21.Others

References

Horii C, Okonogi A, Okubo T, et al. Studies on bioequivalence of kakkonto decoction and its extract preparation (I)*. Shoyakugaku zasshi 2014; 68: 9-12.
Horii C, Okonogi A, Okubo T, et al. Study of the equivalence of kakkonto (葛根湯) extract formulation and decoction (II). *Natural Medicines* 2015; 69: 59-65.

1. 1. Objectives
To select the Pharmacopeia indicator components for evaluation of the equivalence of kakkonto (葛根湯) extract formulation and decoction.

2. Design
Randomized controlled trial (cross-over) (RCT cross-over).

3. Setting
Public recruitment of healthy volunteers from a clinical study registry of a university hospital medical information network center, Japan.

4. Participants
Six healthy volunteers.

5. Intervention
Since the method of allocation to treatment arms was not described in the article, the treatment arms are described in terms of treatment regimen.
Arm 1: Administration orally of kakkonto (葛根湯) decoction (of Pueraria Root 8 g, Ephedra Herb 4 g, Jujube 4 g, Cinnamon Bark 3 g, Peony Root 3 g, Glycyrrhiza 2 g, and ginger 1 g heated and extracted in 500 mL of water, filtered through 4 layers of gauze, and adjusted to 250 mL), washout for 2 weeks, and finally administration of Kracie Kakkonto (葛根湯) Extract Fine Granules 7.5 g (n=6).
Arm 2: Administration orally of Kracie Kakkonto (葛根湯) Extract Fine Granules 7.5 g, washout for 2 weeks, and administration of its decoction (n=6).

6. Main outcome measures
Blood concentrations of ephedrine and pseudoephedrine from mao (麻黄, ephedra herb), puerarin and daidzein from kakkon (葛根, pueraria root), glycyrrhizic acid and liquiritin from kanzo (甘草, glycyrrhiza), and peoniflorin from shakuyaku (芍薬, peony root) at 15, 30, 60, 120 and 240 minutes after administration.

7. Main results
No between-group difference was found in the rates of absorption based on MRT parameters, AUC, Cmax, Tmax, and blood concentrations after taking puerarin from kakkon and ephedrine and pseudoephedrine from mao. At the same time, there was a tendency toward large variation between subjects in the daidzein from kakkon, glycyrrhizic acid and liquiritin in kanzo, and the peoniflorin from shakuyaku.

8. Conclusion
Analysis of blood concentrations of the several pharmacopoeia indicator components contained in kakkonto, namely ephedrine and pseudoephedrine from mao and puerarin from kakkon, suggests they may be indicator components for the equivalence of kakkonto extract formulation and decoction.

9. From **Kampo medicine perspective**
None.

10. Safety assessment in the article
Not mentioned.

11. Abstractor's comments
This study was conducted to evaluate the equivalence of Kampo extract with decoction, the predominant form of this Kampo treatment in daily use. When ephedrine and pseudoephedrine, the main ingredients in kakkonto, were selected as indicator ingredients, their post-dose blood concentrations and absorption rates were similar between the extract and decoction formulation. These results suggested that the various drug formulations prescribed in clinical settings were equally effective and that these indicator ingredients selected from the Japanese Pharmacopeia may be used to show the equivalence between formulations. This study is a pilot study of just six subjects assigned to two groups. , Considering the differences in treatment response between individuals, an increased number of study subjects will be required to obtain more generalizable results. ePilot studies, such as this study, which evaluate pharmacokinetics of Kampo crude ingredient absorption, are of major importance to clinicians who need to anticipate the possible effects of Kampo medicines in daily practice. Further studies are anticipated.

12. Abstractor and date
Ushiroyama T, 31 March 2017.