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Novel 1-(2- Methoxyphenyl)-4-[3-Aryloxy-2-Hydroxypropyl]-Piperazine Derivatives and Their Block Effects on α_1-Adrenoceptor Subtypes

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SUMMARY. Two novel 1-(2-methoxyphenyl)-4-[3-aryloxy-2-hydroxypropyl]-piperazine derivatives (**5** and **8**) and their respective enantiomers were synthesized and biologically tested. Their structures were characterized by ^{1}H NMR, ^{13}C NMR and MS. These compounds were evaluated for their blocking activity and selectivity toward α_{1A}, α_{1B}, and α_{1D}-adrenoceptors. Biological assays *in vitro* indicated that **5** and **9** showed a preferential antagonist profile for α_{1D} and α_{1A}-adrenoceptor than for α_{1B}, which might have improved uro-selectivity compared to the known potent $\alpha_{1D/A}$ antagonist drug naftopidil **1**. It was also found that different configurations exhibited different biological activities and subtype selectivities.

RESUMEN. Dos novedosos derivados de 1-(2-metoxifenil)-4-[3-hidroxipropil-ariloxi-2]-piperazina (**5** y **8**) y sus respectivos enantiómeros fueron sintetizados y probados biológicamente. Sus estructuras se caracterizaron por ^{1}H NMR, ^{13}C NMR y MS. Estos compuestos fueron evaluados para su actividad de bloqueo y la selectividad hacia α_{1A}, α_{1B}, y α_{1D}-adrenoceptores. Los ensayos biológicos *in vitro* mostraron que los derivados **5** y **9** tenían un perfil antagonista preferencial por α_{1D} y α_{1A} más que por , α_{1B}, que podrían haber mejorado la uro-selectividad en comparación con el potente antagonista conocido naftopidil **1**. También se encontró que las diferentes configuraciones exhibieron diferentes actividades biológicas y selectividades de subtipo.

KEY WORDS: α_1-adrenoceptor subtypes, Benign prostatic hyperplasia, Piperazine derivatives.

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