RESEARCH ARTICLE

Spectrophotometric Estimation of the Lansoprazole by Oxidative Coupling Reaction with 2, 4-Dinitrophenyl Hydrazine

Saba H. Jamel[1], Intidhar D. Sulaiman[2]

Department of Chemistry, College of Education for Pure Science (Ibn Al-Haitham), University of Baghdad, Baghdad, Iraq

Received: 05th September, 2020; Revised: 10th October, 2020; Accepted: 19th November, 2020; Available Online: 25th March, 2021

ABSTRACT

A simple, accurate, sensitive, and low-cost technique was advanced to measure the optical spectrum to the determination of lansoprazole in pure form and dosage forms. The method relies on the oxidation of the reagent 2,4-dinitrophenylhydrazine (2,4-DNPHz) with potassium periodate (KIO_4) and coupling with the lansoprazole (LPZ) in the alkaline medium to form a stable with reddish-brown colored dye with a maximum greatest absorption at 484.5 nm. The reaction is carefully completed when optimizing the variable affecting it. The concentration range from 1-30 µg/mL obegs Beer's law and the molar absorptivity value of (13260.132) L/mol.cm. Detection limit was (0.1266 µg/mL) and Sandell's sensitivity value 0.0278 µg/cm^2. The method has been successfully applied to the estimation of lansoprazole in dosage forms.

Keywords: Lansoprazole, Oxidative coupling, Pharmaceutical preparations, Spectrophotometric.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.1.9

How to cite this article: Jamel SH, Sulaiman ID. Spectrophotometric Estimation of the Lansoprazole by Oxidative Coupling Reaction with 2, 4-Dinitrophenyl Hydrazine. International Journal of Drug Delivery Technology. 2021;11(1):52-57.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Lansoprazole is a substituted benzimidazole, [LPZ: chemically known 2-[3- methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl] methyl]sulfinylbenzoimidazole (scheme1). molecular formula is $C_{16}H_{14}F_3N_3O_2S$ and M.wt 369.37gm/mol].[1,2] The proton pump inhibitors (PPIs) are unstable at a low pH.[3] Additionally, PPIs are chemosensitizing cytotoxic drugs, and active against various human tumor cells.[4-6] During the past years, many different analytical methods have been devised and developed to determine the LPZ concentration in various samples of pharmaceutical preparations. These include spectrophotometric and potentiometric methods,[7] Colorimetric,[8] Potentiometry,[9] UV-visible spectrophotometric determination.[10,11] Liquid Chromatography with tandem mass spectrometry (LC-MS/MS),[12-14] reverse phase-high performance liquid chromatography (RP-HPLC),[15,16] chiral LC- MS,[17,18] liquid chromatography with diode array detection (LC-DAD),[19] reverse phase ultra-fast liquid chromatography,[20] LC-chemometric techniques,[21] LC-UV and LC-MS,[22] Capillary zone electrophoresis.[23] The present study aims to recommend a direct and sensitive optical spectrophotometry for estimating the substance lansoprazole by means of the mono-variable method in its pure form and in pharmaceutical preparations. The method depends on oxidations of 2,4-Dinitrophenylhydrazine (2,4-DNPHz) by metal periodate and reaction with lansoprazole in alkali medium to make a colored product.

Experimental

Instruments

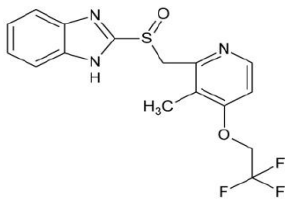
APG instrument, UV-VIS spectrophotometer model T80 (U.K) with (1 cm) matched quartz cells was used for the absorbance measurements. Sartorius BL (210) S electronic balance was used for weighing the samples.

MATERIALS AND METHODS

All chemicals were of analytical reagent grade and were obtained from BDH and the pancreas. The state company supplied standard lansoprazole powder for Drug Industries and Medical Appliances, Samara-Iraq (SDI), India, and United Kingdom (UK).

Lansoprazole Stock Solution (1000 µg/mL)

The standard stocking solution for the (LPZ) was prepared by weighing 0.1 g of pure drug completely precisely and then dissolved in 10 mL of methanol. It was relocated to a 100 mL volumetric flacon and the volume was completed to the mark with methanol.



