

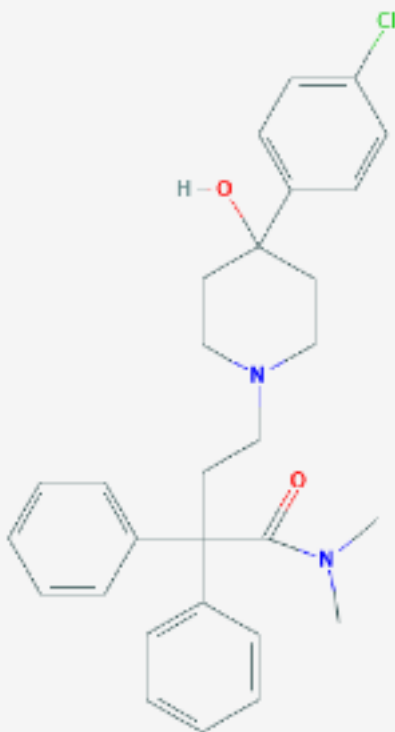
Probability is a major problem [2]

- Pharmacokinetics
 - Up to 40% of drug discovery programs abandoned due to pharmacokinetics - the movement of drugs within the body
 - Low solubility is associated with problems with pharmacokinetics

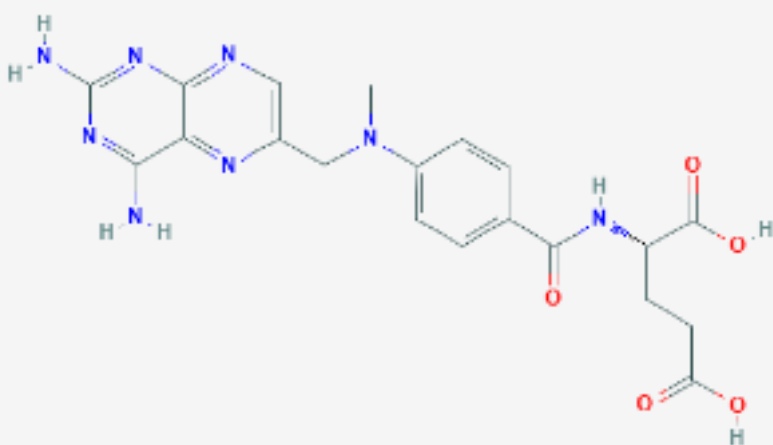
- Precipitation
 - Loperamide (diarrhea drug) can sometimes precipitate when injected
 - Methotrexate (cancer drug) has kidney toxicity due to precipitation

- Polymorphs can affect solubility and have different bioavailability, e.g. ritonavir (HIV drug) had to be reformulated





