Original Article

Spectrophotometric method for quantitative determination of triclabendazole in bulk and pharmaceutical

Abstract

Background: Triclabendazole (TCBZ, 6-chloro-5(2-3 dichlorophenoxy)-2-methyl thio-benzimidazole), an halogenated benzimidazole (BZD) thiol derivative, shows high efficacy against both the immature and mature stages of Fasciola hepatica in sheep and cattle, which is a differential feature compared to other available trematodicidal drugs. As a consequence of its excellent activity against the liver fluke, it has been extensively used and this has inevitably promoted the selection of TCBZ-resistant populations, which is now a worrying problem in several areas of the world. We propose simple ultraviolet spectrophotometric method for the estimation of triclabendazole in 0.1 methanolic HCl for the estimation of the drug. Method was validated as per ICH guidelines. **Materials and Methods:** Spectral absorbance measurements were made on Shimadzu UV-1800 with 10 mm matched quartz cells and dilutions were made in 0.1 M methanolic HCl. **Results:** The LOD and LOQ of triclabendazole at 305 nm were found to be 0.068434 and 2.73×10-4 µg/ml respectively. The calibration was linear in the range of 1–10 µg/ml. Analytical parameters such as stability, selectivity, accuracy, and precision have been established for the method in Endex and Fasinex tablets and evaluated statistically to assess the application of the method. **Conclusion:** Method passes all parameters with in desirable limits and found to be simple, stable, sensitive, reproducible, and accurate for the routine analysis of the drug in pharmaceutical formulations and in pharmaceutical investigations involving triclabendazole.

Key words:
Method development and validation, spectrophotometric method of triclabendazole, Assay of Triclabendazole

Introduction

Triclabendazole (TCBZ, 6-chloro-5(2-3 dichlorophenoxy)-2-methyl thio-benzimidazole), an halogenated benzimidazole (BZD) thiol derivative, shows high efficacy against both the immature and mature stages of *Fasciola hepatica* in sheep and cattle, which is a differential feature compared to other available trematodicidal drugs.[1]

Triclabendazole is effective in humans presenting with infection by the liver fluke *Fasciola hepatica*[2,3] or with the lung fluke *Paragonimus sp*.[4,5]

Preliminary pharmacokinetics in European patients indicate that the absorption of TCBZ might be higher in postprandial than in fasting administration conditions.[3]

The pharmacokinetics of triclabendazole in sheep and goat have been studied.[6,7] Like other sulfide benzimidazoles, triclabendazole is oxidized to sulfoxide and sulfone metabolites in sheep, goat, and cattle.[7,8]

The purpose of the present study was to develop a rapid and simple UV spectroscopic method for assaying triclabendazole in bulk and pharmaceutical dosage forms.

Materials and Methods

Pure drugs of triclabendazole (Ipca Ltd, Ratlam, India),

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methanol (Qualigens Fine Chemicals Ltd, Mumbai) were used for the present study. Tablets were procured from a local pharmacy. Spectral absorbance measurements were made on Shimadzu UV-1800 with 10 mm matched quartz cells.

Method

Different solvent were investigated to develop a suitable UV spectrophotometric method for the analysis of TCBZ in formulations. For selection of media the criteria employed were sensitivity of the method, ease of sample preparation, solubility of the drug, cost of solvents, and applicability of method to various purposes [Figure 1].

- 1 N NaOH (Methanolic)
- 0.1 N NaOH (Methanolic)
- 1 N HCL (Methanolic)
- 0.1 N HCL (Methanolic
- Finally 0.1 methanolic HCL was used for the estimation of triclabendazole.

Standard

The stock solutions having 1 mg/ml solutions of drugs were freshly prepared in 0.1 N methanol. Aliquots of stock solutions were diluted further again using 0.1 N methanol to get the concentration of triclabendazole as 2, 4, 6, 8, 10, and 12 µg/ml at 305 nm to study the verification of Beer's law [Figure 2].

Sample

Tablets containing 900 mg TCBZ was finely powdered. A quantity of powder equivalent to 100 mg TCBZ was accurately weighed and transferred to a 100 ml volumetric flask, dissolved in 0.1 N methanolic HCL, filtered through Whatman filter paper no. 1 and the volume was made up to 100 ml with the same solvent. Aliquots of this solution were diluted with 0.1 N methanolic HCL to get the concentration of 6 µg/ml.

Analytical validation

Linearity

The linearity of an analytical method is its ability to reduce test results that are directly or by a well-defined mathematical transformation proportional to the concentration of analyte in samples within a given range. The range of analytical method is the interval between upper and lower levels of analyte including levels that have been demonstrated to be determining with precision and accuracy using the method. The linear response of TCBZ was determined by analyzing five independent levels of the calibration curve in the range of 1-12 µg/ml in triplicate.

