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Determination of albendazole sulfoxide in human plasma by using liquid chromatography–tandem mass spectrometry

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ABSTRACT

A rapid, simple and sensitive method was developed and validated using liquid chromatography–tandem mass spectrometry (LC–MS/MS) for determination of albendazole sulfoxide (ABZOX) in human plasma. The plasma samples were extracted by protein precipitation using albendazole sulfoxide-d3 as internal standard (IS). The chromatographic separation was performed on Waters Xbridge C18Column (100 × 4.6 mm, 3.5 μm) with a mobile phase consisting of ammonia solution, water and methanol at a flow rate of 0.70 mL/min. ABZOX was detected and identified by mass spectrometry with electrospray ionization (ESI) in positive ion and multiple-reaction monitoring (MRM) mode. The method was linear in the range of 3–1500 ng/mL for ABZOX. This method was successfully applied to the bioequivalence study in human plasma samples.

1. Introduction

Albendazole is an orally administered broad-spectrum antihelmintic. Chemical formula of albendazole is methyl 5-(propyl-thio)-2-benzimidazolecarbamate. The empirical formula is $C_{12}H_{15}N_3O_2S$ and its molecular weight is 265.3 [1]. Albendazole is a white to off-white powder. It is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted to the sulfoxide metabolite prior to reaching the systemic circulation. The systemic antihelmintic activity has been attributed to the primary metabolite, albendazole sulfoxide (ABZOX) [1,2].

Albendazole is present at very low concentrations in plasma samples whereas albendazole sulfoxide is present at higher concentrations [3]. Many analytical methods have been reported for determination of albendazole metabolites in human plasma by high performance liquid chromatography (HPLC) with ultra-violet, fluorescence detection [3–6] and also by using capillary electrophoresis [7]. Many LC/MS–MS methods have been described using liquid–liquid extraction [8–11] or using solid-phase extraction [2].

As a result, the aim of this present study was to develop a simple, rapid, cheap and sensitive method for ABZOX determination using protein precipitation in plasma samples and to apply this method to the samples obtained from clinical trials. In our validated method the lower limit of quantification (LLOQ) is less than all methods described at literature [2–11].

2. Experimental

2.1. Chemicals and materials

Albendazole sulfoxide (98%) and paracetamol were kindly supplied by Toronto Research Chemicals (Toronto, Canada). Albendazole sulfoxide-d3 (internal standard, IS) was purchased from Clearsynth (Mumbai, India). Albendazole was supplied by Sequent Scientific Limited (Karnataka, India). Methanol and ammonia solution 25% were of HPLC grade and were purchased from Merck (Darmstadt, Germany). Lithium heparin blank human plasma was obtained from Equitech Enterprises Inc (Texas,USA). The water used to prepare mobile phase was purified in a Millipore MilliQ water purification system (USA).

2.2. Stock solutions, calibration standards and QCs

Stock standard solutions of ABZOX were prepared in methanol at a concentration of 0.5 mg/mL. Working solutions in the concentration range of 1–100 μg/mL were prepared by diluting in methanol.

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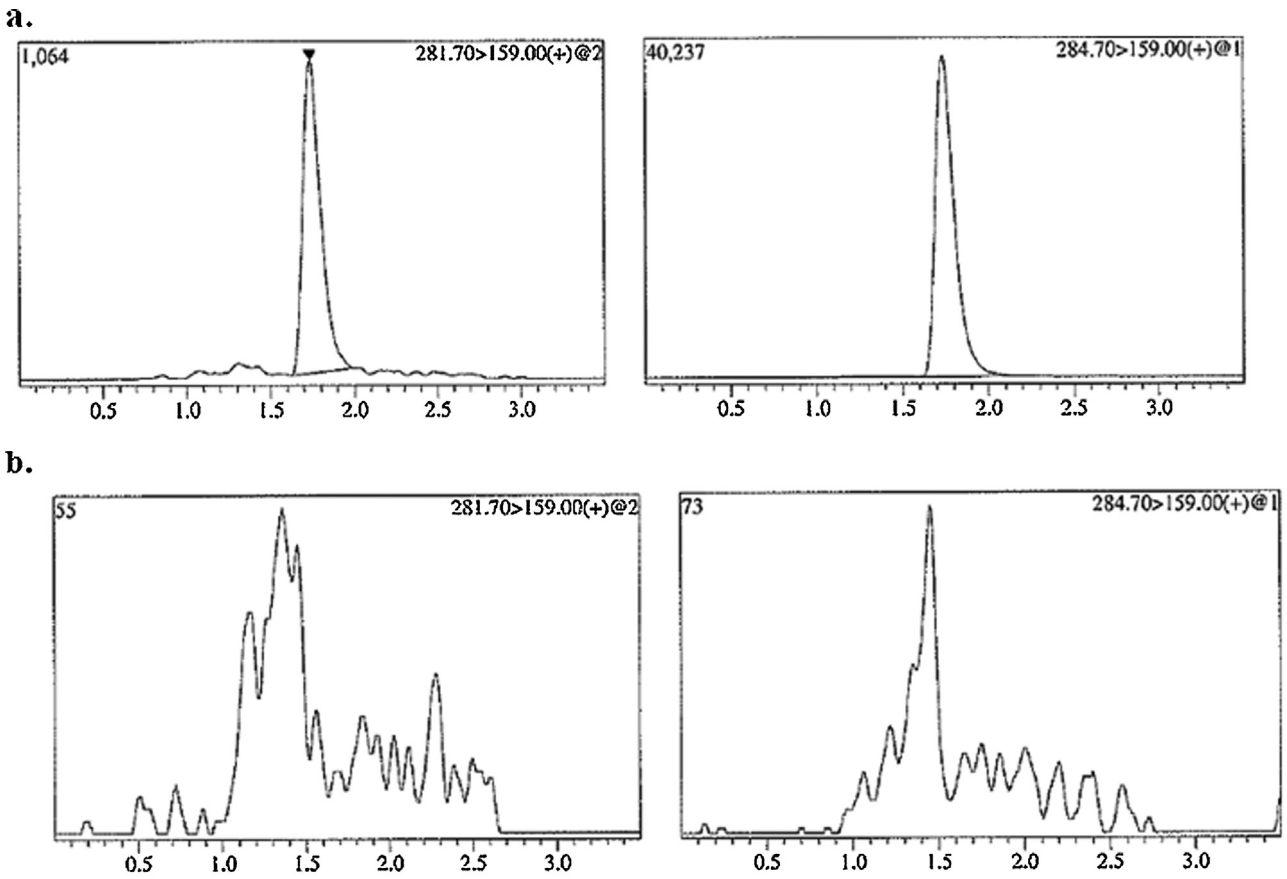

