Acta Pharmaceutica Sciencia
48: 45-54 (2006)

Spectrophotometric Methods for the Determination of Lansoprazole in Capsules

Lansoprazolün Kapsüllerde Tayini için Spektrofotometrik Yöntemler

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Abstract

Three simple, sensitive and accurate spectrophotometric methods for the determination of lansoprazole (L) in capsules have been developed. These methods are based on the ion-pair complexes of L formed with tropaeolin OO (TPOO) and eriochrome black T (EBT) in tartaric acid medium and with bromothymol blue (BTB) in nonbuffer aqueous medium. The coloured products are extracted with chloroform and quantitatively measured at 411 nm with TPOO, at 505 nm with EBT, and at 415 nm with BTB. Beer's law was obeyed over the concentration ranges of 2-18, 2-21 and 4-23 $\mu g.mL^{-1}$ with molar absorptivites of 1.972×10^3, 1.591×10^3 and 1.485×10^3 L. $mol^{-1}.cm^{-1}$ for TPOO, BTB and EBT respectively. These methods have been successfully applied for the assay of drug in capsules. Statistical comparison of the results with the reference method showed good agreement and indicated no significant difference in accuracy and precision.

Key Words: Lansoprazole, spectrophotometry, ion-pair, tropaeolin OO, eriochrome black T, bromothymol blue

Introduction

Lansoprazole(L), (±)2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]-1*H*-benzimid-azole, is a proton pump inhibitor and has been used in the treatment of duodenal ulcers, gastric ulcers and reflux esophagitis (Nagaya *et al.*, 1990). Its chemical structure is given in Figure 1.

Several spectrophotometric methods have been described for the determination of lansoprazole in dosage forms, including, first and second order derivative spectrophotometry (He and Lin, 2000; Özaltın, 1999), based on their reactions with various reagents (Mashru and Banerjee, 1999; Meyyanathan *et al.*, 997; Moustafa, 2000; Puratchikodi *et al.*, 1999), and compensation and chemometric methods (Wahbi, 2002). The drug has been also determined by electrochemical methods (Al-Madi and Al-Zehouri, 2001; Belal *et al.*, 2004; Radi, 2003; Yardimci and Özaltin, 2001), HPLC (Avgerinos *et al.*, 1998; Bin, 1998; Singh and Singh, 1999), capillary electrophoresis (Dogrukol-Ak, 2001), and using supercritical fluid chromatography (SFC) (Del Nozal *et al.*, 2004).

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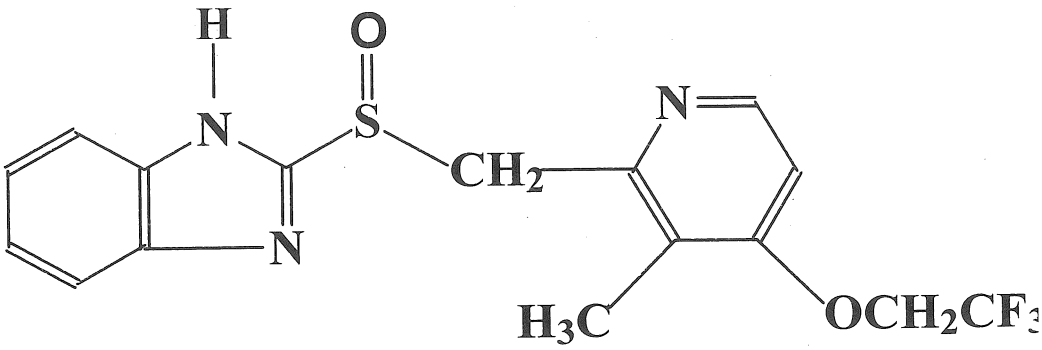

Figure 1. Chemical structure of lansoprazole.

Many chromatographic techniques have been applied for the analysis of L in biological fluids such as HP-TLC (Pandya *et al.*, 1997), HPLC (Aoki *et al.*, 1991 ; Borner *et al.*, 1997; Karol *et al.*, 1995; Landes *et al.*, 1992; Uno *et al.*, 2005; Ye *et al.*, 1998; Zaater *et al.*, 1999), LC-MS (Oliveira *et al.*, 2003), and LC –MS-MS (Miura *et al.*, 2004). Lansoprazole has been also assayed in biological fluids using a flow injection system (Yeniceli *et al.*, 2004). A literature survey revealed that, there was no ion-pair extractive spectrophotometric method for the assay of L in pharmaceutical formulations. The ion pair extractive spectrophotometry method is used commonly in pharmaceuticals (Önal *et al.*, 2005 ; Rahman *et al.*, 2004; Ramesh *et al.*, 2001).

