

Section-III



Chapter-2
RESEARCH
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Dopamine is an endogenous neurotransmitter in the CNS mediating its action via different receptor subtypes which are mainly grouped into two families namely D₁ like and D₂ like family. D₁ like family comprises of D₁ and D₅ receptors while D₂ like family comprises D₂, D₃ and D₄ receptors. Some evidence indicates the existence of D₆ and D₇ receptors also but it is not convincing yet. All the dopamine receptor subtypes are the members of the G protein coupled receptor super family. The D₁ like family is coupled to G_{αs} which upon agonism leads to increased cAMP level while D₂ like family is coupled to G_{αi/o} that results in decreased cAMP level on agonism [55].

Central dopamine receptors are believed to play an important role in the regulation of voluntary movement, feeding, reward, sleep, attention, motivation, memory and learning. Several fused ring systems have been synthesized to evaluate dopamine agonistic activity in the literature for example benzazepines and quinazolines. Keeping this in mind a series of compounds have been synthesized in the Pharmaceutical Chemistry laboratory that were planned to be evaluated pharmacologically for D₁ receptor agonistic potential, with the following objectives in mind.

1. To standardize *in vitro* experiments for assessment of D₁, D₂ and D₃ receptors agonists/antagonists using isolated rat mesenteric artery preparation.
2. To screen the newly synthesized compounds for their D₁ receptor agonistic potentials using isolated rat mesenteric artery preparation.
3. To assess the safety profile of selected potent compounds using OECD guideline.
4. To assess the selected potent compounds using stereotaxic surgery-induced Parkinson's rat model.
5. To evaluate the neurochemical parameters using tissue homogenates.
6. To evaluate the selected compounds for anti-apoptotic property using immunohistochemistry.
7. To estimate neurotransmitter (dopamine) levels in brains of rat dosed with the test compounds or standard drug using high performance liquid chromatography (HPLC)-ECD.