



# Dydrogesterone *versus* Micronized Progesterone

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# Dydrogesterone *versus* Micronized Progesterone Receptor Selectivity

Biological activity	Dydrogesterone	Progesterone
Progestogenic	+	+
Anti-gonadotropic	-	+
Anti-estrogenic	+	+
Estrogenic	-	-
Androgenic	-	-
Anti-androgenic	±*	±
Glucocorticoid	-	+
Anti-mineralocorticoid	±	+

Dydrogesterone is selective for the progesterone receptor, avoiding other receptor-related side effects<sup>1-4</sup>

\*Dydrogesterone has less pronounced anti-androgenic effects than progesterone; + effective; ± weakly effective; - not effective

1. Schindler AE, et al. Maturitas 2008; 61(1-2):171-180. 2. Schindler AE. Maturitas 2009; 65(Suppl 1):S3-S11. 3. Dydrogesterone CCDS. 23 June 2015. 4. Rižner TL, et al. Steroids 2011; 76(6):607-615.

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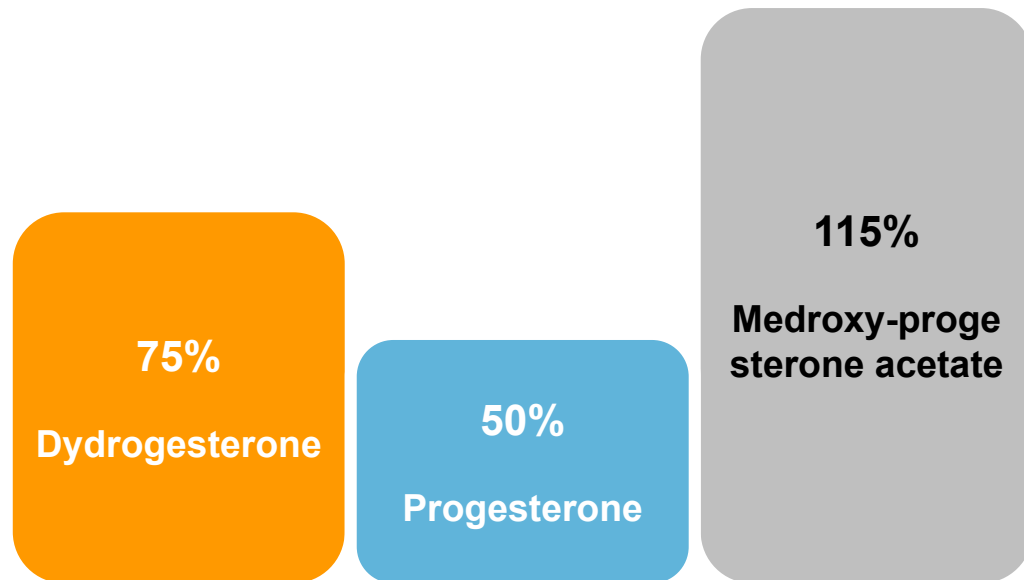
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# Dydrogesterone *versus* Micronized Progesterone Receptor Affinity

Dydrogesterone has ~1.5 times better affinity to progesterone receptors than progesterone<sup>1</sup>

Affinity to progesterone receptor<sup>1</sup>



Dihydrodydrogesterone, the main metabolite of dydrogesterone, also has progestogenic activity<sup>1-3</sup>

1. Schindler AE, et al. Maturitas 2008; 61(1-2):171-180.
2. Schindler AE. Maturitas 2009; 65(Suppl 1): S3-S11.
3. Dydrogesterone CCDS. 23 June 2015.

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# Dydrogesterone *versus* Micronized Progesterone Bioavailability and Oral Administration

Dydrogesterone has ~5.6 times better oral bioavailability than progesterone<sup>1-3</sup>

## Oral bioavailability

28%  
dydrogesterone

<5% progesterone

## Oral dose

100–300 mg  
progesterone

10 mg  
dydrogesterone

Dydrogesterone requires a 10–20 times lower oral dose than micronized progesterone,<sup>1-3</sup> providing clear clinical benefits<sup>4-6</sup>

