ANALYTICAL LETTERS
Vol. 37, No. 6, pp. 1151–1162, 2004

PHARMACEUTICAL ANALYSIS

Adaptation of a Color Reaction for Spectrophotometric Determination of Diclofenac Sodium and Piroxicam in Pure Form and in Pharmaceutical Formulations

A. M. El-Didamony[1,*] and A. S. Amin[2]

[1]Chemistry Department, Faculty of Science, Zagazig University, Zagazig, Egypt
[2]Chemistry Department, Faculty of Science, Benha University, Benha, Egypt

ABSTRACT

A simple, sensitive, and convenient spectrophotometric method for the determination of diclofenac sodium and piroxicam in pure form and in pharmaceutical formulations was developed. The method is based on the oxidation of diclofenac sodium or piroxicam by iron(III) in the presence of *o*-phenanthroline. The formation of *tris*(*o*-phenanthroline) iron(II) complex (ferroin) upon the reaction of diclofenac sodium or piroxicam with an iron(III)-*o*-phenanthroline mixture in acetate buffer solution of

*Correspondence: A. M. El-Didamony, Chemistry Department, Faculty of Science, Zagazig University, Zagazig, Egypt; E-mail: ameldidamony61@msn.com.

DOI: 10.1081/AL-120034060 0003-2719 (Print); 1532-236X (Online)

pH 4.4 and 4.8, respectively, was investigated. The ferroin complex is measured at 510 nm against a reagent blank prepared in the same manner. The optimum experimental parameters for the color production are selected. Beer's law is valid within a concentration range of 1.0–32 $\mu g\,mL^{-1}$ for diclofenac sodium and 1.0–28 $\mu g\,mL^{-1}$ for piroxicam. For more accurate results, Ringbom optimum concentration ranges are 2.0–30 and 2.0–26 $\mu g\,mL^{-1}$ for diclofenac sodium and piroxicam, respectively. The molar absorptivities are 1.15×10^4 and $1.63 \times 10^4\,L\,mol^{-1}\,cm^{-1}$, whereas Sandell sensitivities are 2.78 and 2.03 $ng\,cm^{-2}$ for diclofenac sodium and piroxicam, respectively. The method gave a mean percentage recoveries 99.8 $\pm$ 1.2% for diclofenac sodium and 100.3 $\pm$ 0.8% for piroxicam. The developed method is applied for the determination of diclofenac sodium and piroxicam in bulk powder and in their pharmaceutical formulations without any interference from tablet fillers.

Key Words: Diclofenac sodium; Piroxicam; Spectrophotometry; Pharmaceutical formulations.

INTRODUCTION

Diclofenac sodium [monosodium 2-(2,6-dichloroanilino)phenylacetate] [15307-79-6] is a well known analgesic and anti-inflammatory agent.[1] Piroxicam [4-hydroxy-2-methyl-*N*(2-pyridyl)-2H-1,2-benzothiazine-3-carboxamide1,1dioxide] is a new non-steroidal anti-inflammatory drug which is extensively used in medicine.[2] The USP-NF procedure,[3] for the quantitative determination of these drugs in pure and in pharmaceutical dosage forms is based on high performance liquid chromatography (HPLC). The HPLC methods require expensive equipment and are often timing consuming.

Several methods have been reported for the assay of these drugs whenever pure, in dosage forms, or in body fluids. Piroxicam has been analysed by HPLC,[4–9] spectrophotometry,[10–16] fluorometry,[17] voltammetry,[18–20] potentiometry,[16] and polarography.[20] Diclofenac sodium has also been determined by chromatographic techniques including TLC,[21,22] GC,[23] and HPLC,[9,23–28] colorimetric,[29] capillary electrophoresis,[30] and spectrophotometric procedures.[31–38]

The present study describes a spectrophotometric method for the determination of diclofenac sodium and piroxicam, based on the oxidation of drugs by Fe(III) in the presence of *o*-phenanthroline. The formation of *tris*(*o*-phenanthroline) iron(II) complex (ferroin) upon the reaction of diclofenac sodium or piroxicam with an iron(III)-*o*-phenanthroline mixture in optimum reaction conditions was investigated.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

EXPERIMENTAL

Apparatus

All spectral and absorbance measurements were made on a Perkin–Elmer λ3B spectrophotometer with 10 mm matched quartz cell. An Orion Research Model 601 A/digital ionalyzer, pH-meter with a combined saturated calomel-glass electrode was used for pH measurements.

