

ERECTILE DYSFUNCTION

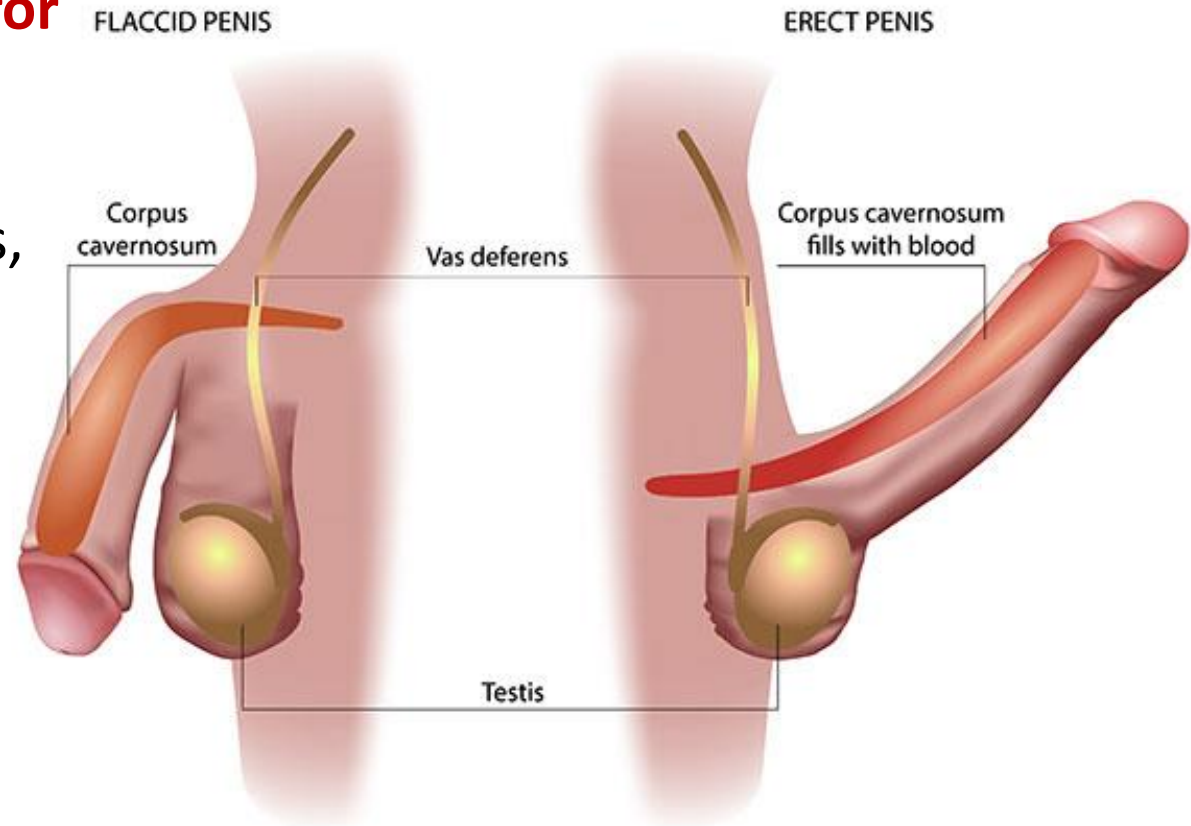
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ED is common urologic disorders in males.

ED is the inability to maintain penile erection for the successful performance of sexual activity.

