

Reproductive Effects and Mechanisms-of-Action of Fetal Exposure to Azole Fungicides



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PhD candidate

DTU Food

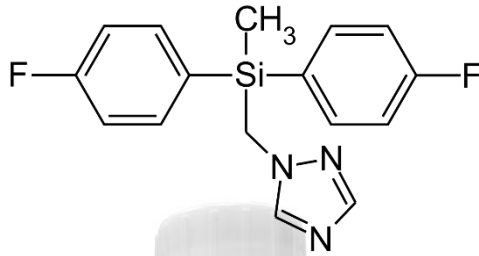
Why azole fungicides?

- They display ED effects, including adverse reproductive outcomes
- Classic MoA is inhibiting CYP enzyme activity, but also several other MoA
- Effects / adverse outcomes can vary greatly

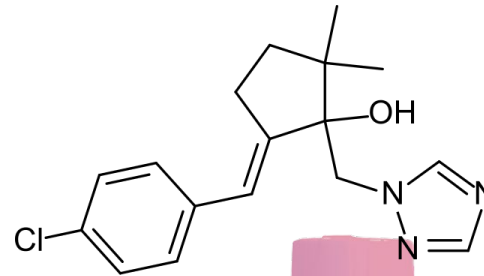


in vitro & *in vivo* endocrine activities; examples

Flusilazole

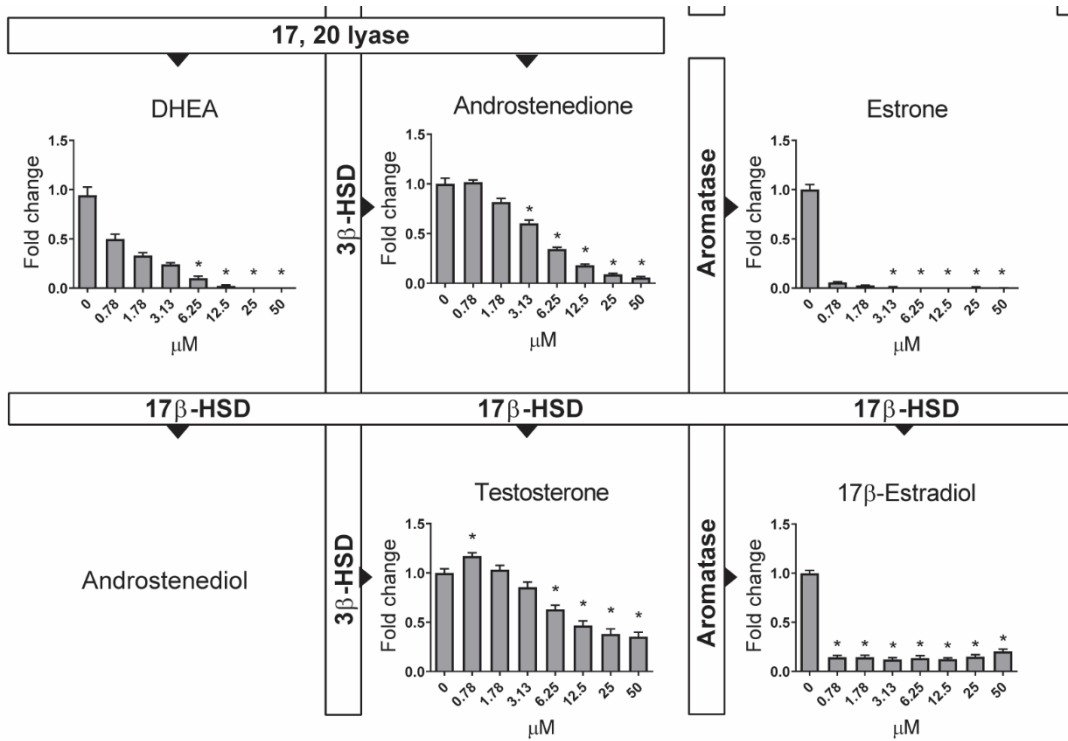


Triticonazole

