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Formulation And Evaluation Of Herbal Transdermal Patch Containing Lantana Weed

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Abstract:

Lantana Kamara is a flowering plant that arrived in India in a family of the Verbenaceae family. A study of kn owledge and scientific chemical principles of traditional medicine and medicinal plants could lead to the disco very of newer, cheaper medicines. Lantana Kamara is known to heal several illnesses and be used in various medical preparations for people. Over the past decades, scientists and researchers around the world have been examining the chemical composition of the entire L plant in detail and biological pharmacological activities. These studies determined the treatment potential of Lantana Kamala by transdermal drug collection. The main goal of developing alternative new forms of doses is to reduce patient-induced inconveniences/problems and increase drug efficacy, success and protection. The aim of this evolutio n is to develop adhesive patches by integrating herbal sources. Although synthetic drugs are developed to treat complex diseases, these drugs are associated with many side effects. This is where nature works, and the herb al sauce on the other side is more effective, safer and easier to get. The current review provides bird's-eye views of ethnobotany, phytochemistry, pharmacology and toxicology of l. Camera Herbal Transdermal Pa tches offer a variety of evaluations including thickness, folding time, physical appearance, weight uniformity, moisture content, drug content, flatness, hygroscopicity, pH, in vitro drug release and stability studies.

Keywords: Lantana Weed, Herbal transdermal patch, verbenaceae.

Introduction: Drug Targeting and Controlled Release of Drug is the aim of the transdermal drug delivery system. Drug delivery systems include Sustain Release system, Delayed release system, Targeted release system, modified release system, extended release system and many more. Local anesthesia and anti-inflammatory activities can be produced by using the Transdermal drug delivery system. It has many advantages over old and traditional drug delivery systems, which is why it has a wide scope now. New innovations in the medical field are there. The First Pass Metabolism can be bypassed by the TDDS, as it tends to enhance the Bioavailability of and drug. The prolong effect of desired drug can be maintained by keeping the drug concentration in the given therapeutic window. Solvent evaporation method is used to develop transdermal patches.

Greek physician introduced the compounding of herbal drugs and other excipients in dosage form. He is widely considered to be "FATHER OF PHARMACY". And his work and practices are called as "GALEN PHARMACY". In 1904, Schwenken Becker generalized that skin was relatively permeable to lipid soluble substance but not to water and electrolytes. Dale Wruster and his student Sherman Kramer stated that the absorption can be enhanced or modified by varying the diffusion area of cell by changing the level of skin hydration. Scopolamine (Hyoscine) patch for treatment of

motion sickness was the First Transdermal Patch to reach the market. Then after scopolamine Nitro-glycerine patches for Angina pectoris were evolved. Before marketing the transdermal scopolamine patches the nitroglycerine ointments was the only transdermal product of nitroglycerine.

ANATOMY OF SKIN

EPIDERMIS: Composed of various layers, the epidermis forms the outermost layer of skin, primarily derived from ectoderm. Its keratinized stratified squamous epithelial characteristics define it, comprising the stratum corneum, stratum lucidum, stratum granulosum, and stratum spinosum.

1. STRATUM CORNEUM: Positioned as the outermost layer of epidermis, stratum corneum prevents the penetration of environmental substances while also minimizing insensible body water loss. Efficiently, this layer protects the body from potential invasions.

2. STRATUM LUCIDIUM: A translucent, thin zone resides between stratum granulosum and stratum corneum, forming this particular layer. Characterized by its exclusive positioning within the epidermal structure, stratum lucidum serves its function seamlessly.

3. STRATUM GRANULOSUM: Within this layer, approximately 3-5 layers of flat cells coexist with non-membrane bound, irregularly shaped granules. Functioning together in unison, these cellular entities orchestrate the overall operation of this stratum.

4. STRATUM SPINOSUM: A zone embodying several layers of polyhedral cells of irregular shaped, this layer provides key structural support. Efficiency in functionality of stratum spinosum ensures unimpeded epidermal activity.