Scheme 1: The structural formula of lansoprazole

**Author for Correspondence: jamelsaba818@gmail.com*

Lansoprazole Working Solution (100 µg/mL)

Prepared by diluting (2.5 mL) of the stock solution to 25 mL in a volumetric flask with methanol.

2,4-Dinitrophenyl hydrazine solution (2, 4-DNPHz) (1×10^{-3}) M

It was prepared by dissolving (0.0198)g of (2,4-DNPHz) in 2 mL of concentrated sulfuric acid (H_2SO_4), it was relocated to a 100 mL volumetric flacon and the volume was completed to the mark with distilled water.

Potassium Periodate Solution (4×10^{-3}) M

The KIO_4 solution is prepared by dissolving (0.092) g in an appropriate volume of distilled water and relocated to a 100mL volumetric flacon, and completing the mark limit distilled water.

Sodium Hydroxide Solution (~3) M

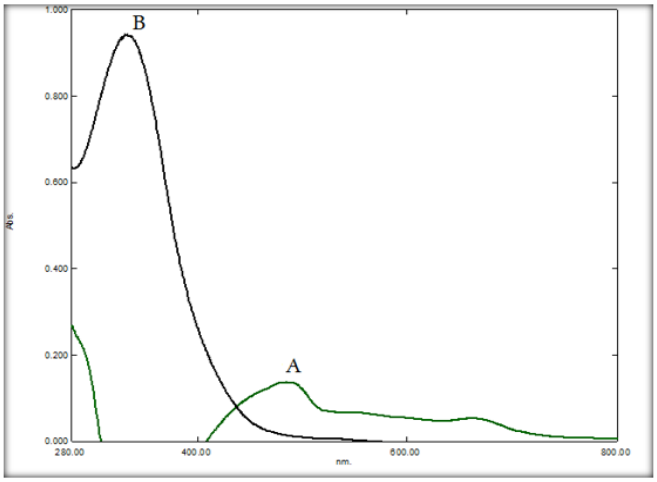
A total of 12 g of NaOH dissolve in a convenient volume of distilled water and relocated to a 100 mL volumetric flacon and completing the mark with distilled water.

Lansoprazole Capsules Solution (600 µg/mL)

The contents of 10 capsules were emptied after vacateing the dosage form mixing them well, then weighing carefully, and the average weight and the quantity taken from the powder are 0.3529 g, and 0.3624 g (containing 30 mg of the drug lansoprazole) of lansoprazole-30mg and lancid-30 mg respectively was accurately weighted, then about dissolved in 15 mL of methanol and stirred for 10 minutes to ensure dissolution of the drug complete, then relocated to volumetric flacon 50 mL, the complete the mark limit with methanol we obtain to 600 µg/mL (LPZ). The solution is filtered to avoid any remaining insoluble or suspended substance-using filter paper No.41 before starting to use the solution. The working solution (100 µg/mL) was freshly prepared and analyzed via the recommended procedure.

General Recommended Procedure for Standardization

In a series of 10 mL volumetric flacons, 1 mL of the standard solution LPZ containing 10–300 µg, 1 mL of 1×10^{-3}M 2,4-DNPHz and 1 mL of 4×10^{-3}M potassium periodate were added to every flacon. The resulting oxidized product was coupled with LPZ followed by 1 mL of 3M sodium hydroxide to every flacon with shaking. After 4 minutes, the solutions were making up to the mark with distilled water, mixed well and left to stand for 10 minutes. The absorbance of reddish-brown colored chromogen was measured at 482.5 nm against the reagent blank.



Wavelength (nm)

Figure 1: Absorption spectra of (a) 10 µg/mL LPZ versus reagent blank, (b) blank solution versus dissolvent under initial test conditions

RESULTS AND DISCUSSION

Absorption Spectra for Primary Test

The method's primary test involved oxidation of 2,4-dintrophenyhydrazin with potassium periodate and reaction with LPZ in an alkaline medium to form a colored product. The test was done by adding 1 mL of 100 µg.mL^{-1} (LPZ), 1 mL of 1 x 10^{-3}M 2, 4-DNPHz, 1 mL of 3 x 10-^{3}M potassium periodate, and then 1 mL of 1M sodium hydroxide in (10) mL volumetric flacon with shaking. After which, the Contents were diluted to the mark with distilled water and mixed well. The absorption was recorded for the stained colored product formed, and the resulting spectrum showed the highest absorption at the maximum wavelength (λ_{max}) versus the reagent blank. Figure 1 shows that the maximum absorption was obtained at a wavelength of 484.5 nm

Optimization of Reaction Variables

The different variables related to the composition of the colored product have been studied by varying the parameters one at a time and controlling all others fixed and optimum conditions have been selected.

