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Spectrophotometric methods for the estimation of cinitapride and pantoprazole in bulk and oral dosage form

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ABSTRACT

Different UV spectrophotometric methods have been developed for the estimation of cinitapride (CNP) and pantoprazole (PNP) in both bulk and capsule dosage form. Both the drugs were well soluble in methanol. CNP and PNP showed maximum absorption at 262nm and 290nm respectively using methanol as solvent. CNP obeyed Beer's law, showing linearity in the range of 4-20and PNP at 5-30µg/ml with correlation coefficient of 1 for both. Method A is based on standard absorbance, method B involves determination of the Area under curve (AUC) and method C makes use of second derivative of the Zero order spectrum. The developed methods were analyzed for specificity, limit of detection (LOD), limit of quantification (LOQ), linearity of response, precision and accuracy. Thus the proposed method could be adopted for routine analysis of the formulation.

KEYWORDS

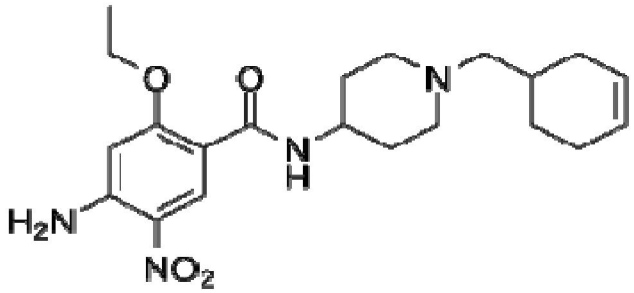
Cinitapride;
Pantoprazole;
Second derivative;
AUC;
LOD;
LOQ.

INTRODUCTION

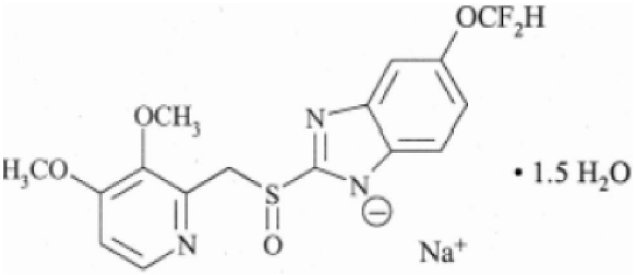
Cinitapride[1,2] (CNP) is a substituted benzamide gastroenteric prokinetic agent acting via complex, but synergistic effects on serotonergic 5-HT2 (inhibition) and 5-HT4 (stimulation) receptor and dopaminergic D2 (inhibition) receptors in the neuronal synapses of the myenteric plexi; it is used as an anti-ulcerative drug. Pantoprazole is an irreversible proton pump inhibitor which, at the therapeutic dose of 40mg, effectively reduces gastric acid secretion[3]. Cinitapride is chemically 4-amino –N-[1-(3-cyclohexen-1-ylmethyl)-4-piperidinyl]-2-ethoxy-5-nitrobenzamide. Pantoprazole is chemically 6-(difluoromethoxy-2-[(3,4-dimethoxy pyridine-2-yl) methyl sulfynyl] -1H-benzimidazole. Extensive literature survey reveals that only first derivative and HPTLC[4] method has been reported so far for the combination. RP HPLC method and UV spectrophotometric methods have been reported for CNP[5,6] and PNP[7,8] individually. The aim of this work is to develop simple, accurate, precise spectrophotometric methods for the determination of pantoprazole and cinitapride in bulk and capsule dosage form. Method A is the standard absorbance method involving the determination of CNP and PNP in methanol followed by measuring the absorbance at 262 and 290nm respectively. Method B involves determination of the Area under curve of the spectrum obtained in method A and method C involves the derivatization of the Zero order spectrum obtained in method A where the second order spectra showed

negative maxima at 262 and 290 nm for CNP and PNP respectively.

Structures[9]



Cinitapride
Mol wt: 402.49



Pantoprazole sodium sesquihydrate
Mol wt: 432.4

MATERIALS AND METHODS

A Shimadzu model uv-1650 double beam uv-vis spectrophotometer with a pair of 1cm matched quartz cells was used to measure absorbance. The capsule dosage form was obtained from the local market. All the solutions were freshly prepared just before the analysis, and methanol used was of analytical grade.

