

## 90. Tetrahydrocannabinol (THC)

**CHEMICAL NAME** = delta-9-tetrahydrocannabinol

**CAS NUMBER** = 1972-08-3

**MOLECULAR FORMULA** =  $C_{21}H_{30}O_2$

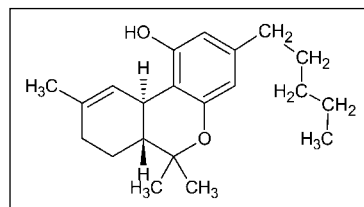
**MOLAR MASS** = 314.5 g/mol

**COMPOSITION** = C(80.2%) H(9.6%) O(10.2%)

**MELTING POINT** = 80°C

**BOILING POINT** = 200°C

**DENSITY** = not reported



Tetrahydrocannabinol (THC) is the main active compound in marijuana. It comes from the plant *Cannabis sativa* (cannabis), which is a dioecious (monoecious varieties do exist) annual herb naturally found in many tropic and temperate regions of the world. Many varieties of cannabis exist, and two related species (*Cannabis indica* and *Cannabis ruderalis*) are main sources of THC. *Cannabis sativa* is also known as hemp, although this name is not unique to the species; its stem is a source of fiber that has been used throughout history for hundreds of applications including rope, twine, paper, and cloth. Hemp seeds are edible and high in protein. The seeds are also a source of fatty oil that can be used for food, cosmetics, medicines, and as a fuel source. *Cannabis* contains chemicals called cannabinoids; of the 60 cannabinoids found in *Cannabis*, one is THC, which is the psychoactive ingredient in marijuana. Marijuana is produced from the leaves and flowers of cannabis, and hashish is a resin collected from the female flowers. The THC content, which determines the effect of cannabis drugs, varies with plant structure, variety, and preparation. Buds and flowers specifically cultivated for drug use have greater THC content than leaves. THC content may vary from a few tenths of a percent to more than 10%, but good quality marijuana has a THC content of approximately 10%, and good hashish and hashish oils generally have THC contents between 30% and 80%.

*Cannabis* use by humans dates from prehistoric times. It was used as a food source, medicine, fuel source, for fiber, and as a recreational drug. Although it is not known how *Cannabis* was first used, fibers and seeds have been found in Neolithic archaeological sites. Pottery

recovered from Taiwan archaeological sites dating from more than 10,000 years ago contain cannabis fiber. The earliest evidence of the medicinal use of *Cannabis* comes from the Chinese Emperor and herbalist Shen-Nung, who lived in the 28th century B.C.E. Shen-Nung wrote a work on herbal medicines in which he recommended *Cannabis* for malaria, beri-beri, gout, constipation, rheumatic pains, and female menstrual problems. The first use of *Cannabis* as a psychoactive agent is unknown, but it is assumed that knowledge of its mind-altering effect was a natural consequence of its medicinal use. Indian and Chinese writings as early as 2000 B.C.E. refer to the psychedelic effect of *Cannabis*, and it was used in religious rituals in both regions. The Greek historian Herodotus (484–425 B.C.E.) wrote about Scythians inhaling *Cannabis* smoke for its euphoric effect. Medieval alchemists used *Cannabis* vapors to clear the mind, and hemp oil was distilled from flowers for use in various formulations.

THC was first isolated from hashish in 1964 by Raphael Mechoulam (1930–) and Yehiel Gaoni at the Weizmann Institute. Mechoulam had obtained 5 kg hashish from Israeli police officials and the earliest scientific work on THC and cannabinoids used this source. In the early 1990s, the specific brain receptors affected by THC were identified. These receptors are activated by a cannabinoid neurotransmitter called arachidonylethanolamide, known as anandamide. Anandamide was named by Mechoulam using *ananda*, which is the Sanskrit word for ecstasy. Anandamide is thought to be associated with memory, pain, depression, and appetite. THC is able to attach to and activate anandamide receptors. These receptors are actually called THC receptors rather than anandamide receptors because researchers discovered that THC attaches to these receptors before anandamide was discovered. The areas of the brain with the most THC receptors are the cerebellum, the cerebral cortex, and the limbic system. This is why marijuana affects thinking, memory, sensory perception, and coordination.

THC in the form of marijuana is the most widely used and available illicit drug in the United States. The potency of marijuana is directly related to its THC content, which averages between 5% and 10% for commercial-grade marijuana. During the last several decades, the THC content of seized marijuana has steadily increased. In 1985, the THC content averaged 3.5%; in 2005, the average was 8%. It is difficult to determine the amount of marijuana produced because of its illegal status. Production in different countries is highly variable depending on growing conditions, weather, and enforcement. Mexico, the chief U.S. supplier, has averaged approximately 10,000 tons of production annually over the last several years, although not all of this is exported to the United States. It is estimated that between 15,000 and 25,000 tons of marijuana are available in the United States, with Americans spending approximately \$10 billion annually on the drug.

*Cannabis* has been used as a medicine for thousands of years, and there are many proponents for the use of medical marijuana. Some common medicinal uses include alleviating nausea associated with cancer therapies, treating glaucoma, alleviating suffering in AIDS patients, and helping multiple sclerosis patients control muscles. Medical marijuana is a controversial issue. Opponents claim that medical marijuana will make the drug more readily available, there are suitable alternatives, it has limited medical efficacy, it is difficult to control, and it has harmful side effects. Proponents claim it relieves suffering, is not addictive, is safe, and is easily administered. The American Medical Association has taken a neutral view and called for more controlled research on the topic. The federal government's view that marijuana use is illegal for all purposes is in direct conflict with several states that have passed medical marijuana laws legalizing limited medical usage. In 2005, the Supreme Court ruled against state

medical marijuana laws and supported the federal government view that users in states where it was allowed medicinally could be prosecuted.

Medical marijuana remains a controversial topic, but synthetic THC, dronabinol, marketed under the trade name Marinol, has been available by prescription since 1986. The dronabinol analog nabilone is another THC prescription drug marketed under the name Cesamet. Marinol and Cesamet, taken as capsules, have Food Drug Administration approval as an anti-nausea agent and appetite stimulant (for AIDS patients), but they are also prescribed for depression and muscle spasms. In 2005, Canada was the first country to approve Sativex, a cannabis spray that relieves pain in people with multiple sclerosis.