Impact of 2, 4-DNPHz Concentration

The impact of the concentration of (2,4-DNPHz) on the absorbance of the colored product has been investigation in the range between 6×10^{-4} – 5×10^{-3}M Figure 2. It has been found that the maximum absorption of the reddish brown color was achieved with 1×10^{-3}M of the reagent. Above that value a decrease in absorbance was observed. Therefore, 1 mL of 1×10^{-3}M was used during the subsequent work.

Impact of Potassium Periodate Concentration

The study for potassium periodate (KIO_4) concentration showed that the reaction depended on KIO_4 as an oxidizing agent. The

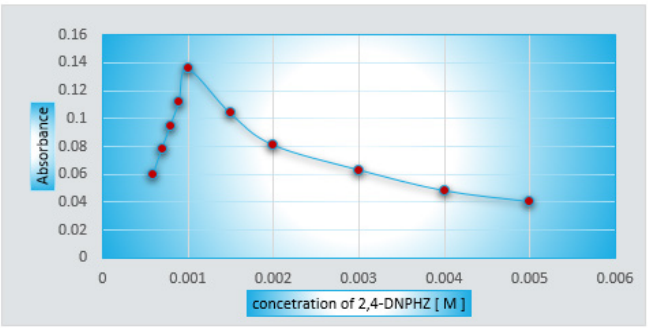


Figure 2: The impact of the concentration of 2, 4-DNPHz on the color development in the determination of 10 µg/mL LPZ.

highest absorption was attained when the concentricity of KIO_4 was 4×10^{-3}M. A reduction this value a decrease in the absorbance reading occurred Figure 3. Therefore, 1 mL of 4×10^{-3}M was used during the subsequent work.

Impact Different Bases

The impact of different alkaline solutions with a concentration of 1M on the absorption intensity of the colored dye formed was investigated. Four types of bases, namely, NaOH, KOH, Na_2CO_3, and NH_4OH were tested, and the results were listed in Table 1. As can be seen it was found that sodium hydroxide shows the maximum absorption intensity of the colored product. Therefore it was selected for subsequent work.

Impact of Sodium Hydroxide Concentration

The impact of sodium hydroxide concentration on absorption measured for consisting colored product was investigated through the use of 1-mL of different concentrations of NaOH solution ranged between (0.5–5.0)M. The results are shown in Figure 4, which shows that add of 1-mL of 3M (NaOH) exhibited a better absorbance. Above this concentration, the absorbance value decreased. Therefore, 1-mL of 3M NaOH was used in all subsequent experiments.

Impact of Coupling Reaction Time

The opimumt time for a reaction of a fixed concentration of 10 µg/mL (LPZ) with 2,4-DNPHz was studied in the presence of the KIO_4 in a alkaline medium. The bsorbance values were recorded in different intervals period and reached 25 minutes. The oxidative coupling reaction is complete at 4 minutes, which are listed in Table 2.

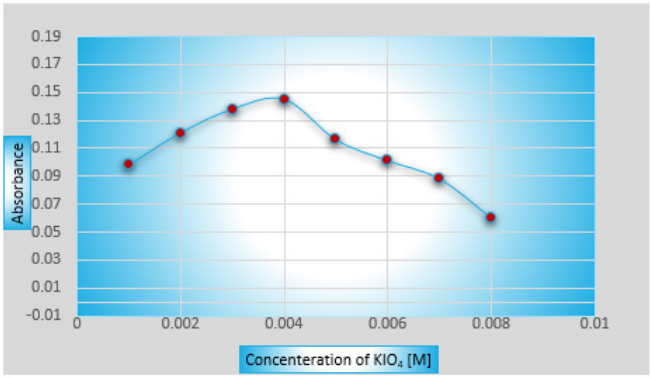


Figure 3: The impact of potassium periodate concentration on the color development in the determination of 10 µg/mL LPZ.

