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Day 1: Discovered in 1847 as an early explosive, #glyceryl trinitrate, or GTN (also known as nitroglycerin) was used in blasting & smokeless gunpowder. In the UK, interest in amyl nitrite (no prescription use now) led to GTN usage for angina from 1867 (stable in solid medicinal form).

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Day 2: [#glyceryl](https://twitter.com/search?q=%23glyceryl) trinitrate is a potent vasodilator. UK uses include angina treatment & prophylaxis, control of myocardial infarction & hypertension for cardiac surgery, anal fissure & prophylaxis of phlebitis (transdermal). Longer-acting nitrate agents can also treat left ventricular heart failure

(cont);Sub-lingual spray 400 mcg x 1-2/no more than 3 uses (shelf-life ~3yrs), sub-lingual tablet 300-600 mcg every 5 mins up to 3 doses (tablets expire 8 weeks after opening), i.v infusion 10-200 mcg/minute

Day 3: MOA #glyceryl trinitrate. Once in smooth muscle cells, denitration leads to release of nitric oxide. This activates guanylate cyclase & ↑cGMP. Less Ca+ into cell allows smooth muscle relaxation. Powerful venodilation lowers cardiac preload. At higher doses, coronary artery vasospasm is relieved & there is lower afterload. All actions ↓ oxygen demand & relieve anginal pain

Day 4: Kinetics – GTN is a prodrug. Rapid absorption from sub-lingual & buccal mucosa > fast pain relief-effect but for < 30 mins. Extensive 1st pass metabolism limits formulations, t½ 1-3 minutes, but some metabolites can last longer (~30 mins). Metabolised in blood vessels/no elimination

Day 5: ADRs common: flushing, headache, postural hypotension, reflex tachycardia, nausea. Uncommon, circulatory collapse, tongue blistering (sub-lingual), exfoliative dermatitis (not exhaustive); NB potential to worsen angina if severe hypotension/reflex tachycardia

Issues such as tolerance & avoiding sudden withdrawal as linked to rebound vasoconstriction; potential for angina, MI & sudden death (caution for all nitrates) may depend on usage of GTN, especially with high continuous dose

Day 6 DDIs #glyceryl trinitrate: All hypotensive agents including alcohol, tricyclic anti-depressants & neuroleptics, severe interaction with phosphodiesterase inhibitors e.g sildenafil (not exhaustive). Note drugs with antimuscarinic effects can cause dry mouth & reduce effectiveness of sublingual GTN tablets.

Day 7: Mechanism for tolerance/cross tolerance to other nitrates largely unknown. Theories include:endothelial dysfunction, activation of counter cardiovascular reflexes e.g RAAS, elevation of opposing neurohormones, e.g norepinephrine & ↓nitrate metabolism (prodrug)