

Twenty-two female subjects (Sub) were allocated randomly to one of two treatments, either drug (D) or placebo (P). Additionally, to all subjects, a two component oral contraceptive was given. The contraceptive components were ethinyl estradiol (EE) and norethindrone (NET). The experiment was designed in order to detect any influence of drug D on the effectiveness of the contraceptive.

On day 8 of each treatment period, blood samples were drawn at 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 24 hours after drug (or placebo) dosing. From these, the area under the plasma concentration vs. time curve (AUC) and the maximum plasma concentration (C_{max}) were calculated for each component (EE and NET) of the oral contraceptive.

Each female subject received either 125 mg of Drug D or a matching placebo tablet two times daily for eight days (16 doses) starting with either Day 1, 2, 3, or 4 of her menstrual cycle as was convenient for the subject. The oral contraceptive administration always started on Day 1 of her menstrual cycle. On the morning of the eighth day of taking either Drug D or placebo, the female subject took her dose of either Drug D or placebo and also the oral contraceptive. Blood samples were drawn immediately prior to dosing and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10, 12, and 24 hours after dosing. The quantities of EE and NET present at each time point were assayed from the plasma samples, and these assay values were used to construct separate plasma concentration vs. time curves for EE and NET for each subject. From the two curves, AUC (pg*hr/ml) and C_{max} (pg/ml) values were calculated. As an example, some plasma concentration vs. time curves are shown in [Figure 1](#).

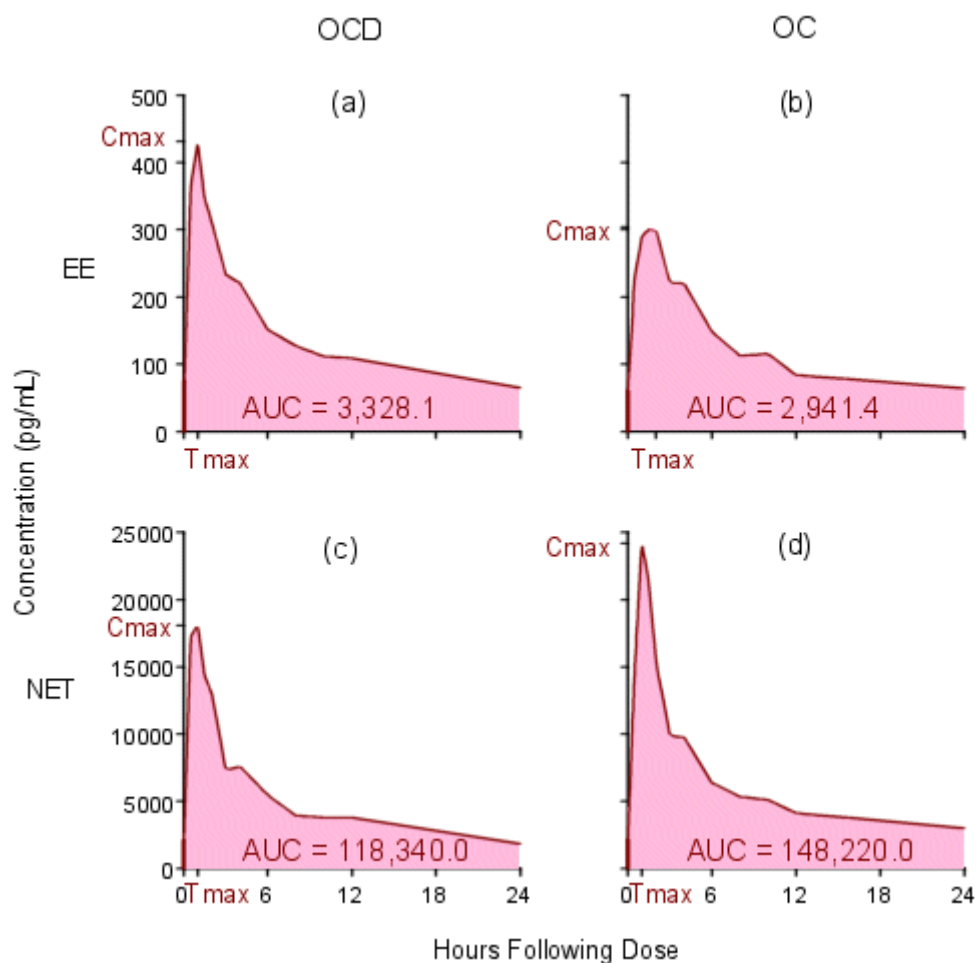


Figure 1. Plasma Concentration vs. Time Curves. The y-axes for EE are not the same as the y-axes for NET. (a) EE OCD; (b) EE OC; (c) NET OCD; (d) NET OC.

Eleven of the female subjects (numbers 2, 4, 5, 8, 9, 12, 14, 16, 18, 20, 21) received Drug D concomitantly with the oral contraceptive combination of EE and NET. The other eleven (numbers 1, 3, 6, 7, 10, 11, 13, 15, 17, 19, 22) received matching placebo.