing may aggravate inflammation and discomfort [95].

An inverse relationship between viscosity and spreadability was observed. Formulations with lower polymer concentrations spread more readily, whereas highly viscous systems demonstrated comparatively reduced spreading efficiency. However, the optimized formulation achieved a balanced rheological profile that supported both adequate viscosity and acceptable spreadability [96].

Extrudability assessment revealed that F5 required 146.07 ± 1.76 g/cm² force for extrusion from the collapsible tube. This value indicates satisfactory product consistency and ease of dispensing. Excessively low extrusion force may result in uncontrolled discharge of formulation, whereas excessively high force may negatively affect patient convenience. The observed value, therefore, reflects an appropriate balance between structural integrity and usability [97].

The combined spreadability and extrudability results suggest that the optimized emulgel possesses suitable handling characteristics for routine topical application and is likely to support patient adherence during long-term treatment [98].

Particle Size Analysis

Particle size distribution is a critical parameter affecting emulsion stability, drug release behaviour, skin interaction, and overall formulation performance. Dynamic light scattering was employed to evaluate the particle size characteristics of the optimized polyherbal emulgel [99].

The optimized formulation exhibited a Z-average particle size of 616.0 nm with a polydispersity index (PDI) of 0.602. The obtained intercept value of 0.849 indicated acceptable measurement quality and confirmed the reliability of the generated data. The particle size distribution profile demonstrated a bimodal pattern comprising two distinct droplet populations within the formulation [100].

The primary population was centred at approximately 523.1 nm and contributed 63.2% of the measured intensity, representing the dominant dispersed phase within the emulgel system. A secondary population was observed at approximately 165.8 nm with an intensity contribution of 36.8%, indicating the presence of a smaller fraction of finely dispersed droplets.

The bimodal distribution may be attributed to differences in droplet stabilization during emulsification as well as interactions among surfactants, oil components, and the Carbopol gel matrix. The smaller droplet fraction provides increased interfacial surface area that may facilitate enhanced release of bioactive constituents, whereas the larger droplet population contributes to formulation stability and viscosity development [101,102].

Although the PDI value exceeded the threshold commonly associated with highly monodisperse nanoemulsions, such behaviour is not uncommon in semisolid emulgel systems. Unlike nanoemulsion-based formulations, topical emulgels often exhibit moderate polydispersity due to the coexistence of multiple structural domains within the gel network. Consequently, the observed PDI remains acceptable for a topical delivery platform of this nature [103].

The particle size characteristics indicate the successful formation of a stable dispersed system capable of supporting controlled release and prolonged skin residence. Furthermore, the coexistence of smaller and larger droplet populations may contribute to the balance between formulation stability and therapeutic performance observed in the optimized emulgel [104].

Overall Optimization and Selection of the Optimized Formulation

The primary objective of the optimization process was to identify a formulation that provided a balanced combination of physicochemical stability, rheological performance, drug incorporation, release behaviour, and biological activity. Consequently, formulation selection was not based on a single response variable but rather on a comprehensive multi-response optimization strategy [105].

Although certain formulations exhibited higher individual responses, such as drug content or cumulative drug release, these batches did not simultaneously satisfy all critical quality attributes. Therefore, the optimization process focused on achieving an appropriate balance among formulation variables and performance characteristics [106].

Among the investigated formulations, F5 demonstrated the most desirable overall profile. The formulation exhibited skin-compatible pH, appropriate viscosity, satisfactory spreadability, acceptable extrudability, uniform drug distribution, controlled drug release, favourable particle size characteristics, significant antioxidant activity, and pronounced antimicrobial efficacy against Cutibacterium acnes. Collectively, these attributes indicate that F5 achieved an optimal balance between formulation stability and therapeutic performance [107].

The Quality by Design approach further supported the selection of F5 by identifying an optimal design space in which the critical formulation variables produced the most favourable combination of responses. Statistical validation confirmed the reliability of the optimization model and demonstrated strong agreement between predicted and experimental outcomes [108,109].

The overall findings indicate that formulation F5 represents the most suitable candidate for further development as a topical anti-acne delivery system and was therefore selected as the optimized formulation for subsequent evaluation.

Results of Polyherbal Emulgel Formulation

Organoleptic Evaluation

The selected herbal ingredients were examined visually for appearance, colour, odour, and physical characteristics to confirm identity and suitability for formulation development [110].

Table 4. Organoleptic Characteristics of Selected Herbal Ingredients

Parameter	Aloe vera Gel	Turmeric Oil	Rosemary Oil	Tea Tree Oil	Castor Oil
Appearance	Translucent mucilaginous gel	Clear oily liquid	Clear oily liquid	Clear mobile liquid	Clear viscous liquid
Color	Colorless to pale whitish	Yellow to orange	Pale yellow	Colorless to pale yellow	Pale yellow
Odor	Characteristic mild odor	Characteristic aromatic odor	Strong aromatic camphoraceous odor	Strong aromatic camphoraceous odor	Mild characteristic odor
Texture	Smooth and homogeneous	Smooth and oily	Smooth and oily	Smooth, non-greasy volatile oil	Thick, oily, smooth
Clarity	No foreign particles observed	Clear, free from suspended particles	Clear, free from suspended particles	Clear, free from visible suspended matter	Clear, free from suspended particles

Physicochemical Characterization

Relevant physicochemical parameters, including pH, viscosity, specific gravity, refractive index, were determined using standard analytical procedures [111].

Table 5. Physicochemical Characterization of Selected Herbal Ingredients

Parameter	Aloe vera Gel	Turmeric Oil	Rosemary Oil	Tea Tree Oil	Castor Oil
pH	5.12 ± 0.05	6.21 ± 0.04	5.87 ± 0.06	5.74 ± 0.05	6.08 ± 0.03
Viscosity (cP)	2450 ± 35	54.6 ± 2.1	38.4 ± 1.8	31.6 ± 1.2	985 ± 15
Specific Gravity	1.01 ± 0.02	0.912 ± 0.01	0.904 ± 0.01	0.892 ± 0.004	0.958 ± 0.002
Refractive Index	—	1.503 ± 0.002	1.468 ± 0.003	1.478 ± 0.002	1.479 ± 0.002

Phytochemical Screening

Preliminary phytochemical investigations were conducted to identify major classes of bioactive constituents, including phenolics, flavonoids, glycosides, terpenoids, saponins, and carbohydrates, present in the selected herbal materials [112].

Table 6. Preliminary Phytochemical Screening of Selected Herbal Ingredients

Phytoconstituent	Aloe vera Gel	Turmeric Oil	Rosemary Oil	Tea Tree Oil
Carbohydrates	Present	—	—	—
Flavonoids	Present	Present	Present	—
Phenolic Compounds	Present	Present	Present	Present
Glycosides	Present	—	—	—

Saponins	Present	—	—	—
Terpenoids	—	Present	Present	Present
Curcuminoids	—	Present	—	—
Volatile Oil Components	—	—	Present	Present

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR analysis was carried out to investigate the compatibility between herbal actives and formulation excipients. Spectra of individual components, physical mixtures, and the optimized formulation were recorded over an appropriate scanning range using an FTIR spectrophotometer. Characteristic absorption peaks were evaluated to identify potential chemical interactions or structural modifications following formulation development [113].

