



Herbal transdermal patches: A review

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Abstract

Drug delivery technologies are now receiving considerable attention from pharmaceutical companies. The main purpose of developing alternative drug delivery technologies is to increase efficiency and safety of drug and provide more convenience for the patient. Substantial research conducted during the past several years has led to the development of technologies that meet the requisite criteria for delivering the drug through a non-invasive route. One of such technologies is transdermal drug delivery. Transdermal patch is a medicated adhesive pad that is designed to release the active ingredient at a constant rate over a period of several hours to days after application to the skin. It has been found that drugs from herbal origin can be utilized with enhanced efficacy by incorporating in transdermal drug patches. Herbal transdermal patches which aids to quit smoking, relieve stress, increase sexuality, insect repellent patches, detoxification, male energizer, postpone menopause are available. Even herbal penetration enhancers like some terpenes are found to be potential enough to replace the conventionally available penetration enhancers like DMSO (Dimethyl Sulfoxide) which has several disadvantages. The present review will try to focus on the delivery of some herbal agents through transdermal route.

Key Words: Transdermal drug delivery, medicated patches, herbal agents.

Introduction

The transdermal delivery is a relatively simple technology to use. The major barrier within the skin is the stratum corneum, the top layer of the epidermis. The stratum corneum consists of keratinized, flattened remnants of once actively dividing epidermal cells. Hygroscopic, but impermeable to water, it behaves as a tough, flexible membrane. The intercellular space is rich in lipids. The stratum corneum is about ten microns thick, but on the palms and soles it ranges up to 600 microns in thickness. Although the stratum corneum is an efficient barrier, some chemical substances are able to penetrate it and to reach the underlying tissues and blood vessels¹. These "successful" substances are characterized by low molecular weight (≤ 500 Da), lipophilicity, and effectiveness at low dosage.

Transdermal absorption occurs through a slow process of diffusion driven by the gradient between the high concentration in the delivery system and the zero concentration prevailing in the skin. Thus, the delivery system must be kept in continuous contact with the skin for a considerable time (hours to days)².

General method of preparation

- Herbs are put in a jar and a spirit of 40% pure ethanol is added (80 proof Vodka, for example)
- The jar is left to stand for 2–3 weeks, shaken occasionally, in order to maximise the concentration of the solution.

To make a more precise tincture, more extensive measuring can be done by combining 1 part herbs with a water-ethanol mixture of 2-10 parts, depending on the herb itself. With most tinctures, however, 1 part water at 5 parts ethanol is used.

METHODS OF PREPARATIONS OF PATCHES :

Method 1).

PVA, PVP were used as the skeletal material of preparation, Glycerol as humectant and plasticizer, Azone and propylene glycol as penetration enhancer. Polyacrylic resin pressure-sensitive adhesives (PSAs) are materials that adhere to a substrate by application of light force and leave no residue when removed. Pressure sensitive adhesives are also important components of transdermal drug delivery systems (TDDS), because they ensure intimate contact between the drug-releasing area of a TDDS and the skin surface, which is critical for controlled release of the drug (Yoshinori *et al.*, 2005).

