β-ADRENERGIC ACTIVITIES OF ENANTIOMERS OF ISOMERIC OCTOPAMINES AND SYNEPHRINES

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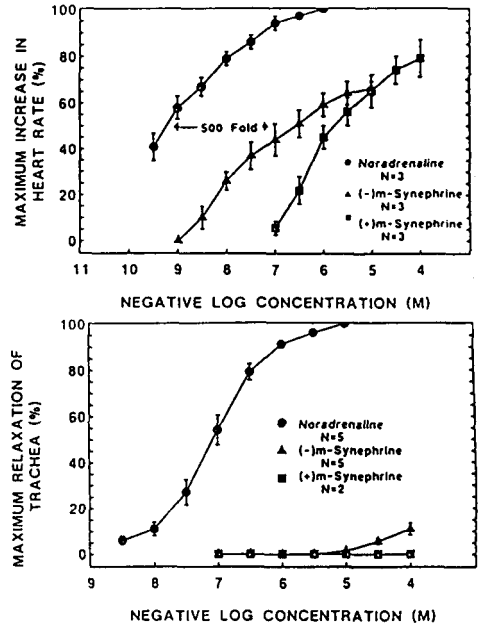
m- and p-Hydroxyphenylethanolamine (octopamine) occur naturally in several sympathetically innervated organs in similar concentrations (1-10 ng/g) and their N-methyl derivatives, the synephrines, are present in substantially greater quantities in adrenal gland (Ibrahim et al, 1985). The adrenergic activities of these compounds have not been measured hitherto and, in order to simulate physiological conditions more closely, the racemate of each compound was resolved for the first time into the corresponding optically pure enantiomorphs by fractional crystallisation of the diastereoisomeric salts formed with an antipode of an appropriate organic acid. The activities of the resultant (+)- and (-)- isomers were determined at β_1 (chronotropic response of isolated guinea pig atrium pretreated with phenoxybenzamine) and β_2 (relaxation of guinea pig tracheal smooth muscle pretreated successively with phenoxybenzamine and carbachol) adrenergic receptors (see figures and Table 1).

Table 1 Relative potencies

Compound	β_1
(-)Noradrenaline	1.00
(-)m-Synephrine	0.01
(-)m-Octopamine	0.0001
(-)p-Octopamine	0.0001
(-)p-Synephrine	<0.00002
(+)m-Synephrine	0.001
(+)m-Octopamine	<0.00002
(+)p-Octopamine	<0.00002
(+)p-Synephrine	<0.00002



The (-)-enantiomers of all four amines behaved as partial agonists for β_1 adrenoceptors with the following potency order: noradrenaline>>m-synephrine> m-octopamine = p-octopamine. The (+)-enantiomers of all four amines were less active than the corresponding (-)-isomers by 1-2 orders of magnitude. The (-)-enantiomers of all four amines behaved as partial agonists (but the activities were too low to establish a potency ranking) and weak partial antagonists at β_2 receptors whilst the corresponding (+)-isomers had no detectable agonist or antagonist effect at these structures.
It is concluded that any potential role for these compounds involving modulation of noradrenaline neurotransmission cannot be mediated via β_1 or β_2 adrenergic receptors.

Ibrahim, K.E. et al (1985) J. Neurochem. 44: 1862-1867