

Formulation and Evaluation of Herbal Transdermal Patches

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ABSTRACT

Various non-invasive administrations have recently emerged as an alternative to conventional needle injections. A transdermal drug delivery system (TDDS) represents the most attractive method among these because of its low rejection rate, excellent ease of administration, and super convenience and persistence among patients. TDDS could be applicable in not only pharmaceuticals but also in the skin care industry, including cosmetics. Because this method mainly involves local administration, it can prevent local build-up in drug concentration and non-specific delivery to tissues not targeted by the drug.

However, the physico-chemical properties of the skin translate to multiple obstacles and restrictions in transdermal delivery, with numerous investigations conducted to overcome these bottlenecks. In this review, we describe the different types of available TDDS methods, along with a critical discussion of the specific advantages and disadvantages, characterization methods, and potential of each method. Progress in research on these alternative methods has established the high efficiency inherent to TDDS, which is expected to find application in a wider range of fields.

KEYWORD: herbal patch, Transdermal drug delivery system, *tridax procumbens*,

drug delivery, in which the aim is to deliver the drug through the skin in a predetermined and controlled rate. TDDS are adhesive drug-containing devices of defined surface area that deliver a predetermined amount of drug to the surface of intact skin at a programmed rate to reach the systemic circulation.

Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first-pass metabolism, respectively. Transdermal route has yielded with oral treatment as the most successful innovative research area in drug delivery, as oral treatment involves attainment and maintenance of drug concentration in the body within a therapeutically effective range by introduction of a fixed dose at regular intervals, due to which the drug concentration in the body follows a peak and trough profile, leading to a greater chance of adverse effects or therapeutic failure; large amount of drug is lost in the vicinity of the target organ and close attention is required to monitor therapy to avoid overdosing.

The limitations of the oral route can be overcome and the benefits of intravenous drug infusions such as to bypass hepatic "first pass" hepatic elimination (HEPE) to maintain constant prolonged and therapeutic effective drug levels in the body can be closely duplicated, without its potential hazards, by transdermal drug administration through intact skin.

Transdermal drug delivery systems (TDDS) is a self-contained distinct dosage form which delivers the drug by means of transdermal patch through the epidermis of the skin at a predetermined and sustained rate with low biological half-life. It provides systemic delivery of drug through increased bioavailability with reduced dosing frequency.

The skin has a number of considerable advantages over other routes of administration when used as a site of drug delivery, including increased patient compliance, the ability to avoid gastric irritation, no hepatic first-

I. INTRODUCTION

Innovations in the area of drug delivery are taking place at a much faster pace as compared with the last two decades. Improved patient compliance and effectiveness are inextricable aspects of new drug delivery systems. A more radical approach has been to explore newer interfaces on the body for introducing therapeutics. One such approach, transdermal drug delivery, makes use of human skin as a port of entry for systemic delivery of drug molecules. Transdermal drug delivery system (TDDS) is one of the systems lying under the category of controlled

pass metabolism thus enhancing the bioavailability, minimize the risk of systemic side effects by reducing plasma concentrations contrast to oral therapy, provide a sustained release of drug at the site of application; rapid termination of therapy by removal of the patch, the reduction of fluctuations in plasma levels of drugs, and avoid pain associated with patch removal.

Skin and drug permeation

The objective of TDDS is to achieve systemic medication through topical application on intact skin; therefore, it is important to review the structural and biochemical features of the human skin and those characteristics that contribute to the barrier function and the rate of drug access into the body via the skin. Anatomically, the skin can be divided into two layers: epidermis and dermis or corium penetrated by hair shafts and gland ducts. The skin is one of the most extensive organs of the human body, covering an area of about 2 m² in an average human adult.

The major skin layers, from inside to outside, comprise the fatty subcutaneous layer (hypodermis), the dermis of connective tissue and the stratified avascular cellular epidermis. This multilayered organ receives approximately one-third of all blood circulating through the body. Epidermis results from an active epithelial basal cell population and is approximately 150- μ m thick. It is the

outermost layer of the skin, and the process of differentiation results in migration of cells from the basal layer toward the skin surface. The epidermis contains no blood vessels; therefore, nutrients and waste products must diffuse across the dermal-

epidermal junction to maintain its vitality. The epidermis consists of five layers, which, from the inside to the outside, are the stratum germinativum (basal layer), stratum spinosum (spinous layer), stratum granulosum (granular layer), stratum lucidum and stratum corneum (SC). Because the SC cell is dead, the epidermis without the SC is usually termed the viable epidermis. The SC is considered as the rate-limiting barrier in transdermal permeation of most molecules. The SC comprises 15-

20 layers of keratin filled corneocytes (terminally differentiated keratinocytes) anchored in a lipophilic matrix.