The aim of this study is to develop three simple, rapid, accurate, sensitive, and inexpensive visible spectrophotometric methods for the determination of L in capsules as alternative methods to the ones published before. These methods were based on the ion-pair complexes of L formed in tartaric acid medium with tropaeolin OO (Orange IV)(TPOO) and eriochrome black T (EBT) and in nonbuffer aqueous medium with bromothymol blue (BTB).

Materials and Methods

Apparatus

(a) *UV-Vis spectrophotometer*: A Shimadzu (Tokyo, Japan) UV-160 A UV-visible spectrophotometer with 1 cm path length glass cells was used for absorbance measurements.
(b) *pH meter*: A WTW pH 526 digital pH Meter with a combined glass electrode (Wissenschaftlich-technische Werkstatten, Weillheim, Germany) was used for pH measurements.

Materials and Reagents

Lansoprazole (L) was kindly supplied by Sanovel Pharmaceuticals (İstanbul, Turkey). Lansor® capsules (Sanovel Pharmaceuticals, İstanbul) was purchased from local drugstore. Each capsule was labeled to contain 30 mg of L. Tropaeolin OO (TPOO) was obtained from The British drug houses ltd.(BDH) (London, England); eriochrome black T (EBT), bromothymol blue (BTB) and tartaric acid were purchased from E. Merck (Darmstadt, Germany). All chemicals and solvents used were of analytical grade. Distilled water was used for the preparation of all solutions.

Standard and Reagent Solutions

Standard stock solution of L was prepared as 0.1 mg/mL in chloroform (2.71×10^{-4} M). TPOO, EBT, and BTB were prepared as 2.43×10^{-3} M, 3.11×10^{-3} M and 3.41×10^{-3} M respectively, in distilled water (for TPOO and EBT) and in 5% alcohol (for BTB). Tartaric acid was prepared as 0.1 M in distilled water.

Procedure of Calibration Graph

Suitable aliquots of the stock solution of L (0.2-1.8 mL in the case of TPOO method, 0.2-2.1 mL in the case of BTB method, and 0.4-2.3 mL in the case of EBT method) were transferred into separate glass stoppered tubes. Then the solutions of the reagent (1 mL) and 0.5 mL 0.1 M tartaric acid (for TPOO and EBT methods) were added , mixed, and the volume of chloroform (extract solvent) was completed to 10 mL. Then the contents were shaken with a vortex mixer for exactly 3 min. The absorbances of the chloroform extracts were measured at 411 nm (for TPOO), at 415 nm (for BTB), and at 505 nm (for EBT) against a reagent blank prepared similarly. The calibration graph was constructed in each case, by considering the absorbance measured at six concentration levels of L and the regression equations were calculated.

Procedure for capsules

The content of ten capsules of Lansor® was emptied, weighed and powdered. An accurately weighed amount of powdered content equivalent to 30 mg of lansoprazole was transferred into a 50 mL calibrated flask. 25 mL of chloroform was added, and the mixture was shaken mechanically for 15 min and then completed to volume with chloroform and filtered. 1 mL of filtrate was put into a calibrated flask, and diluted to10 mL with chloroform. From this diluted final solution, 1 mL was taken and same procedure was applied as described above for the calibration graph. In all methods, the content of the capsules was calculated using the corresponding regression equation of the calibration graph.

Stoichiometric relationship

The stoichiometric ratio of the formed ion-pair complexes was investigated by Job's continuous variation method (Önal *et al.*, 2005). A 2.01×10^{-4} M solution of L was used with comparable solutions of the TPOO, BTB and EBT reagents. For each method, a series of solutions was prepared in which the total volume of the drug and reagent was kept at 3 mL, and the procedure was completed as described for the Calibration Graph.

