Inhibitory Effect of Tien-Kao (Cuminum cyminum L.) Extracts on CYP3A4 Activity in-vitro

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Introduction

Concurrent use of two or more herbs and modern medicines may cause herbal-drug interactions via metabolism-based mechanism. CYP3A4 is one of a major member of the cytochrome P450 enzymes that involved in these metabolism processes. Tien-Kao (Cuminum cyminum L.) is a Thai herb used in traditional stomachic and anti-vertigo remedy. To ensure patient safety, possibility of each herb that cause metabolic herb-drug interaction should be investigated. This research was aimed to study the effect of Tien-Kao’s constituents on CYP3A4 activity in vitro. Metabolic tests were carried out in triplicates using rat liver microsome. Testosterone (TST) was used as a specific probe substrate for CYP3A4 and the amount of 6β-OH Testosterone, major metabolite of TST, was determined by HPLC using UV detector.

Objectives

To investigate the effect of Tien-Kao (Cuminum cyminum L.) extracts on rat CYP3A4 activity.

Methods

- Wistar Rat Livers
- Microsome Preparation
- Determination of Total Protein
- Rat Liver Microsome (RLM)
- + Testosterone
- + NADPH
- + Herbal Extract
- Determination of 6β-TST by HPLC

Metabolic study

Metabolic tests were carried out with RLM in triplicate in vitro using testosterone (TST) as a specific CYP3A4 probe substrate. The amount of 6β-hydroxytestosterone (6β-TST), major metabolite of TST, obtained from each metabolic reaction with or without herbal crude extract was determined using High Performance Liquid Chromatography (HPLC) technique.

HPLC condition

- Column: C-18 reverse phase
- Detected wavelength: 282 nm.
- Mobile phase: Methanol: Water (50:50)
- Flow rate: 1 mL/min
- Injection volume: 100 μL

Data analysis

The amount of 6β-TST found was converted into % inhibition compared to those obtained from the reaction without the herbal crude extract.

Results

Inhibitory effect of Tien-Kao (Cuminum cyminum L.) extracts on rat CYP3A4 enzyme activity

Conclusion

It could be concluded that all three extracts of Tien-Kao (methanol, aqueous and hexane) inhibited CYP3A4 activity in vitro in different degree (3.11%, 10.56% and 27.04% inhibition respectively). Chemical structures of unidentified inhibitors in all extracts should be further investigated.

Benefits

This research benefits for further in-vivo metabolic test. The results from both in-vivo and in-vitro metabolic test will ensure the safety use of Thai herbal medicines.

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References