

# A Review: Extraction and Formulation of Transdermal Patch of *Moringa Oleifera*

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## Abstract:

*Moringa oleifera*, also known as the “Moringa”, “tree of life” or “miracle tree,” is classified as an important herbal plant due to its immense medicinal and non-medicinal benefits. Traditionally, the plant is used to cure wounds, pain, ulcers, liver disease, heart disease, cancer, and inflammation. It is a single family shrub and tree that is cultivated in a whole tropical belt. It belongs to the family Moringaceae . Multiple bio-active compounds such as phenolic acid, flavonoids, alkaloids, natural sugars, vitamins, minerals, and various organic acids are analyzed. Many pharmacological studies has shown the ability of plant as it posses many analgesic, anti-inflammatory, immune-modulatory and many more properties. Formulating it in a transdermal patch will increase its absorption into the systemic circulation as the human skin is readily accessible surface of drug delivery system. There is considerable interest in the as a site of drug application in both systemic and local affect. Thus the review article explores the overall study on the extraction of *Moringa oleifera* and its formulation in transdermal patch.

**Keywords:** Moringa, *Moringa oleifera*, extraction, formulation, transdermal patch.

## Introduction:

*Moringa oleifera* “the miracle tree” thrives globally in almost all tropical and sub-tropical region but it is believed to be native to India, Afganistan, Bangladesh and Pakistan. The Moringa family comprises 13 species (*Moringa oleifera*, *Moringa arborea*, *Moringa rivae*, *Moringa ruspoliana*, *Moringa drouhardii*, *Moringa hildebrandtii*, *Moringa concanensis*, *Moringa borziana*, *Moringa longituba*, *Moringa pygmaea*, *Moringa ovalifolia*, *Moringa peregrina*, *Moringa stenopetala*) out of which *Moringa oleifera* has become well known for its use in nutrition, biogas production, fertilizer, etc. Studies have shown that *Moringa oleifera* is among the most reliable and cheapest alternative for good nutrition. Despite nutritional significance it is not much popular. However due to its taste and hydrophobic nature it is difficult to consume it but if it is directly into the systemic circulation, it will gradually increase the bio-availability and patient compliance as well providing an ease to administer. Hence formulation of transdermal patches of moringa will make it easy to administer along with that it will also increase the bio-availability if the drug as it skips the first pass metabolism. Transdermal Patches are products of Transdermal Drug Delivery System which is defined as “a self-contained discrete dosage form” which is known as patches which when applied to the skin releases the drug through the skin at a controlled rate to the systemic circulation. This review summarizes the medicinal uses of *Moringa oleifera* when formulated in transdermal patch.

### 1) Moringa

It is an herbaceous plant has been extensively used to treat malnutrition. Moringa has nine times more protein than yoghurt, seventeen times more calcium than milk, seven times more vitamin C than orange, twenty five times more iron than spinach and ten times more vitamin A than carrot as shown in the table 1 below. Traditionally it is used for the treatment of anemia, anxiety and asthma.

**Table 1: Nutritious composition of Moringa oleifera leaf per 1 cup**

Nutrients	Quantity
Vitamin B6	19% of the RDA.
Vitamin C	12% of the RDA.
Iron	11% of the RDA.
Riboflavin (B2)	11% of the RDA.
Vitamin A (from beta-carotene)	9% of the RDA.
Magnesium	8% of the RDA.
Protein	2 grams.

#### 1.1) Taxonomical Classification

Kingdom	Plantae
Sub-kingdom	Tracheobionta
Super Division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Sub-class	Dilleniidae
Order	Capparales
Family	Moringaceae
Genes	Moringa
Species	Oleifera

**Table 2: Taxonomical classification of M. oleifera**

#### 1.2) Morphology

It grows rapidly in loamy and well drained sandy soil preferring a height of 500m above sea level. Normally the trees grows upto a height of small to medium size in height. The leaves are naturally trifoliate, the flowers are born on an inflorescence (10-25 cm long) and fruits are generally trifoliate and commonly referred as pods. The trunk grows straight but is occasionally poorly formed.



