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Review

IODINE REPLENISHMENT THERAPY FOR WOMEN: A REVIEW ON TRANSDERMAL IODINE PATCHES

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Abstract:

Iodine deficiency is today's time the leading cause of brain damage not just in India but around the globe, IDD are along with a host of other health complications. Most Iodine Deficiency Disorders are often both invisible and irreversible but at the same time, these are largely preventable. Indian, population is at a greater risk as the soil covering the Indian landmass lacks iodine, therefore the crops grown are also devoid of this element. Iodine-fortified salt mitigates the risk however this cannot compensate for the daily requirement of iodine in women, especially in the vulnerable rural areas of India. Transdermal drug delivery can be simply described as the method of transporting drug molecules across the skin via preformulated patches. These patches stick to the surface of the skin which absorbs the drug molecule and passes it to the bloodstream for further transport. The research aims to develop an alternative means for women in rural India to be equipped with the daily dose required of Iodine by applying a self-adhesive transdermal patch in the form of bindis with an iodine solution. Bindis are traditionally applied on the forehead by women in India. The bindis will work efficiently as a transdermal patch.

Keyword*: Iodine, skin, Patches, Iodine Deficiency Disorders, Transdermal Drug Delivery System, Bindi, Preformulated.*

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INTRODUCTION

Skin being the largest organ of the human body presents a pathway for drug delivery which is of keen interest to pharmacists. Drug delivery through the skin is a growing focus of pharmaceutical research. The skin provides a protective barrier against water loss, injury, and infection.[1]. Drug penetration and permeation through the skin are greatly influenced by the structural properties of the skin and the physicochemical properties of the drug. The human skin consists of three distinct layers, namely, the stratified, avascular, cellular epidermis, the dermis, and the underlying hypodermis of connective tissue. The skin layer that mainly affects drug permeation into the skin is the outermost stratum corneum (SC), or the horny layer. The major components of the SC are the ceramides, fatty acids, cholesterol, cholesterol sulphate and sterol esters, which greatly vary among individuals and body location and provide the SC with its amphiphilic properties. Water plays a crucial role in maintaining the SC integrity and is it also involved in the mediation of some hydrolytic enzymes' activities. The other layers do not act as a barrier in drug penetration.[2]

Advantages of Transdermal Drug Delivery Compared to Other Routes of Administration

Transdermal drug delivery is an attractive alternative to conventional drug delivery systems such as oral and parenteral routes. It provides many advantages over other routes of administration for five reasons:

- It is a non-invasive drug delivery system. It effectively maintains the steady plasma level of the drug and increased drug efficacy.

- It maintains the drug level in the systemic circulation within the therapeutic window (i.e., above the minimum effective concentration but below the level at which side effects become apparent) for prolonged periods, so the drug remains within its therapeutic level.
- The transdermal drug delivery system, compared to an oral and intravenous route of administration, avoids peaks and valleys in plasma levels by providing steady blood concentration.
- It also avoids degradation of the drug in the gastrointestinal tract, eliminates the first-pass effect, and improves patient compliance and acceptability of drug therapy.
- The patch can be removed easily by the patient on an appearance of side effects.[5,6,7]

Disadvantages of Transdermal Drug Delivery System

- Drugs that require high blood levels and Those requiring a daily dose of 10mg or less cannot be administered.
- Transdermal administration is not a means to achieve rapid bolus type drug input.
- The molecular size of the drug should be reasonable to be absorbed percutaneously.
- Possibility of local irritation at the site of application.
- Skin irritation or contact dermatitis due to drug or excipients.
- Skin's low permeability limits the number of drugs that can be delivered in this manner.[5,6,7]

