

the WHO New Delhi report<sup>10</sup>.

#### ACKNOWLEDGEMENTS

We would like to thank FIP Foundation, the Netherlands for the grant that made this study possible. S.C. Basak was a recipient of 2000 FIP Fellowship.

#### REFERENCES

1. Kumar, D., Raghuram, T.C., Radhaiah, G. and Krishnaswamy, K., *Pharmacoeconomics*, 1995, 7, 332.
2. Varma, D., Girish, M., Shafanas, K.K. and Renjit, P.B., *Indian J. Hosp. Pharm.*, 2000, 37, 49.
3. Lakshmi, P.K. and Gayathridevi, S., *Pharm. Prac. Res.*, 2002, 32, 24.
4. Lakshmi, P.K. and Basak, S.C., *Int. Pharm. J.*, 2002, 16, 22.
5. Basak, S.C., Raja, R., Ramesh, S. and Senthikumar, S., *Indian J. Hosp. Pharm.*, 2001, 38, 169.
6. Malik, V., Eds., In; *Drugs and Cosmetics Act, 1940*, 13th Edn., Eastern Book Company, Lucknow, 2001, 90.
7. Basak, S.C., Arunkumar, A. and Masilamani, K., *Int. Pharm. J.*, 2002, 16, 32.
8. Basak, S.C., *Indian J. Pharm. Educ.*, 2004, 38, 19.
9. Helper, C.D. and Strand, L.M., *Amer. J. Hosp. Pharm.*, 1990, 47, 533.
10. The role of pharmacist in the health care system, Report of a WHO Consultative Group (WHO/PHARM/94.569), New Delhi, 1988, 1.

---

## RP-HPLC Estimation of Gatifloxacin in Tablets

---

LAKSHMI SIVASUBRAMANIAN\* AND A. MUTHUKUMARAN

Department of Chemistry, Pharmaceutical Chemistry Unit, Vellore Institute of Technology,  
Deemed University, Vellore-632 014.

Accepted 22 April 2005

Revised 11 November 2004

Received 4 May 2004

**A simple, efficient and reproducible method for the determination of gatifloxacin in tablets has been developed using reverse phase high performance liquid chromatographic method. The elution was done using a mobile phase consisting of 0.01N Na<sub>2</sub>HPO<sub>4</sub> (pH 5.0) and acetonitrile (80:20% v/v) on Waters' Symmetry C<sub>18</sub> 4.6x150 mm analytical column with flow rate of 1 ml/min with detection at 292 nm. An external standard calibration method was employed for quantitation. The elution time was 1.6 min. The linearity range was 5-30 µg/ml for gatifloxacin.**

Gatifloxacin (GFN), 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinoline carboxylic acid is an advanced generation antibiotic<sup>1</sup>. This is used in the treatment of susceptible infections, including respiratory and urinary tract infections. It is official in Martindale's complete drug reference<sup>2</sup>. A survey of literature revealed a few high performance liquid chromatographic methods for its determination in human plasma using UV<sup>3,4</sup> and tandem mass detection<sup>5</sup>. No method has been so far reported for the estimation of GFN from pharmaceutical dosage forms. The present paper aims at reporting an isocratic RP-HPLC method for the determination of GFN in

tablets.

The apparatus used was Water's HPLC SPD chromatograph equipped with dual wavelength detector and model 7725i Rheodyne injector with 20 µl external loop. The column used was Waters' Symmetry C<sub>18</sub>, 4.6x150 mm analytical column, the elution was carried out isocratically at the flow rate of 1 ml/min using Na<sub>2</sub>HPO<sub>4</sub> (0.01 N) at pH 5.0 and acetonitrile 80:20% v/v as mobile phase. The detector was set at wavelength of 292 nm. Responses of peak areas were recorded and integrated using software.