DERMIS: Mesodermally derived and offering essential support to the epidermis, the dermis constitutes a layered network of mucopolysaccharides-rich collagen and elastin fibres, complete with blood vessels, lymphatic nerve endings, and more. Moreover, the thickness of this characteristics layer is around 3-5 mm. Considering these unique factors, the dermis seamlessly aligns with epidermis functionality, laying the groundwork for operation scalability. As you note, it plays a pivotal role in maintaining integral tissue functionality, facilitating broader bodily alignment.

PATCHES:

Transdermal patches are medicated adhesive systems designed to deliver drugs into the bloodstream via the skin. These patches contain a drug coating and utilize transdermal drug delivery systems (TDDS) to improve patient convenience, enhance drug effectiveness, and protect the drug from degradation. Formulated to facilitate drug diffusion through skin layers, transdermal patches enable the drug to reach systemic circulation. To overcome limitations associated with conventional drug administration, controlled-release and novel drug delivery systems have emerged. TDDS patches are self-contained dosage forms applied to the skin that release medication at a controlled rate over an extended period, allowing the drug to reach the bloodstream at a predetermined pace.

Gram-positive bacteria, such as Staphylococcus epidermidis, can cause infectious diseases and skin disorders detrimental to human health. Natural ingredients with antibacterial properties, like those found in *Lantana camara* Linn, can aid in wound healing. *L. camara* possesses a wide range of chemical constituents, including essential oils, phenols, flavonoids, alkaloids, glycosides, phenyl ethanoids, quinines, saponins, steroids, triterpenoids, sesquiterpenoids, and tannins.

The use of herbal medicines is increasing globally, particularly in countries like Indonesia, China, and India, due to their broad pharmacological effects and relatively mild side effects. However, herbal medicine faces challenges related to bioavailability, solubility, absorption of active substances, and stability. Further research is needed to develop traditional medicinal preparations like transdermal patches.

A transdermal patch is a topical preparation that allows a drug substance to penetrate skin tissue and become systemically available. It is a localized treatment option capable of delivering drugs directly to a wound site. The transdermal drug delivery system offers several advantages, including sustained drug release, ease of use,

reduced dosing frequency, and avoidance of first-pass metabolism, decreased gastric irritation, and improved patient compliance.

“Patch-based extract preparations represent an innovative approach to drug delivery, designed to enhance patient compliance, safety, and comfort. A key component of these patches is the polymer matrix, which significantly influences their physical properties. Polymers, formed through polymerization, are broadly classified as either water-soluble or water-insoluble.

Water-soluble (hydrophilic) polymers swell and form a gel-like consistency, creating a natural matrix that facilitates drug diffusion through open pores. Polyvinyl pyrrolidone (PVP) is a prime example, valued for its film-forming capabilities, non-irritating nature, and solubility in skin-safe solvents. Consequently, PVP finds application as a hydrophilic polymer, disintegrant, suspending agent, and a carrier for drugs (typically at concentrations of 10-25%), as well as a dispersing and suspending agent. Conversely, water-insoluble polymers, such as ethyl cellulose (EC), are affected by the ratio of crystalline to amorphous forms of the polymer. Crystals can impede molecular movement and slow drug release. EC, a hydrophobic cellulose derivative, contributes hardness and flexibility to the patch, increasing its viscosity. It is utilized as a coating agent, tablet binder/filler, viscosity-increasing agent, and for sustained-release tablet coatings at concentrations ranging from 3.0 – 20.0%. Combining these two polymer types offers the potential to create patches with optimized physical characteristics."

Basic Component of Transdermal Patch

Transdermal patches typically consist of several layers that are designed to deliver the medication through the skin and into the bloodstream. Figure 1 illustrates the basic component of a medicated patch. The specific composition and structure of the patch may vary depending on the drug being delivered and the desired rate of drug release.

The backing layer is the outermost layer of the patch and serves to protect the other layers from the environment. This layer is usually made of a flexible, waterproof material such as polyethylene or polypropylene. The adhesive layer serves to attach the patch to the skin and keep it in place. It usually consists of a strong, hypoallergenic adhesive that is gentle on the skin. The drug layer contains drugs that are delivered through the skin. It is formulated to release the drugs at a constant rate over a period of time. The rate-controlling membrane serves to control the rate at which the drugs are released from the patch. Membranes are usually made of semi-permeable materials that allow the drugs to pass through the membrane at a controlled rate. Linen acts as a protector for the patch and adhesive. The patch must be removed before being applied to the skin surface.

