Abstract

Prevalence of obesity and associated diseases like type 2 diabetes has increased rapidly during last years. These diseases closely relate to each other. Obesity leads to insulin resistence, which directly precedes type 2 diabetes. Metformin is the most prescribed medicament for type 2 diabetic patients and insulin resistant people. It improves glucose tolerance and insulin resistance. Enzyme AMP-activated protein kinase (AMPK) is strogly involved in metformin action. The latest studies using transgenic models lacking AMPK suggest, that notable part of mechanisms involved in metformin action is independent on AMPK. n-3 polyunsaturated fatty acids (n-3 PUFA), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which are abundant in sea fish, have beneficial effects on metabolism. These fatty acids lower plasma lipids and exert cardioprotective effects. n-3 PUFA also prevent development of insulin resistence and type 2 diabetes in rodents. The aim of this thesis was to characterise acute effects of metformin on glucose homeostasis, impact of short term diet intervention with diet rich in n-3 PUFA on metformin action and the role of insulin stimulated signalling pathways and AMPK. Results suggest that early effect of metformin is dose dependent and that single dose of metformin significantly improves glucose tolerance 60 minutes after administration of the drug. Combination of high dose of metformin and n-3 PUFA did not exert significant additive improvement of glucose tolerance. Howewer, low dose of metformin in combination with n-3 PUFA significantly improved glucose tolerance in comparsion to control group. Next, acute metformin action is not dependent on presence of α2 subunit of AMPK and activation of AMPK in skeletal muscle and liver is not involved in acute metformin action. Measurement of the activity of protein kinase B (Akt/PKB), enzyme responsible for insulin sensitivity, did not reveal involvement of insulin stimulated signalling in liver or skeletal muscle.

Key words: metformin, insulin resistance, n-3 PUFA, AMP-activated protein kinase, glucose tolerance