EXCRETION OF INTRAVENOUSLY ADMINISTERED RADIOACTIVE HYDROCORTISONE IN SKIN SURFACE LIPIDS*

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In a previous paper it was postulated that both androgens and corticosteroids or their metabolites are essential for the development of steroid acne and acne vulgaris. The corticosteroids appear to be required for the induction of follicular keratotic plugging (1). If such be the case, it must be assumed that the steroids or their metabolites reach the pilosebaceous apparatus via the systemic circulation. It has already been shown that steroid compounds in addition to cholesterol are present in the skin surface lipids (2). This study was undertaken in order to determine the extent to which systemically administered corticosteroid compounds appear in skin surface lipid.

METHOD AND MATERIALS

In preparation for this study, which was performed on 4 young, adult, male volunteers, the subjects underwent head soaks in ethyl ether as described previously (2), and three successive total body wipes with fat-free cloths saturated with ether. The surface lipids obtained in this manner were used as controls in the study. The volunteers were then given a fat-free cotton scrub suit to wear, and and intravenous infusion of 500 ml of 5% glucose in water containing 0.03 mg of 4-C^{14}-hydrocortisone (Fig. 1) representing 2 μc of radioactivity was administered. The cotton materials were rendered fat-free by refluxing for 8 hours in benzene on three consecutive days, and then soaking repeatedly in ether until no residue was recovered.

At 6 hour intervals for the 24 hours immediately following the intravenous infusion, head soaks (×3) and total body wipes (×3) were performed in addition to extraction of lipid from the scrub suit by soaking in 700 ml of freshly distilled ether three times. Fresh disposable polyethylene gloves were worn by the investigators carrying out each of these procedures in order to avoid contamination of the samples. The urine for each 6 hour period was also collected. The surface fat and urine collected in these time periods were measured and assayed for radioactivity. The urine radioactivity was measured by combining a 1 ml aliquot of each sample with 10 ml ethanol and 6 ml scintillator solution,† and then assaying the radioactivity in a Packard Tri-Carb Scintillation Spectrometer. The skin surface fat was dried in a desiccator under vacuum over sulfuric acid, and then added to 10 ml ethanol and 6 ml scintillator solution for assay in the scintillation spectrometer. Because of the quenching effects of the sebum, and the small amounts of radioactivity present, it was found that the sebum aliquot had to be no more than 500 mg. The data presented are corrected for the quenching effect of each skin surface lipid sample, which was determined by enriching each sample with 2 μc of C^{14}-labelled benzoic acid and reading the results in the scintillation spectrometer.

RESULTS

Tables I and II show the recovery of radioactivity in skin surface lipid and urine as per cent of administered radioactivity, to the nearest 0.1%. In all cases the recovery of radioactivity in the urine in 24 hours corresponded to that reported by other investigators in similar studies (3). The urine assays were run as an additional control for the study. Also, in all cases some radioactivity was recovered in the skin surface lipids. In all but subject III this amounted to approximately 1% of the administered quantity of radioactivity, and in these individuals the data suggested that no further radioactivity would be excreted in the sebum. In subject III, however, the surface lipid yield was small, and the yield of radioactivity in the 24 hour moiety appeared to be rising. It is felt, therefore, that in this case the 0.4% recovery of radioactivity does not represent the maximum yield which could have been attained had the work been extended for additional hours.

The total amount of skin surface fat collected in 24 hours ranged from 1.85 gm to 4.44 gm. Subjects I and II subsequently had a single additional 24 hour collection of skin sur-

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† 6 gm PPO and 150 mg POPOP in 500 ml toluene.

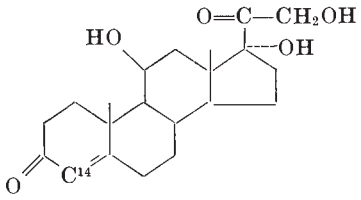

FIG. 1. Chemical Configuration of 4-C^{14}-labelled hydrocortisone.

242 mμ, the wavelength of maximum absorption for hydrocortisone (5) and related steroids (6). This further tends to indicate the incorporation of the recovered radioactivity in a steroid compound, and suggests that this may be hydrocortisone, but it is in no way conclusive.

Since the 24 hour skin surface lipid recovery is far greater when it is taken at 6 hour intervals than when it is taken only once during 24 hours, it seems that the repeated removal of the lipid film promotes increased surface lipid accumulation.

TABLE I

	Subject I		Subject II		Subject III		Subject IV	
	Sebum weight	% Recovery radioactivity	Sebum weight	% Recovery radioactivity	Sebum weight	% Recovery radioactivity	Sebum weight	% Recovery radioactivity
6 hrs.	0.943	0.0	1.446	0.3	0.583	0.1	0.420	0.1
12 hrs.	0.947	0.6	1.126	0.4	0.506	0.1	0.666	1.2
18 hrs.	0.815	0.3	1.091	0.1	0.346	0.0	0.751	0.1
24 hrs.	0.960	0.2	0.776	0.0	0.415	0.2	0.544	0.0
Totals	3.665	1.1	4.439	0.8	1.850	0.4	2.381	1.4

TABLE II

Subject	24 hr. Urine Volume	24 hr. % Recovery Radioactivity
I	1766	94.1
II	2010	89.8
III	1332	97.1
IV	2180	98.6

face lipids under similar conditions, and the total lipid collected was 2.00 gm and 2.19 gm respectively.

DISCUSSION

It appears that radioactivity derived from intravenously administered 4-C^{14}-labelled corticosteroids does appear in skin surface lipid in the amount of about 1% of that administered. Since there is no evidence that the A-ring is broken in normal *in vivo* corticosteroid metabolism (4), it is likely that the radioactivity recovered from the skin surface was incorporated in a steroid compound. Also, it has been shown that skin surface fat does contain noncholesterol steroid compounds, and a spectrophotometric analysis of surface lipids from a subject who had received 200 mg of hydrocortisone intravenously, compared with a blank from the same person, showed a peak only at

SUMMARY

It has been shown that about 1% of the radioactivity from an intravenously administered quantity of 4-C^{14}-hydrocortisone appeared in the skin surface lipid of 4 adult male volunteers in 24 hours. Twenty-four hour recovery of lipids from the total skin surface was much greater when repeated surface defatting collections were made at 6 hour intervals than when made after a single 24 hour period.

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