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Review Paper

Formulation And Evaluation of Herbal Transdermal Patch Containing Cuscuta Reflexa Roxb., Curcumin and Aloe vera Extract for Anti-Inflmmatory Activity

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ABSTRACT

This research focused on creating a plant-based patch with Cuscuta reflexa, curcumin, and Aloe vera to help ease swelling in joints and skin. Because these patches slowly deliver medicine through the skin, they skip digestion issues, stick around longer in the body, plus patients often find them easier to use than pills. Instead of swallowing medication, the formula was turned into thin films using solvents, blended with flexible binders, additives that boost absorption, so active ingredients stay locked in yet ready to spread out gradually.Films made showed consistent thickness along with even weight across samples. One thing noticed was how well they resisted creasing when folded repeatedly. Their outer touch stayed smooth while acidity levels measured close to skin balance. Each patch held steady drug spread without hotspots or gaps visible. Water retention tests ran alongside exposure trials under room settings. Flexibility remained through handling thanks to balanced material blend. Slight dampness presence did not alter structural behavior over time. Appearance stayed clear, intact, never cracked during inspection periods.

INTRODUCTION

Body's reaction to harm - like germs or injured cells - involves swelling, heat, redness, often pain. When short-lived, it helps repair tissues, keeps infections in check. Long-lasting flare-ups, though, link closely to illnesses such as stiff joints, heart issues, brain decline, immune attacks on self. Globally, over two hundred million struggle with these ongoing inflammatory conditions, says WHO. This silent burden shapes much of disease-related suffering and death worldwide [1]. Traditional treatment regimens for inflammation realy heavily on non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and biologics. However, prolonged use of these pharmaceutical

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agents is associated with severe adverse effects such as gastrointestinal ulceration, hepatotoxicity, nephrotoxicity, and immunosuppression [2]. Fewer side effects have sparked curiosity about natural treatments, especially those rooted in plants loaded with powerful anti-inflammatory compounds [3].

Starting at the surface, skin-based treatments skip stomach troubles that pills often bring. Instead of swallowing medicine, a patch sticks on, doing its job without help from digestion. One big plus? The body uses more of the active ingredient when it enters through skin. Side effects stay lower because levels stay steady. If things go wrong, taking off the patch stops delivery fast. Because it is easy to wear, people stick with treatment longer. All told, this method handles drugs in a calmer, smoother way than older forms.[4] The use of transdermal patches A medicated patch that may administer medications directly to the bloodstream through skin portals at a set pace is known as a transdermal patch or transdermal drug delivery system[5]. This feels easiest to take since stopping happens anytime without needing stomach absorption, skips liver processing right away, lasts across several days when needed.

A method using the skin to get medicine into the body works without needles. [4,5] Once applied, the substance moves across the outer layer, slipping into circulation. [4,5]. Few methods beat placing medicine on skin when it comes to steady release throughout the day. Skipping digestion is one benefit, which means less strain on the stomach because absorption happens directly through tissue. Another point worth noting - liver processing gets avoided entirely since the substance enters blood without traveling through that organ first [6].

A patch refers to a way of delivering medicine through the skin. Instead of pills or capsules, this method avoids some problems tied to digestion. Because medicines go straight into the bloodstream, they skip the gut. That means less breakdown from stomach acids or enzymes. Liver processing also gets bypassed entirely. As a result, more of the drug reaches circulation intact. This boost in delivery efficiency shows why patches matter medically.[7]

2. Transdermal Patch Design-

Not every medicine moves through skin the same way - how easily it passes depends on how thick the skin layer is, where it's applied, and how long it stays there. Skin isn't just a wall; it changes some drugs before they enter blood, kind of like filtering them early. Each medication behaves differently once placed on skin, influenced by its own mix of traits. For entry into the body, uncharged molecules have an easier path, especially if they dissolve in fats rather than water. Big molecules struggle - the ones heavier than 500 Daltons often get stuck in the outermost shield of skin. Best chances happen when daily needs stay under 10 milligrams, making small doses more likely to work.

3. Basic Component of Transdermal Patch-

A single look at how these patches work reveals their core parts. Each layer plays a role in moving medicine across skin and into blood. Picture shows what goes inside one of these treatment stickers. How it is built can shift based on which drug is used or how fast it should enter the body. Different needs lead to different designs.[8]

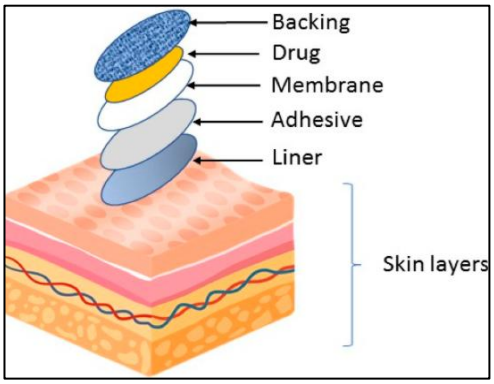


Fig.no. 1 layers of transdermal patch

4. Types of Transdermal Patches [9]

Single-layer drug delivery system:-

The drug in this type of patch is added right in the adhesive layer, which performs 2 functions—first, it securely connects (binds) the various elements of the patch together and holds the patch onto the skin, and second, it is also the medium that allows for the release of the drug. The adhesive material is located between a removable liner (on one side) and a protective backing (on the other side).

