PROGRESS REPORT NO. I

ON

PERCUTANEOUS ABSORPTION

TO

ARMY CHEMICAL CENTER

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OBJECT:

To measure the rate of penetration of chemicals with different physical characteristics and correlate this information to allow some predictability as to what physical characteristics are necessary in a compound for its rapid penetration of intact human skin.

To determine histochemically, the chemical nature of the barrier area.

RESULTS:

The barrier area can be stained rather selectively with maleimide because of its combination with peculiar free sulfhydryl groups in this area. Dinitrofluorobenzene will also stain the barrier area intensely and again probably because of its combination with sulfhydryl groups in that area.

Further work is being done histochemically.

Methodology is established now for measuring penetration of skin by different radioactive organic compounds,

Our principle aims in this project are to:

(1) Correlate physical characteristics of a compound with its ability to penetrate intact human skin and

(2) Investigate the chemistry and morphology of the barrier area of human skin by histochemical techniques.

We have been able to show that the barrier area of human skin contains rather large concentrations of sulfhydryl groups. These sulfhydryl groups differ in such a way that they bind maleimide and can be stained in this way whereas most other known sulfhydryl containing areas of the skin do not bind maleimide in this way. Dinitro-fluorobenzene combines with the sulfhydryl groups of the barrier area to give a clear delineation of this area. The dinitrofluorobenzene staining can be prevented by iodoacetic acid blocking previous to exposure to dinitrofluorobenzene. Hydrolytic enzymes of various types are demonstrable in the barrier area in high concentration. The methods of demonstrating various hydrolytic enzymes histochemically leave reasonable doubt as to the specificity of some of the demonstrated hydrolytic enzymes. We intend

to investigate the barrier area for various types of fatty substances and enzymes which hydrolyze fatty acid esters as well as peptide substrates.

Percutaneous absorption of topical radioactive agents will be measured with a devised skin counting technique. We have been working on this method and now have it to a point where it is reasonable to study absorption of radioactive compounds through human skin. We intend to study primarily chemicals containing C^{14} or S^{35}. These chemicals will have varying physical characteristics which we hope to correlate with the absorption rates.

We are also enthusiastic about a very sensitive method for measuring percutaneous absorption. This involves visible, local, cutaneous biologic reactions to compounds of concentrations of 1×10^{-6} or less. With this method it will be possible to calculate wider ranges of differences in absorption rates through the skin. It also insures the measurement of chemicals that penetrate into the corium itself and not into the appendages only. Once a standard absorption rate is determined for a given compound it is intended to incorporate the chemical media which might damage the barrier area such as disulfide splitting agents, proteolytic and mucolytic enzymes and fat solvents. Also the effects of drying, hydration, heat and cold will be determined in regard to absorption rates of a given compound.