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Short communication

Determination of lansoprazole in pharmaceutical capsules by flow injection analysis using UV-detection

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Abstract

The direct determination of lansoprazole by using a flow injection analysis (FIA) with UV-detection and its application to the pharmaceutical capsules is described, in this study. The best carrier solvent was found to be 0.01 M NaOH and it was determined at optimum conditions such as flow rate of 1 ml min^{-1} and wavelength of 292 nm. Examining the repeatability of the method that was found to be 1.72% for intra-day and 2.13% for inter-day precision using the 8.01×10^{-6} M lansoprazole concentration has validated the method. The linear range of the method was 5.4×10^{-6} to 5.4×10^{-5} M. The limit of detection and quantification was found to be 5.8×10^{-7} and 1.7×10^{-6} M, respectively. The proposed method was applied to the pharmaceutical capsules and very good results obtained. Thus, the FIA method for the quantification of lansoprazole can be proposed as a cheap, rapid, easy, accurate, and precise method for the routine determination in pharmaceutical preparations.

Keywords: Lansoprazole; Flow injection analysis; Pharmaceutical analysis

1. Introduction

Lansoprazole (LNS) {2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl] 1H benzimidazole} is a substituted benzimidazole with antisecretory and antiulcer activities [1]. It is effective in treating various peptic diseases, especially those resistant to treatment with histamine H_2 receptor antagonists, therefore it is successfully used for the treatment of duodenal ulcer, gastric ulcer, reflux oesophagitis and Zollinger–Ellison syndrome [2].

The methods for the determination of LNS in pharmaceutical preparation such as HPTLC [3], HPLC [4,5], spectrophotometry [6,7], capillary electrophoresis [8], polarography [9], adsorptive stripping square-wave and anodic voltammetric assay [10,11] have been reported. According to our best of knowledge, there is no flow injection analysis (FIA) covering the determination of LNS appeared in the literature.

The aim of this study is to develop a simple and validated FIA method for the determination of LNS in pharmaceutical preparations. The validity of the method was tested regarding to precision, linearity, accuracy and the limit of detection and quantification and all the results were evaluated statistically by common statistical tests.

2. Experimental

2.1. Chemicals

The standard material (99.6%) was generously supplied by Sanovel Ilaçları (Istanbul, TR). All the other chemicals used in the experiments were the products of Merck Co. (Darmstat, G) and they were all of analytical grade. Double distilled water was prepared in our laboratory employing all glass apparatus and it was used for the preparation of the solutions. The commercial preparation of LNS, Lanzedin® of Biopharma A.Ş. (Istanbul, TR) was purchased from a local drugstore. It has encapsulated enteric-coated pellets and it contains 30-mg active material.

2.2. Apparatus

An HPLC consisting of a model LC 6A pump, a model of SPD-10A UV-Vis variable wavelength detector, and a model of CR 7A integrator all from Shimadzu (Kyoto, J) were

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used for FIA. Standard solutions and samples were injected to a Rheodyne model of with 20-μL loop injection port from Cotati Co. (California, USA) by 22-G injection needle. The flow rate was 1.0 ml min^{-1}. Carrier solvent was always filtered from a glass filter and sonicated with a model of B-220 from Branson (California, USA) sonicator. Common spectrophotometric studies were conducted using UV-2401 PC Spectrophotometer from Shimadzu (Kyoto, J).

2.3. Preparation of solutions

Carrier solvent was 0.01 M NaOH. Dissolving 0.28 mg ml^{-1} in the carrier solvent, standard stock solution of LNS was prepared. Then, the dilutions of LNS for the calibration studies in the range of 5.4×10^{-6} to 5.4×10^{-5} M were prepared by pipetting the necessary amount of standard solution of LNS.