5. **Multi-layer drug in adhesive:-**

In terms of drug delivery, a patch using multi-layer drug adhesive to deliver a drug is somewhat similar to a patch using single-layer drug adhesive in that both layers of adhesive are responsible for delivering the drug. However, with multi-layer drug adhesive system, there is an additional layer of drug-in-adhesive between the adhesive layers, usually separated by a barrier. Additionally, this patch has a temporary barrier (i.e., a drug layer), which will eventually dissolve, as well as a permanent background layer (i.e., backing).

Drug reservoir-in-adhesive:-

Distinct drug layers are present in this type of transdermal product. Another compartment holds the drug as either a solution or suspension; it is separated from the outside world by the backing (or cover) of the product. In reservoir types of this kind, the rate at which drug is released is constant.

Drug matrix-in-adhesive:-

There are two types of drugs that may be in a semi-solid matrix (known as a "drug layer") - solutions and suspensions. The drug layer is covered by an adhesive layer; however, these adhesive layers may partially cover the other part of the drug layer as well.

2. PLANT OVERVIEW -

2.1 - CUSCUTA REFLEXA :-



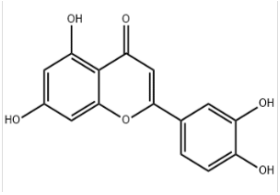
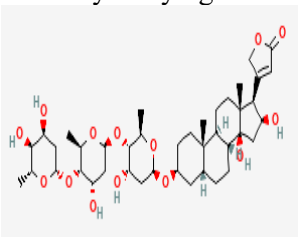
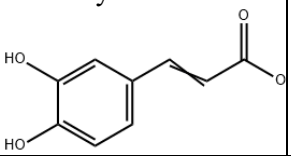
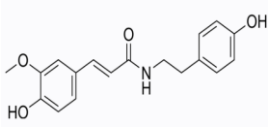
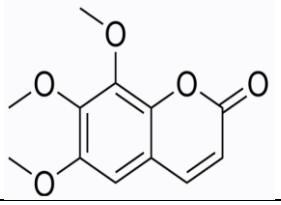
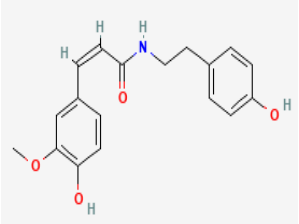
Fig no. 2 cuscuta reflexa Roxb.

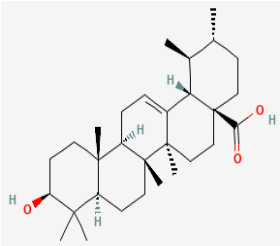
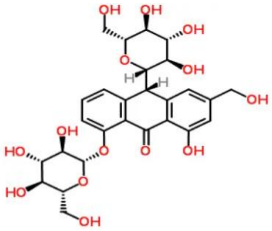
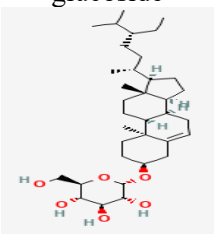
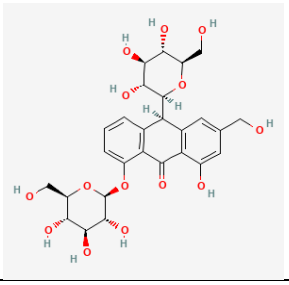
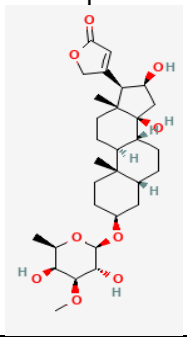
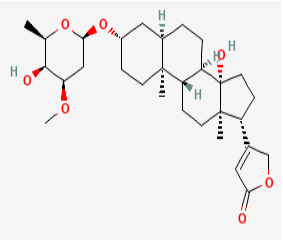
Cuscuta reflexa, commonly known as giant dodder, is a long, thin, light yellowish green, leafless parasitic plant that twines around other plants (i.e., its hosts) [10]. Other common names for this plant include witch's hair, devil's hair and amarbel. The genus Cuscuta belongs to the family Cuscutaceae; however, it has been described as

belonging to the family Convolvulaceae according to the angiosperm phylo-geny project [11,12].

