Stereoselectivity of butylidenephthalide on voltage-dependent calcium channels in guinea-pig isolated ileum.

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Abstract

Two geometric isomers, the Z- and the E- forms, can be separated from synthetic mixtures of butylidenephthalide (Bdph). Z-Bdph (50-100 microM) non-competitively inhibited Ca(2+)-induced contractions in depolarized (K+, 60 mM) guinea-pig ileum longitudinal smooth muscle, with a pD2' value of 3.88 +/- 0.20 (n = 5). However, E-Bdph (20-100 microM) competitively inhibited these contractions with a pA2 value of 4.56 +/- 0.18 (n = 5) which was significantly ($P < 0.05$) greater than the pD2' value of Z-Bdph. In contrast, the two isomers had no stereoselective inhibitory action on Ca2+ influx through pre- or post-junctional membranes of cholinergic nerve endings from which the transmitter acetylcholine is released or on Ca2+ release from intracellular stores. Therefore, the trans-Z and cis-E forms of Bdph might have geometric stereoselectivity for voltage-dependent calcium channels (VDC) in guinea-pig longitudinal smooth muscle. Both isomers might inhibit more selectively the contractile twitch responses evoked by electrical stimulation than by cumulative acetylcholine- or carbachol-induced transient contractions in guinea-pig ileum longitudinal smooth muscle.