DETERMINATION OF FOUR NON-STEROIDAL ANTI-INFLAMMATORY AGENTS AND THEIR METABOLITES IN PLASMA AND URINE BY HPLC

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Most of the non-steroidal anti-inflammatory agents are usually excreted as glucuronide conjugates. However, a few including naproxen, indomethacin, phenylbutazone and sulindac undergo metabolism before conjugation, as shown in Table I.

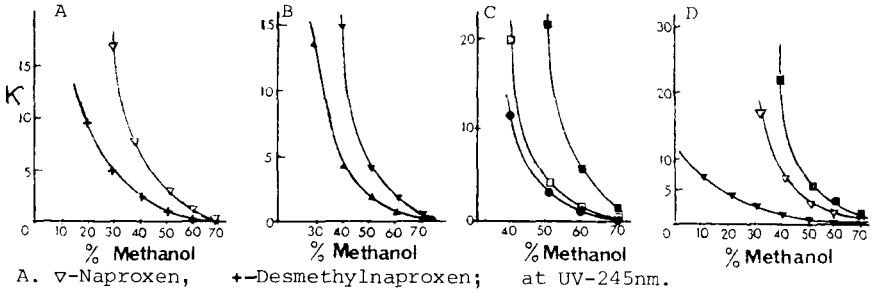
Table I

Drugs	Metabolites	Comments
1. Naproxen	Desmethylnaproxen	Inactive Metabolite
2. Phenylbutazone	Oxyphenbutazone	Active Metabolite
3. Sulindac	Suliphide Derivative	Active Metabolite
	Sulphone Derivative	Inactive Metabolite
4. Indomethacin	Deschlorobenzoylindomethacin	Inactive Metabolite
	Desmethylindomethacin	Inactive Metabolite

HPLC has been used to determine non-steroidal anti-inflammatory agents in plasma and urine (Thomas et al, 1978; Jefferies et al, 1979). The fate of the drug and the rate at which bio-transformation occurs is an important clinical consideration for all drugs, but particularly for those used to treat chronic conditions.

Reversed phase chromatography with aqueous acidic methanol (pH 2.5) was chosen because the metabolites are usually more polar than the parent drug and so elute sooner. The eluent composition was found to govern selectivity and retention, and permits suitable HPLC conditions for the analysis of each drug and its metabolite(s) to be chosen, Fig.1. A short column (50x4 6mm.id.) packed with Spherisorb 5-ODS is used to reduce the analysis time and improve sensitivity. Injection of filtered diluted urine and protein free plasma or ether extracts of plasma means minimal preparation of sample is required.

Figure 1 Effect of Eluent Composition (% Methanol) on Capacity Factor (K)



A. ▽-Naproxen, +-Desmethylnaproxen; at UV-245nm.
B. ▼-Phenylbutazone, ▲-Oxyphenbutazone; at UV-254nm.
C. □-Sulindac, ●-Sulphone, ■-Sulphide; at UV-288nm.
D. ■-Indomethacin, ▽-Desmethylindo.; ▼-Deschloro- ; at UV -260 nm.

This method is simple, rapid and more sensitive than the previously described method for phenylbutazone (Pound and Sears, 1975). No HPLC procedure has been described for the other examples.

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