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Polyherbal Antiarthritic Transdermal Film

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ABSTRACT: The abstract presents the formulation and evaluation of a Polyherbal Antiarthritic Transdermal Film designed for controlled drug release and permeation of therapeutic compounds. The study incorporates *Lysiphyllum strychnifolium* stem extract into a polyvinyl alcohol (PVA) blended film matrix, utilizing a microwave-assisted extraction technique for optimal extraction conditions. The extracted herbal constituents exhibit significant total phenolics and flavonoids content, alongside notable antioxidant activity and nitric oxide scavenging potential. The blank PVA blended film and herbal transdermal patches demonstrate desirable physical characteristics, ensuring compatibility and homogeneity of the ingredients. Through the integration of various natural herbal extracts such as boswellia, evening primrose oil, blackcurrant seed oil, ginger, licorice, cat's claw, and devil's claw, along with pharmaceutically acceptable excipients, the formulation aims to address pain associated with arthritis. Additionally, the development process involves a hot-melt coating technique, encompassing steps such as melting, mixing, coating, laminating, cutting, pouching, and labeling. The kinetics of drug release and permeation behavior of astilbin from the matrix layer are elucidated, fitting well with the Korsmeyer–Peppas and zero-order models, respectively. Consequently, the Polyherbal Antiarthritic Transdermal Film emerges as a promising candidate for herbal medicine applications in the management of arthritic pain.

KEYWORDS: Formulation, evaluation, Polyherbal Antiarthritic Transdermal Film, controlled drug release, permeation, *Lysiphyllum strychnifolium* stem extract, polyvinyl alcohol (PVA), microwave-assisted extraction, laminating, cutting, pouching, labeling, kinetics, astilbin, Korsmeyer–Peppas model, zero-order model.

I. INTRODUCTION

The resurgence of interest in herbal medicine has sparked a significant shift towards exploring alternative therapeutic approaches, particularly in the management of various ailments, including arthritis. Traditional systems of medicine have garnered attention for their perceived efficacy and minimal adverse effects compared to conventional allopathic treatments. As a result, modern herbal formulations have proliferated in the market, ranging from triphala tablets to capsaicin gel, offering novel avenues for disease management. Among these, transdermal drug delivery systems (TDDS) have emerged as a promising modality, facilitating the controlled release of herbal compounds into systemic circulation.

Transdermal drug delivery represents a sophisticated approach to administering medications, bypassing the first-pass metabolism and ensuring a consistent concentration of active compounds in the bloodstream. The application of TDDS offers several advantages over conventional routes, including improved patient compliance, reduced side effects, and enhanced therapeutic efficacy. By utilizing the skin as a conduit for drug absorption, TDDS enables precise control over drug kinetics, maintaining concentrations within the therapeutic window while minimizing fluctuations that may lead to suboptimal dosing or toxicity.

However, despite its potential benefits, transdermal drug delivery is not without challenges. The skin's formidable barrier, particularly the stratum corneum, poses a significant obstacle to drug penetration. Overcoming this barrier necessitates the use of chemical permeation enhancers (CPEs) to augment the transdermal delivery of herbal compounds. These enhancers modify the skin's permeability properties, increasing the thermodynamic activity and partition coefficient of substances to facilitate their passage. Furthermore, formulating an effective transdermal drug delivery system requires careful consideration of physicochemical properties, such as molecular size, half-life, and oral bioavailability, to ensure optimal drug penetration and therapeutic outcomes.

II. RELATED WORK

Polyherbal formulations represent a promising avenue in contemporary pharmacotherapy, leveraging the synergistic interactions between multiple natural herbal extracts to enhance therapeutic outcomes. These formulations have garnered significant attention, particularly within traditional Ayurvedic medicine, due to their potential to amplify therapeutic effects while minimizing adverse reactions. By combining various herbal extracts, such as *Tinospora cordifolia*, *Pterocarpus marsupium*, *Gymnema sylvestris*, *Zingiber officinale*, and *Momordica charantia* for diabetes treatment, or *Zingiber officinale*, *Piper nigrum*, and long pepper for mucous reduction, polyherbal formulations offer a nuanced approach to disease management. Furthermore, the use of polyherbal combinations like Guduchi and curcumin to bolster immunity, or *Cuminum cyminum*, *Piper nigrum*, and *asafoetida* for alleviating bloating issues, underscores the versatility and efficacy of this therapeutic approach.

