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Synthesis of some novel butyrophenone substituted azasteroids and evaluation of antipsychotic activity

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The present study is undertaken to investigate the pharmacological activities of azasteroids, in which the nitrogen is present as heteroatom, also had medicinal importance. Haloperidol has been taken as lead with an aim to have more active azasteroidal antipsychotic agents, certain novel analogues of haloperidol have been synthesized, the major approach implied in present study is to synthesize azasteroidal butyrophenone, in which butyrophenone is attached to the 6 position of azacholesterol, 17a position of azaandrostenolone ring, and 4 position of azaandrostan. In present study the 17a-[3' –(p-flourobenzoyl) propyl]-17 a-aza-D-homo-5-androstan-3β-ol,4-[3'-(p-flourobenzoyl)propyl]-4-aza-5a-androstan-17β-ol,6-[3'-(p-flourobenzoyl)propyl]-6-aza-5a-cholesterol drugs are found to be effective antipsychotics. Compound 1 and Compound 2 show activity comparable to haloperidol. The observed behaviour alterations may be due to dopaminergic supersensitivity in nigrostriatal structure. The present study demonstrated that the administration of 17 a-[3'-p-flourobenzoyl) propyl]-17a-aza-D-homo-5-androstan-3β-ol,4-[3'-(p-flourobenzoyl)propyl]-4-aza-5α-androstan-7βol, 6-[3'-(p-flourobenzoyl)propyl]-6-aza-5α-cholesterol did not aggravate extrapyramidal side effects as compared to Haloperidol. This may be due to its possible affinities for 5-HT receptors. Furthermore neurosteroids are specific mediator of GABAA receptor which regulates the neuronal activity through diverse neurotransmitter mechanism. These neuroactive steroids after neuronal excitability by modulating the activity of several neurotransmitter receptors and thus can influence behaviour.

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