Simple and Rapid Spectrophotometric Determination of Propranolol Hydrochloride as Base Form in Pharmaceutical Formulation through Charge Transfer Complexation

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Abstract

Two simple and selective spectrophotometric methods are described for the determination of propranolol hydrochloride (PPH) as base form (PPL) in bulk drug, and in tablets and capsules. The methods are based on the molecular charge-transfer complexation of propranolol base (PPL) with either 2,4,6-trinitrophenol (picric acid; PA) or 2,4-dinitrophenol (DNP). The yellow colored radical anions formed on dissociation, are quantitated at 425 nm (PA method) or 415 nm (DNP method). The assay conditions were optimized. Beer's law is obeyed in the concentration ranges 2.4-42.0 µg ml-1 in PA method and 9.0-126.0 µg ml1 in DNP method, with respective molar absorptivity values of 4.97 × 103 and 1.66 × 103 l mol-1 cm -1 . The reaction stoichiometry in both methods was evaluated by Job's method of continuous variations and was found to be 1:1 (PPL:PA, PPL:DNP). The developed methods were successfully applied to the determination of PPL in pure form and commercial tablets/capsules with good accuracy and precision. Statistical comparison of the results was performed using Student's t-test and F-ratio at 95% confidence level and the results showed no significant difference between the reference and proposed methods with regard to accuracy and precision. Further, the accuracy and reliability of the methods were confirmed by recovery studies via standard addition technique.

1. Introduction

Propranolol hydrochloride (PPH), a non-selective beta-adrenoceptor antagonist, chemically known as (2RS)-1-[(1-Methylethyl)amino]-3-(naphthalen-1-yloxy) propan-2-ol hydrochloride (Figure 1) [1]. PPH is commonly used in the management of hypertension, angina pectoris, cardiac dysrhythmias, hypertrophic obstructive cardiomyopathy, myocardial infarction, anxiety, essential tremor and migraine. This beta-blocker may work by stabilizing arteries or preventing the central generator of migraine in the brainstem from firing. Of the many beta-blockers, PPH is the most effective for prevention of migraine. The drug is official in British Pharmacopoeia [2] and United States Pharmacopoeia [3], which describe UV-spectrophotometric methods for the assay of PPH after extraction into methanol, and also in Indian Pharmacopoeia [4] which describes a potentiometric titration of drug in ethanol with 0.1 M NaOH. O N OH H2 .Cl Figure 1: Structure of propranolol hydrochloride. Due to its therapeutic and pharmacological relevance, several methods have been reported for PPH and include high-performance liquid chromatography (HPLC) [4], thin layer chromatography [5], UVspectrophotometry [6-9], fluorimetry [10], voltammetry [11] and chemiluminometry [12, 13]. These techniques involve an expensive experimental set up and are not always easily accessible. Few titrimetric [14, 15] and visible spectrophotometric [16-32] methods have also been reported. http://astonjournals.com/csj 2 Research Article Visible spectrophotometry, because of its simplicity and cost-effectiveness, sensitivity and selectivity and fair accuracy and precision is routinely used in many industrial quality control laboratories. Several visible spectrophotometric methods based on different reaction schemes are found in the literature for PPH. Idowu et al. [16] reported a method for the assay of PPH using diazotized 4-amino-3,5-dinitrobenzoic acid (ADBA) as the chromogenic

