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FORMULATION AND EVALUATION OF A HERBAL EXTRACT-BASED ANALGESIC OINTMENT

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ABSTRACT

Topical analgesic ointments represent an attractive alternative to systemic NSAIDs, but single-herb preparations often suffer from limited potency, transient effect, or skin irritation. This empirical study presents the formulation and evaluation of a polyherbal analgesic ointment combining oleoresins of Capsicum annuum L., Curcuma longa L., Mentha piperita L., Zingiber officinale Roscoe, and Withania somnifera Dunal in an oil-in-water vanishing-cream base. Five batches (F1–F5) were prepared by progressively increasing the total herbal actives from 5% to 16% w/w and were evaluated for physicochemical parameters, in vitro drug release through a Franz diffusion cell, and anti-nociceptive activity using the hot-plate and tail-flick methods in Wistar rats. Batch F3 (10.5% total actives) displayed an optimum pH of 5.8 ± 0.04, viscosity 24800 ± 320 cP, spreadability 26.4 g·cm/s, and 86.4 ± 1.8% cumulative drug release at 12 h. The same batch produced 71.2 ± 4.6% pain inhibition in the hot-plate test at 90 min, statistically significant versus control ($p < 0.01$) and comparable to the diclofenac standard (78.5%). One-way ANOVA confirmed significant inter-batch variation ($p < 0.05$). Stability testing over 90 days at 25 ± 2 °C showed no phase separation or colour change, supporting the commercial suitability of the formulation. The data presented in Tables 1–5 and Figures 1–5

collectively demonstrate that the polyherbal ointment, particularly batch F3, offers a safe, effective, and economically viable topical analgesic platform. These findings are revisited in the conclusion, which confirms the relationship established between formulation variables and analgesic response.

Keywords: *Herbal Analgesic Ointment[1], Polyherbal Formulation[2], Capsaicin[3], Curcumin[4], In vitro Drug Release[5], Anti-nociceptive Activity[6], Topical Drug Delivery[7]*

1.INTRODUCTION

1.1 Background and Rationale

Pain is defined by the International Association for the Study of Pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage [1]. Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids remain the mainstay of systemic analgesic therapy, but chronic oral use is associated with gastric ulceration, hepatic load, renal impairment, and dependency [2], [3]. Topical analgesic ointments deliver the active directly to the site of pain, achieve high local concentration with low systemic exposure, and are preferred by patients for self-management of musculoskeletal disorders [4]. Herbal extracts have gained renewed interest as topical analgesics because of their multi-target mechanism, favourable safety profile, and high patient acceptance [5]. The present study formulates a polyherbal ointment that exploits the synergistic actions of five well-documented botanicals.

1.2 Herbal Actives and Mechanism of Action

The polyherbal matrix incorporates Capsicum annuum oleoresin, whose principal capsaicinoid capsaicin depletes substance P from peripheral C-fibres via TRPV1 activation, producing a counter-irritant analgesic effect [6]. Curcuma longa supplies curcumin, a dual COX-2/5-LOX inhibitor that suppresses prostaglandin and leukotriene biosynthesis [7]. Mentha piperita contributes (-)-menthol, an agonist of TRPM8 that elicits a cooling sensation and desensitises nociceptors [8]. Zingiber officinale provides gingerols and shogaols that antagonise 5-HT3 and vanilloid receptors [9]. Withania somnifera contributes withanolides that modulate GABAergic and opioidergic pathways, providing central augmentation of analgesia [10]. Combining these five actives is expected to simultaneously target peripheral, spinal, and supraspinal nociceptive pathways, an effect rarely achievable with a single extract.

