# Oxidation of Dopa in Human Albinism

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The urine of an albino woman contained small quantities of 5-S-cysteinyldopa; 6-hydroxy-5-methoxyindole-2-carboxylic acid, a melanin precursor metabolite, was lacking. The 5-S-cysteinyldopa excretion observed may reflect non-specific oxidation of dopa. Two other albino patients showed normal values for the excretion of 5-S-cysteinyldopa and of 6-hydroxy-5-methoxyindole-2-carboxylic acid. *Key words: Melanin; Pigment; 5-S-Cysteinyldopa; 6-Hydroxy-5-methoxyindole-2-carboxylic acid.* (Received January 28, 1985.)

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Many substances which are precursors of melanin or metabolites of such precursors have been studied as markers of melanin formation. 5-S-Cysteinyldopa (5-S-CD), the key substance in the phaeomelanin pathway, is formed in the melanosome by nucleophilic addition of cysteine to dopaquinone. Since the demonstration of 5-S-CD in the urine of patients with melanoma, and subsequently also in urine from healthy persons, the production and excretion of this substance has attracted a great deal of attention. 5-S-CD has been used as a recorder of metastases from malignant melanoma, and it is also the substance which hitherto has provided the best biochemical information on the functional state of the melanocyte system (1).

A marker of the eumelanin pathway, 6-hydroxy-5-methoxyindole-2-carboxylic acid (6H5MI-2-C), has been demonstrated in the urine of melanoma patients (2). A method for measuring it in urine has been developed, and the substance has been identified and quantified in normal human urine (3).

Oculocutaneous albinism is a hereditary deficiency of pigment in skin, hair, and eyes. It has been differentiated into 10 forms on clinical, biochemical, and ultrastructural grounds, but these forms cannot always be clearly distinguished (4, 5).

We report here the finding of 5-S-CD, but the absence of 6H5MI-2-C, in the urine of a woman with oculocutaneous albinism. Both compounds were present in the urine of two other albino patients.

## MATERIAL AND METHODS

The first patient attended the outpatient department at Lund in summer 1983 for severe sunburn. She had nystagmus, photophobia, a squint, iris transillumination, white hair, white skin, and lacked visible pigment.

In the following winter urine was examined for melanocyte metabolites. A 24-h specimen was collected in a plastic bottle containing 50 ml of acetic acid, and 1 g of sodium metabisulphite. The concentration of 6H5MI-2-C was determined by high pressure liquid chromatography (HPLC) as recently described (3). The concentration of 5-S-CD in the urine was determined by a recently described method (6), but using 5-S-L-cysteinyl-D-dopa as an internal standard (7).

The two other albino patients were previously known at the department in Malmö. They had similar clinical findings as the first patient but had pigmented nevi. They were studied as above.

## RESULTS AND COMMENTS

In the first patient studied the urinary concentration of 5-S-CD was 42 ng/ml of urine corresponding to 7.1 nmol/mmol creatinine. This value is lower than the winter value for a

group of women of fertile age who showed a mean value of 42 nmol 5-S-CD/mmol creatinine, range 12–190. No 6H5MI-2-C could be detected in the patients' urine. Mean value for 6H5MI-2-C in the group mentioned above was 37 nmol/mmol creatinine, range 8–125 (8).

The very presence of cysteinyldopa in the urine of an albino woman in the total absence of melanin suggests that some of the cysteinyldopa in normal urine may be unrelated to pigment formation. Experimental studies support this assumption. Thus small amounts of 5-S-CD have been found in several organs of laboratory animals (9). Non-specific oxidation of dopa of neural or adrenal origin (10) could be responsible for extracutaneous 5-S-CD in albinos (11).

A small basal secretion of 5-S-CD could be the result of metabolized glutathionedopa (12) formed by non-specific dopa oxidation. Methaemoglobin is one of several compounds that can catalyse such non-specific oxidation (13). Further studies of basal excretion levels of 5-S-CD not related to melanin production but to other oxidative reactions in the body would be of greatest biological interest.

The absence of 6H5MI-2-C in the urine has not previously been reported. Covariation in urinary excretion of 5-S-CD and 6H5MI-2-C has been shown; thus, stimulation of the melanocyte by PUVA leads to similarly increased excretion of 5-S-CD and 6H5MI-2-C (14). On the other hand, in genetically determined hyperpigmentation the excreted quantities of 5-S-CD and 6H5MI-2-C do not run parallel. The excretion of 6H5MI-2-C is higher in black Afrincans than in Caucasians, whereas the excretion of 5-S-CD is similar (15).

The total absence of 6H5MI-2-C in the urine of our first albino patient suggests that this compound is formed only when melanin production occurs.

The two other oculocutaneous albino patients showed values for the excretion of 5-S-CD and 6H5MI-2-C within the ranges specified above (25 and 17 nmol 5-S-CD/mmol creatinine, and 12 and 14 nmol 6H5MI-2-C/mmol creatinine, respectively). Normal values for 5-S-CD have also been reported in albinos from Cameroon (16). Such subjects may represent other forms of albinism than the first studied patient. Further investigation of the cysteinyldopa and indole excretion would be helpful in the classification of albinism.

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