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Determination of 2-aminopyridine in piroxicam by derivative UV-spectrophotometry

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Summary

A method for the determination of 2-aminopyridine in piroxicam (bulk material and pharmaceutical formulations) by second-derivative ultraviolet spectrophotometry is described. The procedure is simple and rapid, and provides accurate and precise results.

Piroxicam (Zinnes et al., 1982), or 4-hydroxy-2-methyl-*N*-(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide 1,1-dioxide, is a potent non-steroidal anti-inflammatory, antipyretic and analgesic agent, widely used in the treatment of rheumatological disorders (Brogden et al., 1984).

Among the potential impurities of the drug, 2-aminopyridine can be found as synthesis precursor and decomposition product by acidic cleavage (Hobbs and Twomey, 1979). Several methods to assay piroxicam and its metabolites, in biological fluids and tissues, by HPLC and HPTLC have been reported (Richardson et al., 1986; Riedel and Laufen, 1983; Yi-Hung Tsai et al., 1985). Only one HPLC method has been developed to assay piroxicam in pharmaceutical formulations, but not its impurities (Richards et al., 1987). This paper describes a method for the determination of 2-aminopyridine in piroxicam by derivative ultraviolet spectrophotometry in bulk material and in pharmaceutical forms.

A Perkin-Elmer ultraviolet-visible spectrophotometer Model Lambda 5 was used. Zero-order spectra: scan speed 60 nm/min; spectral slit width 2 nm. Derivative conditions: scan speed 60 nm/min; spectral slit width 2 nm; $\Delta\lambda$ 6. Ethanol and diethyl ether (spectroscopic reagent grade) were purchased from Farmitalia-Carlo Erba (Milan, Italy). Piroxicam (Pfizer Italiana, Latina, Italy) was further purified by several recrystallizations from ethanol. 2-Aminopyridine was purchased from Sigma Chemical Co. (St. Louis, U.S.A.) and used without further purification. Feldene suppositories and capsules were obtained from Pfizer Italiana (Latina, Italy).

Standard solutions were ethanolic solutions containing piroxicam (5×10^{-5} M) and 2-amino-

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pyridine with concentrations in the range 5×10^{-8}–5×10^{-7} M. The determination of 2-aminopyridine can be carried out, in the concentration range examined, by utilizing the peak–trough amplitude between 240 and 244 nm in the second-derivative spectrum and by using the following equation, obtained through regressional analysis of data for the standard solutions previously reported: $h = 4.73 \times 10^4 x + 0.037$ (correlation coefficient 0.9986), where h = peak–trough amplitude between 240 and 244 nm in the second-derivative spectrum, measured on the scale ± 0.3 and x = concentration of 2-aminopyridine (mol/l). The calibration curve was obtained by regressing the values of the peak–trough amplitude of 8 different samples regularly distributed between the lower and the upper concentration value.

Analysis of bulk material: the powdered bulk material was dissolved in ethanol in such a way as to obtain a 5×10^{-5} M solution of piroxicam. After filtration through an HA 0.45 μm filter (Millipore, Bedford, MA, U.S.A.), the solution was analysed by derivative UV-spectrophotometry by using the equation previously reported.

Analysis of pharmaceutical formulations. (a) *Capsules*: the contents of 10 capsules were removed, weighed and combined. An amount of powder equivalent to about 100 mg of piroxicam was accurately weighed and dissolved in ethanol in such a way as to obtain a 5×10^{-5} M solution of piroxicam. After filtration, the solution was analysed by derivative UV-spectrophotometry as previously reported. (b) *Suppositories*: 5 suppositories were crushed and combined. An amount of material equivalent to about 100 mg of piroxicam was accurately weighed into a screw-capped tube, 10 ml of ether–water (1 : 1) was added and the mixture was shaken vigorously for 15 min. The ether layer was removed, dried and evaporated under reduced pressure. The residue was dissolved in ethanol in such a way as to obtain a 5×10^{-5} M solution of piroxicam and analysed as previously described for the capsules.

Fig. 1 shows the derivative spectrum utilized for the determination of 2-aminopyridine in piroxicam. The minimum concentration of this impurity detectable by the described procedure

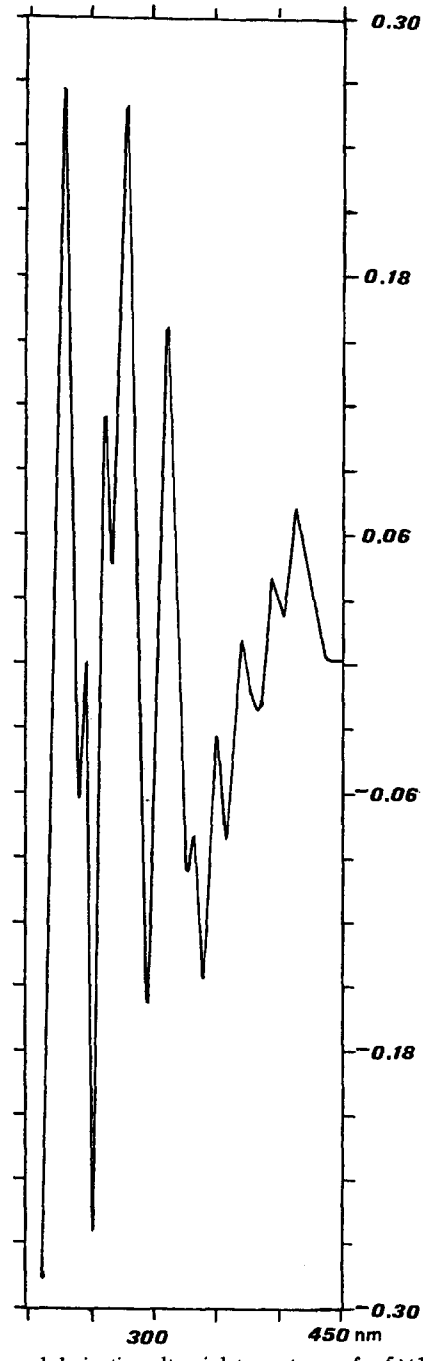

Fig. 1. Second-derivative ultraviolet spectrum of a 5×10^{-5} M ethanolic solution of piroxicam containing 2-aminopyridine (5×10^{-7} M).

was 0.1%. The data employed for the calibration curve and for the analysis of samples are the average of a minimum number of 5 determinations for each sample.

These results have been obtained from the analysis of samples of commercial bulk material, pharmaceutical formulations (capsules and suppositories) containing the drug and capsules added with a known amount of impurity [sample and 2-aminopyridine found (%, S.D.)]: bulk material = 0.1, 0.0019; bulk material = 0; suppositories = 0.1, 0.0021; capsules = 0.1, 0.002; capsules added with 0.1% of 2-aminopyridine = 0.2, 0.0038.

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