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Spectrophotometric analysis of raloxifene hydrochloride in pure and pharmaceutical formulations

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Two simple and sensitive spectrophotometric methods (A and B) for the determination of raloxifene hydrochloride in bulk samples and pharmaceutical formulations are described. Method A is based on the oxidation of the drug with ferric chloride and coupling with potassium ferric cyanide. Method B is based on reduction of the drug with Fehling's reagent. Bluish green color formed in method A absorbs at 735 nm and brown color produced in method B absorbs at 430 nm.

Raloxifene hydrochloride (RXF) methanone [6-hydroxy-2-(4-hydroxy phenyl) benzo[*b*]thien-3-yl]-[4[2-(l-piperidinyl) ethoxy]phenyl]-hydrocholoride is a selective estrogen receptor modulator (SREM) that is used to prevent osteoporosis in postmenopausal patients. It has estrogen-like effect on bone and lipid metabolism. In addition, it is an estrogen antagonist and lacks estrogen-like effects in uterine and breast tissues (Osol 2000; Satoskar and Bandarkar 2001; Budavari 1996; Harrison 2001; Dennis 2003). The drug is not official in any pharmacopoeias. Very few clinical studies have been reported for RXF. The present article reports two new visible spectrophotometric methods based upon the reaction of RXF molecule to undergo oxidation (Vipalava 2002) and reduction (Atherden 1995; Ph Ind 1996).

The optical characteristic such as Beer's law limits, molar, extinction coefficient, sandell's sensitivity, correlation coefficient, slope and intercept data from linear least squares treatment and percent relative standard deviation (from six replicate samples) were summarized in Table 1.

Table 1: Analysis of raloxifene in tablet formulations

Formulation	Label Claim (mg/tab)	Method	% of label claim* ± SD	% COV	S.E of Mean	% Recovery**
Tablet 1	60	M_1	98.8 ± 1.5	1.6177	1.9844	98.70
		M_2	99.9 ± 1.4	1.4219	0.7099	
Tablet 2	60	M_1	99.1 ± 1.5	1.6707	1.8630	98.90
		M_2	99.7 ± 1.6	1.2853	0.8331	

* Mean of six determinations. M_1 – Method A , M_2 – Method B. ** Average of five determinations

Table 2: Optical characteristics and precision

Observation	Method A	Method B
Absorption maxima (nm)	735	430
Beer's law limit (μg/ml)	0–70	0–65
Correlation coeffecient	0.9998	0.9995
Molar absorptivity ($l \cdot mol^{-1}cm^{-1}$)	1.1279×10^4	1.1248×10^4
Sandel's sensitivity ($\mu g/cm^2/0.001$)	2.058×10^{-2}	2.3408×10^{-2}
Regression equation ($y = mx + c$)		
Slope (m)	0.04858	0.04272
Intercept (c)	−0.1129	0.0382
% Range of error (confidence 95%)	0.0037	0.00104

In order to justify the reliability and suitability of the proposed methods, known quantities of pure drug were added to its pre-analyzed dosage forms and the values are listed in Table. 2. There is no interference from other ingredients present in the formulation.

Method A involves oxidation of the drug with 0.5% ferric chloride solution. Oxidation of RXF with 0.5–1 ml 0.5% ferric chloride solution gave a maximum and reproducible absorbance values. The effect of time, temperature of oxidation on absorbance of the colored species were studied by conducting the oxidation at different temperature for different time intervals, oxidation time ranging from 5–15 min at room temperature gave constant reproducible absorbance values.

In method B reduction of RXF with 1–3 ml of Fehling's reagent gave good and reproducible absorbance value. The effect of reagent concentration, time and temperature were studied. Reduction time ranging from 5–45 min at room temperature gave constant and reproducible values. The time beyond 45 min and increasing the temperature gave unpleasant results.

Stability of the chromogens formed in both methods were tested at various time interval. The chromogens were found to be stable up to 48 h.

The proposed methods are simple and sensitive with good precision and accuracy, employing inexpensive and prevalent chemicals, they can be used for the routine quality control analysis of RXF in pure form as well as in pharmaceutical formulations.

Experimental

An Elico SL150 spectrophotometer with 1 cm matched quartz cells were used for all spectral and absorbance measurements. All solutions were prepared in double distilled water and all the chemicals were of analytical grade. Aqueous solutions of 0.5% ferric chloride solution and Fehling's reagent (E. Merck) were used. All other chemicals were procured from commercial sources.