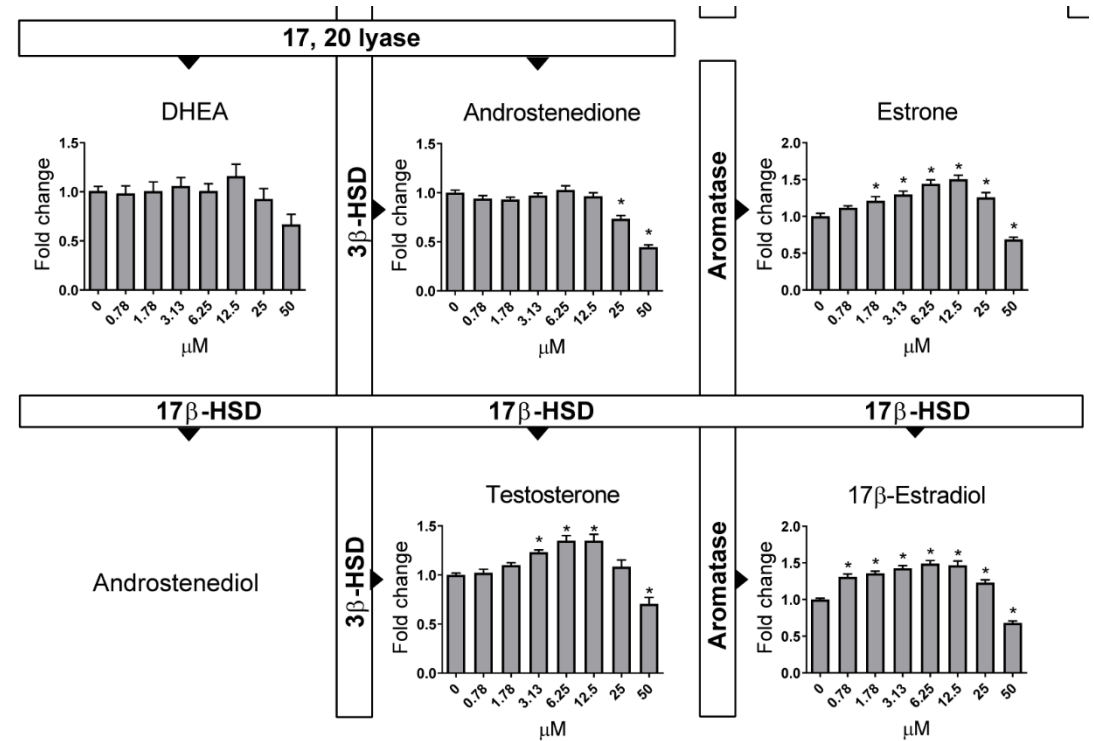


FLUZ disrupts steroidogenesis *in vitro*

flusilazole

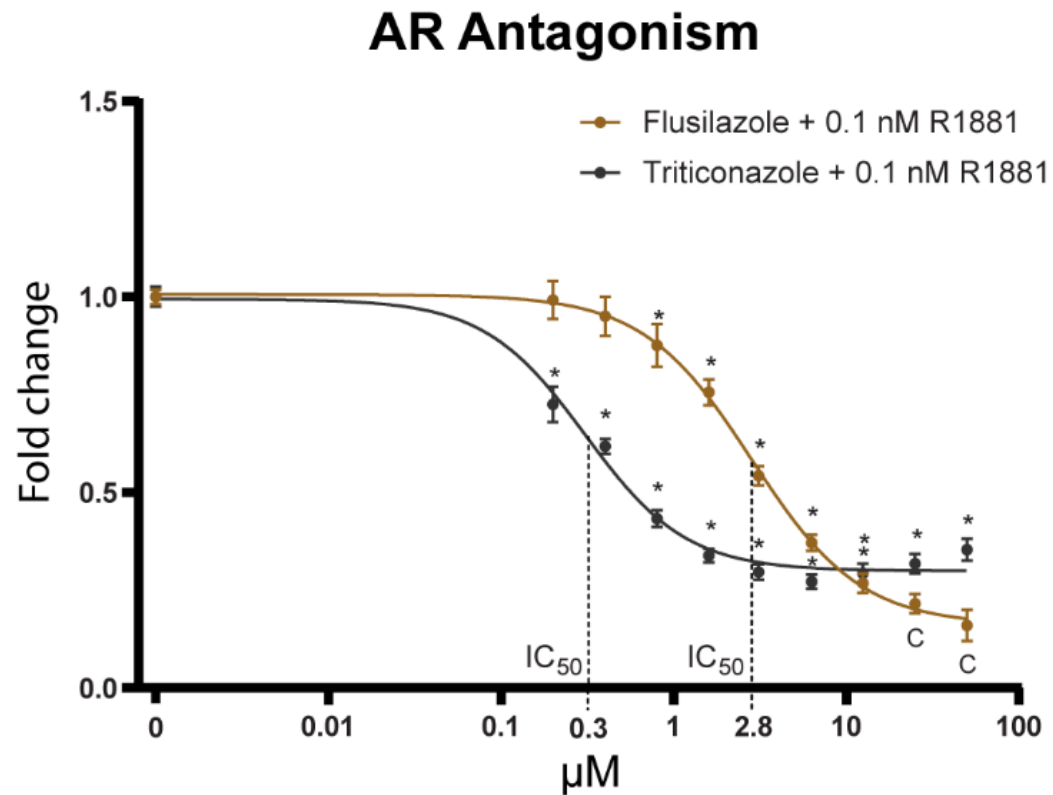


triticonazole



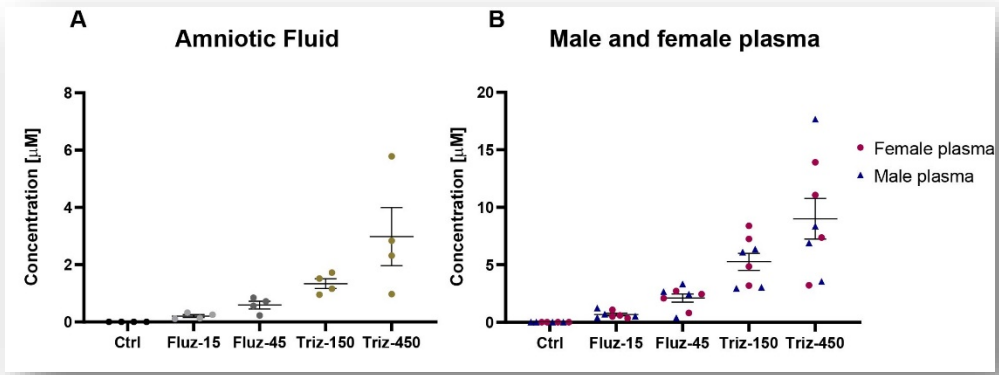
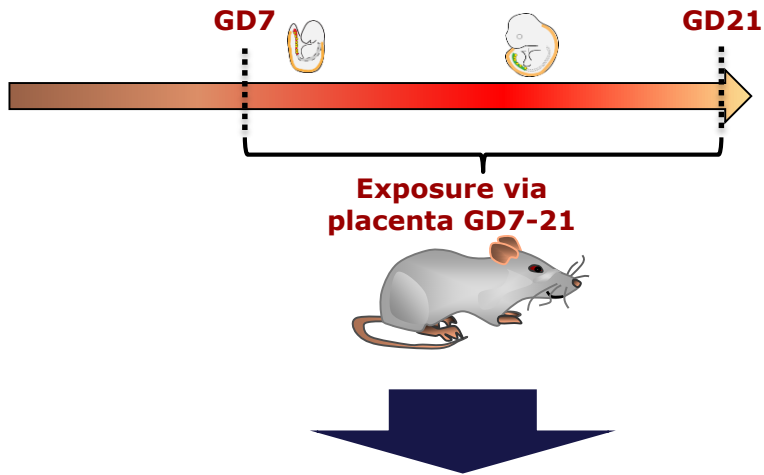
FLUZ and TRIZ are AR antagonists *in vitro*

