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Letter to the Editor

Determination of ketanserin in plasma by reversed-phase high-performance liquid chromatography

Sir,

Ketanserin (3-{2-[4-(4-fluorobenzoyl)-1-piperidinyl] ethyl}-2,4-[1H,3H]-quinazolinedione) is a potent new serotinergic receptor antagonist completely devoid of agonist activity. It has been shown to possess anti-hypertensive properties in experimental animals and man [1—4] and is currently being evaluated as a hypotensive drug. It appears to be free of serious side effects or systemic toxicity in man.

Recently, in this Journal, Kacprowicz et al. [5] have described a high-performance liquid chromatographic (HPLC) method for the determination of ketanserin in human plasma. Independently, in this laboratory, a conceptually similar, though procedurally different, method for the determination of this drug has been developed. The methodology is described briefly below.

A 1-ml sample of human plasma, spiked with 75 ng of the internal standard (R 46594), was treated with 1 ml of borate buffer, pH 10, and extracted with 5 ml of diethyl ether for 15 min. Following centrifugation at 500 *g*, the ether phase was removed, treated with 1 ml of 0.1 *M* sulphuric acid and extracted for a similar period. The ether phase was discarded (following centrifugation) and to the residual aqueous phase were added 100 μl of 4 *M* sodium hydroxide. This aqueous phase was finally extracted with 5 ml of diethyl ether for 15 min; the organic phase was removed following centrifugation, reduced to dryness under nitrogen and reconstituted in 40 μl of mobile phase. A 20-μl aliquot of this solution was injected into the chromatograph.

The liquid chromatograph comprised an Altex Model 100A pump, a 15 cm × 4.6 mm I.D. analytical column packed with 5-μm Ultrasphere ODS particles (both Altex Scientific, Berkeley, CA, U.S.A.) and a Pye-Unicam Model LC-UV ultraviolet detector (Pye-Unicam, Cambridge, Great Britain). The analytical column was fitted with a 5 cm × 4.6 mm I.D. pre-column packed with 30—38 μm Co-Pell ODS (Whatman, Maidstone, Great Britain). The mobile phase consisted of 0.02 *M* K_2HPO_4—methanol (28:72, v/v), final pH 7.2, pumped at a flow-rate of 1.0 ml/min. The UV detector was set at 240 nm.

Using this system k' values for ketanserin and its internal standard were 1.64

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and 2.70, respectively (R_s = 6.90); total analysis time was 10—12 min. With the detector normally operated at 0.005—0.01 a.u.f.s. a nominal limit of detection of 2 ng ketanserin tartrate could be achieved. Calibration was linear over a concentration range of 10—500 ng/ml ketanserin tartrate ($y = 0.012x - 0.024$, r = 0.998) and coefficients of variation for intra- and inter-assay variation throughout this concentration range varied between 4.9—5.7% and 3.7—12.0%, respectively. An extraction efficiency of approximately 60% was normally achieved.

The above technique possesses performance characteristics almost identical to those described by Kacprowicz et al. [5]. The complementary data obtained from the two independent studies indicate that ketanserin, a compound of increasing clinical and pharmacological interest, may be accurately and reliably determined by reversed-phase HPLC at levels consistent with its clinical administration in man.

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