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Assay of Omeprazole in Pharmaceutical formulations by extraction Spectrophotometry

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Four simple and sensitive spectrophotometric methods (A-D) for the assay of omeprazole (OMZ) in pure and dosage forms based on the formation of chloroform soluble ion-associates under specified experimental conditions are described. Four acidic dyes viz. Suprachen Violet 3B (SV 3B, method A), Tropaeolin 000 (TP 000, method B), Bromocresol Green (BCG, method C) and Azocarmine G (AG, method D) are utilised. The extracts of the ion-associates exhibit absorption maxima at 590 nm, 420 nm, 500 nm and 540 nm for methods A, B, C and D respectively. Beer's law and the precision and accuracy of the methods are checked by UV reference method.

OMEPRAZOLE (OMZ), a substituted benzimadazole compound, a prototype anti-secretory agent, is the first of the proton pump inhibitors and is widely used for the treatment of symptomatic gastro-oesophagal reflux. It is official in B.P.[1]. A survey of literature revealed that the reported methods include a single differential pulse polarographic[2], two U.V[3,4] spectrophotometric, besides a few HPLC[5-7]. As there is no report on visible spectrophotometry, the need for a fast, low cost and selective method is obvious, especially for routine quality control analysis of pharmaceutical products containing OMZ.

As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the assay of drugs[8,9], the technique was therefore, utilised in the present work for the estimation of OMZ. The present paper describes four simple and sensitive extraction spectrophotometric methods for the determination of OMZ, based on its tendency to form chloroform extractable ion-association complexes with acidic dyes belonging to different chemical classes viz. SV 3B (CI No. 60730, amino anthroquinone, method A), TP 000 (CI No. 14600, monoazo, method B); BCG (indicator, Sulphophthalein, method C) or AG (CI No. 50085, azine, method D) under specified experimental conditions by exploiting the basic nature of the drug molecule.

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EXPERIMENTAL

A Systronic model 106 and a Milton Roy spectronic 1201 Spectrophotometer which 1 cm matched quartz cells and an Elico LI-120 digital pH meter were used.

All the reagents were of analytical grade and all solutions were prepared in doubly distilled water.

Aqueous solutions of SV 3B (0.2%), TP 000 (0.02%), BCG (0.1%), AG (0.2%) and dilute hydrochloric acid (0.1 M) were prepared. The glycine - HCl buffer solutions (pH 1.3 for method A and pH 1.5 for method D), and potassium acid phthalate buffer solution (pH 3.5 for method C) were prepared[10].

Table 1 : Optical characteristics and precision

Parameter	Methods			
	A	B	C	D
λmax (nm)	590	500	420	540
Beer's Law Limits (μg/ml)	2.5-25.0	1.2-17.5	1.6-16.6	5.0-70.0
Molar absorptivity (lit.mole^{-1} cm^{-1})	8.86×10^3	1.55×10^4	1.31×10^4	3.25×10^3
Sandell's Sensitivity (μg cm^{-2}/0.001 absorbance unit)	0.041	0.020	0.026	0.10
Regression Equation (Y)*				
Slope (b)	2.55×10^{-2}	4.49×10^{-2}	3.79×10^{-2}	9.47×10^{-3}
Intercept (a)	5.8×10^{-3}	-1.60×10^{-3}	4.31×10^{-3}	-2.57×10^{-3}
Correlation Coefficient	0.9999	0.9999	0.9998	0.9999
Relative Standard Deviation (%)**	0.48	0.36	0.81	0.56
% Range of error ** (95% confidence limit)	0.51	0.38	0.85	0.59

* : Y = a + bc where C is concentration

** : Six replicate samples : (Concentration of 15.0, 10.0, 13.3 and 50.0 μg ml^{-1} of pure drug for methods A, B, C and D respectively).

Preparation of standard drug solution

Stock solutions of OMZ (1 mg/ml) was prepared by dissolving 100 mg of OMZ initially in 10 ml of 0.1N NaOH, followed by dilution to 100 ml with distilled water. The working standard were prepared by suitable of the stock solution with distilled water (50 μg/ml for methods A, B and C, 200 μg/ml for method D).

Sample Drug Solutions

Twenty capsules were emptied, pulverized and an amount of powder equivalent to 100 mg of OMZ was weighed and the working solutions for these method (A, B, C & D) were prepared as under standard solution preparation and filtered to remove insoluble portion, if any.

Recommended Procedure

Aliquots of standard OMZ solution (0.5 - 5.0 ml, 50 μg/ml for methods A & C or 0.25 - 3.5 ml, 50 μg/ml method B and 200 μg/ml method D) were placed in a series of 125 ml separating funnels. A volume of 6.0 ml of buffer solution (pH 1.3 method A, pH 1.5 method D, pH 3.5 method C) or 0.1M HCL (method B) and 2.0 ml of SV 3B, TP 000, BCG or AG solutions were added for method, A, B, C & D respectively. The total volume of aqueous phase in each separating funnel was adjusted to 15.0 ml (for method A, B and D) and 10.0 ml (for method C) with distilled water. Then 10.0 ml (for methods A, B or D) or 15.0 ml (for method C) of chloroform was added to each funnel, and the contents were shaken for 2 min. The absorbance of the separated chloroform layer was measured at λmax (590 nm, method A; 500 nm, method B; 420 nm method C; and 540 nm, method D) against a reagent blank within the stability period (5 min-5 h for all four methods). The amount of OMZ present was calculated from calibration graph.

