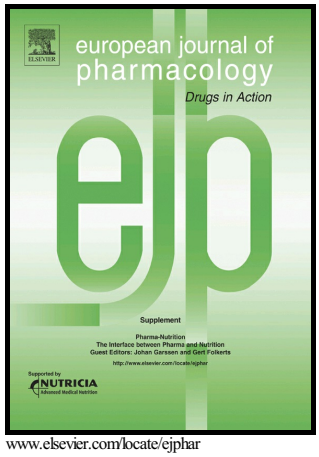

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ABSTRACT

This study describes the association rate and residence time of abediterol, a novel long-acting β_2-adrenoceptor agonist (LABA) in Phase II development for treatment of asthma and COPD, in comparison with indacaterol, olodaterol, vilanterol and salmeterol, for both human β_1- and β_2-adrenoceptors.

Abediterol association and dissociation rates were monitored directly by using its tritiated form. Moreover, association was determined indirectly using experimental K_i and k_{off} obtained from assays performed with unlabelled compound. Dissociation was also studied indirectly by measuring the association rate of ^{3}H-CGP12177 to beta adrenoceptors previously occupied by unlabelled compounds.

Abediterol shows a fast association for the β_2-adrenoceptor (k_{on} $1.4x10^7 \pm 1.8x10^6$ $M^{-1}min^{-1}$) while its dissociation rate is between 30 and 64 times slower than that of the reference LABA compounds tested, with a residence time of 91.3±13.3 min (measured directly) and 185.5±7.5 min (measured indirectly). Abediterol shows kinetic selectivity for the β_2- over the β_1-