Materials and Reagents

All chemicals used were of analytical reagent grade. Diclofenac sodium was obtained from Swisspharma Cairo (under Licence from Ciba-Geigy Ltd, Basle, Switzerland), whereas piroxicam was kindly supplied by Pfizer's Egypt Company, Cairo, Egypt. Voltaren (tablets, ampoules, and suppositories) labelled to contain 25 mg per tablet, 75 mg per ampoule, and 100 mg per suppository of diclofenac sodium were obtained from Swisspharma Cairo (under Licence from Ciba-Geigy, Ltd., Basle, Switzerland). Declophem (tablets, ampoules and suppositories) labeled to contain 25 mg per tablet, 75 mg per ampoule and 100 mg per suppository were obtained from Pharco Pharmaceuticals, Alexandria, Egypt. Feldene (capsules, tablets and suppositories) labeled to contain 10 and 20 mg per capsule, 10 mg per tablet, and 20 mg per suppository of piroxicam were obtained from Pfizer's Egypt Co., Cairo, Egypt (under authority of Pfizer Inc. USA).

o-Phenanthroline–iron(III) mixture. A 0.50 g amount of *o*-phenanthroline monohydrate (Fluka, puriss. P.a.), 5.0 mL of 1.0 M HCl, and 0.40 g of ammonium iron(III) sulphate dodecahydrate (Merck, analytical-reagent grade) were dissolved in and diluted to 250 mL with distilled water. The solution is stable for at least 4 weeks if it is stored in a dark, cool location, e.g., in a refrigerator at 3–4°C.

Stock reference solutions (250 $\mu g\ mL^{-1}$) were freshly prepared from pure samples of diclofenac sodium and piroxicam by dissolving 0.025 g in 100 mL ethanol. Acetate buffer solutions of pH values 3.4–5.6 were prepared as recommended previously.[39]

General Procedure and Calibration

Into a 25 mL calibrated flasks, were pipetted in the order 15.0 mL of acetate buffer solution (pH 4.4 and 4.8 for diclofenac sodium and piroxicam, respectively, as optimum pH value), 0.1–3.2 mL aliquots of the experimental drug

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

solution, and 3.0 mL of *o*-phen-iron(III) mixture, followed by dilution to volume with water. The flasks were stopped, mixed well by shaking and kept for 15 min in a water bath at 60°C ± 1°C, then immediately cooled to room temperature (ca. 25°C ± 1°C) using a cold water bath. The absorbance of the solution was measured at 510 nm against a blank solution which has been treated similarly.

Procedure for Capsules and Tablets

Into a 100 mL calibrated flask an accurately weighted amount of the mixed contents of 20 capsules or tablets, equivalent to 25 mg was transferred quantitatively. The drug was dissolved and diluted to volume with ethanol. The solution was mixed well by shaking and filtered through a suitable filter paper. The assay of the capsules or tablets was completed according to the general procedure.

Procedure for Ampoules

Into a 100 mL calibrated flask, a volume equivalent to 25 mg of diclofenac sodium of the mixed contents of five ampoules was transferred quantitatively and completed to 100 mL with ethanol. The assay of the ampoules was completed according to the general procedure.

Procedure for Suppositories

An accurately weighted amount of the 10 suppositories melted in a small beaker on a water bath with stirring and cool, equivalent to 25 mg was transferred quantitatively in a separating funnel. Dissolve in 40 mL of hot ethanol and after cooling, extract the fatty with 10 mL of ether. Separate the etherial layer and wash it twice with 10 mL of ethanol. Combine the ethanolic extracts and washings into a 100 mL calibrated flask and complete to volume with ethanol. The assay of the suppositories was completed according to the general procedure.

RESULTS AND DISCUSSION

Although diclofenac sodium or piroxicam is relatively stable in both light and air, it is easily oxidized by many redox systems such as:

$$Fe^{3+} + e' \rightleftarrows Fe^{2+}$$

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Iron(III)-*o*-phenanthroline reagent was used for the determination of several drugs. This reagent was utilized for quantitative determination of diclofenac sodium and piroxicam. The method depends on the formation of *tris*(*o*-phenanthroline)iron(II) chelate upon the oxidation reaction of these drugs with an iron(III)-*o*-phenanthroline mixture in acetate buffer of pH 4.4 and 4.8 for diclofenac sodium and piroxicam, respectively. The reaction proceeds through reduction of iron(III) to iron(II) and subsequent formation of the intensive orange–red coloration of the ferroin complex. A detailed study of the optimum chemical conditions for the reduction of phen-iron(III) reaction was performed.

