Pengaruh koadministrasi ekstrak air hibiscus sabdariffa terhadap profil farmakokinetika kaptopril, tekanan darah dan level biomarker sistem renin angiotensin aldosteron = Effect of hibiscus sabdariffa aqueous extract co-administration on the Pharmacokinetic profile of captopril, blood pressure, and biomarker level of renin angiotensin aldosterone system

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Abstrak

Ekstrak air Hibiscus sabdariffa (HS) telah digunakan sebagai pengobatan tradisional pada terapi hipertensi. Banyak orang menggabungkan penggunaan ekstrak air HS dengan kaptopril sehingga dapat berpotensi menimbulkan interaksi. Penelitian ini bertujuan untuk mengetahui pengaruh koadministrasi ekstrak air HS terhadap profil farmakokinetika kaptopril, tekanan darah, dan biomarkersistem renin angiotensin aldosteron (RAAS). Studi farmakokinetika dilakukan terhadap empat kelompok tikus (n = 6). Kelompok I menerima suspensi kaptopril tunggal (CAP; 4,5 mg/200 g BB) sementara kelompok II, III, dan IV menerima koadministrasi ekstrak air HS (15 mg/200 g BB, 30 mg/200 g BB, dan 60 mg/200g BB) dan kaptopril 4,5 mg/200 g BB. Untuk pengukuran tekanan darah dan level biomarker RAAS, digunakan tujuh kelompok tikus (n = 6) berbeda yang terdiri dari satu kelompok sham dan enam kelompok tikus model 2K1C. Pada tikus model 2K1C, hipertensi diinduksi dengan pemasangan mikroklip stainless steel (ID: 0,20 mm) pada arteri ginjal kiri. Kelompok tikus model terdiri dari kontrol negatif (2K1C, tidak diobati), kontrol positif (4,5 mg/200 g BB kaptopril), ekstrak air HS tunggal (30 mg/200 g BB), dan 3 kelompok koadministrasi yang menerima ekstrak air HS (15, 30, atau 60 mg/200g BB) dan kaptopril 4,5 mg/200 g BB. Pemberian ekstrak dan kaptopril dilakukan secara peroral. Seluruh perlakuan dilakukan selama 2 minggu. Ketiga dosis koadministrasi ekstrak HS dapat mempengaruhi profil farmakokinetika kaptopril secara signifikan. Nilai AUC0-t, AUC0-, dan Cmax, pada kelompok tersebut mengalami penurunan, sementara nilai Cl/F dan Vd/F mengalami peningkatan. Seluruh pemberian terapi pengobatan menyebabkan penurunan tekanan darah secara signifikan mendekati kelompok sham. Level renin plasma, aktivitas serum angiotensin converting enzyme (ACE), dan level angiotensin II plasma pada kelompok 2K1C mengalami kenaikan yang signifikan dibandingkan dengan kelompok sham. Aktivitas serum ACE dan level angiotensin II plasma pada seluruh kelompok terapi mengalami penurunan signifikan dan nilainya mendekati kelompok sham. Ekstrak air HS tunggal dapat menurunkan tekanan darah, namun koadministrasi dengan kaptopril tidak memberikan efek tambahan. Oleh karena itu, dapat disimpulkan bahwa pemberian koadministrasi ekstrak air HS dengan kaptopril dapat mempengaruhi profil farmakokinetika kaptopril secara signifikan, namun tidak memberikan pengaruh yang signifikan terhadap penurunan tekanan darah dan level biomarker RAAS.
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Hibiscus sabdariffa (HS) extract has been used as traditional medicine during management of hypertension. Many people co-administered HS aqueous extract with captopril thus predispose herb-drug interaction. The purpose of this study was to determine the effect of HS aqueous extract co-administration on the pharmacokinetic profile of captopril, blood pressure, and biomarker level of renin angiotensin aldosterone system (RAAS). Pharmacokinetic study was performed on four groups of rats (n = g). Group I received

captopril suspension only (CAP; 4.5 mg/200 g BW), while group II, III, and IV received co-administration of Hibiscus sabdariffa extract (15 mg/200 g BW, 30 mg/200 g BW, and 60 mg/200 g BW respectively) and captopril 4.5 mg/200 g BW. Blood pressure and biomarker level of RAAS measurement were performed on another 7 groups (n = 6), a SHAM group and six 2K1C groups. In 2K1C animals, hypertension was induced by placing a stainless micro clip (inner diameter of 0.20 mm) on left renal artery. The 2K1C animals consist of negative control (2K1C, no treatment), positive control (captopril 4.5 mg/200 g BW), HS aqueous extract (30 mg/200 g BW), and three co-administration groups receiving HS aqueous extract (15, 30, or 60 mg/200 g BW) plus 4.5 mg/200 g BW captopril. Extract and captopril administration were given by oral gavage. All treatments were performed for two weeks. Pharmacokinetic profile of captopril was changed significantly by all co-administration doses of HS aqueous extract. The AUC0-t, AUC0-, and Cmax value of those groups were decreased, conversely the Cl/F and Vd/F value were increased. Blood pressure was significantly reduced by all the drug treatments approaching the level of SHAM controls. Plasma renin level, serum angiotensin converting enzyme (ACE) activity, and plasma angiotensin II level were also significantly elevated in the 2K1C group compared to the SHAM group. Both serum ACE activity and plasma angiotensin II level were significantly reduced approaching the SHAM group levels by all the drug treatments. HS aqueous extract can reduce blood pressure but may not provide any additional benefit. Therefore, we can conclude that co-administration of HS aqueous extract with captopril could affect the pharmacokinetic profile significantly, however it didnt have significant effect on the decrease in blood pressure and RAAS biomarker level.