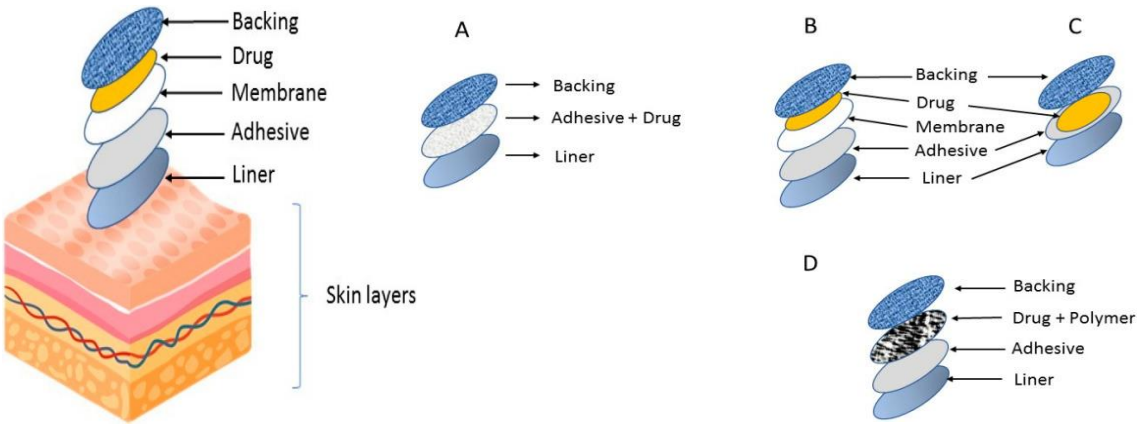

Fig.01-layers of Skin

Types of Transdermal Patches

Generally, there are four main types of transdermal medical patches (drug-in-adhesive, reservoir, matrix, and microreservoir systems), as shown in Figure 2. Most of the patches available on the market are classified as reservoir or matrix systems.

Drug-in-adhesive system

This system is the simplest form of membrane permeation control system. The adhesive layer in this system contains the active ingredient and serves to glue the different layers together. The active ingredient mixture is encapsulated between the liner and the carrier layer.

Reservoir system

In this system, the active ingredient reservoir is placed between the carrier layer and the rate-controlling membrane, and the active ingredient is released through the microporous rate-controlling membrane. The active ingredient can be in the form of a solution, suspension, gel, or dispersed in a solid polymer matrix within the reservoir.

Matrix system

The active ingredient is uniformly dispersed in a hydrophilic or lipophilic polymer matrix. The resulting drug-loaded polymer is deposited into a drug-loaded disk of controlled thickness and surface area.

Micro reservoir System

This system combines the reservoir and matrix dispersion systems. Here, the drug is prepared by first suspending the drug solids in an aqueous solution of a water-soluble liquid polymer and then dispersing that solution uniformly in a lipophilic polymer to create thousands of microscopic drug reservoirs that will not leach.

Advantages of Transdermal Drug Delivery System (TDDS)

Transdermal administration has the following advantages over other conventional administration methods:

1. It improves drug bioavailability and efficacy by bypassing first-pass hepatic, salivary, and intestinal metabolism.
2. It also allows for self-administration.
3. In an emergency, drug delivery can be immediately stopped by removing the patch from the Skin surface and discontinuing use at any time during treatment.
4. Skin is structurally and biologically the same in nearly all people, so inter- and intra-patient Variations are minimal.
5. Avoid gastrointestinal intolerance.
6. It avoids the risks and inconveniences associated with parenteral therapy and improves patient Compliance through ease of use.
7. A stable and optimal time profile of blood levels is achieved, reducing side effects.
8. A single dose releases the drug over a longer period, thus increasing duration of action.
9. Drugs with short biological half-life and narrow therapeutic window are used.
10. Fluctuation in plasma levels of drugs is avoided.
11. Plasma concentration of active drug is maintained.
12. Treatment can be terminated at any time without issue.
13. Elimination of the typical multiple-dosing profile and improved patient compliance.
14. When oral administration is not appropriate, such as due to vomiting or diarrhea, the Transdermal route of administration of the candidate drug is chosen.