Table1. Optical characteristics and statistical data

Parameters	TPOO	BTB	EBT
λ_{max}, nm	411	415	505
Beer's law range, µg/mL[a]	2-18	2-21	4-23
Molar absorptivity, L/mol.cm	1.972 x10^3	1.591 x10^3	1.485 x10^3
Sandel's sensitivity, µg/cm^2 per 0.001 A	0.1873	0.2322	0.2487
LOD, µg.mL^{-1}	0.221	0.379	0.216
LOQ, µg.mL^{-1}	0.735	1.264	0.721
Regression equation Y[b]			
Slope (a)	0.0541	0.0423	0.0454
Intercept (b)	-0.0065	0.0074	-0.0585
Correlation coefficient ®	0.9998	0.9996	0.9999

[a] Calculated from 4 determinations (n = 4)
[b] Y= aX + b, where X is the concentration in µg.mL^{-1}.

Table 2. Comparison of the results obtained by the proposed methods and the reported method for the analysis of L in capsules (each capsule contains 30 mg of L).

Statistical values	TPOO	BTB	EBT	Reported method (Özaltın, 1999)
Mean (mg)	30.11	30.09	30.19	29.99
Recovery ± SD, % (n = 6)	100.36 ± 0.12	100.3 ± 0.28	100.63 ± 0.27	99.96 ± 0.19
Confidence limits	30.11 ± 0.11	30.09 ± 0.25	30.19 ± 0.25	29.99 ± 0.17
t-test[a]	1.31	0.73	1.49	
F-test[a]	0.43	2.22	2.09	

[a] Theoretical values at 95% confidence limit; t = 2.57 and F = 5.05

Results and Discussion

Lansoprazole has a secondary and two tertiary amine groups which are easily protanated easly and forms yellow coloured ion-pair complexes in tartaric acid medium with TPOO and EBT and in nonbuffer aqueous medium with BTB. The absorption spectra of complexes which were quantitatively extracted into chloroform gave maxima at at 411 nm with TPOO, at 505 nm with EBT, and at 415 nm with BTB (Figures 2 and 3).

Optimum ion-pair complex formation conditions with respect to λ_{max}, pH range, solvent, extraction time, amount of the reagents, and stability of the complex formation were investigated.

In order to find the effect of pH on complex formation, phosphate buffer solutions (pH=2.5-5.4) and various concentrations of tartaric acid, oxalic acid, and hydrochloric acid solutions (0.05 M, 0.1 M, 0.5 M and 1M for each acids) were tried and in case of TPOO and EBT methods, 0.5 mL 0.1 M of tartaric acid solution was sufficient for maximum colour formation. In case of BTB method, phosphate buffer solutions (pH = 4-8) were tested, but the ion-pair showed the highest absorbance in nonbuffer solution.

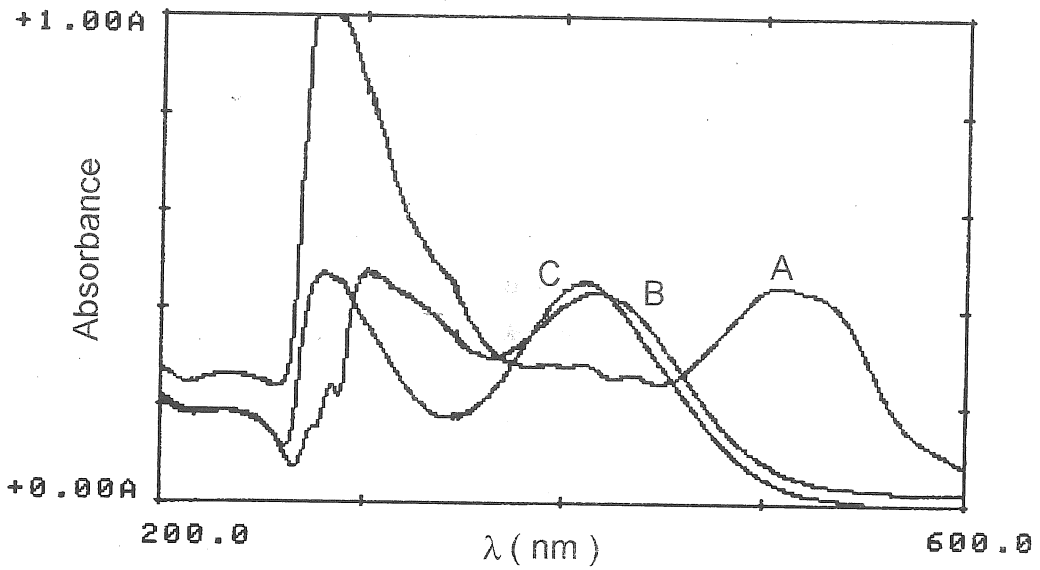

Figure 2. Absorption spectra of the L-ion-pairs in chloroform. (A) L-EBT, (B) L-BTB, (C) L-TPOO. Concentration of the L was 10 μg mL^{-1}.

