Rapid and Sensitive Spectrophotometric Measurement of NonSpecific Beta Blocker Propranolol Hydrochloride Using Three Sulphonphthalein Dyes In Pure Form, Pharmaceuticals and Human Urine

KN Prashanth, K Basavaiah*
MS Raghu Department of Chemistry, University of Mysore, Mysore, Karnataka, India.

Abstract

Three sensitive, selective, rapid and easily reproducible spectrophotometric methods (A-C) have been developed for the determination of propranolol hydrochloride (PPH) as a hydrochloride free base propranolol (PPL) in bulk sample and in its dosage forms. These methods are based on ion-pair formation between propranolol as a hydrochloride and free base and three acidic (sulphonphthalein) dyes; namely bromothymol blue (BTB), bromocresol green (BCG) and bromocresol purple (BCP) which induces an instantaneous bathochromic shift of the maximum in the drug spectrum. The colored products are measured at 420 nm (PPL-BTB complex and PPL-BCP complex) and 425 nm (PPL-BCG complex). The reactions were extremely rapid at room temperature and the absorbance values remained constant for 90 min (method B), and over 24 hrs (method A and C). Conformity to Beer's law in the range 0.4-7.0 µg ml-1 for methods A and B and 0.5-8.4 µg ml-1 for method C enabled the assay of dosage forms of the drug. The proposed methods were compared with a reference method; the results obtained were of equal accuracy and precision. In addition, these methods were also found to be specific for the analysis of PPH in the presence of excipients, which are co-formulated in the drug. Satisfactory results were obtained when applied to spiked human urine. A more detailed investigation of the propanolol hydrochloride ion pair complexes were made with respect to its composition indicated by stability constant values.

Introduction Propranolol hydrochloride (PPH)

(2RS)-1-[(1-Methylethyl)amino]-3-(naphtha len-1-yloxy)propan-2-ol hydrochloride (Figure 1), is a highly effective antihypertensive and antianginal drug. Being a nonselective prototype betaadrenergic receptor-blocking agent, it possesses no other autonomic nervous system activity and specifically competes with beta-adrenergic receptor-stimulating agents for available receptor sites. The drug is widely used in clinical practice for the treatment of cardiac arrhythmia, hypertension and angina pectoris [1], dysfunctional labour, anxiety and migraine [2, 3]. It is also abused in sports involving little physical activity to reduce cardiac, contraction, heart rate and coronary blood flow [4]. Therefore, it has been included in the list of forbidden substances by the International Olympic Committee [5]. Monitoring of propranolol in biological fluids is important not only in clinical practice but also in the field of doping control. The drug is official in BP [6] and USP [8], which describe UV-spectrophotometric methods for the assay of PPH after extraction into methanol, and also in IP [7] 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. http://astonjournals.com/csj 2 Research Article Due to its therapeutical and pharmacological relevance, several methods have been reported for PPH and include thin layer chromatography [9], UV-spectrophotometry [10-13], fluorimetry [14], voltammetry [15] and chemiluminometry [16,17]. These techniques involve an expensive experimental set up and are not always easily accessible. One titrimetric [18] and a few visible spectrophotometric [19-34]

methods have also been reported. 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. A method for the assay of PPH using diazotized 4-amino-3,5-dinitrobenzoic acid (ADBA) as the chromogenic derivatizing reagent reported by Idowu et al. [19]. Bhandari et al. [20] 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 Golcu et al. [21], PPH was reacted with copper (II) or cobalt (II) and the coloured complexes were measured at 548 or 614 nm. El-Ries et al. [22] proposed two spectrophotometric methods based on the charge-transfer complex reaction of PPH with π-acceptors, tetracyanoethylene (TCNE), or chloranilic acid (CLA) to give highly coloured complex species which are quantitated spectrophotometrically, absorbing maximally at 415 or 510 nm. Salem [23] used similar reactions for the spectrophotometric determination of PPH which are based on the reaction of PPH as n-electron 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. [24] 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. [25] 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 colour 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. [26] 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. [27], 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. [28] 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 [29]. A method reported by Basavaiah et al. [30] 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 [31] 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. [32] 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 coloured products with absorption maximum at 515 or 513 nm. Two methods described by Al-Attas et al. [33] 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. [34] 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. The above reported methods suffer from disadvantages like heating step, slow reaction, extraction step, multi step reactions, tedious control of experimental variables and less sensitivity. The present investigation involves the development of accurate, reproducible, and adequately sensitive three spectrophotometric methods based on the formation of ion- pair complexes between hydrochloride free propranolol (PPL) with sulphonphthalein dyes namely bromothymol blue (BTB), bromocresol green (BCG) and bromocresol purple (BCP). The proposed methods were applied to the determination of PPH in pharmaceutical formulation and in human urine. No interference was observed in the assay of PPH from common excipients found in pharmaceutical http://astonjournals.com/csj Chemical Sciences Journal, Vol. 2012: CSJ-80 3 formulation and other biological materials present in urine.