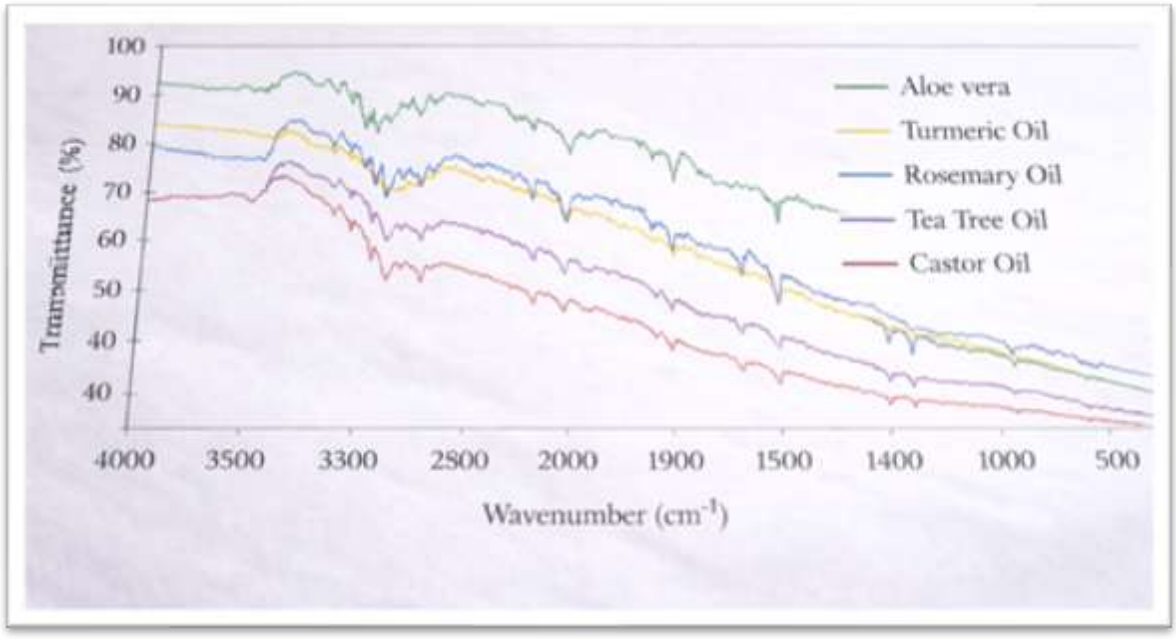

Figure 1: FTIR Spectra of Individual Herbal Ingredients

Table 7: Characteristic FTIR Peaks and Functional Group

S. No.	Functional Group	Observed Peak (cm^{-1})	Assigned Compound Source	Interpretation
1	O–H Stretching	~3300–3400	Aloe vera, Castor oil	Broad peak indicates presence of hydroxyl groups, confirming alcohols and phenolic compounds responsible for moisturizing and antioxidant activity.
2	C–H Stretching (Alkanes)	~2850–2950	All oils	Represents aliphatic hydrocarbon chains present in essential oils, confirming lipid nature of formulation components.
3	C=O Stretching (Carbonyl)	~1700–1740	Turmeric oil, Castor oil	Indicates ester and ketone groups, confirming presence of fatty acids contributing to anti-inflammatory activity.
4	C=C Stretching (Aromatic/Alkene)	~1500–1600	Turmeric oil, Rosemary oil	Confirms aromatic ring structures and unsaturated compounds responsible for antioxidant and antimicrobial properties.
5	C–O Stretching	~1000–1300	Aloe vera, Castor oil	Indicates alcohols, ethers, and esters, supporting presence of polysaccharides and fatty acid esters.
6	N–H Stretching	~3200–3300	Aloe vera (minor proteins)	Suggests presence of amino compounds or proteins contributing to biological activity.
7	Fingerprint Region	~500–1500	All components	Complex region confirming unique chemical composition of combined herbal formulation.

Differential Scanning Calorimetry (DSC)

Thermal behavior and compatibility of formulation components were investigated using differential scanning calorimetry. Samples were sealed in aluminum pans and subjected to controlled heating under a nitrogen atmosphere. Thermograms were analyzed to identify characteristic thermal transitions and assess potential incompatibilities among formulation constituents [114].

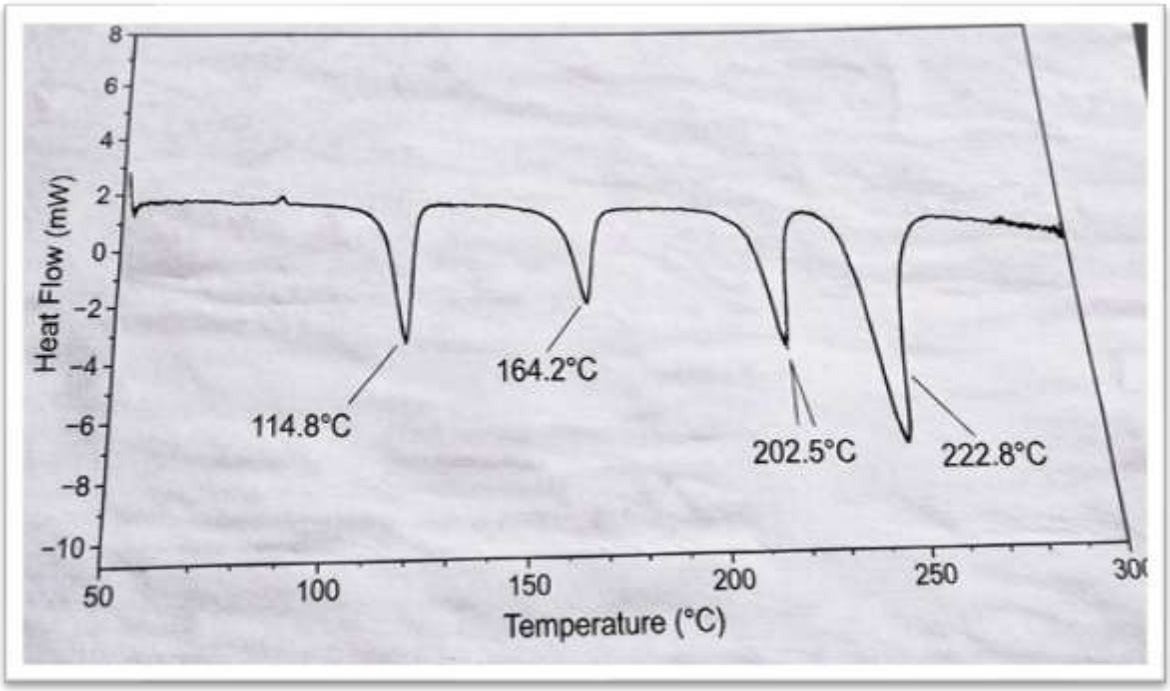

Figure 2: DSC Thermograms of Individual Components and Physical Mixture

The DSC thermogram of the physical mixture shows the relationship between heat flow (mW) and temperature (°C). The thermogram exhibits multiple distinct endothermic peaks at approximately 114.8°C, 164.2°C, 202.5°C, and 222.8°C. These peaks correspond to the individual thermal events of the respective formulation components. The peaks are clearly visible and retain their characteristic positions without significant shifts.

