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Sensitive and selective spectrophotometric assay of piroxicam in pure form, capsule and human blood serum samples via ion-pair complex formation

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HIGHLIGHTS

- Simple, accurate, selective and precise spectrophotometric methods.
- We found that acidic medium is necessary to form ion pair complex between piroxicam with three sulphonphthalein acid dyes.
- The formed complexes were stable.
- Developed and validated method has been used for piroxicam analysis on real pharmaceutical and human serum samples.

GRAPHICAL ABSTRACT

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ABSTRACT

A simple, accurate and highly sensitive spectrophotometric method has been developed for the rapid determination of piroxicam (PX) in pure and pharmaceutical formulations. The proposed method involves formation of stable yellow colored ion-pair complexes of the amino derivative (basic nitrogen) of PX with three sulphonphthalein acid dyes namely; bromocresol green (BCG), bromothymol blue (BTB), bromophenol blue (BPB) in acidic medium. The colored species exhibited absorption maxima at 438, 429 and 432 nm with molar absorptivity values of 9.400×10^3, 1.218×10^3 and 1.02×10^4 L mol^{-1} cm^{-1} for PX–BCG, PX–BTB and PX–BPB complexes, respectively. The effect of optimum conditions via acidity, reagent concentration, time and solvent were studied. The reactions were extremely rapid at room temperature and the absorbance values remained constant for 48 h. Beer's law was obeyed with a good correlation coefficient in the concentration ranges 1–100 μg mL^{-1} for BCG, BTB complexes and 1–95 μg mL^{-1} for BPB complex. The composition ratio of the ion-pair complexes were found to be 1:1 in all cases as established by Job's method. No interference was observed from common additives and excipients which may be present in the pharmaceutical preparations. The proposed method was successfully applied for the determination of PX in capsule and human blood serum samples with good accuracy and precision.

Introduction

Piroxicam is 4 hydroxy-2-methyl-N (2-pyridyl) 2H-1, 2-benzothiazine-3-carbaxamide-1, 1 dioxide (Fig. 1). It is a non-steroidal anti-inflammatory drug (NSAID) belonging to a class of compounds called oxicams [1–4]. Piroxicam was produced for the first time by Pfizer & Co. and studied for almost fifteen years, being introduced in medical practice in 1970 [5]. It is recommended for the treatment of inflammatory, nonspecific infection polyarthritis, acute gout, rheumatic arthritis, osteoarthritis, skeletal disorders,

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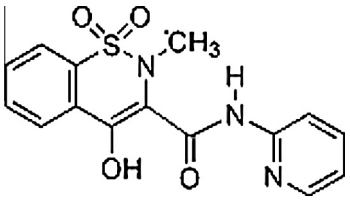

Fig. 1. Chemical structure of PX.

backaches, neuralgia, myalgia and other diseases accompanied by the pain syndrome or an inflammatory process [6,7]. Piroxicam is a potent and extensively used NSAIDs and an anti-arthritic drug with a long biological half-life [8]. The pharmacological action of the piroxicam is related to inhibition of cyclooxygenase (Cox), a key enzyme of prostaglandin biosynthesis at the site of inflammation [4]. The inhibitory effect of piroxicam in prostaglandin E_2 (PGE_2) synthesis is responsible for the ulcerogenic action of piroxicam on the gastrointestinal tract. Piroxicam strongly inhibits Cox-2 activity as well as migration of neutrocytes to inflammatory foci in the presence of prostaglandins. It is fully bio transformed in the liver by hydroxylation of the pyridol ring of the side chain and by coupling with gluconic acid, to inactive metabolites excreted with urine and faeces [9–13]. At high concentrations, gastrointestinal side effects can appear. Therefore, the analysis of piroxicam is important for obtaining optimum therapeutic concentration and for quality assurance in pharmaceutical preparations. The assay of piroxicam in bulk and pharmaceutical preparations is cited in the United States Pharmacopoeia (USP) which is based on liquid chromatography [2]. The great use of the drug posed pressure on the chemist to develop analytical methods for the determination of the drug in commercial dosage forms. Several analytical methods have been reported for determination of piroxicam such as: different versions of chromatography [14–23], derivative spectrophotometry [24], fluorimetric methods [25–28], potentiometry with ion-selective electrodes based on complexes with tricapryl ammonium [29], chemometrical methods [30], polarography [31,32], capillary zone electrophoresis [33,34] and voltammetry [35]. The main problem associated with these determinations is the laborious cleanup procedure required prior to analysis of piroxicam. Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of its simplicity, specificity and low cost.

