Chem. Senses 25: 465–467, 2000

# SHORT REPORT

## Effects of 5α-Androst-16-en-3α-ol on the Pulsatile Secretion of Luteinizing Hormone in Human Females

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### Abstract

We examined the effects of 5α-androst-16-en-3α-ol (3α-androstenol) on pulsatile luteinizing hormone (LH) secretion in human females. The frequency of the LH pulse in the follicular phase was decreased by exposing the women to 3α-androstenol.

### Introduction

Menstrual synchrony, the convergence of the onset date of the menstrual flow, is observed in women living together (Weller and Weller, 1993). Menstrual synchrony has been shown to be mediated by axillary odour (Stern and McClintock, 1998). Axillary odours from women in the follicular phase (FP) of the ovulatory cycle shorten both the time to ovulation and the length of the menstrual cycle in the recipients whereas axillary odours in the ovulatory phase (OP) delay ovulation and lengthen the menstrual cycle. However, the pheromones in the axillary compounds, which regulate both the time to ovulation and the length of the menstrual cycle, have not hitherto been identified.

When we examined the relationship between menstrual synchrony and the ability to smell a putative pheromone, 5α-androst-16-en-3α-ol (3α-androstenol), the women who showed menstrual synchrony had a high sensitivity to 3α-androstenol (Morofushi *et al.*, 2000). It is therefore possible to speculate that human females use 3α-androstenol to synchronize their menstrual cycles. We recently reported that axillary compounds in the FP increased the frequency of pulsatile secretion of luteinizing hormone (LH) and axillary compounds in the OP decreased it, suggesting that axillary compounds change the length of the menstrual cycle by changing the frequency of the pulsatile LH secretion (Shinohara *et al.*, 1999). In the present study, we examined the effect of 3α-androstenol on the pulsatile secretion of LH to explore the possibility that 3α-androstenol is one of the active substances in axillary compounds which regulate the length of the menstrual cycle.

### Materials and methods

Eleven female college students, aged 19–25 years and with a history of regular ovulation, were involved in this study. From 10:00 to 18:00 on days 5–7 after the menstrual onset, blood samples were collected through an i.v. heparin-locked catheter at 10 min intervals. The subjects took 100 kcal isocaloric snacks and 100 ml water hourly for 8 h. They were not exposed to anything for the first 4 h. Afterwards, 2.5 mM 3α-androstenol in 70% isopropyl alcohol (IA) was applied hourly to half of them by wiping above their upper lip with a pad containing the solution for the next 4 h. IA alone was applied to the others in a similar way to 3α-androstenol. Blood plasma was separated by centrifugation at 2000 *g* for 10 min and stored at –30°C until the LH assay (SAPC-S LH RIA kit; Daiichi Radioisotope Laboratory, Tokyo, Japan). The mean of the minimally detectable amount of LH was ~0.3 mIU/ml. The intra-assay coefficients of variation (CV) which were calculated on the basis of duplicated measurement of pooled samples containing 7.78 and 42.1 mIU/ml were 4.17 and 0.66%, respectively. An LH pulse was defined as when both the ascending and descending CVs were >1.7 times the intra-assay CV. The protocol observed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Yokohama City University. The subject gave written