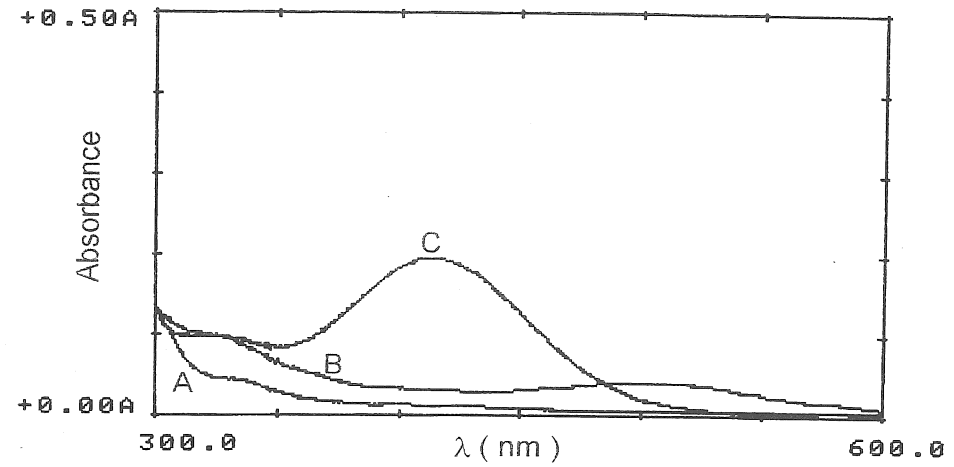

Figure 3. Absorption spectra of the reagents blank against chloroform. (A) L-EBT, (B) L-TPOO, (C) BTB.

To extract the ion-pair complexes from the aqueous phase, a number of immiscible organic solvents such as chloroform, carbontetrachloride, dichloromethane, benzene were examined, and chloroform was selected for its effective extraction. 3 min was used as an optimum shaking time for all three experimental methods. The absorbances of the extracts were observed to be stable for at least 6 h at room temperature in dark.

The effect of reagent concentration was examined separately by measuring the absorbances of the final solutions resulting from reaction mixtures containing a fixed concentration of L and various amounts of the reagents. It was found that 5-fold molar excess of TPOO and EBT and 6-fold molar excess of BTB were sufficient for the maximum absorbances (Figure 4).

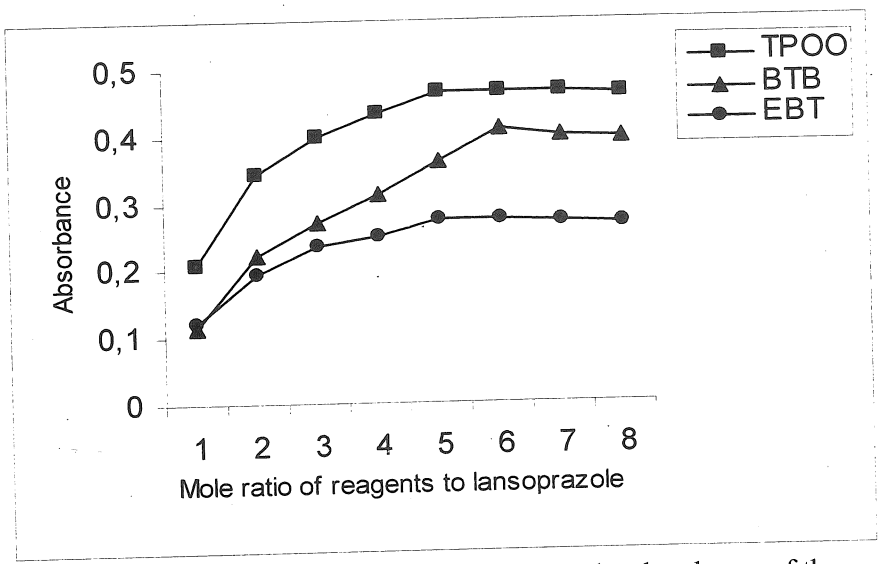

Figure 4. Effect of the reagent concentration on the absorbance of the reaction products.

