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REFERENCES

1. Nandi, R. C., Sarin, J. P. S. and Khanna, N. M., A Process for the Preparation of Polyose from the Seeds of Tamarindus indica, Ind. Pat. No. 142092, 1975.
2. Khanna M, Nandi R. C. and Sarin J. P. S., *Indian Drugs*, 1987, 24, 268.
3. Marshall, K., In; Theory and Practice of Industrial Pharmacy, 3rd Ed, Verghese Publishing House, Bombay, 1987, 88.
4. Pharmacopoeia of India, 3rd Ed, Controller of Publications, New Delhi, vol. II, 1985, A-121.
5. Dwivedi A. K., Kulkarni D. and Singh S., A Process for the Preparation of Sustained Released Tablet Formulation of Verapamil Hydrochloride Using Polysaccharide Polymers. Indian Patent Application No. 433/DEL/95 Dated 14.3.95.
6. Kulkarni D., Dwivedi A. K., Sarin J. P. S. and Singh S., *Ind. J. Pharm. Sci.*, 1997, 59, 1.
7. Martindale : The Extra Pharmacopoeia, 30th Ed., The Pharmaceutical Press, London, 1993, 1257.
8. Patel R. P. and Joshi G. J., *Indian J. Pharma.*, 1958, 20, 279.
9. Higuchi T., *J. Pharm. Sci.*, 1963, 52, 1145.

Spectrophotometric Determination of Atenolol and Timolol Dosage forms via Charge-transfer complexation

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A spectrophotometric method is described for the determination of atenolol and timolol as bulk drug and in dosage forms by complexation of the drug with choranic acid. Job's method revealed a 1:1 complexation between the drug and choranic acid. Quantitative recoveries were obtained from commercially available dosage forms.

TIMOLOL maleate is a β -blocker used in the treatment of hypertension, glaucoma and for prophylaxis after myocardial infraction¹.

Atenolol is popular in the therapy of essential hypertension. For atenolol and timolol maleate, USP² and IP³ describe a nonaqueous titration method using 0.1 N perchloric acid whereas the assay procedure for atenolol tablets and timolol ophthalmic solution is based upon the extraction of the drug and determination of its absorbance^{2,3}. For timolol maleate tablets either alone or in combination with

hydrochorthiazide an HPLC assay procedure is given². A reversed phase HPLC method for the simultaneous determination of atenolol and nifedipine in tablets⁴ and a spectrophotometric method for timolol maleate in eye drops⁵ have been described.

Charge-transfer complexation has been found to be a useful technique for the determination of many drugs which contain electron donor groups. The use of chloranic acid has been described in the determination of several alkaloids^{6,7} in dosage forms. Here we wish to describe a simple and sensitive spectrophotometric method for the

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Table 1 : Analysis of dosage forms by proposed and official method

Dosage form	Recovery, %* proposed method	Recovery, %* official method
Atenolol tablets		
50 mg/tab	98.37 (± 1.55)	98.36 (± 1.13)
100 mg/tab	99.0 (± 0.78)	98.36 (± 1.12)
Timolol tablets		
50 mg/tab	99.06 (± 0.33)	100.45 (± 0.1)
Timolol eye drops		
0.50% w/v	99.30 (± 0.51)	99.94 (± 0.41)
0.25% w/v	99.73 (± 0.70)	99.90 (± 0.50)

* Based on label claim

assay of atenolol and timolol as bulk drug and in dosage forms based on interaction of the drug with chloranilic acid to form instantaneously a 1:1 purple-violet complex.

Atenolol and timolol maleate pure drug powders were gift from Deepharma and Cadila laboratories respectively. Timolol maleate ophthalmic solution, atenolol and timolol tablets were obtained commercially. p-Chloranilic acid (Riedel de Haen) and other chemicals were of analytical reagent grade. Chloranilic acid, 0.005 M and 0.2% w/v solutions were prepared by dissolving p-chloranilic acid in 1,4-dioxan and stored in a dry, amber coloured glass bottle in dark place and is stable upto 6 weeks. Atenolol and timolol maleate solutions (0.005 M each) were prepared in chloroform.

Spectrophotometric measurements were done on Bausch and Lomb Spectronic 21 or on Hitachi Model 150-30 double beam spectrophotometer using 1 cm² silica cells. The contents of three bottles containing 5 ml each of 0.25% w/v (or 0.5% w/v) timolol ophthalmic solution were pooled together. A 10 ml portion was pipetted into a clean, dry evaporating dish and the solution evaporated to dryness. The residue was dissolved in chloroform and transferred to a 10 ml volumetric flask and the volume made up to mark with chloroform.

Twenty tablets are weighed and crushed to a fine powder in a glass pestle and mortar. An aliquot of the powder equivalent to 100 mg of the drug was weighed and transferred to a 100 ml volumetric flask. Chloroform was added and the flask was shaken and then allowed to stand for 1 h. The clear, supernatant solution was used for the assay.