The vegetative part does not contain any roots or fully developed leaves, there is only a stem-like structure. This parasite wraps itself around its host plant and penetrates the host plant's stems through its haustoria. The haustoria then make a direct connection with the host plant's vascular bundles which will allow the parasite to absorb water, carbohydrates, and other nutrient-containing solutions from the host [13]. The flower of this plant is tiny, bell-shaped and white with yellow filaments attached. The seeds & fruit of the plant are formed by the flower. The plant's medicinal properties are often referred to as miraculous due to their traditional use in treating headaches, bone fractures, fevers and rheumatism [14]. Cuscuta relexa has been studied extensively for many years for its antimicrobial acrivies [15,16]. The obligate holostemparasitic Cuscuta reflexa (dodder), is an important traditional medicine in Eastern and Southern Asian Countries where it can be used alone or with other botanicals [17]. Cuscuta shows hepatoprotective, anti-HIV, anti-inflammatory, antioxidant, antiulcer, antidiabetic, antimicrobial, anticonvulsant, antiproliferative, and antiulcer properties and these activities have been mainly attributed to its phytochemical constituents (i.e. flavonoids, saponins, sterols/triterpenoids, and tannins) [18]. C. reflexa Roxb. produces five phytoconstituents, specifically, 2, 3-dihydro-3, 5, 7-trihydroxy-2-(3-hydroxy-4-methoxyphenyl).chromen-4-one (CR-1), 2, 3-dihydro-3, 7dihydroxy-2-(3, 4dihydroxyphenyl) chromen-4-one (CR-2), 6-methoxy-2H-chromen-2-one (CR-3), N-(4-methoxyphenethyl)-3-(3,4dihydroxyphenyl)acrylamide (CR-4), and kN-(4-butylphenethyl)-3-(4-hydroxy methoxyphenyl)acrylamide (CR-5) [19].

Chemical Structure And Pharmacological Activity Of Cuscuta Reflexa Roxb.-

Serial N0.	Chemical Structure	Pharmacological Activity	Serial N0	Chemical Structure	Pharmacological Activity
1.	luteolin 	Anti-inflammatory, Antimicrobial, Cardioprotective and Anticancer activities	7.	16-b-hydroxydigitoxin 	Cardioprotactive activity.
2.	Ethyl caffeate 	Anti-inflammatory activity; Anticancer, Anti-arthritic.	8.	N-Trans-feruloyltramine 	Aintioxidant, Neuroprotective and Anticancer activities
3.	Trimethoxycoumarin (Dimethylfraxetin) 	Gastroprotective. Int-inlamnatory, Antioxidant,	9.	N-Cis-feruloytramine 	Aintioxidant, Antiproliferative, Anti Hyperuricemia and Anticancer activities.

4.	Ursolic Acid 	Anti-inlammatory, Antioxidant, antimicobial, Antigenotoil condition, anticancer	10.	Cuscutaroside A 	antiobesity activity, porcine pancrcatic lipase (PPL), antiplatelet, aggregation activity
5.	b-sitosterol D-glucoside 	Anti inlammatory, Antioxidative, antintimicrobial, Hepato-protective, anticancer	11.	Cuscutaroside B 	Aniobesity activity, porcine pancratic lipase (PPI), antiplatelete ,aggregation activity
6.	Strospeside 	Anti-cancer adivity	12.	Odoroside 	Anti-cancer activity

Ethnobotanical and pharmacological uses of Cuscuta Reflexa Roxb. -

1. Ethnobotanical Uses -

Traditional knowledge indicates that Cuscuta reflexa is used to treat a wide spectrum of human ailments

• In the Kodagu district of Karnataka, tribal communities use a paste prepared from the whole plant mixed with honey to manage epilepsy, administered orally once daily for three days. [20] Cuscuta reflexa, the stem portion of which is indigenous to eastern Himalayas, has also been used by the tribal peoples living in Uttarakhand as a remedy for epilepsy [21]. The Sapera tribe located in Haryana has historically relied upon this plant to assist with fevers [22]. A medicinal concoction made with all parts of Cuscuta reflexa has been administered to help remedy yellowish discoloration of the skin and/or liver problems experienced by those living in Uttarakhand [21]. Additionally, there is evidence that Cuscuta reflexa has had some success in providing relief for individuals suffering from an enlarged liver, providing support for its use to protect the liver [23]. The people living in Assam have historically utilized Cuscuta reflexa as a remedy for various types of gastrointestinal problems such as gas, bloating and/or abdominal discomfort [24]. Additionally, members of tribal communities residing within the North Cachar Hills region of Assam have utilized Cuscuta reflexa to maintain normal hair growth and prevent premature greying or dandruff are considerations of the tribes that rely upon the use of Cuscuta reflexa. [25] Cuscuta reflexa has been found useful for treating jaundice

and viruses and irritated skin for individuals living within the regions of Pakistan and Tripura [26,27]. Pain in muscles finds relief through the outside use of mashed plant parts. [28]. Folks in Odisha have long turned to the liquid from Cuscuta reflexa stems when dealing with malaria [29].

Folks living in Kalahandi have long turned to this plant when dealing with upset stomachs, bloody stools, stiff muscles, puffiness, or creaky joints [30].

Around Budgam in Jammu and Kashmir, people turn to the plant when dealing with sore joints [31].

- Folks who follow old remedies have been known to turn to this plant when dealing with paralysis or issues tied to jaundice [32].
- A skin paste made from the entire plant is used in Uttarakhand for treating eczema, also helping with dandruff [33].
- Away from the mainstream, this herb finds use against breathing issues, stomach troubles, earaches, or trouble urinating across parts of India and Nepal [35].
- Headaches, constipation, sore teeth, or breathing trouble - people nearby often turn to this plant for relief [34,36]. When it comes to blood-related issues, brews made from its leaves play a role [36]. Liver swelling or scar tissue? That's another case where the herb shows up in traditional use [36].

