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Aminoglutethimide as an inducer of oxidative drug metabolism in the rat.

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There is some evidence that when aminoglutethimide is used in the treatment of patients with advanced breast cancer a clinically-significant degree of hepatic enzyme induction may occur. This activity of the drug has been investigated in female rats. After three daily oral doses (60 mg/kg) of aminoglutethimide, the hypnotic effect of hexobarbitone was significantly shortened and plasma levels of dicoumarol were lowered. This pretreatment regimen also diminished an estradiol-induced increase in uterine weight. Electron microscopy of liver from aminoglutethimide-treated rats revealed a proliferation of smooth endoplasmic reticulum. There were significant increases in the metabolism of 4-nitroanisole, dicoumarol and [¹⁴C]estradiol by the 10,000 × g supernatant of liver homogenates from aminoglutethimide-pretreated rats. In these animals, levels of hepatic microsomal protein, cytochrome P-450 and NADPH-cytochrome-C reductase were raised. The results are consistent with aminoglutethimide being a phenobarbitone-like inducer of the hepatic mixed-function oxidases