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Spectrophotometric determination of Omeprazole in Pharmaceuticals

T.S.Rajendra Kumar, Lecturer in Chemistry, S.N.S.R Degree College, Velgode, Kurnool Dt , Andhra Pradesh

Abstract: Omeprazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-pyridinyl) methyl] sulfinyl]-1H-benzimidazole, is a substituted benzimidazole that inhibits gastric secretion by altering the activity of H^+/K^+ ATPase, which is the final common step of acid secretion in parietal cells. It is a lipophilic, weak base with pK_{a1} = 4.2 and pK_{a2} = 9 and will be degraded unless it may be protected against acid conditions . Although its elimination half-life from plasma is short, reported to be about 0.5–3 h, its duration of action with regard to inhibition of acid secretion is much longer allowing it to be used in single daily dose. Omeprazole contains a tricoordinated sulphur atom in a pyramidal structure and therefore can exist in two different optically active forms, (S)- and (R)-omeprazole. Omeprazole was first approved as a racemic mixture, but the (S) isomer was recently introduced on the market. Both enantiomers have a similar inhibitory effect on acid formation in isolated gastric glands from rabbits, but (R)-omeprazole is stereoselectively hydroxylated by cytochrome P450 CYP2C19 enzyme, resulting in an almost twofold increase in the plasma concentration for the (S)-isomer than for racemic omeprazole after the administration of equivalent doses. Omeprazole is metabolized principally by CYP2C19 to generate 5-hydroxy-omeprazole, and a minor pathway, through CYP3A4 enzymes generates omeprazole-sulphone.

It is used in the treatment of peptic ulcers , reflux oesophagitis the Zollinger–Ellison syndrome . Omeprazole is official in the USP 24 and BP 98 . Omeprazole is a racemate. It contains a tricoordinated sulfur atom in a pyramidal structure and therefore can exist in equal amounts of both the S and R enantiomers. In the acidic conditions of the stomach, both are converted to achiral products, which reacts with a cysteine group in H^+/K^+ ATPase, thereby inhibiting the ability of the parietal cells to produce gastric acid.

Key Words: *Beer Law, Absorption Spectrum, HPTLC*

Spectrophotometer

A SHIMADZU (Model No: UV-2550) UV-Visible spectrophotometer with 1 cm matching quartz cells were used for the absorbance measurements.

REAGENTS AND SOLUTIONS

All reagents used were of analytical reagent grade and distilled water was used for the preparation of solutions. A 1000 µg mL^{-1} standard drug solution of omeprazole was prepared by dissolving in 1M hydrochloric acid and the stock solution was diluted appropriately with water to get the working concentration. Ferrous ammonium sulphate solution 1000 µg mL^{-1} was prepared and the solution was diluted appropriately to get the working concentration. Bromate bromide mixture (40 and 50 µg mL^{-1} in $KBrO_3$), 1,10-phenanthroline (0.3%), ammonia (1:1) were used.

PROCEDURES

Spectrophotometric Method A

Aliquots containing 1.00-5.00 µg mL^{-1} of omeprazole was transferred into a series of 10 mL standard flasks. To this, 1 mL of 5 mol L^{-1} HCl and bromate-bromide mixture (40 µg mL^{-1} in $KBrO_3$) were added. The contents were shaken well and were set aside for 5 minutes with occasional shaking. Then, 1 mL of 400 µg mL^{-1} ferrous ammonium sulphate was added and again the flask let stand for 15 minutes with occasional shaking followed by 1 mL of ammonium thiocyanate was added and diluted to the mark with distilled water, the absorbance of each solution was measured at 480 nm against the reagentblank.

Spectrophotometric Method B

Aliquots containing 2.00-12.00 µg mL^{-1} of omeprazole was transferred into a series of 10 mL standard flasks. To this, 1 mL of 5 mol L^{-1} HCl and bromate-bromide mixture (50 µg mL^{-1} in $KBrO_3$) were added. The contents were shaken well and were set aside for 5 minutes with occasional shaking. Then, 1 mL of 350 µg mL^{-1} ferrous ammonium sulphate was added and again the flask let stand for 15 minutes with occasional shaking followed by 1 mL of 1,10 phenenthroline and 1:1 NH_3 solution were added and diluted to the mark with distilled water, and the absorbance of each solution was measured at 510 nm against the reagent blank.

