Melanocyte Metabolites in the Urine of People of Different Skin Colour

L.-E. WIRESTRAND, C. HANSSON, E. ROSENGREN and H. RORSMAN

Departments of Dermatology and Pharmacology, University of Lund, Lund, Sweden

Wirestrand L-E, Hansson C, Rosengren E, Rorsman H. Melanocyte metabolites in the urine of people of different skin colour. Acta Derm Venereol (Stockh) 1985; 65: 345–348.

The urinary excretion of 2 melanocyte metabolites was studied in normal people of different skin type. The sulphur-free indole derivative 6-hydroxy-5-methoxyindole-2-carboxylic acid was excreted in larger quantities by people with genetically dark skin, whereas the excretion of 5-S-cysteinyldopa was not related to pigment type. No correlation between 5-S-cysteinyldopa and 6-hydroxy-5-methoxyindole-2-carboxylic acid excretion emerged. *Key words: 6-Hydroxy-5-methoxyindole-2-carboxylic acid; 5-S-Cysteinyldopa; Melanin; Pigment.* (Received January 15, 1985.)

H. Rorsman, Department of Dermatology, University Hospital, S-221 85 Lund, Sweden.

Skin colour is largely dependent on the quantity and quality of the melanin in the skin. Melanin consists of heterogenous macromolecules formed by dopa oxidation products. Oxidation products of dopa give black, insoluble pigments called eumelanin. Oxidation of dopa in the presence of cysteine gives lighter, soluble polymers called phaeomelanins.

Degradation studies of natural melanins have shown that sulphur is present in all vertebrate melanins (1). Insoluble melanins of the eye too give phaeomelanic products of degradation (2). Electron spin resonance studies on natural melanins from different sources have shown the whole range of melanins including phaeomelanins, eumelanins, and melanins of mixed type (3). The concept of mixed-type melanin with properties of both eumelanins and phaeomelanins is now widely accepted (4).

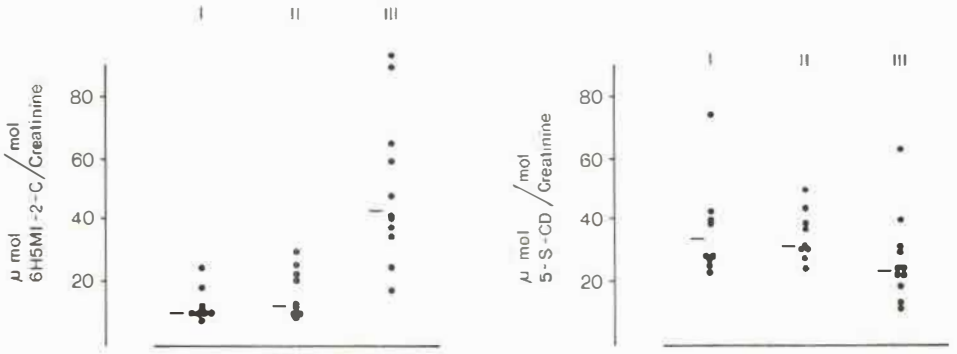

Fig. 1. The concentrations of 6-hydroxy-5-methoxyindole-2-carboxylic acid and 5-S-cysteinyldopa in the urine of people with red hair and fair skin (Group I), blond hair and fair skin (Group II), and black hair and genetically dark skin (Group III). The median is indicated by a bar.

5-S-Cysteinyldopa (5-S-CD) is supposed to be the main sulphur-containing building-stone of melanins, whereas carboxylated and decarboxylated indole derivatives are considered to be the major sulphur-free components (5). In combination with established methods for analysing 5-S-CD (6, 7, 8), a recently developed method for analysis of 6-hydroxy-5-methoxyindole-2-carboxylic acid (6H5MI-2-C) (9, 10) has made possible the study of melanocyte activity in genetically different people under normal conditions and in disease states that affect melanin synthesis. The present study is the first investigation on metabolites of both eumelanin and phaeomelanin in differently pigmented normal people.

MATERIAL AND METHODS

Twenty-nine healthy people of different skin colour took part in the study. They were divided into 3 groups according to skin and hair pigmentation: Group I, Scandinavians with red hair and fair skin (n=9); Group II, Scandinavians with blond hair but more skin pigment than Group I (n=9); Group III, Africans with black hair and genetically dark skin (n=11). Both sexes were represented in all groups, and the age distributions were similar with mean values of about 30 years. The study was performed in December-January, a period with very little sunshine in this part of Sweden. Urine was collected for 24 hours in plastic bottles containing 50 ml acetic acid and 1 g of sodium metabisulphite. Both 6H5MI-2-C and 5-S-CD were analysed within 24 h.

Analysis of the two melanocyte metabolites was performed by HPLC. 6H5MI-2-C was detected by a fluorescence detector (9, 10), and 5-S-CD by an electrochemical detector (7). 6H5MI-2-C and the two diastereomers of 5-S-CD were synthesized by earlier described methods (9, 8).