Arthritis, characterized by chronic inflammation and pain in the joints and surrounding tissues, poses a significant medical challenge globally. Traditional remedies, such as polyherbal formulations, present a compelling avenue for addressing this complex condition. In the quest for innovative solutions, researchers have developed a transdermal patch infused with polyherbal extracts, including *boswellia serrata*, evening primrose oil, blackcurrant seed oil, licorice, ginger, cat's claw, and devil's claw. This formulation aims to synergistically combat arthritis symptoms, leveraging the anti-inflammatory, analgesic, and immune-modulating properties inherent in each herbal constituent. By harnessing the transdermal route, this novel approach seeks to optimize drug delivery, ensuring enhanced efficacy while minimizing systemic side effects and improving patient compliance.

Boswellia serrata, a revered botanical in traditional medicine, offers profound anti-inflammatory and analgesic effects attributed to its rich content of boswellic acids. These bioactive compounds inhibit pro-inflammatory cytokines and the activity of 5-lipoxygenase, making *boswellia serrata* a cornerstone in arthritis management. Similarly, evening primrose oil, abundant in gamma-linolenic acid (GLA), exerts anti-inflammatory actions by modulating immune responses and scavenging free radicals. Likewise, blackcurrant seed oil, with its potent GLA content, complements this anti-inflammatory arsenal by regulating immune function and prostaglandin synthesis.

Licorice, ginger, cat's claw, and devil's claw further enrich the polyherbal formulation with their unique therapeutic contributions. Glycyrrhizic acid from licorice inhibits cyclooxygenase-2 (COX-2), a pivotal mediator of inflammation, while gingerols in ginger suppress prostaglandin synthesis and inhibit leukotriene production. Cat's claw, with its pentacyclic oxindole alkaloids, modulates immune responses and inhibits inflammatory mediators like prostaglandin E2 and tumor necrosis factor-alpha (TNF- α). Finally, devil's claw, enriched with harpagoside, exhibits anti-inflammatory effects by targeting COX-2 and lipoxygenase pathways. Together, these polyherbal extracts offer a comprehensive therapeutic approach for mitigating the multifaceted manifestations of arthritis, presenting a promising avenue for future research and clinical application.

III. MATERIALS & METHODS OF EXTRACTION

The extraction methodologies employed in the formulation of the Polyherbal Antiarthritic Transdermal Film involved meticulous procedures tailored to each botanical constituent, ensuring optimal extraction of bioactive compounds while maintaining purity and standardization.

For *Boswellia serrata*, a multi-step process was undertaken to isolate Boswellic acids, the key therapeutic agents present in the gum resin. This involved reflux extraction using an ethanol-water mixture followed by filtration to eliminate insoluble impurities. Subsequent concentration and precipitation steps facilitated the separation of Boswellic acids from non-polar impurities and lower terpenes. Acidification and filtration further refined the extract, yielding standardized Boswellic acid fractions with a high concentration of bioactive compounds.



Fig: Extraction of Boswellia Serrata

The extraction of Nirgundi essential oil from Vitex negundo leaves employed hydro-distillation, a classical method for volatile oil extraction. After drying and powdering the leaves, hydro-distillation in a closed Clevenger apparatus yielded a pale-yellow essential oil with the desired aroma profile. This meticulous process ensured the retention of volatile compounds while minimizing degradation, resulting in a high-quality essential oil suitable for incorporation into the transdermal formulation.

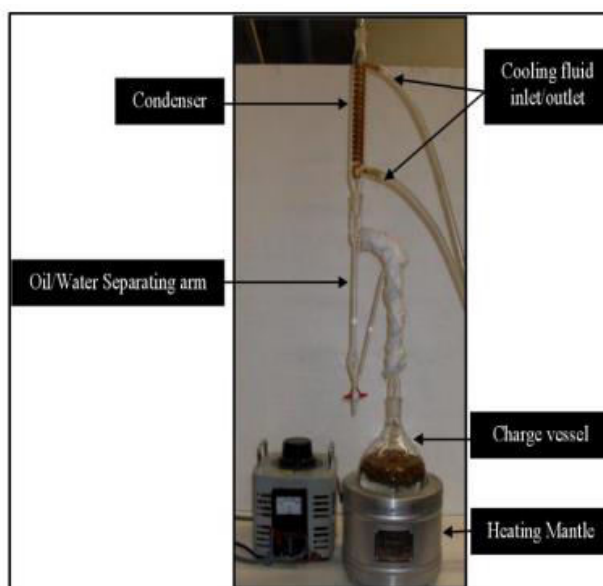


Fig: Extraction of Nirgundi Oil

Capsaicin, sourced from chili peppers, underwent extraction using a Soxhlet apparatus, a widely employed technique for extracting non-volatile compounds. The dried chili pepper powder was subjected to hydro-distillation, with the resulting extract collected and concentrated to obtain the desired capsaicin product. This method ensured efficient extraction of capsaicin, a potent analgesic compound, while maintaining its therapeutic efficacy.