The stoichiometry of ion-pair complexes of the drug with each of reagents was determined by Job's method of continuous variation. The results indicated that the molar ratio of drug to all reagents was 1:1(Figure 5).

Under the described experimental conditions, calibration graphs for three methods were constructed and Table 1 summarizes the values for Beer's law limits, molar absortivity, regression equation, correlation coefficients, Sandel's sensitivity, limit of detection (LOD), and limit of quantitation (LOQ) for each method. The data given in Table 1 indicated that linear relationships were found between the absorbance at λ_{max} and the concentration of the drug in the ranges 2-18, 2-21, 4-23 $\mu g.mL^{-1}$ for the methods using TPOO, BTB, and EBT respectively. The correlation coefficients were 0.9996 - 0.9999 indicating good linearity. The LOD and LOQ values were calculated from the calibration graphs using the equations, LOD = 3SD/*a*, where

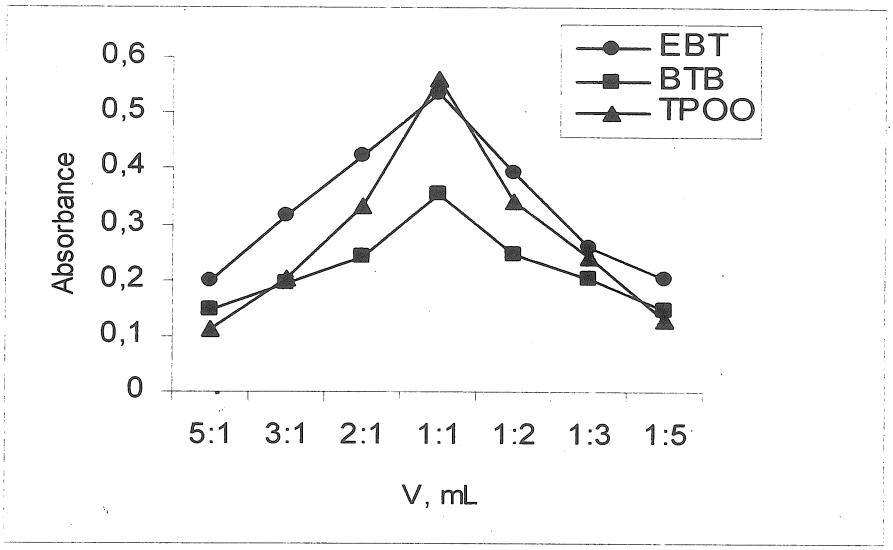

Figure 5. Job's method of continuous variations of L–reagent (drug/reagent = 2.01×10^{-4} M).

SD is the standard deviation of the intercept and *a* is the slope of the calibration graph (Kepekçi and Öztunç, 2005). As seen from Table 2, the mean recoveries were 100.3, 100.36 and 100.63 with the standard deviation values of 0.12, 0.28 and 0.27 for TPOO, BTB and EBT methods respectively. Interferences between different capsule additives and L has been worked previously (Özaltın, 1999) and no interference has been found .Also since formation of the ion pair complex with anionic dye need the presence of a basic group, lansoprazole, lacking a basic center can not interfere with additives (Al-Ghannam, 2006). The results of the proposed methods were compared statistically with those obtained by the reported method based on original UV spectrophotometry (Özaltın, 1999). No significant difference has been found in terms of the means and standart deviations using Student's t-test and F- test at 95% confidence level.

In conclusion, the proposed methods have the advantages of being simple, rapid, accurate, sensitive, inexpensive and suitable for routine quality control analysis of L in capsules.