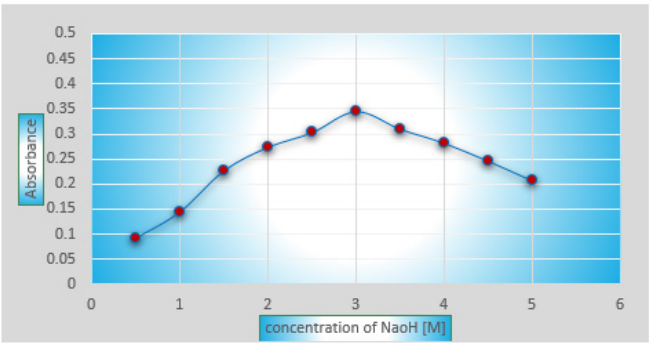


Figure 4: The impact of sodium hydroxide concentration on the color development in the determination of 10 µg/mL (LPZ)

Impact of Reagents Mixing Order

The impact of different orders of components on chromogen formation was investigated by changing the sequence of the addition of the reactants four times, as shown in Table 3. From the results shown, it is obvious that mixing order number one was recommended as it resulted in obtaining a maximum absorbance was used in all subsequent work.

Stability

The stability of the colored complex formed from the LPZ intemtion with the 2,4-DNPHz was studied by measuring the absorbance at various. It was observed that the optimum time stabilization of the colored is 10 minutes in the recommended general procedure and that the color of the produced complex is stable for 60 minutes, as shown in Figure 5.

Final Absorption Spectra

The absorbance spectrum for reddish-brown product, created from the treatment of (LPZ) 10 µg/mL with 2,4-DNPHz in the existence of KIO_4 in alkaline medium under the optimum conditions was recorded and showed maximum absorption at 482.5 nm versus the reagent blank as shown in Figure 6.

Table 1: The impact of different bases on coupling reaction

Base (1M)	*Absorbance*
NaOH	0.145
KOH	0.049
Na_2CO3	0.005
NH_4OH	0.018

Table 2: The impact of coupling reaction time

Time (min)	*Absorbance*
0	0.287
1	0.306
2	0.329
4	0.345
5	0.334
7	0.322
10	0.313
12	0.301
15	0.294
20	0.279
25	0.261

Table 3: Variance of absorbance with the change of reactants addition order in the estimation of 10 µg /mL (LPZ)

NO.	*Sequence*	*Absorbance*
1	Drug+Reagent+Oxidizing agent+Base	0.350
2	Reagent+Oxidizing agent+Drug+Base	0.302
3	Reagen+Drug+Oxidizing agent+Base	0.276
4	Drug+Base+Reagent+Oxidizing agent	0.003

Calibration Curve and Analytical Data

Using the optimum experimental condition, the measured absorbance values at 482.5 nm was plotted against the different standard concentrations of LPZ to create a calibration curve. The plot linearity obtained from the LPZ were at a range concentration of (1-30) µg/mL as shown in Figure 7. The statistical processors of the analytical data are concise in Table 4.

Structure of the Product

Job's method[24] and mole ratio method[25] was used in the determination of the stoichiometry of the reaction between (LPZ) and 2,4-DNPHz. The obtained results Figures 8 and 9 showed that 1:1 lansoprazole to 2,4-DNPHz ratio is obtained. This mechanism was proposed of the reaction between LPZ and 2,4- DNPHz can be represented in Scheme 2.

