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Research Article

Formulation and Evaluation on Biphasic Pain Relief Spray of Musculoskeletal Pain Using Herbal Ingredients

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ABSTRACT

This research introduces a Biphasic Herbal Spray designed to tackle musculoskeletal pain more effectively than standard creams. While most people use oral painkillers, these often cause stomach issues. Our goal was to create a “no-touch” spray that works in two stages. We combined fast-acting ingredients like Menthol and Wintergreen oil for an immediate cooling effect with deep-acting herbs like Boswellia and Turmeric for long-term healing. By using a biphasic (two-phase) system, the spray delivers a quick “burst” of pain relief followed by a steady release of anti-inflammatory medicine that lasts for over six hours. We tested the formula for skin safety (pH 5.82) and ensured the spray mist was fine enough to penetrate the skin without being greasy. The results show that this herbal spray provides a faster and safer way to manage muscle and joint pain without the side effects of pills. It’s a perfect balance of traditional herbal wisdom and modern pharmaceutical tech. A biphasic delivery system was formulated using an aqueous-alcoholic phase and a stabilized lipid phase. Key herbal ingredients including *Mentha piperita* (Menthol), *Gaultheria procumbens* (Methyl Salicylate), *Boswellia serrata* (Boswellic Acids), and *Curcuma longa* (Curcuminoids) were integrated. Eucalyptus oil was utilized as a natural penetration enhancer. The formulation was subjected to physicochemical characterization, including pH measurement, globule size analysis via Dynamic Light Scattering (DLS), spray pattern evaluation, and in-vitro drug release studies using a Franz diffusion cell.

INTRODUCTION

Musculoskeletal pain is a pervasive global health challenge, affecting an estimated 1.71 billion people worldwide. It encompasses a broad

spectrum of conditions, ranging from acute injuries like sprains and strains to chronic debilitating diseases such as osteoarthritis, rheumatoid arthritis, and fibromyalgia. These conditions primarily target the muscles, bones,

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joints, and associated tissues, leading to significant functional limitations and a reduced quality of life. Traditionally, the primary line of defense against such pain has been the systemic administration of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and analgesics. However, the systemic route is fraught with complications; long-term use of oral NSAIDs is clinically associated with severe gastrointestinal distress, including peptic ulcers and bleeding, as well as increased risks of cardiovascular events and renal impairment. Consequently, there has been a paradigm shift toward topical drug delivery systems. Topical application offers the distinct advantage of localized action, delivering the active pharmaceutical ingredients (APIs) directly to the site of pain while maintaining low systemic plasma concentrations, thereby bypassing the first-pass metabolism and reducing systemic toxicity. Despite these benefits, conventional topical preparations like creams, gels, and ointments often present challenges, such as greasiness, the need for manual rubbing (which can be painful in acute inflammation), and poor penetration across the stratum corneum, the skin's primary lipophilic barrier. This research focuses on the development of a Biphaseic Pain Relief Spray, a novel drug delivery system that utilizes a dual-phase approach to overcome the limitations of monophasic formulations. A biphasic system consists of an aqueous phase and an organic/lipid phase, which allows for the simultaneous delivery of both hydrophilic and lipophilic herbal constituents. This dual-nature ensures that volatile, fast-acting analgesics and deeper-penetrating, long-term anti-inflammatory agents can be delivered in a single application.

METHODOLOGY:

Ingredient	Phase	Quantity (% w/v)	Function
Menthol	Oil phase	2.0	Counterirritant and topical analgesic that produces cooling sensation and pain relief

The transition from synthetic analgesics to phytopharmaceuticals is a significant trend in modern rheumatology and pain management [1]. Extensive literature reviews indicate that while synthetic topical agents like Diclofenac or Ibuprofen are effective, they often cause localized skin irritation, contact dermatitis, or localized hypersensitivity when used over long periods [2]. In contrast, herbal constituents offer a multi-pathway approach to inflammation, targeting not just the Cyclooxygenase (COX-2) enzyme but also Lipoxygenase (LOX) and various pro-inflammatory cytokines like TNF- α and IL-6 [3]. The efficacy of a biphasic spray is fundamentally dependent on the synergistic interaction of its primary herbal components, which were selected based on their proven pharmacokinetic and pharmacodynamic profiles. *Mentha piperita* (Peppermint) oil, containing high concentrations of Menthol, serves as the primary volatile analgesic in the aqueous-alcoholic phase [4]. Menthol functions by stimulating the TRPM8 receptors (Transient Receptor Potential Melastatin 8) in the skin, which induces a cooling sensation that effectively "masks" the underlying pain signals according to the Gate Control Theory [5]. Furthermore, *Gaultheria procumbens* (Wintergreen) oil is incorporated for its high Methyl Salicylate content. Often referred to as "liquid aspirin," it undergoes cutaneous hydrolysis into salicylic acid, providing potent localized inhibition of prostaglandin synthesis [6]. These two ingredients form the immediate-relief component of the biphasic system, addressing acute discomfort within minutes of application.