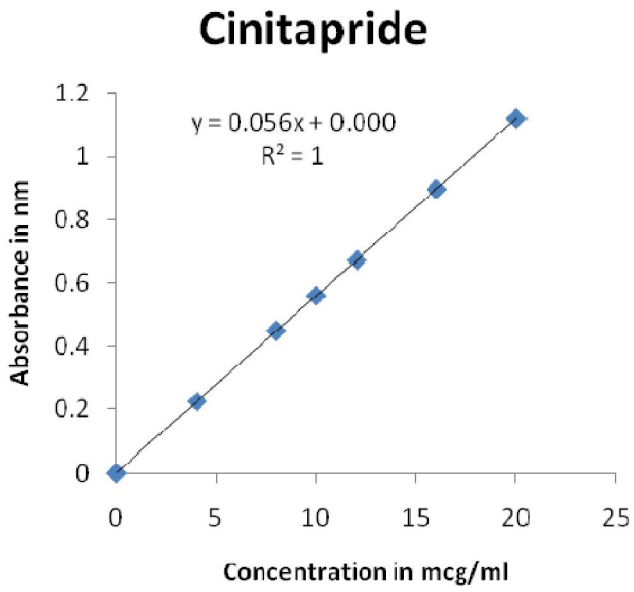


Figure 1 : Calibration chart of CNP

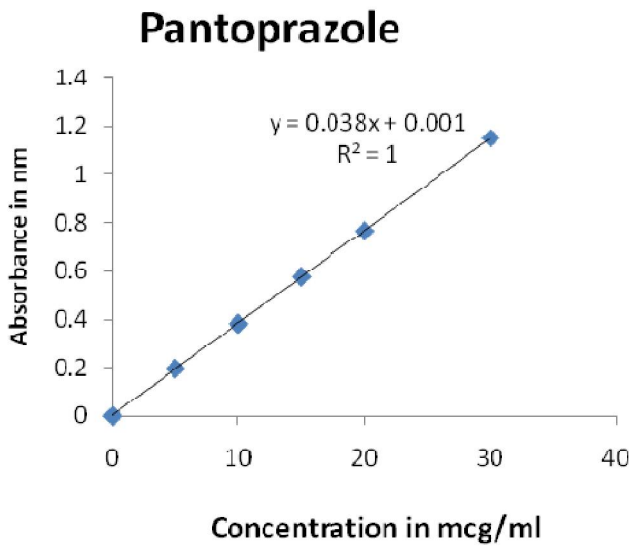


Figure 2 : Calibration chart of PNP

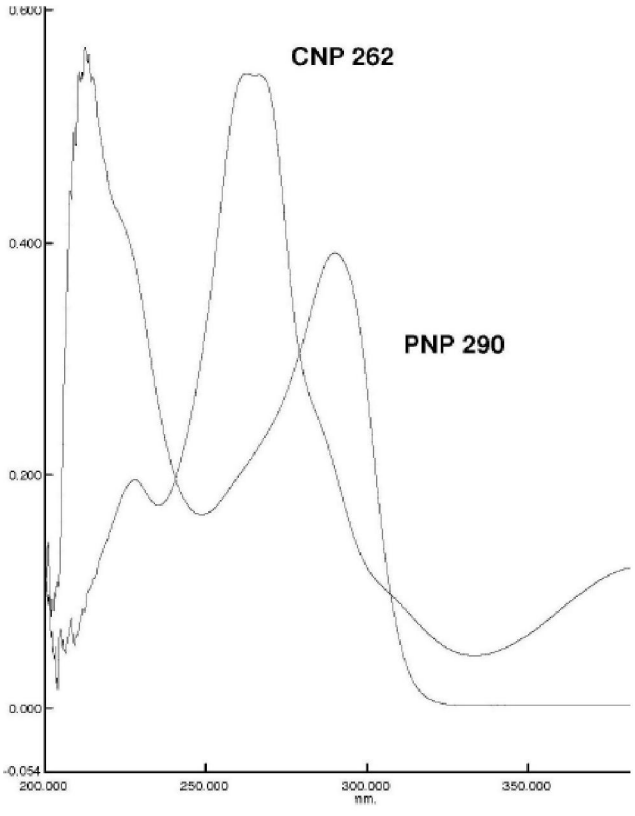


Figure 3 : Overlain spectra of CNP and PNP

Estimation of cinitapride and pantoprazole

Spectral and linearity characterization of CNP and PNP

Aliquot quantity of each standard CNP and PNP

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were weighed in two separate 50ml volumetric flasks. Dissolved in 10 ml of methanol and made up to volume with methanol. Dilutions ranging from 4-20µg/ml of standard CNP and 5-30µg/ml of standard PNP solutions were prepared using methanol. The final dilutions were scanned in ultraviolet region 200-400nm against methanol blank. PNP showed maximum absorption at 290nm and CNP at 262nm (figure 1, 2). Both CNP and PNP obeyed Beer's law[10] in the concentration range of 4-20µg/ml and 5-30µg/ml respectively (figure 3).

Preparation of sample solution

The capsule dosage form contains CNP as extended release tablet and PNP as enteric coated tablet. Thus both the components were analyzed as separate entities.