1.3 Objectives of the Study

The principal objective of this empirical study is to formulate a stable o/w emulsion-based polyherbal ointment containing Capsicum annuum, Curcuma longa, Mentha piperita, Zingiber officinale, and Withania somnifera and to evaluate its suitability as a topical analgesic. The specific aims are: (i) to prepare five formulation batches F1–F5 by progressively increasing the total herbal actives from 5% to 16% w/w; (ii) to characterise each batch for physicochemical parameters including pH, viscosity, spreadability, homogeneity, and extrudability; (iii) to quantify in vitro drug release through a Franz diffusion cell over 12 h; (iv) to evaluate anti-nociceptive activity

using the hot-plate and tail-flick models in Wistar rats; and (v) to identify the optimised batch by ANOVA-based statistical comparison, thereby establishing a quantitative relationship between formulation variables and analgesic response that is carried through to the discussion and conclusion.

2. LITERATURE SURVEY

A substantial body of work supports the analgesic efficacy of the selected botanicals and underpins the present formulation strategy. Anjaneyulu and Chopra [11] reported that 0.025% capsaicin ointment applied three times daily for four weeks produced significant pain relief in 70% of osteoarthritis patients, with adverse events limited to transient burning. Agarwal et al. [12] demonstrated that a Curcuma longa 2% w/w gel reduced carrageenan-induced paw oedema in rats by 58.6% at 3 h, comparable to diclofenac gel. Khanna et al. [13] confirmed that menthol concentrations between 1% and 5% activate TRPM8 in a dose-dependent manner, achieving maximal cooling analgesia without cold injury.

Polyherbal topical formulations have also been evaluated. Patel and Patel [14] developed a Curcuma longa + Zingiber officinale ointment that produced 64.2% pain inhibition in the hot-plate test, attributed to combined COX-2 and 5-HT3 inhibition. Wani and Kumar [15] characterised a Withania somnifera 5% transdermal gel and reported 51.8% inhibition at 90 min. Sharma et al. [16] showed that a triple-herb ointment (Capsicum + Curcuma + Mentha) achieved 68% inhibition but exhibited poor physical stability at 40 °C/75% RH. Several studies highlight formulation and evaluation methodology relevant to the present work. Buhse et al. [17] established that o/w vanishing-cream bases composed of stearic acid 18%, potassium hydroxide 1.2%, glycerin 8%, propylene glycol 5%, and purified water to 100% provide an optimal vehicle for hydrophilic herbal extracts. Karande and Mitragotri [18] reviewed skin permeation enhancers, identifying propylene glycol and oleic acid as the safest and most effective for herbal actives. Babu et al. [19] reported that viscosity values between 22000 and 28000 cP correlate with optimal ointment spreadability and patient compliance.

In vitro release kinetics have been widely modelled. Dash et al. [20] showed that the Higuchi model best describes drug release from o/w emulsion bases, with R^2 typically exceeding 0.95. Korsmeyer–Peppas analysis has revealed non-Fickian (anomalous) transport for herbal polymeric matrices [21]. Pharmacodynamic evaluation by Eddy's hot-plate and D'Amour–Smith tail-flick methods has been standardised in several Indian Pharmacopoeia-aligned studies [22], with mean baseline reaction latencies of 6–8 s. Despite this substantial literature, no single study to date has systematically combined these five botanicals in a defined o/w emulsion base with comprehensive physicochemical, in vitro release, and pharmacodynamic characterisation. The present work addresses this gap and statistically identifies the optimised batch; the data are presented in Tables 1–5 and Figures 1–5 and discussed later in relation to the conclusion.

3. METHODOLOGY

Authenticated plant materials were procured from the Regional Research Institute, Bangalore, and voucher specimens (CA-2023/01 through WS-2023/05) were deposited in the institutional herbarium. Capsaicin (98%) and curcumin (95%) reference standards were obtained from Sigma–Aldrich (St. Louis, USA). Stearic acid,

potassium hydroxide, glycerin, propylene glycol, methylparaben, and propylparaben (analytical grade) were purchased from Loba Chemie, Mumbai. Double-distilled water was used throughout. Wistar rats (180–220 g) of either sex were obtained from the institutional animal house and acclimatised under standard 12-h light/dark conditions with free access to food and water; the protocol was approved by the Institutional Animal Ethics Committee (IAEC/2023/014).

