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Activities of 5-Methylfurfuryltrimethylammonium Iodide and Related Compounds at Vascular Endothelial Muscarinic Receptors of the Rat Aorta

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Abstract—5-Methylfurfuryltrimethylammonium iodide (5-MFT) is a furan analog of muscarine and was studied for its cholinergic activity at vascular endothelial receptors of the rat aorta. Other related compounds have different substitutions at position 5 of the furan ring and include the following compounds: 5-hydroxymethyl- (5-HMFT), 5-chloromethyl- (5-CMFT), 5-bromomethyl- (5-BMFT), 5-iodomethyl- (5-IMFT), and 5-methoxy- (5-MOFT) furfuryltrimethylammonium salts. The furan analogs relaxed helical strips of rat aorta which contracted with norepinephrine (10^{-6} M). These relaxations were endothelial cell-dependent. The ED_{50}'s for muscarinic activities increased in the following order: 5-MFT = ACh < *dl*-muscarine < 5-HMFT = 5-CMFT < 5-MOFT < 5-BMFT < 5-IMFT. Among the furan analogs, 5-MFT was found to be a full agonist at the endothelial cells; other furan analogs were only partial agonists. The affinities and relative intrinsic efficacies of the most potent analogs decreased in the following order: ACh = 5-MFT > *dl*-muscarine > 5-HMFT > 5-CMFT.

Atropine and scopolamine antagonized relaxations by furan analogs. K_B values for atropine and scopolamine against ACh, 5-MFT or 5-HMFT as agonist were not different, indicating that these agonists and antagonists were acting at the same muscarinic receptors. The K_B of atropine and of scopolamine increased when 5-CMFT was used as an agonist, indicating that 5-CMFT may cause relaxation by acting at other sites besides endothelial muscarinic receptors. The endothelial muscarinic receptor might be classified tentatively as of M_2 or M_1 type. These studies did not exclude the possible heterogeneity of the endothelial muscarinic receptors.

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