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SPECTROPHOTOMETRIC DETERMINATION OF TOLMETIN SODIUM IN CAPSULE DOSAGE FORM

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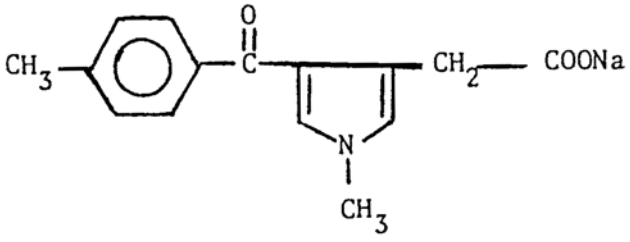
ABSTRACT

Two different U.V. spectrophotometric modes, zero-order and first derivative, have been appied for the quantization of tolmetin sodium (Tolectin® 200 mg) in bulk form and in its pharmaceutical formulation. Direct U.V.-measurement of aqueous solution of the drug at 325 nm exhibits significant linearity at the concentration range 0.1-1.5 mg% with a coefficient of variation (C.V.) 0.34%. The first derivative (d'A) spectrophotometric measurements at 342 nm yield results with a C.V. 0.29%. Drug assay of the capsule gives percent contents of 100A2 ± 0.34 and 100.28 ± 0.29 by adopting zero-order and d'A-spectrophotometry respectively. The reproducibility and accuracy the two proposed methods have been assessed by employing standard additions technique. Accordingly the percent recoveries obtained were 99.60 ± 0.22 and 100.16 ± 0.26 for the zero order and the d'A-spectrophotometry respectively.

Introduction

Tolmetin, 1-methyl-5-(4-methylbenzoyl)-IH-pyrrole-2-acetic acid sodium salt is commonly used as a non-steroidal antirheumatic drug with analgesic properties in man. Extensive clinical trials have established the potency of the drug in the treatment of adult and juvenile rheumatic arthritis and in osteoarthritis (Muller, et al. 1977; Kaplan, et al. 1979).



Tolmetin sodium

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Several procedures involving thin layer chromatography (Giachetti, et al. 1983; Cressman, et al. 1975, Selley, et al. 1974), high performance liquid chromatography (Desiraju, et al. 1982), colorimetry (Ozyadin, 1982) and d[i]rect-current polamgraphy (Poctovo, 1982) were reported for the detection and quantitation of tolmetin in capsule dosage form and tolmetin and its metabolites in biological fluids.

In this work two U.V.-spectophotometric methods, namely, the zero-order and the d'A-spectrophotometry have been proposed for the assay of the drug in bulk and in capsule forms (Tolectin®). The results are encouraging and show that both the zero-order the d'A curves are recommendable to use for the quality control of the drug. Furthermore, the d'A method can be applied to eliminate interference in case of possible co-existing U.V.-absorbing additives in pharmaceutical drug designing and dosage form.

Experimental

Materials:

Authentic tolmetin sodium (Lot No. 87P2427) and tolmetin capsules (Batch No. 124511) were kindly donated by Cilag AG, 8201 Schaffhausen, Switzerland and Cilag Scientific Office in Riyadh, Saudi Arabia, respectively.

Solutions:

Standard drug solutions and sample solution were prepared in distilled water.

Apparatus:

Varian (Techtron Pty. Limited, Springvale, Australia) DMS 90 double beam U.V./ Vis-spectrophotometer with 1-cm quartz cuvettes were used. The instrument was connected to Hewlett Packard X-Y recorder model 7015B.

Standard curve:

From authentic tolmetin sodium, 10 mg, accurately weighed, was dissolved in water using 100 ml volumetric flask. The solution (100µg/ml) was utilized for the preparation of a series of standard solutions in the range 1-15 pg/ml (ppm). The absorbances, A, of the zero-order, and d'A, of the first derivative at 325 nm & 342 nm respectively were measured against water as a blank. The standard curves of the aqueous solutions of the drug at two different days showed practically constant slope. The A(1 percent, 1 cm) and d'A (1 percent, 1 cm) values were found to be 6.30×10^2 and 1.31×10^2 at 325 and 342 nm respectively.