# Dydrogesterone *versus* Vaginal Micronized Progesterone Absorption and Plasma Levels

## Dydrogesterone<sup>1</sup>

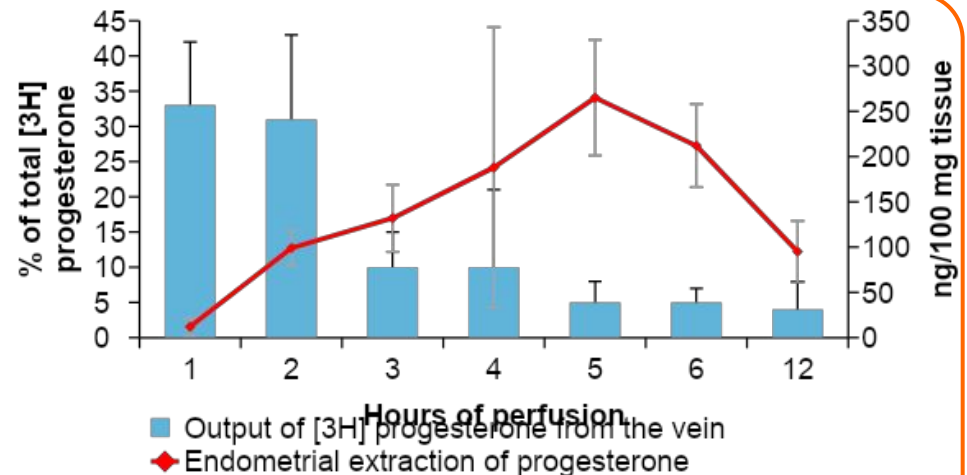
- Has **quick-effect onset** (rapidly absorbed, reaching maximal levels between 30 minutes and 2.5 hours after administration)
- Has a **long, stable effect** (mean terminal half-life is 5–7 hours)

## Vaginal progesterone<sup>2</sup>

Progesterone diffuses through the entire uterus by 4–5 hours, and then decreases concentration after 5 hours

**Venous blood outflow from the uterus was highest in the first 2 hours**

**Vaginal route permits targeted drug delivery for a short period of time**



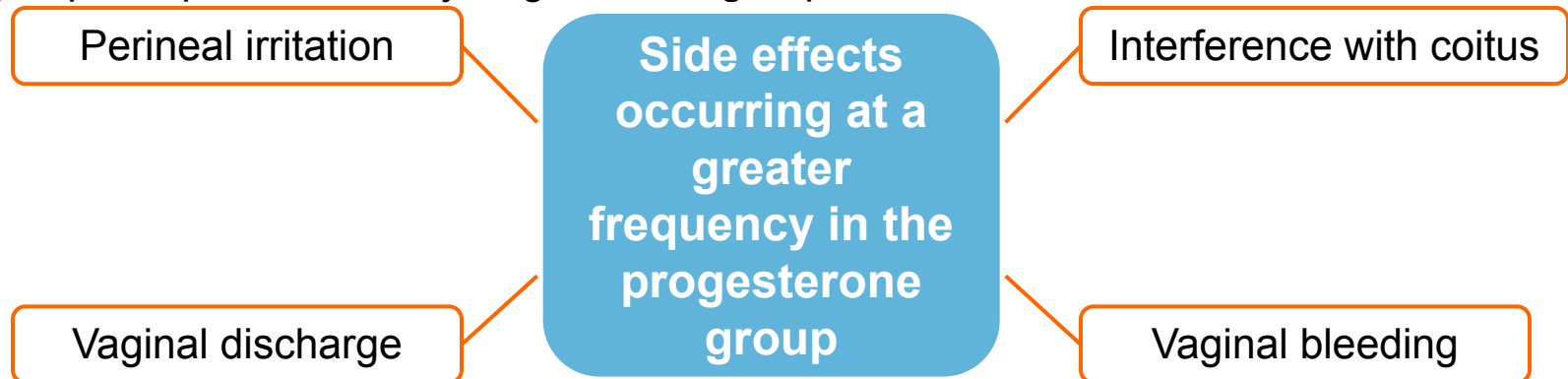
Adapted from Bulletti C, et al. Hum Reprod 1997; 12(5):1073-1079

**Dydrogesterone reaches peak absorption levels more rapidly than vaginal progesterone, and these levels are maintained for a longer duration<sup>1,2</sup>**

