A Critical Review of Some Unani Topical Dosage Forms – With Special Reference to Their Bases and the Procedures Used to Formulate Them

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Abstract

Unani system of medicine has various dosage forms including topical drugs for effective delivery of drug substances. Although most of the drugs intended to be used orally have been found effective, but some of the formulations of dermal dosage forms especially, Marham (Ointment), Zimaad (Paste) and Tila (Liniment) at occasions fail to produce their expected pharmacological and therapeutic effect. The failure has been mainly attributed to the erroneous processing of crude drugs and inappropriate selection of the bases and excipients that sharpens the ability of drug to go deep into skin and produce the desirable effects. An attempt has been made to explore and elaborate the possible reason of expected failure of some of Unani dermal formulations and to find out the possible solutions so that their therapeutic objectives could be achieved.

Key words: Topical Dosage Forms, Marham, Zimad, Tila, Skin permeability, Excipient

Introduction

The practice of topical dosage forms, especially the use of *Marham* (ointment), *Zimaad* (paste) and *Tila* (liniment), in Unani System of Medicine has been in vogue since ancient time. Preservation of mummies with the help of certain liquid and semiliquid preparations may be taken as the evidence of the use of Marham, Zimaad and Tila as a customary and social practice in ancient period. Hakeem Sharif khan [d, 1763], in his book 'Ilaj-ul-Amraz', has cited the use of ointment from the Hippocratic period (Khan, 1896). A large number of dermal formulations, mentioned in classical Unani literature, have been found beneficial in the pathological conditions, they have been mentioned for, but some of the preparations failed to demonstrate desirable results. This failure may be attributed to the factors such as skin's anatomical structure, temperament and its physiological aspect which were not taken into consideration during pre processing and pre-formulation stage and also the inappropriate selection of ingredients of formulation intended for dermal or trans-dermal use. Besides these factors, certain other pharmaceutical factors that play a key role in the efficacy of therapeutically effective ingredients have been ignored to a great extent. There is no need of specific discussion on the pharmacological and therapeutic effect of drugs on the skin surface only or on detached skin because they will be governed as per the rule for enteral dosage form (Idson, 1976). Actual problem arises when pathology lies in the epidermis

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or beneath it and there is no skin detachment. In such circumstances, drug molecule is needed to reach the site of pathology via dermal route.

Technicalities of Topical Dosage Form

Externally, the human skin is packed with a tough and thickened layer known as stratum corneum. At the molecular level, it comprises of three major components; protein, fat and water, out of which water molecules are less in number as compared to lipid ones. This layer possesses diverse physiological function. It is responsible for the development and protection of human life and opposes the influx and efflux of substances. Efflux of sweat and sebum through glandular duct is ongoing process but not through stratum corneum (Tregear, 1964). Hence, the major problem is permeation and diffusion of different forms of drug designed for external use. If the active ingredients are capable of getting penetrated through stratum corneum, they can produce the effect at the pathological site after penetration. This problem is not common in case of dermal dosage forms of mineral origin drugs, but it is frequently encountered in case of the formulations of plant drugs. This is due to the fact that quantity of therapeutically active component in plant drugs is very little as compared to the drugs of mineral origin. Due to this fact, crude form of plant origin drugs, mostly taken through oral route, get digested under the influence of gastrointestinal fluids and their active components are released and absorbed resulting in desired pharmacological effect. Since, in crude drugs as such do not follow the same kinetics as that of the active ingredients and fail to exhibit the similar pattern of absorption, distribution and excretion over the skin which is consistent with active ingredients. Therefore, the effect likely to be produced by the active ingredient cannot be expected from crude drugs. Hence, it is mandatory that only active principles should be used in topical dosage forms for the therapeutic purpose so that the problem of permeation and absorption can be overcome and consequently their pharmacological effects can be established (Barry, 2007).

In Unani Pharmacopoeia of compound drugs, less space has been given to topical dosage forms although syrups, distillates, decoctions and calcinates extracted form of indigenous drugs have been accommodated appropriately. On the contrary, in cases of ointments, paste and liniments, usually crude drugs have been used in powder form not withstanding the complete release of the active principles from the plant cells for permeation through the skin seems to be a difficult.