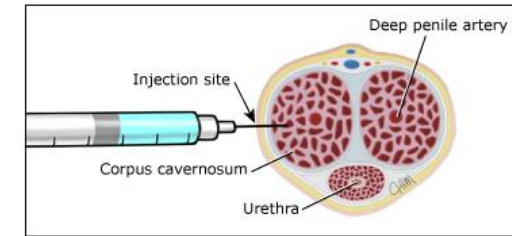
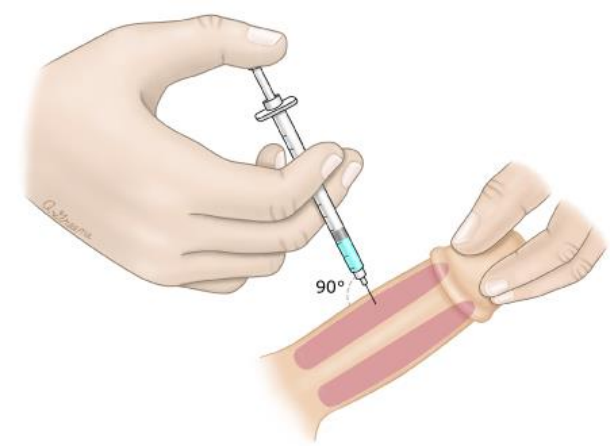
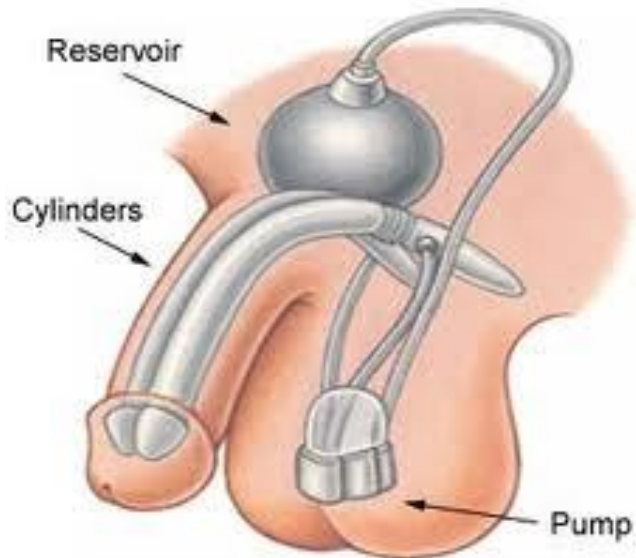
Causes: vascular disease, diabetes, medications, depression,



Drugs for Erectile dysfunction (ED)

Therapy for ED includes

- ✓ Penile implants,
- ✓ Intrapenile injections of *alprostadil*,
- ✓ Intraurethral suppositories of *alprostadil*,
- ✓ Oral phosphodiesterase-5 (PDE-5) inhibitors



Therapies: alprostadil, and oral phosphodiesterase-5 (PDE-5) inhibitors.

Phosphodiesterase-5 inhibitors : (sildenafil, vardenafil, tadalafil, and avanafil)

MoA: PDE inhibit PDE-5, the isozyme responsible for degradation of cGMP in the corpus cavernosum.