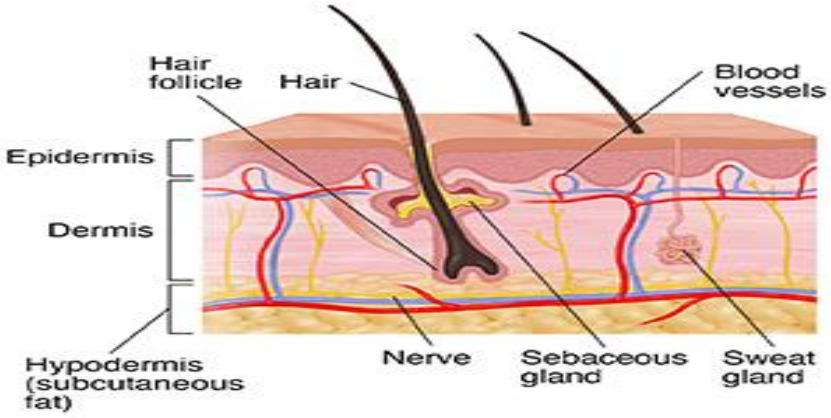

Figure 1: Structure of Skin

TRANSDERMAL ABSORPTION

There are two main subtypes of transdermal patch drug delivery systems viz passive and active.

1. ***Passive transdermal patch drug delivery systems***: These rely only on natural diffusion to transfer the drug from the patch to the skin and into the body. They provide a consistent diffusion rate, depending upon the characteristics of the skin and the design of the patch.
2. ***Active transdermal patch drug delivery systems***: This uses a specific method to aid in the transfer of the drug to the skin and into the body. These methods include chemical enhancers and permeators, physical aids like micro-needles, and low electrical current like iontophoresis. The amount of diffusion depends on the active method used, the drug characteristics, and the skin.[3,4]

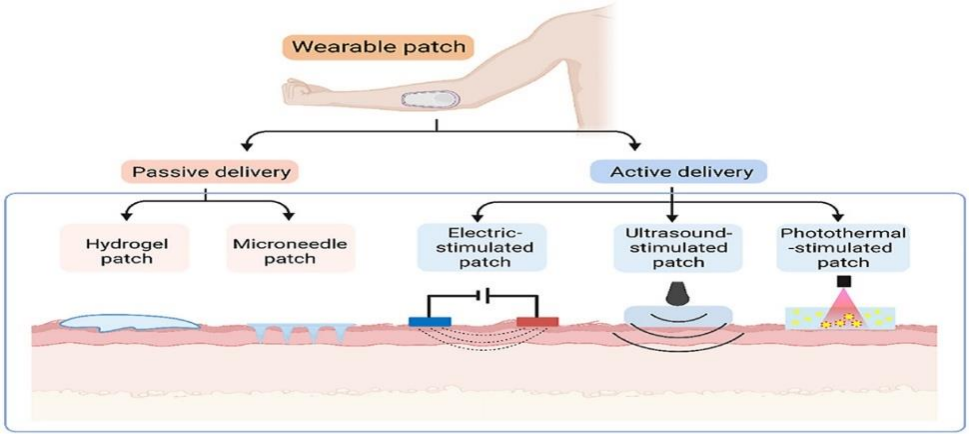

Figure 2: Transdermal Absorption

Dosages of Iodine- Recommended Daily Allowance (RDA)

Maintaining adequate iodine levels is vital for the production of thyroid hormones.These thyroid hormones play a role in a range of biological functions, and they are critical for human metabolism, development, and growth.The daily recommended intake of iodine varies by age and other factors. Here are the recommended dietary allowances (RDAs) for iodine from the Institute of Medicine:

Table 1: RDA of Iodine

S.No	Individual	RDAs
1	Infant	50 mcg/day
2	Children [1-8 years]	90 mcg/day
3	Children [9-13 years]	120 mcg/day
4	Adults	150 mcg/day
5	Pregnant women	220 mcg/day
6	Breastfeeding women	290 mcg/day

Iodine status differs in men and women, and iodine deficiency has more severe consequences for women as it will affect future generations . Women are at a greater risk for Iodine deficiency disorders (IDD) which leads to a range of adverse maternal and fetal outcomes, with the most significant irreversible effect resulting from neurodevelopmental deficits in fetal brain caused by deficient iodine status during early pregnancy.

