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Note

Separation of morphine alkaloids, heroin, methadone and other drugs by ion-exchange chromatography

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The recently reported separation[1] of four opium alkaloids and heroin by high speed liquid–liquid partition chromatography, using extracts of the alkaloids in organic solvents, prompts us to report analysis of similar mixtures using high speed ion-exchange chromatography.

Ion-exchange chromatography has the advantage over liquid–liquid partition chromatography in the analysis of these compounds, that analysis can be carried out directly with aqueous solutions thereby eliminating time-consuming extraction procedures[2] which often introduce error. This note describes the separations of morphine from five associated opium alkaloids, of morphine from heroin and 6-(O-acetyl) morphine (the product of hydrolysis of heroin), of methadone from morphine or heroin, and of the analgesics aspirin, phenacetin, caffeine, paracetamol (N-acetyl-*p*-aminophenol) and *p*-aminophenol.

EXPERIMENTAL

The high speed liquid chromatograph consisted of a high-pressure reciprocating piston pump (Orlita, Type DMP 1515 Giessen), a stainless-steel column (1.0 m in length and 2.1 mm bore) and a variable wavelength ultraviolet photometer (Cecil Instruments, Cambridge) fitted with an 8 flow cell (Du Pont Co., London).

Columns were dry packed with 37–44 μ Zipax strong cation-exchange (SCX) or Zipax strong anion-exchange (SAX) resin (Du Pont Co.). Samples were injected by microsyringe through a septum using a specially designed injection port. Operative pressures were 500–1500 p.s.i. (30–100 atm).

Morphine alkaloid, morphine sulphate, papaverine hydrochloride, thebaine, cryptopine and narcotine alkaloids were gifts from MacFarlane Smith Ltd. Methadone hydrochloride B.P. (Physeptone injections, Burrough Wellcome Co. Ltd.), heroin hydrochloride B.P., diamorphine, aspirin, phenacetin, caffeine and paracetamol were pharmaceutical preparations; *p*-aminophenol was obtained from Koch Light laboratories.

Sample mixtures were prepared either in alcoholic or in acidic aqueous solutions.

RESULTS AND DISCUSSION

Opium alkaloids

Morphine could be eluted from Zipax SCX by aqueous sodium hydroxide/boric acid buffers of pH from 9.2–9.8 and ionic strength from 0.02–0.15 mol·l^{-1} in a few minutes as a symmetrical peak (Fig. 1), but the other main alkaloids accompanying morphine in opium, namely codeine, papaverine, thebaine, cryptopine and narcotine were strongly retained. They could be eluted and well separated from each other in 45 min by the same buffers with the addition of 4–5% of acetonitrile and approximately 1% of *n*-propanol (Fig. 2). This compares with a time of 72 min for the four morphine alkaloids analysed on Corasil by partition chromatography[1]. Morphine was eluted before the accompanying alkaloids in our work but in the work reported in ref. 1 it eluted after the alkaloids. In addition, the symmetry of the peaks was somewhat better when eluted from the cationexchange resin making this method more attractive for quantitative analytical purposes.

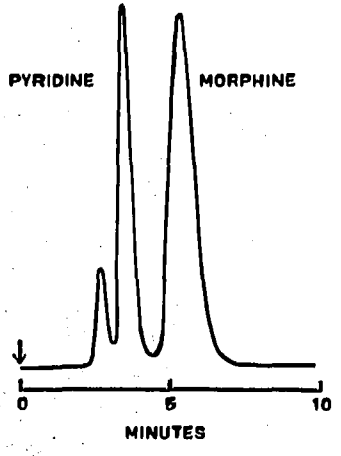


Fig. 1. HSL-chromatogram of morphine and pyridine on Zipax SCX. Mobile phase: aqueous 0.77 *M* NaOH, boric acid added to pH 9.8. Linear velocity, 0.75 cm/sec. Detector: UV, 230 nm; sensitivity, 0.1 AUFS (absorbance units full scale deflection).

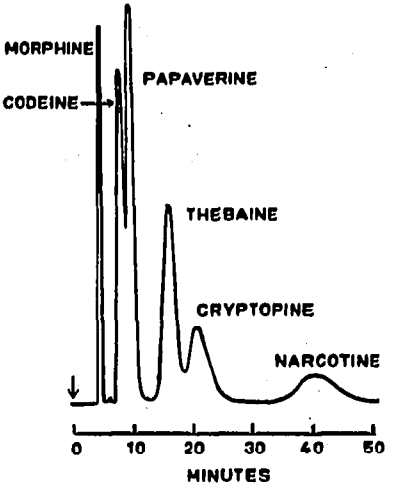
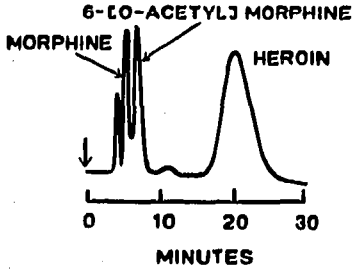


Fig. 2. HSL-chromatogram of morphine alkaloids on Zipax SCX. Mobile phase: 0.2 *M* NaOH, boric acid added to pH 9.5, 0.2 *M* KNO_3, 4% acetonitrile, 1% *n*-propanol. Linear velocity, 0.4 cm/sec. Detector: UV, 254 nm; sensitivity, 0.5 AUFS.

