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Synthesis and Preliminary Pharmacological Evaluation of Methoxilated Indoles with Possible Dopaminergic Central Action

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SUMMARY. Compounds **5-7** were synthesized from 4-tetralones with o-iodoanilines by a radical nucleophilic substitution or SRN1 reaction, and were pharmacologically evaluated in order to establish their possible antagonistic action on the central dopaminergic receptors. Behavioural parameters, such as stereotypy in rats were measured after intracerebroventricular administration of these compounds at doses of 10 μg/5 μL. Our results demonstrate that compounds **5-7** do not affect stereotypy behaviour. However, they inhibit the apomorphine-induced stereotypy behaviour, suggesting the involvement of the central dopaminergic system. Also we observe that there is a concordance between the behavioural profiles induced by our compounds and those reported for clozapine **8** and ziprasidone **9**. It is plausible to suggest that compounds **5-7** could be acting as potential atypical antipsychotic agents. Quantum calculations performed on the basis of a comparative conformational study of their structures indicate a stereoelectronic similarity between the basic nuclei of compounds **4** and **5-7**. In addition Molecular Dynamics (MD) simulations performed on compounds **5-7** at the binding site of dopamine D_2 receptor suggest that these compounds could interact with the human D_2 dopamine receptors.

KEY WORDS: Antagonists, Dopaminergic receptors, Neurotransmitters, Quantum calculations, $S_{RN}1$ Reactions.

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