GFN was obtained from Hetero Drugs Limited, Chennai. Acetonitrile HPLC grade and disodium hydrogen orthophosphate anhydrous AR grade were obtained from S. D. Fine

\*For correspondence

E-mail: lakshmiss@hotmail.com

TABLE 1: DETERMINATION OF GATIFLOXACIN IN TABLETS

Drug	Label claim/ tablet (mg)	Amount Found* (mg)	Recovery studies		
			Amount Added (mg/ml)	Amount recovered (mg/ml)	Percentage Recovery (%)
GFN	400	400.02±0.22	5	4.95	99.6
			15	14.85	99.2
			25	25.12	100.8

\*Mean of three determinations

Chemicals Ltd., Mumbai.

Standard stock solutions of the drug were prepared by dissolving 25 mg of GFN in mobile phase and made up to 25 ml with the same (1000 µg/ml). Working standard solution was prepared by diluting 1 ml of the stock solution to 10 ml with mobile phase (100 µg/ml). The gradient dilutions were prepared by taking 0.5, 1, 1.5, 2, 2.5 and 3 ml of solutions and made up to 10 ml with the mobile phase. 20 µl of the solution from each flask was injected two times. Calibration curve was constructed by plotting mean peak areas against the corresponding drug concentrations. The detector response was found to be linear in the concentration range of 5-30 µg/ml.

Twenty tablets (Gabact, Sarabhai Piramal Pharmaceutical Ltd., Vadodara) each containing 400 mg of gatifloxacin were finely powdered transferred a quantity equivalent to 25 mg in to a 25 ml volumetric flask and added 10 ml of methanol. Then diluted the volume with mobile phase and filtered through Whatman no.1 filter paper. One milliliter of the resulting solution was then diluted to 10 ml with mobile phase. From this 1, 2 and 3 ml samples were taken and their volume was made up to 10 ml each. A chromatogram of these solutions was obtained by injecting 20 µl of each sample into the chromatographic system. There was no interference from diluents and lubricants. The retention time of the drug was 1.6 min (fig. 1). Chromatographic parameters such as peak asymmetry ( $A_s$ ) and capacity factor ( $k$ ) were found to be 1.2 and 1.3, respectively. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.03 and 0.2 ng/ml respectively. Analytical recovery studies were carried out from a series of spiked concentrations added to the analysed dosage form (Table 1).

Analyzing five replicates of fixed amount of GFN

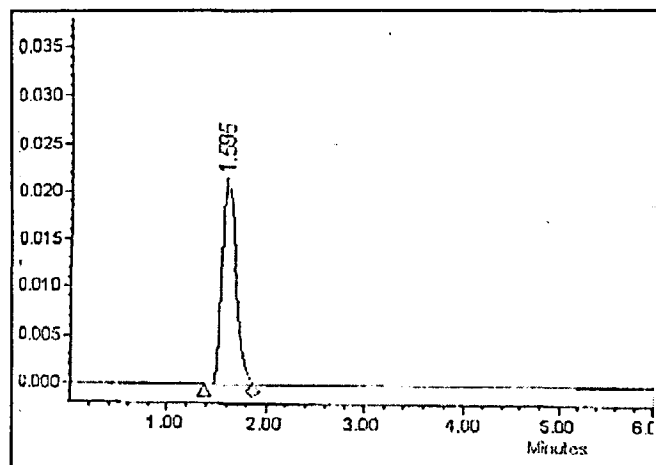


Fig. 1: Chromatogram of gatifloxacin

checked precision and accuracy of the proposed method. The precision of the method was calculated in terms of the relative standard deviation. Low values of relative standard deviation (0.56 %) and percentage errors at 95 % confidence limits (0.78) indicated high precision and accuracy of the proposed method. Hence the present method can be used for the routine analysis of GFN in formulation.

#### ACKNOWLEDGEMENTS

The authors are grateful to M/S Hetero Drugs Limited, Chennai for providing authentic sample of GFN.

