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Assessing potential drug-drug interactions of BST204 with anti-cancer drugs (5-fluorouracil, irinotecan, tamoxifen) using *in vivo* rat models

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Objective: BST204, a fermented ginseng extract, shows anti-tumor effects and can be used as a supplement for cancer patients. This paper was to assess the potential drug-drug interaction of BST204 with 4 anti-cancer drugs (5-fluorouracil, irinotecan, tamoxifen) in male Sprague–Dawley rats.

Methods: The rats (9-11 weeks, 270–310 g) in every study were randomly separated into 4 groups: (1) anti-cancer drug alone; (2) single co-administration of BST204 and anti-cancer drug; (3) multiple dose of vehicle for 7 days+single anti-cancer drug on the 7th day; (4) multiple dose of BST204 for 7 days+single anti-cancer drug on the 7th day. 15 minutes prior to anti-cancer drug administration, BST204 at doses of 400 mg/kg or 1 g/kg (control) were orally administered by gastric gavage tube to the rats. Multi-dose BST204 (1 g/kg or 400 mg/kg) were administrated to rats once a day for continuous 6 days in the 3 and 4 groups. On the 7th day, rats were operated carotid artery surgery for cannulation and then received BST204 or vehicle before chemotherapeutic agents. 30 mg/kg 5-fluorouracil (i.v.), 20 mg/kg irinotecan (i.p.) and 30 mg/kg tamoxifen (p.o.) were administrated to rats and LC-MS/MS was used to detect the concentration of them and their main active metabolites.

Results: There were no statistical significance for AUCinf, t_{1/2}, MRT, CL and V_{dss} of 5-fluorouracil in without and with BST204 groups (P>0.05). For both irinotecan and its active metabolite (SN-38), the AUC_t and C_{max} in without BST204 groups were similar with them in with BST204 groups. AUC or C_{max} of tamoxifen, 4-hydroxytamoxifen, endoxifen, and N-desmethyldoxifen between BST204 and vehicle groups showed no statistical significance. In addition, the C_{max} of tamoxifen were relatively higher in presence of BST204 than in absence of BST204 (P>0.05). It may be associated with P-gp inhibition of 20 (S)-ginsenoside Rh2, which is highly contained in BST204. But, the effect can be ignorable because there was no statistical significance compared with control groups.

Conclusion: The pharmacokinetic interaction of BST204 with the 3 anti-cancer drugs in rats undefined us that the potential impact of BST204 on drug-drug interaction (5-fluorouracil, irinotecan, tamoxifen) can be ignorable.

Biography

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