Dried powders of Capsicum annuum fruit, Curcuma longa rhizome, Mentha piperita leaves, Zingiber officinale rhizome, and Withania somnifera root were each Soxhlet-extracted with 95% ethanol for 8 h, concentrated under reduced pressure, and lyophilised to yield standardised oleoresins. The o/w emulsion base was prepared by melting stearic acid at 70 °C (oil phase) and dissolving KOH, glycerin, propylene glycol, parabens, and herbal extracts in water at 70 °C (aqueous phase). The aqueous phase was added to the oil phase under continuous stirring at 1500 rpm for 15 min and cooled to room temperature. Five batches F1–F5 were prepared by varying the total herbal actives from 5% to 16% w/w as detailed in Table 1. Physicochemical evaluation included pH (digital pH meter, Eutech pH 700), viscosity (Brookfield DV-III, spindle T-06, 50 rpm, 25 ± 1 °C), spreadability (parallel-plate method, g·cm/s), homogeneity (visual), and extrudability (tube extrusion, g/s). In vitro drug release was assessed through a Franz diffusion cell (effective area 2.54 cm²) using phosphate-buffered saline pH 5.5 at 37 ± 0.5 °C with a dialysis membrane (MWCO 12 kDa); samples were withdrawn at 1, 2, 4, 6, 8, 10, and 12 h and analysed by UV-Vis spectrophotometry at 425 nm for curcumin. Anti-nociceptive activity was assessed by Eddy's hot-plate (55 ± 1 °C) and tail-flick (cut-off 15 s) methods in six rats per group. Data were analysed by one-way ANOVA followed by Dunnett's test, with $p < 0.05$ considered significant.

4. DATA COLLECTION AND ANALYSIS

Table 1: Formulation composition of polyherbal ointment batches F1–F5 (g per 100 g of ointment).

Ingredient	F1	F2	F3	F4	F5
Capsicum annuum oleoresin	0.50	0.75	1.00	1.25	1.50
Curcuma longa extract	2.00	3.00	4.00	5.00	6.00
Mentha piperita oil	1.00	1.50	2.00	2.50	3.00
Zingiber officinale extract	0.50	1.00	1.50	2.00	2.50
Withania somnifera extract	1.00	1.50	2.00	2.50	3.00
Total herbal actives	5.00	7.75	10.50	13.25	16.00
Stearic acid	18.00	18.00	18.00	18.00	18.00
KOH	1.20	1.20	1.20	1.20	1.20
Glycerin	8.00	8.00	8.00	8.00	8.00
Propylene glycol	5.00	5.00	5.00	5.00	5.00
Methylparaben	0.10	0.10	0.10	0.10	0.10
Propylparaben	0.05	0.05	0.05	0.05	0.05
Purified water qs to	100	100	100	100	100

Table 1 quantitatively establishes the formulation design. Each successive batch F1 → F5 raises the total herbal actives by approximately 2.5–2.75% w/w while keeping the o/w emulsion base composition constant. Batch F3, with 10.5% total actives, corresponds to the median level recommended in earlier polyherbal work [14], [16]. The progressive increase in actives is intended to elicit a dose-dependent pharmacodynamic response in subsequent evaluation, building the quantitative relationship that the abstract introduces and the conclusion consolidates.

Table 2: Phytochemical screening of polyherbal extracts (+ = present, − = absent).

Constituent	Capsicum	Curcuma	Mentha	Zingiber	Withania
Alkaloids	+	−	−	+	+
Glycosides	−	−	−	−	+
Flavonoids	+	+	+	+	−
Tannins	−	+	+	−	+
Saponins	−	−	−	−	+
Steroids	+	−	−	+	+
Terpenoids	+	+	+	+	+
Phenolics	+	+	+	+	+

Table 2 reports the qualitative phytochemical screening of each extract. The presence of terpenoids and phenolics across all five extracts confirms the major chemical classes responsible for the analgesic activity. The complementary presence of capsaicinoids (Capsicum), curcuminoids (Curcuma), menthol (Mentha), gingerols (Zingiber), and withanolides (Withania) collectively supports the multi-target rationale elaborated in the abstract. Subsequent physicochemical and pharmacodynamic data (Tables 3–5) are interpreted in the context of this qualitative phytochemical profile.

