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## PROFILE OF URINARY EXCRETION IN INDONESIAN VOLUNTEERS AFTER DHEA ADMINISTRATION

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### ABSTRACT

Dehydroepiandrosterone (DHEA) is a major precursor of endogenous steroid biosynthesis. Exogenous DHEA is considered to be a doping drug and listed in the class of prohibited anabolic agents by IOC since January 1997. In the present study, we investigate the urinary excretion of some DHEA metabolites in volunteers after taking DHEA. Thirteen volunteers, 20 – 30 years old, all men, fulfilled the inclusion criteria (healthy, no previous or chronic disease), passed the medical examination (physical exams, blood chemistry determination, chest X-ray), and signed a letter of informed consent. All volunteers had undergone 2 weeks wash-out periode of free medicines, vitamins and all kind of food that influence hormonal level. Each volunteer took 50 mg of exogenous DHEA orally in the morning at h. 8.00 for 5 days. Urine was collected and the DHEA metabolites were determined at various time points for 24 hours before and after DHEA administration.

Urinary excretion glucuronide (and free) metabolites of testosterone (T), epitestosteron (E), androsterone (A), etiocholanolone (Etio), 5 $\alpha$ -androstane-3 $\alpha$ , 17 $\beta$ -diol (5 $\alpha$ -diol), 5 $\beta$ -androstane-3 $\alpha$ , 17 $\beta$ -diol (5 $\beta$ -diol) and DHEA, and also sulfate metabolite of DHEA was determined by GC/MS. The results showed that the T/E ratio at h. 8.00 was  $1.07 \pm 1.15$ , peaked h. 16.00 :  $1.18 \pm 1.21$  before and at 8.00 :  $1.03 \pm 1.15$ , peaked at h. 16.00 :  $2.11 \pm 2.53$  after exogenous DHEA. One volunteer had a high baseline T/E ratio of 3.4 at h. 8.00 before and at h. 15.00, 16.00, and 18.00 respectively were 9.71; 9.13 and 8.55 after exogenous DHEA. The A/Etio ratio at h. 8.00 was  $1.45 \pm 0.54$ ; peaked at h. 20.00 :  $1.82 \pm 0.68$  before and at h. 8.00 :  $0.77 \pm 0.49$ , peaked at h. 12.00 :  $1.51 \pm 0.67$  after exogenous DHEA. The A/Etio curve before exogenous DHEA was entirely above the value obtained after exogenous DHEA. Although the curve of ratio of 5 $\alpha$ -diol/5 $\beta$ -diol after exogenous DHEA was slightly different from that of the curve before exogenous DHEA, it was not statistically significant. The DHEAS/DHEA glucuronide at various time points after exogenous DHEA was significantly higher than that before exogenous DHEA; the ratio of DHEAS/DHEA glucuronide reached a maximum value of  $158.03 \pm 95.63$  after exogenous DHEA in comparison with  $18.49 \pm 16.32$  at h. 16.00 before exogenous DHEA.

To conclude, oral administration of exogenous DHEA of 50 mg once daily for 5 days (1) alter ratios T/E, A/Etio and DHEAS/DHEA glucuronide; (2) One volunteer had a high baseline T/E ratio of 3.4 and after receiving exogenous DHEA the ratio was further increased to 9.71, significantly exceeding

the limit value permitted by IOC 6:1 ; (3) The ratios of DHEAS/DHEA glucuronide after receiving exogenous DHEA in comparison with those before exogenous DHEA were significantly increased at various time points.

**Key words : DHEA, metabolites ratio**

## DESCRIPTION

### OBJECTIVE

To determine the excretion of some steroid metabolites after exogenous DHEA administration

### PARTICIPANTS

Thirteen volunteers, 20-30 years old, all men, fulfilled the inclusion criteria (healthy, no previous or chronic disease), passed the medical examination (physical exams, blood chemistry determination, chest X-ray) and signed a letter of informed consent.

### METHODOLOGY

After two weeks wash-out period of free medicines, vitamins and all kind of food that influence hormonal level, each volunteer took 50 mg of exogenous DHEA orally in the morning at h. 8.00 for 5 days. Urine was collected and the DHEA metabolites were determined at various time points for 24 hours before and after DHEA administration. Urinary excretion glucuronide (and free) metabolites of testosterone (T), epitestosterone (E), androsterone (A), etiocholanolone (Etio), 5 $\alpha$ -androstane-3 $\alpha$ , 17 $\beta$ -diol (5 $\alpha$ -diol), 5 $\beta$ -androstane-3 $\alpha$ , 17 $\beta$ -diol (5 $\beta$ -diol) and DHEA are hydrolyzed by *E. coli* glucuronidase enzyme; the sulfate metabolite of DHEA is hydrolyzed by *Helix pomatia* acyl sulphatase enzyme. All metabolites were determined by GC/MS.