DRUGS FOR ERECTILE DYSFUNCTION

Alprostadil MUSE, CAVERJECT, EDEX

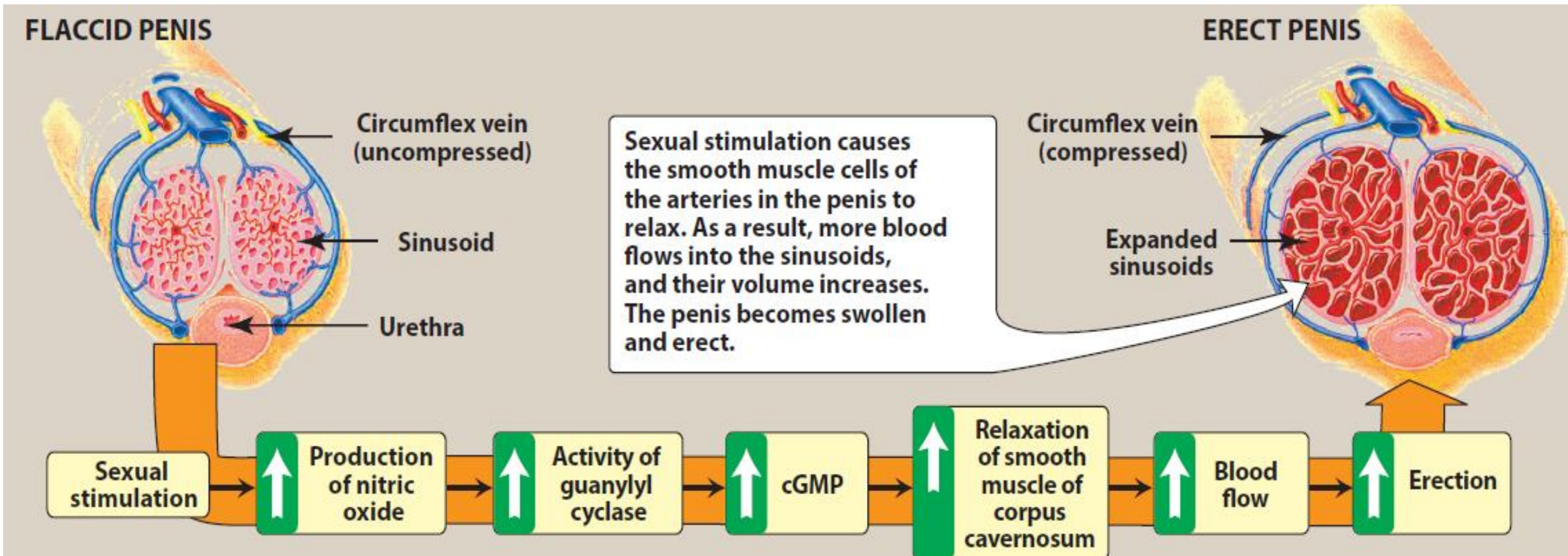
Avanafil STENDRA

Sildenafil VIAGRA

Tadalafil CIALIS

Vardenafil LEVITRA, STAXYN

Drugs for Erectile dysfunction (ED)



Mechanism of penile erection.

cGMP = cyclic guanosine monophosphate

Drugs for Erectile dysfunction (ED)

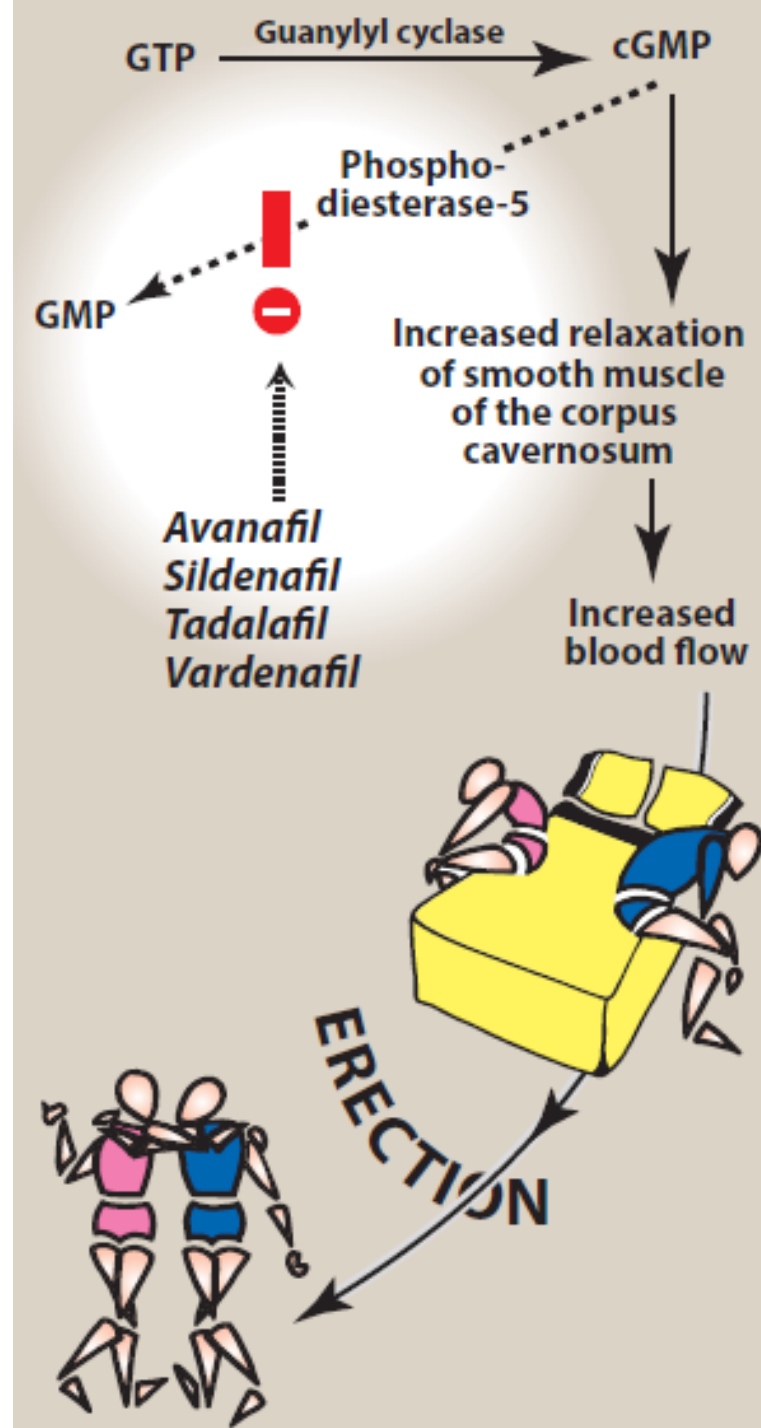
Mechanism of action:

Sexual stimulation results in smooth muscle relaxation of the corpus cavernosum, increasing the inflow of blood.

