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Phytochemicals from Medicinal Plants for Anti- Inflammatory Activity and Their Transdermal Patches

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A B S T R A C T :

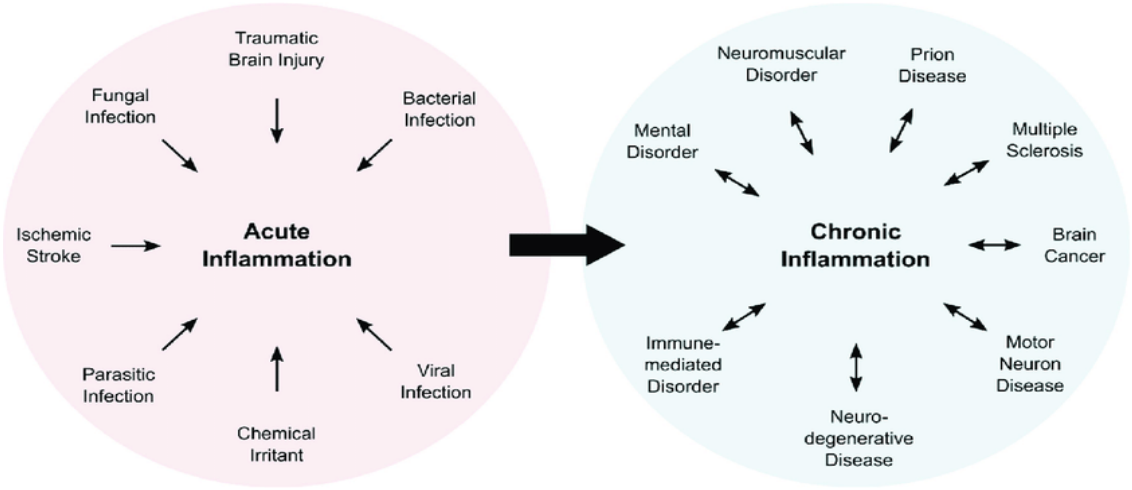
Inflammation is a complex biological response to harmful stimuli, often leading to chronic conditions like arthritis, dermatitis, and other inflammatory diseases. Conventional anti- inflammatory diseases. Conventional anti-inflammatory diseases therapies, including NSAIDs and corticosteroids, frequently cause adverse effects with long term use. As a result, there is increasing interest in plant-based therapies that offer safer and more sustainable alternatives. Medicinal plants are rich in bioactive phytochemicals such as flavonoids, alkaloids, terpenoids, and polyphenols which exhibit potent anti-inflammatory properties through mechanisms like inhibitions of pro inflammatory cytokines, and modulation of key signalling pathways. Transdermal patches offer a promising drug delivery system for these phytochemicals, providing controlled release, enhanced bioavailability and reduced systemic side effects. They enable direct absorption through the skin, bypassing first pass metabolism and maintaining steady therapeutic levels. This review explores the therapeutic potential of various medicinal plants with established anti-inflammatory activities. By synthesizing traditional knowledge with pharmaceutical innovations, this review highlights the role of plant derived phytochemicals in transdermal patches as an effective and non-invasive therapeutic option for inflammation management.

Keywords: Inflammation, Transdermal Patches, Phytochemicals

INTRODUCTION :

Inflammation, a fundamental immune response to injury, infection, or chronic stressors, underlies a wide spectrum of health conditions, ranging from acute musculoskeletal pain to debilitating chronic diseases such as rheumatoid arthritis, inflammatory bowel disease, and atherosclerosis. While conventional treatments like non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids effectively manage inflammation, their prolonged use is often causes adverse effects, including gastrointestinal complications, cardiovascular risks, and immunosuppression. This has and thinning of the skin. Inflammation is of Acute Inflammation and Chronic Inflammation. Acute inflammation is a rapid response to a harmful agent that serves to deliver mediators of host defence, leukocytes, and plasma proteins to the site of injury. It gives an initial response of the body to harmful stimuli. Chronic inflammation is a prolonged process in which tissue destruction and inflammation occur at the same time. In general, for chronic inflammation, the extent and effects of inflammation may vary with the cause of the injury and the ability of the body to repair and overcome the damage. Nonsteroidal anti-inflammatory drugs are the agents which suppresses the inflammation. These agents have also adverse effects such as peptic ulceration and osteoporosis. NSAID'S are one of the common therapeutic agents used for the treatment of pain, fever, and inflammation, these are Diclofenac, Ibuprofen, Naproxen

