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EDITORIAL

PERCUTANEOUS ABSORPTION

The application of ointments to the skin for cosmetic and medicinal purposes goes back to antiquity, but this practice has until recent years been on an empirical basis. Modern advances in dermatology have given a better understanding of the efficacy of such preparations,[1] and emphasis has been placed on the use of different ointment bases, the nature of which may well determine the usefulness of a particular ointment as much as the active ingredient. Many different synthetic bases such as the polyethylene glycols are now available in addition to the traditional fatty materials of animal or mineral origin.

Few drugs can readily penetrate the intact skin and as a method of administration of drugs the percutaneous route has limited value. Nevertheless it may prove useful in certain cases; for example a high concentration of drug can be maintained for intense local action in a particular part of the body, and it may prove effective as an alternative method of administration where oral or parenteral therapy is not feasible. Very important is the recognition of the hazards from percutaneous absorption of many toxic agents used in industry and agriculture.

Several factors determine the degree of absorption of a medicament from the skin. First of all it must penetrate the skin, the main route being through the hair follicles and the sebaceous glands, although some penetration may also occur through the sweat glands. After the drug has passed down the hair follicle the conditions are favourable for absorption. An increase in the skin temperature enhances the absorption of the inuncted material, presumably by lowering the viscosity of the sebum and by the increase in the blood supply. The solubility of the drug in lipoids is important, or its ability to combine with fatty acids in the sebum; the metallic ions of ammoniated mercury may ultimately be absorbed by such a mechanism. The organic phosphorus insecticides such as parathion are soluble in lipoids and water so that absorption of these dangerous agents occurs readily. An ointment base may retard penetration and absorption, or it may

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PERKUTAANSE ABSORBERING

Die aanwending van salf aan die vel vir kosmetiese en geneeskundige doeleindes dateer terug tot die Oudheid, maar hierdie gewoonte was tot 'n paar jaar gelede nog op 'n proefondervindelike basis. Moderne vooruitgang in huidsiekteleer het 'n beter begrip van die werksaamheid van sulke preparate[1] gegee, en klem is gelê op die gebruik van verskillende salfbasisse, die aard waarvan net sowel die bruikbaarheid van 'n besondere salf as die aktiewe bestanddeel mag bepaal. Behalwe die tradisionele vetstowwe van dierlike- of minerale-oorsprong, is baie verskillende sintetiese basisse, soos byvoorbeeld die poli-etileen glikole, nou beskikbaar.

Min geneesmiddels kan maklik deur die ongeskonde vel dring, en as 'n metode van toediening van geneesmiddels, het die perkutaanse roete 'n beperkte waarde. Nogtans mag dit by sekere gevalle nuttig blyk; 'n hoë konsentrasie van geneesmiddel kan byvoorbeeld vir intense lokale werking in 'n besondere deel van die liggaam volgehou word, en dit mag effektief blyk as 'n alternatiewe toedieningsmetode waar mondelinge of parenterale terapie nie doenlik is nie. Dit is baie belangrik dat die gevare deur perkutaanse absorbering van baie giftige stowwe wat in industrie en landbou gebruik word, besef word.

Verskeie faktore bepaal die mate van absorbering van 'n geneesmiddel deur die vel. Eerstens moet dit deur die vel dring, aangesien die hoofroete deur die haarsakkies en die smeerkliere is, alhoewel daar ook 'n mate van deurdringing deur die sweetkliere mag geskied. Ná die geneesmiddel langs die haarsakkie afgegaan het, is die toestande gunstig vir absorbering. 'n Verhoging in die temperatuur van die vel verhaas die absorbering van die ingevryfde stof, vermoedelik deur die viskositeit van die huidsmeer te verlaag, en deur die verhoging in die bloedtoevoer. Die oplosbaarheid van die geneesmiddel in lipoïede is belangrik, asook sy vermoë om met vetsure in die huidsmeer te kombineer; die metaalagtige ione van ammoniakkwik mag uiteindelik deur so 'n meganisme geabsorbeer word. Die insektemiddels met organiese fosfor, soos byvoorbeeld paration, is oplosbaar in lipoïede en water, met die gevolg dat absorbering van hierdie gevaarlike stowwe maklik geskied. 'n Salfbasis mag deurdringing en absorbering vertraag, of dit mag die oordrag van 'n geneesmiddel, weens sy mengbaarheid met die huidsmeer, vergemaklik. In hierdie laasgenoemde verband het dit

facilitate transfer of a drug by its miscibility with the sebum. In this latter respect animal and vegetable oils and fats have proved superior to mineral fats.