The mediator of this response is nitric oxide (NO).

NO activates guanylyl cyclase, which forms cyclic guanosine monophosphate (cGMP) from guanosine triphosphate.

cGMP produces smooth muscle relaxation through a reduction in the intracellular Ca²⁺ concentration.



Drugs for Erectile dysfunction (ED)/ Pharmacokinetics:

A Time to peak concentration

<i>Avanafil</i>	30–45 min
<i>Sildenafil</i>	60 min
<i>Vardenafil</i>	60 min
<i>Tadalafil</i>	120 min

B Half-life

<i>Avanafil</i>	5 hr
<i>Sildenafil</i>	3–4 hr
<i>Vardenafil</i>	4–5 hr
<i>Tadalafil</i>	18 hr

C Food interaction*

<i>Avanafil</i>	No
<i>Sildenafil</i>	Yes
<i>Vardenafil</i>	Yes
<i>Tadalafil</i>	No

Drugs for Erectile dysfunction (ED)



Pharmacokinetics:

Sildenafil and vardenafil should be taken approximately 1 hour prior to anticipated sexual activity, with erectile enhancement observed for up to 4 hours after administration.

The absorption of both drugs is delayed by consumption of a high-fat meal.

Tadalafil has a slower onset of action than sildenafil and vardenafil, but a significantly longer half-life of approximately 18 hours (once-daily dosing).

This results in enhanced erectile function for up to 36 hours.

Furthermore, the absorption of tadalafil is not clinically influenced by food.

The timing of sexual activity is less critical for tadalafil.

Drugs for Erectile dysfunction (ED)



Adverse effects:

The most frequent adverse effects of the PDE-5 inhibitors are **headache, flushing, dyspepsia, and nasal congestion.**

Disturbances in **color vision** (loss of blue/green discrimination) may occur with PDE-5 inhibitors, probably because of inhibition of **PDE-6** (a PDE found in the retina that is important in color vision).

Priapism (a painful, prolonged erection)

Tadalafil does not appear to disrupt PDE-6,

Drugs for Erectile dysfunction (ED)



Drug interactions:

Because of the ability of PDE-5 inhibitors to potentiate the hypotensive activity of NO, administration of these agents in patients taking any form of organic nitrates (for example, nitroglycerin products, isosorbide dinitrate, or isosorbide mononitrate) is contraindicated.

PDE-5 inhibitors may produce additive blood pressure–lowering effects when used in patients taking α -adrenergic antagonists (used to treat hypertension).

Drugs for Erectile dysfunction (ED)/ B. Alprostadil



Alprostadil is synthetic prostaglandin E1 (**PGE1**).

In the penile tissue, PGE1 allows for relaxation of the smooth muscle in the corpus cavernosum.

Alprostadil is available as an **intraurethral suppository** and an **injectable** formulation.

Although PDE-5 inhibitors are considered first-line therapy for the treatment of ED, alprostadil may be used for patients who are not candidates for oral therapies.

Drugs for Erectile dysfunction (ED)/ B. Alprostadil/ 1. Mechanism of action:



It is believed that alprostadil increases concentrations of cyclic AMP (**cAMP**) within cavernosal tissue.

As a result, protein kinase is activated, allowing trabecular smooth muscle relaxation and dilation of cavernosal arteries.

Increased blood flow to the erection chamber compresses venous outflow, so that blood is entrapped and erection may occur.

Drugs for Erectile dysfunction (ED)/ B. Alprostadil/ 2. Pharmacokinetics:



Systemic absorption of alprostadil is minimal.

If any alprostadil is systemically absorbed, it is **quickly metabolized**.

The **onset of action** of alprostadil is 5 to 10 minutes when given as a urethral suppository and 2 to 25 minutes when administered by injection.

The resulting erection may last for 30 to 60 minutes, or longer, depending upon the particular patient.

Drugs for Erectile dysfunction (ED)/ B. Alprostadil/ 3. Adverse effects:

Since alprostadil is not systemically absorbed, adverse systemic effects are rare.

However, hypotension or headache is a possibility due to PGE1-induced **vasodilation**.

Locally, adverse effects of alprostadil include penile **pain**, urethral pain, and testicular pain.

Bleeding from the insertion or injection of alprostadil is rare.

Hematoma, ecchymosis, and rash are possible from alprostadil injection, although these adverse effects are also rare. Alprostadil administration may lead to **priapism**.