Fig No 1: Causes of Acute and Chronic Inflammation



Mechanism Of Anti- inflammatory Activity

Anti-inflammatory mechanisms serve to mitigate inflammation, which is the body's immune response characterized by redness, swelling, heat, and pain, through either natural processes or pharmacological treatments. The body employs pro-resolving mediators, such as lipoxins and resolving, to naturally resolve inflammation by inhibiting the recruitment of neutrophils, facilitating the clearance of debris by macrophages, and decreasing the levels of pro-inflammatory cytokines like TNF-α and IL-1β.Regulatory immune cells, including T regulatory cells (Tregs), release IL-10 to temper excessive immune responses, while cortisol produced by the hypothalamic-pituitary-adrenal (HPA) axis also plays a role in reducing inflammation. On the pharmacological front, non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, work by inhibiting cyclooxygenase (COX) enzymes, thereby alleviating pain and swelling associated with prostaglandin activity. Corticosteroids, like prednisone, act similarly to cortisol by suppressing inflammatory gene expression through the inhibition of NF-κ B and reducing cytokine production ..Biologics, including TNF inhibitors such as adalimumab, specifically target cytokines involved in autoimmune disorders, while antihistamines are effective in blocking histamine during allergic reactions. Immunosuppressants, such as cyclosporine, decrease immune cell activity to manage conditions like transplant rejection. These pharmacological interventions focus on critical pathways, including NF-κ B, arachidonic acid metabolism, and cytokine signalling. Additionally, non-pharmacological strategies, such as diets rich in omega-3 fatty acids or regular exercise, can also foster anti-inflammatory responses. The choice of mechanism is influenced by whether the inflammation is acute or chronic, as well as the particular condition being addressed.

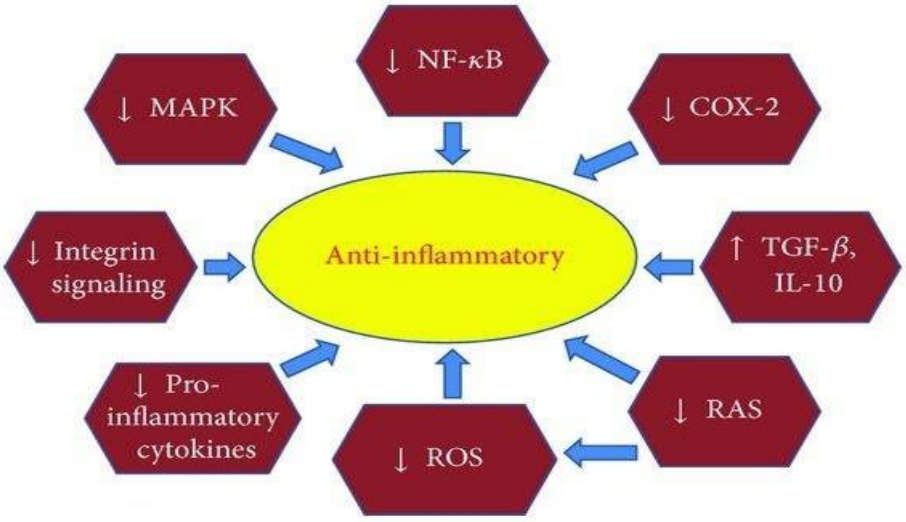


Fig -.No 2: The potential mechanisms of action of anti-inflammatory agents. MAPK: mitogen activated protein kinase; NF-κB: nuclear factor-κB; COX2: cyclo-oxygenase-2; TGF-beta: transforming growth factor-beta; IL-10: interleukin-10; RAS: renin-angiotensin system; ROS: reactive oxygen species.

