New Quinolone and Meroterpenoid Fungal Metabolites with Anti-acetylcholinesterase Activity

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Enhancement of cholinergic neurotransmission by acetylcholinesterase inhibitors have been considered as one potential therapeutic approach against Alzheimer disease. In the course of our screening for selective acetylcholinesterase inhibitors from microbial metabolites, we isolated new quinolone and meroterpenoid compounds from Penicillium citrinum and Aspergillus terreus, respectively. The compounds were isolated by an ethylacetate partition, SiO_2, Sephadex LH-20, ODS, and Chiral HPLC column chromatography. Two new quinolone compounds named quinolactacins A1 and A2 are diastereomeric with a very unique pyrrolo[3,4-b]quinolone skeleton. Five new meroterpenoid compounds named terreulactones A - E are the sesquiterpene lactone type meroterpenoid. Quinolactacin A2 and terreulactone C inhibited acetylcholinesterase with IC_{50} (?M) values of 19.8 and 0.06, respectively. Quinolactacin A2 and terreulactones C showed more than 30 and 3000 times, respectively, selectivity for acetylcholinesterase versus butyrylcholinesterase. Details of their structure and activity will be presented.