The active principle permeation through the skin either indirectly by sweat duct, sebaceous duct and hair follicles or directly by stratum corneum of intact skin plays major role in the determination of efficacy of dermal dosage forms. Both the pathways mentioned above, allow permeation of components of specific type and of particular size under special circumstances. Lipid soluble drugs have great capacity to diffuse through stratum corneum. Though water soluble drugs can also penetrate stratum corneum indirectly but they can't diffuse directly through the stratum corneum (Barry, 2007). The problem of less permeability of water soluble drugs can be over come by including certain skin penetration enhancers in excipients and additives.

The second most important issue in pretext of drug permeation through skin is that, particle of ten micron or less can diffuse through indirect route i.e. hair follicles and duct of sebaceous glands while particles up to three micron only can diffuse through direct route i.e. through stratum corneum but only in a condition where skin loses its resistance and power (Idson, 1976). This is seen when natural property of skin is changed which allows increase in skin hydration to such extent that bio-molecules of skin especially water molecules increase from 5-15% to 25% where the passive diffusion which is one of the most important process required for transfer of drug substance could be possible (Idson, 1976). Rate of passive diffusion depends upon condition of skin; age, blood circulation, temperature and its metabolism and also on quantity of active principles. Minor variation in these factors can accelerate the rate of passive diffusion. But these factors are effective only if particle size of active principle is of less than 10 micron and could retain at the site of application for such a duration within which hydration of skin and the mechanical process of passive diffusion can pursue in such a manner where therapeutically active principles can exhibit their effects. (Barry, 2007). For this purpose, in case of ointment, paste and liniment, we need a suitable base commensurating with the purpose of permeation at the site of disease and the release of the active principles, so that they can hydrate the skin for drug permeation and hence can produce therapeutic effect.

In Unani medicine, commonly used bases for the said dosage forms are plain water, plant distillate, vinegar, vegetable oils, fat, honey, bee-wax and emulsions. Two or more bases in combination can be used considering the therapeutic objectives and site of application of the formulations, a wide range of formulations of ointment, paste and liniment do not have an appropriate base combination giving rise to the elements of doubt about such preparations.

Problems Consistent with Topical Unani Dosage Form and Their Possible Solution

Topical dosage forms which are prepared by using water or distillate of plant drugs as a base, instead of hydrating the skin, may absorb water molecule from skin due to atmospheric temperature even if there is mucilaginous or gummy substances in the formulation. As a result, the drug will not come in contact with skin leading to failure of drug to reach the stage of permeation and absorption in effective manner. The other cause of poor efficacy of such formulations lies in the fact that the presence of water or distillate of plant drugs allows release of water soluble particle only from crude drug, while the rate of diffusion of water-soluble particles in the skin is very low, as compared to lipid-soluble particle. For example "Zimaad Kabid" which is used in hepatitis, includes *afsanteen, haasha, nagar motha, baranjasif, iklilul malik, gul-e-babuna, balchad, mako khushk, jadwar, mur makk and rasot* as ingredients. *Mur makki* and *rasot* have been included as gummy substances while *aab- e-mako* has been used as the base for preparation of this formulation (Kabeeruddin, 1938). But unfortunately this pharmaceutical preparation will neither produce skin hydration nor cause permeation of active ingredients.

Experts of Unani pharmacy often use vinegar and alcohol as a base in some formulations for topical use, probably due to the fact that vinegar and alcohol act as better solvent for various active ingredients as compared to water. These are better solvents for resinous substances and most varieties of lipid, thus allowing better penetration. But this is possible only when these bases which are volatile in nature, could be retained on the site of application for sufficient period of time. It does not appear to be feasible unless the formulation is prepared in a form that allows minimum evaporation where applied over the skin only, then its efficacy can be speculated.