Disadvantage of Transdermal Drug Delivery System (TDDS)

1. Potent drugs are suitable candidates for transdermal delivery
2. Skin irritation may occur in some patient at the site of application
3. The delivery system is not suitable for drugs needs high blood levels
4. This system is uneconomic
5. Dose dumping may occur due to Binding of drug to skin
6. It can be used only for chronic conditions not for acute condition because chronic condition Require drug therapy for a long period of time e.g., hypertension, angina and diabetes etc.
7. Therapeutic performance of the system Affected by Cutaneous metabolism

8. Ionic drugs are not suitable candidate for Transdermal therapy.

LANTANA:

Medicinal plants are an important source of medically important compounds. From ancient times, medicinal plants have been used to treat various health problems. Systematic analysis of these plants provides a wide range of bioactive molecules that can be useful in the development of new medicines. Recently, there has been growing interest in the pharmacological evaluation of various plants used in different traditional medicine systems. In recent years, many traditionally known plants have been extensively studied using modern scientific techniques and their various medicinal properties have been demonstrated. For example, they have anticancer, anti-inflammatory, antidiabetic, anthelmintic, antibacterial, antifungal, hepatoprotective, antioxidant, larvicidal, and other effects. 1-10 Lantana camara Linn. A flowering ornamental plant of the Verbenaceae family. L. camara is also called lantana, wild sage, Surinamese tea plant, Spanish flag, and West Indian lantana. L. Camara is a well-known medicinal plant in traditional medicine, and recent scientific studies have highlighted the potential uses of L. camara in modern medicine. The aim of this review is to document the morphology, distribution, phytochemistry, and medicinal properties of L. camara, as well as future perspectives for further scientific investigation to develop effective therapeutic compounds. Classification: Kingdom: Planifera; Phylum: Angiosperms; Class: Magnoliopsida; Order: Lamiales; Family: Verbenaceae; Genus: Lantana; Species: Lantana camara Linn. Plant description: The morphology of L. camara is shown in Figure 1. L. camara is a vigorous shrub with a low, erect or drooping, squared trunk and strongly recurved leaves with a strong blackcurrant scent. The plant grows to a height of 1-3 metres and up to 2.5 metres wide. The leaves are ovate or oblong, pointed or semi-pointed, toothed, wrinkled on the upper surface and rough on both sides. The leaves are 3-8 cm long and 3-6 cm wide and are green in colour. Leaves and stems are covered with coarse hairs. The small flowers grow in clusters (called umbels). They are usually orange in colour but can vary from white to red in various shades and the flowers change colour over time. The flowers bloom almost all year round in axillary flower heads with yellow throats. The calyx is small, the corolla tube narrow, the margin divided into unequal lobes 6-7 mm wide. The stem is closed in two pairs of 4-folds, the ovary is two-celled, and two are ovulated. The inflorescences are borne in pairs in the axils of opposite leaves. The inflorescence is compact, dome-shaped, 2-3 cm wide, with 20-40 sessile flowers. The root system is very strong, producing new fresh shoots even after repeated cutting. Geographical distribution: L. camara is a tropical plant native to central and northern South America and the Caribbean. L. camara is currently distributed in about 60 countries, including New Zealand, Mexico, Florida, Trinidad, Jamaica, and Brazil. It is also found in many African countries, including Kenya, Uganda, Tanzania, and South Africa. In India, L. camara was probably introduced before the 19th century. Currently, L. camara is distributed throughout India. Kamala is known by different names in different languages in India namely Raimuniya (Hindi), Chaturangi and Vanachedi (Sanskrit), Alipu and Unnichedi (Tamil), Alipu, Poochedi, Konginipoo, Nathachedi (Malayalam), Thilay, Sambhalay, Nonbhalay (Manipuri), Tantani and Ganeri (Marathi), Pulikampa (Telugu), Kakke and Natakhu (Kanadzhi). Ethnopharmacology: L. camara is an important medicinal plant with various medicinal properties in traditional drug systems. It is used to treat various health problems in different parts of the world. The leaves are used to treat cuts, rheumatism, ulcers, colds, tetanus, rheumatism, malaria, cancer, chicken pox, asthma, ulcers, swelling, eczema, tumors, high blood pressure, bilious fever, abdominal organ ataxia, wounds, measles, fever, colds and high blood pressure. In Ghana, a decoction of the whole plant has been used to treat bronchitis, and the roots ground up and dissolved in milk have been given to children for stomach aches and as an anthelmintic. Lantana oil is used to treat skin and itching and to disinfect wounds. A decoction has been applied externally to treat leprosy and scabies. 12-14 Phytochemical Composition: The phytochemical composition of L. camara has been studied extensively over the past few decades. Various parts of L. camara have been reported to contain essential oils, phenolic compounds, flavonoids, carbohydrates, proteins, alkaloids, glycosides, iridoid glycosides, phenylethanoids, oligosaccharides, quinines, saponins, steroids, triterpenes, sesquiterpenoids and tannins as important phytochemical groups.15-18 Pharmacological Studies: L. camara is an important medicinal plant of the Verbenaceae family. Recently, the plant has been attributed with various medicinal properties (Figure 2).

