

TETRAHYDROGESTRINONE (THG) IS A POTENT ANDROGEN AND PROGESTIN

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Tetrahydrogestrinone (THG) is a novel steroid recently identified by a sports doping laboratory as an illicit agent sold to improve elite athletic performance. While its structure is closely related to gestrinone, a 19-nor progestin, and resembles that of trenbolone, a potent banned synthetic androgen, THG was never marketed, so no information on its hormonal properties are known. We therefore examined THG for steroidal bioactivity using yeast transformed with a steroid receptor-reporter system, comparing its bioactivity to other known androgens, nandrolone, 7 α nandrolone (MENT), norbolethone, 5 α -norbolethone, norethandrolone and trenbolone, as well as THG's parent compound, gestrinone. Yeast were stably transformed with human androgen receptor (AR) or progesterone receptor A (PR) cDNA, together with a reporter plasmid containing a β -galactosidase gene under the transcriptional control of an androgen (ARE) or progestin (PRE) reporter element. Bioassays were established by culturing transformed yeast in the presence of the steroids over the range of 1.2×10^{-6} to 5.9×10^{-10} M. The bioassay end-point was β -galactosidase activity in yeast cell lysates. THG showed dose-dependent highly potent activation of AR activity with an EC₅₀ of 0.29 nM compared with other steroids nandrolone (0.12 nM), norbolethone (0.3 nM), 5 α -norbolethone (0.026 nM), gestrinone (0.59 nM), trenbolone (0.78 nM), norethandrolone (0.19 nM) and MENT (0.01 nM). THG also activated PR (EC₅₀ 0.7 nM) with much higher potency than its parent steroid, gestrinone (EC₅₀ 30 nM). We conclude that THG is a potent androgen and progestin. It shows similar potency to the comparator androgens, nandrolone, norbolethone, 5 α -norbolethone and trenbolone. The discovery of this illicit designer androgen raises concern about the possibility of other novel androgens being produced from other marketed synthetic sex steroids.