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Effects of BST204 extract, a purified ginseng dry extract on pharmacokinetics of imatinib in rats

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BST204 is a purified ginseng dry extract that is a highly concentrated mixture of racemic (1:1) Rh2 (not less than 5.0%) and Rg3 (not less than 10.0%) developed by Green Cross Health Science (Republic of South Korea). It is undergoing Phase IIa clinical trials for the treatment of cancer cachexia in Europe. We previously reported that oral dosing of BST204 extract had no effect on the pharmacokinetics of two anti-cancer drugs, 5-fluorouracil, and irinotecan, after intravenous dosing in rats. This study aimed to investigate the influences of BST204 extract on the oral absorption and disposition of imatinib, an oral cancer drug, in rats. Rats were orally administered imatinib (30 mg/kg) alone and in combination with BST204 extract (1 g/kg or 0.2 g/kg) concomitantly, respectively. Plasma concentrations of imatinib and N-desmethyl imatinib were determined using an LC-MS/MS. Pharmacokinetic parameters were calculated using a non-compartment model of WinNonlin software. High oral dose of BST204 extract (1 g/kg) resulted in marked reductions (62.1% decrease) in the maximum concentration (C_{max}) and increases (6-fold) in the time to reach a C_{max} (T_{max}), respectively, as compared with imatinib alone, while the terminal half-life of imatinib was not different between two groups. Similar patterns of N-desmethyl imatinib, which are decreased C_{max} and delayed T_{max}, were observed by co-administration with high oral dose of BST204 extract. In contrast, the pharmacokinetics of imatinib and N-desmethyl imatinib were not altered by orally in combination with low dose of BST204 (0.2 g/kg). In conclusion, high dose of BST204 extract significantly decreased the oral bioavailability of imatinib, and the interaction should occur at the absorption phase, possibly through the inhibition of its intestinal absorption mediated by uptake transporters. We suggest that concurrent intake of BST204 extract with imatinib are better avoided in order to ensure the efficacy of imatinib.

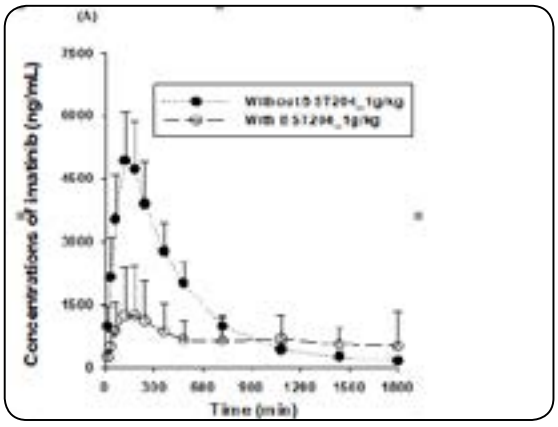

Figure 1: Effects of high dose BST204 extract (1 g/kg) on the pharmacokinetics of imatinib in rats

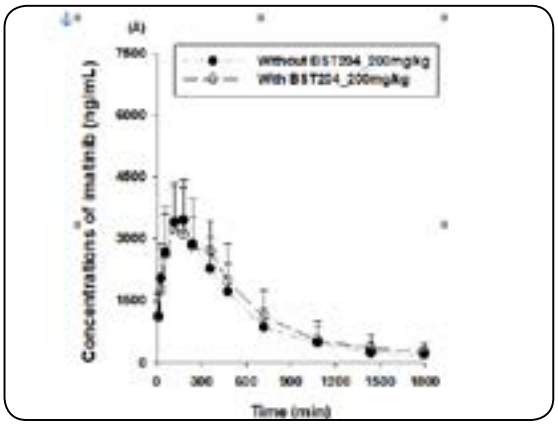

Figure 2: Effects of low dose BST204 extract (0.2 g/kg) on the pharmacokinetics of imatinib in rats.

Biography

Soon Uk Chae is a graduate student with major in Pharmacology/Pharmacokinetics from The Catholic University of Korea. His research interests include: in vitro herb-drug interaction, nonclinical pharmacokinetics and bioanalysis development.

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