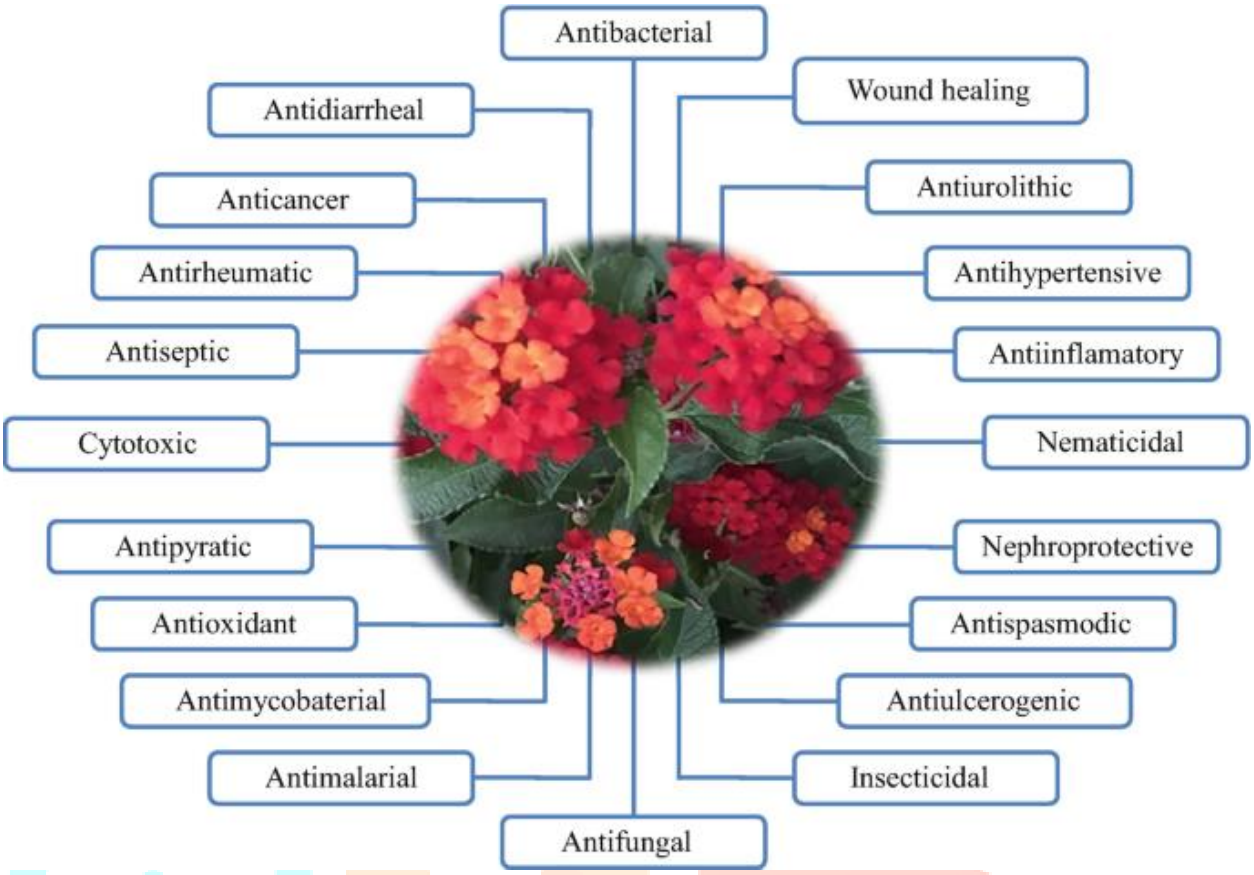

Fig.02- Medicinal Properties of Lantana camara

Components of transdermal patch:

