

## Drug Status Report

**Drug:** *Mitragyna speciosa*<sup>1</sup> (also known as kratom and biak-biak)

### Drug Name Status:

I - Mitragynine is the common name

II - 7-Hydroxymitragynine is the common name

III - Ajmalicine is the common name

IV - Reserpine is the proper name

### Chemical Name:

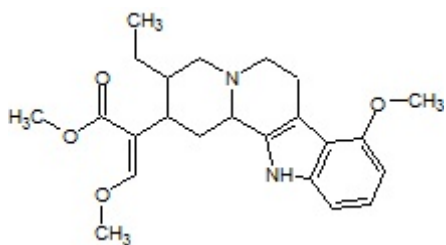
I - (16E,20β)-16,17-Didehydro-9,17-dimethoxy-17,18-seco-20-α-yohimban-16-carboxylic acid methyl ester

II - (16E,20β)-16,17-Didehydro-9,17-dimethoxy-7-hydroxy-17,18-seco-20-α-yohimban-16-carboxylic acid methyl ester

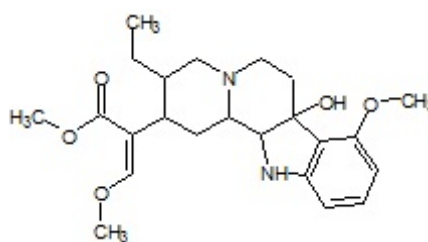
III - 16,17-Didehydro-19-methyloxayohimban-16-carboxylic acid methyl ester

IV - 11,17-Dimethoxy-18-((3,4,5-trimethoxybenzoyl)oxy)yohimban-16-carboxylic acid methyl ester

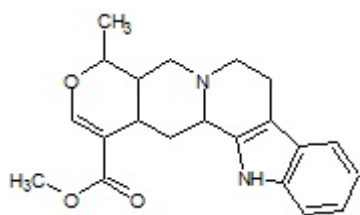
### Chemical structure:



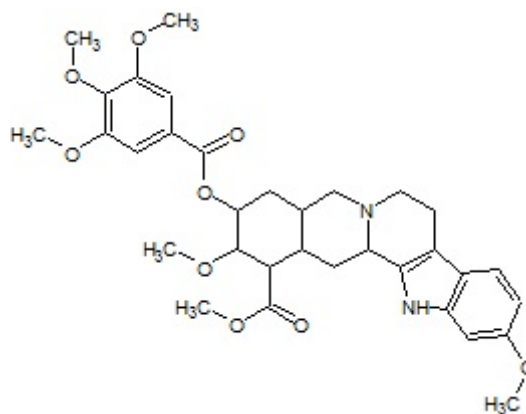
I - mitragynine



II - 7-hydroxymitragynine



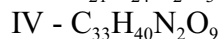
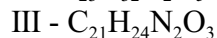
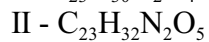
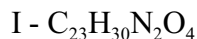
III - ajmalicine



IV - reserpine

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<sup>1</sup> *Mitragyna speciosa* is a tree indigenous to Thailand.

**Molecular Formula:**

**Pharmacological class / Application:** I, II - alkaloid/analgesic; III, alkaloid; IV, alkaloid/antihypertensive

**International status:**

US: *Mitragyna speciosa* and its alkaloids are not listed on the schedules to the US Controlled Substances Act and is not mentioned on the DEA website.

United Nations: *Mitragyna speciosa* and its alkaloids are not listed on the Yellow List - List of Narcotic Drugs under International Control. The plant and its alkaloids are not listed on the Green List - List of Psychotropic Substances under International Control. Mitragynine, one of the alkaloids of *Mitragyna speciosa*, may be controlled in Australia<sup>2</sup>.

Canadian Status: In a review of *Mitragyna speciosa*, Shellard reported<sup>3</sup> that there are more than 40 alkaloids in *Mitragyna speciosa*. The alkaloids described in that review are structurally similar. The three alkaloids, I - III, which have been confirmed to be present in *Mitragyna speciosa* have been included in this report to illustrate the type of alkaloid present in the plant. These alkaloids are structurally similar to reserpine, IV, an antihypertensive. The structural similarity can be more easily seen if the right sides of the molecules are viewed first. They are not structurally similar to any group of drugs controlled by the CDSA.

Mitragynine (I), the major alkaloid in *Mitragyna speciosa*, has been shown to have antinociceptive activity in mice. Its potency is estimated at 1/4 that of morphine. It has also been shown to inhibit guinea pig ileum contraction elicited by electrical stimulation which was reversed in the presence of naloxone<sup>4</sup> suggesting the involvement of opioid receptors. Under similar test conditions - guinea pig ileum - 7-hydroxymitragynine (II) was found to be more than ten times as potent as morphine. The antinociceptive activity of II has been confirmed by others<sup>5</sup>.

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<sup>2</sup> <http://www.tga.gov.au/ndpsc/record/rr200302.htm>

<sup>3</sup> Shellard, EJ, Bulletin on Narcotics, (2), 41-55. (1974)

<sup>4</sup> Takayama, H, Chem. Pharm. Bull. 52(8), 916-928 (2004).

<sup>5</sup> Matsumoto, K, Hatori, Y, Murayama, T, Tashima, K, Wongeripipatana, S, Misawa, K, Kitajima, M, Takayama, H and Horie, S. Eur. J. Pharmacol. 549(1-3), 2006  
Matsumoto, K, Horie, S, Takayama, H, Ishikawa, H, Aimi, N, Ponglux, D, Murayama, T, and

The pharmacological properties - analgesic - of the alkaloids of *Mitragyna speciosa* do not affect their current status under the CDSA. The only time pharmacological activity is a factor in the status of a substance in regard to the schedules to the CDSA is when the substance is a cannabinoid receptor agonist<sup>6</sup>.

Recommendation: *Mitragyna speciosa* and its alkaloids are not included in the schedules to the CDSA and are not controlled substances.

December 22, 2006

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Watanabe, K, *Life Sci.*, 78(1), 2-7, 2005

<sup>6</sup> See the status report on SB-235863 (Nov. 23, 2006)