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Effect of a Dietary Supplement Containing Raspberry Ketone on CYP3A Activity in Healthy Women

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ABSTRACT

Raspberry ketone (RK) is available as a supplement with effect on weight gain suppression. Recent studies have found that various herbal products can affect the activities of drug metabolizing enzymes and drug efflux proteins, and provoke clinically relevant drug-drug interactions. Capsaicin, a molecule having a similar chemical structure to RK, is another well-known cytochrome P450 (CYP) inhibitor. On the other hand, it is totally unclear whether RK has any effect on human CYP activities. In this study, we evaluated the effect of orally administered RK on CYP3A activity by measuring 6beta-hydroxycortisol/cortisol ratio in urine samples. Methods: This clinical study was conducted with approval by the Institutional Review Board at Gunma University Hospital. A total of 7 healthy women aged between 20 and 35 years were included and all of them provided written informed consent. Urine samples were collected from all subjects on the morning of day 5 (± 1 day) of menstrual cycle. In the subsequent RK phase, subjects took 3 tablets (16.7 mg/tab) of RK 3 times daily for 7 days, followed by urine sampling on the morning of day 8. In the control phase, the second morning urine sampling was performed 8 days after the first sampling. Urine 6beta-hydroxycortisol and cortisol concentrations were measured by HPLC UV method and the 6beta-hydroxycortisol to cortisol ratio was compared between the two phases. Results: The mean basal and assessment ratios in the RK phase were 7.49 ± 4.76 and 9.20 ± 8.05, respectively, while the corresponding ratios in the control phase were 5.36 ± 3.17 and 5.19 ± 4.61, showing no significant difference in either phase. Conclusion: RK does not affect CYP3A activity.

It has a chemical structure similar to that of capsaicin and has been shown to reduce weight gain in obese rats [1]. Wang et al reported that 40 rats given raspberry ketone with fattening diet were protected against fatty liver [2]. In another study conducted in human, the participants who takes raspberry ketone concomitant with caffeine, garlic, capsaicin, ginger and synephrine lost 7.8% of their fat mass, compared with the placebo group which lost 2.8% [3]. In Japan, it has been commercially available as a supplement for weight reduction since 2002. A major representative of these products is St. John's wort, which has been shown to induce the expressions of CYP2C9 [4], CYP2C19 [5] and CYP3A4 [6], thereby interfering with the efficacy of warfarin, cyclosporin and oral contraceptives. In our previous study, raspberry ketone had shown little impact on CYP3A activity in rats [8]. On the other hand, it is totally unclear whether raspberry ketone has any effect on human CYP activities. Renal clearance of hydroxycortisol has been reported to be an indicator of CYP3A activity [9], however, the measurement of blood concentration is required. To reduce stress for the subjects, it has been reported that the hydroxycortisol/cortisol ratio in urine samples is available as an indicator of CYP induction [10]. In this study, we investigated the effect of oral administration of raspberry ketone on 6beta-hydroxycortisol/cortisol ratio as an index of Pharmaceutica Analytica Acta ISSN: 2153-2435 Pharmaceutica Analytica Acta Aomori et al., Pharm Anal Acta 2018, 9:6 DOI: 10.4172/2153-2435.1000587 Research Article Open Access Pharm Anal Acta, an open access journal ISSN: 2153-2435 Volume 9 • Issue 6 • 1000587 CYP3A activity in young healthy women who are potential main user of raspberry ketone. Materials and Methods Chemicals and materials Raspberry ketone was kindly supplied by Kanebo (Tokyo, Japan) as Vitarosso Tablet containing 16.7 mg of raspberry ketone in one tablet. He tablet also contains Gymnema sylvestris extract, adlay seed extracts, inositol and ascorbic acid as minor constituents. All other chemicals and reagents were obtained from commercial sources and used without further purLficatLon. Clinical experiments All clinical experimental procedures were approved by the Institutional Review Board in Gunma University Hospital. Seven healthy women aged 20-35 years were included in this randomized crossover open study. All participants gave written consent to participate in the study are they were informed of the study purpose and procedures. He exclusion criteria were use of any prescription drugs including contraceptives, pregnancy, and history of intake of raspberry ketone. We ascertained normal renal and hepatic function in all participants by routine clinical laboratory tests before the following procedures were performed. He participants were requested to abstain from any supplements, herbal tea, St. John's wort, grapefruit juice, alcohol, coffee, and smoking during the study. Subjects were randomized into two study groups. Urine samples were collected from all subjects on the morning of day 5 (± 1 day) of menstrual cycle and the basal hydroxycortisol/cortisol ratio was measured.

In the subsequent raspberry ketone phase, subjects took 3 tablets (16.7 mg/tab) of raspberry ketone 3 times daily for 7 days, followed by urine sampling on the morning of day 8 to calculate the assessment ratio.

Keywords: Raspberry ketone; Supplement; CYP3A; Interaction; Oral contraceptives; 6beta-hydroxycortisol/cortisol ratios Introduction Raspberry ketone (4-(4-hydroxyphenyl) butane-2-on) is an aroma component of red raspberry.