

## Alpha<sub>1</sub>-adrenoceptor antagonistic properties of RW-11b, a 5-arylidenehydantoin derivative

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The  $\alpha_1$ -adrenoceptors contribute to the regulation of blood pressure, play a role in heart contractile function, cardiac rhythm and human prostate smooth muscle contraction. Various  $\alpha_1$ -adrenoceptor antagonists can be useful in the treatment of hypertension and benign prostatic hyperplasia (BPH). Antagonists of  $\alpha_1$ -adrenoceptor are the mainstay of treatment of BPH as they are able to reduce the dynamic component of bladder obstruction and they may reduce the irritant symptoms of the disease. The  $\alpha_1$ -adrenoceptors subclass has been divided into three subtypes:  $\alpha_{1A}$ ,  $\alpha_{1B}$  and  $\alpha_{1D}$  on the basis of pharmacological and cloning studies. Some data point toward a distinct distribution and function of the 3 receptors in different vascular beds and smooth muscles [Eltze et al., Naunyn Schmiedebergs Arch Pharmacol, 2001; Sapa and Kubacka, Eur J Pharm, 2011]. In this context it is necessary to search for new selective  $\alpha_1$ -adrenoceptor antagonists with a well identified pharmacological pro-

file. Analysis of a number of chemical structures of selective  $\alpha_1$ -adrenoceptor antagonists indicates that the majority of active compounds possess arylpiperazine moieties. Thus, we synthesized and tested a 5-arylidenehydantoin derivative with phenylpiperazine moiety, designated as RW-11b, in order to find new selective  $\alpha_1$ -adrenoceptor antagonists. The compound was evaluated on its affinity for  $\alpha_1$ -adrenoceptors in radioligand binding assays ( $K_i = 23$  nM). Since it contains an asymmetric carbon atom, the racemic mixture as well as both enantiomers (R+ and S-) were tested. The antagonistic properties at  $\alpha_1$ -adrenoceptor subtypes were assessed in functional bioassays. It turned out to be the competitive antagonist of  $\alpha_1$ -adrenoceptors with stronger activity at  $\alpha_{1D}$  and  $\alpha_{1A}$  and weaker at  $\alpha_{1B}$  subtype of  $\alpha_1$ -adrenoceptors with no significant differences between racemic mixture and two enantiomers.

## Determination of the molecular mechanism of action of *Epilobium angustifolium* and *Serenoa repens* extracts in enlarged rats prostates – a preliminary study

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In the study we have assessed changes in mRNA expression profile of 5 $\alpha$ -reductase 1 (5 $\alpha$ r1) and 2 (5 $\alpha$ r2) isoenzymes, and signal transduction Mapk3 and RafA kinases in the ventral lobes of the testosterone in-

duced rats prostates under the influence of water extract from *Epilobium angustifolium* and a lipid-sterolic extract from *Serenoa repens* (recommended for BPH treatment).