Fig. 1. MRM chromatograms of 3 ng/mL (LLOQ) of ABZOX spiked with internal standard (a), and blank human plasma (b).

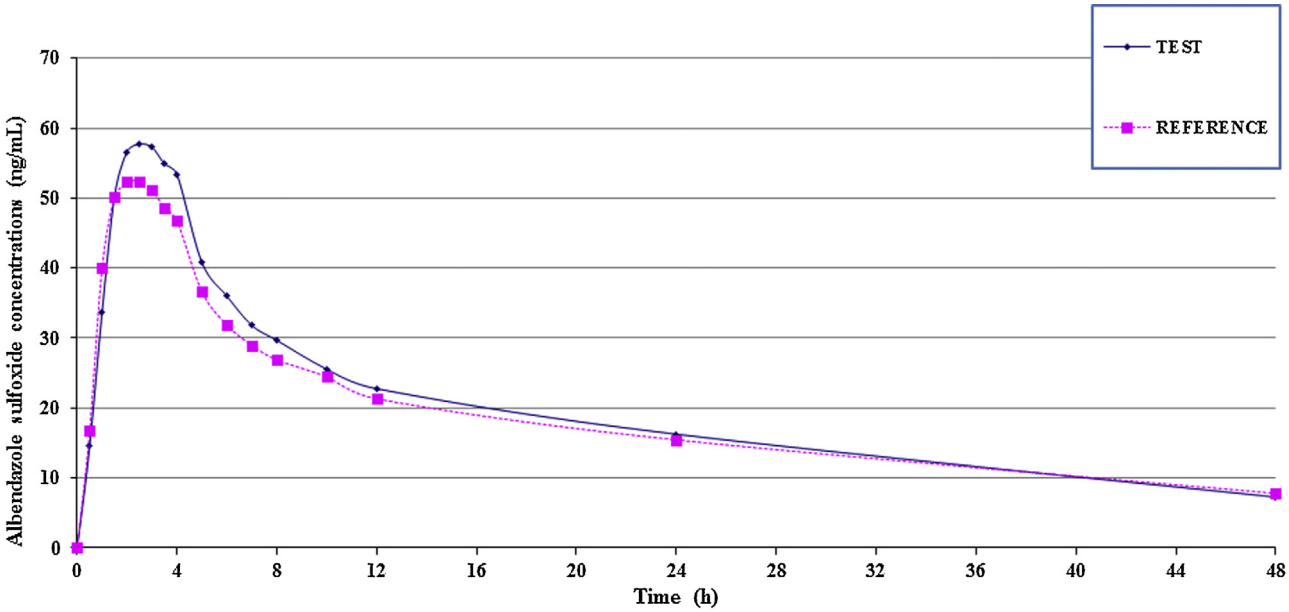

Fig 2. Mean plasma concentrations of test vs. reference after 400 mg dose (one 400 mg tablet) single oral dose (44 healthy volunteers).

Table 1
MS parameters for ABZOX and albendazole sulfoxide-d3.

Compound	Precursor	Product	Dwell time	Q1 pre-bias (V)	Collision energy(V)	Q3 pre-bias (V)
ABZOX	281.70	159.0	100	−30	−40	−25
IS	284.70	159	100	−30	−40	−26