A Pharmacokinetic Study of Micronized Natural Progesterone Extended-Release Tablets

From Madison Pharmacy Associates, Inc.

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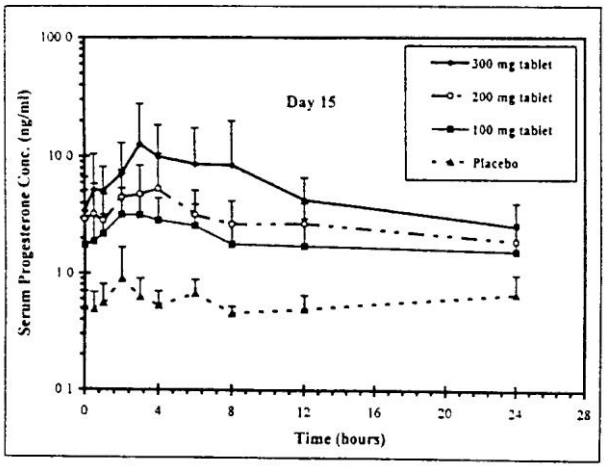
Objective: To define the pharmacokinetic parameters of extended release micronized natural progesterone following daily dosing over two weeks in healthy postmenopausal women.

Methods: Twenty-four postmenopausal women were randomized to receive either placebo, 100, 200, or 300 mg tablets of extended release micronized natural progesterone daily for two weeks. Multiple blood samples were analyzed for serum progesterone concentrations. Pharmacokinetic parameters: maximum serum concentration (Cmax), half-life (t1/2), and area under the curve (AUC) were calculated by non-compartmental analysis.

Results: The median time to reach maximum, serum progesterone concentration was approximately three hours for all doses on both the first and last day of treatment. Steady state concentrations were reached by the fourth day. The maximum serum progesterone concentrations (mean Cmax) on the last day of the study were 2.9 (± 1.9) ng/ml, 5.2 (± 5.0) ng/ml, and 13.5 (± 15) ng/ml for the 100, 200, and 300 mg dose and placebo however, no statistically significant difference among the three doses for AUC, half-life, or Cmax. Given these mean Cmax values, a sample size of 11 in each group would be needed to detect a significant difference in the means with 80% power.



Conclusions: Pharmacokinetic parameters of extended release micronized natural progesterone were defined. Extended release natural progesterone produced serum concentrations of progesterone in the luteal phase range. The average elimination half-life of the 300mg preparation was 18 hours supporting once daily dosing. Extended release micronized natural progesterone was well tolerated. (1998)