The urinary creatinine concentrations were determined at the Department of Clinical Chemistry, University Hospital, Lund.

Wilcoxon's rank sum test was used to test differences between the groups.

RESULTS

Fig. 1 shows the urinary excretion of 6H5MI-2-C and 5-S-CD.

The mean values for 5-S-CD were 36, 34, and 27 μmol/mol creatinine in Groups I, II, and III, respectively. No significant differences between the groups emerged.

The mean values for 6H5MI-2-C were 13, 17, and 50 μmol/mol creatinine in Groups I, II, and III, respectively. The interindividual variations in 6H5MI-2-C concentration were small in Groups I and II, but were greater in Group III. The urinary excretion of 6H5MI-2-C in Group III was significantly greater than that in Groups I and II ($p<0.001$), but there was no significant difference between Groups I and II.

No correlation was found between the indole and cysteinyldopa concentrations in individual people.

DISCUSSION

Redheads excrete not only cysteinyldopa but also indoles, and Africans excrete not only indoles but also cysteinyldopa. The redheads and blonds did not differ with regard to excretion patterns.

Although both the indole derivative and 5-S-cysteinyldopa were found in all pigment types studied, distinct differences in their relative concentrations were found. Most of the Africans had higher concentrations of 6H5MI-2-C than did the Scandinavians, but the cysteinyldopa concentrations did not differ significantly between the groups.

The absence of any correlation between the indole and 5-S-CD in the people studied is remarkable because it has been shown that stimulation of pigmentation by PUVA leads to increased excretion of both compounds (10). It would therefore seem that the constitutional balance between indoles and cysteinyldopas differs from the balance after stimulation of the pigment system.

It should be noted that cysteinyldopa is excreted also in the urine of certain albinos (11), and some of the cysteinyldopa determined in our subjects may have been of extramelanocytic origin. However, there is evidence that 5,6-DHI-2-C is a product exclusively formed in the melanocyte (12).

ACKNOWLEDGEMENTS

This investigation was supported by grants from the Swedish Cancer Society (Project 626-B85-13XA), The Swedish Medical Research Council, The Walter, Ellen and Lennart Hesselman Foundation for Scientific Research, The Edvard Welander Foundation for Scientific Research, and the donation funds of the Faculty of Medicine, University of Lund.

REFERENCES

1. Prota G, Rorsman H, Rosengren AM, Rosengren E. Phaeomelanic pigments from a human melanoma. Experientia 1976; 32: 970–971.
2. Novellino E, Ortonne JP, Voulot C, Chioccara F, Misuraca G, Prota G. Identification of cysteinyldopa-derived units in eumelanins from mammalian eyes. FEBS LETTERS 1981; 125: 101–103.
3. Sealy RC, Hyde JS, Felix CC, Menon IA, Prota G. Eumelanins and pheomelanins: Characterization by electron spin resonance spectroscopy. Science 1982; 217: 545–547.
4. Rorsman H, Agrup G, Hansson C, Rosengren AM, Rosengren E. Detection of phaeomelanins. In: Pigment Cell, vol. 4, ed. Klaus SN. Karger, Basel 1979; 244–252.
5. Rorsman H, Agrup G, Hansson C, Rosengren E. Biochemical recorders of malignant melanoma. In: Pigment Cell, vol. 6, ed. MacKie RM. Karger, Basel 1983; 93–115.
6. Hansson C, Edholm LE, Agrup G, Rorsman H, Rosengren AM, Rosengren E. The quantitative determination of 5-S-cysteinyldopa and dopa in normal serum and in serum from patients with malignant melanoma by means of high-pressure liquid chromatography. Clin Chim Acta 1978; 88: 419–427.
7. Kågedahl B, Pettersson A. Determination of urinary 5-S-cysteinyldopa by high performance liquid chromatography. J Chromatogr 1983; 272: 287–297.
8. Agrup G, Edholm LE, Rorsman H, Rosengren E. Diastereomers of 5-S-cysteinyldopa. Acta Derm Venereol (Stockh) 1983; 63: 59–61.
9. Hansson C. 6-Hydroxy-5-methoxyindole-2-carboxylic acid in normal human urine. Acta Derm Venereol (Stockh) 1984; 64: 185–190.
10. Hansson C, Wirestrand L-E, Aronsson A, Rorsman H, Rosengren E. Urinary excretion of 6-hydroxy-5-methoxyindole-2-carboxylic acid and 5-S-cysteinyldopa during PUVA treatment. Photodermatology 1985; 2: 52–57.

11. Carstam R, Hansson C, Krook G, Rorsman H, Rosengren E, Wirestrand L-E. Oxidation of dopa in an albino woman. Acta Derm Venereol (Stockh) 1985 in press.
12. Ekelund M, Carstam R, Hansson C, Rorsman H, Rosengren E. Urinary excretion of 5-S-cysteinyldopa and 6-hydroxy-5-methoxyindole-2-carboxylic acid: Differences between pigmented and albino mice. Acta Derm Venereol (Stockh) 1985 in press.