ABSTRACT

Iron plays a key role in many metabolic pathways in the cell, but it may become toxic at higher concentrations. Therefore, the maintenance of iron homeostasis is crucial for cell viability and is strictly regulated. This element has also an important role in the host-parasite interaction. Parasites are fully dependent on iron uptake from the host environment. Iron uptake is a very difficult process thanks to effective sequestration of the host's iron supplies, which makes iron almost inaccessible to parasites. Imported iron is mostly transported to the mitochondria where it is necessary for its proper function.

This work is focused on the effect of modified chelators on pathogenic fungi and the chosen kinetoplastid parasites, which cause serious human diseases. These diseases are becoming a great threat due to emerging drug resistances. Modified chelators are able to target mitochondrial functions and affect iron homeostasis, which can lead to a promising antiparasitic and antimycotic effect. Modified chelators in tested organisms can inhibit their gorwth even in nM concetrations, affect mitochondrial respiration, membrane potential and membrane permeability. Thanks to mitochondrial targeting the potency was much higher compared to the unmodified compounds. This work contains also research of new antimicrobial substance halicin identified by the artificial intelligence. We also managed to target this subtance to the mitochondria and improve it's potency.

Keywords: iron, mitochondria, drugs, chelation, parasitic protists, pathogenic fungi