Transdermal Patch

The Transdermal patch is medicated adhesive patch. These are prepared which deliver a therapeutically effective amount of drugs across the skin. The patches provide a controlled release of the medication into the patient. It acts as a carrier for a drug which holding it until the point of application. At this point, the adhesive secures the patch to the skin. It allows the drug access to the skin; it helps the permeation process. It delivers the drugs topically. A transdermal patch containing a high dose of drug into the skin which is retained for a prolonged period of time, gets entered the blood flow through the diffusion process.

Transdermal drug administration generally refers to the topical application which intact in the skin simultaneously minimizes the retention and also metabolism of the drug in the skin. TDD systems are used in the skin disorders, pains, angina pectoris, neurological disorders, etc. TDD systems are considered as the new drug delivery systems which involve the demonstration of clinical safety and effectiveness of the drug. In novel techniques, drug delivery has been investigated in human medicine in recent years. Among the new drug delivery systems, there are mostly used for transdermal applications.

Herbal transdermal patches deliver natural compounds through the skin, offering a non- invasive way to treat various conditions. These patches are designed to release herbal ingredients slowly, bypassing the digestive system for better release.

Phytochemical constituents and their Anti- inflammatory Activity

Phytochemicals are naturally occurring substances sourced from plants, noted for their potential health advantages, particularly their anti-inflammatory effects. These bioactive compounds, which include flavonoids, phenolic acids, alkaloids, terpenoids, and saponins, are synthesized by plants as a defence strategy against environmental challenges, pathogens, and herbivorous threats. Extensive research has shown that these compounds can interact with human biological systems, modulating inflammatory pathways and presenting possible therapeutic applications for inflammatory conditions. The anti-inflammatory properties of phytochemicals arise from their capacity to inhibit critical inflammatory pathways, such as the nuclear factor-kappa B

(NF-κ B) signalling pathway, cyclooxygenase (COX) enzymes, and the generation of reactive oxygen species (ROS). For example, flavonoids like quercetin and curcumin, which is derived from turmeric, have been found to obstruct pro-inflammatory mediators, while terpenoids such as boswellic acid from frankincense demonstrate notable COX-2 inhibition. These mechanisms not only mitigate inflammation but also bolster antioxidant activity, thereby offering further protection to tissues against oxidative harm.

TABLE-1: Phytochemicals Used For Anti Inflammatory Activity

HERBAL EXTRACT	**CHEMICAL CLASS**	**BIOLOGICAL SOURCE**	**FAMILY**	**MECHANISM OF ACTION**
Curcumin	Curcuminoids	*Curcuma Longa*	Zingiberaceae	Inhibits pro inflammatory enzymes such as cox-2, lox
Silibinin	Flavonoid	*Silybum maranium*	Asteraceae	Stabilize cell membranes scavenging free radicals and modulating signaling pathways
Gingerols	Phenolic compounds	*Zingiber Officinale*	Zingiberaceae	Suppress PGE2, NO production
Astibin	Flavonoid	*Lysiphyllum ,strychnifolium*	Fabaceae	Reduce ROS, inhibits IL-6, TNF-alpha and cox-2, antioxidant effects enhance anti Inflammatory
Cannabidol	Cannabinoid	*Cannabis Sativa*	Cannabaceae	Activate CB2 receptors inhibit TNF-alpha, reduce prostaglandins synthesis
Capsaicin	Alkaloid	*Capsicum annuum*	Solanaceae	Depletes substance P, inhibits COX-2 and iNOS; modulates TRPV1 channels to reduce inflammation.
Tectorigenin	Iris tectorum extract	*Isoflavone (Flavonoid)*	Iris tectorum (rhizome)	Blocks NF-κB pathway, reduces COX-2 and iNOS expression—keeps inflammation in check!