The lipids of this extracellular matrix are distinctive in many respects:

- 1) they provide the only continuous phase (and diffusion pathway) from the skin surface to the base of the SC;
- 2) the composition (ceramides, free fatty acids and cholesterol) is unique among biomembranes and particularly noteworthy is the absence of phospholipids;

Advantages and disadvantages of TDDS

Advantages

- Self-administration is possible and continuous, sustained release of drug

- Avoids peak and trough drug levels and longer and multi-day dosing intervals

- Avoids first-pass hepatic metabolism and enzymatic degradation by the gastrointestinal tract and also avoids gastrointestinal irritation

- less frequent dosing improves patient compliance

- Alternate route for patients who are unable to take oral medications

- Dose delivery unaffected by vomiting or diarrhea

- Drug administration stops with patch removal

Disadvantages

- only small lipophilic drugs can be delivered currently through the skin

- Drug molecule must be potent because patch size limits the amount that can be delivered

- Not suitable for high drug doses

- Adhesion may vary with patch type and environmental conditions.

- Skin irritation and hypersensitivity reactions may occur

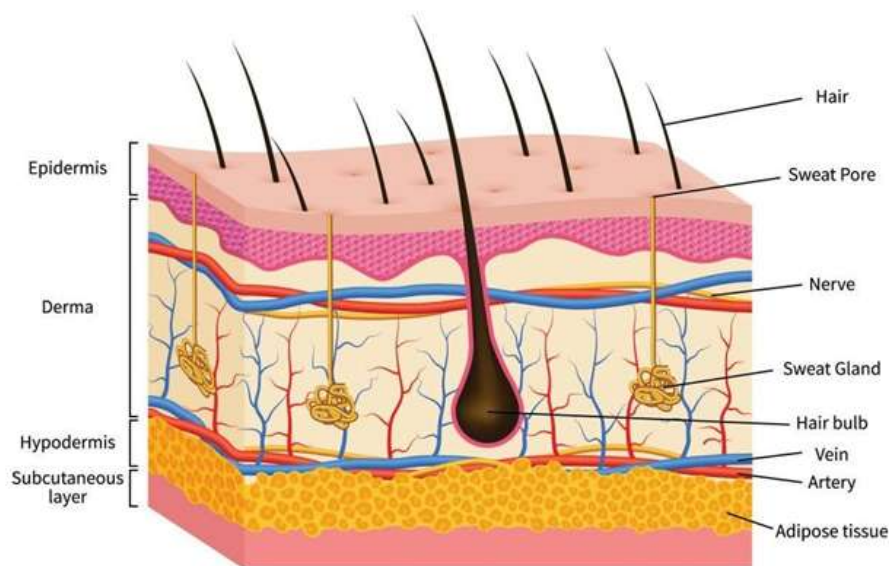


FIGURE:-HUMAN SKIN

Main Ingredients

Used For the Preparation of Herbal Transdermal Drug Delivery System

Liners:

It provides the protection of patches during storage and the liners should be removed previous to use.

Adhesive: It serves to adhere the components of the patch together along with adhering the patch to skin.

Membrane-

It controls the drug release from the multi-layer patches. It's also known as the permeation enhancer.

Drug- Drug reservoir is in direct contact with release liner.

Backing-

protects the patches from outer environment.

MAIN DRUG (API)

TRIDAX PROCUMBENS

Tridax procumbens, commonly known as coat buttons or tridax daisy, is a species of flowering plant in the family Asteraceae. It is native to the tropical Americas including Mexico but it has been introduced to tropical, subtropical, and mild temperate regions worldwide. It is listed as anxious weed in the United States and has pest status in India.



Scientific classification

Kingdom: plantae
Clade: angiosperms
Order: asterales
Family: asteraceae
Genus: Tridax
Species: T. procumbens

Uses in traditional medicine

Traditionally, tridax procumbens has been in use in India for wound healing and as an anticoagulant, antifungal, and insect repellent. Tridax procumbens is also used as

treatment for boils, blisters, and cuts by local healers in parts of India

Chemical compositions

The flavonoid PROCUMBENETIN has been isolated from the aerial parts of Tridax procumbens. Other chemical compounds isolated from the plant include alkylpentacyclic, fatty acid, and polysaccharides. Several main active chemical compounds were found to be present. But toxicological knowledge is scarce and more research described to be needed on this plant.

INGREDIENTS

SR.NO	INGREDIENTS	QUNTITY	ROLE
1	Drug (API) Tridax procumbens		API
2	HPMC	3.5G	Polymer
3	Methenol water	20ML	Solvent
4	Propyleneglycol	0.1ML	Plasticiser
5	Olic Acid	1 ML	Penetration Enhancer

Formulation of Transdermal Matrix Patch

Preparation of casting solutions

The casting solutions were prepared by dissolving weighed quantities of polymers in a mixture of chloroform and methanol in 1:1 ratio. The drug, plasticizer and permeation enhancer were then added to the polymer solutions separately and systematically mixed to form a homogeneous mixture. The resultant solution was kept aside without any disturbance to permit the entrapped air to bubble out.

Preparation of transdermal patches

About 20 ml of the above prepared casting solution were pipetted into circular glass moulds especially designed to hold contents, which is casted on mercury surface. The glass mould containing the casting solutions were allowed to dry at room temperature for 24 hrs and the patches are dried in oven at 40-45° for about 30 minutes to remove the residual solvents. The patches were removed and cut into circular discs with 4.4 cm diameter (15.21 cm² surface area). The patches were wrapped in aluminum foil and stored in desiccator for further studies.