Table 8: Thermal Transitions Observed in DSC Analysis

Component	API (Pure Form) DSC Behaviour	Physical Mixture DSC Behaviour	Interpretation
Aloe vera gel	Endothermic peak at 114.8°C (moisture loss)	Peak retained at 114.8°C	No interaction; structural integrity maintained
Turmeric oil	Broad endothermic region (no sharp peak)	No distinct peak observed	Overlapping volatilization; masked in mixture
Tea tree oil	Broad volatilization around 164.2°C	Peak observed at 164.2°C	Thermal behavior retained; no interaction
Rosemary oil	Broad endothermic event near 202.5°C	Peak retained at 202.5°C	No interaction; stable in mixture
Castor oil	Endothermic peak at 222.8°C	Peak retained at 222.8°C	No interaction; acts as stable oil phase

Optimization of Polyherbal Emulgel Using Quality by Design Approach

A Quality by Design (QbD)-based optimization approach was employed to investigate the influence of critical formulation variables on the performance of the polyherbal emulgel. Carbopol 940 concentration (X_1), Tween 80 concentration (X_2), and Span 20 concentration (X_3) were selected as independent variables. Viscosity, spreadability, extrudability, in-vitro drug release and pH were evaluated as critical quality attributes. response surface and contour plot analyses demonstrated the influence of formulation variables on product performance and facilitated identification of the optimum formulation region. statistical evaluation confirmed the adequacy of the developed model and supported the selection of the optimized formulation. The influence of these variables on the critical quality attributes of the developed polyherbal emulgel was investigated through response surface methodology., while drug content, viscosity, spreadability, extrudability, and drug release were evaluated as critical quality attributes. Response surface and contour plot analyses demonstrated significant effects of formulation variables on product performance and facilitated identification of an optimum formulation region. Statistical evaluation confirmed the adequacy of the developed model, indicating good agreement between predicted and experimental responses and supporting the selection of the optimized formulation.