Iodine is essential for women's health, particularly for thyroid function and fetal development during pregnancy. Here are some key points that highlight the importance of iodine for women:

1. **Pregnancy and breastfeeding:** Iodine is essential for the growth and development of the fetal brain. Pregnant and breastfeeding women need more iodine (220-290 mcg/day) to support their own thyroid function and the development of their babies. Ideally, women should consume at least 150 Î¼g/day of iodine in the long term before pregnancy to ensure there is sufficient iodine in the thyroid gland and sufficient iodine during pregnancy.
2. **Thyroid Health:** Iodine is needed for the production of thyroid hormones that control metabolism, energy and other functions of the body. Women with thyroid problems such as hypothyroidism may need iodine supplements.
3. **Health Benefits:** Iodine has anti-inflammatory properties that can help reduce menstrual pain, bloating, and breast tenderness.
4. **Physical Health:** Iodine has been shown to protect breast tissue and may help reduce the risk of breast cancer.
5. **Food sources:** Add iodized salt, seaweed (such as kelp, dulse, or wakame), dairy products, and some fortified foods to your diet to meet your daily iodine needs.
6. **Fetal Development:** Iodine deficiency during pregnancy can lead to cretinism, a disease that causes mental retardation, deafness, and physical disability in children.
7. **Postpartum thyroiditis:** Iodine may help prevent or control this condition, which causes thyroid swelling and hormonal imbalance after birth.
8. **Menopause symptoms:** Since iodine regulates thyroid hormones, it can reduce hot flashes, night sweats and mood swings.
9. **Polycystic Ovary Syndrome (PCOS):** Iodine may help manage PCOS symptoms such as irregular menstrual periods, weight gain, and acne by supporting thyroid function and hormone balance.
10. **Child support:** Iodine is important for breast milk production and the development of the baby, so it is important to meet the daily iodine needs of breastfeeding adults.

DESIGN OF TRANSDERMAL DELIVERY SYSTEM

The basic components of any transdermal delivery system include the drug dissolved or dispersed in an inert polymer matrix that provides support and platform for drug release.

There are two basic designs of the patch system that dictate drug release characteristics and patch behavior:

1. **Matrix or Monolithic:** The inert polymer matrix binds with the drug and controls its release from the device.
2. **Reservoir or Membrane**: The polymer matrix does not control drug release. Instead, a rate controlling membrane present between the drug matrix and the adhesive layer provides the rate limiting barrier for drug release from the device.[8,9]

COMPONENTS OF TRANSDERMAL PATCHES

1. **Polymer matrix/drug reservoir:** Manufactured by dispersing the drug in a liquid or solid synthetic polymerbase. It must be biocompatible and chemically compatible with other system components such as drugs and penetration enhancers. It must also ensure consistent and effective drug delivery over the intended shelf life of the product and have a safety profile. Polymers used in transdermal drug delivery systems are classified as follows:[10,11,12]
   a) **Natural polymers:** e.g. Cellulose derivatives,gum,zein,shellac, wax, gum, natural rubber, chitosan etc.
   b) **Synthetic elastomers:** e.g. Polybutadiene, hydrin rubber, silicone rubber, polyisobutylene, acrylonitrile, neoprene, butyl rubber, etc.
   c) **Synthetic polymers:** e.g. Polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene etc.
2. **Drugs:** Some of ideal properties of drug & some factors to be consider during preparation of Transdermal patches are as follows:
3. **Backing Laminate:** It is a supportive material which is impermeable to drugs and also to permeation enhancers. They should chemically compatible with the drug, enhancer, adhesive and other excipients.
4. **Pressure Sensitive Adhesive (PSA):** It helps to increase the adherence of the transdermal patch onto the surface of the skin. It can easily be removed from the smooth surface without leaving a residue on it. Examples: Polyacrylates, Polyisobutylene, and silicon-based adhesives.
5. **Permeation Enhancers:** The chemical compounds that enhance the permeability of stratum corneum so as to attain therapeutic levels of the drug candidate. They improve the permeability by interacting with Stratum corneum. Ideal Properties of Permeation Enhancers include their ability to be non-irritating, non-toxic & non- allergic also they should not bind to receptor site. They should be cosmetically acceptable with an appropriate skin feel.