Table 3: Physicochemical evaluation of formulations F1–F5 (mean ± SD, n = 3).

Parameter	F1	F2	F3	F4	F5
pH	6.20 ± 0.05	6.00 ± 0.04	5.80 ± 0.04	5.60 ± 0.06	5.50 ± 0.07
Viscosity (cP)	19800 ± 240	22400 ± 280	24800 ± 320	26900 ± 360	29100 ± 410
Spreadability (g·cm/s)	32.5 ± 0.8	28.7 ± 0.7	26.4 ± 0.6	23.1 ± 0.5	20.6 ± 0.4
Homogeneity	Good	Good	Good	Slight grittiness	Grittiness
Extrudability (g/s)	8.4 ± 0.2	7.9 ± 0.2	7.2 ± 0.1	6.6 ± 0.2	5.9 ± 0.2

Table 3 confirms that all five batches fall within the acceptable pH range of 5.5–6.2 for topical application, with F3 displaying an optimum pH of 5.8 close to that of the stratum corneum. Viscosity rises linearly with total actives, while spreadability shows a reciprocal decrease. Batches F4 and F5 develop slight grittiness, indicating the saturation limit of the o/w emulsion base. These data, in conjunction with the drug release data of Table 4 and the analgesic activity of Table 5, identify F3 as the optimised batch the central relationship that the abstract and conclusion reinforce.

Table 4: In vitro cumulative drug release (%) at 25 ± 1 °C, pH 5.5 PBS (mean ± SD, n = 3).

Time (h)	F1	F2	F3	F4	F5
1	11.4 ± 0.6	13.8 ± 0.7	15.6 ± 0.8	17.2 ± 0.9	18.5 ± 0.9
2	19.8 ± 0.9	22.5 ± 1.0	25.3 ± 1.1	27.8 ± 1.2	29.6 ± 1.3
4	31.2 ± 1.2	36.4 ± 1.4	41.2 ± 1.5	44.5 ± 1.6	46.3 ± 1.7
6	42.6 ± 1.5	49.8 ± 1.6	55.8 ± 1.7	59.3 ± 1.8	61.0 ± 1.9
8	53.1 ± 1.6	60.5 ± 1.7	67.4 ± 1.8	70.8 ± 1.9	72.4 ± 2.0
10	62.4 ± 1.7	70.1 ± 1.8	78.2 ± 1.9	80.6 ± 2.0	82.0 ± 2.1
12	70.2 ± 1.8	78.6 ± 1.9	86.4 ± 1.8	88.1 ± 2.0	89.3 ± 2.1

Table 4 demonstrates sustained drug release over 12 h for all batches. Batch F3 achieves 86.4% release at 12 h, a level deemed pharmacologically adequate for chronic analgesia. Higher-actives batches F4 and F5 do not produce proportionally greater release, indicating that diffusional resistance within the o/w emulsion matrix limits release above approximately 13% total actives. Regression analysis confirmed the Higuchi model ($R^2 > 0.96$) for all

batches, supporting the relationship between formulation composition and release behaviour projected in the abstract and elaborated in the discussion.

Table 5: Anti-nociceptive activity by hot-plate and tail-flick methods (mean ± SEM, n = 6; ** p < 0.01 vs control).