1. Polymer Matrix: To release drug from patches PVP, PVC, Starch

2. Active agent: to get desired Therapeutic Effect Any desired drug

3. Penetration Enhancer: Enhance permeation through skin. Enhancing skin function e.g. SLS, Ethanol etc.

4. Plasticizer: Reduce Brittleness of Patches, they use in the range of 5-20%. e.g. Propylene Glycol

5. Drug Reservoir: Its combination of polymers 1-2 polymers

6. Backing Membrane: Gives strength and support Aluminum Foil

7. Adhesive layer: Helps adhere to skin - 8. Release Liner Act as Protective Layer Teflon, silicon etc.

Extraction of Lantana Leaves:

1. Collect the fresh leaves of lantana from plant.
2. Wash the leaves with the tap water to remove dust, debris from the leaves.
3. Dry the washed leaves naturally.
4. Grind the leaves into fine powder in mortar and pestle.
5. Extract the powder by using solvents like ethanol, ether, petroleum, etc.
6. Filter the extract to separate out filtrate.
7. Store the extract at room temperature.

Method of preparation of Transdermal patch:

1. Asymmetric TPX membrane method
2. Circular Teflon mould method.
3. Mercury substrate method.
4. By using “IPM membranes” method
5. By using “EVAC membranes” method.

1. **Asymmetric TPX membrane method:** These are manufactured using drying or wetting processes. In this TPX, a mixture of solvent (cyclohexane) and non-soluble additives is resolved at 60°C to form a polymer solution. The polymer solution is held at 40°C for 24 hours and poured onto a glass plate. The cast film is evaporated at 50°C for 30 seconds, and the glass plate immediately dives into the solidification pool (temperature manager at 25°C). After 10 min utes, remove the membrane and air dry at 50°C fOr 12 hours with soft circulation.
2. **Circular Teflon foam method:** discovered by Baker and Heller in 1989. The polymer solution in diff erent parts is used as an organic solvent. Then this solution is divided into two parts. In one part, a calc ulated amount of drug is solved, in another part of enhancer is solved in a different concentration and t he two parts are mixed. Then a plasticizer (e.g. dinbutylphthalat) is put into the drug polymer solution. The overall content is stirred for 12 hours and then poured into a circular Teflon shape. The shape is pl aced on an established surface and covered with an inverted funnel to control the solvent evaporation i n a laminar river hood model at 0.5 m/s. The solvent is allowed to evaporate for 24 hours. A dry film i s then formed and should be held at 25 ± 0.5 °C for an additional 24 hours in the dry area containing p ebbles before evaluation of removal of aging effects.
3. **Mercury Substrate Method:** This method dissolves the drug and plasticizer in the polymer solution. Stir for 10-15 minutes to obtain a uniform dispersion. Next, pour onto a flat mercury surface and cover with an upside-down funnel to control the evaporation of the solvent.
4. **When using the "IPM membrane" method:** Disperse the drug in a mixture of water and polymer (propylene glycol and carbomer 940 polymer) and stir on a magnetic stirrer for 12 hours. The dispersion must be neutralized by adding triethanolamine to make it viscous. If the solubility of the drug in aqueous solution is very low, a solution gel can be obtained using a buffer at pH 7.4. The formed gel is absorbed into the IPM membrane.
5. **When using EVAC membranes:** For TD preparation, 1% carbopol reservoir gel, polyethylene (PE), and ethylene-vinyl acetate copolymer (EVAC) membrane are required as the rate-controlling membrane. If the medicine is not soluble in water, prepare the gel using propylene glycol. The drug is dissolved in propylene glycol, add carbopol resin to the above solution and neutralize using a 5% w/w sodium hydroxide solution. Place the drug (gel-like) on the sheet of the background layer covering the specified area. A speed control membrane is placed on the gel and heat seals the edges to form leak-proof protrusions.

