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Spectrophotometric Methods for the Determination of Salmeterol Xinafoate

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Two simple and accurate spectrophotometric methods (A and B) have been developed for the determination of salmeterol xinafoate (SX) and its dosage forms. SX in 0.05 M sodium hydroxide (NaOH) exhibits maximum absorption at a wave length of 247 nm and shows linearity in the concentration range of 1-14 µg/ml in method A. In method B, SX forms a stable bluish green chromogen on treatment with ferric chloride, potassium ferricyanide and hydrochloric acid, showing maximum absorption at 738 nm. The chromogen obeys Beer's law in the concentration range of 0.5-5 µg/ml.

Salmeterol is a direct acting sympathomimetic agent with β-adrenoreceptor stimulant activity and a selective on β_2 receptors[1]. It is a long acting antiasthmatic drug and may be useful in protecting against nocturnal and exercise-induced asthma attacks. Salmeterol is employed in the form of xinafoate and chemically it is, (R.S)-5-{1-Hydroxy-2-[6-(4-phenyl butoxy) hexylamino]ethyl} salicylalcohol-1-hydroxy-2-naphthoate[2]. It is not official in any pharmacopoeia. Literature survey reveals very few analytical methods for estimation of SX including HPLC[3-6] and spectrophotometric methods[7-10].

In the present investigation, SX is dissolved in 0.05 M NaOH and determined at the maximum absorption of 247 nm (method A) and in method B, SX formed a bluish-green coloured chromogen on treatment with ferric chloride, potassium ferricyanide and hydrochloric acid, with a maximum absorption at 738 nm.

MATERIALS AND METHODS

All the reagents used are of analytical grade. Solutions of sodium hydroxide (0.05 M) (Loba Chemie), ferric chloride (0.3% w/v) [CDH], potassium ferricyanide (0.1% w/v) (loba Chemie) and hydrochloric acid (1 N) prepared in doubled distilled water.

A stock solution of SX (1 mg/ml) (pure drug or formulation) was prepared in 0.05 M NaOH and further suitable dilutions were made with 0.05 M NaOH to get working standard solution of 50 µg/ml for method A. For method B accurately weighed amount of SX (pure drug or formulation) equivalent to 50 mg was dissolved in 25 ml of methanol and the volume was made upto 50 ml with double distilled water and further diluted with double distilled water to get working standard solution of 50 µg/ml. As commercial tablets of SX are not available in the market; two tablet formulations each containing 10 mg of SX (Ripsalm-Tab-I and Tab-II) were prepared in our laboratory and estimated.

Method A:

Aliquots of working standard SX (0.2 - 2.8 ml; 1 ml ≡ 50 µg) solutions were transferred into a series of 10 ml graduated test tubes and the volume was made upto 10 ml with 0.05 M NaOH. The absorbance of each solution was measured at 247 nm against a reagent blank.

Method B:

Into a series of 10 ml volumetric flasks, aliquots of working standard SX (0.1 - 1 ml; 1 ml ≡ 50 µg) were trans-

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TABLE 1 : OPTICAL CHARACTERISTICS AND PRECISION

Parameters	Method A	Method B
Beer's Law Limits (μg/ml)	1-14	0.5-5
Sandell's Sensitivity (μg/cm²/0.001 absorbance unit)	0.136	0.0067
Molar extinction coefficient (1. mole^{-1}. cm^{-1})	4.438×10^4	9.037×10^4
% Relative standard deviation**	0.510	0.482
% Range of error		
0.05 confidence limits	±0.4265	±0.4032
0.01 confidence limits	±0.6309	±0.5966
Correlation coefficient	0.99987	±0.9999
Regression equation (Y*)		
Slope (a)	7.31×10^{-2}	0.1506
Intercept (b)	5.06×10^{-4}	(-) 0.00166
Stability	12 h	15 min.

Y* b+ac; Where 'c' is concentration in μg/ml and Y is absorbance unit

** Calculated from eight replicate samples.

ferred and 1ml of ferric chloride (0.3%) solution was added. The flasks were stoppered immediately and shaken well for 5 min. Then 0.5 ml of potassium ferricyanide (0.1% was added into each flask and placed the lids immediately. After 5 min 1 ml 1 N HCl was added and the final volume was made upto 10 ml with double distilled water. The absorbance of each solution was measured at 738 nm against a reagent blank.

The amount of SX present in formulations were estimated by computing from their respective calibration curves. The dosage forms were also analysed by the UV spectrophotometric method by extraction of the drug into methanol and measuring the absorbance at 254 nm after suitable diluation with double distilled water. Spectral and absorbance measurements were made on an ELICO SL-159 UV VIS spectrophotometer by using 1 cm matched quartz cells at the temperature of 30±2°.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, Sandell's sensitivity, stability, molar extinction coefficient, % relative standard deviation (calculated from eight determinations and % range of error (0.05 and 0.01 confidence limits) for the proposed two methods are summarized in Table 1.

Recovery experiments were performed by adding known amount of drug to previously analysed pharmaceutical preparations and also to various excipients used in formulations. When pharmaceutical preparations containing SX were analysed, the results obtained by the proposed methods were in good agreement with the labelled amounts and are comparable with the results of UV spectrophotometric method (in methanol).

In method A, SX exhibits λ_{max} 247 nm in 0.05 M NaOH at which the absorbance of 0.05 M NaOH against double distilled water was negligeable. In method B the formation of bluish green coloured complex is due to the partial oxidation of phenolic hydroxy group of SX with ferricchloride and ferrous ions thus produced form complexes with the reagents for divalent iron like potassium ferricyanide. These results indicated that the proposed methods are simple, sensitive, reproducible and

accurate and can be used for the routine determination of SX in bulk and in solid dosage forms.

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