Visible Spectrophotometric Methods for Estimation of Repaglinide in Tablet Formulation

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Two simple, economical, precise and reproducible visible spectrophotometric methods have been developed for the estimation of repaglinide in tablet formulation. The developed methods are based on the formation of chloroform extractable complex of repaglinide with zincon and methylthymol blue in acidic medium. The extracted complex with zincon shows absorbance maxima at 533.0 nm and linearity in the concentration range of 50-250 µg/ml. The extracted complex with methylthymol blue shows absorbance maxima at 427.0 nm and linearity in the concentration range of 100-500 µg/ml. Results of analysis for both the methods were validated statistically and by recovery studies.

Repaglinide, chemically, (S)-2-ethoxy-4-[2-[[3-methyl-1-[2-(1-piperidinyl)phenyl] butyl]amino]-2-oxoethyl] benzoic acid, is a new nonsulphonyl urea oral hypoglycemic drug[1]. It is used in the treatment of type-2 diabetes mellitus[2]. It is official in USP[3] which describes liquid chromatographic method for its quantitation. Literature survey reveals HPLC[4-6] methods for the estimation of repaglinide from plasma and pharmaceutical formulation. The objective of the present investigation is to develop simple, accurate and economical spectrophotometric methods for the estimation of repaglinide in tablet formulation.

Thermospectronic UV1, UV/Vis double beam spectrophotometer with spectral bandwidth of 2 nm, wavelength accuracy of ±0.5 and 1 cm matched quartz cells was used for analytical method development. All the chemicals and reagents used were of analytical grade. Zincon (2-[α-(2'-hydroxy-5'-sulfophenylazo)-bezylidine]hydrazino) benzoic acid monosodium salt, (Thomas Baker, Mumbai) reagent was prepared in acid phthalate buffer of pH 1.2 and methylthymol blue (CDH, New Delhi) reagent was prepared in acid phthalate buffer of pH 2.0. Both the reagents were prepared in double distilled water and extracted several times with chloroform so as to remove chloroform soluble impurities. Tablet formulation of repaglinide (Torrent, Ahemedabad) was procured from a local pharmacy. Standard solution of repaglinide was prepared by dissolving 100 mg in 100 ml of chloroform to give stock solution of concentration 1 mg/ml of drug.

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For method I, in a series of 10 ml volumetric flasks, aliquots of standard drug solution (1 mg/ml) in chloroform were transferred and diluted with same so as to give several dilutions in concentration range of 50-250 µg/ml of repaglinide. To 5 ml of each dilution taken in a separating funnel, 5 ml of zincon reagent was added. Reaction mixture was shaken gently for 5 min and allowed to stand for 5 min so as to separate aqueous and chloroform layer. The chloroform layer was separated out and absorbance maxima measured at 533.0 nm against a reagent blank. Calibration curve was plotted between concentration of repaglinide and measured absorbance.

For method II, in a series of 10 ml volumetric flasks, aliquots of standard drug solution (1 mg/ml) in chloroform were transferred and diluted with same so as to give several dilutions in concentration range of 100-500 µg/ml of repaglinide. To 5 ml of each dilution taken in a separating funnel, 5 ml of methylthymol blue reagent was added. Reaction mixture was shaken gently for 5 min and allowed to stand for 5 min so as to separate aqueous and chloroform layer. The chloroform layer was separated out and absorbance measured at 427.0 nm against a reagent blank. Calibration curve was plotted between concentration of repaglinide and measured absorbance.

For analysis of tablet formulation, twenty tablets (1.0 mg and 2.0 mg) of repaglinide were weighed accurately and finely powdered. An accurately weighed portion of powdered sample, equivalent to 15 mg of repaglinide was taken in a 50 ml volumetric flask containing 25 ml of chloroform, sonicated for 20 minutes.

TABLE 1: RESULT OF ANALYSIS AND RECOVERY STUDIES

Method	Label claim (repaglinide) mg/tab	% of label claim estimated*	% recovery**	Standard deviation
Method I	1.0	99.11	99.02	0.2350
(Zincon)	2.0	99.30	99.23	0.3126
Method II	1.0	99.24	98.74	0.3350
(Methylthymolblue)	2.0	98.85	99.17	0.5818

*Average of five determinations, **Average of recovery studies at three different concentration levels

The resultant was filtered through Whatman filter paper No. 41 into another 50 ml volumetric flask. The filter paper was washed several times with chloroform. The washings were added to the filtrate and the final volume was made up to the mark with chloroform.

For method I, 5 ml filtrate of the sample solution was diluted to 10 ml with chloroform and treated as per the procedure of the calibration curve. Amount of the drug present in sample was computed from respective calibration curve.

For method II, 5 ml filtrate of the sample solution was treated as per the procedure of the calibration curve. Amount of the drug present in sample was computed from respective calibration curve. The procedure of analysis from tablet formulation for both the methods was repeated five times with two different strengths of tablet formulation. Results of analysis are reported in Table 1.

Recovery studies were carried out for both the methods by the addition of known amount of standard drug solution of repaglinide to pre-analyzed tablet sample solution at three different concentration level. The resulting solutions were analyzed by proposed methods. The results of recovery studies were found to be satisfactory and are reported in Table 1.

These proposed methods were found to be simple, accurate, economical and rapid. Recovery studies were found close to 100 percent that indicates accuracy and precision of the proposed methods. Statistical analysis was carried out and the results of which were satisfactory. Standard deviation and relative standard deviation values were low that indicated reproducibility of the proposed methods. It was observed that excipients did not interfere in the determination of repaglinide. Hence these developed methods could be used for routine estimation of repaglinide in its tablet dosage forms.

ACKNOWLEDGEMENTS

REFERENCES

1. Budavari, S., Eds., In; The Merck Index, 12th Edn., Merck & Co., Inc., Whitehouse Station, NJ, 1996, 8308.
2. Reynolds, J.E.F., Martindale, 33rd Edn., The Complete Drug Reference, Pharmaceutical Press, London, 2002, 334.
3. United State Pharmacopoeia, Asian Edn., USP Convention Inc., Rockville MD, 2003, 1623.
4. Greischel, A., **J. Chromatogr.**, 1991, 568, 246.
5. Gandhimathi, M., Ravi, T.K. and Renu, S.K., **Anal. Sci.**, 2003, 19, 1675.
6. Krishna Reddy, K.V.S.R., MosesBabu, J., Mathad, V.T., Eswaraiah, S., Reddy, S.M., Dubey, P.K. and Vyas, K., **J. Pharm. Biomed. Anal.**, 2003, 32, 461.