# Abstract

**Charles University in Prague**

**Faculty of Pharmacy in Hradec Králové**

**Department of Pharmaceutical Chemistry and Drug Control**

**Author:** **Alena Janoutová**

**Supervisor:** **PharmDr. Jan Zitko, PhD.**

**Title of diploma thesis:** **Pyrazine Derivatives as Potential Antituberculosis Drugs IV**

Drug research, potentially effective against tuberculosis, progress already for several years in the Department of Pharmaceutical Chemistry and Drug Control Faculty of Pharmacy in Hradec Králové.

This study is focused on new derivatives of pyrazinamide (PZA) prepared as potential antituberculars. PZA itself is a well-established first-line antitubercular agent and a constituent of all basic tuberculosis treatment regimens. The design of final compounds was based on the previously synthesized 5-alkylamino-N-phenylpyrazine-2-carboxamides1, which possessed promising in vitro antimycobacterial activity with MIC ranging from 0.78 to 3.13 μg/mL. The object of this study was to test the activity of derivatives with alkylamino chain modified with terminal phenyl, hydroxyl or methoxy group.

Final compounds were prepared by nucleophilic substitution of chlorine with respective amines in refluxing EtOH. Reaction yields, after all purification steps, were 58-87%. Compounds were characterized by $^{1}H$ and $^{13}C$ NMR, IR, elementary analysis and melting point.

Final compounds were tested for *in vitro* antimycobacterial, antibacterial , antifungal and antiviral activity. Only six substances, out of total of 16 newly prepared, showed moderate activity against *M. tuberculosis* H37Rv (MIC =12,5-50 μg/mL, MIC(PZA) = 6,25 μg/mL). For four substances were found low antiviral activity (against more types of Influenza virus). All compounds were ineffective against *M. avium* and other tested

pathogens. All compounds with R2 = Cl were inactive. Detailed structure-activity relationships will be discussed.