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Background/Aims: Azoles are antifungal agents used in both medicine and agriculture. In fungi they typically work by damaging the fungal cell membrane by inhibition of cytochrome P450 enzymes, primarily CYP51. However, in mammals azoles can have endocrine disrupting effects and fetal exposure to certain azoles can disrupt reproductive development.
We have tested an agricultural azole fungicide, triticonazole, for its endocrine disrupting potential, both in vitro and in vivo.
Method: Triticonazole was tested with in vitro assays for Androgen Receptor (AR) interaction and steroid hormone synthesis disruption. An in utero rat developmental toxicity study was furthermore conducted: time-mated Sprague Dawley rats were exposed to two concentrations (150 or 450 mg/kg bw/day) by oral gavage on gestational days 7-21 and dissections were carried out on gestational day 21. Blood and amniotic fluid were collected from dams and pups for pharmacokinetic and hormone measurements. Anogenital distance was measured and reproductive tissues collected from the fetuses.
Results: Triticonazole showed strong AR antagonism and capacity to disrupt steroid biosynthesis in vitro. Following gestational exposure to triticonazole (150 or 450 mg/kg bw/day), a shorter male anogenital distance was apparent in both dose groups. Additional studies are currently on-going to further characterize molecular effects in reproductive tissues.
Conclusions: Triticonazole is an endocrine disrupting chemical that appears to act by anti-androgenic mechanisms.