1. Dydrogesterone CCDS. 23 June 2015.  
2. Bulletti C, et al. Hum Reprod 1997; 12(5):1073-1079.

# Dydrogesterone *versus* Vaginal Micronized Progesterone Safety and Tolerability

- Both oral and vaginal micronized progesterone are metabolized by the liver<sup>1,2</sup>
  - Progesterone is associated with a risk of cholestasis in pregnancy, therefore it is only licensed in the UK for use up to Week 12 of gestation in ART/IVF and only by the vaginal route
- It is estimated that more than 10 million pregnancies have been exposed to dydrogesterone. So far, there have been no indications of a harmful effect of dydrogesterone use during pregnancy<sup>3,4</sup>
- A randomized controlled trial in 853 infertile women compared the efficacy and tolerability of 20 mg/day oral dydrogesterone and 90 mg 8% vaginal progesterone gel used for luteal support. Numerically more local side effects occurred in the progesterone group compared to the dydrogesterone group<sup>5</sup>



ART, assisted reproductive technology; IVF, *in vitro* fertilization

1. Utrogestan 200 mg oral capsules. SPC UK. October 2013. 2. Utrogestan 200 mg vaginal capsules. SPC UK. October 2013. 3. Queisser-Luft A. Early Hum Dev 2009; 85(6):375-377. 4. Dydrogesterone CCDS. 23 June 2015. 5. Tomic V, et al. Eur J Obstet Gynecol Reprod Biol 2015; 186:49-53.

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# Dydrogesterone *versus* Vaginal Micronized Progesterone Preference and Acceptability

- In studies that compared oral *versus* vaginal formulations of non-progestin drugs, women prefer to use oral formulations than vaginal ones<sup>1,2</sup>
- Application of vaginal tablets requires a private, clean room; whereas tablets can be taken orally, anywhere

**A comparative study between dydrogesterone and vaginal micronized progesterone for luteal support<sup>3</sup>**

**Vaginal discharge  
or irritation**

Dydrogesterone  
group: 0%

Progesterone  
group: 10.5%

**Satisfaction  
with tolerability  
of treatment**

Dydrogesterone  
group: ~95%

Progesterone  
group: ~73%

Statistically significant difference ( $p < 0.05$ )

1. Arvidsson C, et al. Eur J Obstet Gynecol Reprod Biol 2005; 123(1):87-91.  
2. Bingham JS. Br J Vener Dis 1984; 60(3):175-177.  
3. Chakravarty BN, et al. J Steroid Biochem Mol Biol 2005; 97(5):416-420.

# Conclusions

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## Dydrogesterone

- Is produced from a natural source<sup>1</sup> like other progestogens
- Is very similar to progesterone, but has enhanced oral bioavailability<sup>2,3</sup>
- Is highly selective and has a high affinity for progesterone receptors<sup>2,3</sup>
- Is metabolized into compounds that are either progestogenic or inactive<sup>2,3</sup>
- Has a fast onset of action and long, stable effect<sup>4</sup>
- Is well tolerated and has a favorable safety profile in all approved indications, including pregnancy<sup>4-9</sup>

Note: the effectiveness and safety records of dydrogesterone are based on the body of evidence for treatment of threatened<sup>5,6,10,11</sup> and recurrent miscarriage<sup>7</sup>

1. University of Maryland Medical Center. Complementary and Alternative Medicine Guide. Wild yam. <http://umm.edu/health/medical/altmed/herb/wild-yam>.  
2. Schindler AE, et al. Maturitas 2009; 65(Suppl 1):S3-S11. 3. Schindler AE, et al. Maturitas 2008; 61(1-2):171-180. 4. Dydrogesterone CCDS. 23 June 2015. 5. El-Zibdeh MY, Yousef LT. Maturitas 2009; 65(Suppl 1):S43-S46. 6. Pandian RU. Maturitas 2009; 65(Suppl 1):S47-S50. 7. El-Zibdeh MY. J Steroid Biochem Mol Biol 2005; 97(5):431-434. 8. Dutta DK. Asian J Obstet Gynae Pract 2001; 5(2):3-5; 9. Queisser-Luft A. Early Hum Dev 2009; 85(6):375-377. 10. Omar MH, et al. J Steroid Biochem Mol Biol 2005; 97(5):421-425. 11. Carp H. Gynecol Endocrinol 2012; 28(12):983-990.