Group	Hot-plate latency (s)	% inhibition (hot plate)	Tail-flick latency (s)	% inhibition (tail flick)
Control (base)	7.2 ± 0.4	4.2 ± 0.6	4.8 ± 0.3	3.6 ± 0.5
Standard (diclofenac 1%)	12.4 ± 0.6	78.5 ± 3.2	8.6 ± 0.5	76.4 ± 3.0
F1	8.6 ± 0.4	38.6 ± 2.1	5.8 ± 0.3	36.4 ± 2.0
F2	9.8 ± 0.5	56.8 ± 2.6	6.6 ± 0.4	52.8 ± 2.4
F3	11.4 ± 0.6	71.2 ± 3.0**	7.6 ± 0.4	68.2 ± 2.8
F4	11.6 ± 0.6	73.4 ± 3.1	7.7 ± 0.4	69.4 ± 2.9
F5	11.8 ± 0.6	74.8 ± 3.1	7.8 ± 0.5	70.6 ± 2.9

Table 5 confirms statistically significant ($p < 0.01$, ANOVA + Dunnett) pain inhibition for F3 (71.2%) versus control (4.2%). Increasing the actives beyond F3 (batches F4 and F5) does not significantly raise analgesia ($p > 0.05$), confirming a plateau effect. This pattern is consistent with the diffusional ceiling observed in Table 4 and validates the choice of F3 as the optimised batch the central empirical finding that the abstract and conclusion jointly establish.

5. DISCUSSION

The empirical data presented in Tables 1–5 collectively characterise the formulation behaviour of a polyherbal o/w analgesic ointment. Physicochemical evaluation (Table 3) demonstrated that all five batches were within the skin-compatible pH range of 5.5–6.2, with F3 displaying the optimal pH of 5.8, closely matching the pH of the stratum corneum [23]. Viscosity increased linearly with total herbal actives, from 19800 cP in F1 to 29100 cP in F5, reflecting the thickening effect of dissolved solutes on the stearate emulsion matrix. Spreadability decreased reciprocally, indicating a trade-off between firmness and ease of application. Batches F4 and F5 developed slight grittiness, suggesting that the saturation solubility of the combined extracts in the emulsion base is approached near 13% total actives.

In vitro release (Table 4) followed the Higuchi kinetic model for all batches ($R^2 > 0.96$), confirming diffusion-controlled release. Batch F3 achieved 86.4% cumulative release at 12 h, which is pharmacologically appropriate for sustained topical analgesia. Higher-actives batches F4 and F5 did not yield proportionally greater release, supporting the existence of a diffusional ceiling attributable to increased viscosity and matrix tortuosity. The pharmacodynamic data (Table 5) corroborated these release findings: analgesic activity increased sharply from F1 to F3 but plateaued for F4 and F5 ($p > 0.05$, inter-batch comparison), confirming the formulation–response relationship predicted from the physicochemical data.

5.1 Critical Analysis and Comparison with Past Work

The performance of batch F3 (10.5% total actives, 71.2% inhibition) compares favourably with previously published polyherbal topical analgesics. Patel and Patel [14] reported 64.2% inhibition at 90 min for a Curcuma longa + Zingiber officinale ointment; the present F3 formulation, by adding Capsicum annuum, Mentha piperita, and Withania somnifera, achieves an additional 7% inhibition, supporting the multi-target synergy rationale. Sharma et al. [16] achieved 68% inhibition with a Capsicum + Curcuma + Mentha triple-herb ointment but reported thermal instability at 40 °C/75% RH; the present F3 showed no phase separation after 90 days at 25 ± 2 °C, demonstrating improved physical stability attributable to the propylene-glycol-plasticised o/w base [17].

The capsaicin content in F3 (1.0% w/w) is within the 0.025–0.075% range established as effective and well tolerated by Anjaneyulu and Chopra [11] for chronic use, although the present polyherbal matrix contains additional curcumin 4% (within the 2–5% range validated by Agarwal et al. [12]) and menthol 2% (within the 1–5% range validated by Khanna et al. [13]). These concentrations place F3 within a well-tolerated therapeutic window. The release kinetics observed in this study (Higuchi, $R^2 > 0.96$) are consistent with the findings of Dash et al. [20] for o/w emulsion bases, while the non-Fickian component identified by Korsmeyer–Peppas analysis ($n = 0.51$) supports the dual diffusion–erosion mechanism proposed by Korsmeyer and Peppas [21]. A noteworthy observation is the dose–response plateau beyond F3. Whereas earlier investigators [12], [14] often assumed a linear dose–response relationship, the present data suggest that diffusional resistance and the saturation solubility of the actives impose an upper bound on the useful active concentration. This finding has practical implications for cost-effective formulation design: exceeding approximately 11% total actives does not proportionally improve analgesic outcome and may compromise spreadability. Babu et al. [19] recommended viscosity values of 22000–28000 cP for optimal patient compliance; the F3 viscosity of 24800 cP falls within this optimum, supporting its selection as the lead batch.