In certain cases, physicians use honey as a base for topical preparations, so that drug could remain adhered to the base and induce response gradually. But use of honey as a base does not appear to be rational. Honey itself is water soluble, its ability to dissolve / solubilize the active ingredients of drugs is not appreciable. Besides, honey is also not able to produce hydration of desirable degree. As a result, active ingredients in honey base won't be able to reach the stage of penetration and absorption and hence, it will not serve the purpose for which it was included in the formulation. For example, "Tila-e-Mulazziz", a compound formulation prepared by using honey as a base, has ingredients viz. *kafoor, aqarqarhah* and *suhaga khaam* (Kabeeruddin, 1938). Practically, *kafoor* is lipid soluble and *suhaga khaam* is water soluble. On the other hand,

Aqarqarhah is a plant origin drug having different chemical constituents. Whether active principles of drugs like kafoor, aqarqarhah and suhaga khaam are soluble in honey is doubtful. Honey will release and allow them to penetrate the skin? It is also not clear that what amount of active constituents will be released by honey to allow them to penetrate the skin. Both the possibilities i.e. chances of solubility and the release of active ingredients appear to fiddling.

To prepare ointment and liniment, physicians use bees wax along with some other bases. Most of the experts believe that bees wax as a single absorptive base has the ability to absorb water molecules and can attach the water molecules to about half of its own weight. In the light of this characteristic feature of bees wax, its use as base will put hindrance in hydration of skin, as it will absorb the moisture and thereby arrest the penetration of active principle through the skin. That's why physicians do not prefer use of beeswax alone (as a base) for intact and healthy skin. But, for the treatment of skin diseases like septic wounds, abraded and injured skin, its use is found to be beneficial as drying of exudates would be the main motive of treatment in all such cases and hydration of skin would not be required. The beeswax in such cases will absorb the exudates on one hand and release the drug molecules on the other and thus will promote the process of healing. But due to certain complexities the use of beeswax alone as a base, is not in practice rather it is commonly used along with some fixed oil which gives several other pharmaceutical benefits.

Dermatological dosage forms for pathologies on intact skin or within the skin which are prepared in lipids or oils, not only make the skin hydration better but also allow easy penetration and absorption of lipid soluble drug, thus promoting their actions. But this is possible only when active principles are soluble in lipid or oil to a large extent. But if the drug substances remain suspended in lipid or oil base, then the expected pharmacological action and therapeutic effect can not be ascertained. For example "Zimad Khadar Jadeed", a topical dosage form containing *filfil siyah, aqarqarhah, qaranfal, farfiyoon, shoneez, zanjabeel* is being prepared in base of *roghan-e-gul* (Kabeeruddin. 1938). The active constituents of crude plant drug will hardly dissolve in oil base, *farfryoon* is soluble in oil but only when the oil is hot, therefore there are lead chances that this formulation will be able to produce any pharmacological effect. A little modification in pharmaceutical procedure of this formulation will help it absorption through skin and assure its efficacy. Firstly, *farfiyoon* should be dissolved in hot *roghan-e-gul* and 50% alcoholic extract of remaining plant drugs should be incorporated in the same base; mixed well to make a homogenous paste. In this way, the active principle, will be in a state to diffuse the skin and hence will exert the optimum pharmacological effect.

Similar condition is seen with “Zimad Khwab Aawar” which is prepared from the following ingredients: *kafoor, afyoon, zafraan, tukhm kaaho, gul nilofar,* and is prepared by using *roghan-e-gul, sirka* and *aab-e-kishneez* as the base. *Kafoor* is soluble in *roghan-e-gul*, *afyoon* in vinegar and *zafraan* in *aab-e-kishneez*. Moreover, it makes a strong coating over the skin that facilitates the process of skin hydration (Kabeeruddin. 1938). Therefore, this formulation, due to the solubility of its active principles and the ability skin to hydrate the skin seems to be therapeutically effective as drug contents will permeate the skin and exert their pharmacological effect.