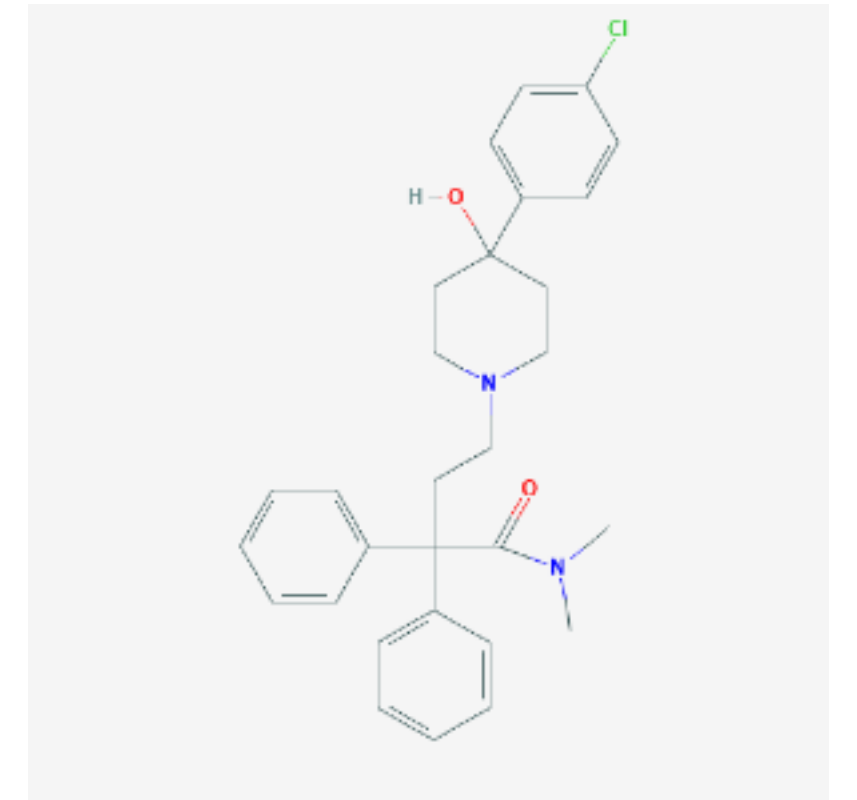
Loperamide



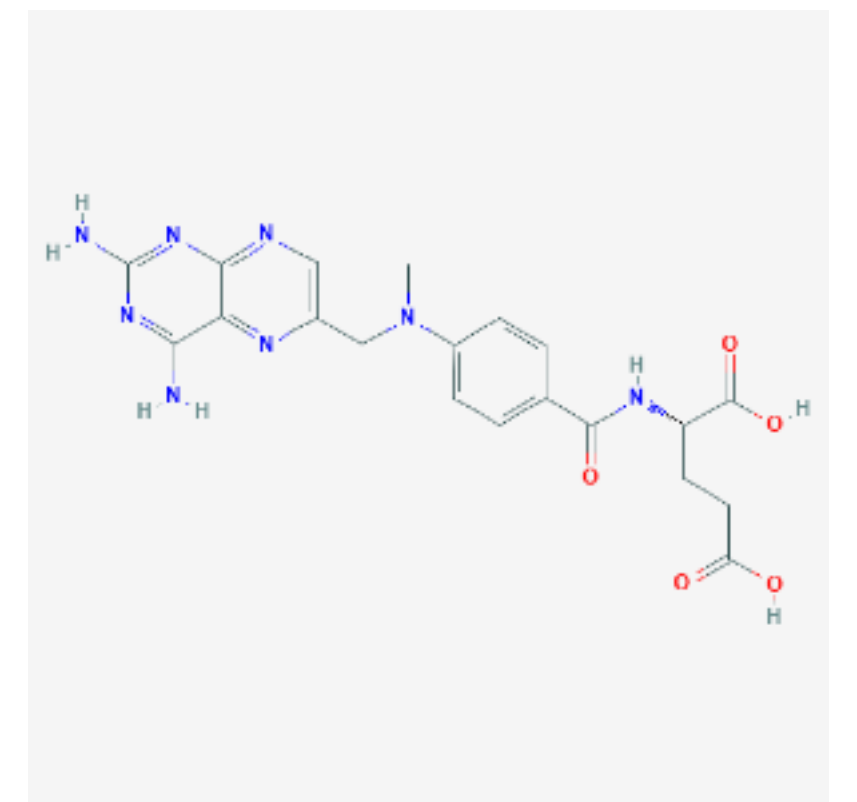
Methotrexate

Poor solubility is a major problem [2]

