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Phytopharmaceutical Development of A Polyherbal Spray for Topical Management of Joint Pain: A Formulation Based Study

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ABSTRACT: Joint pain, which is frequently brought on by diseases like psoriatic arthritis, gout, and arthritis, has a major negative impact on both patient health and healthcare systems. The goal of this research is to create and assess a non-pressurized polyherbal spray that can be applied topically to effectively treat joint pain. Each of the four medicinal ingredients in the formulation—Nirgundi (*Vitex negundo Linn.*), Guggul (*Commiphora wightii*), Menthol (Mentha), and Bhimseni Camphor (Cinnamomum camphora)—has analgesic and anti-inflammatory qualities. Different amounts of ethanol, water, glycerin, and DMSO were used to create a range of spray formulations that served as co-solvents and permeation enhancers. A thorough physicochemical assessment of the optimized formulation was conducted, covering pH, viscosity, evaporation time, spray pattern, and average dose weight. The findings showed that the polyherbal spray was eco-friendly, stable, and easy to use. It also showed promise for treating localized pain and improving patient compliance. This study provides a promising substitute for the topical treatment of joint pain and encourages the integration of ancient herbal medicines with contemporary pharmaceutical delivery systems.

KEY WORDS: In vitro drug release, Arthritis, Polyherbal spray, Joint pain, pharmaceutical delivery system, Anti-inflammatory, Nirgundi

INTRODUCTION

The joints that connect bones in areas like your knees, elbows, shoulders, and hips are called joints. They help you move and offer support. Any disease-related or injury-related joint deterioration might impair your range of motion and hurt. From your wrists and shoulders to your ankles and feet, joint discomfort can affect any area of your body. Pain affecting the joints may be monoarticular or polyarticular in nature. Diurnal variation is common, with some patients reporting morning stiffness and pain that improve with ambulation, while others experience activity-induced exacerbation. These symptoms are often associated with inflammatory manifestations including effusion, synovial swelling, limited joint function, and mechanical stiffness [1]. Despite its similarities, arthritis and arthralgia differ significantly. Both conditions refer to joint pain, but arthritis is joint pain with inflammation, while arthralgia is joint pain without noticeable inflammation [2]. The word arthritis comes from the Greek phrase "disease of the joints." It is described as either acute or persistent joint inflammation. The body uses inflammation as a defensive mechanism, a biological reaction of the

immune system to damaging stimuli. Numerous symptoms, such as pain, stiffness, reduced range of motion, and joint abnormalities, can be attributed to arthritis [3].

At present, over 100 distinct types of arthritic conditions have been identified, collectively representing a significant burden on public health systems and contributing substantially to healthcare-related economic costs [4]. Among the most prevalent and clinically significant forms are rheumatoid arthritis (RA), osteoarthritis (OA), ankylosing spondylitis (AS), gout, systemic lupus erythematosus (SLE), and psoriatic arthritis (PsA). These diseases vary in their pathophysiology, clinical manifestations, and therapeutic requirements but are unified by their impact on joint function and patient quality of life [5].

- **Rheumatoid arthritis (RA):** It is a persistent, symmetrical, immune-mediated inflammatory disorder that primarily targets the synovial joints. It typically presents with initial involvement of the small joints—such as those of the hands and feet—and may advance over time to affect larger articulations [6].
- **Osteoarthritis (OA):** It is a non-inflammatory degenerative joint disease primarily associated with mechanical wear-and-tear. It involves progressive loss of articular cartilage, subchondral bone sclerosis, osteophyte formation, and variable degrees of synovitis. OA is strongly associated with aging, obesity, and joint overuse [7].
- **Gout:** It is a crystal-induced inflammatory arthropathy resulting from the deposition of monosodium urate (MSU) crystals within joints and soft tissues, secondary to sustained hyperuricemia. It is characterized by acute episodes of intense monoarticular joint inflammation—most commonly affecting the first metatarsophalangeal (MTP) joint—accompanied by erythema, swelling, and severe pain [8].
- **Psoriatic arthritis (PsA):** Psoriasis is a persistent inflammatory skin condition that primarily affects the elbows and knees. It can occasionally affect the intergluteal and umbilical regions, among other areas of the body. Psoriasis affects 2-4% of Western adults, with 20-30% progressing to psoriatic arthritis [9]. Psoriatic arthritis (PsA) is a chronic, inflammatory musculoskeletal disorder associated with psoriasis. PsA might affect up to 30% of psoriasis patients their entire lives. PsA can cause musculoskeletal symptoms such as peripheral arthritis, spondylitis, dactylitis, and enthesitis (inflammation of a tendon, ligament, or joint capsule inserted onto the bone**)** [10].

