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Characterization of the brown pigment of the mucosa of the urinary tract

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Summary. The brownish discoloration of the mucosa of the urinary tract which is present in 10–42% of the patients with chronic abuse of analgesics containing phenacetin is, like the discoloration of liver, skin and cartilage, due to lipids similar in type to those in the lipid component of lipofuscin.

Key words: Phenacetin abuse – Pigmentation – Urinary tract

Introduction

In chronic abuse of analgesics containing phenacetin a brownish discoloration of skin, cartilage, liver, kidneys, and of the mucosa of the lower urinary tract may be present (Berneis and Studer 1967 and 1969; Bianchi et al. 1972; Dubach and Nussberger 1972; Gloor 1982; Hofer et al. 1979; Munck et al. 1970).

In the skin (Berneis and Studer 1969) and the rib cartilage (Bianchi et al. 1972), the pigment is made up of lipids similar to the lipid components of lipofuscin. The brownish discoloration of the liver and the kidneys is partially due to an increase in lipofuscin itself (Bianchi et al. 1972).

Since it has not yet been shown that the pigment in the mucosa of the urinary tract is identical or similar to that in other sites, such as skin cartilage etc, and not a phenacetin metabolite, this study was undertaken to characterize the pigment.

Material and method

Rib cartilage, abdominal skin and ureter were investigated. The tissues were collected at autopsy of a 54-year-old man with a clinically documented phenacetin abuse of 15 years, chronic uraemia and haemodialysis since 8 years.

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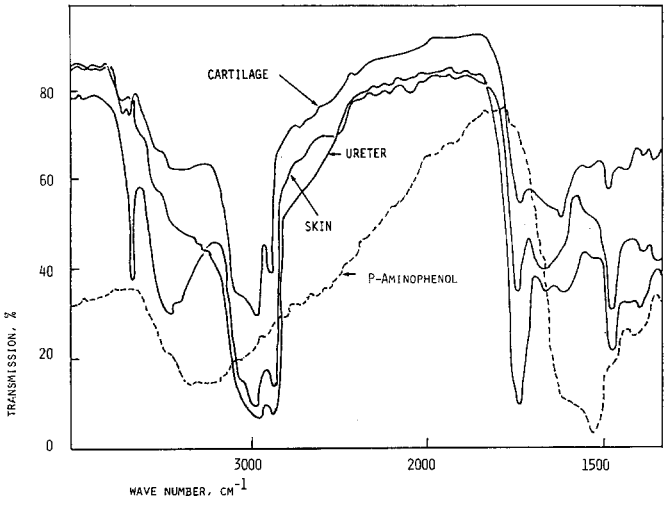
Table 1. Composition of the tissue samples of the skin, cartilage and ureter

	Petroleum ether extract		Methanol ether extract		Dry residue		Water content
	mg	%	mg	%	mg	%	%
Skin	4.99	0.49	22.71	2.26	244.18	24.3	73.00
Rib cartilage	56.25	5.61	42.75	4.25	407.88	40.7	49.40
Ureter	36.58	3.63	26.44	2.62	96.75	9.6	84.17



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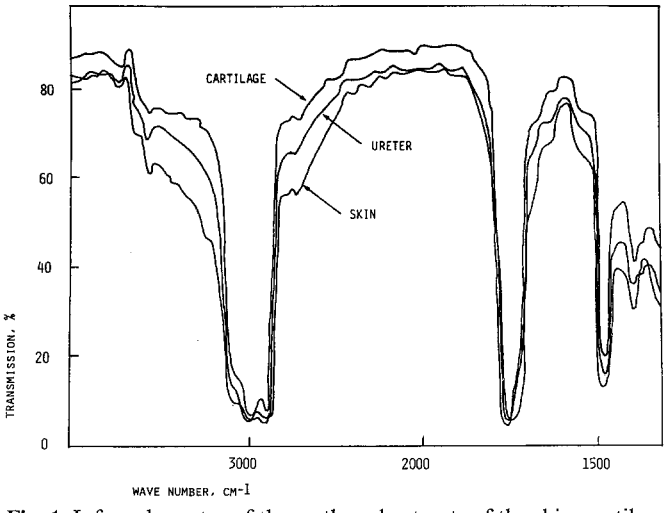

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Fig. 1. Infrared spectra of the methanol extracts of the skin, cartilage and ureter, in comparison to the spectrum of p-aminophenol (Paracetamol)

Fig. 2. Infrared spectra of the petroleum ether extracts of the skin, carilage and ureter

The frozen tissue samples were first extracted with petroleum ether, and then with methanol until they were completely decolored.

