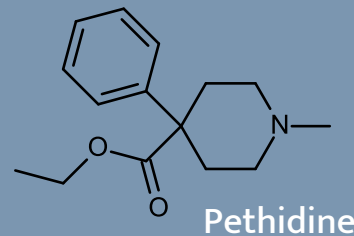


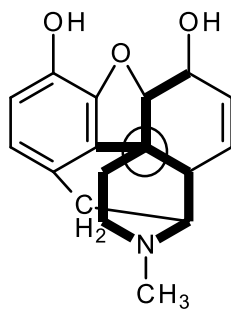
# PETHIDINE

Molar Mass : 247.3 g mol<sup>-1</sup>  
Melting point : 186-189 °C

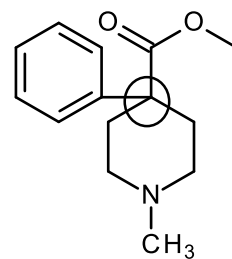


Pethidine is a synthetic analgesic drug used to relieve pain. It was developed during world war II in Germany by Eisleb and Schaumann in 1939. Pethidine was the most widely used drug in the late 20<sup>th</sup> century. In a survey done in 2004, of the top 10 drugs used in the US, pethidine injection was third on the list.

It is also known by the names Dolantin<sup>®</sup>, Demerol<sup>®</sup> and Meperidine. It is structurally similar to morphine. According to Schaumann, grouping of 1-methyl-4-phenylpiperidine via quaternary carbon atom is the carrier of analgesic effect of morphine and this is also present in pethidine. The pKa of pethidine is 8.59 i.e. it is basic in nature.



Morphine



Pethidine

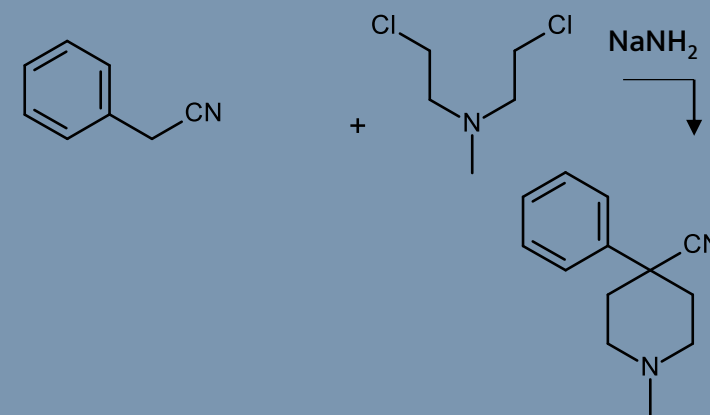
## History of analgesics

The word analgesia was introduced in the literature with the discovery of morphine by German pharmacist Friedrich Sertürner in 1803.

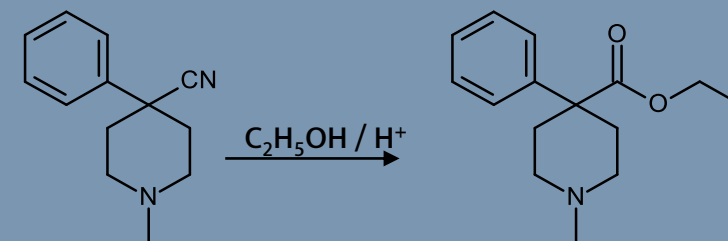


## Synthesis of pethidine

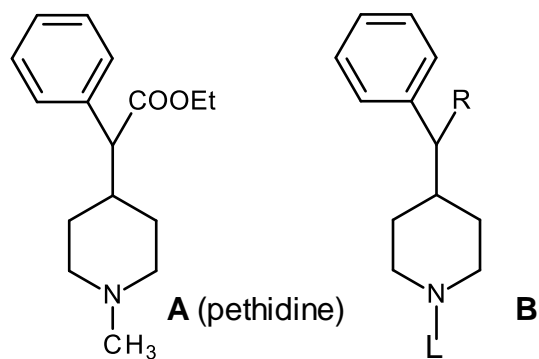
Synthesis of pethidine involves condensation reaction between *N,N*-bis-(2-chloroethyl)-*N*-methylamine and benzyl cyanide to give piperidine derivative.



Cyano group of the piperidine derivative is hydrolyzed to give carboxylic acid and further esterified to give pethidine.



