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Note

Rapid determination of alminoprofen in plasma by high-performance liquid chromatography

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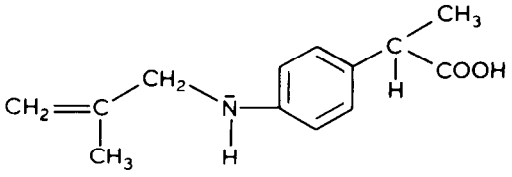
Alminoprofen is a derivative of propionic acid (2-methylallylaminophenyl propionic acid) with the following molecular structure:



It is a relatively new non-steroidal anti-inflammatory agent with a rapid antalgic activity that has been shown in unpublished clinical studies.

Determination of levels of alminoprofen in plasma and urine has been reported by Premel-Cabic et al. [1], who used a gas chromatographic—mass spectrometric technique. Premel-Cabic et al. [2] published also a simple gas chromatographic method. No method for the high-performance liquid chroma-

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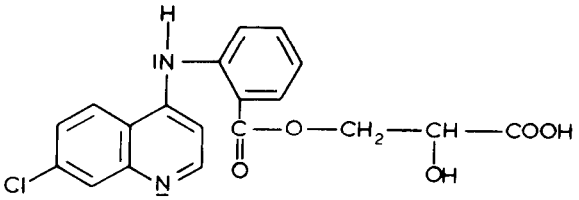
tographic (HPLC) measurement of alminoprofen in biological samples has yet been described.

This paper proposes a reversed-phase HPLC method with UV detection, which can be used readily to monitor therapeutics or intoxication poisoning. Its advantage is a rapid and easy extraction preceding a rapid separation.

EXPERIMENTAL

Chemicals and drugs

The following reagents were used: glacial acetic acid (UCB, Belgium); methanol (Normapur Prolabo, France); diethyl ether (Prolabo, France); distilled water; alminoprofen (graciously provided by Dr. Bouchara's laboratory); glafenic acid (internal standard) with the following molecular formula:



Standard solutions of alminoprofen and internal standard were prepared by dissolution in the mobile phase.

Apparatus and technique

The chromatographic system consisted in a Chromatem 38 solvent delivery pump (Touzart et Matignon, France) and a Rheodyne injector fitted with a 50-μl loop. The column was a μBondapak C_{18} (30 cm × 4.6 mm I.D.; 10 μm) (Waters Assoc., U.S.A.). The detector was a variable-wavelength Schoeffel spectrophotometer. The detection wavelength was 235 nm (0.2 a.u.f.s.). All chromatograms were recorded on a CSA 10-mV recorder (France) at a chart speed of 2.5 mm/min.

Mobile phase. The mobile phase was methanol—water (50:50) with 1% glacial acetic acid. The flow-rate was 0.85 ml/min. This mobile phase was thoroughly degassed.

Extraction. To 1 ml of human plasma were added 50 μl of a solution of 200 μg/ml internal standard, 100 μl of 0.017 *M* glacial acetic acid and 7 ml of diethyl ether. The mixture was shaken for 10 sec in a vortex mixer (Bioblock, France). The solution was then centrifuged for 10 min at 2000 *g* at 3°C, and the supernatant was discarded. The lower organic phase was transferred to a clean glass tube and evaporated to dryness in a vortex evaporator (Buchler, NJ, U.S.A.). The residue was dissolved in 200 μl of the mobile phase; a 50-μl aliquot was injected into the chromatograph with Hamilton syringe.

Calibration. The standard curve was obtained by adding alminoprofen to drug-free plasma, to achieve concentrations of 4, 8, 10, 20 and 40 μg/ml. Standard plasma was extracted under the experimental conditions described above. The peak height ratios of alminoprofen over internal standard were plotted versus concentration.

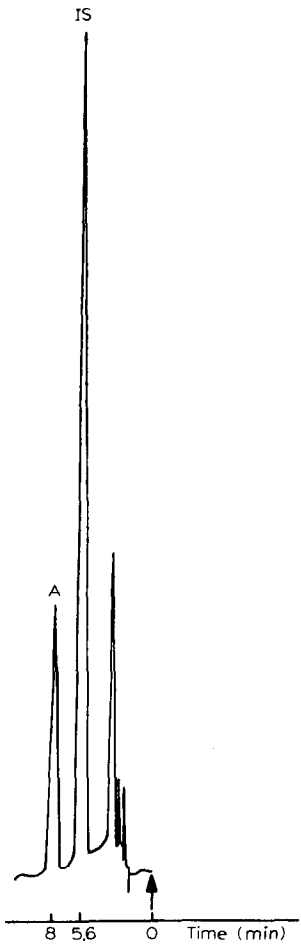


Fig. 1. Typical chromatogram obtained from a plasma extract containing 17 μg/ml alminoprofen. Peaks: A = alminoprofen; IS = internal standard.

RESULTS

Fig. 1 shows a typical chromatogram of plasma of an healthy volunteer (2 h after an oral administration of 150 mg of alminoprofen).

Assay technique

The calibration curve was linear from 4 to 40 μg/ml, with the equation $y = 0.0280(\pm\ 0.0002)x\ -\ 0.006(\pm\ 0.006)$; $r = 0.991(\pm\ 0.0017)$, where y is the ratio of the peak height of alminoprofen and x the concentration of alminoprofen in μg/ml; r is the correlation coefficient.

Precision

The reproducibility of the method was checked for three plasma concentrations, 8, 10 and 20 μg/ml; the coefficients of variation were 6.4, 9.8 and 11.3%, respectively.

Recovery

The reproducibility of alminoprofen was assessed by comparing the peak height after an injection of a pure solution of alminoprofen with that obtained after an injection of extracted plasma containing the same amount of alminoprofen. The percentage recovery of the extraction procedure is shown in Table I.

Sensitivity

The threshold of sensitivity of this technique was 1 μg/ml of plasma.

Application

This HPLC—UV method gives reproducible results, and is sensitive enough for the determination of alminoprofen in human plasma. It is also easy to perform and cheap. It has been used in a study of plasma concentrations of alminoprofen after oral administration of 300 mg of this drug to healthy patients. Results are shown in Tables II and III.

TABLE I

RECOVERY OF ALMINOPROFEN FROM HUMAN PLASMA

Mean ± standard deviation over ten determinations at each concentration.

Alminoprofen (μg/ml)	Recovery (%)
4	70.10 ± 0.63
10	68.41 ± 0.85
20	62.20 ± 1.14
Mean ± S.D.	66.90 ± 4.16

TABLE II

PLASMA CONCENTRATIONS OF ALMINOPROFEN AFTER AN ORAL DOSE OF 300 mg IN TWELVE HEALTHY PATIENTS

Time after administration (min)	Level of alminoprofen (mean ± S.D., μg/ml)
60	30.6 ± 14.1
120	27.7 ± 11.9
180	19.5 ± 10.7

TABLE III

SOME PHARMACOKINETIC PARAMETERS IN HEALTHY PATIENTS AFTER AN ORAL DOSE OF 300 mg ALMINOPROFEN

Parameter	Mean ± S.D.
C_{max} (μg/ml)	35.2 ± 15.2
T_{max} (h)	1.64 ± 0.62
$T_{½}$ (h)	3.2 ± 1.9

CONCLUSION

In this short paper we have described a simple and rapid technique for the determination of alminoprofen in plasma. Sensitivity and reproducibility are sufficient to allow us to elucidate the pharmacokinetics of this drug.

REFERENCES

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2 A. Premel-Cabic, D. Chaleil, R. Bonniot, P. Riberi, G. Streichenberger and P. Allain, Thérapie, 36 (1981) 41.