Table 2

Analysis of pharmaceutical formulations of Omeprazole by proposed and reference procedures

Pharmaceutical formulations	Labelled amount (mg)	Amount found by proposed methods*(mg) A	B	C	D	Reference method[3]	% Recovery by proposed method** A	B	C	D
Capsule I	20	19.9±0.16	19.8±0.17	19.9±0.19	20.0±0.18	19.8±0.27	99.4±0.90	99.0±1.35	99.5±0.79	99.8±0.50
		F = 2.84	F = 2.52	F = 2.01	F = 2.25					
		t = 1.04	t = 0.3	t = 0.95	t = 1.35					
Capsule II	20	19.8±0.41	19.9±0.15	19.7±0.42	19.9±0.34	19.9±0.27	99.8±0.82	99.5±0.84	99.5±0.84	99.4±0.40
		F = 2.30	F = 3.24	F = 2.48	F = 1.58					
		t = 0.64	t = 0.26	t = 2.03	t = 1.26					
Capsule III	20	19.9±0.17	20.0±0.18	20.2±0.13	19.9±0.16	19.9±0.12	99.1±0.85	99.9±0.83	100.0±0.90	99.8±0.82
		F = 2.25	F = 2.29	F = 1.17	F = 1.77					
		t = 0.41	t = 0.81	t = 0.82	t = 0.49					
Capsule IV	20	19.9±0.15	19.9±0.09	19.8±0.27	19.9±0.17	19.9±0.14	99.7±0.92	99.5±0.78	98.7±1.27	99.4±0.74
		F = 1.14	F = 2.19	F = 4.99	F = 1.47					
		t = 0.27	t = 0.58	t = 0.92	t = 0.08					

* : Average ± standard deviation (n = 6). The F- and t-values refer to comparison of the proposed method with the reference method. Theoretical values at 95% confidence limits F = 5.05, t = 2.57.

** : Recovery 10 mg added to the preanalysed pharmaceutical preparation (Average of three determinations).

RESULTS AND DISCUSSION

Optimum operating conditions used in the procedures were established adopting variation of one variable at a time (OVAT) method. The optical characteristics such as Beer's law limits, molar absorptivities, regression equations and correlation coefficients obtained by linear least squares treatment of the results are given in Table 1. The precision and accuracy were found by analysis of six separate samples containing known amount of the drug and the results are summarized in Table 1. The relative standard deviation and % range of error at the 95% confidence level are also given in Table 1.

These methods were applied for the determination of OMZ in capsules. The results obtained from the proposed and reference methods[3] were compared statistically by means of student t- test and by the variance ratio F-test and no significant difference (Table 2) was observed. It indicates that none of the usual excipients employed in the formulation of dosage forms interfere in the analysis of drug by the proposed methods. As an additional check of accuracy, recovery experiments were performed by the standard addition method. These results are also summarised in Table 2. The stoichiometric ratio of the drug to dye was determined by the slope ratio method[11] and was found to be 1:1 in methods A, B and C and 2:1 in method D.

The order of sensitivity among the proposed method and UV reference method (R) in the determination of OMZ is B>C>A>R>D. The λmax order is A>D>B>C>R. The λmax of all the four proposed methods were considerably higher than that of reference method. The higher λmax of the proposed method is a decisive advantage since the interference from the associated ingredients shall be far less at higer wave lengths. Thus all the proposed

methods are simple and sensitive with good precision and accuracy and can be used for the routine quality control analysis of OMZ in pure form as well as pharmaceutical formulations depending upon the availability of chemicals and nature of other ingredients present in the sample.

REFERENCES

1. **British Pharmacopoeia**, HMSO, London 1993 (Addendum 1995), 1590.
2. Oezaltin and Temizer Aytekin, **Electronalysis** (N.Y.), 1994, 6, 799.
3. Zhixum, Xe, **Yaowu Fenxi Zazhi**, 1991, 11, 276.
4. Dhumal, S.N., Dikshit, P.M.; Ubhary, I.I. and Gaitonde, C.D., **Indian Drugs.**, 1991, 28, 565.
5. Pan, T.Y. and Zhenbang, G.H. **Zhongguo Yiyao Gongye Zazhi.**, 1993, 24, 466.
6. Ray, S. and De, P., **Indian Drugs.**, 1994, 31, 543.
7. Mathew, M., Das Gupta, V. and Bailey E., **Drug Dev. Ind. Pharm.**, 1995, 21, 965.
8. Foster, R., **J. Phys. Chem.**, 1980, 84, 2135.
9. Das Gupta, V., **Ind. J. Pharm.**, 1973, 35, 77.
10. Lurie, Ju., **Hand Book of Analytical Chemistry.**, Moscow, Mir Publishers, 1975, 253.
11. Irving, H., Rossotti, E.J.C. and Williams, R.J.P., **J. Chem. Soc. (London)**, 1995, 11, 1906.