**Visual representation of M. oleifera leaf**



**Authentication of *M. oleifera* leaf by Department of Botany RTM Nagpur University, Maharashtra, India. 440033**

**1.3) Therapeutic Uses**

In modern era many studies have been conducted which concludes that moringa shows cholesterol lowering, diuretic, anti-hypertensive anti-spasmodic anti-ulcer, hepatoprotective anti-tumor, anti-cancer, anti-bacterial, anti-fungal and anti-oxidant activities. It has numerous medicinal uses which have been recognized in the ayurveda medicine system as shown in table below:

Name of Ayurvedic Text	Form of Plant Used	Treatment
Charaka Samhita (1000 BC- 4th Cent. AD)	Powder Decoction	Used for treatment of worms and headache, Ascites, edema Hiccough and asthma, deafness, tinnitus in the ear, worm's manifestation.
Ashtanga Hridaya (7th Cent. AD)	Oil	Ear ache, deafness, and tinnitus in the ear
Kashyapa Samhita (6-7th Cent AD)	Decoction Oil	Puerperal disorder, sleeplessness Edema
Sharangadhara Samhita (13 Cent. AD)	Decoction	Conjunctivitis
Yogaratanakara (17th Cent. A.D.)	Decoction	Enlargement of spleen, worm edema, Ascites, fever, abscess.

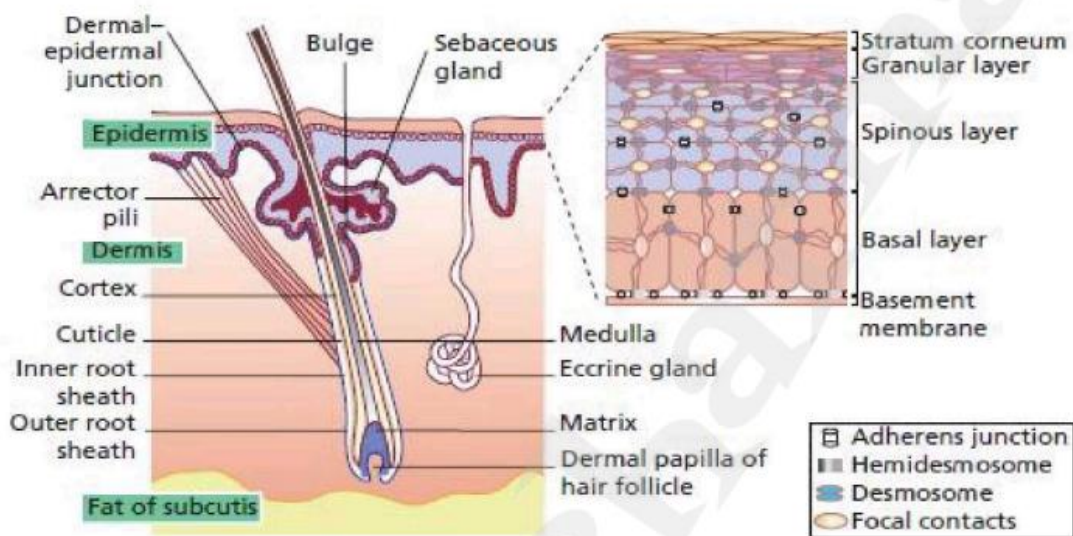
**Table 3. Medicinal Uses of *M. oleifera* in Ayurveda Medicine System**

## 2) Transdermal Drug Delivery System

“Transdermal Patches” are the products of “Transdermal Drug Delivery System” (TDDS) is a part of controlled drug delivery system which is based on the principle of passive diffusion of or on Fick's law of diffusion. It is a painless method of delivering of drugs systematically by applying the a drug formulation onto intact and healthy skin. The drug initially penetrates through the stratum corneum and then passes through the deeper epidermis and dermis without drug accumulation in the dermal layer. When drug reaches the dermal layer it becomes available for the systemic absorption via dermal microcirculation. The Transdermal Drug Delivery System provides leading edge over parental and oral routes by increasing the patient compliance and avoids the first pass metabolism respectively. It not only provides controlled and constant administration of drug but also allows continuous input of drug with short biological half life and eliminates pulsed entry into systemic circulation.