To make compounds related to pethidine, R or L group shown in the structure B are replaced with different substituents which results in modification in the analgesic activity of pethidine. When carbethoxy ( $R=COOC_2H_5$ ) is replaced by propionyxy ( $R=OCOC_2H_5$ ), analgesic activity increases 20 times irrespective of the structure of the substituent L attached to N.



In human body, pethidine is metabolized in the liver by microsomal enzymes. Pethidine is excreted from the body in a form which depends on pH of the urine.

Highly acidic urine contains high amount of pethidine and norpethidine, whereas alkaline urine contains pethidinic and norpethidinic acids or its conjugates.

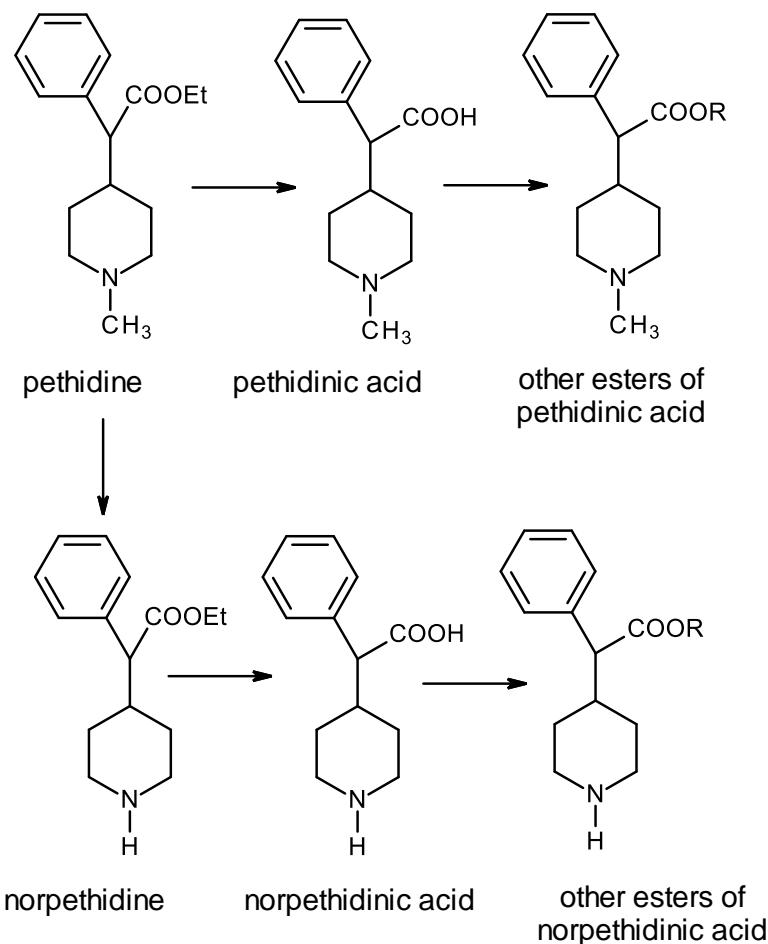
### Did you know???

Pethidine drug was given to women to relieve labour pain. Later, it was banned at some places after it was found to cause respiratory problems in babies.

## Toxicity

Research revealed that pethidine is more harmful than morphine since one of its metabolic products, norpethidine is toxic. Pethidine is banned in some countries.

Products of metabolism of pethidine is shown below.



Though pethidine has side effects, it is prescribed or used on patients when the benefits are higher than the side-effects.

Pethidine is mainly used to relieve moderate to severe pain, during surgery or post surgery.

## References and Further Reading

1. Stevens, L. J. (1956). The Literature of Analgesics. A Key to Pharmaceutical And Medicinal Chemistry Literature *Advances in Chemistry*, 3–11. <https://doi.org/10.1021/ba-1956-0016.ch001>
2. Asatoor, A. M., London, D. R., Milne, M. D., & Simenhoff, M. L. (1963). The Excretion Of Pethidine And Its Derivatives. *British Journal of Pharmacology and Chemotherapy*, 20(2), 285–298. <https://doi.org/10.1111/j.1476-5381.1963.tb01468.x>
3. Pethidine - A Little Shot Of Something Not So Nice. (1993). Retrieved from <https://www.aims.org.uk/journal/item/pethidine>

## Image sources

Images taken from unsplash and wikimedia commons.

## Now, can you find?

1. Name some analgesics that are most commonly used.
2. Give some examples of drugs from phenyl piperidine family?

For more questions, refer Indian National Chemistry Olympiad questions (2017 paper): (problem 3)- <https://olympiads.hbcse.tifr.res.in/>