ASSAY

Method A: Standard absorbance method

Estimation of CNP

20 tablets of CNP were accurately weighed and crushed to fine powder. Tablet powder equivalent to 10mg of the CNP was weighed in a 100 ml volumetric flask, shaken vigorously with sufficient amount of methanol for half an hour. Finally the solution was made up to volume with methanol. The solution was well shaken and filtered through Whatmann filter paper (No.41). The first few ml of the filtrate was discarded and aliquot quantity of the filtrate was diluted to obtain a final concentration of 10µg/ml of CNP. The absorbance of the resulting solution was measured at 262nm against methanol blank.

Estimation of PNP

20 tablets of PNP was accurately weighed and crushed to fine powder. Tablet powder equivalent to 50mg of PNP was weighed in a 100ml volumetric flask, shaken vigorously with sufficient amount of methanol for half an hour and finally made up to volume with methanol. The resulting solution was filtered through Whatmann filter paper (No.41). The first few ml of the filtrate was discarded and sufficient quantity of the filtrate was diluted with methanol to obtain a final concentration of 15µg/ml of PNP. The absorbance of the resulting solution was measured at 290nm against methanol blank.

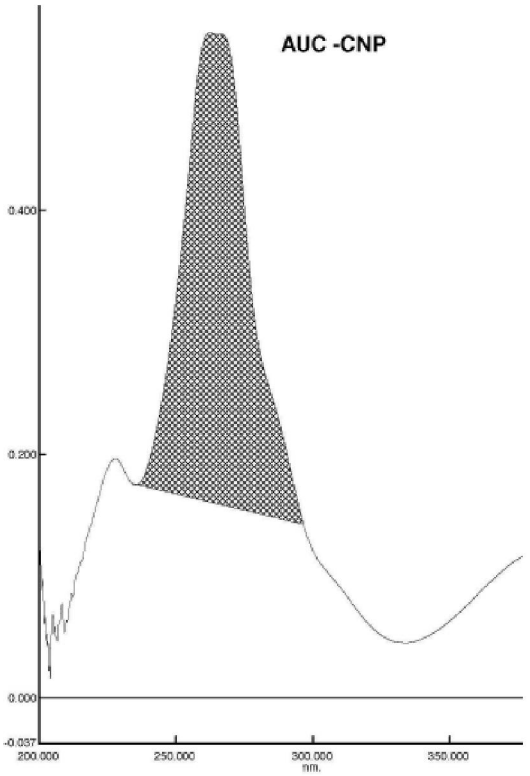

Figure 4 : AUC of CNP

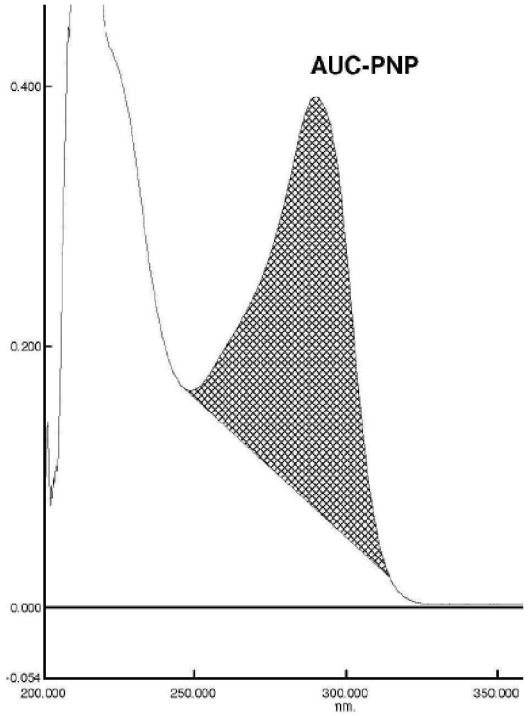

Figure 5 : AUC of PNP

Method B: Area under the[11]

The AUC (area under curve) method involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected

wavelengths λ1 and λ2. The wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. The standard spectra obtained in the linearity characterization and the sample spectra obtained in method A were used. The AUC for CNP (figure 4) were determined between 239.8 and 296.4nm for both standard and sample. Similarly for PNP, the AUC (figure 5) between 248.4 and 314.0 nm for both standard and sample were determined. The calibration graph was plotted between AUC and concentration.

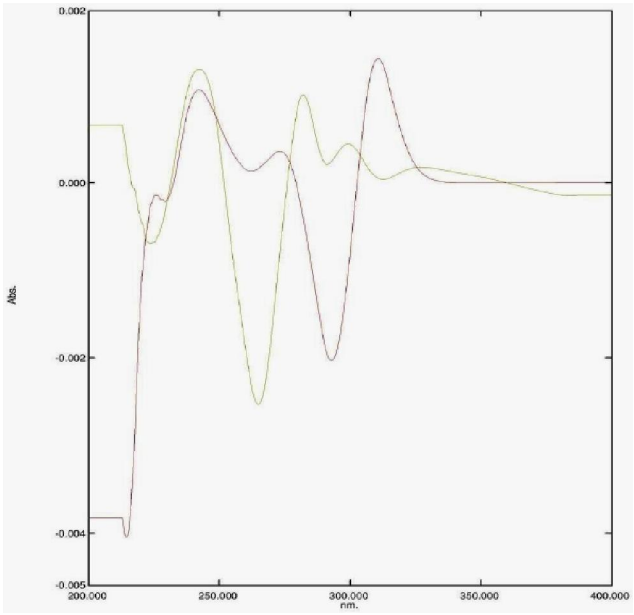

Figure 6 : Overlain second derivative spectra of CNP and PNP

The sample AUC was interpolated on the respective linearity chart of the AUC and the concentration was determined.