- *Stably Transfected Human Androgen Receptor Transcriptional Activation Assay (AR-Eco)*
- *Approx 10-fold difference in IC₅₀: Fluz = 2.8 μM; Triz = 0.3 μM*



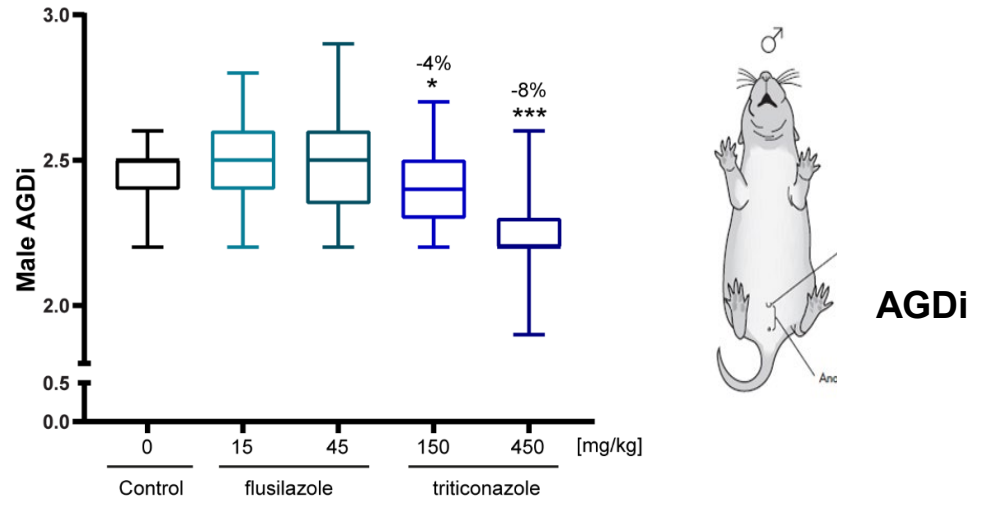
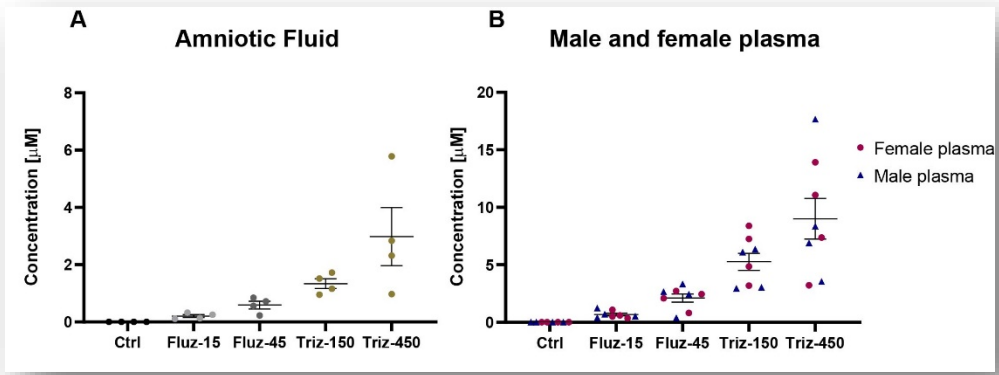
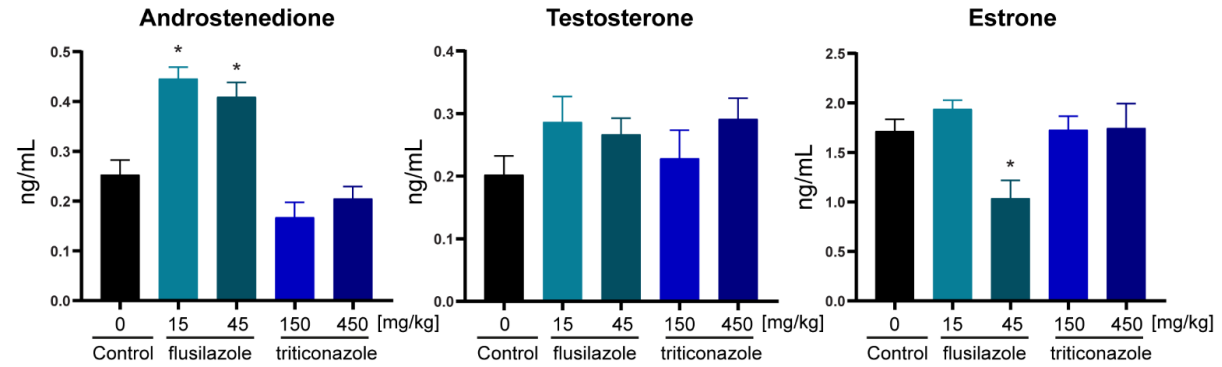
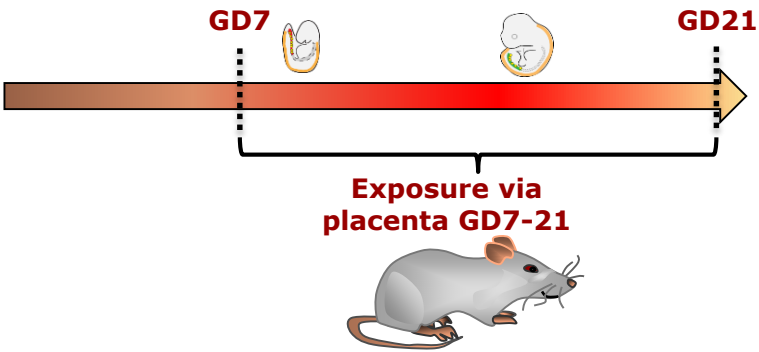
FLUZ and TRIZ have different effects *in vivo*