Effect of pH

The effect of pH was investigated in different buffer medium namely, universal, thiel, borate, and acetate buffer solutions of pH ranges 2.0–12.0.[39] The results indicated that the reduction process occurs in slightly acidic medium and the optimum buffer solution was the acetate. The optimum pH for diclofenac sodium was in the range 3.8–5.0, whereas for piroxicam was in the range 4.3–5.3. The pH value 4.4 and 4.8 was selected for further study to diclofenac sodium and piroxicam, respectively, since the results are highly concordant at this pH values. The amount of buffer added to 25 mL of solution was also investigated and found to be 15 mL which gave marginally the highest absorbance values.

Effect of Time and Temperature

The reaction was tried on cold and it was found that diclofenac sodium required about 2 hr for complete color development and 15 min heating at $60^{\circ}C \pm 0.5^{\circ}C$ on thermostatic water bath. Piroxicam needed about 90 min on cold and 15 min heating at $60^{\circ}C \pm 0.5^{\circ}C$ on thermostatic water bath. For this reason; the heating time was selected to be 15 min for both drugs. Further increase in the heating time does not cause any change in color intensity, while raising the temperature above 80°C, the color intensity and the absorbance start to decrease.

Effect of Reagent Concentration

The results obtained showed that at least 2.5 mL solution of the prepared reagent should be present to achieve maximum color development (Fig. 1).

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

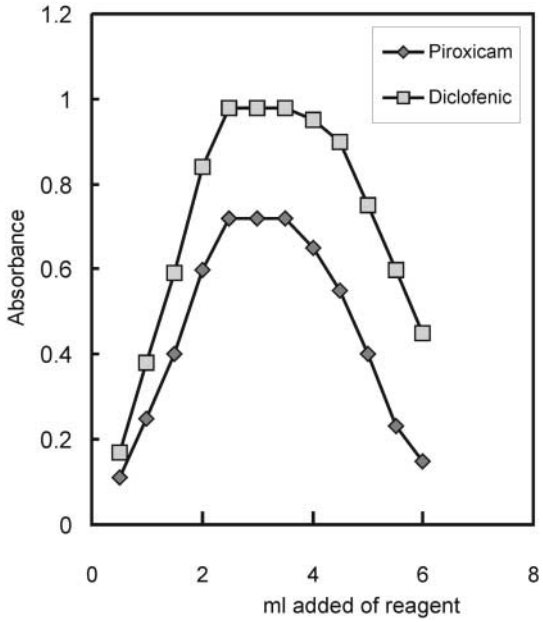

Figure 1. Effect of reagent concentration on the complexation of 20 μg mL^{-1} of piroxicam and diclofenac sodium. *(View this art in color at www.dekker.com.)*

However, 3.0 mL of reagent was used in the present study to insure complete color formation and quantitative reaction at the upper limit of the calibration curves. The color formed under these conditions was stable for more than 12 hr.

Absorption Spectrum and Calibration Graph

The absorption spectrum of the well known ferroin complex was scanned in the double beam mode against a reagent blank in the range 400–600 nm. Automatic base line correction was employed, while the same base line was determined and checked with both samples and blank cells filled with reagent blank solution.

The calibration graph was obtained according to the above general procedure. The linearity (six replicates for seven different concentrations) was checked by a linear least-squares treatment. All the spectral characteristics and the measured or calculated factors and parameters are summarized in Table 1.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Table 1. Spectral and analytical characteristics.

Parameter	Values	
	Diclofenac sodium	Piroxicam
λ_{max} (nm)	510	510
ε ($L\,mol^{-1}\,cm^{-1}$)	1.15×10^4	1.63×10^4
Sandell's sensitivity ($ng\,cm^{-2}$)[a]	2.78	2.03
Regression line equation: $A = mC \pm z$[b]		
m (slope $\pm$ S.D.) ($n = 5$)	0.036 ± 0.002	0.049 ± 0.001
z (intercept $\pm$ S.D.) ($n = 5$)	-0.006 ± 0.061	$+0.0037 \pm 0.044$
Correlation coefficient (r) ($n = 42$)[c]	0.9988	0.9995
Optimum concentration range ($\mu g\,mL^{-1}$)	1.0–32	1.0–28
Ringbom concentration range ($\mu g\,mL^{-1}$)	2.0–30	2.0–26

[a]Average of six determinations (the values obtained are referred to diclofenac sodium or piroxicam).
[b]A = absorbance; C = concentration.
[c]Six replicates for seven different concentrations.

