Summary

Myocardial remodelling represents a major issue in the current cardiology research and is related to the increasing incidence of heart failure in our population. The changes characterising cardiac remodeling include mainly cardiomyocyte apoptosis/necrosis, disequilibrium between the synthesis of ECM components and their degradation and the reinduction of fetal genes.

The aims of this doctoral thesis are: study of myocardial remodeling in L-NAME-induced hypertensive rats and the possibilities of pharmacological modulations by means of melatonin and substances involved in renin-angiotensin-aldosterone system.

Methodical emphasis is put on myocardial protein profile and hydroxyprolin (a marker of fibrosis) evaluation. Additionally, it focuses on the detection of metalloproteinases by means of zymography and on monitoring of cardiac troponins T (cTnT) and I (cTnI) concentration levels, as markers indicative of cardiomyocyte necrosis, using Elisa method and Western blot.

Our study has proved that a preventive administration of melatoninu at a dose of 10 mg/g in L-NAME-induced hypertensive subjects did not result in myocardial protein profile changes of statistical significance. Likewise, hydroxyproline levels, a marker of fibrosis, were comparable to control group. These results combined to the blood pressure reduction of statistical significance In conclusion, these promising data demonstrate usefullness of further research aimed at use of melatonin in the treatment of cardiovascular diseases.

Pharmacological studies performed on the basis of a regression model are technically demanding and, therefore, are very rarely reported in the literature. Although, the effort focused on the regression of a hypertrophy already developed reflects more accurately the clinical practice. Spironolactone administration had no beneficcial effect on changes in protein profile. Spironolactone administration resulted in left ventricular weight loss, nevertheless collagen and noncollagen proteins were more abundant. We can suppose that the left ventricular hypertrophy of early stages of spironolactone treatment is related to a significant reduction in volume of circulating liquid.

Furthermore, the study has proved that daunorubicin-induced dilatation cardiomyopathy, characterised by reduction in levels of Metabolic and contractile proteins and by significant increase in collagen, is associated with time-dependent changes in gelatinase A (MMP-2). MMP are supposed to be responsible for significant changes in the structure of collagen network involved in the development of fibrosis.

We used the model of neonatal ventricular cardiomyocytes to assess the time and dose dependance of the cardiac troponin release in response to daunorubicin exposure. Our study reports that the cardiac troponin level represents a more efficient biochemical marker than lactatedehydrogenase to asses cardiotoxicity *in vitro*. In addition, a direct correlation between cTnT (Roche) and cTnI has been proved using a new generation of sets ADV AxSYM troponin I (Abbott) ion aexperimental studies both *in vitro* and *in vivo*.