Ashwagandha	Withanolides	*Withania somnifera (root, leaves)*	Modulates immune response reduce stress	Surge in adaptogenic supplements
Rosmarinic Acid	Polyphenol (Caffeic Acid Derivative)	*Rosmarinus officinalis* (Rosemary)	Lamiaceae	Inhibits 5-LOX, complement system, and pro-inflammatory cytokines (IL-8, TNF- α); antioxidant
Verbascoside	Phenylethanoid Glycoside	*Stachytarpheta indica*	Verbenaceae	Inhibits COX-1, 5- LOX, and IL-8; antibacterial and antioxidant effects complement anti- inflammatory action.
Resveratrol	Polyphenol	*Vitis vinifera*	Vitaceae	Activates sirtuins, inhibits NF-κB, reduces TNF-α, IL-6
Epigallocatechin gallate (EGCG)	Catechin	*Camellia sinensis*	Theaceae	Inhibits NF-κB, reduces TNF-α, IL-6
Andrographolide	Diterpenoid lactone	*Andrographis paniculata*	Acanthaceae	Inhibits NF-κB, reduces TNF-α, IL-1β, IL-6, Inos
Baicalin	Flavonoid (flavone glycoside)	*Scutellaria baicalensis*	Lamiaceae	Inhibits NF-κB, reduces TNF-α, IL-1β, IL-6, oxidative stress
Harpagoside	Iridoid glycoside	*Harpagophytum procumbens*	Pedaliaceae	Inhibits COX-2, reduces PGE2, TNF-α, inflammatory mediators
Tanshinone IIV	Diterpenoid quinone	*Salvia miltiorrhiza*	Lamiaceae	Inhibits NF-κB, MAPK; reduces TNF- α, IL-6, pro- inflammatory cytokines

Kaempferol	Flavanoid	*Plant derived*	Flavanol	reduce inflammation- induced diseases such as intervertebral disc degeneration, colitis, post-menopausal bone loss, and acute lung injury.4 Furthermore, it has been found to inhibit angiogenesis in VEGF-stimulated HUVECs by modulating the VEGF/VEHGR-2
Gooseberry	Alkaloids	*Phyllanthus acidus*	Phyllantaceae	It inhibits pro-inflammatory cytokines like TNF-α, IL-1β, and IL-6 by suppressing the NF-κ B signaling pathway,
Tulsi	Terpinoids	*Ocimum sanctum*	Lamiaceae	Tulsi inhibits pro- inflammatory pathways, including the arachidonic acid metabolism (via cyclooxygenase and lipoxygenase enzymes) and the release of inflammatory mediators like histamine and prostaglandins.
Panax ginseng	Triterpenoid saponins (Ginsenosides)	*Ginseng radix*	Araliaceae	Inhibits NF-κB and pro-inflammatory cytokines (e.g., TNF-α, IL-6) via ginsenosides like Rg3 and Rb2
Licorice root.	Triterpenoid saponins (e.g., glycyrrhizin), flavonoids	*Glycyrrhiza glabra*	Fabaceae	Inhibition of COX and LOX
Danshen	Diterpenoids	*Salvia miltiorrhiza*	Lamiaceae	Tanshinones inhibit NF-κ B and pro-inflammatory cytokines (e.g., TNF- α, IL-6), while salvianolic acids suppress COX-2 and iNOS expression.
Wormwood	Sesquiterpene lactones	*Artemisia absinthium*	Asteraceae	Flavonoids and phenolic acids inhibit pro-inflammatory cytokines TNF- α, IL-6 and reduce oxidative stress
Dioscorea nipponica	Steroidal Saponins	*Dioscorea nipponica*	Dioscoreaceae	Inhibit pro- inflammatory cytokines TNF- α, IL-1β, IL- by suppressing NF- κ B signaling.

