α-ADRENERGIC ACTIVITIES OF ENANTIOMERS OF ISOMERIC OCTOPAMINES AND SYNEPHRINES

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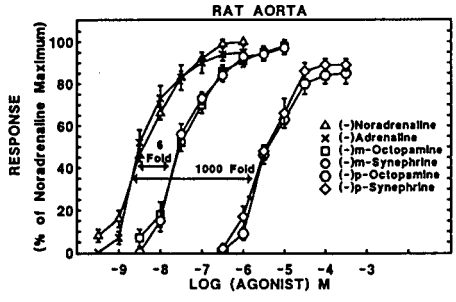
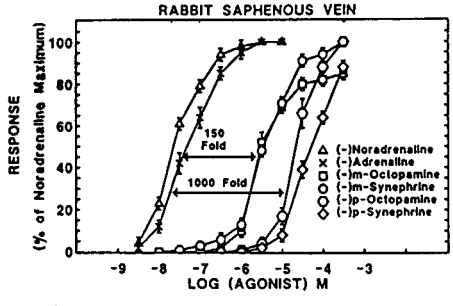
m- and p-Hydroxyphenylethanolamine (octopamine) and the corresponding N-methyl derivatives, the synephrines, occur naturally (in sympathetically innervated organs and adrenal gland respectively; Ibrahim et al, 1985) but their physiological roles are unknown. The racemate of each amine was resolved and the dose-response curves determined for the activities of the corresponding enantiomorphs on α_1 (rat aorta) and α_2 (rabbit saphenous vein) adrenoceptors (see figures and Table 1).

Table 1 Relative potencies

Compound	α_1	α_2
(-)Adrenaline	1.51	0.53
(-)Noradrenaline	1.00	1.00
(-)m-Octopamine	0.16	0.006
(-)m-Synephrine	0.16	0.007
(-)p-Octopamine	0.001	0.001
(-)p-Synephrine	0.001	0.0006
(+)Noradrenaline	0.03	0.02
(+)m-Octopamine	0.02	0.001
(+)m-Synephrine	0.0004	0.0002
(+)p-Octopamine	0.0002	0.00008
(+)p-Synephrine	0.00002	<0.00002





The rank order of potency of the (-)-isomers and (+)-forms (for both α_1 and α_2-adrenoceptors) was, respectively: NA>m-octopamine ▫ m-synephrine> p-octopamine ▫ p-synephrine and NA>m-octopamine>m-synephrine>p-octopamine>p-synephrine. However, the potency of each (+)-isomer was 1-2 orders of magnitude less than that of the corresponding (-)- form, the differences being greater for the synephrines than the octopamines on both types of receptor.

Ligand binding studies were performed on α_1 and α_2 binding sites from rat cerebral cortex (using ^{3}[H]-prazosin and ^{3}[H]-yohimbine respectively). The (-)-isomers were more active than the (+)- forms and the rank order of affinities of the former for both α_1 and α_2 sites was NA>m-octopamine = m-synephrine>p-synephrine>p-octopamine.

It is concluded that m- and p-octopamine have similar potencies at α_1-(and also at α_2) adrenoceptors and that they can be considered to be naturally occurring α_1 selective amines. However, if m- and p-octopamine are co-released with NA in amounts proportional to their concentrations in vivo, their low activities at both types or receptor render this potential mechanism an unlikely one for any physiological role.

Ibrahim, K.E. et al (1985) J. Neurochem. 44: 1862-7