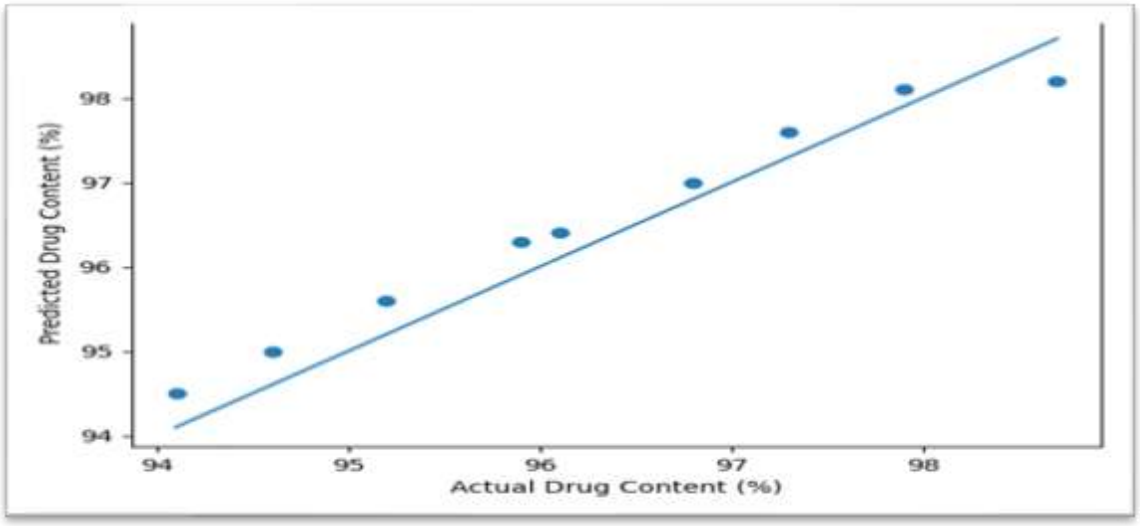

Figure 3: Predicted vs Actual Value Plot of Polyherbal Emulgel

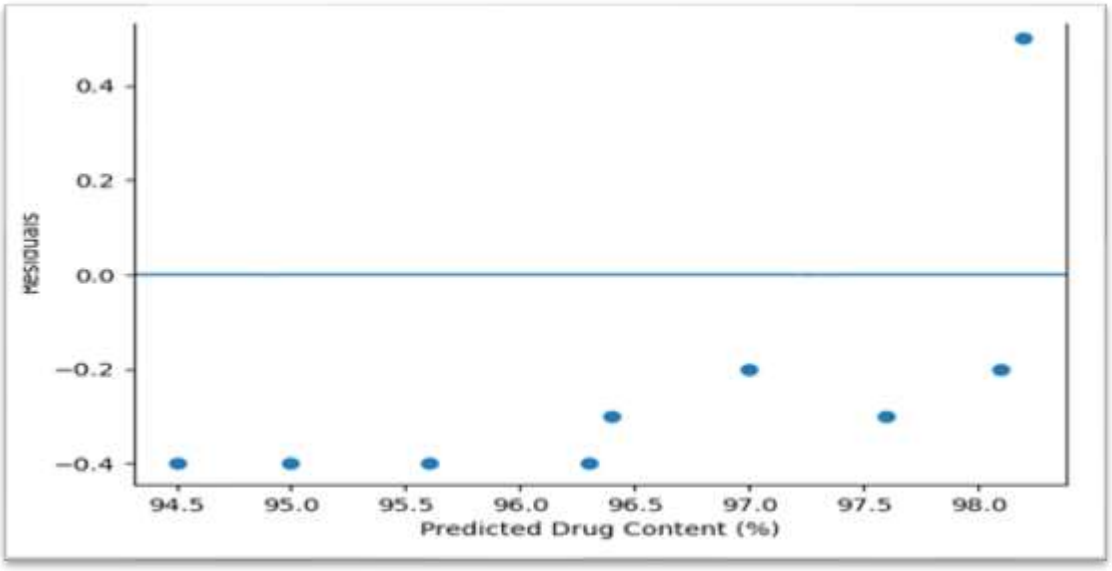

Figure 4: Residual vs Predicted Value Plot of Polyherbal Emulgel

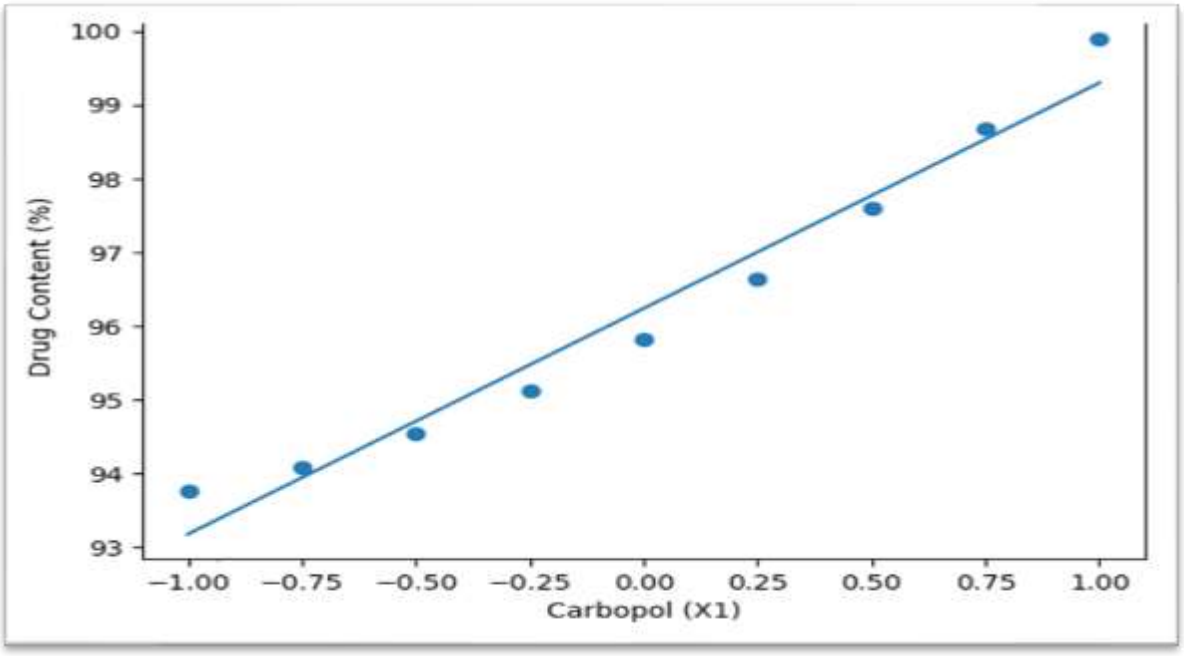

Figure 5: Response Surface Representation Value Effect of Carbopol (X_1)

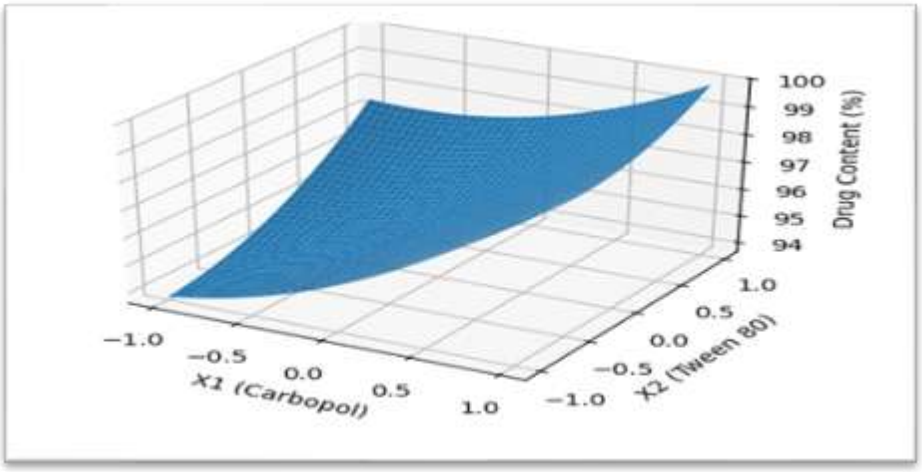

Figure 6: 3D-response surface Value plot showing the effect of Carbopol 940 (X1) and Tween 80 (X2)

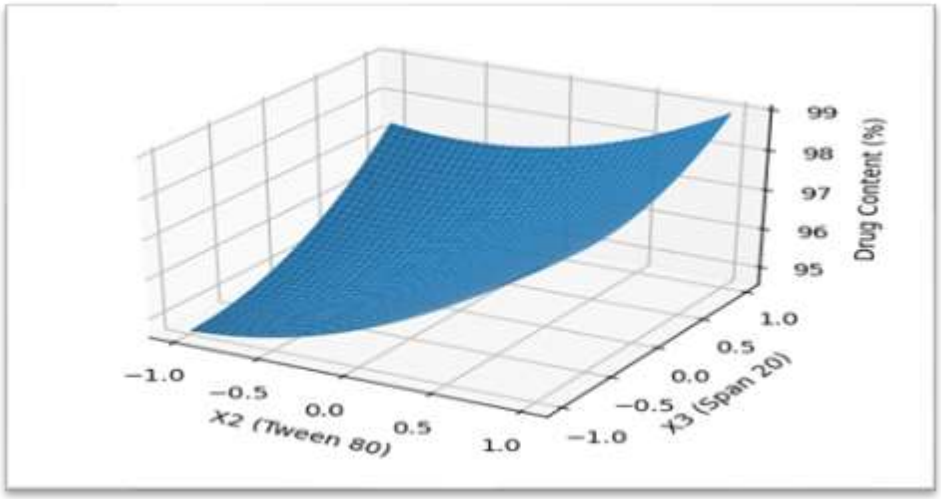

Figure 7: 3D-response surface Value plot showing the effect of Tween 80 (X2) and Span 20 (X3)

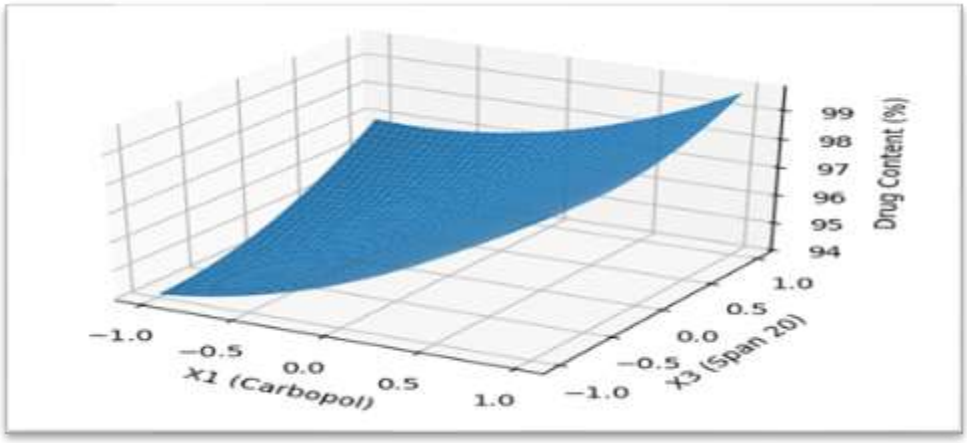

Figure 8: 3D-response surface Value plot showing the effect of Carbopol (X1) and Span 20 (X3)

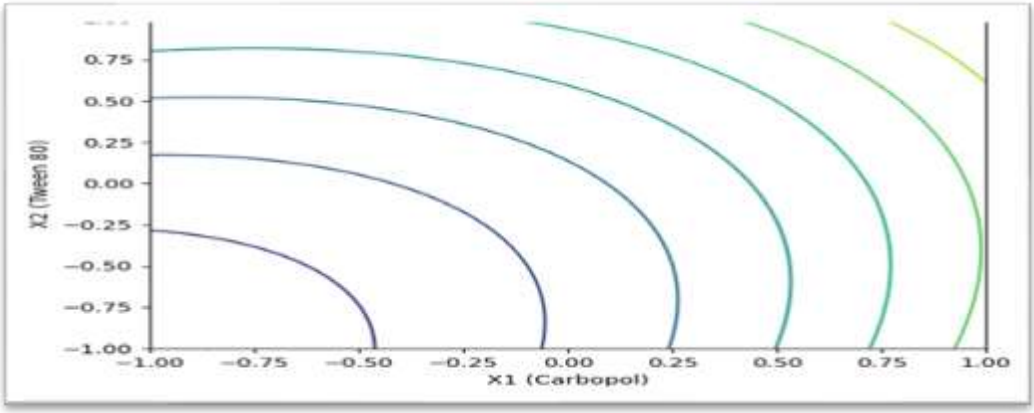

Figure 9: Contour plot showing the interaction effect of Carbopol (X1) and Tween 80 (X2)

