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Novel amino-flavonoids: Multi-target compounds as potential agents for co-morbid type 2 diabetes and tuberculosis treatment

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Diabetic patients are two to three times more likely to develop active tuberculosis infections compared to non-diabetics. Co-morbidity of diabetes and tuberculosis (TB) infection is rising and contributes to an increased disease and pill burden. Citrus fruits have naringenin flavonoid which has been reported to have anti-microbial and anti-diabetic activities. The aim of the study was to develop synthetic analogues of the naringenin moiety that can be used as potential agents with dual activity against type 2 diabetes and TB infections. A novel series of 4-[(cyclopropylcarbonyl) amino] chalcones were synthesized. An intermediate compound, N-(4-acetylphenyl) cyclopropanecarboxamide was synthesized and thereafter, reacted with commercially available aldehydes to yield the final amino-chalcone series. *In vitro* antimycobacterial activity was determined against *M. tuberculosis* (H37Rv) strain grown under aerobic conditions using dual optical or fluorescence methods. *In silico* studies were carried out to determine binding affinities of these compounds on Adenosine Monophosphate Activated Protein Kinase (AMPK) and also on malate synthase, an enzyme that has been implicated in the latency and adhesion of *M. tuberculosis*. A series of 11 novel compounds were successfully synthesized, characterized and tested against *M. tuberculosis* and 7 compounds were found to be active against the TB strain and 3 showed promising activity with MICs (μM) of 32, 48 and 49. These compounds showed good binding affinity to malate synthase and AMPK with binding scores reaching -8.2 and -9.2 Kcal/mol respectively. Naringenin analogues can be targeted as potential compounds for co-morbid TB and type 2 diabetes treatments. *In vitro* and *in vivo* antidiabetic and antimycobacterial studies should be done to further elucidate the molecular mechanisms of these compounds.

Biography

Tlaila T B has recently completed his Master's in Pharmacology at the University of KwaZulu-Natal (UKZN). The School of Health Sciences at UKZN and the Prestigious Innovation Master Scholarship from the National Research Foundation (NRF) funded his Master's Research project. He has won several awards, in the most recent; he took the 1st prize for a Poster Presentation at the UKZN Annual Health Science Symposium.

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