2.4. Application of method to LNS capsules

Ten Lanzedin® capsules, each containing 30 mg LNS, were accurately weighed, emptied carefully and the mass of the collected content was determined. The empty shells were weighed and the net fill weight of each capsule was calculated. The capsule contents were finely powdered in a mortar. A sufficient amount of pellet equivalent to the average weight of capsule content was accurately weighed, transferred to a 50-ml flask and 0.01 M NaOH was added to dissolve the active material. It was magnetically stirred for 10 min and made up to the volume with carrier solvent. Then, the solution was centrifuged at 5000 rpm for 10 min. The supernatant was diluted with the related solutions to achieve the flow injection analysis.

3. Results and discussion

LNS is an acid labile medicine and has therefore been formulated as encapsulated enteric-coated pellet formulation to prevent from gastric decomposition and improve systemic bioavailability [2]. The stability of LNS has been shown previously [7,10], therefore 0.01 M NaOH solution was choosen as a carrier solvent and a dissolution medium to provide enough stability for the experiments. This solution has also been used to dissolve LNS in the previous reports [6–9,11].

The optimum instrumental parameters were investigated for an available analysis regarding peak morphology and other advantages in the 0.01 M NaOH solution. Since the maximum absorbance of LNS in this solution appears at 292 nm, the detection was performed at this wavelength during the FIA experiments. The effect of flow rate on the peak responses was studied in the range of 0.4–3.0 ml min^{-1}. The flow rates in the range of 0.6–1.0 ml min^{-1} could be usable, but peak tailing was observed at higher flow rates than 1.0 ml min^{-1}. Optimum flow rate exerting the peak symmetry to provide suitable integration output was obtained at 1.0 ml min^{-1} and employed, in the rest of experiments.

3.1. Peak area precision

The precision of the peak area of LNS was examined by using constant concentration of 8.01×10^{-6} M LNS by injecting eight times in the consecutive days. The peak area responses of LNS (mean value ± S.D.; $n = 8$ for each set) were found to be, in turn, 109,341 ± 2378, 109,563 ± 2670, 109,332 ± 1881 for intra-day. Inter-day repeatability was calculated by pooling the peak area responses of the intra-day (mean value± S.D.; total sets $n = 24$) as 109,412 ± 2333. The R.S.D.% value is about 2% exhibiting the sufficient method precision and this limit is accepted as an analytical points' of view.

3.2. Linearity

Calibration equations were constructed employing the peak area responses versus LNS concentration in the range of 5.4×10^{-6} to 5.4×10^{-5} M injecting six different concentrations as three sets. The flow diagram of LNS for calibration studies is shown in Fig. 1. Calibration curves showed good linearity in the mentioned range as demonstrated in Table 1.

Certain analytical parameters such as limit of detection (LOD) and limit of quantification (LOQ) values were calculated computing the processed of integrated peak from flow diagram. LOD and LOQ values were estimated as [(standard deviation of repeatability)/slope of regression equation)] by multiplying with 3.3 and 10, respectively. They were found to be 5.8×10^{-7} M for LOD and 1.7×10^{-6} M for LOQ.

3.3. Accuracy of the method

LNS has been produced as an encapsulated micropellet form. The pharmaceutical form of capsule is prepared

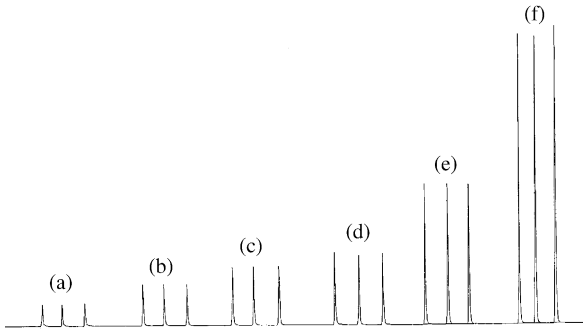

Fig. 1. Calibration runs for the determination of LNS. Triplicate signals for each LNS reference solution from left to right: (a) 5.4×10^{-6} M; (b) 7.6×10^{-6} M; (c) 1.08×10^{-5} M; (d) 1.30×10^{-5} M; (e) 2.59×10^{-5} M; (f) 5.40×10^{-5} M.