Flusilazole 15 mg/kg and 45 mg/kg
 Triticonazole 150 mg/kg and 450 mg/kg



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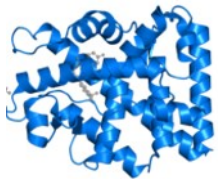


Conclusions on ED effect screen

Flusilazole and Triticonazole both have endocrine disrupting properties, but have dissimilar effects on reproductive parameters

Triticonazole

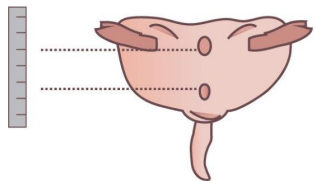
In vitro



**Most potent
AR antagonist**

In vivo

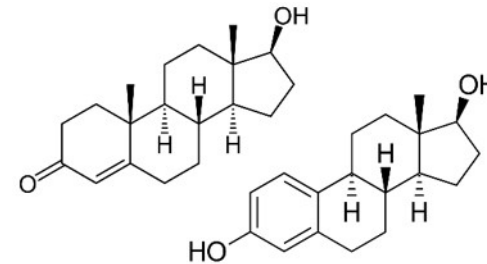
GD21



short AGD

Flusilazole

In vitro



**Most potent
Steroidogenesis disruptor**

In vivo

GD21



***altered blood
hormone profile***

Draskau et al 2019



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In vitro and *in vivo* endocrine disrupting effects of the azole fungicides
triticonazole and flusilazole[☆]

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Thank you for your attention!

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