Novel indole-containing condensed tetracyclic systems with promising high antitubercular and antiviral activity: synthesis and *in vivo* study

Description:

The basic statistics of the present-day global "tuberculosis problem" are well known: one-third of the global population is considered infected; 6 million new cases each year; 20% of adult death and 6% of infant deaths are attributable to TB. The increased incidence of drug-resistant tuberculosis certainly highlights the need for new antitubercular drugs. Equally urgent is the need for new antiviral agents, especially with the growing concern for the next influenza pandemic.

We propose to combine the expertise of Georgian and USA scientists to pursue the general goal of developing of a new novel generation compounds with antitubercular and antiviral activity, based on the original indole-containing tetracyclic systems - benzo[b]thiophene indoles.

Our strategy is based on literature precedents that show that the combination of two pharmacologically active bicyclic systems in one molecule can promote the increase of biological activity of the molecule and expand the spectrum of its pharmacological action.

In the present study, the basic bicyclic system is indole. Since the nature of the second bicyclic system is crucial for the pharmacological activity of tetracyclic construction, we have chosen benzo[b]thiophene as the bicyclic partner for.

The research team of Prof. T.Khoshtaria has more than 30 years expertise and experience in the synthesis and study of condensed tetracyclic systems. Among the vast number of synthesized heterocyclic compounds, their derivatives of isomeric benzo[b]thiophene indoles were found to have the most promising tuberculostatic and viral activity.

Innovative Aspect and Main Advantages:

Several years ago we began collaborating with the US NIH's NIAID-sponsored compound screening programs, the Tuberculosis Antimicrobial Acquisition and Coordinating Facility (www.taacf.org) and the Antimicrobial Acquisition and Coordinating Facility (www.niaid-aacf.org), which provides us with **free** compound screening services against tuberculosis and 30 viruses (including influenza A and B strains), respectively. More than 150 compounds were sent for preliminary screening. **Many of them have been shown to have high (96 - 100%) anti-tubercular and antiviral (IVA (H1N1), IVA (H3N2) and IVB) *in vitro* activities, as we predicted.**

All possible six isomers of benzo[b]thiophene indoles (see Fig.1) - precursors of new heterocyclic systems were originally synthesized.

Within the STCU project, the following specific tasks are planned:

1. Preparation of isomeric benzo[b]thiophene indoles and their derivatives;
2. Screening and pharmacological study of the prepared compounds against Mycobacterium tuberculosis H37Rv and Viruses such as Flu A and Flu B.

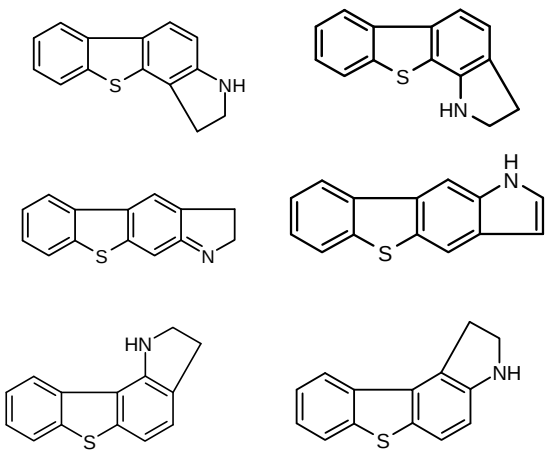

Fig.1 Structure of synthesized isomers of benzo[b]thiophene indoles

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Areas of Application:

Medicine

Stage of Development:

Positive results of i*n vitro* screening

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