Özet

Lansoprazol'ün kapsüllerde miktar tayini için üç basit, hızlı ve duyarlı metot geliştirildi. Bu metotlar lansoprazolün tropaeolin OO ve eriokrom siyahı T ile tartarik asitli ortamda ve brom timol mavisi ile tamponsuz sulu çözeltilerinde iyon çifti kompleks oluşumuna dayanmaktadır. Renklenen ürünler kloroforma ektre edildi ve maksimum absorbans değerleri TPOO ile 411 nm, EBT ile 505 nm ve BTB ile 415 nm de ölçüldü. L konsantrasyonunun doğrusal olduğu aralık TPOO, BTB ve EBT metotları için sırasıyla 2-18, 2-21 ve 4-23 ug.mL^{-1} ve molar absorbtiviteleri sırasıyla 1.972×10^3, 1.591×10^3 and 1.485×10^3 L. mol^{-1}.cm^{-1} dir. Bu metotlar lansoprazol içeren kapsüllere başarıyla uygulandı. İstatistiksel olarak referans mototla kıyaslandığında iyi bir uyum gösterdi ve doğruluk ve kesinlik bakımından bir fark göstermedi.

References

Al-Ghannam, S.M. (2006). A simple spectrophotometric method for the determination of beta-blockers in dosage forms. *J Pharm Biomed Anal.*40:151-156.

Al-Zehouri, J.M., Al-Madi, S.H. (2001). Polarographic method for the determination of lansoprazole in dosage form and spiked human urine. *Saudi Pharm. J.* 9: 99-105.

Aoki, I., Okumura M., & Yashiki, T. (1991). High performance liquid chromatographic determination of lansoprazole and its metabolites in human serum and urine. *J. Chromatogr.* 571 : 283-290.

Avgerinos, A., Karidas, T., Potsides, C., Axarlis, S. (1998). Determination of lansoprazole in biological fluids and pharmaceutical dosage by HPLC. *Eur. J. Drug Metab. Pharmacokinet.* 23: 329-332.

Belal, F., El-Enany, N., Rizk, M. (2004). Anodic polarographic determination of lansoprazole and omeprazole in pure form and in pharmaceutical dosage forms. *Yaowu Shipin Fenxi* 12: 102-109.

Bin, L. (1998). Determination of lansoprazole in raw material and its tablets by RP- HPLC. *Guangdong Yaoxueyuan Xuebao* 14: 247-249.

Borner, K., Borner E., Lode, H. (1997). Quantitative determination of lansoprazole in human serum by HPLC. *Chromatographia* 45: 450-502.

Del Nozal, M.J., Toribio, L., Bernal, J.L., Alonso C., Jimenez, J.J. (2004). Chiral separation of omeprazole and several related benzimidazoles using supercritical fluid chromatography. *J. Sep Sci.* 27: 1023-1029.

Dogrukol-Ak, D., Tuncel, M., Aboul-Enein, H.Y. (2001). The determination of lansoprazole in pharmaceutical preparation by capillary electrophoresis. *Chromatographia* 54: 527-530.

He, K., Lin, C. (2000). Determination of lansoprazole in capsules by UV spectrophotometry. *Zhongguo Yiyuan Yaoxue Zazhi* 20: 92-93.

Karol, M.D., Granneman G.R., Alexander, K. (1995). Determination of lansoprazole and five metabolites in plasma by high-performance liquid chromatography *J. Chromatogr. B Biomed. Appl.* 668: 182-186.

Kepekçi Ş.E., Öztunç A. (2005). Determination of maprotiline hydrochloride by ion-pair extraction using bromophenol blue and bromocresol purple. *Acta Pharmaceutica Turcica*, 47: 65-71.

Landes, B.D., Miscoria G., Flouvat, B. (1992). Determination of lansoprazole and its metabolites in plasma by high-performance liquid chromatography using a loop column. *J. Chromatogr.* 577: 117-22.

Mashru, R., Banerjee, S.K. (1999). Spectrophotometric determination of lansoprazole in bulk drug and dosage form. *East. Pharm.* 42: 125.

Meyyanathan, S.N., Raj, J.R.A., Suresh, B. (1997). Spectrophotometric determination of lansoprazole in its dosage forms. *Indian drugs* 34: 403-406.

Miura, M., Tada H., Suzuki, T. (2004). Simultaneous determination of lansoprazole enantiomers and their metabolites in plasma by liquid chromatography with solid-phase extraction. *J. Chromatogr. B* 804: 389-395.