Method C: Second derivative[12]

Derivative spectrophotometry involves the conversion of normal spectrum to its first, second or higher derivative spectrum. The second derivative (D^2) spectrum is the plot of the curvature of the D^0 spectrum or a plot of $d^2A/ d\lambda^2$ against λ. The zero order spectra obtained in the linearity characterization and method A were derivatized to get second order spectra. CNP showed a negative maxima at 262nm and PNP at 290nm (figure 6). The amplitude of the negative maxima were measured and plotted against concentration to determine the linearity. The sample amplitudes were interpolated on the respective linearity chart of the derivative spectra and the concentration was determined

Recovery studies

The recovery studies were carried out on spiked samples by adding predetermined amount of standard drugs to the respective sample. About 20, 40 and 100% of standard drugs were added to the sample solutions and the absorbance was measured against methanol blank. The percentage recovered was calculated. The recovery studies were performed at three levels to confirm the accuracy of the above said methods.

TABLE 1 : Optical parameters of CNP and PNP

S.No	Optical Parameter	Cinitapride			Pantoprazole		
		Method			Method		
		A	B	C	A	B	C
1.	Wavelength λmax	262 nm	262nm	262nm	290 nm	290nm	290nm
2.	Molar absorptivity	22557.89	---	---	14746.97	----	----
3.	Beer's law limit µg/ml	4-20	4-20	4-20	5-30	5-30	5-30
4.	Regression equation	y = 0.056x + 0.000	y = 0.882x + 0.052	y = 0.478x + 0.085	y = 0.038x + 0.001	y = 0.955x - 0.095	y = 0.215x + 0.035
5.	Slope	0.05602	0.882	0.478	0.03815	0.955	0.215
6.	Intercept	0.00029	0.052	0.085	0.001	-0.095	0.035
7.	Correlation coefficient	1.0	0.9990	0.999	1.000	0.9990	0.999
8.	Sandell's sensitivity	0.0178	----	----	0.0260	----	----
9.	LOD	0.03366	---	---	0.4144	----	----
10.	LOQ	0.10200	----	----	1.2560	----	---
11.	RSD	0.4710	0.9901	1.1310	0.8022	0.9548	0.4782

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TABLE 2 : Result of tablet assay

Drug	Method A		Method B		Method C	
	% Amount Present ±SD	RSD %	% Amount Present ±SD	RSD %	% Amount Present ±SD	RSD %
CNP	100.85± 0.65	0.6445	101.24± 1.0	0.9901	100.91± 1.14	1.13
PNP	100.82± 0.80	0.9825	99.79± 0.952	0.9548	99.63± 0.476	0.478

***mean of three determinations**

TABLE 3: Recovery studies

Drug	Amount of drug added		% Recovery by the proposed methods		
	Sample	Standard	Method A	Method B	Method C
CNP	8µg/ml	1.6	101.35	100.75	100.75
		3.2	100.67	99.22	101.20
		8.0	99.99	100.74	99.49
PNP	15µg/ml	3.0	100.75	100.35	101.00
		6.0	101.30	99.70	101.00
		15.0	100.46	98.36	101.02

***mean of three determinations**

RESULTS AND DISCUSSIONS

CNP and PNP both were found to obey Beer's law in the concentration range of 4-20µg/ml and 5-30µg/ml. Both PNP and CNP showed good linearity shown by correlation coefficient value equal to 1.0. The optical parameters of CNP and PNP with respect to all the three methods are presented in TABLE 1. The percentage of the individual drugs in the formulation according to the four methods were calculated and presented in the TABLE 2. The results of the analysis showed that the amount of drugs were in good agreement with the label claim of the formulation. The accuracy of the proposed method were determined by recovery studies. The recovery studies were carried out on spiked samples and calculated for all the three methods. The percentages recovered were found to be in the range of 98-101 represented in TABLE 3 which showed that the excipients in the formulation do not interfere with the analysis.

CONCLUSION

The above methods developed for the estimation of CNP and PNP were found to posses good linearity of response, specificity and accuracy. The methods are simple, economical and easy to perform. Thus the proposed methods could be applied for routine analysis of these drugs.

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