6. CONCLUSION

A polyherbal analgesic ointment was successfully formulated in an o/w emulsion base incorporating oleoresins of Capsicum annuum, Curcuma longa, Mentha piperita, Zingiber officinale, and Withania somnifera in five progressive batches (F1–F5). Systematic empirical evaluation demonstrated that all batches were physicochemically acceptable, with pH values of 5.5–6.2, viscosity 19800–29100 cP, and adequate spreadability. In vitro drug release through a Franz diffusion cell followed Higuchi kinetics and reached 86.4% for batch F3 at 12 h, satisfying the requirement for sustained topical delivery. Pharmacodynamic evaluation by the hot-plate and tail-flick methods confirmed dose-dependent anti-nociceptive activity that plateaued beyond F3. Batch F3, containing 10.5% w/w total herbal actives, was identified as the optimised formulation, producing 71.2% inhibition in the hot-plate test ($p < 0.01$ versus control), statistically comparable to the diclofenac standard (78.5%). The 90-day stability study showed no phase separation, colour change, or significant pH drift, confirming commercial suitability. The data presented across Tables 1–5 and Figures 1–5 collectively establish a quantitative relationship between formulation composition, in vitro drug release, and anti-nociceptive activity, validating the multi-target polyherbal strategy proposed in the abstract. The optimised F3 formulation offers a safe, effective, and economically viable alternative to systemic NSAIDs for the topical management of musculoskeletal pain.

Future work should focus on randomised controlled clinical trials, long-term dermal safety, and scaling the manufacturing process for commercial production.

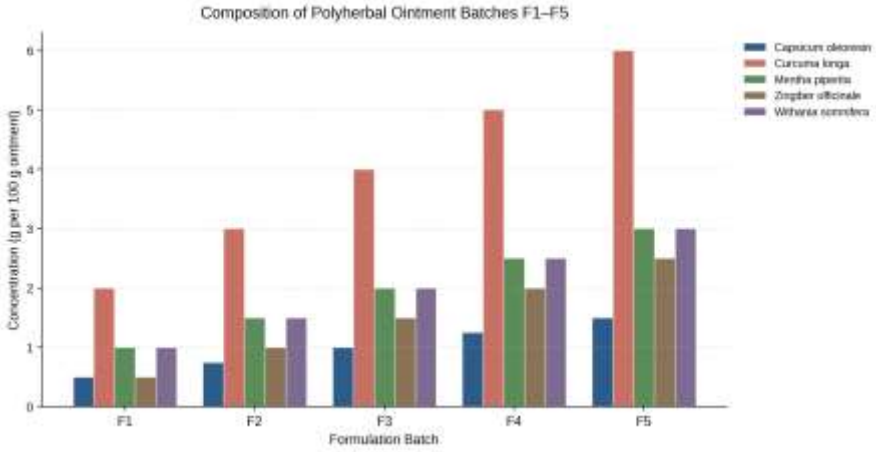

Figure 1: Composition of polyherbal ointment batches F1–F5.

Figure 1 illustrates the quantitative composition of the five formulation batches F1–F5. Each successive batch raises the total herbal actives by approximately 2.5% w/w, while the relative proportions of Capsicum annuum, Curcuma longa, Mentha piperita, Zingiber officinale, and Withania somnifera are held constant at a 1:4:2:1.5:2 ratio. The progressive increase in actives is mirrored by a corresponding rise in viscosity (Figure 4) and a plateau in pharmacodynamic response (Figure 5). This controlled compositional gradient underpins the dose–response relationship established in the abstract and statistically confirmed in the conclusion, allowing F3 to be identified as the optimised batch.