Table 2: Ideal properties of drugs

S.No.	Parameter	Properties
1.	Half life	Less than 10 hours
2.	Dose	Less than 20 mg/day
3.	Molecular Weight	Upto 400 Dalton
4.	Oral Bioavailability	Poor
5.	Skin irritation	none

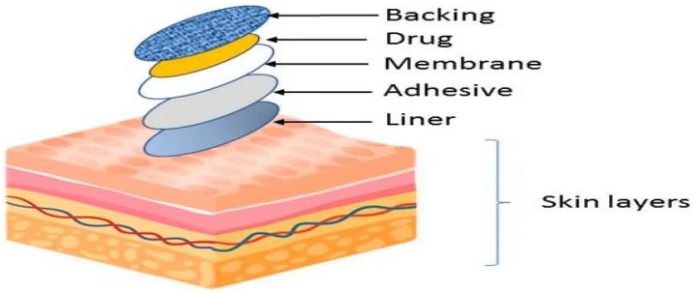

Figure 3: Components of TDDS

Drug penetration pathways

There are critically three ways in which a drug molecule can cross the intact stratum corneum: via skin appendages (shunt routes); through the intercellular lipid domains; or by a transcellular route. The drug in question is likely to permeate by a combination of these routes, with the relative contributions of these pathways to the gross flux engineered by the physicochemical properties of the molecule.

1. **THE APPENDGEAL ROUTE:** Skin appendages provide a continuous channel directly across the horny layer. The drug penetration is blocked the hair follicles and sweat ducts (typically 0.1% of skins surface area), thus limiting the area available for direct contact of the applied drug formulation.
2. **TRANSCELLULAR ROUTE:** Drugs entering by this route pass through corneocytes, containing hydrate keratin, which provide an aqueous environment for hydrophilic natured drugs to move. The cells are surrounded by a lipid envelope which connects the cells to the interstitial lipids. Separating keratinized skin cells are multiple lipid bilayers; there are estimated to be up to 20 such lamellae between each corneocyte. Therefore, the diffusion pathway for a drug via the transcellular route requires some partitioning and diffusion steps.
3. **INTERCELLULAR ROUTE:** In this pathway the drug moves by diffusing through the continuous lipid matrix. This route works as an obstacle for few reasons. First, the stratum corneum, the interdigitating nature of the corneocytes yields a tortuous pathway for intercellular drug permeation. Secondly, the intercellular domain is a region of alternating structured bilayers. Consequently, a drug must sequentially partition into, and diffuse through repeated aqueous and lipid domains. This route is used for small uncharged molecules penetrating the skin. [13-16]

METHODS OF PREPARATION

1. **SOLVENT CASTING METHOD:** For this purpose, 12-well plates (diameter 2 cm) were chosen. Polymers (PVA and PVP) were weighed accurately and dissolved in 10 mL of the mixture of water and in ethanol solution of various percentages by volume, diluted from 70% ethyl alcohol and put aside to form a clear solution. The active ingredient (10 *w*/*w*%) was dissolved in the abovementioned solution and mixed until a clear solution was obtained. PEG 400 and propylene glycol were used as plasticizers. The resulting homogeneous solution was cast in the plates and dried at 40 °C for predetermined time intervals. The dried patches were further studied from different \
aspects. [17,18]

General Procedure for Preparation of Iodine Transdermal patch:

The Iodine Transdermal patches were prepared by solvent casting technique.

1. Various polymers were used as a film forming polymer.
2. Accurately weighed quantity of polymer was dissolved in specified quantity of suitable solvent.
3. Weighed quantity of plasticizer was added to the above solution and dissolved by using magnetic stirrer.
4. Weighed quantity of Iodine was dissolved in 10 ml of appropriate solvent, separately.
5. Solution of 2% Iodine was added to previously prepared solution of polymer and plasticizer, and mixed thoroughly. The above solution kept aside for 1 day for removal of air bubbles.
6. Then casted on petriplate and dried overnight to form the film.
7. Then the film was carefully removed and cut into suitable size i.e. 2cm x 2cm.

