Summary

Vascular resistance is mainly determined by the contraction of vascular smooth muscle (VSM), which is regulated by the phosphorylation of myosin light chain (MLC). VSM contraction is initiated by calcium influx into the VSM cells, which is mediated by transient receptor potential (TRP) channels and L-type voltage-dependent calcium channels (L-VDCC). On the other hand, calcium sensitization is a mechanism enhancing vascular contractile response at a given level of intracellular calcium by RhoA/Rho kinase pathway-mediated inhibition of myosin light chain phosphatase. In this thesis I present the data about i) the role of TRP channels in the mechanisms of vascular smooth muscle contraction, ii) enhanced contractility of arteries from spontaneously hypertensive rats (SHR), and iii) the differences in contraction of arteries from normotensive and hypertensive rats related to the role of RhoA/Rho kinase pathway in three types of experimental hypertension (SHR, Ren-2 transgenic rats and salt-sensitive Dahl rats).

In the study concerning TRP channels, I compared the effects of three commonly used non-selective TRP channels inhibitors (2-APB, SKF-96365, FFA) on isolated arteries. Among them 2-APB was the most interesting because the observed inhibitory effects of 2-APB were dependent on the type of contraction stimulus and also on Na^+ presence in bathing solution. In the study on enhanced contractility of SHR arteries the participation of several mechanisms was suggested to be responsible: the increased influence of norepinephrine vascular varicosities, insufficient opening of K^+ channels and especially altered membrane potential. Both calcium entry and calcium sensitization contribute to the adrenergic vasoconstriction of arteries. Calcium entry seems to be more important in rats with genetic hypertension (SHR and Ren-2 TGR), in which the role of calcium sensitization is attenuated. On the other hand, the role of calcium sensitization is enhanced in contraction of arteries in hypertensive salt-sensitive Dahl rats.

Better understanding of mechanisms of vascular smooth muscle contraction in health and disease might be important for future drug development.