### 2.1) Permeation through skin

Skin is a multi-layered organ composed of many histological layer. The major divisions of skin from top to bottom are epidermis, dermis and hypodermis.



Anatomy of Skin

#### 2.1.1) Epidermis

Microscopically the epidermis is further divided into five layers namely they are stratum corneum, granular layer, spinous layer, basal layer and basement membrane. The stratum corneum forming the outermost layer of the epidermis is exposed to the external environment and it is the most important layer for the transdermal drug delivery system as its composition allows to keep water within the body and foreign substances out of the body.

#### 2.1.2) Dermis

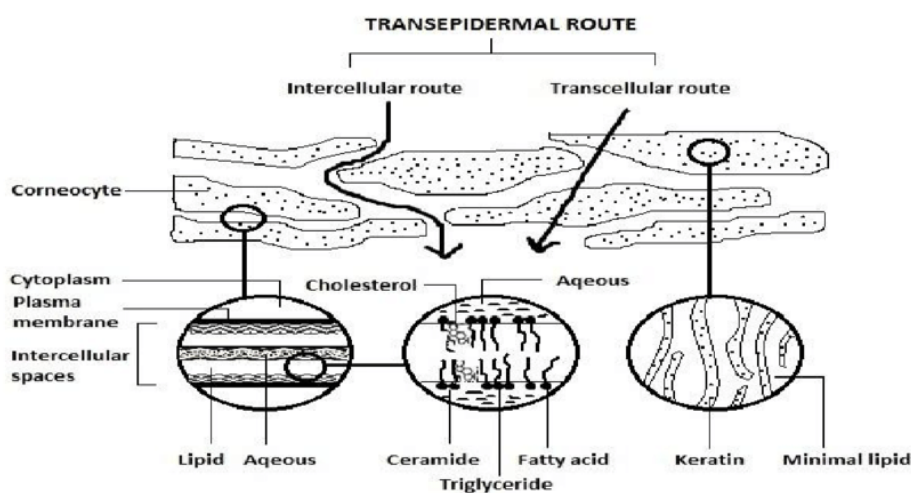
It consists of extensive microvasculature network structure like sweat glands, hair follicles, and smaller blood vessels. Therefore, in order to deliver drug through skin the drug must pass through the epidermis to the dermis where it can be absorbed by capillaries into the circulatory system.

### 2.1.3) Hypodermis

It is the third layer below the dermis which is elastic in nature and includes large amount of fat cells that work as a shock absorber for blood vessel and nerve endings.

### 2.2) Routes of skin permeation

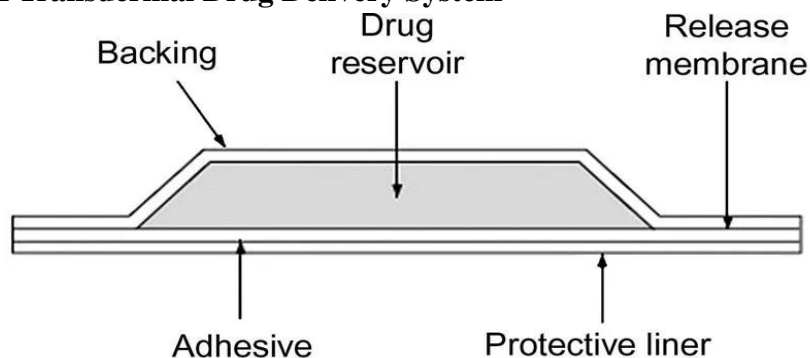
The main route of transport for water-soluble molecules is transcellular. It involves the passage through the cytoplasm of corneocytes and lipid arrangement of the stratum corneum<sup>9</sup>. The pathway of transport for lipid soluble molecules is intercellular; it implicates the passage apparently through the endogenous lipid within the stratum corneum. The transcellular and intercellular route is collectively known as trans-epidermal route as shown below:



**In fig. Diagrammatic representation of Trans-epidermal Route**

Solute molecules may penetrate the skin through the hair follicles, sweat duct or through the sebaceous glands. These passages are collectively known as shunt or appendageal route. It is generally accepted that the skin appendages comprise of approximately 0.1% of fractional area for drug permeation. Thus, the main focus is to develop permeation strategies through the stratum corneum rather than through the appendages. The main barriers to absorption are the dead cells of the SC, restricting the inward and outward movement of drug substances and having high electrical resistance. The SC is a heterogeneous tissue, composed of flattened keratinized cells.