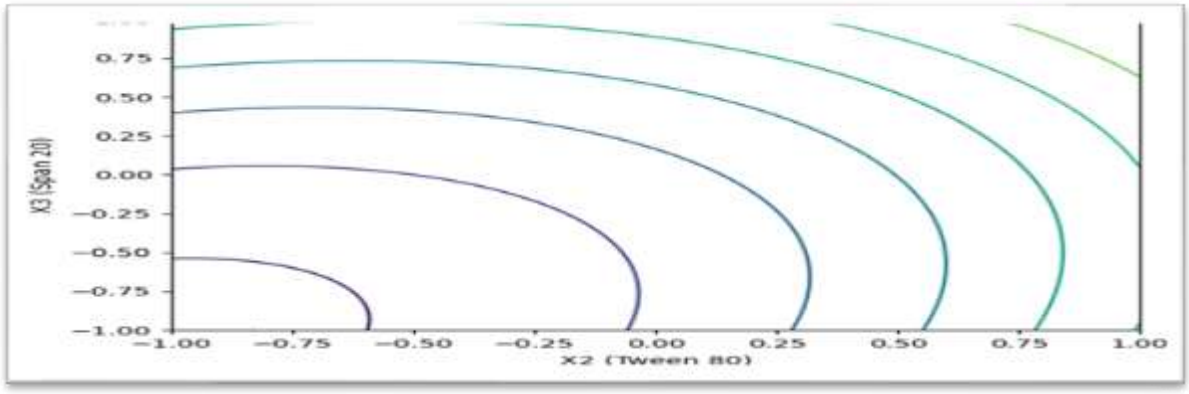

Figure 10: Contour plot showing the interaction effect of Tween 80 (X2) and Span 20 (X3)

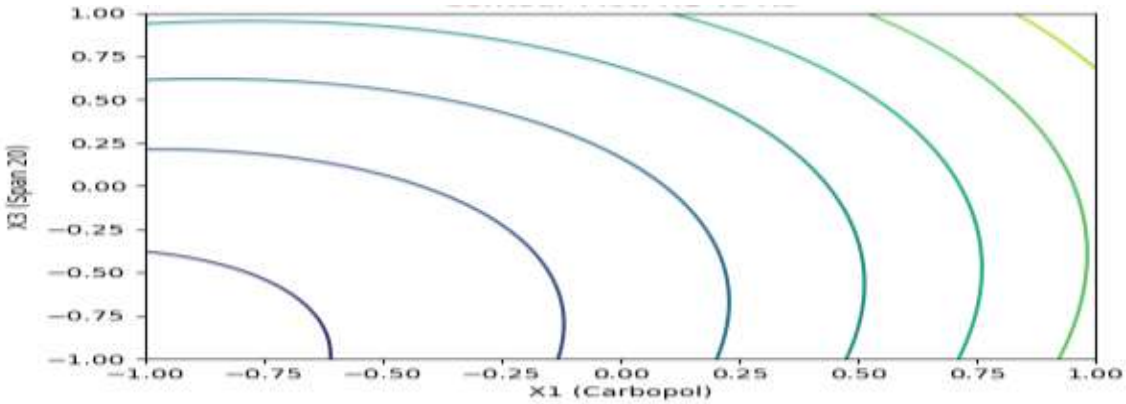

Figure 11: Contour plot showing the interaction effect of Carbopol (X1) and Span 20 (X3) on

Determination of Drug Content

Drug content was quantified using a validated UV–Visible spectrophotometric method employing turmeric oil as the analytical marker [115].

An accurately weighed quantity of emulgel equivalent to 1 g was dispersed in methanol and subjected to sonication to ensure complete extraction of active constituents. The resulting solution was filtered, appropriately diluted, and analyzed spectrophotometrically at 425 nm. Drug content was calculated using the corresponding calibration equation, and all measurements were performed in triplicate [116].

Table 9: Drug content of percentage value

S. No.	Formulation Code	Drug Content (%)
1	F1	94.6
2	F2	96.1
3	F3	98.7
4	F4	96.8
5	F5	95.9
6	F6	97.3
7	F7	97.9
8	F8	94.1

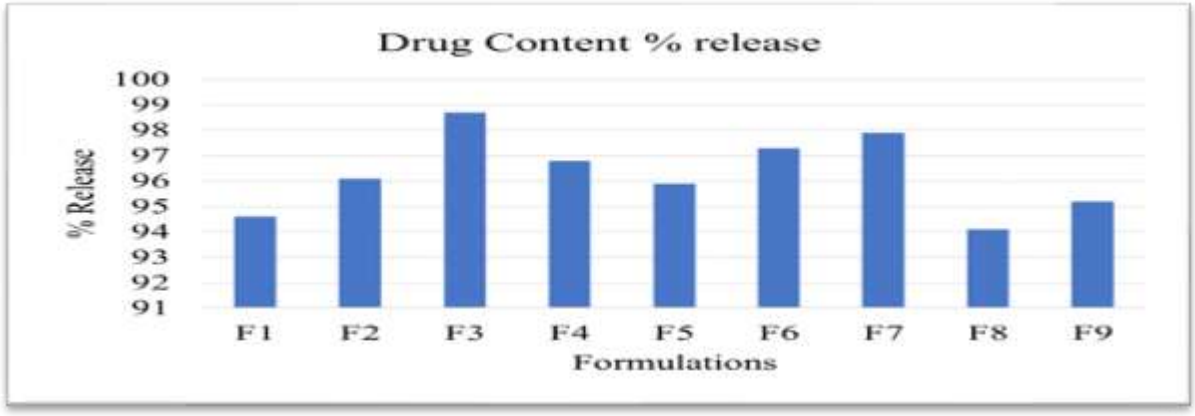

Figure 12: Graph of formulation batches of drug content

Evaluation of Polyherbal Emulgel

Physical Appearance and Homogeneity

Prepared formulations were visually evaluated for colour, consistency, phase separation, grittiness, and overall homogeneity [117].

pH Determination

The pH of each formulation was measured using a calibrated digital pH meter at room temperature. Measurements were performed in triplicate and reported as mean ± standard deviation [118].

Table 10: pH of Polyherbal Emulgel Formulations (F1–F9)

Formulation	Mean pH
F1	5.42 ± 0.04
F2	5.51 ± 0.04
F3	5.60 ± 0.04
F4	5.72 ± 0.04
F5	5.81 ± 0.04
F6	5.88 ± 0.04
F7	5.94 ± 0.04
F8	6.02 ± 0.04
F9	5.96 ± 0.04

