extract may be due to the antioxidant property of the flavonoids and free phenolic compounds present in the extract.

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Spectrophotometric Determination of Propranolol Hydrochloride in Pharmaceutical Preparations

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Two simple, sensitive and accurate spectrophotometic methods are described for the determination of propranolol hydrochloride either in pure form or in pharmaceutical preparations. Each method involves nitration of the drug with uranyl nitrate or thorium nitrate in sulphuric acid medium. The yellow coloured nitro derivative has an absorption maximum at 377 nm. The nitro derivative obeys Beer's Law in the concentration range of 2-32 µg/ml and 1-30 µg/ml for uranyl nitrate and thorium nitrate respectively. The optium reaction conditions and other analytical parameters are evaluated. The influence of substrates commonly employed as excipients with propranolol drug has been studied. Results of analysis of pure drug and its dosage forms by the proposed methods are in good agreement with those of the official method.

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Propranolol hydrochloride (PLH) belongs to beta-adrenoceptor antagonist class of compounds. It is currently used for treating anginapectoris, hypertension, migraine, cardiac arrhythmias, anxiety, thyrotoxicosis and glaucoma[1]. In view of its importance, various methods have been developed for the determination of PLH. The methods used for its determination include spectrophotometry[2,3], conductometry[4], HPLC[5,6] and spectroflurimetry[7]. The official methods normally involve non–aqueous titrimetry or ultraviolet spectrophotometry[8,9]. The widespread use of this drug has necessiated the development of simple and sensitive spectrophotometric methods for its routine quality control.

The present work reports two simple, sensitive and accurate spectrophotometric methods for the determination of PLH using thorium nitrate or uranyl nitrate in sulphuric acid medium. Each method is based on the nitration of the naphthalene ring with uranyl nitrate or thorium nitrate in sulphuric acid medium to yield a yellow coloured nitro product. Nitration of PLH takes place when the reaction mixture is warmed on a water bath (70-80°) for about 1-2 min. The method involving thorium nitrate is more sensitive (ε=6.259X10^3 l/mol.cm) than the method involving uranyl nitrate (ε =5.524X10^3 l/mol.cm). The methods have been successfully applied for the assay of PLH in pharmaceutical preparations.

All spectral measurements were made using a Hitachi UV–visible spectrophotometer model U-2001 with 1 cm matched quartz cells. All chemicals used were of analytical reagent or pharmaceutical grade and quartz processed high purity water was used throughout.

Standard solution of PLH (Cipla Ltd.) was prepared by dissolving 50 mg of the drug in 50 ml distilled water. The solution was further diluted to get the final concentration of 200 µg/ml. One percent solution each of uranyl nitrate and thorium nitrate was prepared separately in distilled water. Sulphuric acid (5 M) was used for the study.

Aliquots of standard solution containing 10-320 µg of PLH were transferred into a series of 10 ml volumetric flasks. Three millilitres of uranyl nitrate or thorium nitrate was added to each flask. The acid concentration in each flask was adjusted to 1.5 M using sulphuric acid (3ml, 5M). The contents were mixed well and kept on a water bath (70-80°) for 1-2 min. When the yellow coloured nitro product was formed, the contents were cooled to room temperature, diluted to 10 ml with distilled water and mixed well. The absorbances were measured at 377 nm against the corresponding reagent blank.

Synthetic mixtures containing 50 mg of PLH and various excipients were prepared in the laboratory. These mixtures were talc (150 mg), sucrose, starch and lactose (200 mg), gelatin (50 mg) and magnesium stearate (100 mg), talc, starch and magnesium stearate (100 mg), sucrose(150 mg), lactose (200 mg) and gelatin(50 mg).

A portion of the mixture was accurately weighed, diluted to 50 ml with distilled water in a volumetric flask, shaken well and then filtered. An appropriate aliquot of the solution was taken and the standard procedure was followed for the analysis of the drug content.

