Cannabinol: degradation leads to opportunity?

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Cannabinol (CBN) is the cannabinoid which is generally indicative of the age of the cannabis plant. This is because CBN is formed from degradation of THC on exposure to heat and UV light, and this conversion occurs over time—subject to storage conditions. As well being a degradation product of THC, it has also shown to be a rapid metabolite of THC in the blood (McCallum et al., 1975).

![Chemical diagram showing the degradation of THC to CBN](image)

**Figure 4: The degradation of THC to CBN, which occurs in the presence of heat and UV light. The reaction is a partial hydrogenation of one of the aromatic rings of THC.**

CBN acts as a weak agonist to CB₁ and CB₂, about 4 times less potent at CB₁ compared to THC (Rhee et al., 1997). CBN exhibited a much higher inhibitory constant (Ki) than THC (about 6 times higher) on brain CB1 receptors, indicated in brain synaptosomal binding experiments (Rhee et al., 1997). Hence it does not bind to CB₁ with the same affinity as does THC. This could provide the explanation behind CBN’s minimal psychoactive effects. CBN is metabolised to 11-OH-CBN (via 11-hydroxylation), which is twice as potent as CBN on CB₁ receptors but can only exhibit partial agonist activity at the CB₂ receptor (Rhee et al., 1997). Even though it is more potent on brain CB₁ receptors than CBN, it is still three times less potent than THC on these receptors (Rhee et al., 1997). It has shown to have less than 10% of the psychoactive and cardio acceleratory effects of THC in humans (Howlett, 1987). In another study the effects of CBN were considered to be less intense (both physiologically and psychologically) in humans subjects compared with the effects of THC (Hiltunen and Järbe, 1986).
CBN’s pharmacological effects might point towards it being a credible therapeutic compound. It might be a good compound to manipulate the CB₁ mediated effects on the Endocannabinoid system, without the well-known behavioural effects which are associated with the strong CB₁ agonists. It was able to exhibit dose-dependent increase in feeding in rats, without the motor incoordination that is caused by stronger CB₁ agonists such as THC (Farrimond et al., 2012). Therefore repeated dosages of CBN can be delivered with the same appetite inducing effects as THC, but without the side effect of motor incoordination typically seen with THC. CBN has shown to cause small reductions in Intraocular pressure (IOP) in animals models (Colasanti et al., 1984, Green et al., 1978). It has shown to inhibit pro-inflammatory cytokines such as IL-2, CREB and NF-kB, which point to possible pleiotropic effects of this compound (Herring et al., 2001). In further studies, CBN has shown to inhibit the binding of transcription factors to the AP-1 site, which is thought to regulate the production of IL-2 (Faibert and Kaminski, 2000). IL-2 is a critical autocrine T-cell growth factor, and is thought to be the main mediator in many autoimmune conditions, and CBN may be a possible immunosuppressant for these conditions.

Weak agonism of CB₁ as well as low affinities of CBN for brain CB₁ receptors make the case for CBN’s validity as a possible therapeutic compound. It can be used for appetite stimulation in subjects with anorexia, used as an anti-depressant (with little side effects) as possibly an anti-inflammatory compound.
References


