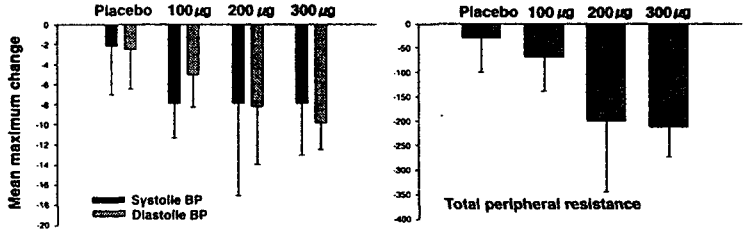
Pharmacokinetic and Pharmacodynamic Evaluation of a Novel K^+ Channel Activator, SKP-450, in Healthy Volunteers

JH Sohn[1], MD, KS Yu, MD, KS Bae, MD, JY Cho, PhD, KJ Kang[2], RN,
JH Lee[2], MT, IJ Jang, MD, PhD, SG Shin, MD, PhD

Dept. of Pharmacol. and Clin. Pharmacol. Unit, Seoul Nat'l Univ. College of Med. and Hospital, Inje Univ.[1], Pusan.
Clinical Trial Center[2], Clinical Research Institute, Seoul Nat'l Univ. Hospital

To evaluate the pharmacokinetic and pharmacodynamic characteristics of a novel K^+ channel activator SKP-450, a single-blind, randomized, placebo-controlled, parallel group study was conducted in 28 healthy volunteers. The volunteers were randomly allocated to single dose groups of 100㎍, 200㎍, or 300㎍. The 200 ㎍ group was further studied for food interaction in a crossover fashion. Drug concentrations in plasma were measured by HPLC. PD effects were evaluated by serial measurements of blood pressure (BP), pulse rate, hemodynamic parameters (cardiac index & total peripheral resistance: TPR using computerized impedance cardiography), and also by measuring plasma renin activity and aldosterone concentrations.

Dose	Tmax(hr)	Cmax(ng/ml)	$t_{1/2}$(hr)	AUC(ng · hr/ml)	CL/F(L/hr)
100㎍	1.13	2.78	2.51	12.34	10.67
200㎍	1.17	4.68	2.27	19.92	10.75
200㎍(food)	3.01	3.85	2.87	23.03	9.03
300㎍	1.00	6.57	2.18	35.96	9.66



SKP-450 was generally well tolerated, showed linear PK properties, and was expected to show significant reduction in BP & TPR.