Summary

Carbon-based nanomaterials (CNMs) have unique physical-chemical properties, which make them appropriate candidates for both industry and medicine. However along with production, there are growing concerns about their effects on human organism. For this reason, CNMs are frequent topic of toxicological studies. A key step in the clarification of their safety is to evaluate their interaction with the components of the immune system, particularly their ability to cause inflammation. For some allotropes e.g., pristine graphene derivatives, significant results are still missing or incomplete. For these reasons, this dissertation deals with the evaluation of the proinflammatory effect of two types of pristine graphene platelets (GPs), which represent common intermediate in the processing of other graphene derivatives, and which can penetrate to body via inhalation. For comparison, our work also includes an evaluation of the proinflammatory effect of multiwalled carbon nanotubes (MWCNTs).

Professional phagocytes, particularly monocytes and macrophages represent key cells in processing and elimination of foreign and damaged or abnormal elements. Since phagocytes also represent main mediators of inflammation, we selected human primary monocytes and human monocytic cell line THP-1 differentiated in macrophages as a biological model for testing of CNMs. In both models, rapid endocytosis of all CNMs was confirmed by transmission electron microscopy. Cell viability was assessed via measurement of lactate dehydrogenase (LDH) and HMGB1 (High-Mobility Group Box 1) release. The direct proinflammatory effect was assessed by detection of NLRP3 inflammasome activity and IL-1β production. Activation of NLRP3 by canonical and alternative pathways was observed only in the case of MWCNTs. As possible mechanism was microscopically detected Cathepsin B leakage caused by lysosome damage. In case of GPs, there was neither disruption of cell integrity nor acute inflammation. Potential inhibition of inflammation was denied by co-exposure of GPs with a representative proinflammatory stimulator. On the contrary, we observed an enhanced response, based on which we further evaluated a modulatory effect in the form of testing of cell reactivity against selected bacteria. Monocytes and THP-1 macrophages pre-treated by CNMs were subsequently analysed for phagocytic activity (using microscopy and flow cytometry) and for production of IL-6, TNF-α and IL-10 (using ELISA or reporter cell-based biological assays). The effect of CNMs on the differentiation of primary monocytes was monitored by microscopy and flow cytometry. Results confirmed immunomodulatory effect for all three CNMs.