
Poster

[P27-10] P27-10: Pharmacokinetics and pharmacogenetics

Chair: Andrew Somogyi, Australia

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[P27-10-8] Inhibitory effects of flavonoid-containing vegetables on CYP3A4 activity in recombinant CYP3A4 and LS180 cells

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Background

Human intestinal absorption and drug metabolism vary to a large extent among individuals. For example, cytochrome P450 (CYP) 3A4 activity has large individual variation that cannot be attributed to only genetic differences. Various flavonoids in vegetables, such as kaempferol and quercetin, possess inhibitory effects, and some fruit juices have also been found to inhibit CYP3A4 activity in clinical study. Therefore, differences in daily intake of flavonoid-containing vegetables may induce individual variation in intestinal bioavailability of CYP3A4 substrate. To identify the vegetable that strongly inhibits CYP3A4, we investigated effects of vegetables juice, and juice prepared from individual vegetables, on CYP3A4 activity using recombinant CYP3A4 and LS180 cells in this study.

Methods

Five vegetables juices (VJ-o, Kagome Original[®]; VJ-g, Kagome 30 kinds of vegetables and fruits[®]; VJ-p, Kagome Purple vegetables[®]; VJ-r, Kagome Sweet Tomato[®]; and VJ-y, Kagome Fruity Salada[®]; KAGOME Co. Ltd., Aichi, Japan) and nine vegetable (cabbage, Japanese radish, onion, tomato, eggplant, carrot, Chinese cabbage, green pepper, and lettuce) juices from individual vegetables were centrifuged (1,630×g, 10 min) and filtered using filter paper and 0.45-μm membrane filters. CYP3A4 activities were measured using the metabolic activity of testosterone by recombinant CYP3A4 and the metabolic activity of Luciferin-IPA (selectively reacted with CYP3A4, and hardly reacted with CYP3A5 and CYP3A7: Promega, Madison, WI, USA) in human colon adenocarcinoma LS180 cells that strongly expresses CYP3A4.

Results

VJ-o, VJ-y, and juices prepared from cabbage, onion or green pepper strongly inhibited testosterone metabolism in recombinant. But VJ-g, VJ-p, VJ-r, and juices prepared from Japanese radish, tomato, eggplant, carrot, Chinese cabbage, and lettuce did not affect or weakly inhibited that. In addition, VJ-o, VJ-y, and juices prepared from cabbage and onion significantly inhibited CYP3A4 activity in LS180 cells.

Conclusions

This study showed that some vegetables juice and juice prepared from individual vegetables could significantly inhibit CYP3A4 activity. Therefore, variation in the daily intake of vegetables such as cabbage and onion may be one of the factors responsible for individual differences in intestinal bioavailability of

CYP3A4 substrate.