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Drug Absorption through the Skin – An Ancient and Modern View

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ABSTRACT

The skin is adapted to serve many different roles, since it is the major interface between the body and environment; Skin offers an accessible and convenient site for administration of medication. There is greatsignificance in targeting the skin as a site for drug application for systemic and local effect. The stratum corneum layer- outermost layer of the skin acts as barrier for many drugs. Modification or refinement of materials used may alter the absorption. So a thorough knowledge of dermal absorption is needed. In *SushrutaSamhita* the role of *Thiryakdhamani's* in the absorption of drugs applied on skin surface, has been explained. He has mentioned the different time period taken by a drug, to enter through *romakupa*, *Twacha*, *Rakta*etc after *Abhyanga*. Through this paper an attempt is made to review briefly the absorption through skin in an ancient view, by comparing it to recent understanding of the skin absorption, in order to design safe and effective formulations to treat skin disorders.

KEYWORDS

Twacha, *Topical absorption*, *Skin*

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INTRODUCTION

Topical absorption is one of the greatly booming alternative drug delivery system. The human skin is available surface for the release of drug. Absorption of water soluble substance through the skin is insignificant, but some lipid soluble substance can infiltrate skin, like fat soluble vitamins (A, D, E, K), few drugs, and gases oxygen, carbon dioxide[1].Skin is primarilyfunctioning as a selective barrier for diffusion or elimination of a varioussubstances.*Abhyanga*, *parisheka*, *avagaha*, *seka*, *pralepa*etc are few topical drug delivery methods practiced by *ayurvedic* physicians since ages. It is also indicated in classics that skin acts as barrier for the drugs applied on its surface[2].

AIM

Aim of this conceptual study is to assess the view of *Ayurveda* and contemporary science concerning absorption of drugs through skin.

Based on structural and functional properties, we recognize two major types of skin: thin (hairy) and thick (hairless). Transdermal absorption is most rapid in regions of the skin where stratum corneum layer is thin, such as scrotum, face, and scalp[12].

Twak is a structure which covers[13]. *Twacha* is the structure which completely covers *medas*, *shonita* and all other *dhatus* of the body[14]. It is one among five *gnanendriyas*[15] and *moola* of *mamsavahasrotas*[16, 17].*AcharyaSushruta*has explained seven layers of *twak*. They are *Avabhashini*, *Lohita*, *Shweta*, *Tamra*, *Vedini*, *Rohini*, *mamsadahara* respectively[18].

Avabhasini is the outermost layer and it expresses all *varnas* and illuminates five types of *chaya*.*Lohita* is the second layer of skin. The name indicates that this layer is also pigmented and the diseases occurring in this are pigmentation disorders.

Shweta is the third layer of skin. The name implies that it is clear layer. *Tamra* is the fourth layer. *Kilasa*&*Kushta* are diseases that are likely to occur in this layer. *Vedini* is the fifth layer of skin. It forms *adhishtana* of *Visarpa* and *Kushta*. The name suggests the presence of sensory receptors in this layer. *Rohini* is the sixth layer. *Mamsadhara*is the seventh layer. *Bhagandara*, *Vidradhi*, *Arsas* are likely to occur in this layer.The diseases present in this layer also show abnormal growth. *Granthi*, *Apachi*, *Shleepada*, *Galaganda* are likely to occur in this layer[18].

Factors influencing absorption in skin according to classics

Role of *Bhrajakapitta*

Bhrajakapitta, which is present in the *twak*, digests the drugs applied on the skin through the *parisheka*, *abhyanga*, *lepan*,*avagaha* etc[19].Any drug applied on skin, will be first digested by *Bhrajakagni*, then further processing or absorption takes place[18.]

Direction of application

Drugs which are applied in opposite direction to that of hair direction will enter *romakupa* quickly and enters *swedavaahisiras*(structure which carry sweat)[20].

Thickness of application

It is mentioned that the thickness of *alepa* should be same as that of thickness of wet skin of *Mahisha*[20].

Time taken by drug to traverse twak

In the concept of *Abhyanga*, *Acharya's*havetold that, after *abhyanga*drugs enters body through romakupa in- 300 *matrakala*. It reaches *twak* by 400 *matrakala*, to reach/cross *rakta* 500 *matrakala*, *mamsa* in 600 *matrakala*, *Meda* in 700 *matrakala*, *asthi* in 800 *matrakala*, *majja* in 900 *matrakala*[2].