Assay of tolmetin sodium capsules:

The contents of ten capsules of (Tolectin®) were carefully emptied, accurately weighed and the average mass of capsule content was computed. A quantity of powder from the mixed sample containing approximately 10 mg of tolmetin sodium was accurately weighed and dissolved in 100 ml water using 100 ml volumetric flask. The absorbances were measured at 325 nm and 342 nm utilizing zero-order and first derivative modes, respectively.

The concentration of unknown sample is computed either from the standard curve or from an equivalent linear regression equation worked out by taking the values of A (1 percent, I cm) or d'A (1 percent, 1 cm).

Results and Discussion

The zero-order absorption spectrum of tolmetin sodium in aqueous solution exhibit typical peaks at 245 and 325 nm in the spectral range 200-440 nm. Comparatively, the first derivative spectrum at similar concentration of the drug shows characteristic maximum at 300 nm and minimum at 342 nm. The sensitivity at both wavelengths is practically the same and consequently d'A-measurements could be carried out at any of them. Fig. 1, compares the zero-order and the first derivative spectra, while Table 1 summarizes the spectrophotometric dam of the drug.

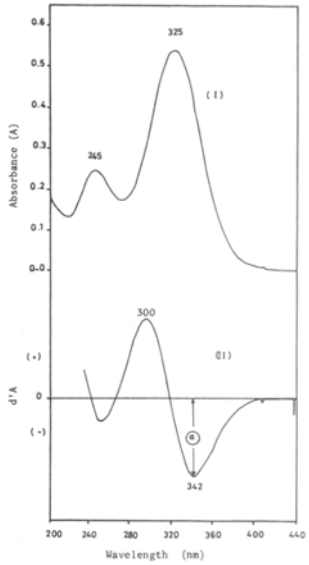

Fig. 1. The absorption spectra of an aqueous solution 8 μm/ml of tolmentin sodium using zero-order (I) and first-derivative (II) spectrophotometric modes; (a) is the peak-height at wavelength of measurement.

Table 1: Spectrophotometric Parameters for Authentic Tolmetin Sodium.

Zero-order	First-derivative
A (1 percent, 1 cm) 6.30 x 10^2 at 325 nm	d'A (1 percent, 1 cm) 1.31 x 10^2 at 342 nm
1.53x 10^4	3.21 x 10^4
Regression equation:	Regression equation:
A = 0.618C* - 0.004	d'A = 1.270C* - 1.016
r = 0.9995	r = 0.9997

C*=mg/100ml.

Linear regression equation (Table 1) showed correlation coefficients (r) of 0.9997 and 0.9995 at 95% confidence limits for A- and d'A-measurements. These correlation coefficients indicate statistically significant linearity between absorbances in zero-order and first derivative spectrophotometry and concentration in the range 1-15 µg/ml of the drug.

The zero-order and the derivative spectrophotometric procedures have been applied for the assay in the capsules gave precise percent results, 100.42 ± 0.33 (n = 6) and 100.28 ± 0.26 (n = 6) for the zero-order and the first derivative methods respectively. The accuracy and reproducibility of both procedures have been assessed by adopting the standard additions technique, where different added amounts (20-80%) of claimed tolmetin sodium in Tolectin® were tried. The concomitant added percent recoveries obtained were 99.60 ± 0.22 (n = 6) and 100.16 ± (126 for the zero order and first derivative methods respectively.

In conclusion it can be stated that the two proposed spectrophotometric methods are rapid, simple, precise and accurate; and any of them is suitable for quality control of totmain sodium. However, the first derivative method has the advantage of eliminating irrelevant absorption due to possible interfering co-existing substances.

Table 2: Determination of Tolmetin Sodium by Zero-Order and First-Derivative Spectrophotometry.

		Zero-Order Method		First-Derivative Method	
Pharmaceutical Preparation	Nominal concentration µg/ml	% Found ± SD*	% of Added recovery ± SD*	% Found ± SD*	% of Added recovery ± SD*
Tolectin® capsules (200 mg)	1-15 (n=6)	100.42 ± 0.33 (n=6)	99.60 ± 0.22 (n=6)	100.28±0.26 (n=6)	100.16±0.26

SD* = Standard deviation.

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