2. Pharmacological uses of <u>Cuscuta Reflexa Roxb. -</u>

1. Anti inflammatory activity- Cuscuta reflexa extracts calm swelling because they block substances that cause inflammation [37].

2. Antioxidant Activity- Free radicals meet their match in this plant, thanks to flavonoids along with phenolics working against oxidation. [38]

3. Hepatoprotective Activity - Cuscuta reflexa shields liver cells when toxins attack. Damage slows down because of its presence. Liver performance gets better over time. This shift happens quietly but clearly. Evidence backs it up. Reference number thirty-nine holds the details.[39]

4. Antimicrobial Activity- Some lab tests reveal these extracts can block bacteria and fungi that cause disease. [40]

5. Antidiabetic Activity- Blood sugar drops when using this plant, while metabolism gets a boost. [41]

6. Hair Growth Promoting Activity- Follicles get a boost – this remedy has long supported thicker strands by tackling shedding [38,40].

Mechanism Of Action Cuscuta Reflexa Inflammation-

When Cuscuta reflexa steps in, inflammation doesn't flare up as hard because it blocks signals like TNF-a, IL-1β, along with IL-6. This quieting effect happens since the plant sukstance puts a brake on NF-KB - this chain reaction means fewer molecules that drive swelling get made [42] .

Starting with enzyme interference, the substance blocks both COX and LOX pathways, cutting down on prostaglandin plus leukotriene production tied to swelling and discomfort [43]. From another angle, cuscuta reflexa shows strong power against oxidation, thanks to flavonoid and phenol presence that mops up harmful oxygen molecules, shielding tissues from damage-linked irritation [44].

When inflammation happens, it keeps lysosomal walls steady so harmful enzymes stay contained. Proteins that could harm tissues are less likely to spill out because of this effectA sudden shift happens when a plant-based substance interferes with an essential process Swelling might tie to an enzyme. Nitric When iNOS slows down, oxide amounts go lower. That shift happens because the system isn't pushing as hard Less of this gas leads to quieter inflammation across the body. Studies support these actions with measurable outcomes.

Each finding ties back to how the herb influences internal reactions. Evidence shows consistent patterns across tests. [45] Another set of data confirms lower NO output when the plant is present. [46] Immune cells move differently when this substance guides how macrophages plus neutrophils reach swollen areas [47].

2.2 – CURCUMA LONGA –

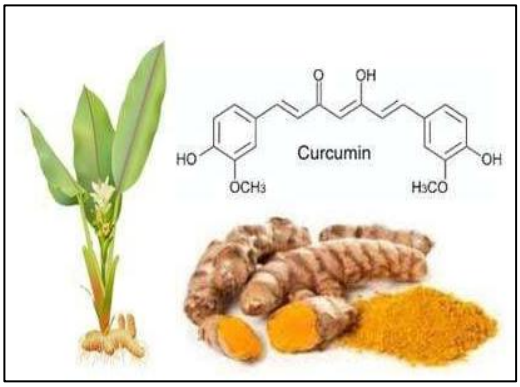


Fig.no. 3 curcumima longa (Turmeric)

Yellow spice curcumin from curcuma longa l plant related to ginger called Haldi, Haridra, even Indian saffron in some places. Found inside dried stems underground, not roots - those get turned into powder. This plant grows wild in warm parts of Asia, mainly India. Now grown across hot zones worldwide too. Research looks at how it might help with joint pain, memory loss, and some types of tumors. Countries making most of it. Down south in India, Andhra Pradesh gets things moving. Where the soil drains fast, heat finds a friend. First worldwide? That title goes to India. Not far after comes China, tagging close. Then Pakistan follows, just a step slower. Thailand shows up next, unhurried. Behind it trail Indonesia, Sri Lanka, Bangladesh, Myanmar - no rush at all. Over that point, Tamil Nadu steps into the mix. Heading upward, Karnataka slips in beside it, with Maharashtra tagging along soon after. To the eastern stretch, Odisha tosses in its part. Close to the edge, West Bengal leans in quietly. Far past where eyes usually wander, Assam sends something down from deep in the northeast. Roots take months to mature before digging begins. Not every region suits its growth pattern. Farmers let the leaves turn yellow before yanking out entire plants. Following that After that, cleaning happens first. Then boiling follows. Drying comes next. What is left gets ground down afterward. Final color glows deep orange, almost glowing under light. Used widely beyond medicine - as dye, flavor, ritual item. Smell sharp when crushed, slightly bitter on tongue. Though popular, effects still under close watch by researchers. Each batch varies based on earth, rain, care taken during drying phase. Some batches stronger than others depending on farming methods used. Even storage time changes potency over weeks.

Bioactive Components Curcumin Demethoxycurcumin Bisdemethoxycurcumin Volatile Oils Turmerone Zingiberene.