1. Preparation of solutions

Stock solution containing 1 mg/ml of pure RXF was prepared by dissolving 100 mg of the drug in methanol. Working standard solutions were prepared by further dilution of the stock solution with methanol to get 20 mg/ml of RXF for both the methods.

2. Analytical procedure for method A

Aliquots of standard RXF solution (0.2–1 ml) were taken in a series of 10 ml volumetric flask and 1 ml of 0.5% ferric chloride solution was added followed by potassium ferric cyanide, thoroughly mixed and absorbance measured at 735 nm against blank solution. A calibration curve has been drawn by plotting the absorbance reading against concentration of the drug. The amount of the drug was calculated from the standard calibration graph.

3. Analytical procedure for method B

Aliquots of standard RXF solution (0.2–1 ml) were taken in a series of 10 ml volumetric flask and 1 ml of 0.5% ferric chloride solution was added follow by potassium ferric cyanide, thoroughly mixed and absorbance measured at 430 nm against blank solution. A calibration curve has drawn by plotting absorbance reading against drug concentration. The amount of the drug was calculated from the standard calibration graph.

4. Analytical procedure for the the formulation

A tablet powder equivalent to 100 mg RXF was weighed accurately and transferred to a 100 ml volumetric flask. The content was dissolved in methanol and made up to the volume with methanol. The procedure mentioned in method A and method B is repeated.

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References

Atherden LM Eds., (1995) Aldehydes and ketoness. In: Bently and Drivers (ed) Pharmaceutical Chemistry, 8th ed., Delhi, p. 356–357.
Budavari S (1996) (ed) The Merck Index, 11th ed., Whitehouse station, p. 1394.
Dennis JC (2003) Sex hormones. In: Drugs Facts and Comparisions, 57th ed., St. Louis, Missouri, p. 259–261.
Harrison TR (2001) Endocrinology and hormone antagonists. In: Principles of Internal Medicine, Vol II, 15th ed., New York, p. 2234.
Osol A (2000) In: Remington (ed) The sciences and practice of pharmacy, 20th ed Vol II, Philadelphia, p. 1386.
Pharmacopoeia of India (1996) Ministry of Health and Family welfare, Government of India, New Delhi, p. 370.
Satoskar RS, Bandarkar SD (2001) Calcium, Phosphorous and Magnesium in metabolism. In: Pharmacology and Pharmacotherapeutics, 17th Ed., Bombay, p. 990–991.
Vipalava P (2002) New spectrophotometric analysis of atenolol in pure and pharmaceutical formulation. Indian J Pharm Sci (64) 129–132.

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Determination of peroxide values using ethyl acetate as solvent

Analytical methods in respect to environmental and economical concern, part 21*

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Peroxide values of fixed oils can be determined in ethyl acetate, an easily biodegredable solvent instead of chloroform according to PH. EUR. 2002, method A. Potentiometric indication is recommended. Further investigations are necessary to explain the high blank values obtained, when ethyl acetate is used.

The peroxide value is the number that expresses the quantity of peroxide in 1000 g of the substance in milliequivalents of active oxygen. The peroxide-number is an important indication of the degree of rancidity of fats (Bracher 2002). PHARM. EUR. 2002 determines the peroxide value according to two methods. Method A uses chloroform as solvent and is applied in most of the monographs. In order to avoid the use of environment hazardous chlorinated hydrocarbons, method B employs 2,2,4-trimethylpentane (isooctane). But the latter method is not without problems. Since trimethylpentane floats on the aqueous layer, the transition of the iodine from the organic phase into the aqueous medium is delayed very much. PH. EUR. recommends to add a small amount of a high HLB nonionogenic emulsifier for example polysorbate 60. A validation is necessary, if method B is used instead of method A.

Ethyl acetate can replace chloroform in the determination of the iodine value of fixed oils (Hilp 2004a). But starch solutions do not yield the characteristic blue colour with iodine in the presence of ethyl acetate. Above all, with application of 0.01 M $Na_2S_2O_3$ the change of the indicator is difficult to recognise. Nevertheless, if potentiometric titration is used, a definite potential jump (Hilp, 2002b, 2004a) can be observed. Furthermore, ethyl acetate shows a fine distribution in water, when stirred. A fast transition of iodine in the aqueous phase can be recognised.

The Table shows the determination of peroxide values of three fixed oils. On purpose, old arachis oils and sesame oil, whose expiration date was exceeded, were used to get a high peroxide value. PH. EUR. 2002 demands for castor oil a peroxide value not over 10.0, because only recently pressed oil yields a value below 5.0 (Arens and Brühl 2002).

When using ethyl acetate as solvent high blank values are conspicuous. Above all, the registration of the poten-