## ABSTRACT

Charles University in Prague Faculty of Pharmacy in Hradec Králové Department of Pharmacology and Toxicology Candidate: Alena Růžičková Supervisor: Dr. Přemysl Mladěnka, Ph.D. Title of Thesis: The effects of coumarins on the cardiovascular system

Coumarins constitute a very large category of natural polyphenolic substances, which are composed of a benzene and a  $\alpha$ -pyrone ring. Coumarin is the basic compound, called also 1,2-benzopyrone. Cardiovascular diseases are still the major cause of morbidity and mortality in the world. That is the reason why a research aimed at substances which could have positive effect on these diseases is very beneficial. It appears that coumarins seem to be promising medicaments for certain cardiovascular diseases. Besides the well-known anticoagulant effect of warfarin and its related substances have some coumarins antiplatelet, antioxidant, antihypertensive, antiedematogenic, hypolipidaemic and anitarrhythmic effects.

effect of mediated of Antiplatelet coumarin is by inhibition cAMP-phosphodiesterase, lowering of intracellular Ca<sup>2+</sup> or by inhibition of thromboxane synthesis. Antihypertensive effects are partly linked with antioxidant activity, but also inhibition of cGMP phosphodiesterase, calcium channel blocking and increased production of prostaglandins have probably significant influence. Antioxidant effects may be, in addition to direct scavenging effect, mediated by the inhibition of COX-1 and 5-lipoxygenase and chelation of iron. Hypolipidaemic and antiarrhythmic effects are also linked to an ability to scavenge free radicals or inhibit their production. Mechanism of antiedematogenic effect is unknown.

Finally, it can be noted that despite the large number of known coumarin shows that the majority of their potentially beneficial effects are mediated by similar mechanisms, namely by the inhibition of production of reactive oxygen species, calcium channel blocking and by the increase of cAMP or cGMP due to inhibition of corresponding phosphodiesterase.