repurposing of rimonabant

**Conclusion:** A sila analogue turned out to be the most potent antimycobacterial compound (MIC, 31 ng/mL) from this series with an excellent selectivity index. Optimization of the series to improve its ADME properties is currently in progress.

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**Orbital tuberculosis: Clinical and microbiology profile**

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**Background:** Mycobacterium tuberculosis infection of the eye is common in India, but the orbital infection is extremely rare. Orbital tuberculosis occurs as a result of hematogenous spread or direct extension from the neighboring structures. In this study we have reviewed the clinical and microbiology features of orbital tuberculosis.

**Methods & Materials:** Medical and Microbiology records of patients with orbital tuberculosis positive for M.tuberculosis in culture between June 2010 and May 2015 reviewed. The study data included demographic details of the patients, clinical presentation, interventions and reports of other investigations performed. Incision biopsies/Pus aspirate/FNAC specimen obtained from patients were subjected to direct microscopy by Ziehl Neelsen staining, inoculated on to Lowenstein Jensen(LJ) medium and histopathology.

**Results:** A total of 6 patients with orbital tuberculosis were identified during the study period. Four of six patients were females. The age ranges of the patients from 7 years to 29 years. Four patients were less than 15 years, two patients were within 15 to 30 years. All the patients were immunocompetent. Two patients presented with lacrimal gland mass with proptosis, one patient with chronic orbital cellulitis, one patient with orbital cellulitis and tuberculosis osteomyelitis, one with upper lid mass with chorioidal granuloma and one patient with upper lid mass. Mantoux test was performed in 4/6 patients and positive in all the four patients. Chest X was performed in 5/6 patients and no abnormality was noted in all these patients. ESR was elevated in 3/5 patients. Histopathology diagnosis was available for 5 patients and 4/5 patients showed granulomatous inflammation with caseous necrosis, one with tuberculosis osteomyelitis. Direct smear was positive for acid fast bacilli and culture grew Mycobacterium tuberculosis on LJ medium in all the patients. All the patients were started on anti tuberculosis treatment.

**Conclusion:** Orbital tuberculosis should be considered as a differential diagnosis in immunocompetent patients with orbital swelling and abscess in TB endemic countries. In majority of patients orbital tuberculosis occurs without systemic involvement.

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**The urgency of effective antitubercular drug development – new promising structures derived from natural terpenoids**

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**Background:** Despite the availability of highly efficacious treatment for decades, tuberculosis (TB) remains a major global health problem. The widespread transmission of resistant variants of Mycobacterium tuberculosis, which does not respond to any of the commercial drugs, threatens health security of both developed and developing world. The urgent need of new antimycobacterial agents and development pathways is becoming more and more apparent.

**Methods & Materials:** More than 200 new diverse structures, including more than 50 new synthetic chiral compounds derived from natural terpenoids (+)-camphor and (-)-fenchone were synthesized. The compounds were evaluated for their in vitro antimycobacterial activity by proportional method against reference strain Mycobacterium tuberculosis H37Rv and multidrug resistant Mycobacterium tuberculosis strain 43.

**Results:** The quantitative structure–activity relationship (QSAR) revealed several structural requirements: two hydrogen bond donors, two or three rings and no large branched substituents. We describe the design of a set of nine novel camphane-based derivatives following these requirements. Four of them showed activities in the nanomolar range, significantly higher than the activities in the initial set. Many structures showed promising antimycobacterial activity by proportional method against reference strain Mycobacterium tuberculosis H37Rv and multidrug resistant Mycobacterium tuberculosis strain 43.

**Conclusions:** All the patients were started on anti tuberculosis treatment.

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Conclusion: When developing new drugs against Mycobacterium tuberculosis, it is important to note that this bacteria has a solid and chemically resistant cell wall. Therefore, anti-TB agents are specific and do not act on other pathogenic bacteria, and vice versa - the huge variety of available antibiotics does not affect the mycobacteria. For all tested compounds there is no correlation between their antimycobacterial activity and activity against other microorganisms. This indicates that the action of all potent derivatives ( (+)-camphor and (-)-fenchones) are specific to the Mycobacterium tuberculosis. All of them are stable, non-toxic against human cells and show antimycobacterial activity in the nanomolar range being 60 times more active than ethambutol. These results can be considered an important starting point for design of new effective antitubercular drugs.