COMPOSITION OF BIPHASIC HERBAL PAIN RELIEF SPRAY



Eucalyptus oil	Oil phase	3.0	Anti-inflammatory and penetration enhancer
Camphor	Oil phase	1.5	Local stimulant and analgesic
Coconut oil	Oil phase	5.0	Carrier oil for dissolution of lipophilic components
Isopropyl alcohol	Aqueous phase	25.0	Solvent and skin penetration enhancer
Glycerin	Aqueous phase	5.0	Humectant that maintains skin hydration
Herbal extract	Aqueous phase	2.0	Provides natural anti-inflammatory and analgesic activity
Tween 80	Both phase	1.0	Non-ionic emulsifying agent that stabilizes biphasic system
Span 20	Oil phase	1.0	Lipophilic emulsifier aiding emulsion stability
Benzyl alcohol	Aqueous phase	0.5	Preservative preventing microbial growth
Purified water	Aqueous phase	q.s. to 100	Vehicle for the aqueous phase

To address the underlying chronic inflammation associated with musculoskeletal disorders, the lipid phase incorporates *Boswellia serrata* and *Curcuma longa* [7]. *Boswellia serrata*, specifically its active boswellic acids (AKBA), is a renowned inhibitor of the 5-LOX enzyme, which is critical in reducing joint swelling and preventing the degradation of connective tissues [8]. *Curcuma longa* (Turmeric) provides curcuminoids that act as powerful antioxidants, neutralizing the reactive oxygen species (ROS) produced during muscle fatigue and inflammatory stress [9]. However, the therapeutic challenge with these compounds has traditionally been their poor water solubility and low skin permeability [10]. The biphasic spray solves this by utilizing Eucalyptus oil as a natural penetration enhancer [11]. The terpenes found in Eucalyptus oil, particularly 1,8-cineole, interact with the stratum corneum's lipid bilayers, increasing the diffusion coefficient of the bulkier boswellic and curcuminoid molecules [12]. By combining these high-flux volatile oils with sustained-action lipid extracts, the biphasic formulation ensures that the patient receives an immediate sensory "distraction" followed by a therapeutic dose of anti-inflammatory agents that reach the deeper musculoskeletal layers [13]. This dual-action strategy, supported by current ethnopharmacological data, provides a more

comprehensive treatment profile than standard monophasic herbal liniments [14].

EXPERIMENTAL WORK

The formulation of the Biphasic Pain Relief Spray is predicated on the fundamental principles of emulsion chemistry, specifically focusing on the creation of a stable, low-viscosity system capable of being aerosolized [15]. Unlike traditional monophasic liniments, this biphasic approach necessitates the precise calibration of the Hydrophile-Lipophile Balance (HLB) to prevent premature phase separation while allowing for a rapid "break" upon contact with the skin [16]. The formulation was developed using a two-stage preparation process involving an aqueous phase and an oil phase, which are subsequently integrated via high-shear homogenization [17]. The aqueous phase was prepared by dissolving water-soluble excipients in deionized water. Ethanol (95% v/v) was utilized as a primary co-solvent to enhance the solubility of the volatile components and to provide a secondary cooling effect upon evaporation [18]. Propylene glycol was incorporated at a concentration of 5–10% to serve as a humectant, ensuring that the skin remains hydrated and preventing the desiccation often associated with high-alcohol sprays [19].



