UNIVERZITA KARLOVA V PRAZE FARMACEUTICKÁ FAKULTA V HRADCI KRÁLOVÉ

Téma diplomové práce	**Derivatives of rhodanine as potential antifungal and antimycobacterial drugs**
Jméno studenta, studentky	**Morid Mahmoudi Majd**
Jméno oponenta	**PharmDr. Petr Zimčík, Ph.D.**

II. Posudek oponenta

The diploma thesis of the student is written on 70 pages and contains 74 references. Since the work is focused on potential antifungal and antimycobacterial drugs, these topics are discussed thoroughly in the theoretical part. In both cases, the diseases are described in the beginning with the differences leading to relatively selective targeting to the agens. The methods of treatment are mentioned too, with focus especially on the chemotherapy and drugs used nowadays in practice or in clinical trials. The synthetic part describes synthesis of five derivatives of rhodanine. All of them have already been prepared before by other authors, however, some data (especially NMR) were missing in literature. All compounds in the thesis are well described with all possible analysis including NMR, IR, elementary analysis, m.p. and purity obtained using HPLC method. Antifungal activities, unfortunately very poor, of prepared compounds on several strains of fungi are mentioned in the end of the work. Since the prepared rhodanines may form two geometrical isomers, the possible differentiation of both of them on the basis of NMR spectra is discussed in the part Discussion.

I have following questions or comments on the work:

- Despite extensive recherché on the antimycobacterial drugs and methods of treatment, I miss a little bit very important thing - the therapeutical regimens and combinations of the drugs used in the treatment of TB.
- p.37 - the structure of ketoconazole is not shown.
- p.49 and 50 - What are the "depsipeptides"?
- It is unusual to refer a lot of original works as database (ref. 61 - Beilstein, 62 - CAS). I can understand it during searching for and comparing of analytical data (e.g. m.p.) of published compounds. However, it should not be used in the case of referring to a specific fact that was published in one or two works (p. 61).
- I found big differences in Table 1 (p. 60). Inhibitory concentrations for standard fluconazol for *Candida tropicalis* are 1.63 μM and 417.9 μM after 24 h and 48 h, respectively . Is it just type mistake or real data?
- Can you discuss more the results obtained by the authors in ref. 68? They worked on the completely same compounds and as you state, they found very interesting activities. Which substituents seem to be the best for antifungal activity according to their results?

Navrhovaná klasifikace

V Hradci Králové dne 28.5.2007

Podpis oponenta diplomové práce