Mechanism of Action of curcumin on Inflammation-

Starting beneath the skin's outer layer, curcumin moves slowly through a patch placed on the surface. This method lets it reach sore areas without rushing into the bloodstream. A consistent amount builds up right where swelling occurs. Because absorption happens gradually, unwanted reactions elsewhere in the body stay low [48]. Blocking NFx signaling happens when curcumin steps in. It stops NF-KB from turning on, which normally switches up genes tied to inflammation. This factor drives production of certain enzymes along with inflammatory signals [49]. Because it lowers levels of TNF-a, IL-1β, IL-6, and IL-8, curcumin helps calm inflammation [50].

Curcumin blocks COX-2 along with LOX enzymes, cutting down production of prostaglandins and leukotrienes that play a role in discomfort and swelling [51]. When curcumin steps in, it slows down a trigger called iNOS that usually revs up nitric oxide. Less of this molecule

means less harm to tissues caught in inflammation's grip. [52] Stopping damage before it spreads, curcumin tackles harmful molecules known as ROS. It also blocks the breakdown of fats through oxidation, a process tied to cell stress. Inflammation sparked by oxidative harm gets cut off early. When the body faces internal chaos, these steps work to hold tissue structure steady. [53] Curcumin Beyond the surface of MAPK pathways, changes begin to unfold in ERK, JNK, yet also p38. Behavior shifts quietly without warning A slowdown occurs in making compounds linked to inflammation when shift happens. [54]

Ethnobotnical and pharmacological uses of Curcumin -

Ethnobotanical Uses of Curcumin-

From the root of Curcuma longa comes curcumin, a compound seen often in old healing methods. Wound care and managing skin infections are common uses handed down through time. [55] Pain in the joints finds relief through its use, historically part of healing practices. [56] Helps with digestion while addressing gut issues too. [57] Found in old plant-based remedies meant to guard the liver.[58]. Helps with coughing, stuffy nose, plus breathing issues. [56] Works naturally to fight germs and microbes [55,57]. Folks once turned to it for clearer skin, passed down through old routines. [58]

Pharmacological Uses –

1. Fighting swelling – Curcumin blocks substances like COX-2 and NF-κB that drive inflammation, calming the body's response [59]
2. Fighting oxidation happens when curcumin grabs loose radicals, boosting helpers like superoxide dismutase along the way. [60]
3. Curcumin stops tumors from starting, growing, or spreading - triggering cell death in abnormal cells instead [61]
4. Certain microbes find it tough to survive when curcumin is around. It fights bacteria, viruses, through different means. Fungi also face challenges under its influence. Evidence supports these effects across several studies.[62]
5. Fresh studies show curcumin shields liver tissue when toxins attack. Oxidative strain fades under its influence too.[63]
6. A sharp twist in brain health comes from curcumin - it eases oxidative stress while quietly blocking the buildup of harmful plaques seen in degenerative conditions. This root-derived compound steps in where few others reach, slowing damage through quiet but steady interference. Brain cells stay more resilient when faced with relentless chemical wear. Not magic, just molecules doing precise work beneath the noise .[61,62]
7. Blood vessel health gets a boost from curcumin. This compound helps lower bad cholesterol numbers. It also slows down damage to fats in the body caused by oxidation. Better flow through arteries shows up with regular intake. Protection for the heart emerges through these shifts. [61,62]

2.3 ALOE VERA –



Fig. no. 4 Aloe vera

Aloe vera answers to tags such as Ghritkumari, sometimes called Kumari, or known across regions as Indian Aloe. Still Out here, where sand stretches wide, something squat refuses to vanish. Its broad leaves clamp shut on every drop, as if daring the sun to take more. Sturdy still, though

close to earth, it waits. Beneath the surface hides something unexpected. Hidden inside those narrow, pointed leaves is a transparent layer filled with gel. This tough green plant thrives where heat and drought are common. Most often found in warm zones near the equator. Its roots trace back to the arid lands of the Arabian Peninsula. Belonging to the Asphodelaceae group shapes how it grows and spreads. From hot, dry areas comes a plant that thrives without much water. Mostly seen across parts of India, Africa, and Mexico today. Rajasthan, Gujarat, along with Tamil Nadu host its growth inside India. Across continents now, fields carry this crop in large stretches.

Found inside: long-chain sugars called Acemannan. Moving on, Aloin steps in - part of the anthraquinone group. Then there is aloe-emodin, working alongside it. Plant-based fats appear too - Luperol leads here. Another one joins, campesterol, quietly present. Sitosterol tags along, doing its part. Flavonoids scatter throughout, adding structure. Vitamins show up - one after another - A, then C, followed by E. Enzymes enter the mix, bradykinase among them. Each piece fits without drawing attention.

Mechanism Of Aloe Vera In Inflammatory Processes :

Aloe vera's active parts - acemannan, aloin, aloe-emodin - slip through the skin's outer layer when delivered via patch or gel. Once inside, they roll out slowly, hitting the sore spot just right. Steady release keeps healing levels stable where it matters most [64]. Irritation fades fast once Aloe vera gets involved, shutting down messages such as TNF-a, IL-1p, and IL-6 deep in the skin, easing redness where it starts [65]. Soon after, pieces of the plant disrupt a process tied to COX-2, an agent usually linked to unease; when blocked, there is less buildup of prostaglandin E, which helps reduce puffiness and tenderness [66]. When NE-KB signals slow down, acemannan plus similar sugars block triggers that would otherwise ramp up body-wide irritation. [67] Instead of sparking damage, elements like flavonoids, vitamin C, along with E, found in aloe vera mop up harmful molecules before swelling can take hold. [68]. Less nitric oxide comes out when Aloe steps in, blocking the enzyme that makes too much during swelling. Fibroblasts grow stronger under Aloe's touch through the skin, building more collagen to mend irritated areas quickly [69]. Moisture stays locked in, thanks to Aloe's hold on water balance, while the outer shield of skin rebuilds itself, keeping irritants out and calming ongoing flare-ups [70].