Analysis of Dosage Forms

To determine the content of omeprazole in conventional tablets (label claim: 20 mg/ tablet), the sample stock solution was prepared by grinding the tablet using a mortar and pestle and transferring to a 100 mL volumetric flask by washing with 1M hydrochloric acid. The solution was shaken for 30 minutes and filtered through Whatman no.1 filter paper and the clear solution was made up to 100 mL. Pipetted out 2 mL (Method A) and 4 mL (Method B) in to a 10 mL calibrated flasks, subjected to analysis by the proposed method. The results are listed in table 9.1A and 9.1B.

RESULTS AND DISCUSSION

In this method bromate in acid medium acts as an oxidizing agent and there is the formation of nacent oxygen. The formed nacent oxygen oxidizes bromide to bromine and the *insitu* generated bromine oxidizes the drug. The unreacted bromine is determined by two different scheme. The reduction of residual oxidant by iron(II) resulting in the formation of iron(III). In method A, resulting iron(III) is complexed with thiocyanate and measured at 480 nm . In method B unreacted bromine is treating with a measured excess of iron(II) and remaining iron(II) is complexed with 1,10 phenanthroline and measured at 510 nm . The reaction mechanism are shown in scheme . Preliminary experiments are performed to fix the reagent concentration. In the present method all parameters influencing the color development are investigated and are incorporated in the recommened procedure.

In method A, omeprazole when added in increasing concentration to a fixed concentration of bromate-bromide mixture, there is a decrease in the concentration of bromate-bromide mixture. When known volume of Fe(II) is added to the same mixture, unreacted oxidant is reduced by a fixed amount of iron(II) and it shows a propotional decrease in the concentration of iron(III). The result could be observed by decrease

in the absorbance with the increase in the concentration of omeprazole In method B, omeprazole when added in increasing concentration to a fixed concentration of bromate-bromide mixture, there is a decrease in the concentration of bromate-bromide mixture. When the decreasing amount of oxidant are reacted with a fixed amount of iron(II), it shows a proportional increase in the concentration of iron(II). As a result there is a propotional increase in the absorbance with the increasing concentration of the drug. Hydrochloric acid medium is found to be ideal for both the steps in method A and B, addition of excess of acid are not preferable since they would require large quantities of ammonia to raise the pH to 4, required for iron(II)- phenanthroline complex formation.

Analytical Data

Adherence to Beer's law is studied by measuring the absorbance values of solutions varying in drug concentration. The analytical parameters such as molar absorptivity and Sandell's sensitivity values are calculated and found to be 3.00×10^4 L mol^{-1} cm^{-1}, 0.011 µg cm^{-2} for spectrophotometric method A and 2.70×10^4 L mol^{-1} cm^{-1} and 0.013 µg cm^{-2} for spectrophotiometric method B respectively. The correlation coefficients, intercepts and slopes for each methods were found to be ¨0.9998, 0.102, ¨0.014 (method A) 0.9871, 0.074, 0.071 (method B) respectively. Beer's law is obeyed in the concentration range 1.00-5.00 □J P/$^{-1}$ for spectrophotometric method A and 2.00-12.00 □J P/$^{-1}$ of omeprazole for spectrophotometric method B. The calibration graphs are described by the equation: Y = a + b X (where Y = absorbance, a = intercept, b = slope and X = FRQFHQWUDWLRQ LQ □J mL^{-1}) obtained by the method of least squares. The results for the determination of pure drug are shown in Table 9.1C and 9.1D, show the sensitivity, validity, and analytical features of the method. Adherences to Beer's law for the determination of omeprazole for spectrophotometric method A and B are shown in fig.

Interference Study

To investigate the effect of excipients and fillers on the measurements involved in the methods, standard addition method is carried out. It is observed that talc, starch, glucose did not interfere in themeasurement.

COMPARISON OF THE PROPOSED METHOD WITH EARLIER METHODS

Reagent	Range	□max (nm)	Molar absorptivity (L mol^{-1} cm^{-1})	Method	Ref.
Ferric chloride	10.00	660	2.10×10^4	Spectrophotometry	[44]
Chloramine T	32.00	420	1.19×10^4	Spectrophotometry	[44]
Folin Ciocalteau	2.40	540	7.40×10^4	Spectrophotometry	[44]
N-bromosuccinimide	10.00	770	2.85×10^4	Spectrophotometry	[44]
Proposed methods					
Thiocyanate	1.00-5.00	480	3.00×10^4	Spectrophotometry	
1,10 -Phenanthroline	2.00-12.00	510	2.70×10^4	Spectrophotometry	

RESULTS OF ASSAY OF FORMULATIONS BY THE PROPOSED METHOD (METHOD A)

Brand name	Labeled amount (mg)	Amount found[a] (mg)	% Label claim ± SD	$b_{t\text{-test}}$
Omicap	20.00	20.06	100.30 ± 0.21	0.65
Omez	20.00	19.95	99.75 ± 0.15	0.76

[a]Average of five determinations

[b]Tabulated t-value at 95% confidence level is 2.31 Omicap- Micro Labs Limited, India Omez-Dr. Reddy's Pharmaceutical Limited.