An aliquot of assay solution was transferred to a 10 ml volumetric flask, 2.5 ml of 0.25% chloranilic acid solution was added and the solution was mixed and diluted to 10 ml with dioxan. The absorbance was measured at the corresponding λ max (534 for atenolol and 530 nm for timolol) against a blank solution prepared by mixing 2 ml CHCl₃ with 2.5 ml chloranilic acid and dioxan added to 10 ml.

In dioxan-chloroform medium atenolol and timolol react instantaneously to give a purple colour with absorption maxima at 534 and 530 nm respectively. Chloranilic acid in dioxan-chloroform mixture is golden-yellow with λ max at 428 nm and a minimum near the λ max of the complexes. Chloranilic acid exists in three forms⁸, the natural yellow H₂A at very low pH, the dark violet HA which is stable at pH 2 and the pale violet A²⁻ stable at high pH. As the reaction product of chloranilic acid with atenolol and timolol are purple, it is possible that HA⁻ is the form of chloranilic acid involved in the complexes. The colour of the complexes is stable for at least 24 hr if the solutions are kept in dark.

Both continuous variation and molar-ratio methods showed that 1:1 complexes are formed as expected from the single donor centre in the drugs. Using Benesi-Hildebrand equation⁹, the molar absorptivities were 1.64 x 10³ and 0.85 x 10³ and stability constants were 2.3 x 10³ and 3.6 x 10⁴ for atenolol-chloranilic acid and timolol-chloranilic acid complexes respectively. Plots of absorbance of complex vs concentration of the drug were found to be linear in the concentration range 0.025-0.250

mg/ml (regression coefficient $r = 0.9896$) for atenolol and $0.02 - 0.17$ mg/ml ($r=0.9998$) for timolol.

The accuracy of the method was tested by recovery experiments on known amounts of bulk drug. The proposed method gave recoveries of 99.0 ± 0.9 and 99.54 ± 0.43 for atenolol and timolol respectively which were comparable to those obtained by the official method (99.10 ± 0.69) for atenolol and 99.87 ± 0.78 for timolol).

Various dosage forms of the two drugs were assayed by the proposed as well as by the official method (Table 1). The recovery values are based on the amount found and those calculated to be present according to the nominal concentration of the product. Pharmaceutical excipients likely to be present in the dosage forms e.g. starch, lactose, talc, magnesium stearate in tablets and buffers, preservatives in eye-drops exhibited no interference during the assay procedure. The proposed method is useful in routine analysis and quality control of these drugs.

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REFERENCES

1. Franz, D. N. In Gennaro, A. R., Ed. Remington : The Science and Practice of Pharmacy, 19th ed., Vol. II, Mack Publishing Co., Easton, 1995, 1013.
2. USP/NF 1995, U.S. Pharmacopoeial Convention, Rockville, 1995, 1554.
3. Indian Pharmacopoeia 1996, Government of India, Ministry of Health & Family Welfare, Delhi, 1996, 72.
4. Erram, S. V. and Tipnis, H. P., *Indian Drugs*, 1992, 29, 436.
5. Sreedhar, K., Sastry, C.S.P., Reddy, M. N. and Sarkar, D. G., *Indian Drugs*, 1994, 31, 389.
6. Elsayed, M. A. and Agarwal, S. P., *Talanta*, 1982, 29, 535.
7. Agarwal, S. P. and Elsayed, M. A., *Analyst*, 1981, 106, 1157.
8. Schwarzenbach, G. and Suter, H., *Helv. Chem. Acta*, 1941, 24, 617.
9. Benesi, H. A. and Hildebrand, J. H., *J. Am. Chem. Soc.*, 1948, 70, 2832.

Spectrophotometric determination of Pentazocine in pharmaceutical formulations

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Four simple and sensitive visible spectrophotometric methods have been described for the determination of pentazocine, based either on the formation of chloroform soluble, coloured ion-association complex between pentazocine and the dye [Alizarine Red S, λ_{\max} : 435 nm or Tropaeolin 000, λ_{\max} : 490 nm] or by finding the oxidant (N-bromosuccinimide or potassium permanganate) reacted with pentazocine using a dye [Celestine Blue λ_{\max} : 540 nm or Fast Green FCF, λ_{\max} : 625 nm].

A survey of literature revealed a few reported visible spectrophotometric methods¹⁻¹³ for the estimation of pentazocine (PZ). This paper describes the development of four more visible spectrophotometric methods for its determination by exploiting its basic

behaviour and reducing characteristics. Methods A and B are based on the formation of chloroform soluble ion-association complex between the drug and the dye [Alizarine Red S (ARS; method A) or Tropaeolin 000 (TP 000, method B)]. Methods C and D are indirect ones, Method C, involving the addition of excess

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