Fig: Extraction of Capsaicin

Similarly, the extraction of curcumin from turmeric utilized Soxhlet extraction, leveraging the solvent's ability to efficiently extract non-volatile compounds. Fine turmeric powder underwent hydro-distillation to extract curcumin, followed by evaporation to concentrate the extract. This process yielded a purified curcumin product suitable for incorporation into the polyherbal transdermal film.

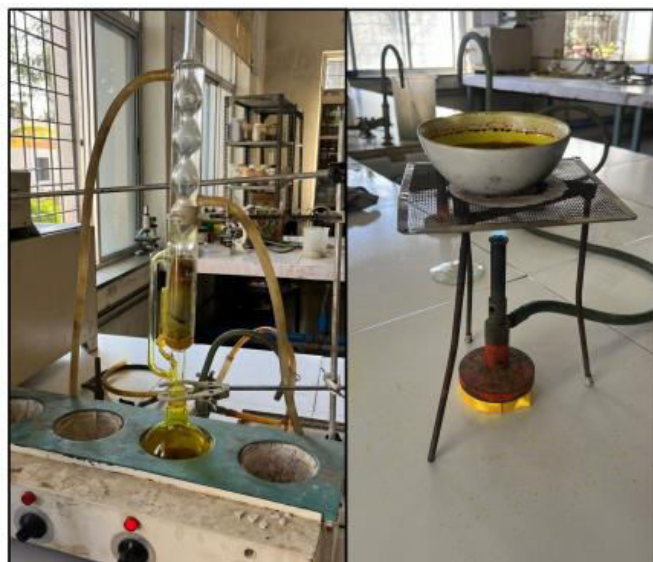


Fig: Extraction of Curcumin

These meticulously designed extraction methodologies ensured the isolation of bioactive compounds from each botanical source, facilitating the development of a standardized and therapeutically potent Polyherbal Antiarthritic Transdermal Film.

IV. PREPARATION & EVALUATION OF POLYMERIC FILM

The preparation of the Polyherbal Antiarthritic Transdermal Film involved the meticulous execution of the solvent casting method, also known as the solvent evaporation technique, to ensure the uniform incorporation of therapeutic compounds into the polymer matrix. Initially, all four herbal extracts, namely boswellic acid, Nirgundi oil, capsaicin,

and curcumin, were dissolved in ethanol. Subsequently, the polymer base, comprising Hydroxypropyl methylcellulose (HPMC) dissolved in an ethanol-water mixture (1:1), along with appropriate quantities of propylene glycol (PG) and polyethylene glycol (PEG), was prepared. Continuous stirring facilitated the homogenization of the solution, resulting in a uniform dispersion of herbal extracts within the polymer matrix. The final solution volume was adjusted to 20 ml to ensure consistency. A definite volume of this solution was then poured onto a film former maintained at a temperature of 50-60°C for 30 minutes to facilitate film formation. The solvent casting method enabled the creation of a polymeric film with a homogeneous distribution of herbal extracts, laying the foundation for subsequent evaluation.

Following the preparation of the medicated polymeric film, a comprehensive evaluation was conducted to assess various parameters critical to its performance and efficacy. Organoleptic characteristics, including appearance, color, clarity, flexibility, and smoothness, were visually inspected to gauge the film's aesthetic and physical attributes. Moreover, the film's thickness was measured using an electronic vernier caliper, ensuring uniformity across multiple points. Percentage flatness, an indicator of the film's structural integrity, was determined by measuring the length of strips cut from different regions of the film. Surface pH, moisture content, folding endurance, uniformity of weight, moisture uptake, and UV absorption maxima were meticulously assessed to ascertain the film's physicochemical properties and performance characteristics. These evaluations provided valuable insights into the film's suitability for transdermal application, guiding further optimization and refinement.

