

Prace poglądowe i monografie

RECEPTORY KANNABINOIDÓW I ICH ENDOGENNE I EGZOGENNE LIGANDY

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CANNABINOID RECEPTORS AND THEIR ENDOGENOUS AND EXOGENOUS LIGANDS.

ABSTRACT – Considerable progress has been noted in recent years in the research into cannabinoid action, due to the discovery of two separate receptors (CB1 and CB2) and two endogenous agonists of these receptors (anandamide and 2AG). The course of biosynthesis and metabolism of anandamide has been identified and a number of its decomposition inhibitors have been synthesized. The latter contribute to the explanation of the endogenous agonists role in the regulation of various physiological processes. Many exogenous receptor agonists with a high power of action have been obtained, including not only structural analogs of cannabinoids, but also compounds from other chemical groups: derivatives of aminoalkylindole, diarylpyrazole, arylbenzofuran and arylbenzothiophen. Owing to these substances, CB1 and CB2 receptors' biochemical and pharmacological properties, as well as their localization in the brain, in the immunological system and in other tissues have been established. On the grounds of the existing research findings highly selective new agonists and antagonists can be expected to appear not only for CB1, but also for CB2.

The discovery of the endogenous cannabinoid system has revealed new perspectives for application of both natural cannabinoids and their synthetic analogs, as well as structurally different ligands of receptors. A number of new compounds (agonists and antagonists) have been developed: they may modulate the system either directly (through selective activation or inhibition of CB1 and/or CB2) or indirectly (through inhibition of these receptors endogenous ligands uptake to tissues or their enzymatic hydrolysis).

Attempts have been made to apply some cannabinoids in therapy, namely of cannabidiol (having a neuroprotective action), CT3 (analgesic and anti-inflammatory action), anandamide (analgesic and antineoplastic action), and S141716A (antipsychotic action).

Thus, research into cannabinoid receptors has increased our knowledge about their structure, joint action with biologically active proteins, and their mechanisms underlying signal transmission. These research findings are of not only cognitive, but also practical value – some ligands of CB1 and CB2 receptors may be expected to be applied as medication in the treatment of various diseases in the near future.

Key words: CB1 and CB2 receptors, G proteins, exogenous ligands, anandamide.

WSTĘP

Dowody stosowania rośliny *Cannabis sativa* przez ludzi istnieją od ponad 4000 lat (33), a obecnie marihuana jest najpowszechniej używanym narkotykiem. W Ameryce Północnej i Europie używa ją regularnie ponad 20 milionów ludzi, a