Twenty tablets were powdered thoroughly. An accurately weighed portion of the powder equivalent to about 50 mg of PLH was transferred into a 50 ml volumetric flask and diluted upto the mark with distilled water. The solution was shaken well and filtered through Whatman filter paper no. 42. The amount of the drug in each tablet was determined using the standard procedure described above. The results of analysis are given in Table 1.

Propranolol undergoes nitration with thorium nitrate or uranyl nitrate in acid medium to form a yellow coloured nitro derivative. Nitration of PLH was carried out by heating the reaction mixture on a water bath (70-80°) for 1-2 min. The stability of the coloured species depends upon the nature and strength of the acid medium. The yellow coloured species was found to be unstable in hydrochloric acid medium and did not form in acetic acid medium. The maximum intensity of the colour was obtained in the range of 1.25-2.0 M sulphuric acid. Hence 1.5 M sulphuric acid was maintained in subsequent studies.

The effect of the concentration of thorium nitrate or uranyl nitrate was studied by measuring the absorbances at 377 nm for solutions containing a fixed concentration of PLH and varying amounts of nitrates. The constant absorbance readings were obtained in the range of 2-4 ml of 1% of thorium nitrate or uranyl nitrate. However, a volume of 3 ml of thorium nitrate or uranium nitrate in a total volume of 10 ml was used for the analysis of PLH. The absorbance readings remained constant for more than 150 min. The order of addition of reagents had no effect on absorbance.

The yellow coloured species obeyed Beer's law in the concentration range of 1-30 and 2-32 µg ml^{-1} of PLH with molar absorptivity values of 6.259X10^3 and 5.524X10^3 L/

TABLE 1: ANALYSIS OF PROPRANOLOL IN FORMULATIONS.

Propranolol Formulations	Label claim (mg/tablet)	Amount found (mg) Developed methods			Recovery ±SD* % Developed methods	
		BP/USP method	Thorium nitrate	Uranyl nitrate	Thorium nitrate	Uranyl nitrate
Tablet I	10.0	9.99	9.98	9.95	98.95 ± 0.8	99.12 ± 0.71
Tablet 2	40.0	40.08	39.92	39.89	99.82±1.9	99.12±1.02
Tablet 3	80.0	80.15	80.06	80.08	98.89±1.1	99.01±0.66
Tablet 4	10.0	9.95	9.93	9.96	98.91±1.1	98.95±0.71
Tablet 5	40.0	39.94	39.95	39.97	99.97±0.5	99.14±0.86
Tablet 6	80.0	79.66	79.75	79.68	99.94±0.9	99.11±0.53

*Average of five determinations.

mol.cm for thorium nitrate and uranyl nitrate methods, respectively. The Sandell's sensitivity values as calculated from Beer's law data were found to be 0.0414 and 0.0469 μg/cm² for thorium nitrate and uranium methods respectively. Regression analyses of Beer's law plots at 377 nm revealed a good correlation (r=0.9995 and 0.9998). Graphs of absorbance versus concentration showed low intercept values (0.0051 and – 0.0015) and slope (0.235 and 0.212) and are described by a regression equation, Y=a+bX (where Y is the absorbance of a 1 cm layer, b is the slope, a is the intercept and X is the concentration of the drug in μg/ml), obtained by the least squares method. The low relative standard deviation values (0.93 and 0.95) and the range of error at 95% confidence level (0.64 and 0.81) for the analyses of five replicates of 20 μg/ml of PLH indicated good precision and accuracy of the proposed methods.

The extent of interference by commonly associated excipients such as magnesium stearate, talc, gelatin, starch, lactose, and sucrose was determined by measuring the absorbance of a solution containing 20 μg/ml of propranolol. An error of ± 2.0% in the absorbance reading was considered tolerable. The proposed methods were found to be free from interferences by the excipients in levels found in dosage forms. In order to test the accuracy of the methods, recovery experiments were performed on synthetic mixtures. The percentage recovery values were found to be 99.5 and 99.4 with RSD values of 1.1 and 0.9 for thorium nitrate and uranyl nitrate methods, respectively for the analyses of five replicates.

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