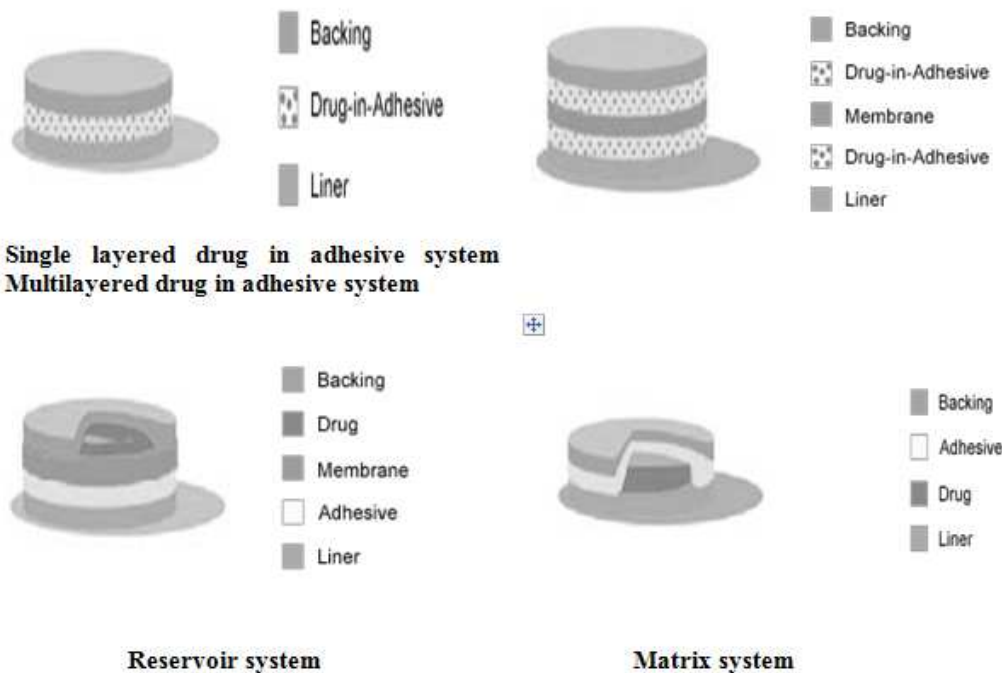
Method 2)

PVA (1 g) and PVP (1g) were weighed in requisite ratios and mixed in 10 ml distilled water, stirred the mixture over a hot water bath until dissolved. After the mixture was cooled down to 25 °C, added Sinomenine (0.3 g), propylene glycol (0.5 ml), glycerol (0.5 ml), azone (0.3 ml) and the pressure-sensitive adhesives (2 ml), mixed together using a mechanical stirrer (IKA, RW16, Germany) at 800 rpm for 15 min under occluded condition (Paola *et al.*, 2003). The mixture was then cast on the release liner with a micrometer adjustable casting knife (R. K. Coat Instruments, UK) set at 500 μm , and was dried at 80°C for 25 min. The total area of one formulation is about 300 cm^2 . The patches were covered with backing laminate

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Types of transdermal patches:**Fig.1 Types of transdermal patches.**

and cut into appropriate sizes. Drug loading for Sinomenine was about 1 mg per cm².

Stability test**1. Centrifugal test**

10 g of transdermal CHM agent was put into the centrifuge tube with a scale, centrifuged 3000 r/min for 30min, while observing whether there is the phenomenon of layering and emulsion breaking.

2. Cold and heat test

The transdermal CHM agents were placed in test tube with plug, kept in a 55°C incubator for 6 h and -15°C refrigerator for 24 h to observe whether the layered, demulsification, mildew, as well as color and uniformity of change occurs (Wu et al., 2008).

3. Accelerating test

The transdermal CHM agents were placed in test tube with plug, kept for three months in a constant temperature incubator of temperature (40 ± 2 °C) and relative humidity of 75% to observe whether the stratification, demulsification, mildew, as well as color, uniformity of change occurs (Wu et al., 2008).

4. In vitro diffusion**Skin treatment**

The abdominal skin of mice was employed with the subcutaneous fat tissues being removed, soaked in saline and kept in 4°C refrigerator for further use.

EVALUATION OF MEDICATED PATCHES :**1) Weight Variation Test :**

The study was carried out on 9 films obtained from 100ml of casting solution. The mean weight of the film as well as the deviation from the mean was obtained.

2) Measurement of film thickness:

The study was carried out on 5 randomly selected films. The thickness of two glass slides held together was recorded first with the help of a micrometer screw gauge ; the films were placed Between the two glass slides and the thickness was measured at 5 different points and the mean values were calculated. The data for thickness measurement is recorded .

3) Hardness Determination:

The apparatus employed for hardness determination consisted of a sharp needle 12cm

long, 2mm thick and tapering to form a pointed end between 11th and 12th cm, passing down a wooden mechanical frame. The sharp pointed end of the needle rested on a flat surface with metal lining. The upper blunt end of the needle was connected to a circular wooden plate on which increments of weights could be placed. The upper part of the needle was connected to an electric wire continuous with two 1.5-volt batteries and a threevolt electric bulb and the circuit was completed by connecting the wire to the metal plate above which the

film is placed. The sharp end of the needle rested on the film. Increments of weights were added on to the surface of wooden plate and when the hardness of the film is exceeded, the sharp end.

