

At present, a very rapid increase in morbidity from so called civilization diseases, which are based on insulin resistance and obesity is a significant global problem, including Poland. It is known that both factors can lead to the development of type 2 diabetes mellitus or cardiovascular system diseases, which are commonly a threat to human life. Recent data of World Health Organization indicate that the prevalence of diabetes in Poland reached 9.5% and overweight 64% in year 2014. It is also known that increased amount of fatty acids in a diet exceeding energetic demands of the human body leads to adipocytes overgrowth as well as accumulation of lipids in other tissues e.g. cardiac muscle.

Therefore, there is constant exploration of a new therapeutic methods, which are aimed at prevention of the above mentioned disturbances or decreasing effects triggered by them. For several decades one of the area, which is an enormous field for investigation of such methods is **endocannabinoid system (ECS)** as well as **phytocannabinoids**. From the literature it is known that there is elevated activity of certain components of the endocannabinoid system during development of obesity or diabetes. However, recently intensive studies connected with properties and effects of phytocannabinoids action have been conducted, being a plant derived compounds (cannabis, *Cannabis sativa*) and used by mankind from centuries. The main phytocannabinoids, which are investigated, are **cannabidiol (CBD)** and its isomer Δ^9 -tetrahydrocannabinol (Δ^9 -THC). Due to the fact that Δ^9 -THC is a dominant psychoactive substance, CBD seems to be a potential therapeutic agent. It was indicated that CBD can induce variety of therapeutic effects and exhibits for instance anti-inflammatory (compared to acetylsalicylic acid), anti-oxidative, antiemetic, antitumor, neuroprotective and importantly cardioprotective activity. CBD evokes many different pharmacological effects, which mechanisms in majority are not known nowadays. Moreover, studies conducted on mouse model of type 1 diabetes confirmed protective action of CBD, as an agent that prevents the occurrence or diminishes effects provoked by this disturbance. Lipolytic effect and/or increased activity of mitochondria was also shown in hepatocytes in a model of nonalcoholic fatty liver disease as the result of CBD action.

In the light of the above data the main assumption of this project is **the evaluation of the probable CBD's impact on lipid metabolism in rat's cardiac muscle by regulation of fatty acid protein transporters expression (FAT/CD36, FABPpm, FATP1,4,6) in high fat diet induced obesity accompanied by insulin resistance**. It seems to be relevant to determine alternations in expression of the above transporters because this proteins are mainly responsible for the rate of long chain fatty acids (LCFA) transport into cardiomyocytes. Apart from that it is crucial to investigate the influence of CBD on cellular localization the above mentioned transporters i.e. in plasma membranes, low density microsomes or mitochondria and probable rate of their translocation. Furthermore, the impact of CBD on intramyocardial and plasma content of pivotal lipid fractions i.e. free fatty acids (FFA), phospholipids (PL), diacylglycerols (DAG), triacylglycerols (TAG), cholesterol (Chol) and selected sphingolipids (e.g. ceramide, CER) will be assessed. Studies indicates that some of these compounds (DAG and CER) can impair insulin signaling pathway, which is the background for the development of resistance to this hormone. Moreover, intensified intracellular transport of LCFA, considerably exceeding cell oxidative abilities, leads to increased accumulation of lipids, and heart contractile dysfunction (one of the elements of diabetic cardiomyopathy). Thus, the rate of LCFA transport will be assessed not only by the expression of protein transporters but also the rate of uptake and oxidation of radiolabeled palmitic acid in *in vitro* conditions (heart perfusion). This project will also evaluate the influence of CBD on existence of probable correlations between the expression of LCFA protein transporters (total, plasmalemmal and mitochondrial) and the rate of palmitic acid uptake and oxidation as well as intramyocardial content of the above mentioned lipid fractions.

Proposed project will reveal new, so far unknown, effects and mechanisms of CBD action in respect of cardiac muscle lipid metabolism in increased availability of dietary fatty acids. Moreover, we will also demonstrate for the first time, whether CBD takes part in the regulation of LCFA transport into cardiomyocytes with the participation of protein transporters. Additionally, the above studies will contribute in the expanding of knowledge on the role of CBD as potential therapeutic factor in obesity or metabolic syndrome treatment. Importantly, described research project is original and has significant therapeutic demands as well as applicable potential and what makes it even more important is accessibility of a drug containing extract from cannabis (*Sativex*) in Poland.