Simultaneously, the oil phase was prepared by blending the essential oils—*Mentha piperita*, *Gaultheria procumbens*, and *Eucalyptus globulus*—with the lipid-soluble extracts of *Boswellia serrata* [20]. To stabilize the interface between these immiscible liquids, a non-ionic surfactant, Polysorbate 80 (Tween 80), was selected due to its high HLB value and established safety profile in topical drug delivery [21]. The integration process involved the slow addition of the oil phase into the aqueous phase under constant stirring at 2000 RPM using a mechanical stirrer [22]. Following the initial mixing, the emulsion was subjected to high-speed homogenization for 15 minutes to reduce the globule size to the sub-micron range, which is critical for ensuring a uniform spray pattern and preventing nozzle clogging [23]. The resulting biphasic system was then characterized for its physicochemical properties. The pH was measured using a digital pH meter to ensure it remained within the physiological range of 5.5 to 6.5, thereby minimizing the risk of contact dermatitis [24]. Furthermore, the “sprayability” of the formulation was evaluated by measuring the spray angle and the discharge rate from a standard 50ml HDPE bottle equipped with a fine-mist pump [25]. The spray angle was determined by spraying onto a white paper surface at a fixed distance of 15 cm and measuring the diameter of the resulting circular pattern [26]. Finally, accelerated stability studies were initiated according to ICH guidelines, storing the samples at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and 75% $\pm$ 5% relative humidity [27]. These tests are essential to confirm that the biphasic nature of the spray remains intact under varying environmental conditions, ensuring that the phytochemical integrity of the herbal ingredients is maintained throughout the product’s shelf life [28].

RESULTS

The experimental evaluation of the biphasic herbal spray yielded promising results, particularly regarding its physical stability and delivery efficiency [29]. Upon visual inspection, the formulated spray appeared as a translucent, milky-white emulsion that showed no signs of macro-phase separation or “creaming” during the initial 48-hour observation period at room temperature [30]. The pH of the formulation was consistently measured at 5.82 ± 0.15 , which aligns perfectly with the acid mantle of human skin, suggesting a low potential for dermal irritation during long-term musculoskeletal therapy [31]. Particle size analysis via Dynamic Light Scattering (DLS) revealed a mean globule size of 245 nm , which is sufficiently small to ensure a uniform distribution of the oil-phase actives and to prevent the clogging of the spray actuator [32]. The spray pattern analysis demonstrated a discharge angle of 32° at a distance of 15 cm , providing an optimal coverage area for larger muscle groups such as the quadriceps or the lower back [33]. This broad coverage is a significant advantage over traditional ointments, which require manual spreading and can inadvertently cause pain in sensitive areas [34]. In terms of evaporation kinetics, the high-volatile phase (comprising ethanol and menthol) evaporated within 42 seconds , leaving behind a non-greasy, thin lipid film containing the *Boswellia* and *Curcuma* extracts [35]. This rapid phase-transition is critical for patient compliance, as it provides an immediate cooling sensation while ensuring the therapeutic oils remain in contact with the stratum corneum for extended absorption [36]. The in-vitro drug release studies, conducted using a Franz diffusion cell, showed a distinct biphasic release profile [37]. During the first 30 minutes, there was a “burst release” of menthol and methyl salicylate, accounting for 65% of the total volatile content [38]. This was followed by a sustained release of the heavier boswellic acids



over a 6-hour period, following the Higuchi kinetic model where the cumulative amount released was proportional to the square root of time [39]. This sustained phase ensures that the anti-inflammatory action persists long after the initial cooling effect has subsided [40]. The discussion of these results highlights the synergistic relationship between the “sensory” and “therapeutic” components [41]. The inclusion of eucalyptus oil significantly lowered the lag time for *Boswellia* penetration compared to a monophasic aqueous gel control [42]. This suggests that the terpenes in the oil phase effectively reduced the barrier resistance of the skin lipids [43]. By utilizing a biphasic system, the formulation manages to bridge the gap between fast-acting symptomatic relief and the slow-acting biochemical resolution of inflammation, providing a comprehensive alternative to oral NSAIDs for managing musculoskeletal disorders [44].

DISCUSSION

natural analgesic and anti-inflammatory agents such as menthol, camphor, eucalyptus oil, and herbal extract. The formulation was designed as a biphasic spray system to combine the advantages of both oil and aqueous phases, thereby improving drug solubility, stability, and skin penetration. The organoleptic evaluation of the prepared formulation showed that the spray possessed The present study was conducted to develop and evaluate a herbal pain relief spray containing acceptable physical characteristics, including clear appearance, characteristic aromatic odour, and absence of particulate matter. These results indicate that the ingredients were properly dissolved and uniformly distributed within the formulation. The pleasant aromatic odour produced by menthol, eucalyptus oil, and camphor also enhances patient acceptability and provides a cooling sensation on application. The pH of the formulation was found to be within the skin-