### 2.3) Components of Transdermal Drug Delivery System



**In Fig. Diagrammatic representation of Transdermal Patch**

- Polymer matrix/ drug reservoir
- Drug
- Permeation Enhancers
- Pressure sensitive adhesives
- Backing laminates
- Release liner
- Other excipients like plasticizers and solvents

## 2.4) Methods of preparation of Transdermal Drug Delivery System

### a. Asymmetric TPX membrane method-

This method was discovered by Burner and John in 1994. By this method prototype patch can be prepared by using heat sealable polyester film (type 1009, 3m) with a concave of 1cm diameter as the backing membrane. Drug dispersed on concave membrane, covered by a TPX [poly (4-methyl-1-pentene)] asymmetric membrane, and sealed by an adhesive.

### b. Circular Teflon mould method

It was discovered by Baker and Heller in 1989. Polymeric solution in various proportions is used as an organic solvent. Then that solution is divided in two parts. In one parts calculated amount of drug is dissolved & in another part enhancers in different concentration are dissolved, and then two parts mixed together. Then plasticizer (e.g., Di-N-butyl phthalate) is added into the drug polymer solution. The total contents are to be stirred for 12 hrs. And then poured into a circular Teflon mould. The moulds are to be placed on a levelled surface and covered with inverted funnel to control solvent vaporization in a laminar flow hood model with an air speed of 0.5 m/s. The solvent is allowed to evaporate for 24 h. After which a dried film formed & that is to be stored for another 24 h at  $25\pm 0.5^{\circ}\text{C}$  in a desiccator containing silica gel before evaluation to eliminate aging effects.

### c. Mercury substrate method

In this method drug & plasticizer get dissolved in polymeric solution. It stirred for 10-15 min to produce homogenous dispersion then it is poured into levelled mercury surface, covered with inverted funnel to control solvent evaporation

### d. By using IPM membrane method

In the mixture of water & polymer (propylene glycol containing Carbomer 940 polymer) drug get dispersed and stirred for 12 hrs. in magnetic stirrer. The dispersion is to be neutralized and made viscous by the addition of triethanolamine. If the drug solubility in aqueous solution is very poor then solution gel is obtained by using Buffer pH 7.4. The formed gel will be incorporated in the IPM membrane.

### e. By using EVAC membrane method

Preparation of TDS, 1% Carbopol reservoir gel, polyethylene (PE), ethylene vinyl acetate co-polymer (EVAC) membrane is needed as rate control membrane. If the drug is insoluble in water, then use propylene glycol for gel preparation. Drug is dissolved in propylene glycol, Carbopol resin will be added to the above solution and neutralized by using 5% w/w sodium hydroxide solution. The drug (in gel form) is placed on a sheet of backing layer covering the specified area. A rate controlling membrane will be placed over the gel and the edges will be sealed by heat to obtain a leak proof device.

### f. Preparation of TDDS by using Pro-liposomes

By carrier method using film deposition technique pro-liposomes are prepared. Drug and lecithin ratio should be 0.1:2.0 taken as an optimized one from previous references. For the preparation of pro-

liposome in 100ml round bottom flask take 5mg of mannitol powder, then it is kept at 60-70°C temperature and the flask is rotated at 80-90 rpm and dried the mannitol at vacuum for 30 minutes. After drying, the temperature of the water bath is adjusted to 20- 30°C. Drug and lecithin are dissolved in a suitable organic solvent mixture, a 0.5ml aliquot of the organic solution is introduced into the round bottomed flask at 37°C, after complete drying second aliquots (0.5ml) of the solution is to be added. After the last loading, the flask containing pro-liposomes are connected in a lyophilizer and subsequently drug loaded mannitol powders (pro-liposomes) are placed in a desiccator overnight and then sieved through 100 mesh. The collected powder is transferred into a glass bottle and stored at the freeze temperature until characterization.