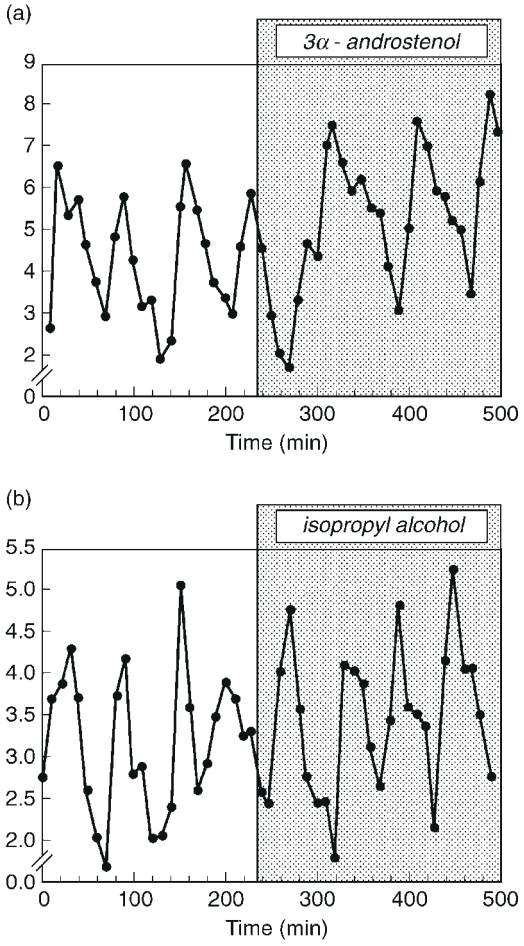


**Figure 1** Representative examples of the effect of 3α-androstenol **(a)** and isopropyl alcohol **(b)** on pulatile LH secretion.

informed consent after the procedures had been fully explained.

## Results

As seen in a representative subject (Figure 1a), the intervals between consecutive peaks of pulsatile LH secretion were 70, 70 and 70 min before the application of 3α-androstenol, but after the start of the application the intervals became longer: 90 and 80 min. On the other hand, IA alone had no effect on the interpulse intervals: 60, 60 and 50 min before IA application and 60, 60 and 60 min during the application (Figure 1b). The mean (± SE) interpulse interval between LH pulses ($n$ = 6) was significantly ($P < 0.05$, paired $t$-test) increased from 53.9 ± 3.9 to 66.0 ± 1.5 min in response to 3α-androstenol. No change in the mean interpulse interval between LH pulses was observed in response to IA ($P > 0.05$, paired $t$-test). The mean interpulse intervals between LH pulses ($n$ = 5) before IA application and during the application were 54.0 ± 4.9 and 53.8 ± 4.7 min, respectively. The data were expressed as the frequency are shown in

**Table 1** Effects of 3α-androstenol and isopropyl alcohol on the frequency (the number of pulses/4 h) of LH pulses

| | 3α-Androstenol | Isopropyl alcohol |
|---|---|---|
| Before application | 4.57 ± 0.81 (6) | 4.59 ± 0.88 (5) |
| During application | 3.64 ± 0.21 (6) | 4.59 ± 0.83 (5) |

Data are the mean ± SE. Numbers in parentheses indicate the number of subjects.

Table 1. 3α-Androstenol decreased the frequency while IA alone had no effect.

## Discussion

The present results demonstrate that the frequency of pulsatile secretion of LH is decreased by exposing women to 3α-androstenol. This finding indicates that 3α-androstenol retards the growth and maturation of ovarian follicles and consequently delays the timing of ovulation. It is therefore possible that 3α-androstenol is involved in menstrual synchrony by increasing the period of menstrual cycles.

3α-Androstenol is known to be secreted from the axillae in humans (Gower and Ruparelia, 1993). The steroid has been demonstrated to act as a pheromone in pigs (Gower and Ruparelia, 1993). It is secreted in the saliva of the boar and acts as a pheromone effective in eliciting the characteristic immobilization response of the estrous sow to the advance of her mate (Gower and Ruparelia, 1993). (*Z*)-7-Dodecen-1-yl acetate is used as a pheromone by the females of more than 126 species of insects and the elephant (Rasmussen *et al.*, 1996). 3α-Androstenol has been reported as affecting women's mood (Gower and Ruparelia, 1993) and sexual arousal (Gower and Ruparelia, 1993), so it also may not be a species-specific pheromone.

Furthermore, women whose menstrual cycles became synchronized with that of room-mates within 3 months had higher olfactory acuity for 3α-androstenol than non-synchronized women, suggesting that the ability to perceive the odour emitted by 3α-androstenol is related to the menstrual synchrony (Morofushi *et al.*, 2000). We recently showed that the frequency of the LH pulse was increased by axillary compounds in the FP, which shorten the menstrual cycle, and decreased by axillary compounds in the OP, which lengthen it (Shinohara *et al.*, 1999). Together with these findings, the present results suggest that 3α-androstenol may be a pheromone included in axillary compounds secreted in the OP, which lengthen the menstrual cycle.

## References

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*Accepted May 17, 2000*