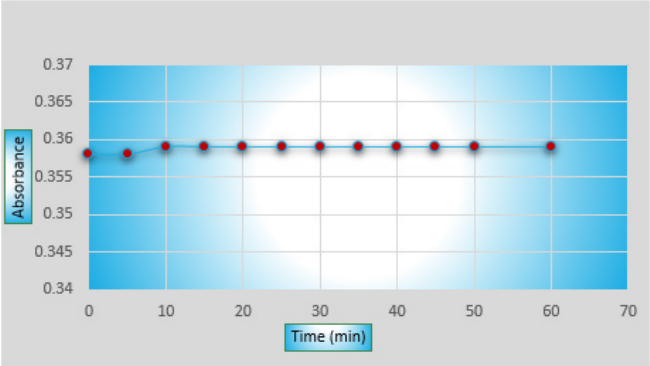


Figure 5: The stability of the colored product with time

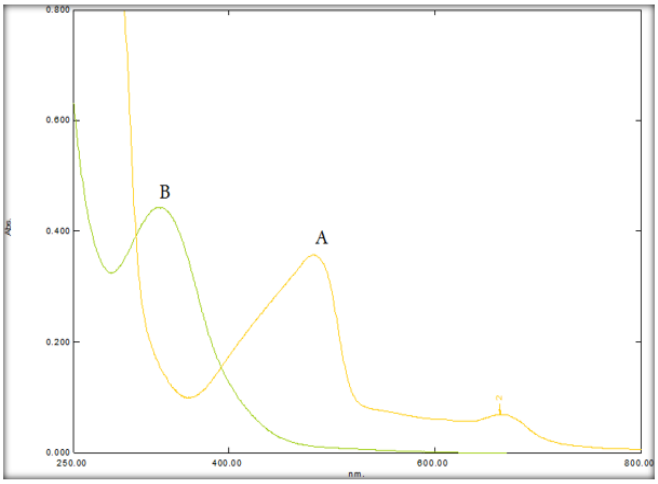


Figure 6: Absorption spectra of (a) 10 µg/mL (LPZ) versus reagent blank, (b) blank solution versus solvent under the optimum conditions

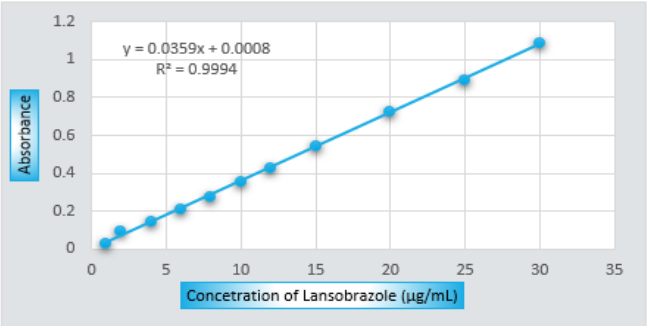


Figure 7: Calibration curve for the determination of LPZ under optimum conditions

Comparison of the Methods

Table 5 shows a comparison between the proposed method and that of other literature analytical methods throughout some analytical parameters.

Precision and Accuracy

The accuracy of the method and its precision was tested by analyzing three replicate samples of LPZ in three various levels (within Beer's law range), the results listed in Table 6 indicate passable accuracy and precision of the method.

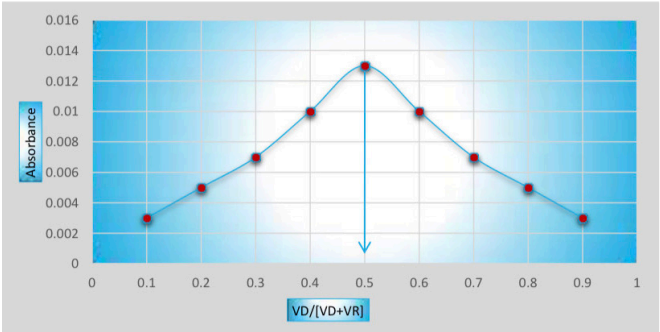


Figure 8: Continuous variation method for the reaction of (LPZ) with 2,4-DNPHz

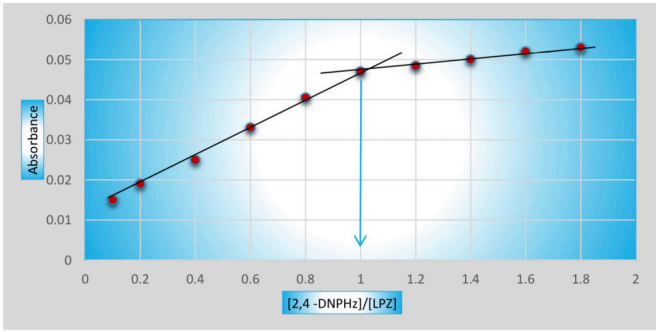


Figure 9: Mole ratio method for the reaction of LPZ with 2,4-DNPHz

Table 4: Optical characteristics and statistical data for the determination of LPZ