#### REFERENCES

1. Budavari, S., Eds., In; The Merck index, 13th Edn., Merck & Co., Inc., Whitehouse Station, NJ, 2001, 4388.
2. Parfitt, K., Eds., In; Martindale, The Complete Drug Reference, 33rd Edn, the Pharmaceutical press, London, 2002, 3078J.
3. Overholser, B.R, Kays, M.B. and Sowinski, K.M, *J.Chromatogr. B. Anal. Tech. Biomed. Life. Sci.*, 2003, 798, 167.

4. Liang, H, Kays, M.B. and Sowinski, K.M, *J. Chromatogr. B. Anal. Tech. Biomed. Life. Sci.*, 2002, 772, 53.
5. Vishwanathan, K, Bartlett, M.G. and Stewart, J.T, *Rapid Commun. Mass Spectrom.*, 2001, 15, 915.

---

## Synthesis, Hydrolysis Kinetics and Pharmacodynamic Profile of Novel Prodrugs of Flurbiprofen

---

NEHA GAIROLA, DEEPIKA NAGPAL, SUNEELA S. DHANESHWAR\*, S.R. DHANESHWAR AND S.C. CHATURVEDI

Department of Pharmaceutical Chemistry, Bharati Vidyapeeth Deemed University,  
Poona College of Pharmacy, Erandwane, Pune-411 038.

Accepted 30 April 2005

Revised 2 December 2004

Received 1 July 2004

**Amide conjugates of flurbiprofen with various amino acid methyl esters were synthesized by Schotten-Baumann technique using prodrug concept. Their physico-chemical characterization was carried out by analytical and spectral methods. They were subjected to *in vitro* hydrolysis in hydrochloric acid buffer (pH 1.2), phosphate buffer (pH 7.4) and 80% human plasma (pH 7.4). The amides were screened for analgesic, antiinflammatory and ulcerogenic activities. They showed comparable analgesic and antiinflammatory activities with appreciable decrease in the ulcer index. Amide conjugate of flurbiprofen with phenylalanine was found to be the most active, even more than the parent drug flurbiprofen.**

Nonsteroidal antiinflammatory drugs (NSAIDs) form a class of therapeutic agents that are most widely used world over because of their analgesic, antipyretic and antiinflammatory effects. It is estimated that, currently, over 40 million people worldwide take NSAIDs daily. Although they are very effective agents, their gastrointestinal (GI) side effects are significant and serious with endoscopically visible gastroduodenal ulceration occurring in 30% patients after 12 weeks therapy. In fact, between 55% to 60% of the hospital admissions for GIT bleedings are related to NSAIDs and the treatment to GI adverse effects accounts for 30% of the total cost of the treatment. The study of Cioli *et al.*<sup>1</sup> suggests that the direct tissue contact of NSAIDs plays an important role in the production of GIT lesions and the reported literature confirms that gastric side effects of flurbiprofen, 2-(2-fluorobiphenyl-4-yl)-propionic acid are due to presence of -COOH group in the parent drug moiety<sup>2</sup>. In order to reduce this side effect, a structural modification like an amide or

ester, has to be carried out to mask COOH group temporarily. A strategic group attached to mask COOH group will not only protect the vulnerable group and stabilize the molecule but it will also direct the drug to its target site.

The rationale behind selection of amino acid as a promoity is as follows<sup>3-5</sup>. Important reporting has been made by Meyers *et al.* in 1979 that many amino acids possess marked antiinflammatory activity against gelatin induced hind paw edema in rats and have healing effect on gastric lesions produced by NSAIDs. So these prodrugs may have additional advantage of producing nontoxic amino acids as byproducts, which upon cleavage may give a synergistic antiinflammatory effect with NSAIDs along with gastro protective effect. By proper selection of amino acids, polarity, solubility profile and acid-base properties of a given drug molecule can be altered completely. The body's handling of nutritional substances suggests that use of a nutrient moiety as a derivatizing group might also permit more specific targeting for enzymes involved in the terminal phase of digestion along with modifying physico-chemical properties, which limit GI drug absorption. N-acylation of amines to give amide

---

\*For correspondence

E-mail: suneeladhaneshwar@hotmail.com