

**Thebaine Cas No. : 115-37-7**

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Active Pharmaceuticals Ingredients Manufacturers

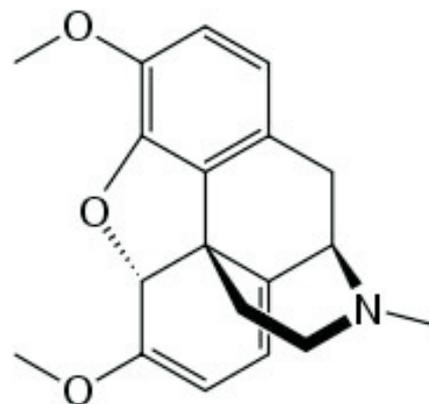


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**Taj Pharmaceuticals Ltd.****Thebaine****CAS No. : 115-37-7**

CAS number 115-37-7  
Molecular formula C<sub>19</sub>H<sub>21</sub>NO<sub>3</sub>  
Molar mass 311.37 g mol<sup>-1</sup>

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**OTHER INFORMATION**

The consumption of poppy seeds in various foods may lead to a positive opiate result in urine subjected to testing for drugs of abuse. As a natural constituent of poppy seeds, thebaine was investigated as a possible marker for poppy seed consumption. Poppy seeds were examined for opiate content by gas chromatography-ion trap mass spectrometry (GC-MS) after extraction with methanol. Urine samples spiked with thebaine and urine from subjects given 11 g of poppy seeds were tested for the presence of thebaine, codeine, and morphine. Street heroin, one morphine and one codeine tablet, and urine from individuals who had used heroin were also examined for thebaine. Urine specimens were screened by enzyme immunoassay (EMIT) and confirmed for thebaine by GC-MS using a solid-phase extraction method. The GC-MS assay showed a linear response over a range of 1-100 ng/mL and a limit of detection of 0.5 ng/mL. Thebaine was detectable in the urine of poppy seed eaters in concentrations ranging from 2 to 81 ng/mL. Because thebaine was absent in powdered drugs and the urine of true opiate drug users, thebaine is proposed as a direct marker for poppy seed use.

The 14-hydroxymorphinans, such as, oxycodone, naloxone, naltrexone, nalbuphine and nalmefene are important opiate derivatives due to their behavior as potent analgesics and/or narcotic antagonists. The most practical synthetic routes to the preparation of these pharmaceuticals have utilized the alkaloid, thebaine, as a starting material. Other important opiate derivatives such as the ring-C bridged compounds buprenorphine and etorphine are also most practically prepared from thebaine.

In accordance with one conventional process, thebaine is oxidized to 14-hydroxycodeinone by use of m-chloroperbenzoic acid in an acetic acid trifluoroacetic acid mixture or by a mixture of hydrogen peroxide and formic acid. 14-hydroxycodeinone is catalytically reduced to oxycodone. Oxycodone is a product sold for use as an analgesic and its production consumes large amounts of thebaine.

Oxycodone can be, in turn, O-demethylated with boron tribromide to yield oxymorphone. After blocking of the hydroxyl groups with a suitable blocking agent, such as, acetyl groups, the oxymorphone derivative is reacted with cyanogen bromide in a von Braun demethylation to yield an N-cyanodihydronormorphinone derivative that is thereafter hydrolyzed to 14-hydroxydihydronormorphinone (noroxymorphone). Noroxymorphone can be readily converted to nal-compounds by N-alkylation with appropriate alkyl halide, or acylation with appropriate acyl halide or anhydride, followed by reduction. A more generally applicable process, converts the oxycodone of the above process to noroxycodone by the von Braun N-deethylation followed by conversion to a 3-O-methyl-nal-compound using N-alkylation with an appropriate alkyl halide, or by alkylation with an appropriate alkyl halide, or acylation with appropriate acyl halide or anhydride, followed by reduction. The 3-O-methyl-nal-compound is reacted to a nal-compound by O-demethylation.



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**T h e b a i n e**

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One reason for the limited availability of thebaine, and its high cost, is that total synthesis is difficult. U.S. Pat. Nos. 4,613,668 and 4,795,813 discuss the scarcity of thebaine and teach the total synthesis, or alternative synthesis, of the 14-hydroxymorphinans. Yet, the demand for thebaine remains.

A second reason for the limited availability of thebaine, and its high cost, is that the primary source of thebaine is extraction from the poppy plant, *Papaver somniferum*. Morphine is the major alkaloid that accumulates in capsules of *Papaver somniferum*. Thus, the supply of thebaine is to a great degree limited to some fraction of the demand for morphine.

Further synthetic routes to the preparation of the 14-hydroxymorphinans are known using the alkaloid, oripavine, as a starting material.

Oripavine has not been used as a starting material for the 14-hydroxymorphinans in any practical sense because it is not recoverable from *Papaver somniferum* in any practical yield. Thus, there is now no real shortage of this material, but only because there has never developed any demand for it.

#### DRUG DESCRIPTION

Thebaine is an opiate alkaloid. A minor constituent of opium, thebaine is chemically similar to both morphine and codeine but has stimulatory rather than depressant effects, causing strychnine-like convulsions at higher doses.[3] Thebaine is not used therapeutically, but can be converted industrially into a variety of compounds including oxycodone, oxymorphone, nalbuphine, naloxone, naltrexone, buprenorphine and etorphine.

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The Controlled Substances Act (CSA) was enacted into law by the Congress of the United States as Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[1] The CSA is the federal U.S. drug policy under which the manufacture, importation, possession, use and distribution of certain substances is regulated. The Act also served as the national implementing legislation for the Single Convention on Narcotic Drugs

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