Dr. Wilder Penfield was a Canadian neurosurgeon. He came across a female patient having epilepsy. He conducted surgery on the brain of the patient. He stimulated various points of cerebral cortex with the help of mild electric current. To his surprise on stimulation of certain points the patient started recalling details of incidents that had occurred years before. She could recall that she was in kitchen calling her son. She had also described all details like accompanying noises, kitchen arrangement as if the incident was brought alive to her. The final opinion was that without the electric stimulation given to parts of cerebral cortex the woman would never have recalled the incident. He came to a conclusion that brain and psychological lives are intimately connected.
OBJECTIVE OF THE STUDY:

From our preliminary studies it was concluded that some compounds among twelve compounds synthesized for the screening of anticonvulsant activity possess significant protection against strychnine-induced convulsions in albino mice. From the literature it was found that the compounds which showed activity in the strychnine model possess significant anxiolytic activity. This property has paved the way for the screening of these compounds for antianxiety and antipsychotic behavioral models.

Our prime objective of the study was to identify the molecules which possess anxiolytic and antipsychotic activity among the selected succinimide mannich bases in the doses selected for these activities.

Synthesizing selected mannich bases of succinimide and characterization of the compounds by means of physical (mp and TLC) and spectroscopical methods.

Screening of the compounds for assessing general CNS behavior by means of Gross CNS behavior, Rotarod test for motor coordination, Pentobarbital induced hypnosis and locomotor activity.

Screening of the compounds for anxiolytic activity by using different behavioral models such as Elevated plus-maze method, Staircase model, Light and dark model and Foot-shock induced aggression in mice.

Screening of the compounds for antipsychotic activity by using different behavioral models such as Condition avoidance response by pole climbing apparatus and Apomorphine induced climbing behavior models.
Rationale behind the selection of Succinimide Mannich Bases:

Although the succinimide molecule itself doesn’t possess any marked biological activity, the substituted succinimide derivatives possess a vast variety of pharmacological activities in the biological system. The approved succinimide derivatives such as Ethosuximide, Methosuximide and Phensuximide against petitmal type of epilepsy are of the examples. The latest drug of this kind is an anti-anxiety drug Sunepitron, which acts on 5HT-1A auto receptors as an agonist to produce anxiolytic activity. All those active anticonvulsants possess either an alkylating group in the 2nd position or N-methyl substitution for delivering a better activity. Chen and Bass et al (1964) concluded that CNS depressant activity might be a property of succinimide nucleus after their work on 3-ethyl-2-methyl phenyl succinimide. The majority of works done so far were concentrated only on its anti-convulsant activities. So, in an attempt we have synthesized a series of succinimide mannich bases with different secondary amines to study their beneficial neuropharmacological effects.

After preliminary investigation of these succinimide mannich bases on various anticonvulsant models such as Maximal electroshock seizure (MES), Maximal Metrazole seizures (MMS) and Strychnine-induced convulsions, we have found that the synthesized compounds were not active in MES and MMS models. But, on strychnine induced convulsions, a few succinimide derivatives showed promising activity in reversing the effect of strychnine (4mg/kg) given intraperitoneally and protected the animal completely from strychnine toxicity even after 24 hr observation. The convulsant action of strychnine is due to interference with postsynaptic inhibition mediated by glycine. Glycine is an important inhibitory transmitter to motoneurons and interneurons in the spinal cord and strychnine acts as a selective, competitive antagonist to block the inhibitory effect of glycine receptors. Strychnine sensitive postsynaptic inhibition in higher centers of the CNS is also mediated by glycine. Compounds that reverse the action of strychnine have been shown to possess anxiolytic properties.
Further, a survey of literature shows that except for small alkyl substitution not much attention has been paid to N-substitution. Therefore, it was thought worthwhile to study N-substituted succinimide derivatives for their psychopharmacological activities with a special reference to CNS depressant activities such as anxiolytic and neuroleptic activities.

The compounds which exerted activity against strychnine induced convulsions have some structural similarities. The compounds which showed the activity have methyl group either on the nitrogen of the secondary amine involved in the reaction or on the branched aliphatic side chain or on the aromatic ring attached to the secondary amine. This interesting fact has been supported by the work done by G.B. Singh. This also forms a basis for the selection of the four succinimide manich bases for the evaluation of CNS depressant activities in the present study.