4) Determination of folding endurance:

A film of 5.5 cm x 3 cm dimension was used in each case. The film to the extent of 0.25 cm was fixed on either side with the help of metal clips. Folding of the film was accomplished by two aluminum L-clamps held in position by the metal clips which, when come closer together, gently press the film along the vertical direction and guide the film to fold upwards. While one of the clips remained stationary, the other metal clip was made to move to and fro by means of a piston connected eccentrically to a rotating wheel with a variable speed regulator. The number of rotations (counts) executed at a fixed speed to break the film was recorded. The average values of 5 such runs for folding endurance for patches. The assembly for folding endurance determination is displayed in Fig.2



Figure 2. Apparatus for determination of folding endurance of the Patch.

5) Determination of drug content:

The drug content was estimated by diazotization reaction of salbutamol sulphate and subsequent coupling with Para nitro aniline in alkaline solution. The resulting colour intensity was measured at 485 nm against a reagent blank. The chromophore obeys Lambert – Beer law in the concentration range of 1 - 8 μ gm/ml of salbutamol sulphate. The average data for three determinations of drug content in the films are recorded.

USE OF HERBAL TRANSDERMAL THERAPY:

There are different patches that are available to lose weight, quit smoking, help to relieve stress and even increase sexuality, insect repellent patches, detoxification, male energizer, better sleeping, postpone menopause etc.

1.anti-smoking patch

Anti-smoking patch is an innovative cessation aid designed to help you give up smoking safely and naturally, without putting more nicotine into your body.

With its unique blend of ingredients, zero nicotine patches offers you the best possible chance to finally kick the habit for good! They are applied to your skin, and put a dose of nicotine into your body

2.kick the nicotine habit naturally: Zero nicotine is safe and easy to use. Each zero nicotine patch contains a dose of the most effective herbal ingredients, formulated to alleviate the symptoms of nicotine withdrawal while cleansing the system of all smoking-related toxins. To break free from smoking, you need to break free from nicotine. Zero nicotine's all-natural formula contains no nicotine and eliminates, rather than replenishes, the level of nicotine in your body, helping you break the habit. Used in conjunction with proven cessation program, zero nicotine can help you be free of tobacco in thirty days or less. It is a well-known fact that withdrawal from nicotine is very unpleasant. In fact, it is the single thing that causes even the most committed "quitters" to go back to smoking. The researchers have discovered a way to combine the all-natural healing properties of a unique variety of traditional herbal formulas to completely and naturally eliminate your body's need for nicotine. Detailed list of ingredients used in anti smoking patch are. Gotu Kola, Hops, Skullcap, Oat, Peppermint, Ginger, Gentian, Myrrh, Safflower, Eucalyptus, Licorice Root, Sarsaparilla, Bayberry.

3.herbal body detox foot patch

The bodies detox foot patches are based on molecular reform therapy.

Molecular reform therapy has four major components.

- 1) Detoxification- To remove waste and toxins from the body. (Non digestive and other chemical toxins must be eliminated from the body)
- 2) Increasing Oxygen intake- to enhance metabolism
- 3) Balance Nutrition - To supply the body with all essential nutrients (Need 49 nutrients daily to perform the proper function.)
- 4) Heath Regulation - To promote mental heath and health restoration.

According to Chinese medical knowledge, our human body has over 360 acupuncture points, with more than 60 acupuncture points found on the soles of the foot. Known as the "second heart", these are the reflex zones of our internal organs, and potential homes for toxins. When the blood circulates to the soles, the Detox Foot Patch can absorb toxins released from the acupressure points. Circulation of blood and lymphatic fluids reach their furthest point in the soles of the feet before being return 'pumped' back up into the higher portions of the body. Unfortunately in today's society, seemingly too much of our time is spent perusing sedentary activities. This can lead to circulatory dysfunction and an inhibited flow of the lymphatic fluids in the body (the lymphatic system in fact has no pumping organ like the circulatory system, and thus relies upon sufficient motion and bodily activity

to precipitate fluid motion) as they begin to accumulate in the ankles and lower legs due to gravity. The body detox foot patch contains all natural ingredients, which are described as below:- Bamboo Vinegar, Wood Vinegar, Tourmaline, Eucalyptus.