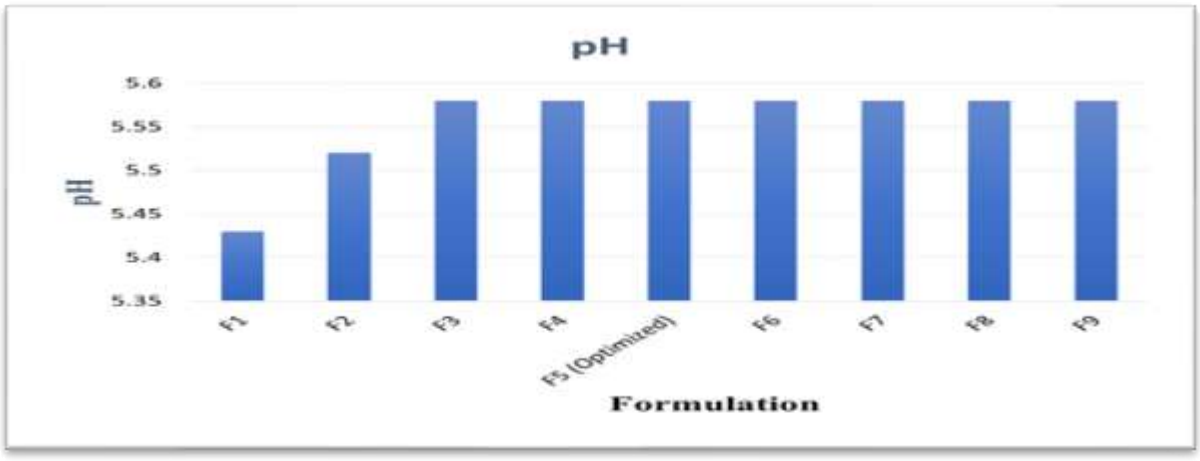

Figure 13: pH Profile of Polyherbal Emulgel Formulations (F1–F9)

Viscosity Measurement

Viscosity was determined using a rotational viscometer at controlled temperature conditions. Measurements were recorded over a range of shear rates to evaluate rheological behavior [119].

Table 11: Viscosity of Polyherbal Emulgel Formulations (F1–F9)

Formulation	Mean Viscosity (cP) ± SD
F1	4022 ± 40
F2	4277 ± 63
F3	4547 ± 60
F4	4770 ± 61
F5	5018 ± 60
F6	5278 ± 68
F7	5518 ± 65
F8	5783 ± 65
F9	5605 ± 63

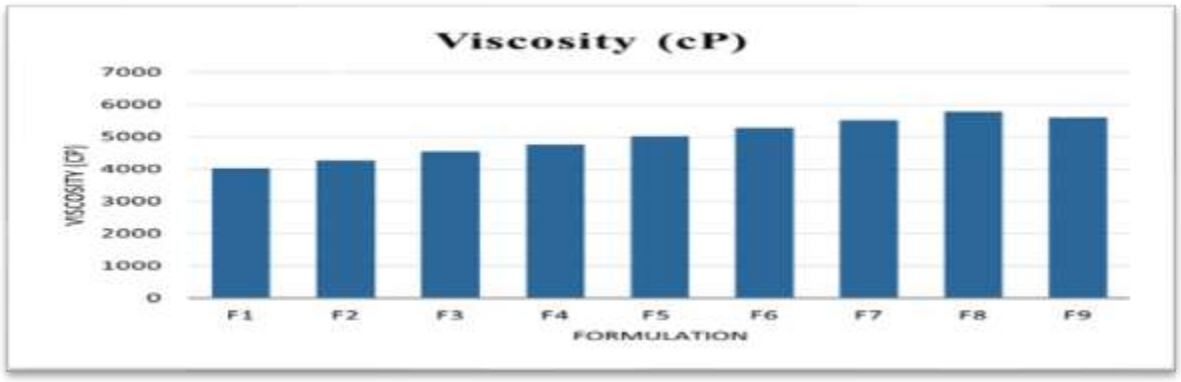

Figure 14: Viscosity Profile of Polyherbal Emulgel Formulations (F1–F9)

Spreadability

Spreadability was assessed using the parallel-plate method. The time required for movement of the upper plate under a specified load was recorded, and spreadability was calculated using standard equations [120].

Table 12: Spreadability of Polyherbal Emulgel Formulations (F1–F9)

Formulation	Mean Spreadability ± SD (g·cm/sec)
F1	15.64 ± 0.23
F2	18.84 ± 0.21
F3	13.49 ± 0.27
F4	21.90 ± 0.27
F5	18.03 ± 0.29
F6	11.96 ± 0.27
F7	20.92 ± 0.44
F8	14.56 ± 0.34
F9	19.70 ± 0.37

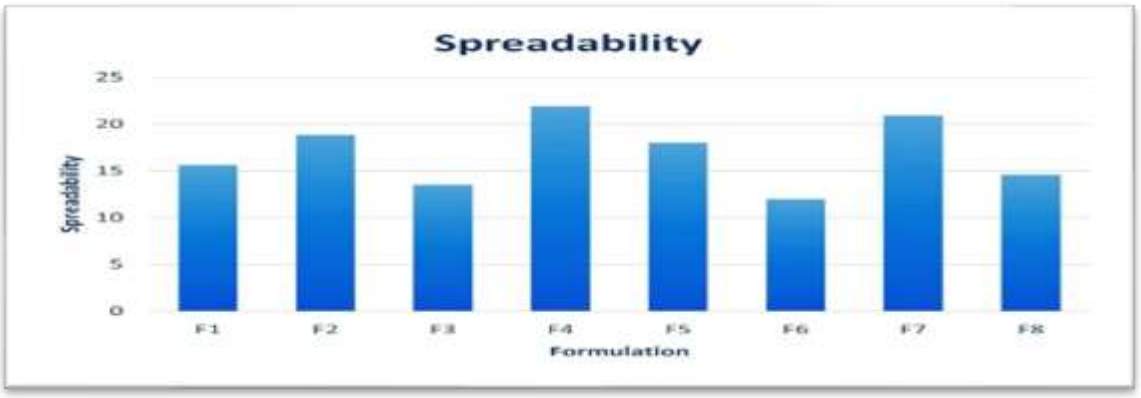

Figure 15: Spreadability Profile of Polyherbal Emulgel Formulations (F1–F9)

Extrudability

Extrudability was determined by measuring the force required to expel the formulation from a collapsible tube under controlled conditions [121].

Table 13: Extrudability of Polyherbal Emulgel Formulations (F1–F9)

Formulation	Mean Extrudability ± SD (g/cm²)
F1	136.27 ± 2.17
F2	150.43 ± 1.86
F3	124.47 ± 1.67
F4	162.83 ± 2.36
F5	146.07 ± 1.76
F6	112.40 ± 2.11
F7	159.17 ± 2.36
F8	130.33 ± 1.96
F9	152.57 ± 2.26

Figure 16: Extrudability Profile of Polyherbal Emulgel Formulations (F1–F9)

Rheological Characterization

Flow behaviour was investigated by plotting viscosity against shear rate. The rheological profile was analyzed to determine pseudoplasticity and shear-thinning characteristics of the developed emulgel [122].

Particle Size Analysis

Particle size distribution and polydispersity index (PDI) of the optimized formulation were determined using dynamic light scattering (DLS). Measurements were performed at ambient temperature following suitable dilution. The Z-average diameter, PDI, and particle size distribution profile were recorded [123].