#### g. By using free film method

In this process firstly cellulose acetate free film is prepared by casting it on mercury surface. And 2% w/w polymer solution is prepared by using chloroform. Plasticizers are to be added at a concentration of 40% w/w of polymer weight. Then 5 ml of polymer solution is poured in a glass ring which is placed over the mercury surface in a glass petri dish. The rate of evaporation of the solvent can be controlled by placing an inverted funnel over the petri dish. The film formation is noted by observing the mercury surface after complete evaporation of the solvent. The dry film will be separated out and stored between the sheets of wax paper in a desiccator until use. By this process we can prepare free films of different thickness can be prepared by changing the volume of the polymer solution.

### 2.5) Factors affecting Permeation

The principle transport mechanism across mammalian skin is by passive diffusion through primarily the trans-epidermal route at steady state or through trans-appendageal route at initially, non-steady state.

The factors that affect the permeability of the skin are classified into following three categories:

#### A. Physicochemical properties of the permeate molecule

- **Partition co-efficient:** Drug possessing both water and lipid solubility are favourably absorbed through the skin. Transdermal permeability co-efficient shows a linear dependence on partition co efficient. Varying the vehicle may also alter a lipid/water partition co-efficient of a drug molecule. The partition co-efficient of a drug molecule may be altered by chemical modification without affecting the pharmacological activity of the drug.
- **Molecular size:** There is an inverse relationship existed between transdermal flux and molecular weight of the molecule. The drug molecule selected as candidates for transdermal delivery tend to lie within narrow range of molecular weight (100-500 Dalton).
- **Solubility / Melting point:** Lipophilicity is a desired property of transdermal candidates as lipophilic hydrophilic molecules. Drugs with high melting points have relatively low aqueous solubility at normal temperature and pressure. molecules tend to permeate through the skin faster than more.
- **pH condition:** The pH mainly affects the rates of absorption of acidic and basic drugs whereas unchanged form of drug has better penetrating capacity. Transport of ionizable species from aqueous solutions shows strong pH dependence. According to pH partition hypothesis only the unionized form of drug can permeate through the lipid barriers in significant amount.

### B. Physicochemical properties of the drug delivery system partition

- **The affinity of the vehicle for the drug molecules:** It can influence the release of the drug molecule from the carrier. Solubility in the carrier determines the release rate of the drug. The mechanism of drug release depends on whether the drug is dissolved or suspended in the delivery/carrier system and on the interfacial i. partition co-efficient of the drug from the delivery system to skin tissue.
- **Composition of drug delivery system:** Composition of drug delivery system may affect not only the rate of drug release but also the permeability of the SC by means of hydration.
- **Enhancement of transdermal permeation:** Due to the dead nature of the SC the release of the drug from the dosage form is less. Penetration enhancers thus can cause the physicochemical or physiological changes in SC and increase the penetration of the drug through the skin. Various chemical substances are found to possess such drug penetration enhancing property.

### C. Physiological and pathological condition of the skin:

- **Skin age:** Foetal and infant skin appears to be more permeable than mature adult skin and therefore percutaneous absorption of topical steroids occurs more rapidly in children than in adults whereas, water permeation has shown to be same in adults and in children.
- **Lipid film:** The thin lipid film on skin surface is formed by the excretion of sebaceous glands and cell lipids like sebum and epidermal cell which contain emulsifying agent may provide a protective film to prevent the removal of natural moisturising factor from the skin and help in maintaining the barrier function of the SC.
- **Skin hydration:** Hydration of SC can enhance transdermal permeability. The rate of penetration study of salicylic acid through skin with dry and hydrated corneum showed that when the tissues were hydrated, the rate of penetration of the most water-soluble esters increased more than that of the other esters.
- **Skin temperature:** Raising skin temperature results in an increase in the rate of skin permeation. Rise in skin temperature may also increase vasodilation of blood vessels, which are in contact with skin leading to an increase in percutaneous absorption.

### 3) Conclusion

Transdermal drug delivery system is useful for topical and local action of the drug. The drugs which shows hepatic first pass effect and unstable in GI conditions are the suitable candidate for TDDS.

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