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Commentary

The Endocannabinoid System – A Look Back and Ahead

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Over the last few decades research on the cannabinoids has gone through several distinct phases:

A. Research on plant cannabinoids (mostly on tetrahydrocannabinol (THC) and cannabidiol (CBD))
B. Research on endogenous cannabinoids (mostly on anandamide and 2-arachidonoyl glycerol (2-AG))
C. Research on endogenous anandamide-like endogenous fatty acid amides with amino acids and ethanol amines.

Plant cannabinoids While many dozens of plant cannabinoids are known today, most research is still on THC and CBD (Fig. 1).

CBD was isolated in the late 1930s, but its structure was elucidated only in 1963 (Mechoulam & Shvo, 1963). In 1964, when its structure was elucidated, pure THC was isolated (Gaoni & Mechoulam, 1964) and later synthesized. The psychoactivity of cannabis preparations (marijuana, hashish etc.) is mostly due to THC, but the other constituents may affect the activity of THC. Some of its metabolites are also psychoactive.

Thousands of publications have been published on the plant cannabinoids and some of them are already in use as therapeutic drugs. THC has been approved as a drug (named Marinol) for enhancement of appetite, and is also used to prevent vomiting due to cancer chemotherapy (Abrahamov & Mechoulam, 1995).

Of particular interest is CBD, which does not cause the typical cannabis psychoactivity, but is a potent antiepileptic drug (Cunha et al., 1980) and is used in many countries in pediatric epilepsy. It is being evaluated in other therapeutic areas (graft versus host disease, Yeshurun et al., 2015, schizophrenia, Leweke et al., 2012, and auto-immune diseases, for example Weiss et al., 2006).

The endogenous cannabinoids Anandamide (Devane et al., 1992) and 2-arachidonoyl glycerol (2-AG) (Mechoulam et al., 1995) were discovered in the 1990s. Both compounds bind to the cannabinoid receptors CB1 and CB2. They are involved in a very large number of human diseases, mostly as neuroprotective entities (Pacher & Kunos, 2013).

Endogenous fatty acid amides with amino acids and ethanol amines A large number of compounds of these types have been discovered in the brain and other tissues, and some of them have been shown to be of major importance in a large spectrum of biological functions and diseases. Thus, oleoyl serine is an anti-osteoporotic molecule (Smoum et al., 2010) and arachidonoyl serine is a vasodilator and lowers brain damage (Cohen-Yeshurun et al., 2011).

Numerous pharmaceutical companies are now involved in research in all the above areas.

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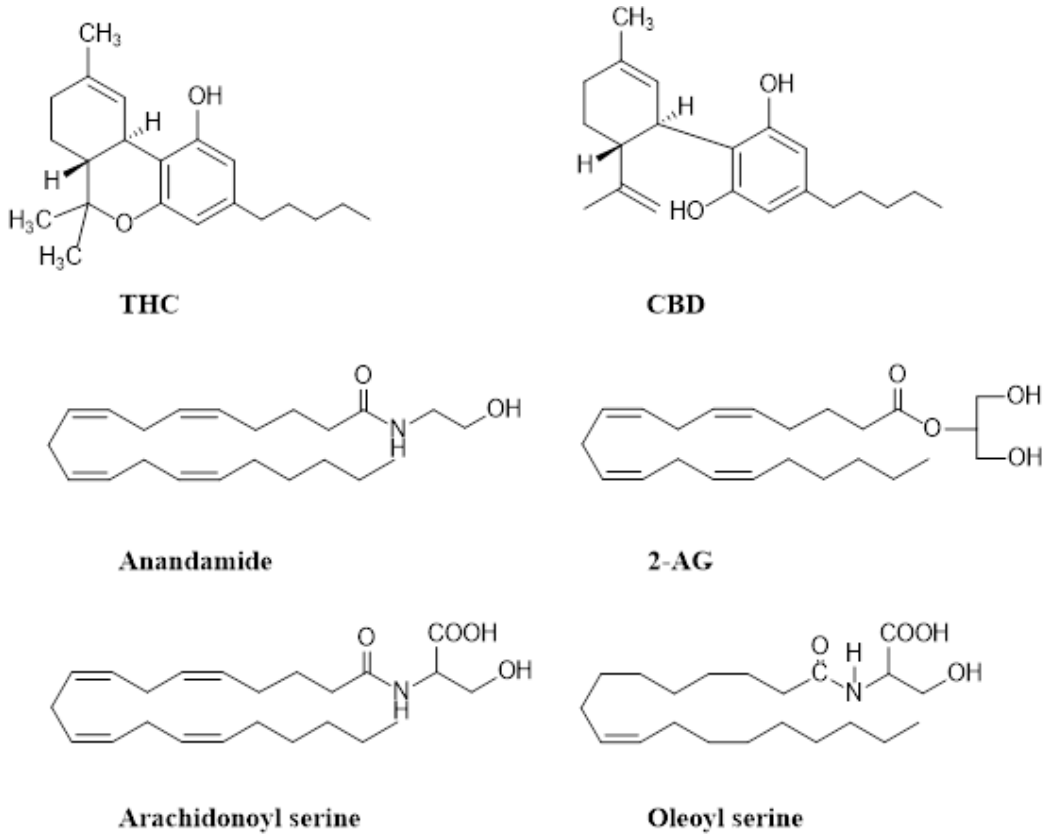

Figure 1: Cannabinoid compounds.

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