Abstract

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Chemistry and Pharmaceutical analysis

Student: Mgr. Marie Molnárová

Supervisor: Prof. PharmDr. Martin Doležal, Ph.D.

Co-advisor: PharmDr. Ondřej Janďourek, Ph.D.

Title of rigorous work: Pyrazine derivatives as a potential drugs

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Tuberculosis is a global problem because it is the most common cause of death among infectious diseases. The complication of therapy is the rise of multiresistant and extremely resistant strains. The synthesis of novel substances is focused to gain safer and active drugs.

This work is focused on the synthesis of pyrazine derivatives in which substitution of pyrazine cycle with various substituents is used. It follows up the research which is established at the Department of Pharmaceutical Chemistry, Pharmaceutical Faculty in Hradec Králové.

The pyrazinamide is the first line antituberculotic drug. The previous studies proved that substitution of pyrazine ring with various substituents can increase the antituberculotic and/or antifungal activity. In this work it is used aminodehalogenation reaction, the 2-chloropyrazine, as a starting substance, reacts with ring-substitued benzylamine in microwave reactor. In this way the products like *N*-benzylpyrazine-2-amine are gained.

The microwave reactor for the synthesis of substances was used. For separation it was used preparative chromatography, CombiFlash. The solids were gained by recrystallization in vacuum evaporator. The identity of new synthesized derivatives was proved by NMR spectroscopy on the Department of Organic and Bioorganic chemistry. The substances were tested on their antibacterial, antifungal and antimycobacterial activity on the Department of Biological and Medical Sciences (antibacterial and antifungal activity) and in the Faculty Hospital in Hradec Králové, the Department of Clinical Microbiology (antimycobacterial activity).