Evaluation of Herbal Transdermal Patch :

Thickness: The thickness of the transdermal film is determined by a travel microscope, dial knife, screw knife, or micrometer at various points of the film. . Individual weights are not significantly different from average weight. The solvent is chosen, making the drug easy to dissolve freely. The weight of the selected area is measured before it is dissolved in the solvent. The entire content is constantly shaking on a shaker that has left for 24 hours, followed by setting and filtration. Drugs in solution are evaluated by appropriate analytical methods.

Content Uniformity Test: This test is used as a gold standard for chemically measuring the content of active ingredients in each unit dose. The test is completed by running an assay to determine the content of drug substances in the polymer film of the patch. According to the USP, the process consists of two phases. The first

stage tests 10 randomly selected units. This is followed by a second stage, which is carried out with another 20 units if the first stage fails.

Moisture Content: The prepared films are weighed individually and kept in a desiccator containing calcium chloride at room temperature for 24 hours. The films are weighed again at regular intervals until a constant weight is reached. The percentage of moisture content is calculated using the formula - Moisture Content (%) = (Initial Weight - Final Weight) Final Weight of Raw Material

Moisture Absorption: The weighed films are left at room temperature for 24 hours. They are then removed and exposed to a relative humidity of 84% in a drying engine using a saturated solution of potassium chloride until a constant weight is reached. Moisture absorption, such as less than % water absorption, is calculated = Final weight - Initial weight 100 initial weight

Flatability: Transdermal patches have a smooth surface and should not be limited over time. This can be demonstrated in flatness studies. To determine flatness, a strip from the center and two are cut from either side of the spot. The length of each strip is measured, and the length of the length is measured by determining the stenosis rate. A zero percentage narrowing corresponds to 100% flatness. % shrinkage = (L1-L2) 100L1 L2 = Final length of each strip = Initial length of each strip Microscopy: The distribution of drugs and polymers in the membrane can be examined using scan electrons Microscope. In this inspection, sections of each sample are cut off and then attached to the stump with double adhesive tape. The sections are then coated with a palladium alloy of gold using a thin coating process using an ion spark to make them electrically conductive. The sections are then examined under a scanning electron microscope.

Adhesion studies: The therapeutic efficacy of TDD may be influenced by the quality of patch-skin contact. Adhesion of TDD to the skin is achieved using PSA. PSA is defined as an adhesive that can be adhered to a surface by applying light pressure. The adhesive properties of TDDS can be characterized by the following factors:

i. **Peeling adhesive properties:** The force required to remove the adhesive coating from the test substrate. It is tested by measuring the force required to pull a single coated adhesive tape applied at an angle of 180◦. If the substrate does not contain residue, the test will pass.

ii. **Tack properties:** The ability of the polymer to adhere to the substrate with little contact pressure. Adhesion is determined by the molecular weight and composition of the polymer, and the use of the curing agent in the polymer. This includes thumb tuck test, rolling ball test, quick stick (peel tack), and probe tuck test. Thumb tack tests are performed by touching the surface of the pressure sensitive adhesive with your thumb and feeling the force necessary to break the adhesive. Thus, the force required to remove the thumb made by the adhesive is a measure of the tack. For the roller ball test, the distance is measured that a stainless steel ball travels with the adhesive facing upwards. The less tack there is, the further the ball travels.

iii. **Quick Stick (Peel Tack) Test:** The peel force had to break the bond between the adhesive and the substrate by pulling the tape away from the substrate at 90° SES. Trial tap tests are performed using a probe that makes contact with the adhesive surface and is withdrawn at a predefined speed. The force required is measured to settle the connection after a short contact time. The test can be performed using a texture analyzer.

Conclusion:

The present review of herbal transdermal patch of lantana camera will shows the better antifungal and another medicinal properties than the synthetic transdermal patch. This herbal transdermal patch will also reduce the side effects of chemicals, and it will be used for all kind of age patients. This patch will also show the wound healing property and it available worldwide so the formulation will be affordable for all population and it will take less time for preparation.

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