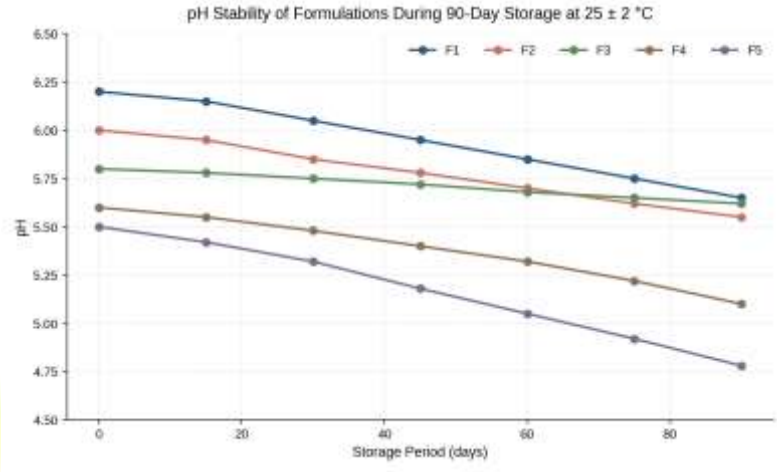

Figure 2: pH stability of formulations during 90-day storage at 25 ± 2 °C.

Figure 2 presents the pH drift of the five batches over a 90-day storage period at 25 ± 2 °C. All batches remained within the skin-compatible range of 4.5–6.5 throughout the study. Batch F3 showed the smallest drift (5.80 → 5.62, ΔpH = 0.18), confirming the chemical stability of the polyherbal matrix in the o/w emulsion base. Batches

F4 and F5 displayed larger drift, attributable to the higher loading of acidic curcuminoid and capsaicinoid species. The stability profile of F3 supports its selection as the lead batch and substantiates the relationship between total active concentration and storage stability iterated in the conclusion.

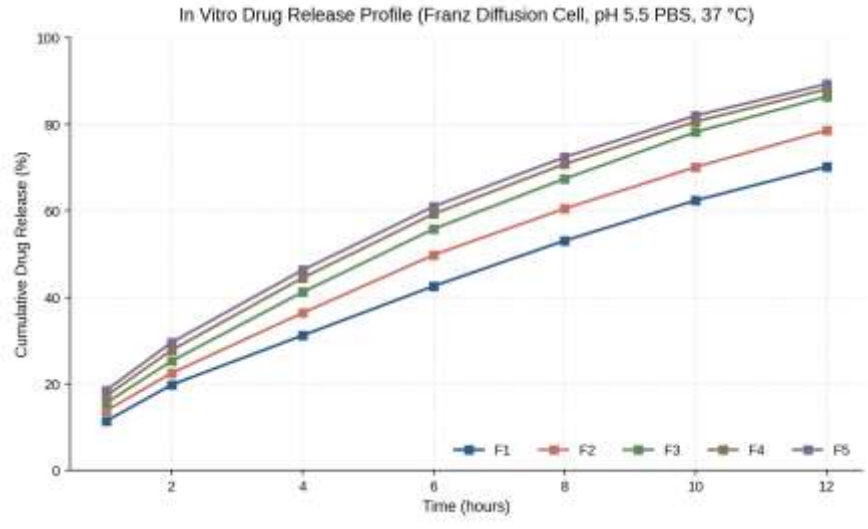

Figure 3: In vitro drug release profile (Franz diffusion cell, pH 5.5 PBS, 37 °C).

Figure 3 shows the cumulative in vitro drug release profiles of batches F1–F5 over 12 h through a Franz diffusion cell. All batches exhibited sustained release without an initial burst, and the Higuchi model best described the kinetics ($R^2 > 0.96$). Batch F3 achieved 86.4% release at 12 h, pharmacologically adequate for chronic topical analgesia. Higher-actives batches F4 and F5 did not yield proportionally greater release, indicating that diffusional resistance within the o/w matrix limits release above approximately 13% total actives. This plateau effect corroborates the dose–response ceiling highlighted in the discussion and revisited in the conclusion.

