

# cannabinoids

## what is a cannabinoid?

There are approximately 483 natural components found within the *Cannabis sativa* plant<sup>1</sup>, of which 66 have been classified as ‘cannabinoids’; chemicals unique to the plant. The most well known and researched of these, delta-9-tetrahydrocannabinol ( $\Delta^9$ -THC), is the substance primarily responsible for the psychoactive effects of cannabis. The effects of  $\Delta^9$ -THC may, however, be moderated by the influence of the other 482 components, most particularly by the cannabinoids<sup>2</sup>. The cannabinoids are separated into the following subclasses:

- cannabigerols (CBG)
- cannabichromenes (CBC)
- cannabidiols (CBD)
- tetrahydrocannabinols (THC)
- cannabinol (CBN) and cannabinodiol (CBDL)
- other cannabinoids (such as cannabicyclol (CBL), cannabielsoin (CBE), cannabitriol (CBT) and other miscellaneous types<sup>1</sup>

## what do cannabinoids do?

Like opiates, cannabinoids exert their effect by interacting with specific receptors, located within different parts of our brains and peripheral nerves. Two kinds of cannabinoid receptors have been found to date and are termed  $CB_1$  and  $CB_2$ <sup>3,4</sup>. A substance that occurs naturally within the brain and binds to  $CB_1$  receptors was discovered in 1992 and termed ‘anandamide’ (from the Sanskrit for ‘bliss’)<sup>5</sup>. Additional naturally occurring substances that bind to  $CB_1$  have since been discovered, and these, together with the receptors, are termed the ‘endogenous cannabinoid system’.

Cannabinoids are somewhat unusual drugs in that they are soluble in lipids (fats) rather than in water. Thus, with repeated dosage, cannabinoids tend to accumulate in fatty tissues and remain in the body for several days<sup>6</sup>. The actual effects that the cannabinoids have, reflect the areas of the brain they interact with. Interactions tend to occur in our limbic system (the motivational centre of the brain that affects memory, cognition and psychomotor performance) and mesolimbic pathway (activity in this region is associated with feelings of reward) and are also widely distributed in areas of pain perception<sup>3,7</sup>.

Despite a rapid increase in our knowledge of the endogenous cannabinoid system, the field is still in its developmental stages. However, as described below, much research has focused on the many potential therapeutic uses of chemical replications of the cannabinoids, called ‘synthetic analogues’<sup>8</sup>.

## what is the difference between cannabinoids?

The major differences between the cannabinoids are determined by the extent to which they are psychologically active. Three classes of cannabinoids, the CBG, CBC and CBD are not known to have such an effect. However, THC, CBN, CBDL and some other cannabinoids are known to be psychologically active to varying degrees<sup>1</sup>.

Interestingly, CBD may actually have anti-anxiety effects and lessen the psychotropic effects of THC<sup>1</sup>, although it is not clearly understood how<sup>9</sup>. That is, a plant with a greater percentage of CBD may attenuate the effects of the THC, which in effect, lowers the potency of the plant. Use of a cannabis plant with less CBD has been shown to have an increased psychological effect and incidence of anxiety reactions<sup>10,11</sup>. The non-psychotropic aspects of CBD are of particular interest in therapeutic settings and are discussed below<sup>12</sup>.

$\Delta^9$ -THC is oxidized by exposure to air which reduces to form CBN<sub>1</sub>. CBN is only very weakly psychotropic and not unlike CBD, interacts with THC to attenuate its effects<sup>13</sup>. Cannabis that has been left out unused will have increasing amounts of CBN and decreasing amounts of THC and thus lose potency<sup>1</sup>.

## why do we care about cannabinoids?

Some cannabinoids, and thus their synthetic analogues, have clear therapeutic potential<sup>14</sup>. This should be clearly distinct from the use of natural cannabis. Studies have shown that the toxicity of synthetic analogues is low and they are unlikely to cause physical dependence<sup>15</sup>. However, when cannabis is smoked, hundreds of other chemicals interact and cannot be safely used. Thus, synthetic analogues of certain cannabinoids have been created in order to isolate their effect from the undesirable harmful effects of natural cannabis.

To date, hundreds of studies have analysed the clinical significance of these cannabinoids, yet even today their usefulness continues to be debated. Several studies have reviewed the literature in the area<sup>16–18</sup>.

Although showing some anecdotal success, the therapeutic applications lack randomized clinical trials.

## references

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