ABSTRACT

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Department of Pharmaceutical Chemistry and Drug Control
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Title of Doctoral Thesis **Derivatives of thiazole as potential drugs**

The doctoral thesis is focused on preparation of thiazole derivatives. Sixty seven compounds were prepared, thirty one of them are original. Structure-activity relationships between the chemical structure, physical properties and biological activities of the evaluated compounds are discussed. First from five series were 5-benzylidenerhodanine derivatives and 5-hetarylmethylidenerhodanine derivative. Compounds were gained by Knovenagel condensation of rhodanine with aromatic or heterocyclic aldehydes. At the same time the earlier prepared condensation product of rhodanine and ketones derived mainly from substituted acetylpyrazines were further tested for biological properties. The next part was given to the preparation of condensation products of *N*-substituted rhodanine with aromatic and heterocyclic aldehydes or ketones. Last series of compounds are of 5-(1-hetarylalkylidene)hydrazonothiazolidine-4-one derivatives prepared by cyclization of analogous thiosemicarbazones.

The prepared compounds were evaluated for their antifungal and antimicrobial activity *in vitro*. Selected compounds were further tested for their antimycobacterial activity, ability to inhibit electron transport in spinach (*Spinacia oleracea* L.) chloroplasts and reducing chlorophyll content in alga *Chlorella vulgaris*. Significant antifungal activity in the whole range of selected pathogenic fungi has been achieved in a group of 5-(1-hetarylalkylidene)hydrazonothiazolidine-4-ones. The presence of heterocyclic nitrogen in the neighboring position of the alkylidene substituent was essential for antifungal activity. Moderate antibacterial activity was observed for 5-benzylidenerhodanine derivatives. Substances with the highest activity in this group carried a halogen or nitro substituent on the aromatic ring. *In vitro* evaluation showed sensitivity to derivatives of 5-benzylidenrhodanine only in *Staphylococcus* strain. Compounds derived from *N*-substituted rhodanines exhibited no antifungal or antibacterial activity. The ability of the inhibition of the growth of *Mycobacterium tuberculosis* was very low by all prepared compounds. 90% reduction of chlorophyll content in alga *Chlorella vulgaris* was found in the group of nitrobenzylidenerhodanines. The influence of other compounds on photosynthetic processes was not significant.