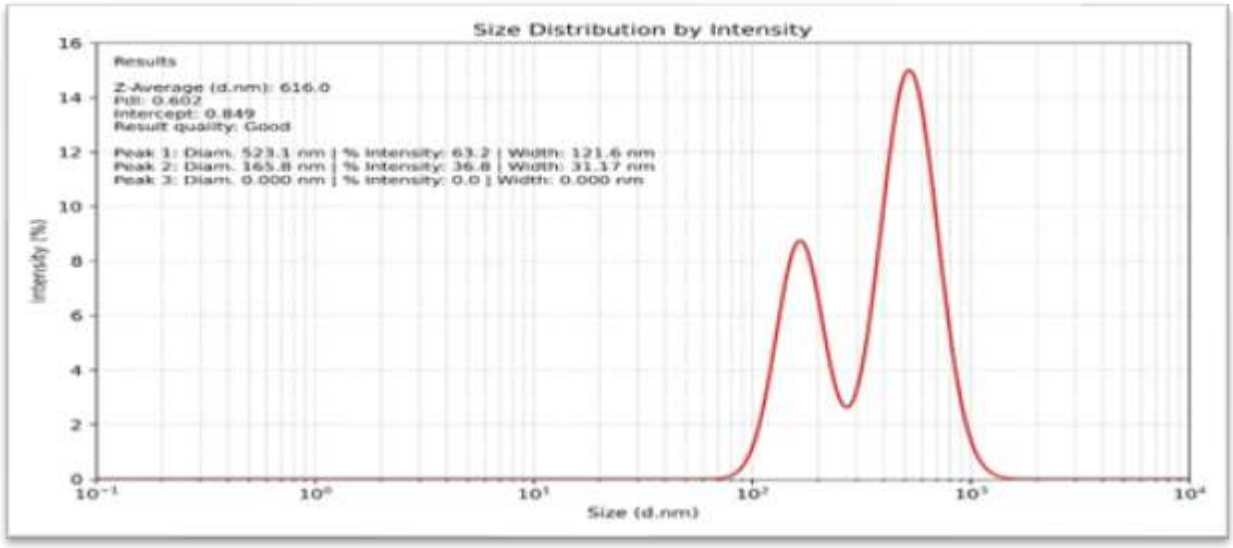

Figure 17: Particle size of Polyherbal Emulgel

In-Vitro Drug Release Study

Drug release studies were performed using a Franz diffusion cell assembly. A suitable synthetic membrane was mounted between donor and receptor compartments. The receptor medium was maintained under continuous stirring at controlled temperature conditions [124].

At predetermined time intervals, aliquots were withdrawn and replaced with fresh dissolution medium to maintain sink conditions. Samples were analyzed spectrophotometrically, and cumulative drug release was calculated [125].

Table 14: Cumulative Percentage Drug Release of Polyherbal Emulgel Formulations (F1–F9)

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	12.4 ± 1.2	11.2 ± 1.0	10.5 ± 0.9	9.6 ± 1.1	8.7 ± 0.9	8.3 ± 1.0	7.6 ± 1.1	6.9 ± 0.8	7.2 ± 0.9
30	21.8 ± 1.5	20.4 ± 1.3	19.2 ± 1.2	18.3 ± 1.3	16.5 ± 1.2	15.9 ± 1.3	14.8 ± 1.4	13.6 ± 1.1	14.1 ± 1.2
60	38.6 ± 1.8	36.9 ± 1.6	35.1 ± 1.5	33.8 ± 1.7	32.8 ± 1.4	31.5 ± 1.6	29.9 ± 1.7	27.5 ± 1.4	28.3 ± 1.5
120	59.2 ± 2.1	56.8 ± 1.9	54.3 ± 1.8	52.6 ± 2.0	56.9 ± 1.8	54.7 ± 1.9	52.1 ± 2.0	48.9 ± 1.8	50.4 ± 1.9
180	72.5 ± 2.4	70.1 ± 2.2	68.7 ± 2.0	66.9 ± 2.2	68.4 ± 2.1	66.8 ± 2.2	64.3 ± 2.3	60.8 ± 2.0	62.7 ± 2.1
240	83.1 ± 2.6	81.5 ± 2.5	80.2 ± 2.3	78.4 ± 2.4	78.2 ± 1.9	76.9 ± 2.5	74.8 ± 2.6	70.5 ± 2.3	72.8 ± 2.4
300	91.8 ± 2.8	89.7 ± 2.7	88.6 ± 2.5	86.9 ± 2.6	86.5 ± 2.3	85.2 ± 2.7	83.6 ± 2.8	79.4 ± 2.6	81.6 ± 2.7

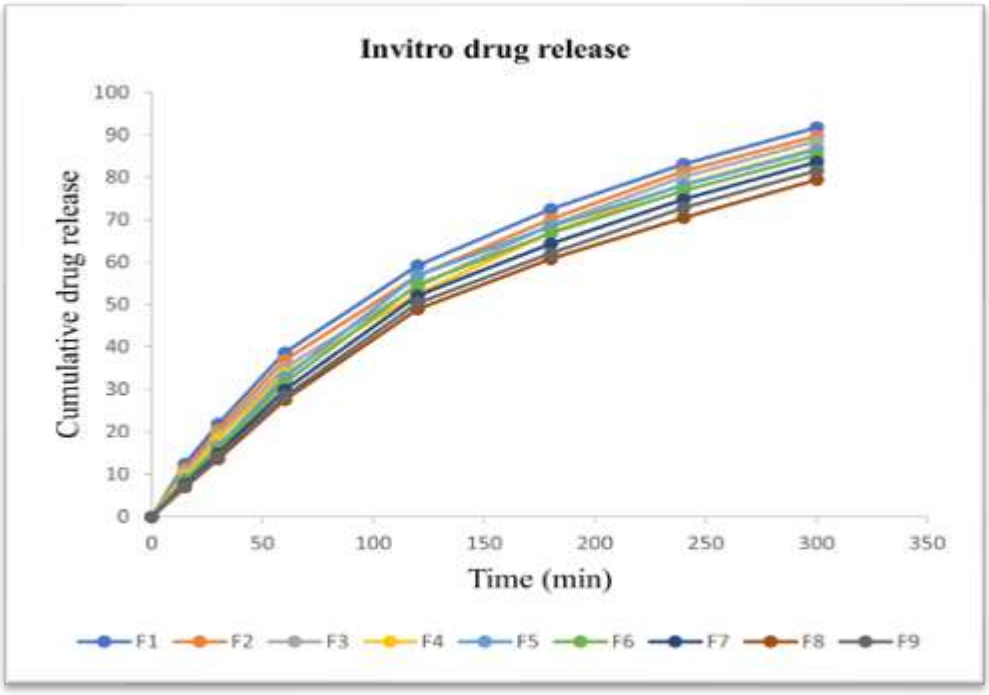

Figure 18: In-Vitro Drug Release Profile of Polyherbal Emulgel Formulations (F1–F9)

Drug Release Kinetic Analysis

The in-vitro drug release data of the optimized polyherbal emulgel formulation were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models to elucidate the mechanism of drug release. The linear regression plots obtained for all models were compared based on their correlation coefficient (R^2) values. The kinetic parameters, including the release exponent (n) obtained from the Korsmeyer–Peppas model, were used to characterize the release behavior of the formulation. The model exhibiting the highest correlation coefficient was considered the best fit and was used to explain the predominant drug release mechanism. [126,127].