### RESULTS

The results showed that the T/E ratio at h. 8.00 was  $1.07 \pm 1.15$ , peaked h. 16.00 :  $1.18 \pm 1.21$  before and at 8.00 :  $1.03 \pm 1.15$ , peaked at h. 16.00 :  $2.11 \pm 2.53$  after exogenous DHEA. One volunteer had a high baseline T/E ratio of 3.4 at h. 8.00 before and at h. 15.00, 16.00, and 18.00 respectively were 9.71; 9.13 and 8.55 after exogenous DHEA. The A/Etio ratio at h. 8.00 was  $1.45 \pm 0.54$ ; peaked at h. 20.00 :  $1.82 \pm 0.68$  before and at h. 8.00 :  $0.77 \pm 0.49$ , peaked at h. 12.00 :  $1.51 \pm 0.67$  after exogenous DHEA. The A/Etio curve before

exogenous DHEA was entirely above the value obtained after exogenous DHEA. Although the curve of ratio of  $5\alpha$ -diol/ $5\beta$ -diol after exogenous DHEA was slightly different from that of the curve before exogenous DHEA, it was not statistically significant. The DHEAS/DHEA glucuronide at various time points after exogenous DHEA was significantly higher than that before exogenous DHEA; the ratio of DHEAS/DHEA glucuronide reached a maximum value of  $158.03 \pm 95.63$  after exogenous DHEA in comparison with  $18.49 \pm 16.32$  at h. 16.00 before exogenous DHEA.

## CONCLUSION

To conclude, oral administration of exogenous DHEA of 50 mg once daily for 5 days (1) alter ratios T/E, A/Etio and DHEAS/DHEA glucuronide; (2) One volunteer had a high baseline T/E ratio of 3.4 and after receiving exogenous DHEA the ratio was further increased to 9.71, significantly exceeding the limit value permitted by IOC 6:1 ; (3) The ratios of DHEAS/DHEA glucuronide after receiving exogenous DHEA in comparison with those before exogenous DHEA were significantly increased at various time points.

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Figure 1. Ratio of T/E in average

