عنوان مقاله:

Synthesis, Evaluation of Vasorelaxant Activity, and Molecular Docking of Pyranopyrazole Derivatives as Calcium Channel Blockers

محل انتشار:

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خلاصه مقاله:

Pyranopyrazole analogs are novel synthetic compounds with many biological activities. In this research,we synthesized six new pyranopyrazole derivatives using a biocompatible catalyst and evaluated their vasorelaxant and calcium channel binding properties in isolated rat thoracic aorta. Male Sprague-Dawley rats (n=۴۲) were used. The thoracic aorta was isolated and divided into four ۴ mm rings. Each ring was connected to a pressure transducer and a hook in an organ bath. The rings were treated with KCl (۴۰ mM) solution and the increased contractions were recorded. After washing out and maintaining the baseline tension, the tissues were pre-incubated with different concentrations of nifedipine (۱۰-۱۰ to ۱۰-۶ M) or each of the synthetic compounds (۱۰-۹ to ۱۰-۵ M) for ۲۰ minutes, and exposed once again with KCl (۴۰ mM). The concentration-response curves were plotted and their pIC۵۰ (negative logarithm of the required concentrations of compounds to achieve half-maximal relaxation) and Rmax (percent of compounds-evoked maximum relaxation) were calculated. Molecular docking studies were carried out using AutoDock software. Homology modeling was done to make the human Cav۱.۲ (hCav۱.۲) protein pdb file. The results showed that all compounds sat efficiently in the calcium channel active site. Also, we found that all compounds (except compound ۶) significantly attenuated the KCl-induced contractions of isolated aorta rings in a concentration-dependent manner, although not as potent as nifedipine. Data were analyzed using one-way analysis of variance (ANOVA) followed by

Tukey’s test. In conclusion, most of our new pyranopyrazole analogs showed vasorelaxant and calcium channel .blocking activities and could be good candidates for further investigations to develop new antihypertensive drugs

کلمات کلیدی:

Pyranopyrazoles, Heterogeneous catalyst, molecular docking, vasorelaxant, Calcium channel blockers