Ethnobotnical and pharmacological uses of Aloe Vera –

1. Ethnobotanical Uses

Healing wounds? That is where it started long ago. Burn treatments often relied on its soothing touch. Skin troubles like eczema find relief through gentle application. Acne shows up less when this comes into play. Infections sometimes fade after contact. Constipation found an old ally in herbal practice. Digestive discomfort eased across generations. Cooling the skin happens without harsh reactions. Moisture sticks around longer once applied. Minor cuts calm down with regular use. Inflammation backs off slowly but surely.

2. Pharmacological Uses

1.Anti-inflammatory activity – From the gut comes relief when aloe vera blocks signals that cause swelling [72].

2.Antioxidant activity – Free radicals get balanced out by its mix of vitamins along with phenols [73].

3.Antimicrobial activity – Aloe vera works on bacteria, also tackles fungi, while handling some viruses too [74].

4.Wound healing activity – From plant leaves, a clear substance boosts skin repair by encouraging new tissue growth [71]

5.Antidiabetic activity – Fewer sugars in the bloodstream often mean cells react more sharply to insulin. [73]
6.Gastroprotective activity – Few know how aloe vera guards the gut wall - yet helps heal sores inside. [72]

3. Rationale for Multi-Herbal Synergy –
Choosing Cuscuta reflexa, curcumin, and Aloe vera isn't random - it follows how they work together in healing. Used long ago in India and China, Cuscuta reflexa treated swelling and joint pain [75,76]. Even though curcumin packs a strong effect, it struggles to pass through skin because it is large - weighing 368.38 g/mol - and repels water [77]. Alongside Aloe vera, whose makeup includes natural saponins and fatty acids, the defense layer of skin weakens, letting active ingredients move through more easily [78]. What also happens is that Aloe vera gel helps the patch stick better to moist surfaces while reinforcing how well it holds together, making wear easier on the user [79].

4. METHODOLOGY-

4.1 - Identification and collection the herbal plant:
1. Cuscuta Reflexa :- Mainly the aerial parts (stem) of Cuscuta reflexa is collected from regional forest area, it is generally collected during the growing season when the parasite is well developed on its host.
2. Aloe vera : - Fresh aloe vera leaves were collected manually from local garden area.
3. Eight to nine months after planting, turmeric gets pulled from the soil. That is when the leafy tops turn yellow and start drying up. Workers dig up whole plants by hand at that stage. Once unearthed, the knobby parts get carefully removed. Dirt comes off through thorough washing. Then they go into pots to be boiled slowly. After cooking, they spend time in open air until fully dry. A light polish gives them a smooth outer layer. Only then do they move to storage spaces.

4.2 - Drying and size reduction of herb :-
1. Cuscuta Reflexa: the herb Cuscuta Reflexa will be shade dried at 5-7 days (to prevent the disruption of Phyto constituent for heat.
2. Turmeric rhizomes: - after the collection, wash turmeric rhizomes and then boil 30-45 min. (To reduce microbes,) For shade drying turmeric rhizomes spread on tray 10-15 day until completely dry.
3. The size reduction of Cuscuta reflexa roxb. Is done by using mortar and pastle and size reduction of dried turmeric roots is done by using electrical grinder.

4.3 - Extraction of plant material: -
1. Cuscuta refexla roxb - Coarse crude drugs of approximately 20g were used for extraction by soxhelation with the help of DCM for 24 hours. The extract was concentrated by evaporating the solvent in Rota vapor for 2 hrs then weighed, stored in a refrigerator at 4C.
2. Phytochemical screening - The phytochemical examination was caried out for DCM extract as per standard method. [80]

2. Aqueous extraction of aloe vera - [81,82]
The scaly Aloe vera leaves were thoroughly washed with water to remove the yellow latex. The outer layer was peeled out, and the gel matrix was collected and blended. To the weighed gel matrix of water was added and stirred using magnetic stirrer for 3 hours to form a homogenous solution. The solution was then filtered using filter paper, collected and stored.