Repeatability (Precision on replication)

It is a precision under a same condition (same analyst, same apparatus, short interval of time, and identical reagents) using the same sample. Method precision of the experiment was performed by preparing the standard solution of TCBZ (6 µg/ml) for three times and analyzed as per the proposed

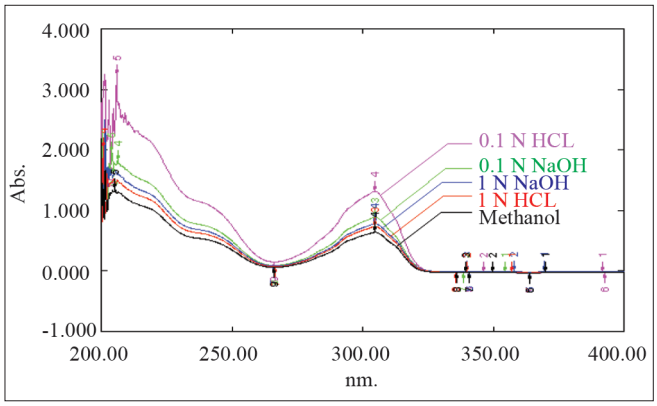

Figure 1: Overlay spectra of drug in different solvents

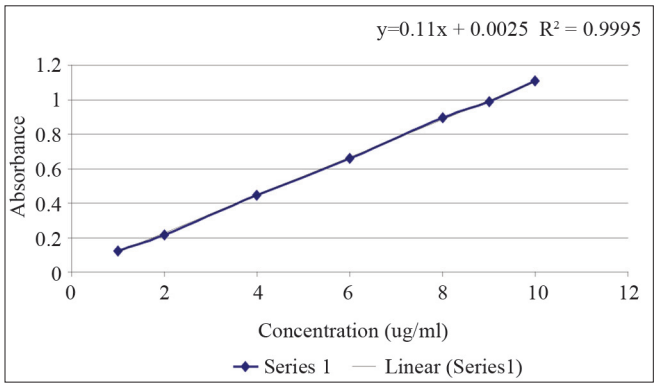

Figure 2: Calibration curve of TCBZ

method. Percentage relative standard deviation (%RSD) or coefficient of variation (CV) was not more than 2%.

Intermediate precision

It expresses within laboratory variations as on different days analysis or equipment within the laboratory. Variation of results within same day is called intra-day precision and variation of results amongst days called inter-day precision. The intra-day precision (CV) was determined for standard solution of TCBZ for three times on the same day. The inter-day precision (CV) was determined for standard solution of TCBZ for three days.

Accuracy

The accuracy of the proposed method was studied by recovery experiments. This was performed by adding 80, 100, and 120% of the nominal concentration of drugs standard solutions of TCBZ to the standard drug and pharmaceutical tablet solutions within the linearity range. Three samples were prepared for each recovery concentration level. The results obtained show excellent recovery of ≥98% for all the three drugs.

Specificity

The specificity of the method was tested by adding a known quantity of standard drug solutions to the tablet excipients

placebo solutions. The tablet excipients placebo solution (without drug) was prepared by mixing the common tablet excipients such as magnesium stearate, starch, lactose, and microcrystalline cellulose with proportions of drug to excipients ratio. From the UV spectra and absorption of excipients alone and the excipients spiked with the drugs. It is clear that no significant interference was found in the drug absorption during analysis.

Regression analysis of calibration curves and summary of validation parameters

Parameter TCBZ S.D.

Wavelength (nm) 305 nm

Limit of quantitation (μg/ml) 0.00273256

Limit of detection (μg/ml) 0.068434

Regression equation

Intercept (α) 0.0027 0.031496

Slope (β) 0.11 0.042957

Correlation coefficient (r) 0.9995 0.030179

Recovery

Product B 99.032 0.323452

Product A 98.97 0.8234

Precision

Repeatability 103 0.0301054

Intra-day precision 97.38 0.039

Inter-day precision 100.5 0.009

Specificity mean difference % interference

Specificity 0.09 1.54 %

Conclusion

The proposed method was found to be simple, accurate, and précised for estimation of drugs without interference. All the validation parameter was found in satisfactory level. This method can give excellence results and can be employed for the routine analysis of drug in bulk and pharmaceutical products.

References

1. Boray J, Crowfoot P, Strong M, Allison J, Schellenbaum M, von Orelli M, *et al*. Treatment of immature and mature *Fasciola hepatica* infections in sheep with triclabendazole**.** *Vet Rec* 1983**;113:**315-7.
2. Chen MG, Mott KF. Progress in assessment of the morbidity due to Fasciola hepatica infection: A review of the recent literature. Trop Dis Bull 1990;87:R1-38.
3. Loutan L, Bouvier M, Rojanawisut B, Stalder H, Rouan MC, Buescher G, *et al*. Single treatment of invasive Fascioliasis with triclabendazole. Lancet 1989;8659:383.
4. Ripert C, Couprie B, Moyou R, Gaillard F, Appriou M, Tribouley-Duret J. Therapeutic effect of triclabendazole in patients with paragonimiasis in Cameroon: A pilot study. Transac Roy Soc Trop Med Hyg 1992;86:417.
5. Calvopiña M, Paredes W, Guderian RH, Poltera AA. Eficacia del triclabendazole en Paragonimiasis pulmonar humana refractaria a la emetina, bithionol y praziquantel. Parasitología al Dia 1993;17:44-6.
6. Kinabo LD, Bogan JA. Pharmacokinetics and efficacy oftriclabendazole in goats with induced fascioliasis. J Vet Pharma Thera 1988;11:254-9.
7. Hennessy DR, Lacey E, Steel JW, Prichard RK. The kinetics of triclabendazole disposition in sheep. J Vet PharmaThera 1987;10:64-72.
8. Bogan JA, Mahammed ANA, Formica G. Pharmacokinetic studies with triclabendazole/fenbendazole combination in sheep and cattle. Rio de Janeiro, Brazil: World Assoc Adv Vet Parasit Abstracts; 1985;165:38.

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