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Almirall, R&D Centre, Laureà Miró 408-410, 08980 Sant Feliu de Llobregat, Barcelona, Spain.

**\*Corresponding author:** Israel Ramos, israel\_amos75@hotmail.com, Tel:+34647660231.

## ABSTRACT

This study describes the association rate and residence time of abediterol, a novel long-acting  $\beta_2$ -adrenoceptor agonist (LABA) in Phase II development for treatment of asthma and COPD, in comparison with indacaterol, olodaterol, vilanterol and salmeterol, for both human  $\beta_1$ - and  $\beta_2$ -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  $^3H$ -CGP12177 to beta adrenoceptors previously occupied by unlabelled compounds.

Abediterol shows a fast association for the  $\beta_2$ -adrenoceptor ( $k_{on}$   $1.4 \times 10^7 \pm 1.8 \times 10^6$   $M^{-1}min^{-1}$ ) while its dissociation rate is between 30 and 64 times slower than that of the reference LABA compounds tested, with a residence time of  $91.3 \pm 13.3$  min (measured directly) and  $185.5 \pm 7.5$  min (measured indirectly). Abediterol shows kinetic selectivity for the  $\beta_2$ - over the  $\beta_1$ -

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