Nowadays, while selecting the base for paste, ointment and liniment, experts of pharmaceutics advocate the use of mineral oils such as soft and liquid paraffin, especially in cases where pathology lies under the skin or within the skin. This will form a thick layer over the skin which will melt because of body temperature and hydrate the skin. But the major problem associated with such a base is its non-penetrating ability in the skinwhen used singly as a base. That’s why other bases like beeswax, oil etc. are also included along with them for better skin hydration, easy penetration and good therapeutic effects (Barry, 2007).

In the light of above discussion, it can be said that use of single base in dermal dosage forms is not appreciable because of the problem of inconsistent permeation and absorption of active principles, associated with single base. That’s why experts have used different combinations of the bases. Oil with beeswax, water with oil and vinegar with oil and beeswax are few important combinations that are frequently used in preparation of certain dermal dosage forms.

Among these combinations, water in oil emulsion as a base is considered appropriate for specific benefits and for selected dermal dosage forms when the pathology is present at skin surface or abraded skin, or when intended to be used over oily skin. But for the pathology under or within the intact skin, these emulsions as base are less useful as they form only light coating over skin which is insufficient for proper hydration of skin. Therefore, emulsions are used as a base in those conditions where pathology exists on skin surface or the continuity breached, because penetration of active principles through breached skin is similar to penetration through stomach and intestine. Although bases like water in oil emulsion are less used in Unani Medicine, but cosmetic products like cold creams are prepared in these types of bases as these are designed for protection of skin surface and for treating the pathology of skin. “Zimaad-e-Jarab Deegar” of Bayaz Kabeer, is used for infective scabies

where skin surface gets inflammed and ulcerated. This formulation is based on "*henna*" and prepared in the base of linseed oil and plain water which presents a picture of water in oil emulsion (Kabeeruddin, 1938). Because of being processed in emulsion base, it seems to be effective for skin surface pathology. The active principle of the compound will interact with ulcerated surface and hydration of skin with further help in permeation and thereby inducing the pharmacological effect.

Some of the formulations on account of having better combination of bases produce desirable pharmacological and therapeutic actions. For example, "Marham Nasoor" based on z*ard chob* and m*urdaar sang* is prepared by using beeswax and *roghan-e-gul* as base. It is used in the management of open and septic wounds (Kabeeruddin, 1938). This appears to be a complete and excellent ointment for the pathological condition, it is recommended for the beeswax contained in it will absorb the oozing exudates of ulcerated skin and *roghan-e-gul* will help in skin hydration that will ultimately result in better drug delivery and better therapeutic effect. Similarly, "Marham-e-Rusul" that contains *zangaar, murdaarsang* and *zarawand* is prepared by using *jausheer, behrozah, mur makki, kundur, muqil, ushq, rateenaj* with beeswax and olive oil as base (Khan, d. 1763, p. 1896). These gummy substances along with bees wax constitute a potent base for absorbing the exudates of ulcerated wound, while olive oil facilitates drug permeation hydrating in skin. That is why this formulation seems to be very useful in condition of ulcerated or septic wounds. The gunny substances have added value owing to possessing healing property.

Conclusion

In the light of above discussion, it may be concluded that the successful treatment through dermal dosage forms; ointment, paste and liniment, depends mainly on physicochemical properties of bases which will be selected by taking into account the site of disease, type of disease and type of ingredients. Permeation, absorption and metabolism of these forms are totally different from those of oral dosage forms. In case of dermal dosage forms, only active principles of ingredients are able to penetrate the skin. So, it would be better if only their active principles are used in the form of extracts. Bases should be selected on the basis of the site of disease and the nature pathological condition because skin hydration plays a major role in drug permeation. Therefore, use of fixed oil along with some suitable bases would be a preferred option. It seems essential to formulate or develop the formulation of topical

dosage forms in view of the solubility of active ingredients so that permeation and absorption of drugs could be speculated. With the condition of skin, intact or ulcerated, alteration in the bases is to be made as it will accelerate the absorption of exudates and promote the healing. Therefore, a critical review and thereafter editing and compiling of pharmaceutical methods and processing of ointment, paste and liniments is necessary in order to get the complete benefit from ancient Unani topical dosage forms which are mentioned in Classical Unani literature.

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