Absorption spectra were taken of the petroleum ether and the methanol extracts, both in the infrared and visible ranges according to the method previously described (Bianchi et al. 1972).

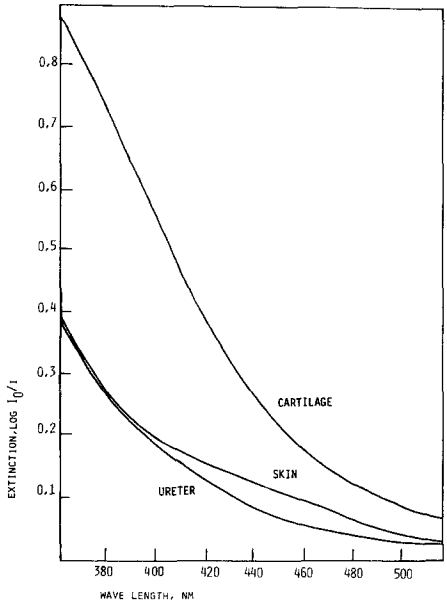

Fig. 3. Absorption spectra of the methanol extracts of the skin, cartilage and ureter in the visible range

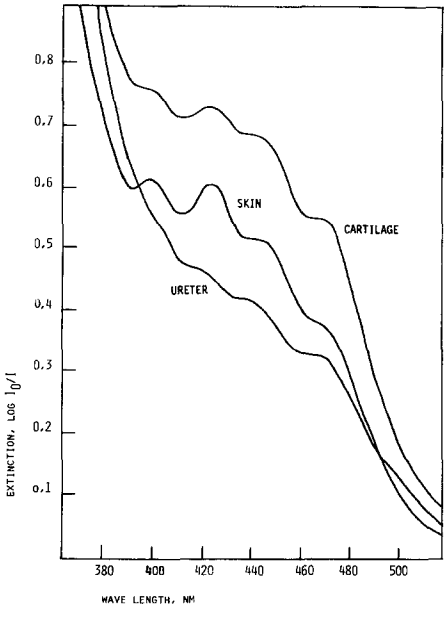

Fig. 4. Absorption spectra of the petroleum ether extracts of the skin, cartilage and ureter in the visible range

Results

The lipids extracted from the skin are mainly soluble in methanol, whereas the lipids from the cartilage and the ureter are approximately equally soluble in methanol and petroleum ether (Table 1).

The infrared spectra of the methanol and the petroleum ether extracts of the tissue samples are in good correspondence (Figs. 1 and 2). Comparison with the absorption spectrum of p-aminophenol yields no correspondence with the curve of the lipids (Fig. 1).

In the petroleum ether and methanol extracts, a pigment of yellow-brown color appears in all curves between 380 nm and 480 nm (Figs. 3 and 4). In the cartilage the concentration of the pigment is higher.

Discussion

On the basis of our findings, the brown pigment which appears in the mucosa of the urinary tract in chronic abuse of analgesics containing phenacetin is very similar to that found in the skin and cartilage (Berneis and Studer 1969; Bianchi et al. 1972). It is a lipogenic pigment which greatly resembles the lipid component of lipofuscin (Berneis and Studer 1969; Bianchi et al. 1972). It is safe to say that the pigment is not melanin, a blood decomposition product, phenacetin or a phenacetin metabolite (Berneis and Studer 1969; Munck et al. 1970). Thus, in contrast to the assumptions of others (Nanra et al. 1978) there is no relation between the brown discoloration of the mucosa of the urinary tract and the dark discoloration of the urine in analgesic abuse (Dubach et al. 1972) which may be due to the presence of phenacetin metabolites (Miller et al. 1970; Nanra et al. 1978).

It has been shown previously (Munck et al. 1970) that the brownish discoloration of the mucosa of the urinary tract is accompanied by an increase in lipids, especially of cholesterol esters, in the mucosa. Histologically this was noticed in swollen collagen fibres and capillary basement membranes of the mucosa.

The pathogenic relationship between the capillary sclerosis of the mucosa of the urinary tract, which is pathognomonic for the chronic abuse of analgesics containing phenacetin and the lipid deposition is not yet known (Mihatsch et al. 1979). The brownish discoloration of the lower urinary tract is always associated with the capillary sclerosis but not vice versa. While capillary sclerosis occurs in about 80% of the patients with long standing phenacetin abuse, the brownish discoloration – although difficult to quantify – is significantly rarer (about 10–42%) (Gloor 1982; Hofer et al. 1979).

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