RESULTS OF ASSAY OF FORMULATIONS BY THE PROPOSED METHOD (METHOD B)

Brand name	Labeled amount (mg)	Amount found[a] (mg)	% Label claim ± SD	$b_{t\text{-test}}$
Omicap	20.00	19.98	99.90 ± 0.19	0.23
Omez	20.00	19.93	99.65 ± 0.08	1.96

[a] Average of five determinations

[b]Tabulated t-value at 95% confidence level is 2.31 Omicap- Micro Labs Limited, India Omez-Dr. Reddy's Pharmaceutical Limited

EVALUATION OF ACCURACY AND PRECISION OMEPRAZOLE (METHOD A)

Amount taken (µg mL^{-1})	Amount found[a] (µg mL^{-1})	Recovery (%)	SD	RSD (%)
1.00	0.97	97.00	0.02	2.06
2.00	1.93	96.50	0.03	1.55
3.00	2.99	99.60	0.03	1.00
4.00	3.98	99.50	0.02	0.50
5.00	4.96	99.20	0.04	0.81

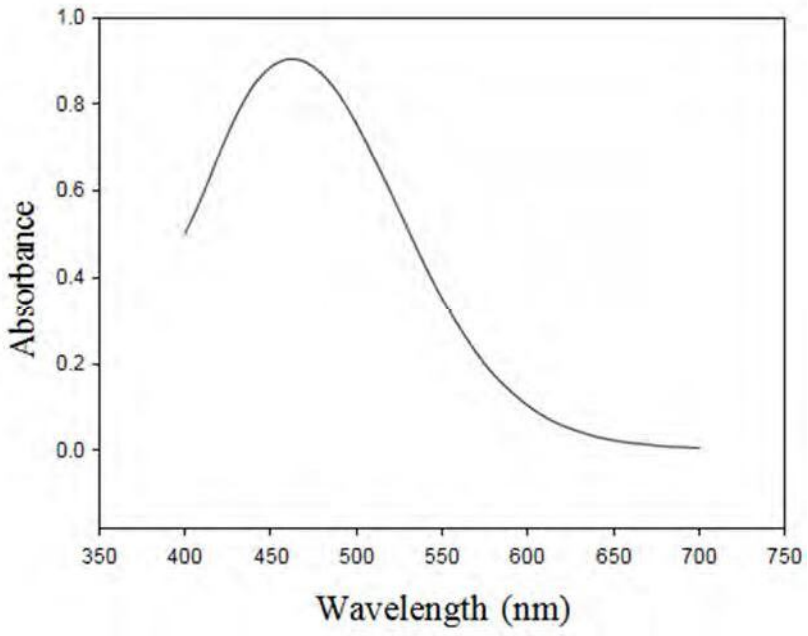
a-Average of five determinations, SD- Standard deviation

EVALUATION OF ACCURACY AND PRECISION OMEPRAZOLE (METHOD B)

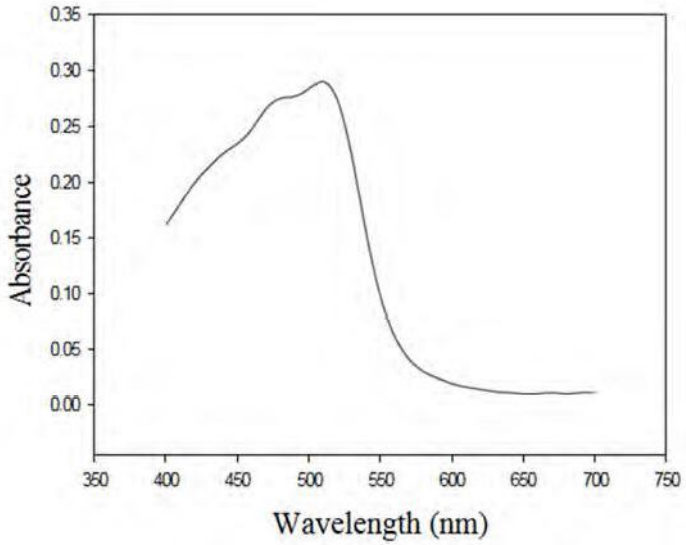
Amount taken ($\mu g\ mL^{-1}$)	Amount found[a] ($\mu g\ mL^{-1}$)	Recovery (%)	SD	RSD (%)
2.00	1.98	99.00	0.02	1.01
4.00	3.93	98.25	0.02	0.51
6.00	6.02	100.30	0.03	0.49
8.00	7.98	99.75	0.02	0.25
10.00	10.01	100.10	0.04	0.40