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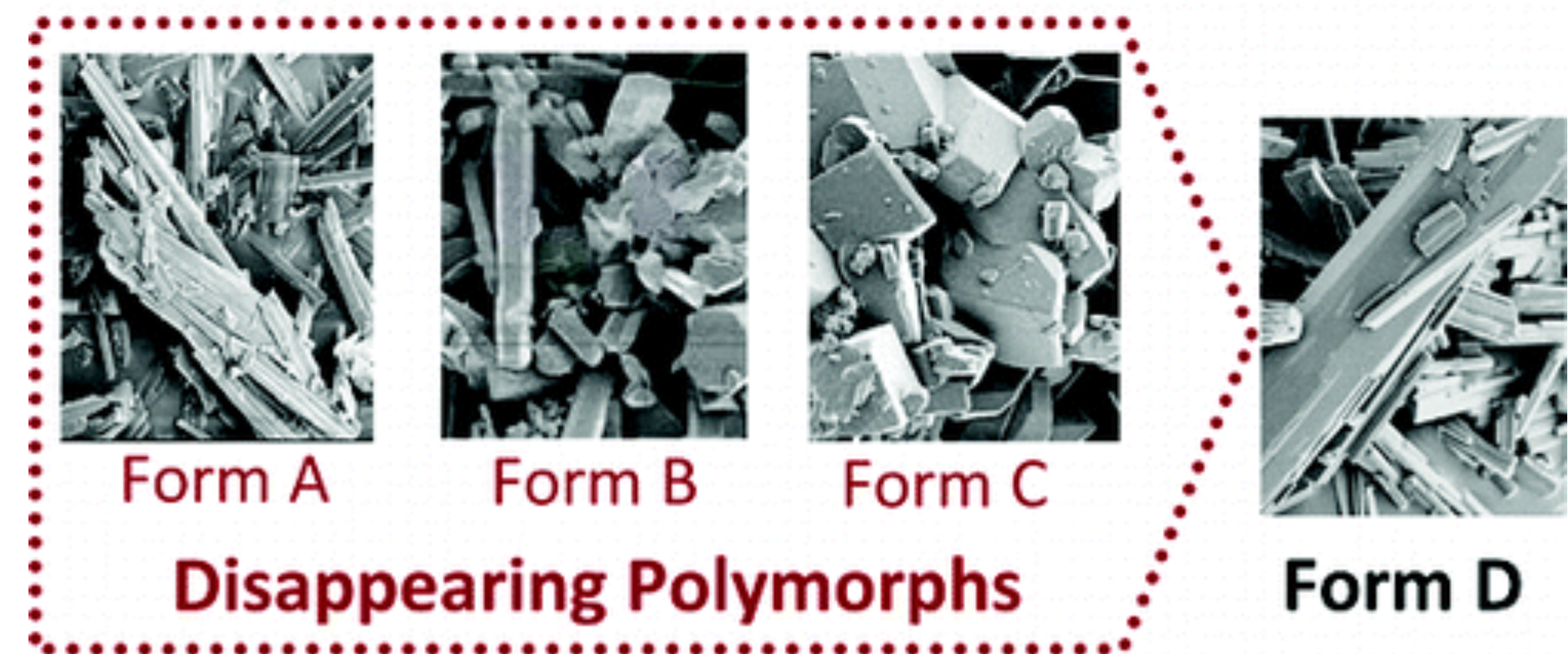
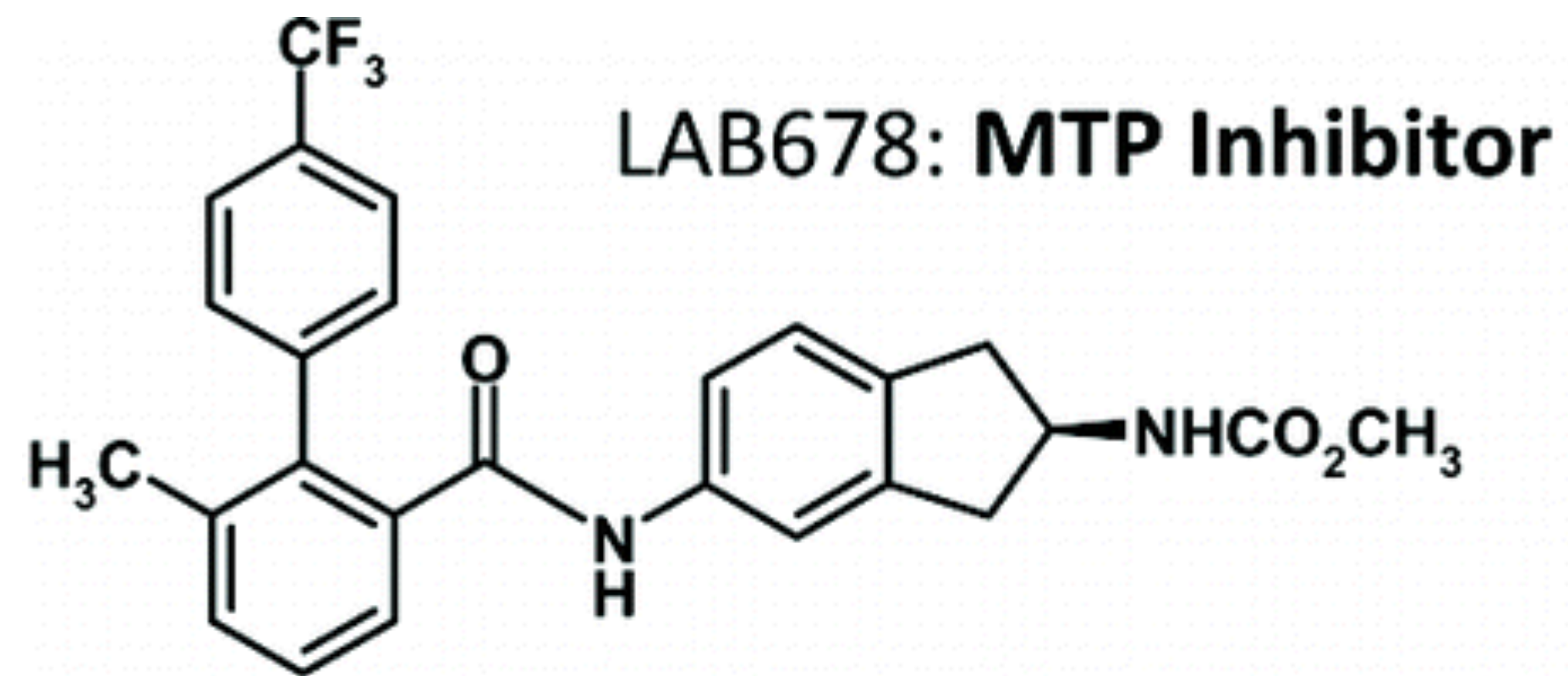


Loperamide



Methotrexate

Polymorphs are chemical engineering problem



Chemical structure and SEM images from [4]