Table 1
Calibration results of LNS flow injection determination related with statistical analysis pumping through 1.0 ml min^{-1} flow rate and at 292 nm detection wavelength

	Intra-day			Inter-day
	Day 1 ($n = 6$)	Day 2 ($n = 6$)	Day 3 ($n = 6$)	Whole days ($n = 18$)
Slope	1.32×10^{10}	1.34×10^{10}	1.33×10^{10}	1.33×10^{10}
Intercept	6964	5664	7052	6560
Correlation coefficient	0.9997	0.9999	0.9998	0.9998
S.D. of regression equation	3049	6018	11610	15980
R.S.D.% of slope	0.56	1.09	2.11	1.68
Confidence limits ($P < 0.05$)	$\pm 6.11 \times 10^{7}$	$\pm 1.21 \times 10^{8}$	$\pm 2.33 \times 10^{8}$	$\pm 9.41 \times 10^{7}$

Table 2
The results of method accuracy ($n = 6$)

Added LNS (M)	Found LNS (M) (mean ± S.D.)	Recovery (%)	Accuracy (%)	R.S.D.%
5.4×10^{-6}	$6.2 \times 10^{-6} \pm 2.0 \times 10^{-7}$	114.4	14.44	3.22
1.08×10^{-5}	$1.2 \times 10^{-5} \pm 2.4 \times 10^{-7}$	108.3	8.33	2.03
5.4×10^{-5}	$5.8 \times 10^{-5} \pm 1.1 \times 10^{-6}$	106.8	6.85	1.85

by mixing the acid protective micropellets with iron oxide, titanium dioxide and sugar. The intermediate precision which corresponds the effect of the ingredients in the pharmaceutical materials was examined by preparing a synthetic ingredient composition. To achieve the test, certain amount of LNS solutions (5.4×10^{-6}, 1.08×10^{-5} and 5.4×10^{-5} M) was spiked into each tube ($n = 6$), which contains synthetic mixture of capsule excipient, and they were left for a while. Then, LNS solutions were recovered by adding definite volume of carrier solvent and the method accuracy was determined using calibration equation of the pooled plot. The results are illustrated in Table 2. The accuracy was evaluated as percentage error [(found concentration-spiked concentration)/spiked concentration] × 100%, and precision was evaluated by the coefficient of variation (CV%, R.S.D.% [(S.D./mean) × 100]). The acceptance criteria are not higher than 15% deviation from the nominal value for accuracy and not more than 15% CV for precision [12]. It was found that these additives had no effect on the accuracy of the LNS determination and accuracy and precision results obtained is in accordance with these criteria.

3.4. Application of the method to LNS capsules

The application of the developed method for the determination of LNS was performed in the encapsulated micropellet containing 30-mg active material. Sharp peaks of LNS appeared with no interference originating from the matrix and other ingredients and carried the characteristics of standard LNS. The method gives a clear picture of the total drug present in pharmaceutical capsules found to be 30.4 ± 1.1 (mean ± S.D., $n = 6$). The content of a capsule is also being in the limits of official requirements [13].

As it was concluded that, FIA has certain advantages regarding simplicity, versatility, high sampling frequency, and degree of automation and low expense of reagents and samples providing the technique suitable for satisfying the increasing demand for control and routine analysis in many fields of analytical chemistry [14]. This method is considerable time saver when comparing to the previous methods such as the spectrophotometric, chromatographic, capillary electrophoretic and electrochemical methods [3–11] and has the superiority at least ninety injections per hour which is very appreciable number for routine analysis laboratories. It also offers simple instrumentation and lower running cost. The sample preparation step is easy and provides LNS monitoring without affecting the inactive ingredients. The injected sample volume is as low as 20 μl. The linear range is comparable to previously reported methods [6,7,9,11]. Although the chromatographic methods have better sensitivity than FIA, sensitivity in this method is better than capillary electrophoresis. Main disadvantage of the method is the unsuitable selectivity in the complex biological matrix such as plasma or urine and cannot be applied without certain processes of the LNS from the matrix.

The FIA method progressed with this study can be practically used for the direct determination of LNS active ingredients in control laboratories as rapid, accurate, reliable, and sensitive method.

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