

2-Methoxyestradiol and Disorders of Female Reproductive Tissues

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Abstract

2-Methoxyestradiol (2ME) is an endogenous metabolite of 17β -estradiol. Once thought of as a mere degradation product, 2ME has gained attention as an important component of reproductive physiology and as a therapeutic agent in reproductive pathologies such as preeclampsia, endometriosis, infertility, and cancer. In this review, we discuss the involvement of 2ME in reproductive pathophysiology and summarize its known mechanisms of action: microtubule disruption, inhibition of angiogenesis and stimulation of apoptosis. Currently, the clinical uses of 2ME as a single agent are limited due to its poor water solubility and thus low bioavailability; however, 2ME analogs and derivatives have been recently developed and tested as cancer treatments. Despite some isolated success stories and ongoing research, 2ME derivatives have not yet provided the expected results. The adjuvant use of 2ME derivatives with chemotherapeutic agents is hindered by their intrinsic toxicity confounding the unwanted secondary effects of chemotherapy. However, due to the well-tested tolerance of the body to high doses of native 2ME, it may be the combination of native 2ME with conventional treatments that will offer novel clinically relevant regimens for cancer and other reproductive disorders.