Kudsu	Isoflavones	*Pueraria thunbergiana*	Fabaceae	Suppresses pro- inflammatory cytokines TNF- α, IL-6 by inhibiting NF-κ B signaling. Leaf extracts also downregulate COX-2 and iNOS expression, mitigating inflammation in models like LPS- induced macrophage activation.
Wild Angelica	Coumarins	*Angelica sylvestris*	Apiaceae	Coumarins and flavonoids inhibit pro-inflammatory cytokines TNF- α, IL-6 and pathways like NF-κ B, reducing inflammation. Phenolic acids also contribute by scavenging free radicals.
Camellia sinensis	Flavanoids	*Camellia*	Theaceae	EGCG inhibits NF-κ B and MAPK pathways, reducing pro-inflammatory cytokines
Borage	Flavanoids	*Borago Officinalis*	Boraginaceae	GLA (from seed oil) is metabolized into dihomo-γ-linolenic acid (DGLA), which increases prostaglandin
Boswellic acid	Triterpenoids	*Boswellia serrata*	Burseraceae	Inhibits 5-lipoxygenase (5- LOX), reducing leukotriene synthesis
Aloe barbadensis miller)	Anthraquinones	*Aloe vera*	Asphodelaceae	inhibit pro- inflammatory cytokines TNF-1α, IL-6 and NF-κ B signaling.
Burdock	Polyphenols	*Arctium lappa*	Asteraceae	decrease levels of inflammatory markers like IL-6 and h s-CRP in patients with knee osteoarthritis.
Sage	Terpenes	*Salvia officinalis*	Lamiaceae	Inhibit inflammatory mediators

Essential Oils With Anti Inflammatory Activity.

Essential oils are potent, volatile aromatic compounds extracted from various parts of plants, including leaves, flowers, stems, roots, and seeds, typically through methods such as steam distillation or cold pressing. These oils have been employed for thousands of years in traditional medicine, aromatherapy, and skincare due to their therapeutic properties, particularly their anti-inflammatory effects. Inflammation serves as a natural defense mechanism against injury or infection; however, if it becomes chronic, it can result in conditions like arthritis, dermatitis, or muscle pain ..Essential oils

offer a natural approach to managing inflammation, thanks to their bioactive components—terpenes, phenols, and aldehydes—that interact with the body's inflammatory pathways. The anti- inflammatory properties of these oils stem from their ability to influence key biological processes, including the suppression of pro-inflammatory cytokines (such as TNF-α and IL-6), reduction of oxidative stress, and inhibition of enzymes like cyclooxygenase (COX) and lipoxygenase (LOX), which play significant roles in the inflammatory response. Unlike synthetic anti-inflammatory medications, essential oils provide a holistic benefit, combining anti-inflammatory effects with analgesic, antimicrobial, and soothing properties ..They can be applied topically (often mixed with a carrier oil), inhaled through aromatherapy, or, less frequently, ingested under professional guidance, making them valuable for treating inflammation-related conditions. Common essential oils recognized for their anti-inflammatory properties include lavender (Lavandula angustifolia), tea tree (Melaleuca alternifolia), frankincense (Boswellia carterii), eucalyptus (Eucalyptus globulus), and chamomile (Matricaria chamomilla), among others .Each oil contains unique active compounds, such as linalool, boswellic acid, or 1,8-cineole, that contribute to their therapeutic effects .Ongoing scientific research continues to validate their mechanisms and effectiveness, alongside anecdotal evidence.

TABLE-2 ; Essential Oils used for anti- inflammatory action.

