Supplementary materials

First-in-human safety, tolerability and pharmacokinetics of single-dose kukoamine B mesylate in healthy subjects: A randomized, double-blind, placebo-controlled phase I study

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Supplementary Table S1. Baseline characteristics of the participants

Characteristics	0.005 mg/kg (n=4)	0.02 mg/kg (n=6)	0.04 mg/kg (n=6)	0.08 mg/kg (n=6)	0.12 mg/kg (n=6)	0.24 mg/kg (n=6)	0.48 mg/kg (n=6)	Placebo (n=12)
Age, years, mean±SD	29.0±8.37	24.7±3.39	29.0±4.86	31.2±4.31	35.0±6.13	32.5±5.24	29.0±9.55	32.7±5.66
Male, n (%)	2 (50.0)	3 (50.0)	3 (50.0)	4 (66.7)	2 (33.3)	4 (66.7)	3 (50.0)	9 (75.0)
Weight, kg, mean±SD	62.5±3.17	61.1±7.87	71.2±5.92	65.5±8.16	65.0±9.22	70.0±12.6	68.6±8.70	69.2±5.43
Height, cm, mean±SD	164.5±4.8	167.0±10.0	168.2±9.1	164.3±5.5	161.7±7.0	168.5±12.0	167.0±9.3	168.5±8.4
BMI, kg/m^2, mean±SD	23.1±1.86	21.8±0.96	25.2±1.11	24.2±1.68	24.7±1.57	24.6±1.99	24.6±2.42	24.4±1.57
Han nationality, n (%)	3 (75.0)	6 (100.0)	6 (100.0)	6 (100.0)	5 (83.3)	5 (83.3)	6 (100.0)	11 (91.7)

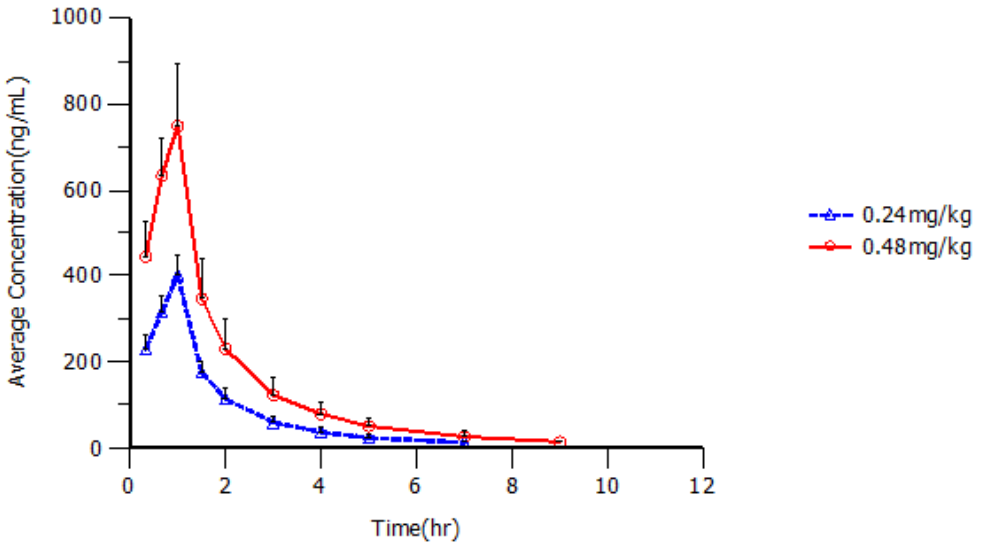
Abbreviations: BMI: body mass index; SD: standard deviation

Supplementary Table S2. Whole blood pharmacokinetic parameters in the 0.24- and 0.48-mg/kg KB dose groups

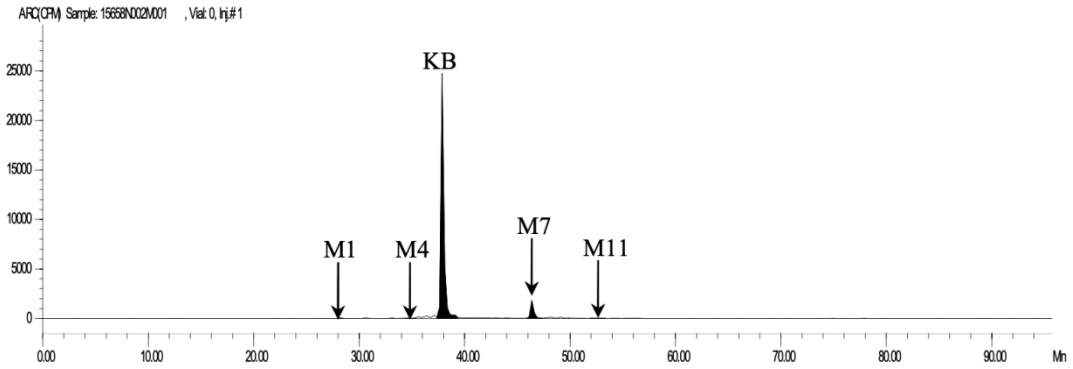
	0.02 mg/kg (n=6)	**0.04 mg/kg (n=6)**
$AUC_{0\text{-}25h}$, h*ng/mL	675.67 ±118.01	1360.79 ±336.80
AUC_{inf}, h*ng/mL	675.32 ±117.58	1361.25 ±338.19
AUC_{last}, h*ng/mL	643.55 ±109.22	1325.35 ±329.06
CL, L/h	18.16 ±1.78	18.85 ±7.22
C_{max}, ng/mL	401 ±46.8	750 ±141
Ke, l/h	0.45 ±0.09	0.39 ±0.05
MRT, h	1.19 ±0.18	1.41 ±0.29
T_{max}, h	1.00 (1.00-1.00)	1.00 (0.67-1.00)
Vd, L	41.17 ±6.22	47.92 ±17.04
$T_{1/2}$, h	1.59 ±0.29	1.78 ±0.19

Notes: All data were described as "mean ± standard deviation," except T_{max} was described as "median (range)".

Abbreviations: AUC: area under the curve; CL: clearance; C_{max}: maximal concentration; ke: elimination rate constant; MRT: mean residence time; T_{max}: time to peak drug concentration; $T_{1/2}$: half-life; Vd: distribution volume



Supplementary Figure S1. Mean whole blood concentration-time curves (semi-log) in the 0.24 and 0.48 mg/kg KB dose groups



Supplementary Figure S2. Liquid chromatography of KB and metabolites in urine samples from participants received 0.12, 0.24 and 0.48 mg/kg KB