3.Extraction of turmeric –
To extract curcumin from dried powdered roots (rhizomes) of turmeric (Curcuma longa), the Soxhlet method is used. Dried turmeric rhizomes are ground into powder form and placed into a

thimble (a type of container) within the Soxhlet apparatus. An appropriate solvent is added (usually ethanol or methanol) to the round-bottom flask, then heated until vaporized, and then cooled in the condenser; resulting in the solvent being cycled repeatedly through the ground turmeric rhizomes, leading to continuous extraction of curcumin. After multiple cycles of the extraction process, the curcumin-containing solvent is collected from the flask; then concentrated using a rotary evaporator to yield curcumin crude extract after collection has occurred. [83]

4.4 - Formulation of Herbal Transdermal Patch Using Solvent Casting

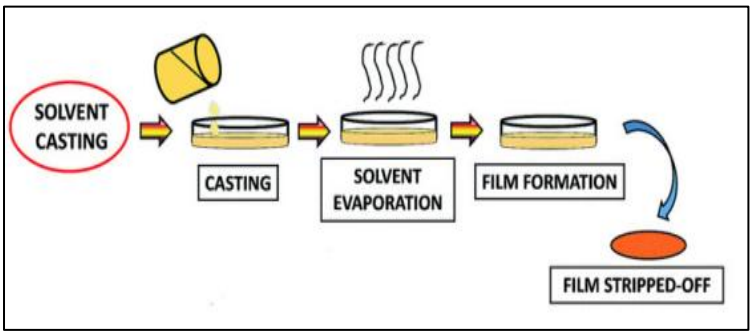


Fig. No. 2.Steps of Transdemal Patch

Preperation By Solvent Casting Method

Formulation process of the transdermal patches via the solvent casting method. The polymers (PVA, PVP) and the plasticizers (PEG 400 and propylene glycol) were measured into the mixture of ethanol and purified water. In the next step, the active substance was incorporated into the composition, and then this mixture was heated until we obtained a viscous but clear solution, which was poured into a 12-well plate and dried at 40°C.

A typical solvent casting formulation includes the following components:

Polymers: are cellulose based (hydroxypropyl methylcellulose, hydroxypropyl cellulose, polyvinyl alcohol)

plasticizers : (glycerin, propylene glycol)

solvents : (ethanol, dichloromethane)

There are a number of reasons why the solvent casting method is especially good for making herbal transdermal patches. First, it makes sure that the herbal actives are evenly spread throughout the polymer matrix, which makes sure that the drug release profiles are always the same. Second, it makes it possible to process at low temperatures, which is very important for keeping the thermolabile compounds in herbal extracts safe. [84] Third, it lets you choose different polymers and design formulations, which lets you change the patch's properties like tensile strength, swelling index, and drug release kinetics. [85]

solvents extracted from plants: (cuscuta reflexa, curcumin, Huile d'olive)

penetration enhancers: (aloe vera)

antioxidants/stabilizers : must be included to maintain the stability of phytoconstituents.

The first step is to take out and standardise the bioactive compounds.Ethanol or methanol is usually used to extract cuscuta reflexa while it is being refluxed. After that, the extract is filtered and concentrated under low pressure. Using uV-spectrophotometry or HPLC, the extract is then standardised for its flavonoid and phenolic content.[86] Curcumin is either extracted from turmeric rhizomes or utilised in its purified state, whereas Aloe vera gel is derived from the inner leaf parenchyma and is stabilised to inhibit enzymatic degradation. [87]

To begin mixing, all the components must be in place before beginning to combine the active ingredient and a polymer solvent. An excellent way to combine these is to create a homogeneous solution of each component using HPMC to dissolve (water and ethanol) dispersed with a surfactant (Tween 80) in the case of curcumin. Cuscuta reflexa extracts and aloe gels are added after hemp has solids removed by mixing thoroughly without pausing until the mixture reaches a uniform thickness. The next step involves removing any trapped air from the thickened compound by pressing it to the floor of a smooth surface like a glass or teflon see-through sheet/tray submerged in a warm room, which takes approximately 1-2 days for the liquid to evaporate. The final step consists of cutting out uniform pieces of the patch from the dried/solidified flat sheet and packaging those pieces into sealed boxes where they are protected from moisture and light

5. THERAPEUTIC MECHANISM AGAINST INFLAMMATION -

Curcumin and Aloe vera work together in the skin patch to change how Cuscuta reflexa works, hitting multiple targets at once. Curcumin is helpful because it is a potent anti-inflammatory agent by altering the NF-KB pathway to reduce the signals that trigger inflammation (such as IL-1β, IL-6, TNF-a).[89] Flavonoids including quercetin and kaempferol are both present in cuscuta reflexa, and they both also protect against free radicals and inhibit lipoxygenase enzymes that produce leukotrienes.[90]] Aloe vera increases blood flow to the area, helps tissues heal, and stops mast cells from releasing histamines, which lowers inflammation caused by histamines.[91] The patch's long-lasting release keeps therapeutic levels high at the site of inflammation, whether it's arthritic joints, muscle strains, or skin irritations.

5. EVALUATION PARAMETERS –

1- Physical Appearance -

Color: Yellowish light, sometimes shifting toward green (curcumin mixed with plant extract causes the tint) .

Surface: Smooth even surface without air bubbles

Transparency: Semi Transparent Opaque

Odor: Mild Herbal Smell

Acceptance: Fine if smooth throughout, without splits or tacky spots on top.

2- Thickness -

Method: Digital vernier caliper

Range: 0.2 – 0.5 mm

Acceptance: Fine if it stays mostly even - up to 0.05 millimeters of difference passes.