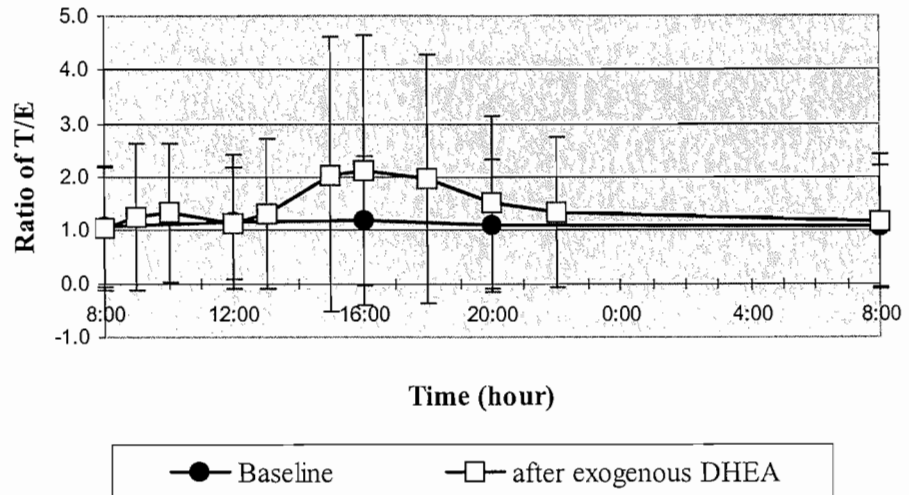


Figure 2. 5a-diol/5b-diol ratio in average

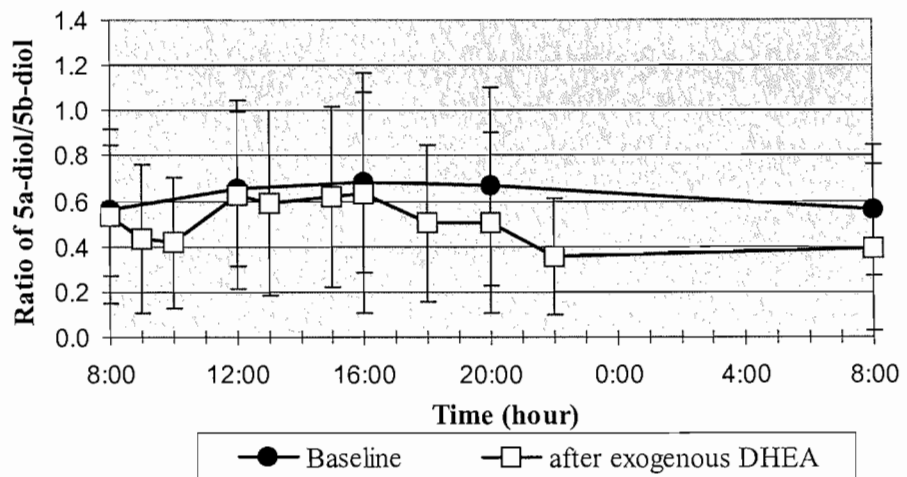


Figure 3. Ratio of A/Etio in average

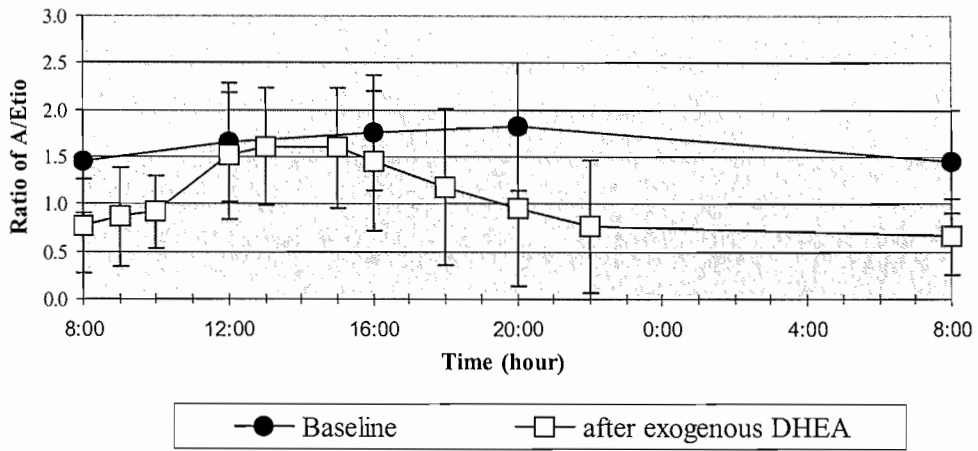
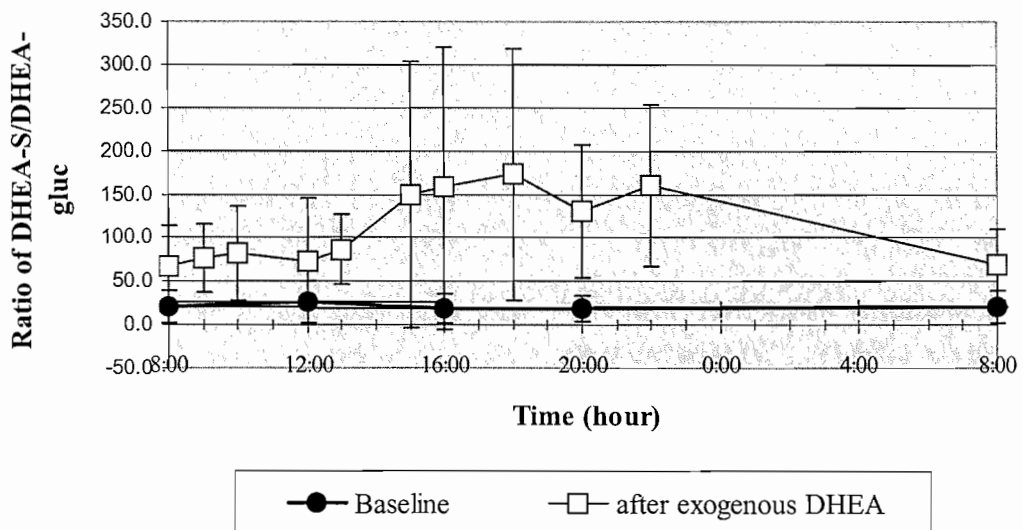


Figure 4. Ratio of DHEA-S/DHEA-glucuronat



**Figure 5. Ratio of T/epiT in volunteer S6**