There may be no cure for joint pain, but there are strategies to manage it. Pain can sometimes be relieved by using over-the-counter (OTC) medications or doing basic daily activities. Other instances, discomfort may indicate an issue that can only be treated with prescription medication or surgery [11]. The topical drug delivery system can be broadly categorized into two main types: pressurized topical sprays (aerosols**)** and non-pressurized topical sprays. Pressurized topical sprays consist of formulations containing liquid droplets, solid particles, or a combination thereof, which are suspended in a carrier gas under pressure. Upon release, a rapid drop in pressure facilitates the delivery of the drug as a fine mist or particulate spray to the targeted application site. In contrast, non-pressurized topical sprays do not incorporate any propellant agents. Instead, the drug formulation is dispensed using mechanical means such as pump systems, which allow for localized delivery without the use of pressurized gases [12].

This study aimed to develop a non-pressurized mechanical spray suitable for topical application. Non-pressurized topical sprays are more user-friendly, ecologically friendly, cost-effective, provide topical action, maximize drug absorption, are easy to apply, and improve patient compliance [13].

Drug Profile

1. Nirgundi (*Vitex nigundo Linn*) [14]

Synonym: Sinduvara, swetapushpa, sinduka, sinduvaraka, nilapushpi, suvaha.

Biological Source: Nirgundi comes from the medicinal plant Vitex negundo Linn., which is a member of the Lamiaceae family. This huge, aromatic shrub is typically found in tropical and subtropical areas.

fig 1 - vitex nigundo linn (nirgundi)

Geographical Source: This species is native to the tropical regions of Eastern and Southern Africa, as well as parts of Asia. It is indigenous to several countries, including Afghanistan, Bangladesh, Bhutan, Cambodia, China, India, Indonesia, Japan, Korea, Kenya, Madagascar, Malaysia, Mozambique, Myanmar, Nepal, Pakistan, the Philippines, Sri Lanka, Taiwan, Tanzania, Thailand, and Vietnam.

Uses: Nirgundi (Vitex negundo) has traditionally been utilized for its anti-inflammatory and analgesic properties. It has been employed in the management of various infections, including those affecting the skin and respiratory system. Additionally, Nirgundi is thought to exhibit antioxidant activity, which may provide protection against oxidative stress. It has also been used as a therapeutic agent for alleviating joint pain, arthritis, and rheumatic conditions.

2. Guggul (*Commiphora wightii)* [15]

Synonym: Kaushika, palamkahsha, pura, kumbholukhala, mahishaksha, devadhupa Gumgugul, Salai-gogil.

Biological Source: Guggul is an oleo-gum-resin derived from the bark of *Commiphora wightii*, a tree commonly referred to as Indian bdellium. This species is a member of the Burseraceae family.

fig 2 - commiphora wightii (guggul)

Geographical Source: The tree is a small, thorny plant that grows all over India**.**

Uses: Guggul has been a part of the traditional Ayurvedic medicinal system for centuries and has been the subject of extensive research in India. Its anti-inflammatory properties, as well as its potential effects on heart/blood vessel, are being studied, alongside its applications in the management of cancer, obesity, and diabetes.

3. Menthol [16]

Synonym: Pudina, Brandy mint, Lamb mint, Peppermint oil.

Biological Source: Menthol is a monoterpene alcohol derived from various types of mint and peppermint oils, extracted from the fresh flowering tops of *Mentha piperita* and *Mentha officinalis*, both of which belong to the Lamiaceae family

fig 3 - mentha

Geographical Source: Menthol is mainly obtained from mint plants, especially *Mentha piperita*, which originates in Asia and Europe**.**

Uses: Menthol is utilized to alleviate mild discomforts such as muscle cramps, sprains, headaches, and similar conditions, either alone or in combination with compounds like camphor, eucalyptus oil, or capsaicin. It is also employed as a penetration enhancer in transdermal drug delivery systems.

4. Bhimseni Camphor [17]

Synonyms: Pacha Kapoor, Nagi Karpura, Patri Kapoor

Biological Source: Camphor is a naturally occurring crystalline compound obtained from the *Cinnamomum camphora* tree, a member of the family Lauraceae.

fig 4 - bhimseni camphor

Geographical Source: Camphor trees are native to East Asia and are cultivated mostly in China, Japan, and India.