The aim of this study was to develop a simple, accurate, precise and extraction-free spectrophotometric method based on the formation of ion-pair complexes between PX with sulphonphthalein dyes such as: BPB, BTB and BCG. This method was validated by the statistical data. The proposed method was applied for determining PX in capsule and human blood serum samples with satisfactory results. No interference was observed in the assay of PX from common excipients in levels found in pharmaceutical formulation.

Experimental

Apparatus

All absorption spectra were made using RAY LEIGH UV-1800 spectrophotometer (Beijing Beifen–Ruili, China) with 1 cm matched quartz cells. The pH measurements were carried out with a Metrohm 827 pH lab pH meter (Herisau, Switzerland).

Reagents and solutions

All the chemicals and reagents were in analytical grade (Merck–Germany) and used without further purification. Piroxicam (PX) was kindly supplied by Sobhan Pharmaceutical (Rasht, Iran). Capsule formulation of piroxicam was procured from a local pharmacy for analysis.

- A stock solution of pure PX (200 μg mL^{-1}) was prepared by dissolving 20 mg of PX with methanol in a 100 mL calibrated flask. Working standard solutions of drug were prepared daily from the stock solution by appropriate dilution with methanol.
- Solutions of bromocresol green (BCG), bromothymol blue (BTB), bromophenol blue (BPB) were prepared by dissolving an accurately weighted amount of the dyes in methanol and then diluted to the mark with water in a 100 mL calibrated flask separately. These solutions are stable for one week if kept in refrigerator.

General recommended procedure for PX in pure form

Aliquots of PX in the concentration range stated in Table 1 were transferred into a series of 5 mL calibrated flasks. 1.5 mL Potassium hydrogen phthalate buffer solution of pH 3–3.5 was placed and 1.5 mL of BPB, BTB and BCG solutions (50 μg mL^{-1}) were sequentially added. The solutions were dilute to the volume with methanol. After 15 min (at 23 ± 2 °C), the absorbance of the yellow ion-pair complexes were measured at 432, 429 and 438 nm for PX–BCG, PX–BTB and PX–BPB complexes, respectively against a reagent blank similarly prepared without adding PX solution. To obtain the standard calibration graph, plot the values of absorbance against the drug concentration, Fig. 2.

Procedure for the assay of PX in capsule

The content of ten capsules was evacuated, weighed and finely powdered and the average weight of a capsule was calculated. An amount of the capsule powder equivalent to 10 mg of PX was weighed accurately and transferred into a 100 mL beaker, dissolved in 25 mL of methanol then filtered through a Whatmann No. 41 filter paper and washed with methanol into a 100 mL calibrated flask. The solution was completed to the mark with methanol. An aliquot of the diluted solution was used for the determination of PX according to the procedure mentioned above. As seen in Table 2, determination of PX can be well done by this method. It is found that RSD% is lowest for PX–BTB complex.

Procedure for the assay of spiked human blood serum

The proposed methods have been successfully applied for the determination of PX in spiked human blood serum samples. Human blood serum was 40-fold diluted with distilled water. In order to determine PX in human blood serum, 1 mL of fresh and diluted serum was placed in a 5 mL calibrated flask. After addition of drug, buffer and reagents solutions into the flask (proceed as described in general procedures), the absorbance of the complex was measured at the optimum wavelength of each method. A blank value was determined by treating PX-free plasma in the same way. So the proposed method can be satisfactory applied to estimation of PX in human plasma (Table 3). As can seen that the proposed method provided acceptable accuracy and precision for the PX in human serum samples. In all cases the spiked recoveries were satisfactory, showing no obvious matrix interferences.

Results and discussion

Spectral characteristics

The nitrogenous drugs are present in positively charged protonated forms and anionic dyes of sulphonphthalein group