Sensitivity, Accuracy, and Precision

The mean Sandell sensitivity as calculated from Beer's law is presented in Table 1. In order to determine the accuracy and precision of the method, solutions containing three different concentration of diclofenac sodium or piroxicam i.e, 8.0, 16.0, and 24.0 $\mu g\,mL^{-1}$, were prepared and analysed in quintuplicate. The measured standard deviation (S.D.), relative standard deviation (R.S.D.), the standard analytical error and confidence limits, (Table 2) can be considered satisfactory, at least for the level of concentrations examined.

Application in Pharmaceutical Analysis and a Statistical Comparative Study

The method was applied to the spectrophotometric determination of diclofenac sodium or piroxicam in commercial pharmaceutical formulations. The results obtained were compared statistically by the Student's *t*-test and the variance ratio *F*-test with those obtained by applying the official method for diclofenac sodium[1] and piroxicam[2,3] on samples of the same batch and given in Table 3.

The Student's *t*-test values obtained at the 95% confidence level and five degrees of freedom[40] did not exceed the theoretical tabulated value of

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

Table 2. Evaluation of accuracy and precision of the proposed method.

Drug	Added ($\mu g\,mL)^{-1}$	Found ± S.D.[a] ($\mu g\,mL^{-1}$)	R.S.D. (%)	Standard error	Confidence limits
Diclofenac sodium	8.0	8.02 ± 0.081	1.72	0.027	8.02 ± 0.10
	16.0	15.95 ± 0.06	1.37	0.035	15.95 ± 0.07
	24.0	23.90 ± 0.12	1.84	0.054	23.90 ± 0.14
Mean			1.64	0.039	
Piroxicam	8.0	7.97 ± 0.10	1.51	0.045	7.97 ± 0.12
	16.0	16.10 ± 0.12	1.79	0.054	16.10 ± 0.14
	24.0	23.90 ± 0.11	1.33	0.049	23.90 ± 0.13
Mean			1.54	0.049	

[a]Mean of five determinations.

Table 3. Determination of diclofenac sodium and piroxicam by the proposed method and statistical comparison with the official method.[1,3]

		Recovery[a] ± S.D. (%)			
Sample	Formulation	Proposed	Official	t[b]	F[c]
Voltaren[d]	25 mg/tablet	99.20 ± 0.091	98.00 ± 0.162	1.24	2.63
	75 mg/ampoule	100.40 ± 0.067	102.00 ± 0.173	1.93	2.78
	100 mg/ suppository	101.00 ± 0.119	97.50 ± 0.211	1.56	2.90
Declophem[d]	25 mg/tablet	100.80 ± 0.108	99.00 ± 0.157	1.11	2.71
	75 mg/ampoule	98.60 ± 0.134	97.50 ± 0.182	1.26	3.11
	100 mg/ suppository	99.20 ± 0.112	102.70 ± 0.226	1.47	2.93
Feldene[e]	10 mg/capsule	98.60 ± 0.121	103.00 ± 0.288	1.71	2.40
	20 mg/capsule	100.80 ± 0.115	98.00 ± 0.177	1.98	2.51
	10 mg/tablet	101.00 ± 0.127	97.20 ± 0.263	1.43	2.98
	20 mg/ suppository	99.00 ± 0.126	102.80 ± 0.259	1.78	2.51

[a]Average of six determinations.
[b]Calculated *t*-value; tabulated *t*-value for five degrees of freedom; and $p = 0.05$ is 2.57.
[c]Calculated *F*-value; tabulated *F*-value for five degree of freedom; and 95% confidence limits is 5.05.
[d]Diclofenac sodium product.
[e]Piroxicam product.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

$t = 2.57$, indicating no significant difference between the methods compared. The F-value (5.05) also showed that there is no significant difference between the precision of the proposed method and the official method. The proposed method can be used for quality control and routine analysis of the investigated drugs in bulk as well as in their dosage forms.

