Cannabinoid Pharmacology: Implications for Additional Cannabinoid Receptor Subtypes


In the early 1990s, basic research on marijuana and the brain revealed that the mammalian brain contains an endogenous cannabinoid system that is responsive to cannabinoids in marijuana, including its primary psychoactive ingredient, delta-9-tetrahydrocannabinol (THC).

Anandamide, the first endocannabinoid to be discovered, acts at two types of cannabinoid receptors: CB₁ receptors, located primarily in the brain, and CB₂ receptors, located primarily in the periphery. The chemical structure of THC allows it to enter the brain and body tissues and organs and to mimic some of the effects of anandamide by activating these receptors. Unlike THC, however, anandamide may also act at novel non-CB₁, non-CB₂ cannabinoid receptors.

This paper reviews research conducted prior to its 2002 publication date suggesting anandamide may have other sites of action in the brain. Evidence for this hypothesis includes the observation that anandamide produced a number of pharmacological effects in mice lacking CB₁ receptors that were not produced by THC and that could not be explained by anandamide’s rapid metabolism.

While the scientific evidence is not yet conclusive almost a decade later (2011), the collective results suggest the possibility of additional cannabinoid receptors in the brain and periphery. Nevertheless, through continued investigation of the endocannabinoids and their actions on cannabinoid and noncannabinoid receptors in the brain and periphery, scientists have demonstrated that the endocannabinoid system plays an important role in physiological functioning and is likely to be involved in processes such as pain, appetite regulation, and brain reward.