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P24. EXPLORATION OF THE RELATIONSHIP BETWEEN LIPOPHILICITY AND RESIDENCE TIME IN 5-HT7 RECEPTOR LIGANDS

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The 5-HT7 receptor is a G protein-coupled receptor (GPCR), activated by the neurotransmitter serotonin (5-hydroxytryptamine, 5-HT). It is involved in many physiological events such aslearning and memory, but also in neurological and neurodevelopmental disorders such asFragile X syndrome, the most common form of inherited intellectual disability, and autistic spectrum disorder. The molecular bases of these diseases are unknown, so it is important to study the pharmacology of 5-HT7 through the development of selective drugs, such as N-(4-cyanophenylmethyl)-4-(2-diphenyl)-1-piperazinehexanamide (LP-211), a brain penetrant and selective 5-HT7receptor agonist. Previous studies showed that, when LP-211 was pre-bound to the 5-HT7 receptor, it remains strongly bound to it. The same experiment, performed using an analogue of LP-211, showed a different result, suggesting that the residence time of these 5-HT7 receptor ligands is structuredependent. Based on preliminary results, we hypothesized that the residence time of this class of compounds can be related to the lipophilicity of the molecule. To test this hypothesis, we have studied the residence time of a series of 5-HT7 ligands characterized by different lipophilic properties (clogP).