4.herbal slim patch / diet patch / weight loss patch

It is 100% made of natural herbs and processed to soft patch form with transdermal technology (to reduce the overburden of vital organ). It looks smooth, soft and smells slightly herbal. It is the natural way to lose weight permanently. After years of research, it was discovered that a small amount of this unique combination applied to the skin (transdermaly) caused miraculous weight loss. The weight loss patch eliminates hunger while burning fat. Actually, the way it works is truly extraordinary. When the diet patch is placed on the skin, this releases weight-regulating substances. The body slowly absorbs these elements, resulting in a "boost" to the thyroid gland. This increases the metabolism and activates fat burning mechanisms. The thyroid controls your metabolism, which in turn burns fat and decreases appetite. Detailed list of ingredients used in herbal slim patch are. Fucus vesiculosus, Guarana, 5-HTTP, Zinc Pyruvate, Flax seed oil, Lecithin, L-Carnitine, Zinc Citrate

5.herbal anti-rheumatic patch

Rheumatic diseases have affected mankind since ages and are one of the commonest inflammatory conditions in developing countries. Rheumatoid arthritis (RA) forms a major prototype of rheumatic diseases and is a common cause of disability. RA is both an extra vascular immune complex disease and a disorder of cell-mediated immunity leads to chronic inflammation, granuloma formation and joint destruction. The etiopathogenesis of RA involves diverse and complex factors such as genetic background, rheumatic factor (circulating antibodies), immune complexes, compliment activation, lymphocytes, arachidonic acid metabolites; free oxygen radicals etc. Currently synthetic drugs form a major line of treatment in the management of arthritis. The conventional drug treatment of RA consists of analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs) and cortico-steroids. These agents act at various sites in the schema of pathogenic mechanisms. An important problem in the drug therapy in the elderly RA patients is the lack of compliance. They have other illnesses for which they may be taking medicines. Transdermal delivery thus offers a better route of delivery, reported to have better patient compliance. Transdermal drug administration generally refers to topical application of agents to healthy intact skin either for localized treatment of tissues underlying the skin or for systemic therapy. For transdermal products the goal of dosage design is to maximize the flux through the skin into the systemic circulation and simultaneously minimize the retention and metabolism of the drug in the skin. The

main ingredients used in Anti-rheumatic herbal patch are Boswellic acid, Curcumin.

6. herbal cholesterol patch

Transdermal Patches contain a very small dose which is slowly delivered directly into the blood stream over a 24 hour period. This is the most efficient method of delivery of Vitamins and Nutrition to the body as compared to Tablets and Capsules which must first travel through the digestive system before reaching the blood stream. It is applicable to helps lower Cholesterol, Triglycerides, LDL, Lp (a) lipoprotein, and raise HDL. Side effects like flushing due to high dosage Niacin are absent when applied through Transdermal Patches without any loss in potency or efficiency. About 90% of Vitamins and Minerals being water soluble are immediately excreted from the body by way of urine after traveling through the digestive system and are therefore wasted. Those of us who have taken B-Complex have seen our urine become yellow in color within half an hour of taking an oral dose. It is the balance approximately 10% that actually reach the blood stream and are used as nutrition to be delivered to the center of the cell where it is really required. Cholesterol patches work best when taken with nutritional supplement organic magnesium on a daily basis.

In short, one can roughly equate one 50mg Transdermal Patch to about a 500mg Oral dose taken two to three times a day in actual effectiveness but without the discomfort associated with oral intake.

The main ingredients used in herbal cholesterol patch are Vitamin B-Complex 5mg, Niacin 20mg, Organic Vitamin C 20mg, Commiphora Mukul 20mg, Organic Chromium 100mg.