Parameter	*Value*
λ max (nm)	482.5
Color	Raddish brown
Regression equation	y=0.0359[LPZ]+0.0008
"Linearity range" (µg/mL)	1-30
"Calibration sensitivity" (mL/µg)	0.0359
"Correlation coefficient" (r)	0.9996
"Correlation of linearity" (R^2)	0.9994
"Molar absorptivity" (L/mol.cm)	13260.132
"Sandell's sensitivity" (µg/cm^2)	0.0278
"L.O.D" (µg /mL)	0.1266
"L.O.Q" (µg /mL)	0.3838

Table 5: Analytical parameters for the analysis of lansoprazole by the proposed method compared to other methods

Methods	*Linear range µg/mL*	*Correlation Coefficient (R)*	*C.V% range*	*Ref.*
proposed method	1.00 - 30.00	0.9996	0.1588-0.7989	–
Analysis Flow-injection	0.01-20.00	0.9998	–	26
RP-UPLC	5.00 – 30.00	0.9989	–	27
Spectrophotometric	(20.00-70.00) – (6.00-16.00)	0.9989-0.9993	0.2 – 0.78	28
Spectrophotometric	0.250-20.00	0.9999	0.88-3.97	29

Table 6: Valuation of the accuracy and precision of the proposed method for the estimation of (LPZ)

Conc. of (LPZ) µg/mL			
Taken	*Found**	*E.R%*	*C.V%*
4.000	4.0259	0.6499	0.7989
10.000	9.9034	-0.9656	0.4296
20.000	20.2468	1.2349	0.1588

*Average of three measurements

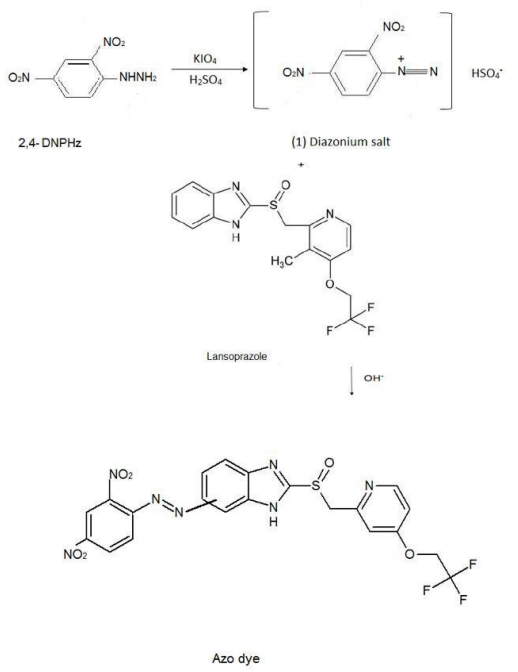
Table 7: Retrieval values for 10 µg/mL of (LPZ) in the existence of 1000 µg /mL of various excipients

Excipients		*Lansoprazole Conc.*		
Name	*Conc.(µg/mL)*	*Taken (µg/mL)*	*Found (µg/mL)*	*Recovery Name (%)*
Lactose	1000	10.000	9.9498	99.4986
Glucose			9.9777	99.7772
Sucrose			9.922	99.22
Starch			10.0891	100.8914

Table 8: Estimation of lansoprazole in dosage form capsules by proposed method

Sample	*Weight Found* (mg)*	*Concentration (µg/mL)*			
		Taken	*Found**	*Recovery %*	*C.V %*
Lancid-30 mg	29.96	10.000	9.894	98.94	0.561
	30.01	20.000	20.005	100.02	0.834
Lansoprazole-30 mg	30.01	10.000	10.003	100.03	0.277
	29.93	20.000	19.922	99.61`	0.698

*Average of three measurements



Scheme 2: The suggested reaction mechanism between LPZ and 2, 4-DNPHz

Interference Study

To ensure the selectivity of the proposed method, the effect of the interfering has been studied by various excipients, which are often associated with pharmaceutical preparations by measuring the absorption of the solution include 10 µg/mL of LPZ and 1000 µg /mL of excipient. The results in Table 7 show that the studied excipients do not interfere in the estimation of LPZ in its dosage forms.