Essential oil	**Source of Origin**	**Mechanism of action**	**Uses**
Lavender Oil	Lavender plant (*Lavandula angustifolia*), Lamiaceae family	Calms down inflammation by quieting enzymes like COX-2 and reducing troublemakers like	Easing joint pain, soothing irritated skin, or just helping you relax.
Eucalyptus Oil	Eucalyptus tree (*Eucalyptus globulus*), Myrtaceae family	Thanks to 1,8- cineole, it knocks out inflammation signals (PGE2, TNF-α) and slips through skin easily to cool things off.	Clearing up chest congestion, soothing sore muscles, or speeding up wound healing
Tea Tree Oil	Tea tree shrub (*Melaleuca alternifolia*), Myrtaceae family	Terpinen-4-ol steps in to hush histamine and inflammatory culprits like COX- 2 and IL-1β—perfect for tackling skin flare-ups.	Fighting acne, calming dermatitis, or tackling inflamed spots with bacteria.
Peppermint Oil	Peppermint herb (*Mentha piperita*), Lamiaceae family	Menthol cools things down by blocking COX-2 and IL-6, plus it tricks your nerves	Relieving muscle aches, soothing headaches, or giving a cooling anti- inflammatory boost.
Frankincense Oil	Frankincense tree (*Boswellia carterii*), Burseraceae family	Boswellic acids team up to shut down 5-LOX and cytokines like TNF-α	Easing arthritis stiffness, calming long-term inflammation, or repairing skin.
Chamomile Oil	Chamomile flower (*Matricaria chamomilla*), Asteraceae family	Chamazulene and bisabolol tame COX-2 and 5- LOX, plus they hush histamine to settle your skin down nicely.	Soothing eczema, calming irritated patches, or helping wounds heal faster.
Rosemary Oil	Rosemary bush (*Rosmarinus officinalis*), Lamiaceae family	Carnosic acid and 1,8-cineole zap 5- LOX and PGE2, while antioxidants pitch in to dial down inflammation.	Easing joint soreness, relaxing tight muscles, or even helping your scalp feel better.
Clove Oil	Clove Oil	Eugenol takes on COX-2 and 5- LOX,	Numbing toothaches, soothing joint pain, or doubling as a pain-relief buddy.

		cutting back PGE2	
Evening Primerose Oil	Fatty Acids	*Oenothera biennis*	GLA converts to dihomo-γ-linolenic acid (DGLA), increasing prostaglandin E1 (PGE1) and cAMP
Turmeric Oil	Turmeric root (*Curcuma longa*), Zingiberaceae family	Curcumin and turmerones gang up on NF-κB and COX-2, slashing TNF-α and oxidative stress for a deep clean	Tackling chronic inflammation, arthritis, or stubborn skin issues.

Marketed Herbal Transdermal Patches And Their Used For Anti Inflammatory Activity

Herbal transdermal patches are novel delivery systems that deliver plant derived active constituents across the skin to fight against inflammation. These patches provide a controlled, sustained release of anti-inflammatory substances, sidestepping the digestive tract to maximize bioavailability and minimize side effects. Sold worldwide or on a regional basis, they contain herbs such as Siegesbeckiae Herba, Curcuma longa (turmeric), and Centella Asiatica, which contain their respective bioactive components kirenol, curcumin, and asiaticoside. .Used to treat arthritis, muscle aches, wound healing, and postoperative inflammation, these patches combine traditional herbalism with advanced technology, presenting a natural alternative to synthetic anti-inflammatory drugs.

Table-3 :Marketed Herbal transdermal Patch for Anti Inflammatory Activity

PATCH	**ACTIVE CONSTITUENT**	**USES**
Phynova Joint and Muscle Relief Patch	Siegesbeckiae Herba (kirenol)	Relief of rheumatic and muscular pain
Curcumin Transdermal Patch	Curcumin (from Curcuma longa	Reduces inflammation in wounds, arthritis, and post- surgical pain
Centella Asiatica Patch	Centella Asiatica (asiaticoside, madecassoside)	Promotes wound healing with anti-inflammatory benefits
Tulsi Patch	Ocimum sanctum (linoleic acid, flavonoids	Anti-inflammatory and analgesic effects for wound healing.

Conclusion

Herbal transdermal patches represent a promising advancement in the administration of anti-inflammatory medications, combining the therapeutic properties of phytochemicals with the advantages of controlled and non-invasive drug delivery. This review highlights the effectiveness of various herbal extracts in reducing inflammation through transdermal systems, enhanced by their ability to bypass first-pass metabolism and improve bioavailability. The collaboration between natural components and sophisticated patch technology offers an environmentally friendly and patient-focused alternative to conventional treatments. With a growing interest in natural therapies, herbal transdermal patches hold significant potential to revolutionize anti-inflammatory treatment, provided that existing challenges are addressed through thorough scientific research and innovation.

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