In summary, the preparation and evaluation of the Polyherbal Antiarthritic Transdermal Film involved a systematic approach encompassing solvent casting method, thorough incorporation of herbal extracts into the polymer matrix, and comprehensive assessment of various parameters to ensure the film's quality, efficacy, and suitability for therapeutic use in arthritis management. This rigorous methodology lays the groundwork for the development of a robust transdermal delivery system capable of providing targeted relief and improved patient outcomes in the treatment of arthritic conditions.

V. RESULT

The study aimed to develop a Polyherbal Antiarthritic Transdermal Film as a novel drug delivery system targeting inflammatory conditions like rheumatoid arthritis (RA) and osteoarthritis. The formulation incorporated four phytopharmaceuticals known for their anti-inflammatory properties: Boswellic acids, Nigundi oil, Curcumin, and Capsaicin. The selection of these constituents was based on their proven therapeutic efficacy and safety profile. Doses were determined based on reported topical doses from the literature, considering the direct permeation of drugs into the bloodstream without undergoing first-pass metabolism in transdermal drug delivery systems.

Moisture content in the matrix-type film was observed to increase with the concentration of hydrophilic polymers, impacting the film's drying process and brittleness. However, overall, the moisture uptake of the transdermal film remained low, contributing to reduced bulkiness. Three batches of the prepared films underwent evaluation for various parameters, including physicochemical characteristics.



Fig: Film Former & Transdermal Film

Upon storage, the optimized formulation demonstrated stability without significant changes in its physicochemical parameters. This stability over time suggests that the formulation maintains its integrity and efficacy under specified storage conditions. These findings underscore the potential of the Polyherbal Antiarthritic Transdermal Film as a stable

and effective therapeutic option for managing inflammatory conditions such as RA and osteoarthritis, paving the way for further development and clinical translation.