Morphine, heroin and methadone

Aqueous solutions of heroin hydrochloride, unless freshly prepared, are contaminated by 6-(O-acetyl)morphine and morphine resulting from hydrolysis. On Zipax SCX heroin, 6-(O-acetyl)morphine and morphine can be separated using a sodium hydroxide/boric acid buffer of varying ionic strength and pH between 9 and 10 which contains 5–15% of acetonitrile (Fig. 3) but using a purely aqueous buffer only morphine and 6-(O-acetyl)morphine can be eluted (Fig. 4).

Methadone is eluted from Zipax SAX by a sodium hydroxide/boric acid



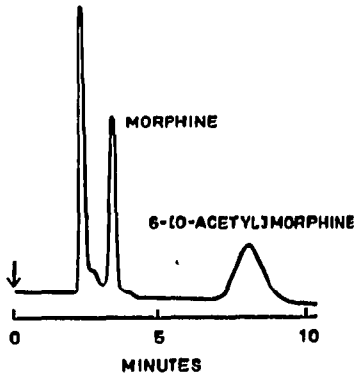


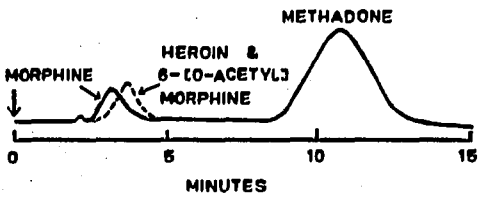
Fig. 3. HSL-chromatogram of morphine and 6-(O-acetyl)morphine on Zipax SCX. Mobile phase: 0.15 *M* NaOH, boric acid added to pH 9.8. Linear velocity, 0.75 cm/sec. Detector: UV, 230 nm; sensitivity, 0.4 AUFS.

Fig. 4. HSL-chromatogram of heroin, 6-(O-acetyl)morphine and morphine on Zipax SCX. Mobile phase: 0.04 *M* NaOH, boric acid added to pH 9.3, 12% acetonitrile, 2% *n*-propanol. Linear velocity, 0.44 cm/sec. Detector: UV, 280 nm; sensitivity, 0.1 AUFS.

buffer of pH 9.8 and is well separated from morphine or heroin, although the latter components are not completely resolved (Fig. 5).

Aspirin analgesics

Analyses of the analgesics aspirin, phenacetin, caffeine and paracetamol have been previously reported[3–5]. Schmit[3] reported the analysis of tablets containing codeine, caffeine, phenacetin, aspirin and phenobarbital on Zipax SCX within 30 min and Du Pont have reported the analysis of tablets containing aspirin, phenacetin and caffeine on Zipax SCX[4] or SAX[5] and of tablets containing caffeine, paracetamol and aspirin on Zipax SAX within a few minutes. The chromatogram of Fig. 6 shows the separation of components in both types of tablets in presence



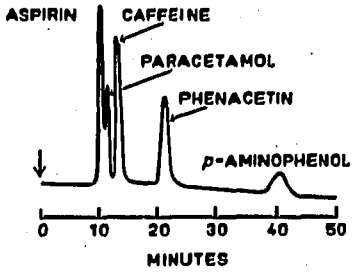


Fig. 5. HSL-chromatogram of methadone, morphine and heroin on Zipax SAX. Mobile phase: 0.15 *M* NaOH, boric acid added to pH 8.8. Linear velocity, 0.75 cm/sec. Detector: UV, 230 nm; sensitivity, 0.1 AUFS.

Fig. 6. HSL-chromatogram of aspirin, caffeine, phenacetin, paracetamol and *p*-aminophenol on Zipax SCX. Mobile phase: 0.004 *M* Na_2HPO_4, 0.0034 *M* KH_2PO_4, 0.001 *M* boric acid, pH 5.8. Linear velocity, 0.19 cm/sec. Detector: UV, 252 nm; sensitivity, 0.1 AUFS.

of *p*-aminophenol, the hydrolysis product of paracetamol and phenacetin. The analysis can be much accelerated if resolution of the first two components can be sacrificed.

A detailed study of the parameters which influence the chromatographic behaviour of opium alkaloids and the above analgesics in ion-exchange systems is now in progress and will be reported later[6].

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