Role of TiryagDhamani's

When *Snehavagahana* is done, it nourishes body by entering through *sira*, *romakupa* and *dhamani's*[2]. The openings of *tiryagdhamani's* are attached to the hair follicle. Tiryag dhamani's carry *sweda* outside the body and *rasa* within the body. Once the drug gets digested in the *twak*, the potency of the drug carried inside the body through tiryag dhamani's[21].

Fundamentals of skin permeation

Recent studies specified skin permeability to lipid soluble drugs. Also it was eminent that different layers of skin are not evenly permeable. Epidermis is less permeable than dermis. All uncertaintiesregarding stratum corneum permeability were eliminated and using isotopic tracers, it was proposed that stratum corneum hamper permeation to a great extent[22].

Permeation Pathways

Any substance applied on the skin surface appears to have 3 potential pathways, across the epidermis:(1) Via sweat ducts (2) acrosshair follicles &sebaceous glands which falls under Appendageal route,(3) throughthe stratum corneum which is also called epidermal route[26]. Epidermal route has two ways of transportation Transcellular&Inter cellular.

Appendages vary from 0.1% to 1% from forearm to forehead, so it provides a very little area for the absorption of the drug. Appendageal route is considered as low resistant shunts as the sebaceous glands are filled with lipoid sebum and sweat glands with aqueous *sweat*[23, 24, 25].

Epidermal route is of two types:

(a)Transcellular route - transportation of particleacross epithelial cells, is considered

as polar route.Keratin matrix present in the Corneocytes is hydrated and polar in nature. Transportationhere needs repetitive partitioning among the polar background and lipophilic domain adjoining the corneocytes(b) Inter cellular - transportation of particle between the cells[30].

The primary pathway taken by a drug is chosen by the partition co-efficient. Hydrophilic drugs partition mostly to intracellular domains and lipophilic drugs pass across the st.corneumthrough intercellular route[22].

Few factors that are accountablefor the skin permeation are as follows:

Age of the skin, condition of the skin, blood supply of the skin, its anatomical site, metabolism of the skin, hydration of the skin, Temperature, pH , diffusion co-efficient, drug concentration, partition co-efficient.[22]

The advantages of topical administration are they GIT irritation can be avoided, an alternate for oral administration of medicine; first pass metabolism can be avoided and non-invasive. Disadvantages are the skin barrierfunction, skin dermatitis or irritation[27-29].

DISCUSSION

With our better considerate of the structure and function of the skin and how to alter these properties, more and more new drug products can be amplified for topical drug delivery. Ayurveda has implicated the significance of skin as an anatomical entity and acquainted with the advantage of topical delivery way back.

The time taken by a drug to enter the structures in various levels of the body, which is explained in *ayurvedic*classics, clearly mean that more time will be taken by a drug to cross *twak*(i.e. 400-500 matrakala); once it traverses *twak* later the absorption is rapid that is (i.e.100 matrakala). This implies the barrier property of stratum corneum of skin.

In contemporary science negligible importance is given to appendageal route for absorption. However, in *ayurveda* major importance has been given to appendageal route. In recent years renewed interest has been shown by researchers in targeting appendages that is follicular delivery. This is attained by manipulating the target molecule or by modifying the formulation as reviewed by Lu et al[31].Successful drug application entails numerous considerations. In consideration of the essential function of the skin, that is protection & containment, it would be intricate to target skin for drug delivery.

CONCLUSION

A careful analysis of *Ayurveda* treatises reveals that there was wide-ranging approach concerning pharmacology by *Acharyas*. The mode of action of topical products overall mentioned in classics implies incredible awareness regarding topical drug delivery system. The pharmacodynamic& kinetic measures of *ayurvedic* drugs are not easy to explicate in terms of modern pharmacology. It is not the single chemical entity, which acts as a receptor & elicits a response. Mode of action of a drug depends upon rasa, *guna*, *veerya,vipaka*, *prabhava* of it and on the *panchabhouthik* composition of the drug and *adhikarana*(site of action). Technological advancements lead to enhanced disease prevention, diagnosis and treatment with increase in quality of life. The properties of the drug, selection of in-vivo model and the status of patient's skin are all important for safe and effective drug delivery.

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