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Fast determination of itraconazole by liquid chromatography tandem mass spectrometry

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PURPOSE / OBJECTIVES

Itraconazole is a broad-spectrum triazole antifungal agent. It is poorly soluble in water and these properties make the oral absorption of itraconazole difficult. Therapeutic drug monitoring can be considered because the itraconazole concentration differs between individuals. The aim of this study was to develop a simple, fast and accurate tandem mass spectrometric method for determination of itraconazole.

MATERIALS & METHODS

Mass spectrometric analyses were performed using an Shimadzu LC-20-AD (Kyoto, Japan) coupled with a ABSCIEX API 3200 triple quadrupole mass spectrometer (USA) equipped with an electrospray ion source (ESI) operating in positive mode. The ions used to quantify were selected as m/z 705.3>392.4 for itraconazole and m/z 475.2>58.0 for internal standard (sildenafil). Chromatographic separation was performed on a C18 column (4.6×50 mm, 5 µm) with a mobile phase consisting of 1% formic acid in water and of 1% formic acid in acetonitrile at a flow rate of 1 ml/min. The sample preparation procedure was briefly, 100 µL sildenafil and 600 µL methanol were added to 250 µL sample and vortexed for 30 s. Afterward, the mixture was centrifuged at 2000 × g for 10 min and 25 µL of supernatant was injected.

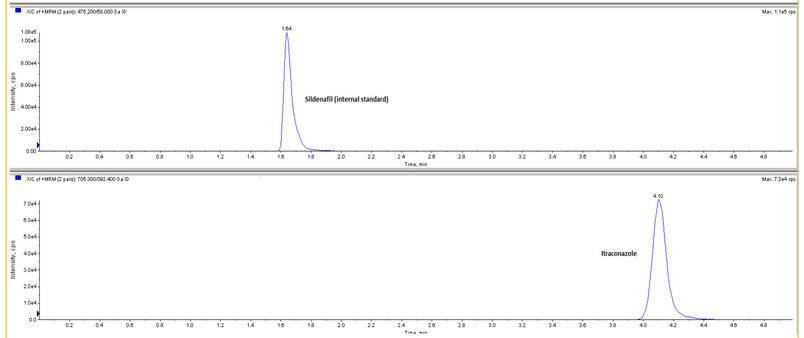
RESULTS

The standard curves for itraconazole was linear within the range of 1,22-10.000 ng/ml with a correlation coefficient r ≥ 0.995. The lower limit of quantification (LLOQ) was 2,44 ng/ml. Total run time was 5 minutes. The intra- and inter-day imprecision values were below 8.5% and 11.9%, respectively. Inter-day accuracies ranged between 87.8–114.8%. The recovery values varied between 95.9 and 103.8% and matrix effect values were less than 12.5%.

We developed a fast, accurate and simple method for measuring itraconazole levels. This method allows the determination of nonadherent patients and toxic levels with a wide linearity range.

RESULTS

Figure 1. Chromatogram of 150 ng/mL itraconazole standard solution in methanol.



SUMMARY/CONCLUSION

We developed a fast, accurate and simple method for measuring itraconazole levels. This method allows the determination of nonadherent patients and toxic levels with a wide linearity range.