FIGURE: HERBAL TRANSDERMAL PATCH

Evaluation Parameters of Transdermal Patch

Folding Endurance

A strip of specific area (2 cm*2 cm) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film was folded at the same place without breaking gave the value of the folding endurance.

Tensile Strength

The tensile strength of the patch was evaluated by using the tensiometer (Erection and instrumentation, Ahmedabad). It consists of two load cell grips. The lower one was fixed and upper one was movable. Film strips with dimensions of 2*2 cm were fixed between these cell grips, and

force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in kg.

Thickness

Patch thickness was measured using digital micrometer screw gauge at three different places, and the mean value was calculated.

Drug Content

A specified area of patch (2 cm*2 cm) was dissolved in 100 mL methanol and shaken continuously for 24 h. Then the whole solution was ultrasonicated for 15 min. After filtration, the drug was estimated spectrophotometrically.

etrically at wavelength of 281 nm and determined the drug content.

Flatness

The results showed that none of the formulations have variation in the strip lengths before and after longitudinal cut, indicating 100% flatness and 0% constriction, and thus they can maintain a even surface when applied to the skin.

Weight variation

The weight of the prepared transdermal patches for different formulations ranged between 286±0.008 to 566±0.017 mg. The variation in weight uniformity of the prepared patches was within acceptable range

In Vitro Drug Release Studies

In Vitro drug release studies were performed by using a Franz diffusion cell with a receptor compartment capacity of 60 mL. The cellulose acetate membrane was used for the determination of drug from the prepared transdermal matrix-type patches. The cellulose acetate membrane having a pore size 0.45 μ was mounted between the donor and receptor compartment of the diffusion cell. The prepared transdermal film was placed on the cellulose acetate membrane and covered with aluminum foil. The receptor compartment of the diffusion cell was filled with phosphate buffer pH 7.4. The whole assembly was fixed on a hot plate magnetic stirrer, and the solution in the receptor compartment was constantly and continuously stirred using magnetic beads, and the temperature was maintained at 32±0.5°C, because the normal skin temperature of human is 32°C. The samples were withdrawn at different time intervals and analyzed

for drug contents spectrophotometrically. The receptor phase was replenished with an equal volume of phosphate buffer at each sample withdrawal.

In Vitro Permeation Study

An in vitro permeation study was carried out by using Franz diffusion cell. Full thickness abdominal skin of male Wistar rat weighing 200 to 250 g was used. Hair from the abdominal region was removed carefully by using an electric clipper; the dermal side of the skin was thoroughly cleaned with distilled water to remove any adhering tissues or blood vessels, equilibrate for an hour in phosphate buffer pH 7.4 before starting the experiment, and was placed on a magnetic stirrer with a small magnetic needle for uniform distribution of the diffusant. The temperature of the cell was maintained at 32 ± 0.5°C using a thermostatically controlled heater. The isolated rat skin piece was mounted between the compartments of the diffusion cell, with the epidermis facing up into the donor compartment. Sample volume of 5 mL was removed from the receptor compartment at regular intervals, and an equal volume of fresh medium was replaced. Samples were filtered through Whatman filter and were analyzed using Shimadzu UV1800 double-beam spectrophotometer (Shimadzu, Kyoto, Japan). Flux was determined directly as the slope of the curve between the steady-state values of the amount of drug permeated (mg*cm) versus time in hours and permeability coefficient was deduced by dividing the flux by the initial drug load (mg*cm).

EVALUATION RESULT

SR.NO	EVALUATION TEST	RESULT
1	THICKNESS TEST (mm) ± S.D	0.120 ± 0.007
2	WEIGHT VARIATION (MG) ± S.D	322 ± 0.006
3	DRUG CONTENT (%) ± S.D	97.83 ± 1.42

4	FLATNESS (%)	100
5	FOLDING ENDURANCE \pm S.D	60 \pm 5.12
6	TENSILE STRENGTH (kg/mm ²) \pm S.D	0.438 \pm 0.036

II. RESULT

The pre formulation study was performed in order to assure the accuracy of drug sample and determination of various parameters for formulation of transdermal patches has been performed successfully.

III. CONCLUSION

In this study different matrix type patches were prepared by varying polymer combination and polymer ratios. *Tridax procumbens* flowers were selected for present study. Both phytochemical and chemical test were performed for the selected plant parts. Methanolic extracts were prepared by liquid extraction methods. By performing chemical valuation the extracts showed positive response towards Alkaloids, glycosides, amino acids. The herbal transdermal patches were formulated and prepared and were evaluated and the results were found to be positive. Folding endurance results indicated that the patches would not break and would maintain their skin integrity with general skin folding when applied. The moisture uptake of the formulations was within the limits which could protect the formulations from microbial contamination and reduce bulkiness. Good uniformity of drug content was observed in all the patches.

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