7.herbal plasters patches

Plaster Patches are Self Adhesive, Warm, a soft, flexible, Pain Relieving Plaster/Patch. Once applied, its ingredients are absorbed into the skin to stimulate blood circulation. It's quick permeating and warm action provides speedy Temporary Pain Relief and comfort for hours. Plasters are specially used by those who suffer from chronic or prolonged Sore Muscles, Arthritis Pain, Painful Joints, Sprains, Backache, Bruises, Shoulder Pain, Arthraiga, Rheumatic Pain, Neuralgia, and Fracture Pain. There are main two type of plaster patches are Cool plaster patch and Mild hot plaster patch Cool plaster patch provides Rapid, Soothing Pain Relief and Alleviates swelling, with a Cool Refreshing Feeling owing to its "Cool pack effect". Mild Hot plaster patch provides a Rapid, Soothing Relief of Pain, especially caused by chronic diseases. By Deep Heating and improving the capillary Blood Circulation and Metabolism of the effected area owing to its "Hot pack effect". Both Cool and Mild hot works while exerting potent Anti - Inflammatory and Analgesic Effects through the Transdermal Absorption of Active Ingredients. Patches hold a High Moisture Contents in a water-soluble Polymer Base, which enables the Deep Penetration of active ingredients in to the affected area,

and provides Sustained Effects through the Continuous Release of its moisture. Plaster Patches design with its "Special Net - Shaped Gel Base", Has an Excellent Affinity to the skin. It may be removed cleanly and easily, even from hairy skin surfaces, Without Pain. Due to its Transdermal Therapeutic System, Plaster Patches can be used safely by the elderly and feeble.

Herbal Plasters Size 4" x 5.5" includes natural herbs like: Powdered Philodendron Bark, Capsicum Extract, Zanthoxylum Fruit, Gardenia Fruit Methyl Salicylate.

METHOD OF APPLICATION OF PATCHES

Apply the patch to your skin. Do not cut or damage the patch. A cut or damaged patch can be very dangerous because you may get too much medicine. Select a clean, dry area of skin above your waist on your front or back. Transdermal Patches are applied on different parts of body like clean dry and hairless skin, back shoulders, inside of wrist, crease of elbow, upper arm, mid abdomen, behind knee, under the arch of foot. The upper back is a good spot to put the patch on children or people who are confused because it will be hard for them to remove the patch. Do not apply the patch to oily, broken, burned, cut, or irritated skin. Use only water to clean the area. Do not use soap or alcohol to clean the skin because this can increase the effects of the medicine. If the area is hairy, clip the hair with scissors, but do not shave. Take the patch out of its wrapper, and take off the protective strip over the sticky part. Do not use a patch if the packaging or backing is damaged. Do not touch the sticky part with your fingers. Press the sticky surface to the skin using the palm of your hand. Press the patch to the skin for 30 seconds. Wash your hands at once. Take off the old patch before putting on a new patch. Apply each new patch to a different area of skin. If a patch comes off or causes irritation, remove it and apply a new patch to different site. To get rid of used patches, fold the patch in half with the sticky sides together. Then, flush it down the toilet. Replace the patch every 3 days or as directed by your doctor or health care professional. Follow the directions on the prescription label. Do not take more medicine than you are told to take. Talk to your pediatrician regarding the use of this medicine in children. While this drug may be prescribed for children as young as 2 years old for selected conditions, precautions do apply. If you forget to replace your patch, take off the old patch and put on a new patch as soon as you can. Do not apply an extra patch to your skin. Do not wear more than one patch at the same time unless told to do so by your doctor or health care professional.

Conclusion :

Plant products serves as an alternative to synthetic because of its local accessibility, eco friendly nature and lower prices compared to the synthetic products. It has

been proved that herbal drugs or drugs from natural origin can be utilized in better form with enhanced efficacy by incorporating them through transdermal route. There are various herbal patches available to lose weight ,quit smoking relieve stress, increase sexuality, as insect repellent, male energizer, to postpone menopause ,which proves the potential of these natural formulations. Thus herbal transdermal patches can create wonders in the field of healthcare and is an upcoming area which should be explored further

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