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Repeated Medication of Shaoyao-Gancao-tang Restores Bioavailability of Its Two Glycosides Reduced by Antibiotics in Rats

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[Purpose] Shaoyao-Gancao-tang (SGT, 芍薬甘草湯) may be used together with antibiotics amoxicillin and metronidazole (AMPC-MET) in peptic ulcer therapy. It is known that plasma concentrations of paeonimetabolin I (PM-I) and glycyrrhetic acid(GA), the metabolites derived from glycosides paeoniflorin(PF) and glycyrrhizin(GL) in SGT by intestinal bacteria, are markedly reduced by combined antibiotics.[1,2)] The present study aimed to investigate appropriate medication regimens able to reduce the negative effect of antibiotics on bioavailabilities of PF and GL in SGT.

[Method] Rats were subjected to three kinds of treatments: administration of AMPC-MET (single dose) alone; repeated oral administration of SGT(daily dose of 10-fold human dose) for 14 days starting 24h after pretreatment with or without AMPC-MET. Plasma concentrations of PM-I and GA were examined as previously reported.[1,2)] PF-[3)] and GL-[1)] metabolizing activities of intestinal bacteria in rat feces were also determined.

[Results and Discussion] GL-metabolizing activity in rat feces was markedly reduced by AMPC-MET and took 11.83±0.40 days to recover. Repeated medication of SGT after AMPC-MET treatment significantly shortened the recovery time to 3.67 ± 0.21 days. Plasma GA concentration decreased by the antibiotics was also markedly restored by the repeated medication of SGT. Similar results were observed for PF-metabolizing activity and plasma PM-I concentration. The present findings suggest that repeated medication of SGT starting 1 or 2 days after AMPC-MET treatment speeds recovery of the reduced bioavailability of GL and PF in SGT. Similar strategies for medications may also be useful for combination therapy of antibiotics and other traditional Chinese formulations to ensure efficacy of the contained bioactive glycosides.

1) He J-X., et al., *Biol Pharm Bull,* 24, 1395-1399, 2001; 2) He J-X., et al., *J Pharm Pharmacol,* 55, 313-321, 2003; 3) He J-X, et al., *Chem Pharm Bull,* 50, 1233-1237, 2002.

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