derivatizing reagent. Bhandari et al. [17] reported a method based on the reaction of PPH with 1-chloro-2,4-dinitrobenzene, forming a complex, which absorb maximally at 314.6 nm. In a method reported by Golcuet al. [18], PPH was reacted with copper (II) or cobalt (II) and the colored complexes were measured at 548 or 614 nm. El-Rieset al. [19] proposed two spectrophotometric methods based on the chargetransfer complex reaction of PPH with π-acceptors, tetracyanoethylene (TCNE), or chloranilic acid (CLA) to give highly colored complex species which are quantitated spectrophotometrically at 415 or 510 nm. Salem [20] used similar reactions for the spectrophotometric determination of PPH which are based on the reaction of PPH as nelectron donor with the sigma-acceptor iodine and π-acceptors such as 7,7,8,8-tetracyaniquinodimethane, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, tetracyanoethylene, bromanil and chloranil. The resulting CT complexes were measured at 365, 840, 420, 470, 450 and 440 nm, respectively. Hussain et al. [21] reported a method based on the redox reaction of PPH with cerium (IV) in H2SO4 medium on heating and the developed color was measured at 478 nm. El-Emam et al. [22] reported a method based on oxidative-coupling reaction in which a mixture of an acidic solution of MBTH and PPH was treated with cerium (IV) and the resulting orange color peaking at 496 nm was measured. In addition to direct methods described above, several indirect methods based on a variety of reaction chemistries are also found in the literature. A spectrophotometric method proposed by Basavaiah et al. [23] makes use of the reaction between chloride of PPH and mercury(II) thiocyanate in which thiocyanate ions displaced complexed with iron(III) for subsequent measurement at 460 nm. In a spectrophotometric method reported by Basavaiah et al. [24], the unreacted cerium(IV) sulphate was treated with iron(II) and the iron(III) was complexed with thiocyanate and measured at 480 nm. Similar method reported by Basavaiah et al. [25] is based on the oxidation of PPH by a known excess of CAT in acid medium followed by determination of the unreacted oxidant by reacting with metal and sulphanilic acid. The same authors reported another spectrophotometric method in which the unreacted oxidant metavanadate was determined by reacting with diphenylamine, and the absorbance measured at 560 nm [26]. A method reported by Basavaiah et al. [27] involves the addition of a known excess of bromate-bromide mixture to an acidified solution of the drug and determination of the unreacted bromine by its bleaching action on methyl orange acid color and the absorbance measured at 510 nm. El-Didamony [28] reported three methods based on oxidation-bromination reaction of PPH by bromine, generated in situ by the action of acid on a bromate-bromide mixture, followed by determination of unreacted bromine by three different reaction schemes. In one method the residual bromine was determined by indigo carmine dye. In the other two methods, the residual bromine was determined by treating with a known excess of iron(II) and the resulting iron(III) was complexed with thiocyanate or the residual iron(II) with 1,10-phenanthroline. Gowda et al. [29] reported two procedures, similar to the above, in which PPH was oxidized by a known excess of NBS in H2SO4 medium followed by the reaction of unreacted oxidant with promethazine hydrochloride (PH) or methdilazine hydrochloride (MDH) to yield red colored products with absorption maximum at 515 or 513 nm. Two methods described by Al-Attas et al. [30] based on the oxidation of PPH by a known excess of N-bromosuccinimide (NBS), in an acidic medium followed by the reaction of excess oxidant with amaranth dye. Sastry et al. [31] devised one more method by treating PPH with a known excess of NBS in HCl medium, and after 10 min, the unreacted oxidant was determined by reacting with celestine blue and measuring the absorbance at 540 nm. Most of the reported spectrophotometric methods suffer from one or the other disadvantage such as use of heating/extraction step, critical dependence on pH, narrow linear range, poor sensitivity, use of multi reagents/ multi step reactions, longer contact time etc. as summarized in Table 1. The

methods based on C-T complexation reactions and using σ and π acceptors [19, 20] are less sensitive and have narrow linear ranges. Though substituted phenols (picric acid and dinitrophenol) have found wide applications as C-T complexing agents in the assay of pharmaceuticals [32-34], they have not applied for the assay of PPH. In this work, we demonstrate the use of picric acid and dinitrophenol as C-T complexing agents for the simple, rapid, sensitive and selective assay of PPH in pharmaceuticals. The methods are based on the formation of C-T complex of PPH base (PPL) with picric acid (method A) or dinitrophenol (method B) followed by the measurement of the absorbance of the colored species at 420 nm. The methods were demonstrated to be accurate, precise, robust and rugged, and eminently suited for rapid analysis in routine work.