CONCLUSION

The proposed method is simple, accurate, and offers advantages of reagent availability and stability, less time consumption and high sensitivity compared to the official methods (based on HPLC). Although the color development of ferroin complex at room temperature requires 120 and 90 min in the reaction with diclofenac sodium and piroxicam, respectively, for completion, this can be shortened to 15 min by raising the temperature to $60^{\circ}C \pm 0.5^{\circ}C$. The proposed method is suitable for the determination of diclofenac sodium and piroxicam in pharmaceutical formulations without interferences from excipients such as starch and glucose or from common degradation products, suggesting applications in bulk drug analysis.

REFERENCES

1. Reynolds, J.E.F. *The Extra Pharmacopoeia "Martindale,"* 30th Ed.; The Pharmaceutical Press: London, 1982; 250.
2. Florey, K. *Analytical Profile of Drug Substances*; Academic Press: London, 1981; Vol. 15, 509–531.
3. *Supplement 2 to the United States Pharmacopeia*, 24th Rev.; *The National Formulary*, 19th Rev; The United States Pharmacopeial Convention: Rockville, MD, 2000.
4. Chen, X.; Xi, N.; Ge, S.; Sun, S. HPLC determination of piroxicam in human serum and its pharmacokinetic parameters. Yaoxue Xuebao **1986**, *21* (9), 692–697.
5. Ge, S.; Cheng, Q.; Wang, X.; Xi, N. High-performance liquid chromatography determination of piroxicam contents in piroxicam suppositories. Yaoxue Xuebao **1988**, *23* (1), 38–41.
6. Jiang, X.; Ge, S.; Wang, X.; Xi, N. High-performance liquid chromatography method for determining piroxicam in body fluids. Zhongguo Yaoli Xuebao **1991**, *12* (4), 381–384.
7. Maya, M.T.; Pais, J.P.; Morais, J.A. A rapid method for the determination of piroxicam in plasma by high-performance liquid chromatography. J. Pharm. Biomed. Anal. **1995**, *13* (3), 319–322.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

8. Chen, H.; Mi, Z.Y.; Liu, W.Z. Study on an high-performance liquid chromatography method for the determination of piroxicam in gels. Fenxi Kexuse Xuebao **2000**, *16* (6), 470–473.
9. Gaudiano, M.C.; Valvo, L.; Bertocchi, P.; Manna, L. RP-HPLC study of the degradation of diclofenac and piroxicam in the presence of hydroxyl radicals. J. Pharm. Biomed. Anal. **2003**, *32* (1), 151–158.
10. Kumar, Y.; Talwar, S.K.; Rathore, Y.K.S.; Sethi, P.D.; Jain, C.L. Spectrophotometric estimation of piroxicam in pharmaceutical formulations through cobalt(II) and copper(II) chelation. Indian Drugs **1990**, *28* (3), 139–141.
11. Sánchez-Pedreño, C.; Garcia, M.S.; Albero, M.I.; Rodriguez, J. Flow injection spectrophotometric determination of piroxicam. J. Pharm. Biomed. Anal. **1993**, *11* (10), 933–938.
12. Ródenas, V.; Garcia, M.S.; Sánchez-Pedreño, C.; Albero, M.I. Simultaneous determination of piroxicam and its major metabolite 5-hydroxypiroxicam in human plasma by derivative spectrophotometry. Analyst **1998**, *123* (8), 1749–1752.
13. Klopas, A.; Panderi, I.; Parissi-Poulou, M. Determination of piroxicam and its major metabolite 5-hydroxypiroxicam in human plasma by zero-crossing first-derivative spectrophotometry. J. Pharm. Biomed. Anal. **1998**, *17* (3), 515–524.
14. Amin, A.S. Spectrophotometric determination of piroxicam and tenoxicam in pharmaceutical formulations using alizarin. J. Pharm. Biomed. Anal. **2002**, *29* (4), 729–736.
15. Gowda, B.G.; Seetharamappa, J.; Melwanki, M.B. Indirect spectrophotometric determination of propranolol hydrochloride and piroxicam in pure and pharmaceutical formulations. Anal. Sci. **2002**, *18* (6), 671–674.
16. El Ries, M.A.; Mohamed, G.; Khalil, S.; El Shall, M. Spectrophotometric and potentiometric determination of piroxicam and tenoxicam in pharmaceutical preparations. Chem. Pharm. Bull. **2003**, *51* (1), 6–10.
17. Escandar, G.M. Spectrofluorimetric determination of piroxicam in the presence and absence of β-cyclodextrin. Analyst **1999**, *124* (4), 587–591.
18. Acuña, J.A.; De La Fuente, C.; Vázquez, D.M.; Tascón, M.L.; Sánchez-Batanero, P. Voltammetric determination of piroxicam in micellar media by using conventional and surfactant chemically modified carbon paste electrodes. Talanta **1993**, *40* (11), 1637–1642.
19. Paniagua, A.R.; Vazquez, M.D.; Tascon, M.L.; Sanchez-Batanero, P. Voltammetric determination of piroxicam after incorporation within carbon pastes. Electroanalysis **1994**, *6* (3), 265–268.
20. Gonzalez, M.; Vazquez, M.D.; Tascon, M.L.; Sanchez-Batanero, P. Contribution to the electrochemical behaviour study of piroxicam in different aqueous-organic media and electrodes by using polarographic and voltammetric techniques. Electroanalysis (N.Y.) **1994**, *6* (5–6), 497–504.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