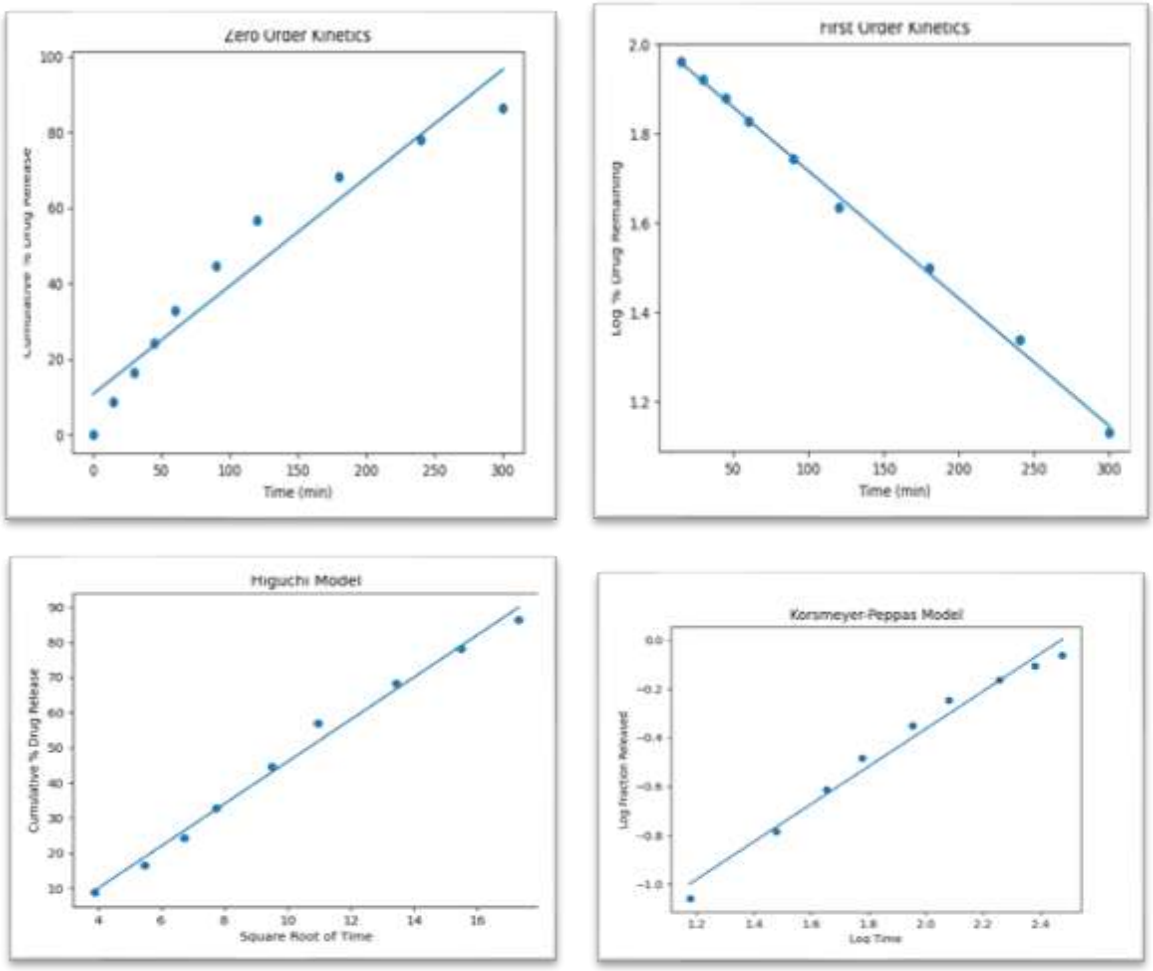

Figure 19: Comparative drug release kinetic plots of the optimized polyherbal emulgel formulation fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models.

Antioxidant Activity

The antioxidant potential of the optimized formulation was evaluated using the DPPH radical scavenging assay [128].

Different concentrations of the formulation were reacted with DPPH solution and incubated under controlled conditions. Absorbance was measured spectrophotometrically, and percentage radical scavenging activity was calculated relative to a control solution. Ascorbic acid was used as the reference standard [129].

Antimicrobial Activity

Antimicrobial efficacy against Cutibacterium acnes was evaluated using the agar well diffusion technique [130]. Sterile agar plates were inoculated with standardized bacterial suspensions, and wells were loaded with predetermined concentrations of the formulation. Following incubation, zones of inhibition were measured and compared with those produced by a marketed clindamycin formulation [131].

Table 15: Percentage zone of inhibition of Test and Marketed Formulation Cutibacterium

S. No.	Formulation	Concentration	Zone of Inhibition (mm)	% Inhibition (vs Marketed)
1	Optimized Polyherbal Emulgel (F5)	150 mg/mL	17.8 ± 0.35	90.8
2	Marketed Drug (Clindamycin 1%)	1% w/v	19.6 ± 0.30	100

Figure 20: Comparative Zone of Inhibition of Optimized Polyherbal Emulgel and Marketed Drug Against Cutibacterium acnes

Table 16: Diameter and Percentage Zone of Inhibition at Different Concentrations

S. No.	Concentration (mg/mL)	Zone of Inhibition (mm)	% Inhibition*
1	25	9.8 ± 0.34	47.6
2	50	12.9 ± 0.42	62.6
3	75	14.7 ± 0.31	71.4
4	100	17.1 ± 0.37	83.0
5	125	18.5 ± 0.29	89.8
6	150	19.7 ± 0.26	95.6

Statistical Analysis

All experiments were performed in triplicate, and results were expressed as mean ± standard deviation.

Response Surface Methodology and analysis of variance (ANOVA) were employed to evaluate the significance of formulation variables and their interactions. Statistical significance was considered at a confidence level corresponding to $p < 0.05$. Model adequacy was assessed using adjusted R^2, predicted R^2, adequate precision, and lack-of-fit analysis [132].

Table 17: Model Summary Statistics for Drug Release

Parameter	Value	Interpretation
R^2	0.958	Indicates that 95.8% of the variability in drug release is explained by the model
Adjusted R^2	0.941	Adjusted for the number of variables; confirms strong model fit
Predicted R^2	0.917	Demonstrates good predictive ability of the model

Adequate Precision	18.72	Signal-to-noise ratio > 4 indicates adequate model discrimination

Conclusion

The present investigation successfully developed and optimized a polyherbal anti-acne emulgel containing Aloe vera, tea tree oil, rosemary oil, and turmeric oil using a Quality by Design-based formulation strategy. The systematic optimization approach enabled the identification of critical formulation variables and their influence on the physicochemical and functional characteristics of the developed delivery system.

Compatibility studies performed using FTIR and DSC confirmed the absence of significant interactions between the herbal actives and formulation excipients, indicating the suitability of the selected components for formulation development. Statistical optimization demonstrated that Carbopol concentration and surfactant composition significantly influenced formulation performance, while response surface methodology effectively identified an optimal formulation region.

The optimized formulation exhibited desirable physicochemical characteristics, including acceptable pH, favourable rheological behaviour, satisfactory spreadability, and suitable extrudability. Particle size analysis revealed the formation of a stable dispersed system, while in vitro release studies demonstrated sustained drug release, governed predominantly by a non-Fickian transport mechanism.

Biological evaluation further highlighted the therapeutic potential of the developed formulation. The optimized emulgel demonstrated substantial antioxidant activity and significant antimicrobial efficacy against Cutibacterium acnes, with activity approaching that of a marketed clindamycin formulation. These findings suggest that the combined action of the incorporated herbal constituents may provide a multifaceted approach to acne management by simultaneously addressing microbial proliferation, oxidative stress, and inflammatory processes.

Overall, the developed polyherbal emulgel represents a promising topical delivery platform with favourable pharmaceutical and biological characteristics. The formulation may offer a potential alternative or adjunct to conventional anti-acne therapies and merits.

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