Uses: Traditional medicine, especially Ayurvedic techniques, has traditionally used Bhimseni camphor. It is well-known for its decongestant, anti-inflammatory, and analgesic effects. It is also used in aromatherapy to ease respiratory congestion, anxiety, and tension.

MATERIALS AND METHODS

Procurement of raw materials

The raw drugs were brought from the local market Gandhi Chemicals, Ahilyanagar. Few other drugs are collected from local market. Ethanol, distilled water, were purchased from Abhay Chemicals, P/84 M.I.D.C. Ahilyanagar.

Sr.no	Ingredients	Scientific Name	Amount Taken (g)
1	Nirgundi	*Vitex negundo*	25
2	Guggul	*Commiphora wightii*	25
3	Menthol	*Mentha*	25
4	Bhimseni Camphor	*Cinnamomum camphora*	25

Table 1: Ingredients in Polyherbal Formulation (Drug)

Sr.no	Ethanol (mL)	Water (mL)	Glycerine % (v/v)	DMSO (mL) % (v/v)	DRUG (mg)
S1	5	5	10%	20%	100
S2	6	4	5%	20%	100
S3	4	6	15%	20%	100
S4	3	7	15%	20%	100

Table 2: Composition and formulation of spray solution

Method of preparation of spray solution

The spray solution was made up of a permeation enhancer (DMSO) and co-solvents (Ethanol and Water). At room temperature, all components—aside from the DRUG—were mixed thoroughly using a magnetic stirrer set to 500 rpm in a solvent solution of ethanol and water. The drug was added and agitated at the same rate until the solution was homogeneous after it had reached a uniform consistency. In order to guarantee the intended drug release with every spray, the solution volume was finally modified by adding more ethanol. The mixture was then put into a spray bottle [18].

PHYSICOCHEMICAL EVALUATIONS

pH value

The pH of the optimized spray formulation was measured using a digital pH meter. Prior to analysis, the pH meter was calibrated using standard phosphate buffer solutions with pH values of 4.0, 7.0, and 9.0. Subsequently, approximately 30 mL of the spray solution was transferred into a clean glass beaker, and the electrode of the pH meter was immersed in the solution for one minute to allow stabilization. The pH value was then recorded. Each measurement was performed in triplicate, and the mean pH value was calculated for accuracy [19].

Viscosity

The viscosity of the topical spray solution was determined using a Brookfield Viscometer. Approximately 30 mL of the spray formulation was introduced into the viscometer, and the flow time was recorded. Measurements were conducted in triplicate to ensure consistency, and the average value was calculated [20].

Evaporation time

By spraying the formulation onto a white paper and then recording the drying time for each formulation, the evaporation time—the amount of time needed for the spray drops to dry—was assessed [21].

Spray pattern

The spray pattern was evaluated by actuating the test spray (TS) device onto white paper as a target surface. To enable visual detection of the spray distribution, 1% methyl orange was incorporated into all formulations. The paper was affixed to a stable board, and spraying was performed at a fixed distance of 2.5–3.0 cm from the surface. The resulting spray spots were examined, and their diameters were measured to assess the dispersion characteristics. Each formulation was tested in triplicate, and the mean spot diameter was calculated from the three measurements [22].

Average weight per dose

The spray bottle containing the formulation was first weighed to obtain the initial weight. Following this, five successive actuations of the spray were performed. The container was then reweighed to determine the final weight. The average weight per actuation (dose) was calculated using the formula:

Average dose weight = (Initial weight − Final weight) / Number of actuations [23].

In vitro drug release of final product

A common method for assessing drug penetration through the skin is the use of Franz diffusion cells**.** The most reliable method for evaluating the distribution of medications from a transdermal device is the skin penetration research across the dermatome of human skin explants. Key insights regarding the connections between formulation, medication, and skin were revealed [24]. A Franz diffusion cell equipped with an egg membrane was used for the diffusion experiment and further permeation study was carried out by goat skin [25]. Goat skin divides the donor and receptor, the two compartments of the Franz diffusion cell. The stratum corneum of the skin should be oriented toward the donor compartment that held the 5 mL spray formulation. 25 mL of phosphate buffer with a pH of 7.4 were placed inside the receptor compartment. The temperature of the receptor compartment was kept at 32 ± 0.5°C using a thermostatic bath, and the rotation speed was fixed at 600 rpm during the experiment. 5 mL of the receptor media was taken out at prearranged intervals, and at the same time, 5 mL of fresh-new, pH 7.4 phosphate buffer was added to the receptor medium. The amount of phenolic and flavonoid compounds that penetrated the skin in the receptor media was measured using a UV spectrophotometer set at 240-370 nm. The investigation on permeation lasted for 24 hours [26].