Various modern synthetic agents have been introduced to enhance the percutaneous absorption of drugs, but more research is needed to find the best compounds for this purpose. In assessing their value many factors need to be taken into account in addition to those considered above. Thus the method of application, which may include friction, massage, and mechanical pressure, and the duration of application, must be taken into consideration. The methods that have been used measure either skin penetration or systemic absorption. Comparisons need to be made with standard preparations under the same conditions. At the best it is usually only possible to make general statements, since strictly valid mathematical assessments can rarely be made. Microscopic sections or auto-radiographs or chemical methods have been used to determine penetration of the skin by specially selected agents. For the assessment of absorption physical and chemical tests have been performed on blood, urine, faeces, or a particular tissue, while radio-active substances have increased the value of such methods. Pharmacological effects have also been measured in studies of the absorption of certain drugs.

In recent years certain oil-soluble vitamins and hormones have been administered through the skin. In this way vitamin-K preparations have been used in newborn infants. As far as oestrogens are concerned the natural hormones are found to be better absorbed than synthetic compounds, for instance to promote breast development in the hypogonadal female; their use in cosmetic preparations may produce systemic effects and is possibly not without danger.

Apart from the sensitization that may occur when certain drugs are applied to the skin, there is the danger of harmful systemic effects when chemicals are absorbed from the skin, especially if large areas of damaged skin are the site of application. Even such apparently innocent substances as boric acid and borax have caused fatal poisoning in babies in this way.

1. Hadgraft, J. W. and Somers, G. F. (1956): J. Pharm. Pharmacol., **8**, 625.

geblyk dat dierlike en plantaardige olies en vette baie voortrefliker as minerale vette is.

Verskeie moderne sintetiese stowwe is ingestel om die perkutaanse absorbering van geneesmiddels te verhaas, maar verdere navorsing is nodig om die beste verbindings vir hierdie doel te vind. By die bepaling van hulle waarde moet baie faktore, behalwe dié wat hierbo oorweeg is, in ag geneem word. Dus moet die metode van aanwending, wat vrywing, massering en meganiese druk kan insluit, asook die duur van die aanwending, in ag geneem word. Die metodes wat gebruik is, meet òf deurdringing van die vel òf absorbering in die liggaam. Vergelykings behoort gemaak te word met standaard preparate onder dieselfde toestande. Op die beste is dit gewoonlik slegs moontlik om algemene bewerings te maak, aangesien streng matematiese berekenings selde gemaak kan word. Mikroskopiese deursnitte, of outoradiograwe, of chemiese metodes is gebruik om deurdringing van die vel deur spesiaal uitgesoekte stowwe, vas te stel. Vir die berekening van absorbering is fisiese en chemiese toetse op bloed, urien, ontlasting, of 'n besondere weefsel uitgevoer, terwyl radio-aktiewe stowwe die waarde van sulke metodes laat toeneem het. Farmakologiese uitwerkings is ook by hierdie studies van die absorbering van sekere geneesmiddels gemeet.

Gedurende die afgelope jare is sekere vitamiene en hormone wat in vet oplosbaar is, deur die vel toegedien. Preparate van vitamien-K is op hierdie wyse by pasgebore suigelinge gebruik. Wat estrogene betref, is dit gevind dat natuurlike hormone beter geabsorbeer word as sinteitese verbindings, soos byvoorbeeld om borsontwikkeling by 'n hipogonadale vrou te bevorder; hulle gebruik in kosmetiese preparate mag uitwerkings op die liggaam veroorsaak, en is waarskynlik nie sonder gevaar nie.

Behalwe die gevoeligmaking wat mag voorkom wanneer sekere geneesmiddels aan die vel aangewend word, is daar die gevaar van skadelike uitwerkings op die liggaam as chemikalieë deur die vel geabsorbeer word, veral waar die gebied van aanwending groot gedeeltes van beskadigde vel is. Self sulke skynbaar onskuldige bestanddele soos boorsuur en boraks het op hierdie wyse noodlottige vergiftiging by babas veroorsaak.

1. Hadgraft, J. W. en Somers, G. F. (1956): J. Pharm. Pharmacol., **8**, 625.