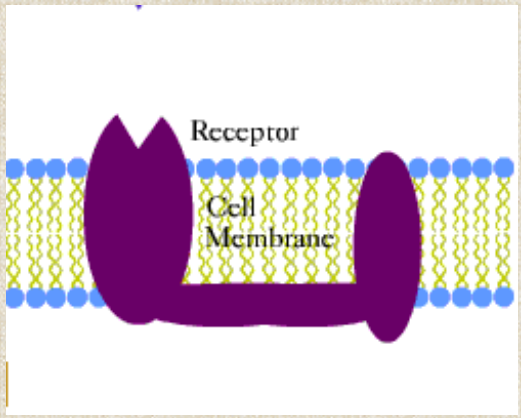
The Cannabinoid Revolution

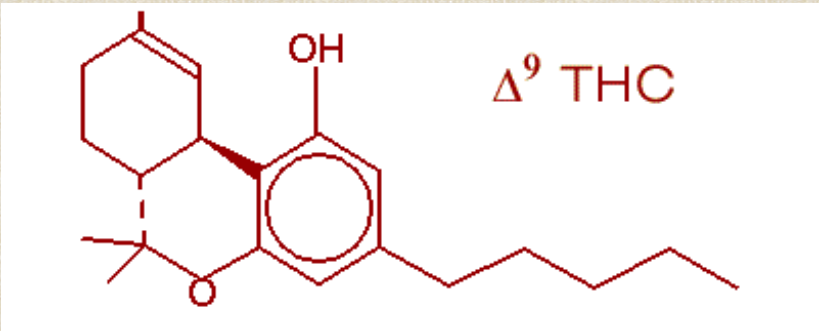
Humans have been using the leaves and flowers of the cannabis sativa and cannabis indica plants as medicine for at least 5000 years. Cannabis products were routinely used as medicine in America prior to the Prohibition fervor of the 1920s that led to cannabis' current federal legal status as an irredeemably harmful narcotic of zero medicinal value. It's only been over the past ten years scientists researching the human brain have found a biochemical explanation for the medicinal uses of cannabis reported by physicians over the past several thousands of years.



Cannabinoids were discovered to work through the chemical receptor system modelled above, which allows molecules to influences processes inside cells without penetrating cell membranes.

In the sixties and seventies marijuana was believed to act as a "dirty drug" like alcohol, producing a sense of well-being by disrupting the cell membranes throughout the brain. But at the same time pharmacologists were investigating the pain- and nausea-relieving properties of the most active ingredient of marijuana, THC (tetra-hydra-cannabinol, shown below), and molecules like it they were able to synthesize in the lab (1).

Some researchers speculated that THC and other "cannabinoids" acted by targeting specific " chemical receptors" in the brain. (2) Such a receptor system enables certain special molecules to work across the membranes of cells without having to puncture or otherwise disrupt them. The researchers were guessing that THC might belong to such a special class of molecules.



THC is one of hundreds of known molecules that bind to cannabinoid receptors.

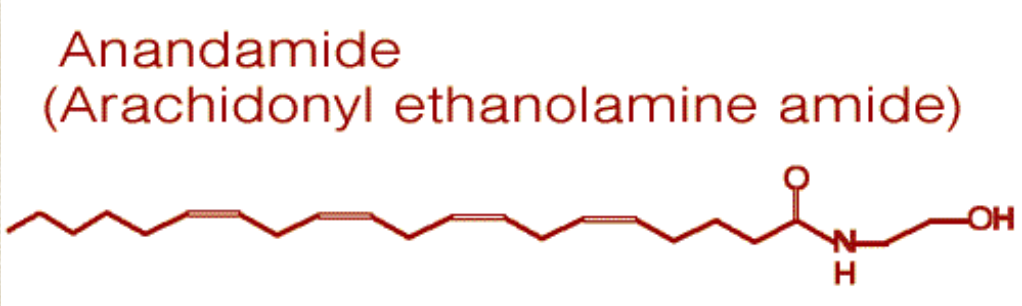
In 1984 THC and several artifical cannabinoids created by drug companies were shown to inhibit the action in nerve cells of a substance called adenylate

cyclase commonly associated with chemical receptor processes in the brain. (2)

In 1988 research was published showing that cannabinoids produced analgesia in animals in a way that matched precisely the way cannabinoids inhibited adenylate cyclase in nerve tissue cultures. The cannabinoid receptor was officially born in a model based on the relationship observed between the molecular structures and relative potencies of the known cannabinoids. (3)

In 1990 series of papers reported evidence and provided details for the conceptual framework of the cannabinoid receptor. The cannabinoid receptor in the brain was identified to work through a "G-protein inhibitory second messenger" system (4) and the gene responsible for making the receptor protein was cloned (5). The locations of cannabinoid receptors in the brains of humans, rats, dogs, guinea pigs and monkeys were mapped using a new synthetic cannabinoid called CP55940, which binds to the CB1 receptor about 500 times more strongly than THC (6).

The existence of cannabinoid receptors in the brain implied there must be a natural brain cannabinoid. In 1992 a team of scientists managed to distill the "endogenous cannabinoid" from the brain of a pig. They named it "anandamide" after "ananda", the Hindu word for internal bliss. (7)



Anandamide was the first natural brain cannabinoid, or "endogenous ligand of CB1", to be isolated by scientists. A few others have since been found.

A second type of cannabinoid receptors was then found to exist in the spleeen and immune system, showing that cannabinoids function naturally as immunomodulators. (8) The brain cannabinoid receptor is now referred to as **CB1** and the immune receptor is called **CB2**.

In 1994 a team of pharmacologists in France discovered a molecule that can block CB1 (but doesn't seem to affect CB2). (9) This "cannabinoid antagonist" is a useful tool for pharmacologists and neuroscientists seeking to understand the neurobiological actions of anandamide in the brains of humans and other animals.

The 5000-year history of medical use of marijuana was made sense of scientifically at long last when the observed properties of cannabinoid receptors in the brain and immune system were described in the context of the medical uses of cannabinoids. (10)

The anti-emetic, anti-convulsant, anti-anxiety, analgesic, antiseizure, and anti-inflammatory properties alleged for marijuana by five millenia of medical users are completely consistent with what has been discovered about the function and role of cannabinoid receptors during the **Cannabinoid Revolution.**

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