EFFECTS OF ATORVASTATIN AND SILYMARIN ON HMCGR AND ABCG5/8 PROTEIN CONTENT IN AN ANIMAL MODEL OF CARDIOVASCULAR DISORDERS

Poruba M.[1], Rácová Z.[1], Hüttl M.[2], Malínská H.[2], Večeřa R.[1]

[1]Department of Pharmacology, Faculty of Medicine and Dentistry, Palacky University Olomouc, Olomouc, Czech Republic
[2]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

The complications of atherosclerosis are common causes of cardiovascular morbidity and mortality. As prevention of increased cardiovascular risk, typically lipid-lowering drugs are used. This include atorvastatin, the most used statin in the Czech Republic. Additionally, there are many nutraceuticals such as silymarin with proofed benefits for human health.
In this study, we compared the effects of atorvastatin, silymarin - the extract from the seeds of milk thistle, or both. Atorvastatin is known as an inhibitor of the key enzyme in the biosynthesis of cholesterol - 3-hydroxy-3-methylglutaryl Coenzyme A reductase (HMGCR). ABCG5 and ABCG8 proteins are transporters responsible for cholesterol efflux from the liver into bile. As an animal model, the spontaneously hypertensive rats with chronic inflammation (SHR-CRP) were used. These rats are a model of cardiovascular disorders with the left ventricular dysfunction.
In this study, the SHR-CRP rats were fed standard laboratory diet (SLD) for four weeks or SLD supplemented with atorvastatin (5 mg/kg/day b.wt.) or silymarin (300 mg/kg/day b.wt.) or combination of both. Animals were sacrificed in a fed state since cardiovascular events are associated with postprandial states. Whole blood and organs were collected for subsequent analysis. For the determination of protein content of enzymes and transporters in the liver, the Western blot techniques were used.
Atorvastatin alone significantly increased the protein content of HMGCR in rat liver. A diet containing the combination of atorvastatin and silymarin increased HMGCR protein content slightly higher than atorvastatin alone. Although there were no effect of atorvastatin on ABCG5 and ABCG8 protein content, a combination of atorvastatin and silymarin significantly increased their amount in rat liver.
This study has shown the positive effects of silymarin in animals treated by atorvastatin. The increase in cholesterol elimination via transporters in the liver is probably compensated by the increase in cholesterol biosynthesis. Although the experimental diet increased the HMGCR protein content, this increase was associated with decreased cholesterol level rather than its increase.
This study was supported by the Czech Science Foundation, Czech Republic [grant number 17-08888S].