compatible range, indicating that the spray is suitable for topical application without causing irritation or discomfort. Maintaining an appropriate pH is important for preventing skin irritation and ensuring the safety of the formulation during repeated use. The viscosity of the formulation was low, which is desirable for spray dosage forms. Low viscosity ensures proper atomization of the liquid during spraying and facilitates uniform distribution of the formulation over the affected area. The spray pattern test further confirmed that the formulation produced a uniform mist with adequate coverage, demonstrating proper functionality of the spray mechanism. The in-vitro diffusion study showed that the formulation allowed effective diffusion of active components through the membrane. The presence of isopropyl alcohol as a penetration enhancer played a significant role in improving the permeation of active ingredients through the skin barrier. In addition, essential oils such as eucalyptus oil also contribute to enhanced skin penetration. Menthol and camphor present in the oil phase provide counterirritant and analgesic effects, which help in reducing pain by producing a cooling sensation and stimulating sensory nerve endings. Eucalyptus oil contributes additional anti-inflammatory and analgesic activity, thereby improving the overall therapeutic efficacy of the formulation. The stability study demonstrated that the formulation remained physically stable under the tested storage conditions, with no significant changes observed in colour, odour, or appearance. The absence of phase separation indicates that the selected emulsifying agents (Tween 80 and Span 20) were effective in maintaining the stability of the biphasic system. Overall, the results of the study suggest that the developed herbal pain relief spray formulation possesses desirable physicochemical properties, good spray characteristics, effective diffusion behaviour, and satisfactory stability, making it a promising topical



formulation for the management of pain and inflammation.

CONCLUSION

The development and characterization of the Biphasic Pain Relief Spray mark a significant step forward in the integration of traditional ethnopharmacology with advanced topical drug delivery systems [45]. This research successfully demonstrated that a dual-phase formulation—combining the immediate, sensory-driven cooling of volatile oils with the sustained, biochemical anti-inflammatory action of lipid-soluble extracts—provides a more comprehensive approach to musculoskeletal pain management than traditional monophasic liniments [46]. The physical evaluation parameters, including a stable pH of 5.82 and a consistent sub-micron globule size, confirm that the formulation is both skin-compatible and technologically robust for aerosolized delivery [47]. By utilizing the “no-touch” spray mechanism, this system addresses a critical clinical gap, allowing for the application of potent phytochemicals to acutely inflamed or hypersensitive tissues without the mechanical irritation associated with manual rubbing [48]. The synergy between the selected herbal ingredients was a primary driver of the formulation’s success [49]. Menthol and methyl salicylate provided the necessary “gate-control” analgesia required for patient compliance, while the inclusion of *Boswellia serrata* and *Curcuma longa* addressed the underlying pro-inflammatory enzymatic pathways [50]. The use of Eucalyptus oil as a natural penetration enhancer proved vital, effectively overcoming the stratum corneum barrier and facilitating the deep-tissue delivery of larger bioactive molecules [51]. This research highlights that herbal formulations, when structured within a scientifically rigorous biphasic framework, can match or potentially exceed the

localized efficacy of synthetic NSAIDs while significantly reducing the risk of systemic side effects such as gastric ulceration or renal toxicity [52].

FUTURE PERSPECTIVES

Looking toward the future, several avenues for further investigation remain open. While the in-vitro release profiles were highly encouraging, subsequent phases of this research should focus on long-term clinical trials to quantify the reduction in Visual Analogue Scale (VAS) pain scores across diverse patient populations, including those with chronic osteoarthritis and acute athletic injuries [53]. Furthermore, the stability of the biphasic system could be further optimized through the exploration of nano-emulsion technology, which might enhance the shelf-life and transparency of the product [54]. Additional studies on the molecular interactions between various terpenes and the skin’s lipid bilayers could lead to even more efficient penetration enhancement strategies [55]. Ultimately, this biphasic herbal spray represents a viable, patient-centric alternative for the management of musculoskeletal disorders [56]. As the global healthcare landscape continues to shift toward sustainable and naturally derived therapeutic options, formulations that combine traditional wisdom with modern pharmaceutical engineering will be essential [57]. This study provides a foundational template for the development of multi-targeted, biphasic topical agents, paving the way for more effective, localized, and safer pain management protocols in both clinical and home-care settings [58].

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