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Date: Saturday, March 5, 2016
Time: 12:45-14:15
Room: Hall 3 (Posters & Exhibition)

Genotypes of mycobacterium tuberculosis isolated from blood of active tuberculosis patients


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Background: Tuberculosis is an infectious disease caused by the bacillus Mycobacterium tuberculosis. Mycobacteremia is a key event in the pathogenesis of tuberculosis and development of extra-pulmonary TB. Genotyping of M. tuberculosis isolates is useful for surveying the dynamics of TB infection, identifying new outbreaks, and preventing the disease. We attempted to estimate the prevalence of M. tuberculosis bacteremia and its genotypes.

Methods & Materials: Suspected cases of tuberculosis were screened for mycobacteremia by culturing 5 ml of peripheral blood sample in the MB/BacT® culture system (bioMérieux, France). Flashed positive bottles were screened for M. tuberculosis using in-house multiplex PCR and further screened for drug susceptibility. All isolates were subjected to spoligotyping, 24 loci MIRU-VNTR, TbD1® and RD analysis. Genotyping analysis was performed using SIT-VIT web and MIRU-VNTRplus online tools.

Results: Blood culture was performed from 469 patients (306 extrapoluminary, 50 pulmonary and 113 disseminated TB cases). Seventy seven (16.4%) of these blood cultures were positive by MB/BacT®. Of the 77 isolates, 36 (11.7%) were patients with extra-pulmonary TB, 34 (30%) disseminated TB, and 7 (14%) pulmonary tuberculosis. Among the culture positives 67 (87%) were identified as M. tuberculosis and 10 (13%) as mycobacteria other than tuberculosis using in-house multiplex PCR. Spoligotyping identified 65 isolates (97%) belong to 16 previously described Share Types, while the remaining two isolates had unique/un-identified Share Types patterns based upon SIT-VIT web. Among them ST26 (CAS1_DEL) was more predominant (49.2%) followed by ST25 (CAS1_DEL) (9.2%), ST1 (Beijing) (9.2%) and ST19 (EAI2_MANILLA) (7.6%). Largest number of clustering of isolates was detected in Beijing (100%), CAS (97.4%), and EAI (81.8%) by spoligotyping. TbD1 analysis showed that majority of the isolates (83.5%) were modern lineages (TbD1+) and 11 (16.4%) isolates belong to ancient lineage (TbD1-). All the ancient lineage isolates belong to EAI lineage.

Conclusion: CAS lineage was predominantly found among mycobacteremia patients. This pattern is not different from the predominance of mycobacterial isolates genotyped from pulmonary TB cases.

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Diagnostic performance of RT-qPCR method by targeting 85B mRNA in the laboratory diagnosis of Mycobacterium tuberculosis infection: A preliminary study in Turkish patients

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Background: The problems with any PCR method using DNA sequences as targets for amplification include false-positive results, the inability to detect a difference between viable and nonviable organisms and the inability to determine drug susceptibility. Instead of DNA detecting assays, using RT-qPCR to assess the expression of the 85B mRNA gene of M. tuberculosis indicates the presence of a viable organism. In this study, we used the mRNA coding for 85B antigen complex which is present in all mycobacteria. We aimed to assess the diagnostic performance of RT-qPCR method by comparing with the real-time PCR Cobas TaqMan MTB kit.

Methods & Materials: A total of 54 cases including 32 (17 males, 15 females) patients with confirmed tuberculosis and 22 (13 males, 9 females) individuals without tuberculosis were included as patient and control groups, respectively. The mean ages of 30 males and 24 females were 37.06 ± 8.86 and 36.75 ± 8.96, respectively. Decontamination with N-acetyl-L-cysteine and sodium hydroxide (NACL–NaOH) at 2% and Mycobacterial Growth Indicator Tube (MGIT) 960 system was used for the laboratory diagnosis of sputum samples. Decontaminated samples were used for the manual extraction of M. tuberculosis DNA and 85B mRNA. Extracted DNA was used for Cobas TaqMan MTB DNA qPCR kit (Roche Diagnostics) in a cobas TaqMan 48 analyzer. For RT-qPCR method, total RNA was extracted from the sputum specimen using standard TRIzol protocol (Invitrogen) and 85B mRNA analyses were performed on LightCycler 480 II system.

Results: A significant difference was detected between patients and control groups by RT-qPCR method (p<0.001) and Cobas TaqMan MTB DNA qPCR kit (p=0.0027). Sensitivity, specificity, positive and negative predictive values and kappa coefficient were determined as 97%, 95%, 97%, 95%, 0.89% for RT-qPCR method and 91%,