Moustafa, A.A.M. (2000). Spectrophotometric methods for the determination of lansoprazole and pantoprazole sodium sesquihydrate. *J. Pharm. Biomed. Anal.* 22: 45-58.

Nagaya, H., Satoh, H., Maki, Y. (1990). Possible mechanism for the inhibition of acid formation by the proton pump inhibitor AG-1749 in isolated canine parietal cells. *J. Pharmacol. Exp. Ther.* 252:1289-1295.

Oliveira, C.H., Barrientos-Astigarraga, R. E., Abib, E., Mendes, G. D., Da Silva D.R., De Nucci, G. (2003). Lansoprazole quantification in human plasma by liquid chromatography-electrospray tandem mass spectrometry. *J. Chromatogr. B* 783: 453-459.

Önal, A., Kepekçi, Ş.E., Öztunç, A. (2005). Spectrophotometric methods for the determination of the antidepressant drug paroxetine hydrochloride in tablets. *Journal of AOAC International* 88: 490-495.

Özaltın, N. (1999). Determination of lansoprazole in pharmaceutical dosage forms by two different spectroscopic methods. *J. Pharm. Biomed.* 20: *Anal.* 599-606.

Pandya, K.K., Mody, V.D., Satia, M.C., Modi, I.A., Modi, R.I., Chakravarthy, B.K., Gandhi, T.P. (1997). High-performance thin-layer chromatographic method for the detection and determination of lansoprazole in human plasma and its use in pharmacokinetic studies. *J. Chromatogr. B* 693: 199-204.

Puratchikodi, A., Krishnamoorthy, G., Jaykar, B., Valarmathy, R. (1999). Spectrophotometric method for the determination of lansoprazole. *East. Pharm.* 42: 127.

Rahman, N., Ahmad Khan, N., Hejaz Azmi S.N.(2004). Extractive spectrophotometric methods for the determination of nifedipine in pharmaceutical formulations using bromocresol green, bromophenol
blue, bromothymol blue and eriochrome black T. *Farmaco.* 59: 47-54.

Ramesh, K.C., Gowda, B.G., Melwanki, M.B., Seetharamappa, J., Keshavayya, J.(2001). Extractive spectrophotometric determination of antiallergic drugs in pharmaceutical formulations using bromopyrogallol red and bromothymol blue. *Anal Sci.* 17: 1101-3.

Radi, A. (2003). Anodic voltammetric assay of lansoprazole and omeprazole on a carbon paste electrode. *J. Pharm. Biomed. Anal.* 31:1007-1012.

Singh, D.K., Singh, R.A. (1999). Determination of lansoprazole by high performance thin layer chromatography in pharmaceuticals dosage forms. *East. Pharm.* 42: 113-115.

Uno, T., Yasui-Furukori, N., Takahata, T., Sugawara K., Tateishi, T. (2005). Determination of lansoprazole and two of its metabolites by liquid-liquid extraction and automated column-switching high performance liquid chromatography: application to measuring CYP2C19 activity. *J. Chromatogr. B* 816: 309-314.

Wahbi, A.A.M., Abdel-Razak, O., Gazzy, A.A., Mahgoub H., Moneeb, M.S. (2002). Spectrophotometric determination of omeprazole, lansoprazole and pantoprazole in pharmaceutical formulations. *J. Pharm Biomed. Anal.* 30: 1133-42.

Yardimci, C., Ozaltin, N. (2001). Electrochemical studies and differential pulse polarographic analysis of lansoprazole in pharmaceuticals. *Analyst* 126: 361-366.

Ye, L.M., Li, Z.W., Hong Z., Qian, G.S. (1998). Determination of lansoprazole by direct injection of plasma and high performance liquid chromatography with column switching. *J. Chin. Pharm. Sci.* 7: 197-200.

Yeniceli, D., Dogrukol-Ak D., Tuncel, M. (2004).Determination of lansoprazole in pharmaceutical capsules by flow injection analysis using UV-detection. *J. Pharm Biomed. Anal.* 36: 145-148.

Zaater, M.F., Najib N., Ghanem, E. (1999). A rapid high-performance liquid chromatographic determination of lansoprazole in human serum. *Saudi Pharm. J.* 7: 123-129.

Received: 02.01.2006
Accepted: 08.05.2006