Applying in Pharmaceutical Preparation

The application of the method for the assay of lansoprazole in drug has been applied successfully and the results obtained in Table 8 for each sample in three replicates.

CONCLUSIONS

The proposed technique enables accurate, rapid, and easily estimation of lansoprazole. The technique is free of excipients interference. The general applicability of the new current for routine quality control procedures was well known by the Lansoprazole assay in both pure and pharmaceutical preparations.

REFERENCES

1. Cartwright, Anthony C. The British pharmacopoeia, 1864 to 2014: medicines, international standards and the state. Routledge, 2016.

2. Azzarito T, Venturi G, Cesolini A, Fais S. Lansoprazole induces sensitivity to suboptimal doses of paclitaxel in human melanoma. Cancer letters. 2015 Jan 28;356(2):697-703.
3. Ferrari S, Perut F, Fagioli F, Del Prever AB, Meazza C, Parafioriti A, Picci P, Gambarotti M, Avnet S, Baldini N, Fais S. Proton pump inhibitor chemosensitization in human osteosarcoma: from the bench to the patients' bed. Journal of translational medicine. 2013 Dec;11(1):1-7.
4. De Milito A, Canese R, Marino ML, Borghi M, Iero M, Villa A, Venturi G, Lozupone F, Iessi E, Logozzi M, Mina PD. pH-dependent antitumor activity of proton pump inhibitors against human melanoma is mediated by inhibition of tumor acidity. International journal of cancer. 2010 Jul 1;127(1):207-219.
5. Marino ML, Fais S, Djavaheri-Mergny M, Villa A, Meschini S, Lozupone F, Venturi G, Della Mina P, Pattingre S, Rivoltini L, Codogno P. Proton pump inhibition induces autophagy as a survival mechanism following oxidative stress in human melanoma cells. Cell death & disease. 2010 Oct;1(10):e87.
6. Azzarito T, Venturi G, Cesolini A, Fais S. Lansoprazole induces sensitivity to suboptimal doses of paclitaxel in human melanoma. Cancer letters. 2015 Jan 28;356(2):697-703.
7. Nassar MY, El-Shahat MF, Khalil SM, El-Moety EA. Optimization and validation of spectrophotometric and potentiometric methods for determination of lansoprazole and omeprazole in pure and capsules. Indian Journal of Pharmaceutical Sciences. 2017 Aug 31;79(3):420-430.
8. Nassar MY, El-Moety EA, El-Shahat MF. Synthesis and characterization of a ZnMn 2 O 4 nanostructure as a chemical nanosensor: a facile and new approach for colorimetric determination of omeprazole and lansoprazole drugs. RSC advances. 2017;7(69):43798-43811.
9. Rahman N, Khan S. Experimental design approach in the optimization of potentiometric method for lansoprazole determination using lansoprazole-tungstate based ion-selective electrode. Industrial & Engineering Chemistry Research. 2018 Jul 2;57(29):9351-9361.
10. Abdulrahman SA, Devi OZ, Basavaiah K, Vinay KB. Use of picric acid and iodine as electron acceptors for spectrophotometric determination of lansoprazole through a charge-transfer complexation reaction. Journal of Taibah University for Science. 2016 Jan 1;10(1):80-91.
11. Bhim A, Buchiy FV, Raj HA, Jain VC. Simultaneous determination of Itopride Hydrochloride and Lansoprazole in Synthetic Mixture using Spectrophotometric technique (First order Derivative Method). PharmaTutor. 2015 Jul 1;3(7):38-45.
12. Luo L, Wen X, Du Y, Jiang Z, Guo X. Enantioselective analysis of lansoprazole in rat plasma by LC–MS/MS: Application to a stereoselective pharmacokinetic study. Biomedical Chromatography. 2018 Nov;32(11):e4345.
13. Bhattacharya S, Sarkar P, Khanam J, Pal TK. Simultaneous determination of paclitaxel and lansoprazole in rat plasma by LC–MS/MS method and its application to a preclinical pharmacokinetic study of investigational PTX-LAN-PLGA nanoformulation. Journal of Chromatography B. 2019 Aug 15;1124:331-339.