a- Average of five determinations, SD- Standard deviation

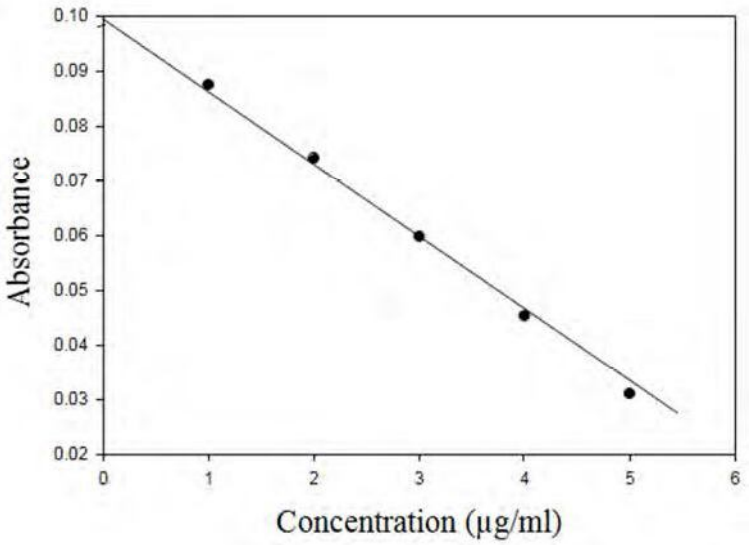
ABSORPTION SPECTRUM OF OMEPRAZOLE FOR METHOD A



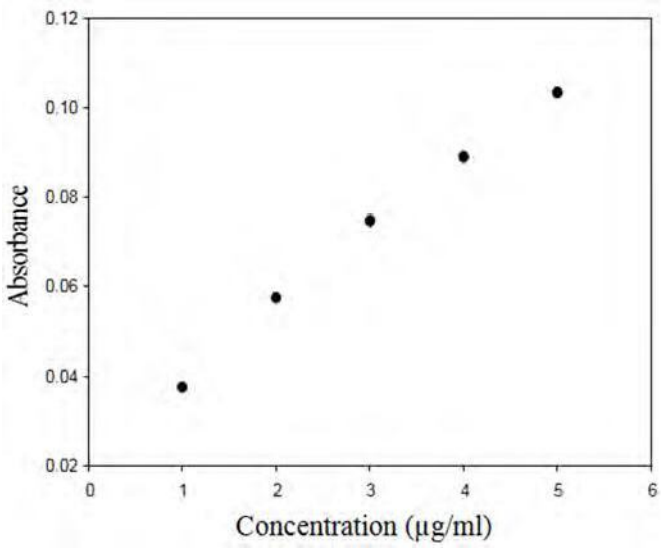
ABSORPTION SPECTRUM OF OMEPRAZOLE FOR METHOD B



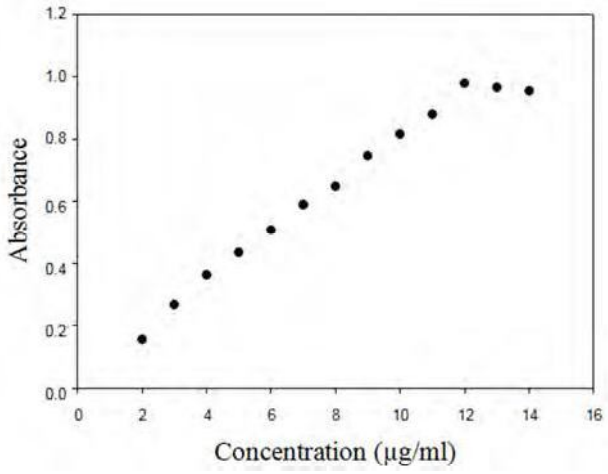
ADHERENCE TO BEER'S LAW FOR METHOD A



ADHERENCE TO BEER'S LAW FOR METHOD A
(Plotted by substracting test solution from the blank)



ADHERENCE OF BEER'S LAW FOR METHOD B



CONCLUSIONS

The proposed methods are accurate and precise as indicated by good recoveries of the drugs and low RSD values. All the analytical reagents are inexpensive, have excellent shelf life, and are available in any analytical laboratory. The proposed method can be applied for routine analysis and in quality control laboratories for quantitative determination of the cited drugs both in the pure and dosage forms.

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