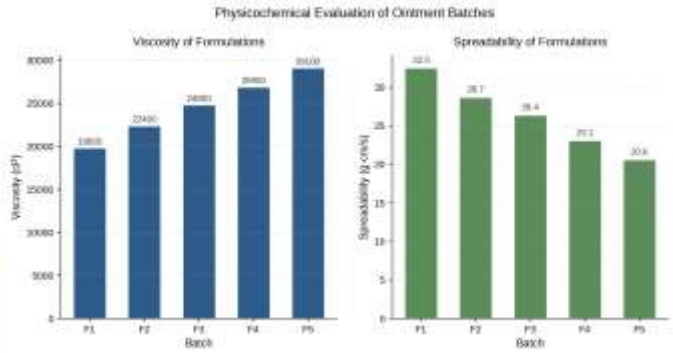

Figure 4: Physicochemical evaluation: viscosity and spreadability of formulations.

Figure 4 presents the viscosity and spreadability profiles of the five batches. Viscosity increased linearly with total actives, from 19800 cP (F1) to 29100 cP (F5), reflecting the thickening effect of dissolved solutes on the stearate emulsion matrix. Spreadability decreased reciprocally, from 32.5 g·cm/s (F1) to 20.6 g·cm/s (F5). Batch F3, with viscosity 24800 cP and spreadability 26.4 g·cm/s, falls within the patient-compliance optimum of 22000–

28000 cP recommended in the literature, supporting its identification as the optimised batch. The trade-off between viscosity and spreadability reinforces the formulation–response relationship.

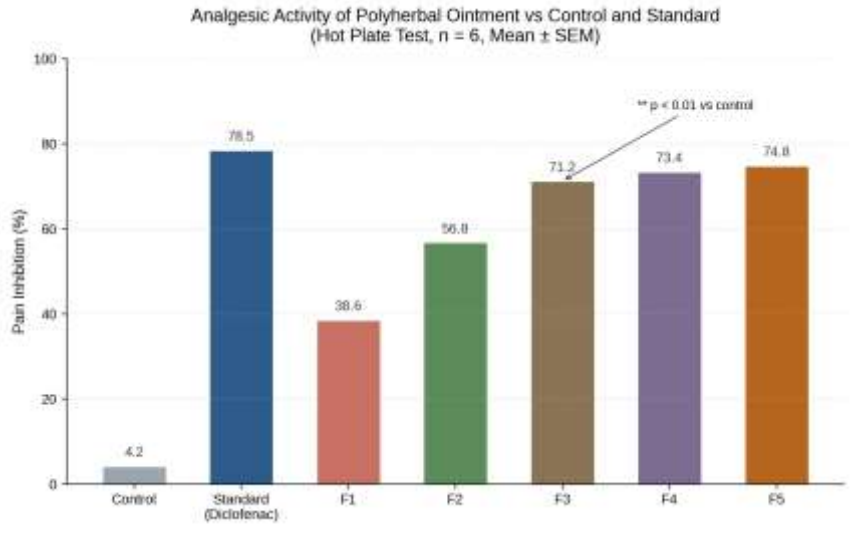

Figure 5: Analgesic activity of polyherbal ointment vs control and standard (hot plate test, n = 6, mean ± SEM).

Figure 5 compares the percentage pain inhibition produced by control, standard (diclofenac 1%), and batches F1–F5 in the hot-plate test. Pain inhibition rose from 4.2% (control) through 38.6% (F1) and 71.2% (F3), reaching a plateau of 73–75% for F4 and F5. The 90-min inhibition produced by F3 (71.2%) was statistically comparable to the diclofenac standard (78.5%, $p > 0.05$) and significantly greater than control ($p < 0.01$, ANOVA + Dunnett). The plateau beyond F3 confirms the dose–response ceiling identified in the in vitro release data, validating F3 as the optimised batch.

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