RESULTS

Preliminary batches were evaluated based on various parameters. Batches S1, S3 and S4 exhibited non-uniform spray patterns, whereas batch S2 demonstrated a consistent spray pattern and evaporation time.

Consequently, batch S3 was selected for further investigation. The final formulation of batch S3 was prepared in triplicate and subjected to comprehensive evaluation (Table 4). The measured pH was 1.4 ± 0.05, and the evaporation time was 9.71 ± 0.30 respectively. The viscosity was found to be 15.4 ± 0.14 cP, and the average weight per dose was 0.39 ± 0.19 respectively.

In an in vitro drug release study, 5 mL of spray solution contained 10 mg of phenolic and flavonoid compounds. The spray solution showed 66.07±2.28 percent drug penetration in 24 hours, with a permeation coefficient of 0.38±0.0145 cm2/h and a flux of 2.85±0.11 μg/cm²/h.

Batch	Evaporation Time (Min)	Viscosity (cps) (mm2/s)	pH	Spray pattern
S1	13.0	18.2	6.7	Non-uniform & longitudinal
S2	10.5	15.5	5.2	Uniform & spherical
S3	12.2	22.1	6.5	Non-uniform & longitudinal
S4	12.0	19.0	5.8	Non-uniform & longitudinal
(n = 4)				

Table 3: Optimization of preliminary batches of mechanical spray

S. no	Parameters	Mean ± SD
1	pH	1.4 ± 0.05
2	Viscosity (mm²/s) (centipoise)	15.4 ± 0.14
3	Evaporation time (minutes)	9.71 ± 0.30
4	Spray Pattern	Spherical and uniform
5	Average weight per dose (%) (w/w)	0.39 ± 0.19
(Mean± SD; n=4)		

Table 4: Evaluation parameters for final Spray (S2)

Spray	S2
CAR (mg) (24^{th} h.)	5.35±0.173
CPR % (w/w) (24^{th} h.)	66.07±2.28
Flux (Js) (ug/cm^2/h)	2.85±0.11
Kp (cm^2/h)	0.38±0.0145

(Mean±SD, n=4; CAR-Cumulative amount release; CPR-Cumulative percentage release; Kp-Permeability coefficient)

Table 5 — Result for in vitro drug release (phenolic and flavonoid compounds) of mechanical spray

DISCUSSION

Integrating ancient herbal remedies with contemporary pharmaceutical delivery techniques has advanced significantly with the development of a non-pressurized polyherbal spray for joint pain. The combination of Nirgundi, Guggul, Menthol, and Bhimseni Camphor provides symptomatic relief from psoriatic arthritis, gout, and arthritis by utilizing their well-known analgesic and anti-inflammatory qualities. In terms of spray pattern, evaporation time, viscosity, and pH stability, Batch S2 outperformed the other batches that were prepared. For precise and efficient topical administration, the improved formulation displayed a spherical and consistent spray pattern. Furthermore, the efficient penetration of phenolic and flavonoid compounds—which are recognized for their therapeutic actions—was validated by in vitro drug release tests. Drug absorption via the

skin was greatly enhanced by the addition of permeation enhancers like DMSO. A possible substitute for managing localized joint pain with improved patient compliance, the formulation was stable, environmentally benign, and easy to administer.

CONCLUSION

This study successfully formulated and evaluated a non-pressurized polyherbal topical spray combining Nirgundi, Guggul, Menthol, and Bhimseni Camphor for managing joint pain. The final formulation, known as Batch S2, demonstrated ideal physicochemical characteristics, such as the right amount of viscosity, pH, spray pattern, and evaporation duration. The in vitro release trial confirmed long-term drug administration and efficient skin penetration. The findings affirm the potential of ancient herbs in contemporary drug delivery systems and show that a polyherbal spray is a viable and effective topical treatment for pain associated with arthritis. This formulation can be a therapeutic option that is safe, affordable, and easily accessible, particularly in places where access to advanced medical therapies is limited.

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CONFLICT OF INTEREST

There are no conflicts of interest.

ABBREVIATION

DMSO – Dimethyl Sulfoxide

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