



## Nitroglycerin synthesis

The industrial manufacturing process often reacts glycerol with a nearly 1:1 mixture of concentrated sulfuric acid and concentrated nitric acid. This can be produced by mixing white fuming nitric acid—a quite expensive pure nitric acid in which the oxides of nitrogen have been removed, as opposed to red fuming nitric acid, which contains nitrogen oxides—and concentrated sulfuric acid. More often, this mixture is attained by the cheaper method of mixing fuming sulfuric acid, also known as oleum—sulfuric acid containing excess sulfur trioxide—and azeotropic nitric acid (consisting of about 70% nitric acid, with the rest being water).

The sulfuric acid produces protonated nitric acid species, which are attacked by glycerol's nucleophilic oxygen atoms. The nitro group is thus added as an ester C–O–NO<sub>2</sub> and water is produced. This is different from an electrophilic aromatic substitution reaction in which nitronium ions are the electrophile.

The addition of glycerol results in an exothermic reaction (i.e., heat is produced), as usual for mixed-acid nitrations. If the mixture becomes too hot, it results in a runaway reaction, a state of accelerated nitration accompanied by the destructive oxidation of organic materials by the hot nitric acid and the release of poisonous nitrogen dioxide gas at high risk of an explosion. Thus, the glycerin mixture is added slowly to the reaction vessel containing the mixed acid (not acid to glycerin). The nitrator is cooled with cold water or some other coolant mixture and maintained throughout the glycerin addition at about 22 °C (72 °F), much below which the esterification occurs too slowly to be useful. The nitrator vessel, often constructed of iron or lead and generally stirred with compressed air, has an emergency trap door at its base, which hangs over a large pool of very cold water and into which the whole reaction mixture (called the charge) can be dumped to prevent an explosion, a process referred to as drowning. If the temperature of the charge exceeds about 30 °C (86 °F) (actual value varying by country) or brown fumes are seen in the nitrator's vent, then it is immediately drowned.

## **Medical uses**

Three different forms of nitroglycerin: intravenous, sublingual spray, and the nitroglycerin patch.

Nitroglycerin is used for the treatment of angina, acute myocardial infarction, severe hypertension, and acute coronary artery spasms.

## **Angina**

GTN is useful in decreasing angina attacks, perhaps more so than reversing angina once started, by supplementing blood concentrations of NO, also called endothelium-derived relaxing factor, before the structure of NO as the responsible agent was known. This led to the development of transdermal patches of glyceryl trinitrate, providing 24-hour release. However, the effectiveness of glyceryl trinitrate is limited by development of tolerance/tachyphylaxis within 2–3 weeks of sustained use. Continuous administration and absorption (such as provided by daily pills and especially skin patches) accelerate onset of tolerance and limit the usefulness of the agent. Thus, glyceryl trinitrate works best when used only in short-term, pulse dosing. Glyceryl trinitrate is useful for acute myocardial infarction (heart attack) and pulmonary edema, again working best if used quickly, within a few minutes of symptom onset, as a pulse dose. It may also be given as a sublingual or buccal dose in the form of a tablet placed under the tongue or a spray into the mouth for the treatment of an angina attack.

## **Other uses**

Tentative evidence indicates efficacy of glyceryl trinitrate in the treatment of various tendinopathies, both in pain management and acceleration of soft tissue repair.

GTN is also used in the treatment of anal fissures, though usually at a much lower concentration than that used for angina treatment.

GTN has been used to decrease pain associated with dysmenorrhea.

### What is the difference between nitroglycerin to explode and for your heart?

Chemically there is no **difference between** the **nitroglycerin** used in dynamite and that used in **heart** medication. In its pure form, **nitroglycerin** is a contact explosive, with physical shock causing it to **explode**, and it degrades over time to even more unstable forms.

### What is the most common side effect of nitroglycerin?

**Headache, dizziness, lightheadedness, nausea, and flushing** may occur as your body adjusts to this medication. If any of these effects persist or worsen, tell your doctor or pharmacist promptly. **Headache** is often a sign that this medication is working.

### What does nitroglycerin do to the body?

**Nitroglycerin** works by relaxing the smooth muscle and blood vessels in your **body**. This increases the amount of blood and oxygen that reaches your heart. In turn, your heart doesn't work as hard. This reduces chest pain.

### Synthesis of Glycerol

