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Drug interaction between oral atorvastatin and verapamil in healthy subjects

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The aim of this study was to investigate the effect of atorvastatinon the pharmacokinetics of verapamil and its major metabolite, norverapamil in healthy subjects. Twelve healthy male subjects followed a randomised cross-over study comprising two treatment periods. The pharmacokinetic parameters of verapamil and norverapamil in healthy volunteers were measured after administration of verapamil (60 mg, PO) in the presence or absence of atorvastatin (40 mg, PO). The pharmacokinetics of verapamil were significantly altered by the coadministration of atorvastatin compared with the control group (given verapamil alone). the presence of atorvastatin significantly ($p<0.05$) increased the area under the concentration-time curve (AUC) of verapamil by 48.1%, and significantly ($p<0.05$) decreased the total plasma clearance (CL/F) of verapamil by 32.5%, while there was no significant change in the time to reach the peak plasma concentration (T_{max}), reach peak plasma concentration (C_{max}) and the elimination rate constant (K_{el}) and the terminal half-life ($t_{1/2}$) of verapamil in the presence of atorvastatin. The pharmacokinetic parameters of norverapamil were nosignificant differences in the healthy subjects coadministered with atorvastatin compared with that of the control group. Since oral verapamil is a substrate for P-gp and CYP3A, the enhanced oral bioavailability of verapamil might be due to the decreased efflux and metabolism of verapamil in the intestine. The present study has demonstrated an interaction between verapamil and atorvastatin, which is likely due to an inhibition of intestinal metabolism and efflux pump resulting in increased oral bioavailability.

Key words: verapamil, norverapamil, atorvastatin, pharmacokinetic, rats