14. Elkady EF, Fouad MA, Jaadan BM. LC–MS/MS bioassay of four proton pump inhibitors. Journal of Chromatography B. 2018 Feb 15;1076:61-69.
15. Meher MK, Bhangale C, Dholas R, Prashant VA, Pawar R. Analytical Method Development, Validation And Forced Degradation Studies Of Lansoprazole By RP-HPLC. Asian Journal of Pharmaceutical Research and Development. 2018 Aug 23;6(4):21-29.
16. Smerikarova M, Bozhanov S, Maslarska V. Development and validation of a RP-HPLC method to quantify amoxicillin, tinidazole, esomeprazole and lansoprazole in a mixture. Indian Journal of Pharmaceutical Sciences. 2020 Jan 31;81(6):1122-1127.
17. Sun L, Cao Y, Jiao H, Fang Y, Yang Z, Bian M, Zhang H, Gong X, Wang Y. Enantioselective determination of (R)-and (S)-lansoprazole in human plasma by chiral liquid chromatography with mass spectrometry and its application to a stereoselective pharmacokinetic study. Journal of separation science. 2015 Nov;38(21):3696-3703.
18. Sun LN, Zhang Y, Yang YQ, Shen Y, Ying YW, Su YW, Zhang XH, Liu Y, Huang X, Wang YQ. Simultaneous enantioselective determination of omeprazole, rabeprazole, lansoprazole, and pantoprazole enantiomers in human plasma by chiral liquid chromatography–tandem mass spectrometry. Journal of Separation Science. 2020 Aug;43(16):3183-3196.
19. Horta RP, do Amaral B, Peralta-Zamora PG, Silva BJ. Evaluation of a hollow-fiber liquid-phase microextraction technique for the simultaneous determination of PPI drugs in human plasma by LC-DAD. Journal of chromatographic science. 2018 Jul 1;56(6):564-573.
20. Panda SS, Ravi Kumar Bera VV, Beg S, Mandal O. Analytical quality by design (AQbD)-oriented RP-UFLC method for quantification of lansoprazole with superior method robustness. Journal of Liquid Chromatography & Related Technologies. 2017 May 28;40(9):479-485.
21. Aktaş AH, Sarıdağ AM. Liquid Chromatographic–chemometric techniques for the simultaneous HPLC determination of lansoprazole, amoxicillin and clarithromycin in commercial preparation. Journal of chromatographic science. 2017 Sep 1;55(8):798-804.
22. Kostolanská K, Peš O, Zendulka O, Máchal J, Juřica J. Determination of lansoprazole, 5-hydroxylansoprazole, and lansoprazole sulfone in human plasma for CYP2C19 and CYP3A4 phenotyping. Chemical Papers. 2019 Dec;73(12):2955-2963.
23. Chung HK, Truong QK, Mai XL, Choi Y, Kang JS, Mar W, Kim KH. Determination of S-(−)-lansoprazole in dexlansoprazole preparation by capillary zone electrophoresis. Archives of pharmacal research. 2017 Aug;40(8):962-971.
24. Job P. Spectrochemical Methods of Analysis. Wiley, New York, 1971;346.
25. Christian GD. Analytical Chemistry. Fifth ed., Wiley, New York, 1994; 385–386.
26. Khan MS, Asghar M, Yaqoob M. Lansoprazole Determination in Pharmaceutical Formulations by Flow Injection Coupled with Acidic KMnO4–Quinine Chemiluminescence System. Analytical Sciences. 2019:19P039.
27. Singh SU, Choudhary NI, Rai JY, Siddiqui IN, Sharma SU. A validated RP-UPLC method development for simultaneous estimation of lansoprazole and naproxen in bulk and tablet dosage form. Asian J Pharm Clin Res. 2013;6(4):150-152.
28. Rizwana IF, Prakash KV, Mohan GK. Extractive spectroscopic determination of lansoprazole in pharmaceutical dosage form. Chem. Sci. Trans. 2014;3(4):1390-1395.
29. Mandil H, Sakur AA, Allabban AA. Development and Validation of Spectrophotometric Method for the Determination of Lansoprazole in Bulk and Pharmaceutical Formulation Through Ion-Pair Complex Formation Using Bromocresol Green. Research journal of Pharmacy and Technology. 2017 May 1;10(5):1417-1425.