

Hypertension is the prevalent cause of cardiovascular disease that leads to heart hypertrophy and failure, oxidative stress, renal failure and, ultimately, to death. The discovery of endogenous cannabinoids and the fact that they are involved in the pathology of hypotension associated with hemorrhage, sepsis, cirrhosis and myocardial infarction indicate that cannabinoids play a greater role in human and animal pathophysiology than initially anticipated. Anandamide (AEA) is the first and the best examined of the endogenous cannabinoid ligands discovered. The up-regulation of the endocannabinoid system is suggested to be a pathophysiological response to buffer increases in blood pressure in hypertension.

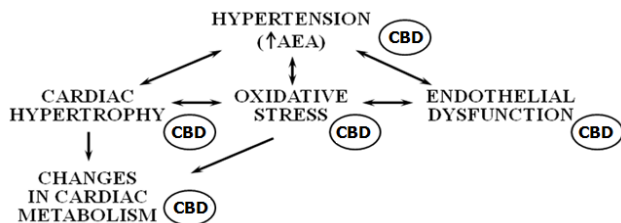


Fig. 1. Cross-talk between hypertension, cardiovascular function, oxidative stress and cardiac metabolism. AEA – anandamide; CBD – cannabidiol.

**Phytocannabinoids**, i.e. preparations of *Cannabis sativa* have been used for centuries not only for recreational purposes but also for effective treatment of malaria, glaucoma, **hypertension** and rheumatic and or labour pain.  $\Delta^9$ -Tetrahydrocannabinol ( $\Delta^9$ -THC) is the most popular phytocannabinoids with the strongest hallucinogenic activity mediated via central cannabinoid CB<sub>1</sub> receptors. In recent years, a great attention has been paid to **CANNABIDIOL (CBD)**. Cannabis containing high levels of  $\Delta^9$ -THC and low levels of CBD is generally referred to as “marijuana” whereas that containing high levels of CBD and very low levels of  $\Delta^9$ -THC is referred to as “industrial hemp” or hemp”. Cannabidiol is not psychoactive compound as  $\Delta^9$ -THC and, additionally, it diminishes the central effects of  $\Delta^9$ -THC. This attribute has been applied in the preparation Sativex, which in Poland, is allowed for the treatment of neuropathic pain during multiple sclerosis in adults. Currently (data from March 2015) medical marijuana has been approved in 23 states of the USA and 10 states have legalized CBD-only.

Cannabidiol possesses very complex and unspecific mechanisms of action. It plays both antagonistic and agonistic role in stimulation of various receptors or enzyme activities. Cannabidiol possesses a great therapeutic potential, because of its strong anti-inflammatory action (hundred times more potent than aspirin), **anti-oxidant** (stronger than vitamin E), anticonvulsant, antiemetic, antipsychotic, anxiolytic and antitumoral properties. Cannabidiol inhibits degradation and uptake of AEA leading to increase in the level of AEA. In a several, often controversial papers were described the influence of CBD on the cardiovascular system underlying its beneficial effects in cardioprotection and diabetes. However, there is no data regarding its role in the hypertension. Hypertension is a common factor for the development of oxidative stress and cardiac hypertrophy, conditions that modulate heart metabolism (Fig. 1). Thus, **the aim of our study is the complex examination of the influence of CBD, given acutely and chronically, on the cardiovascular system, oxidative stress and heart metabolism in experimental model of primary and secondary hypertension.**

The project will be realized by 4 units of the Medical University of Białystok (Poland): (1) the examination of cardiovascular parameters under *in vivo* and *in vitro* conditions – the group of Prof. Barbara Malinowska from the Department of Experimental Physiology and Pathophysiology; (2) the determination of oxidative stress parameters – the group of Prof. Elżbieta Skrzydlewska from the Department of Inorganic and Analytical Chemistry; (3) the heart metabolism determination— the group of Prof. Adrian Chabowski from the Department of Physiology and (4) the histological examination – the group of Prof. Irena Kasacka from the Department of Histology and Cytophysiology.

The complex examination of the influence of CBD on the cardiovascular system, oxidative stress and heart metabolism will extend the basal knowledge about the various positive and negative (potential side effects in other indications) effects of CBD not only in hypertension but also under physiological conditions. Understanding the acute and chronic effects of CBD in preclinical studies is a rational first step for clinical studies and for future research of this compound. Moreover, our project might add strictly scientific facts to the emotional discussion about the legalization of medical marijuana.