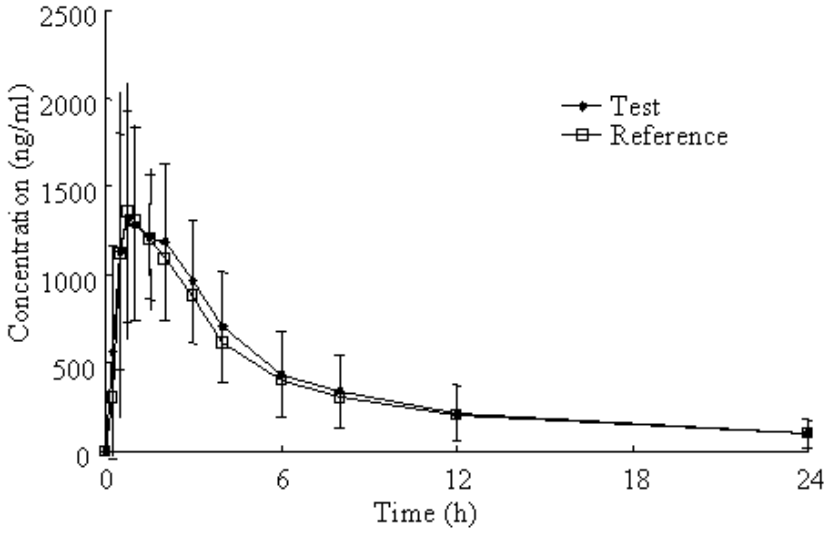

Fig. 3. Plasma concentration versus time curve for two voriconazole tablet formulations in healthy volunteers (n=20). Data are mean±S.D.

Table 3. Pharmacokinetic parameters of voriconazole in test and reference formulations (mean ± S.D., n=20)

Parameter	Voriconazole	
	Test formulation	Reference formulation
C_{max} (ng/ml)	1640.05±564.77	1772.08±676.26
T_{max} (h)	1.3±0.8	1.1±0.7
$T_{1/2}$ (h)	6.99±2.47	7.40±2.98
AUC_{0-t} (ng.h/ml)	8827.98±4243.32	8122.76±3740.73
$AUC_{0-\infty}$ (ng.h/ml)	9971.75±5409.05	9412.17±5006.66

According to the present study, the relative bioavailability of the test formulation was 109.28% (mean AUC_{0-t}) and 107.53% (mean $AUC_{0-\infty}$). There were no significant differences between the two formulations on the basis of assessment by a two one-sided t-test. The 90% confidence intervals of test to reference ratio (after log-transformation) of the AUC_{0-t} (101.20-115.07%) and $AUC_{0-\infty}$ (97.43-113.75%) were within the bioequivalence criteria range of 80–125%, and that of C_{max} (after log-transformation) was within 70–143%. Based on these, the two tablet formulations were found to be bioequivalent.

CONCLUSIONS

A simple, rapid and sensitive LC-MS/MS method is reported for the determination of voriconazole in human plasma. Moreover, the devised method fully meets FDA guidelines, and has high sensitivity and specificity. The method allows high sample throughput (more than 150 samples per day), making it suitable for PK or bioequivalence studies of voriconazole.

REFERENCES

1. L.A. Jeu, F.J. Piacenti, A.G. Lyakhovetskiy, H.B. Fung, *Clinical Therapeutics*, **25**, 1321(2003).
2. L. Purkins, N. Wood, P. Ghahramani, K. Greenhalgh, M.J. Allen, D. Kleinermans. *Antimicrob. Agents Chemother.*, **46**(8), 2546 (2002).
3. H.M. Lazarus, J.L. Blumer, S. Yanovich, H. Schlamm, A. Romero, *J. Clin. Pharmacol.*, **42**(4), 395 (2002).
4. L.Purkins, N. Wood, K. Greenhalgh, M. J. Allen, S. D. Oliver, *Br. J. Clin. Pharmacol*., **56**(1), 10 (2003).
5. R. Hyland, B.C. Jones, D.A. Smith, *Drug Metab. Dispos*., **31**(5), 540 (2003).
6. Y. Ikeda, K. Umemura, K. Kondo, K. Sekiguchi, S. Miyoshi, M. Nakashima, *Clin. Pharmacol. Ther*., **75**(6) 587 (2004).
7. J. Smith, N. Safdar, V. Knasinski, W. Simmons, S.M. Bhavnani, P.G. Ambrose, D. Andes, *Antimicrob. Agents Chemother.*, **50**(4), 1570 (2006).
8. D.A. Stopher, R. Gage, *J. Chromatogr. B Biomed. Sci. Appl.*, **691**(2), 441 (1997).
9. R. Gage, D.A. Stopher, *J. Pharm. Biomed. Anal*., **17**(8), 1449 (1998).
10. S. Perea, G.J. Pennick, A. Modak, A.W. Fothergill, D.A. Sutton, D.J. Sheehan, M.G. Rinaldi, *Antimicrob.*