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In vitro evaluation of antimycobacterial activity of N-aryl-1,4-dihydro pyridine-3,5-dicarboxamides against Mycobacterium bovis BCG

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It has been reported previously that 4-(nitrophenyl)- dihydropyridines having carboxamides in 3 and 5 positions show anti-tuberculosis activity. These compounds inhibit enoyl reductase, an enzyme envolved in mycolic acid biosynthesis.
Objectives: The purpose of the present study was to synthesize new 4-imidazolyl – N, N'-diaryl -1, 4-dihydropyridine-3,5-dicarboxamides, having possible anti-tuberculosis activity.
Material and Methods: A series of 4-imidazolyl N, N'-diaryl -1, 4-dihydropyridine-3, 5-dicarboxamides were prepared. They were screened as antitubercular agents against one type of fast growing Mycobacterium (M. smegmatis). Some of them are better than INH and they were tested against BCG. Minimum bactericidal concentrations (MBCs) were determined using agar proportion method
Results: Thirty one compounds were tested in vitro against M. smegmatis. Five of them were chosen and tested against BCG. Isoniazid (Sigma Chemical Co.) was used as reference drugs. Minimum bactericidal concentration (MBC) was determined using agar proportion method in Muller Hinton Agar medium in first item and Lowenstein-Jensen medium in second item.
Discussion: Comparison of the activities of tested compounds indicates that compounds 27 with N,N-bisphenyl-4-[3-(4-fluorobenzyl)-2-methylthioimidazole-5-yl]-2,6-dimethyl-1,4-dihydropyri dine-3,5-dicarboxamide with MBC=16 and 33with N,N-bisphenyl4-[1-(2-chlorobenzyl)-2-methylthioimidazole-5-yl]-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxamide with MBC=32 group at C-3 and C-5 positions of the 1,4-dihydropyridine ring was the most potent among the tested compounds. They were better than INH and other compounds against M. tuberculosis BCG. The other substituents did not show good antitubercular activity.
Conclusions: The results demonstrate that a substituted imidazole group is a suitable equivalent for nitro phenyl group which was previously reported in the structure of anti tubercular 1, 4-dihydropyridinedicarboxamides
Key words: Anti-tuberculosis, Dihydropyridine, M. smegmatis, BCG