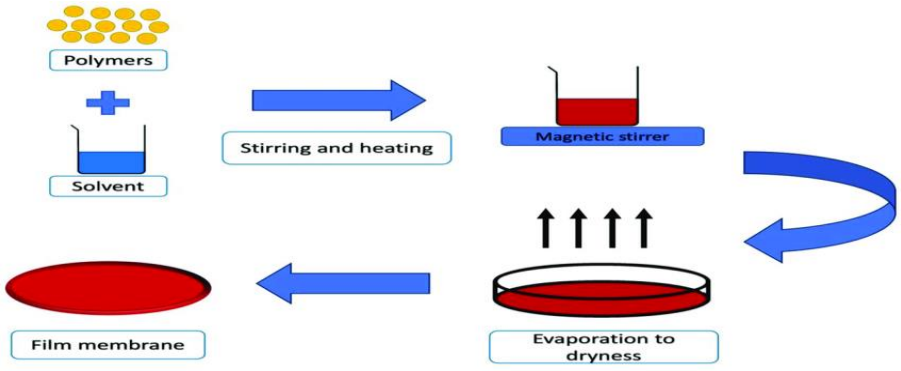

Figure 4: Solvent casting method

EVALUATION OF TDDS

1) **Thickness of the patch:** The thickness of the drug-loaded patches estimated via screw gage micrometer at 3 different points on the patches. Average values and standard deviation values of the three readings were calculated for every drug-loaded patch.
2) **Physical appearance:** Every patch was visually inspected for color, clarity, flexibility, and smoothness

3) **Uniformity of weight:** The patches were subjected to weight variation test by weighing all the patches on a digital weighing machine. Average weight and standard deviation values were then calculated.
4) **Folding endurance:** The test was done to check the efficiency of the plasticizer and the strength of the patch prepared using polymer. The folding endurance is the number of folds required to break any polymeric patch. The folding endurance was measured manually by folding a small strip of the film (2 × 2 cm) at the same place until it broke. The number of times the patch could be folded at the same place without cracking gives the value of folding endurance. Three patches of each type were taken for the test.
5) **Flatness study:** Flatness study was conducted to appraise that the prepared transdermal patches possess a smooth surface and shall not constrict with time. Three longitudinal strips were cut from the film at three different portions. The length of each strip was measured and the variation in length because of non-uniformity in flatness.
6) **Surface pH:** Patches were kept in 0.5 ml of double distilled water for 1 hour in glass tubes and were allowed to swell. A combined glass electrode was brought near the surface of patch and pH readings were taken after allowing an equilibration period of 1 min.
7) **%age moisture absorption/water vapor absorption:** This test is performed to test the physical stability and integrity of the films in high humid conditions in the environment. The prepared films were individually weighed accurately and exposed to 85 ± 5% relative humidity in a desiccator containing 100 ml of saturated solution of potassium chloride at room temperature. During this period, the films were weighed at regular intervals. The percent moisture absorption was determined from the following formula:

% moisture uptake= (Final weight -- Initial weight)/Initial weight×100

8) **% moisture content:** This test is used to know the integrity of films under dry conditions. The individual transdermal films are kept in a desiccator containing fused anhydrous calcium chloride at room temperature. During this period, the films were weighed at regular time intervals of 24, 48, and 72 h. The percentage moisture content was determined by using the following formula:

% Moisture content= (Initial weight -- Final weight)/Initial weight×100

CONCLUSION

We aimed to compile the currently available knowledge about iodine by developing a suitable transdermal formulation whose bioavailability can be increased by using penetration enhancers. Our study highlights the relevance of choosing appropriate excipients as it highly affects the formulation in many aspects. The use of iodine patches will be able to solve the problem faced by women because of Iodine deficiency. The patches carved in the form of bindi will be easily self administered by the women.

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