21. Shinde, V.M.; Tendolkar, N.M.; Desai, B.S. Simultaneous determination of paracetamol and diclofenac sodium in pharmaceutical preparation by quantitative TLC. J. Planar Chromatogr.- Mod. TLC **1994**, *7* (1), 50–53.
22. Sun, S.W.; Fabre, H. Practical approach for validating the TLC assay of an active ingredient in pharmaceutical formulation. J. Liq. Chromatogr. **1994**, *17* (2), 433–445.
23. Chawla, J.L.; Sodhi, R.A.; Sane, R.T. Simultaneous determination of chlorzoxazone, paracetamol, and diclofenac sodium by different chromatographic techniques. Indian Drugs **1996**, *33* (4), 171–178.
24. Miller, R.B. High-performance liquid-chromatographic determination of diclofenac in human plasma using automated column switching. J. Chromatogr., Biomed. Appl. **1993**, *127* ((2) J. Chromatogr. 616), 283–290.
25. Kubala, T.; Gambhir, B.; Borst, S.I. Specific stability indicating high-performance liquid chromatography method to determine diclofenac sodium in raw materials and pharmaceutical solid dosage forms. Drug Dev. Ind. Pharm. **1993**, *19* (7), 749–757.
26. Li, K.; Zhao, F.L.; Yuan, Y.S.; Tan, L. Determination of diclofenac sodium in human plasma by RP-HPLC. Yaowu Fenxi Zazhi **1995**, *15* (5), 17–19.
27. Giagoudakis, G.; Markantonis, S.L. An alternative high-performance liquid-chromatographic method for the determination of diclofenac and flurbiprofen in plasma. J. Pharm. Biomed. Anal. **1998**, *17* (4–5), 897–901.
28. Lala, L.; D'Mello, P.M.; Naik, S.R. HPTLC determination of diclofenac sodium from serum. J. Pharm. Biomed. Anal. **2002**, *29* (3), 539–544.
29. Mathur, S.C.; Kumar, Y.; Prasad, P.B.N.; Rao, A.C.S.; Rathore, Y.K.S.; Gupta, S.C. A simple colorimetric estimation of diclofenac sodium in dosage forms. Indian Drugs **1994**, *31* (9), 447–448.
30. Prado, M.S.A.; Steppe, M.; Tavares, M.F.M.; Kedor-Hackmann, E.R.M.; Santoro, M.I.R.M. Method validation for diclofenac sodium in pharmaceutical by capillary electrophoresis. J. Capillary Electrophor. **1999**, *6* (3–4), 125–129.
31. Agrawal, Y.K.; Upadhyay, V.P.; Menon, S.K. Spectrophotometric determination of diclofenac sodium. Indian J. Pharm. Sci. **1988**, *50* (1), 58–60.
32. Agrawal, Y.K.; Shivramchandra, K. Spectrophotometric determination of diclofenac sodium in tablets. J. Pharm. Biomed. Anal. **1991**, *9* (2), 97–100.
33. Kamath, B.V.; Shivram, K.; Oza, G.P.; Vangani, S. Use of charge transfer complexation in the spectrophotometric determination of diclofenac sodium. Anal. Lett. **1993**, *26* (4), 665–674.
34. Kamath, B.V.; Shivram, K. Spectrophotometric determination of diclofenac sodium via oxidation reactions. Anal. Lett. **1993**, *26* (5), 903–911.
35. Botello, J.C.; Pérez-Caballero, G. Spectrophotometric determination of diclofenac sodium with methylene blue. Talanta **1995**, *42* (1), 105–108.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016