3- Weight Variation

Method: Digital balance

Range : A single patch holds between 100 and 300 milligrams. Size plays a role - take one that measures two centimeters by two, for example. The exact amount varies based on dimensions. Larger versions carry more. Smaller ones hold less. Milligram range shifts accordingly. Shape does not affect dosage. Only surface area matters here.

Acceptance: Variation should be ±5–10%

4- Surface pH -

Method: A splash of water touches the test strip first. Following that, the device checks acidity levels. Moisture activates the material before reading begins. Then numbers appear on screen quietly

Range: 5.5 – 7.0

(Skin compatible, no irritation)

Great when dealing with swelling: around 6.0 to 6.5

5- Folding Endurance (Flexibility) -

Method: Fold repeatedly at same place Range: > 200 folds

Good patch: Flexes a lot without snapping. Tough under pressure, it bends further than most. Holds up when twisted or stretched. Resists cracks even

when pushed hard. Stays intact after repeated strain

6. Tensile Strength:

Range: 0.5 to 2 kg/cm²

Acceptance: The patch shouldn't rip when you handle it

7. Percentage Elongation:

Range : 10% to 30%

Indication: Shows that it is flexible, which is important for the area where joints move.

8. Moisture Content:

Range: 2–8%

Low moisture means better stability.

9. Moisture Uptake:

Range : 5% to 15%

Too high → patch gets sticky

10. Drug Content Uniformity:

Range: 85–115% of the labelled content.

All patches should have the same amount of drug in them.

11. In-vitro Drug Release –

Expected Release: 60 to 80 percent of the drug will be released in 8 to 12 hours.

Good for long-lasting anti-inflammatory effect

12. Study on Skin Irritation

Observation: No redness (erythema)

No swelling (oedema)

Score: 0 (No irritation)

13. Adhesion Test:

The patch should stay on for 6 to 12 hours without falling off.

Important for applying to joints

6. FUTURE PROSPECT-

In-vivo Pharmacological Studies: Ahead of clear answers, studies with animals need to come first. Trials Figuring out if the updated mix calms swelling comes first. Before anything else happens, making sure it's safe matters just as much. Every single one A single trial means little unless others match it. Without repetition, findings stay uncertain. What matters shows up again, not just once. Patterns matter more than outliers ever could. Trust builds slowly through repeated outcomes. One result alone cannot carry weight Over time, hitting the mark again could open doors once thought out of reach.

Clinical Evaluation: Testing on people might show how well a treatment works for issues like joint stiffness, sore muscles, or swollen skin. Sometimes results come from watching changes over weeks. Other times clues appear right away when symptoms shift. Responses vary, yet patterns often emerge through careful observation. Each case adds pieces to the picture without giving full proof alone.

Permeation Enhancement Strategies: Penetration helpers or modern delivery methods - like tiny particles or small needles - might boost how well medicines pass into the skin.

Stability Studies:- Facing varied surroundings, products need lasting checks to pin down how long they stay usable. Storage rules come from watching them age in heat, cold, and dampness alike.

Formulation Optimization and Scale-Up: A fresh mix might work better when making big batches for market sale - this version spreads easily through skin, uses plants, keeps costs low. Production scales up without heavy expenses tagging along. Selling it wide becomes realistic under standard factory rules.

Exploration of Additional Phytoconstituents: Some plant-based remedies that reduce swelling or ease pain might work better when used together. A mix could boost how well they treat symptoms. Using certain herbs at once may improve results. When paired, natural options for discomfort might have stronger effects. Combining specific types can increase healing power.

Patient Compliance and Safety Studies A closer look at how the patch affects skin, sticks to the body, plus what users think might shape better versions down the line.

Targeted and Smart Drug Delivery Systems:
Fine-tuned skin patches - reacting to triggers, releasing medicine at precise spots - lift results beyond standard care. What matters most shows up in how evenly they deliver doses over time. Shifts happen quietly: timing adjusts itself without outside help. Performance grows when materials respond just right to body signals. Success hides in delays that stretch release exactly where needed.

CONCLUSION

Finding its roots in natural ingredients, a patch made from Cuscuta reflexa, curcumin, and Aloe vera was developed to test how well it reduces inflammation through the skin. Built using a common lab technique called solvent casting, each version held steady in thickness while varying slightly in weight - nothing too extreme. Bend without breaking? Yes, they managed that quite well. Skin-friendly acidity levels came through on testing, so irritation seems unlikely. All things considered, these traits line up well for something meant to sit on human skin. Over time, the lab-tested medicine slowly released its key parts, helping keep effective amounts in the body while cutting down how often doses are needed. Instead of acting alone, the chosen plant-based ingredients worked together, boosting their ability to ease inflammation by blocking certain triggers and stress-related cell responses. Despite skipping liver processing, medicine absorbed through skin reaches bloodstream more directly. This method often means less waste, stronger effect, fewer doses each day. Picking a treatment becomes easier when it lines up with how someone already lives. The A fresh mix grabs attention through calming joint puffiness along with soothing irritated skin Some find relief without tough reactions. Rather than tablets, This method skips shots, delivering consistent results through a patch. Secure to use Early tests reveal solid performance in everyday situations. The data points toward Older ways of handling these problems might soon be swapped out.

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