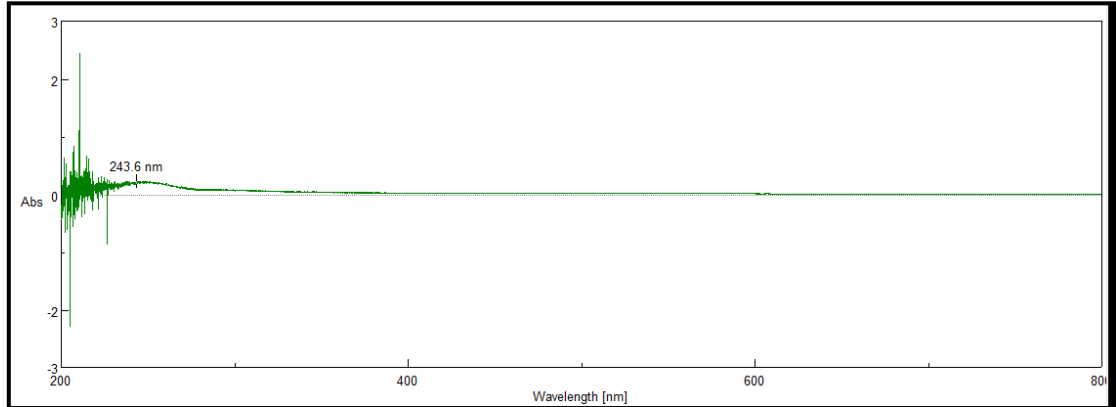


Fig: UV spectra of Boswellic acid in ethanol

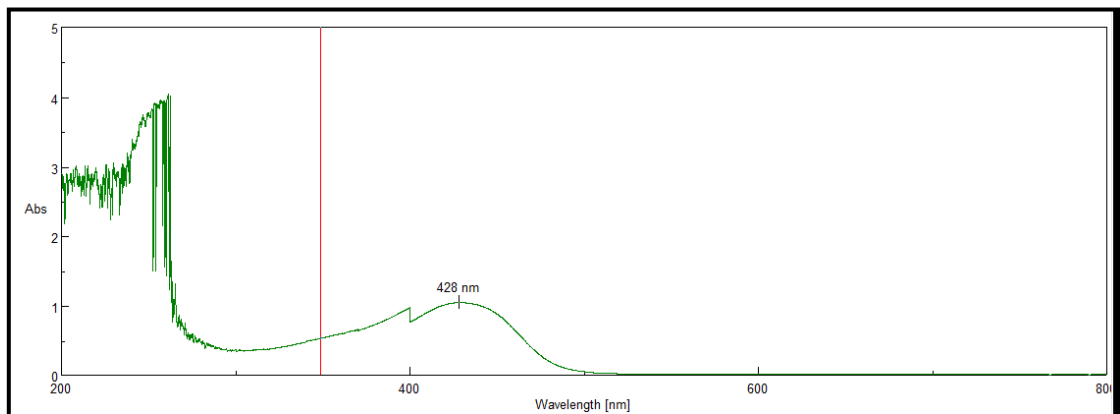


Fig: UV spectra of curcumin in ethanol

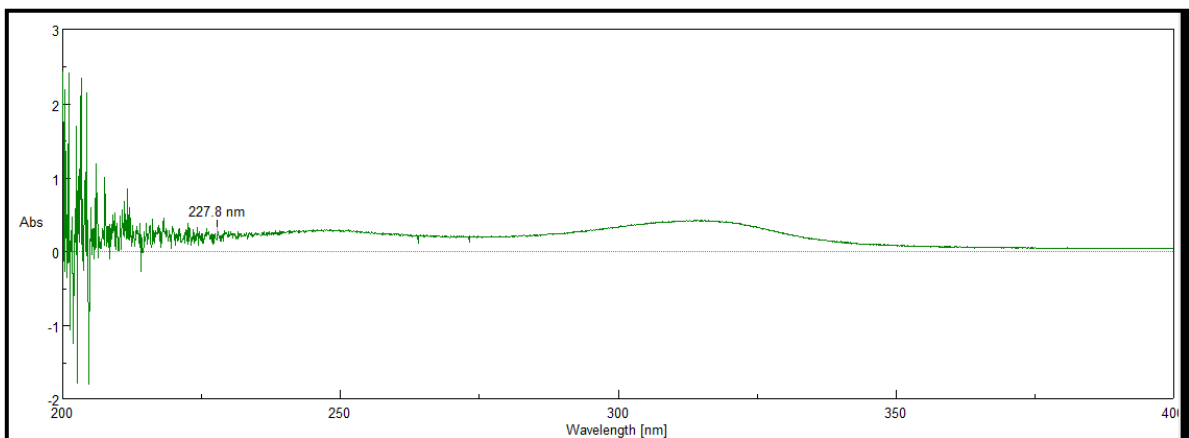


Fig: UV spectra of Capsaicin in ethanol

Sr. No.	Parameters		TDP- 1	TDP- 2	TDP-3
1.	Thickness (mm)		0.1748	0.1794	0.1932
2.	% Flatness	Initial length	10	10	9.8
		Final length	10	10.2	9.9
		% flatness	100	99.99	99.98
3.	Surface pH		7.46	7.4	7.5
4.	% Moisture Content		4.0	3.86	3.63
5.	Folding Endurance		65	61	69
6.	% Moisture Uptake		3.83	3.66	3.67

Table: Result of various parameters of Transdermal film

Sr. No	Weight Uniformity (gm)	Average Weight (gm)
TDP - 1	0.09	0.085
	0.087	
	0.08	
TDP - 2	0.089	0.089
	0.088	
	0.09	
TDP -3	0.08	0.08
	0.08	
	0.081	

Table: Result of Uniformity of Weight Parameter

VI. CONCLUSION

In conclusion, the present study demonstrates the feasibility and potential of incorporating herbal drugs into modern dosage forms, particularly in the form of transdermal films, as an alternative route of administration. Utilizing phytochemicals traditionally employed in Ayurvedic medicine for various disorders, including arthritis and inflammation, this study aimed to formulate and evaluate herbal transdermal films containing *Boswellia serrata*, *Vitex negundo*, Curcumin, and Capsaicin. As scientific reports on the formulation of transdermal drug delivery systems combining these phytoconstituents are scarce, this study fills an important gap in the literature, showcasing the therapeutic potential of such herbal formulations. While this study represents an initial step in exploring the efficacy of herbal transdermal films, further optimization and characterization are warranted, particularly regarding the inclusion of enhancers to improve drug release across the skin. Nonetheless, the future of herbal transdermal films in the pharmaceutical industry appears promising, driven by increasing consumer demand for natural remedies, advancements in technology, and a growing body of research supporting the efficacy of herbal ingredients in disease management. This research underscores the importance of exploring herbal formulations as viable options in modern drug delivery

systems, offering novel therapeutic avenues for the treatment of various ailments, including inflammatory conditions like arthritis.

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