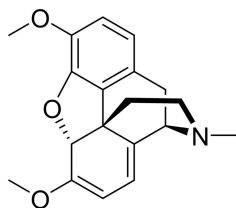




Thebaine



Chemical formula:	$C_{19}H_{21}NO_3$
IUPAC name:	(4R,7aR,12bS)-7,9-dimethoxy-3-methyl-2,4,7a,13-tetrahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinoline
CAS number:	115-37-7
Alternative Name(s):	(-)-thebaine, paramorphine
Molecular weight:	311.37

Thebaine Base

Thebaine is an opiate alkaloid extracted from the opium poppy (*Papaver somniferum*) and is an intermediate in the morphine biosynthesis pathway. While not used as a medicine itself, thebaine extracted from poppy plants (commonly known as anhydrous thebaine alkaloid or ATA) is a key starting material (KSM) for the semisynthesis of various active pharmaceutical ingredients (APIs) for several essential medicines. This includes medicines used in post-surgery and severe acute pain, overdose rescue medication, and addiction treatment medications.

Chemical synthesis is generally not practical for the commercial manufacturing of thebaine¹. Historically, poppy farming has been the only commercial source of thebaine—it is extracted from the straw of cross-bred cultivars of opium poppy that produce higher levels of thebaine than basic poppy strains. The agricultural nature of pharmaceutical supply chains results in significant challenges in inventory and quality control.

Biosynthetic Thebaine

Antheia is the first supplier of biosynthetic thebaine. Antheia's proprietary thebaine-producing yeast strains² are capable of yields sufficient to make industrial microbial fermentation an efficient, controlled, sustainable, and reliable alternative to existing agricultural extraction. The company's biomanufacturing platform reduces production lead time from years to weeks and adds more transparency, reliability, compliance, efficiency, and flexibility pharmaceutical supply chains.

Additionally, because Antheia's thebaine is produced biosynthetically, it is not vulnerable to global supply chain issues and can enable rapid-response production to meet sudden changes in demand. The quality, reproducibility, and security of the supply chain of APIs is greatly improved in the controlled environment of a fermentation vessel, compared to the year-to-year variation inherent in field-grown crops.

Regulatory and Quality Standards

Antheia manufactures all KSMs and APIs under cGMP conditions and will have all appropriate regulatory filings related to its materials. In addition, appropriate regulatory submissions are being prepared and will be submitted to support customers who use thebaine and need to reference and access necessary process-related information.

Every product lot is thoroughly characterized and analyzed against approved specifications and comes with a certificate of analysis (CoA). KSMs and APIs produced via fermentation will perform at the same quality levels as those extracted from plants.

Safety Data Sheet

Thebaine is a Schedule II controlled substance in the U.S. A thebaine SDS will be provided upon request.

Antheia's Mission: Rapid response biomanufacturing for the future of KSM and API production

Antheia is a science and technology company developing next-generation plant-inspired medicines. Antheia was founded in 2015 to transform pharmaceutical supply chains and ensure equitable access to essential medicines.

Today, nearly half of KSMs and APIs for medicines are sourced from nature, including many common and essential drugs. The inherent complexity of these molecules does not lend itself to commercially viable chemical synthesis. As a result, the pharma industry is beholden to agriculture-based supply chains that have high latency and lack the flexibility to meet sudden changes in demand. These critical supply chains are also vulnerable to natural disasters, climate change, pests, and disease.

Modern healthcare requires greater consistency, predictability, and agility in pharmaceutical manufacturing to produce essential medicines.

Applying synthetic biology, Antheia has pioneered a new approach to reconstruct drug-producing, biosynthetic pathways in engineered brewer's yeast (*Saccharomyces cerevisiae*) to manufacture KSMs and APIs. This fermentation-based approach has many advantages over agriculture-based extraction, including:

- **More resilient and efficient pharmaceutical supply chains**

An agile, on-demand platform for improved transparency, greater process consistency, and better control across the supply chain.

- **Accelerated manufacturing cycles and reduced inventory**

APIs can be produced in weeks, rather than the years needed to grow, harvest, extract, and purify compounds from plants.

- **Domestic and localized manufacturing**

Fermentation allows localized production in the U.S. and other key regions to reduce lead times, improve supply chain transparency, and ease export/import requirements.

To discuss Antheia's products or technology, please reach out to

info@antheia.bio

or visit our website for more information:

www.antheia.bio

References:

1. Reed JW, Hudlicky T. The quest for a practical synthesis of morphine alkaloids and their derivatives by chemoenzymatic methods. *Acc Chem Res.* 2015;48(3):674–687.
2. Galanie S, Thodey K, Trenchard IJ, et al. Complete biosynthesis of opioids in yeast. *Science.* 2015;349 (6252):1095–1100.