CHAPTER-1
INTRODUCTION

1.1. Neuropsychopharmacology

Neuropsychopharmacology is an interdisciplinary science consisting of psychopharmacology (effects of drug on mind) and neurosciences. The term Neuropsychopharmacology is originated from Greek word (neuro; nerve, pharmakon; drug action and logia; study). It focuses mainly on neurological disorders and its pathogenesis, drug action and level of awareness (Lopez-Munoz and Alamo, 2009).

Developments in neuropsychopharmacology have direct impact on the studies pertaining to, affective disorders, psychotic disorders, anxiety disorders, neurodegenerative disorders (Parkinson and Alzheimer’s), eating and sleeping behavior (Lopez-Munoz and Alamo, 2009). During the year 2007, World Health Organization (WHO) have reported that neuropsychiatric disorders affect people of all origin, irrespective of their age, sex, education or income and about 6.8 million people die every year due to neurological disorders.

Anxiety affects one-eighth of the world population and gained research significance in the area of psychopharmacology during the last decade (Cha et al., 2004). Anxiety can be defined as a constant and extreme or unreasonable fear that significantly interferes with everyday life (Cryan et al., 2005). Benzodiazepines (BZDs) are the main classes of anxiolytic drugs which cause side effects such as sedation, blurring vision, nausea and dry mouth (Lader and Morton, 1991).

Depression is a persistent mental disability clinically characterized by pervasive low mood, loss of hope and lack of interest in daily activities with high mode of inferiority complex and high risk of suicidal tendency (Perahia et al., 2009). It is an important universal public-health issue with high lifetime prevalence ranging from 2 to 15% (Moussavi et al., 2007). Antidepressant therapies include
drugs with exceptional structural chemical diversity and most of them increase monoaminergic neurotransmission. Although majority of the antidepressant drugs ameliorate depressive symptoms, they also cause multiple unwanted side effects like sleeping disturbances, dry mouth, addiction etc., and unfortunately 30% of depressive patients do not react appropriately to the first-line treatment (Fava and Rush, 2006).

Dementia is a syndrome that leads to memory impairment, affects thinking behavior and also leads to difficult in performing everyday chores. World Health Organisation (2010) have estimated that the number of people living with dementia worldwide to be 35.6 million and thus it is expected to double by 2030 and would rapidly increase by 2050. Nootropic drugs (piracetam, vinpocetine) are mainly available in the market for cognitive impairment which ultimately causes undesirable side effects (Keim et al., 2004).

Parkinson’s disease (PD) is a long term, progressive, neurodegenerative disorder with an estimated prevalence of 31 to 328/100,000 people worldwide i.e., approximately more than 1% of the population over 65 years of age are affected with PD (Pradeep and Venkataraman, 2012). There have been noteworthy advances in PD therapy including surgical and pharmacological interventions. Though, levodopa is considered as the best standard drug for treatment of PD, numerous complications such as motor fluctuations, hallucinations, and psychosis has resulted from its long-term therapy (NCCC, 2006).

Due to the undesirable side effects exhibited by synthetic drugs, investigations for more efficient and well-tolerated drugs from plant resources are need of the hour. The need for the discovery and development of new pharmaceuticals for the treatment of neurological disorders demands that all approaches towards drug discovery be exploited. The promising approaches are the use of natural products that have many distinctive and vital contributions to drug discovery (Newman et al., 2003). Recently scientists have focused on either
flavonoidal phytoconstituents or flavonoid enriched extracts that possess neuroprotective effects (Vauzour et al., 2000).

1.2. Medicinal plants as novel therapeutics

Identification and characterization of novel medicinal plants to cure neurodegenerative diseases have increased the interest of scientific community in recent years. Approximately there are about 120 traditional medicines that are being used for the therapy of Central Nervous System (CNS) disorders in Asia. In the Indian system of medicine the following medicinal plants have shown promising activity in neuropsychopharmacology: Allium sativum (garlic), Bacopa monniera (bhringi), Centella asiatica (gota kola-vallarai), Celastrus paniculatus (Black Oil plant), Nicotiana tabaccum (tobacco), Withania somnifera (aswagandhdha-Indian ginseng), Ricinus communis (castor oil plant), Salvia officinalis (sage), Ginkgo biloba (maidenhair tree), Huperiza serrata (tassel ferns), Angelica sinensis (female ginseng), Uncaria tomentosa (cat’s claw), Hypericum perforatum (St. John’s Wort), Physostigma venosum (Calabear bean), Acorus calamus (sweet flag), Curcuma longa (turmeric), Terminalia chebula (myrobalan), Crocus sativus (saffron), Enhydra fluctuans (helencha), Valeriana wallichii (Amantilla), Glycyrrhiza glabra (liquorice) and so on (Kumar et al., 2006)

Valeriana officinalis (Hattesohl et al., 2008; Benke et al., 2009), Piper methysticum (Sarris, 2007), Passiflora spp (Dhawan et al., 2001; Grundmann et al., 2009) are well to treat anxiety disorders. Hypericum perforatum (Rahimi et al., 2009; Kasper et al., 2008), Celastrus paniculatus (Nalini et al., 1995; Rekha and Dhingra, 2014), Crocus sativus (Akhondzadeh et al., 2004) have performed well in treating mild to moderate depression. Among these, H. perforatum was commercially accepted as an antidepressant agent for clinical purposes. Bacopa monniera (Das et al., 2002) and Centella asiatica (Veerakumar and Gupta, 2002) plants are well known nootropic agents widely used for the treatment of dementia. Likewise, Mucuna pruines (Manyam et al., 2004) and Ocimum sanctum
(Pemminati et al., 2007) species are specifically used in the treatment of Parkinson’s disease.

*Hypericum hookerianum* is a small woody yellow flowered shrub found in India which is commonly known as the golden lotus of *H. perforatum*. These *Hypericum* species are mainly used for the treatment of neurodegenerative diseases. Different extracts of *H. hookerianum* have been reported to possess wound healing (Mukherjee and Suresh, 2000), antibacterial (Mukherjee et al., 2001), antitumor (Dongre et al., 2007) and antiviral (Vijayan et al., 2010) properties.

Therefore, the present study was designed to evaluate the neuropsychopharmacological effects of *H. hookerianum* (aerial parts) in Swiss Albino mice. The mechanism of therapeutic effects of *H. hookerianum* suggests that this particular species can be used as alternative therapy for treating neurological disorders like anxiety, depression, amnesia and parkinson.

The scope of the present study is to analyze the neuropsychopharmacological activities of *H. hookerianum* in animal models and to formulate the novel pharmacotherapeutic agents to treat psychiatric and mental disorders.

### 1.3. Objectives of the study

The present work mainly focuses on the neurotherapeutic like effects of *H. hookerianum* in stress (physiological) and neuroleptic (reserpine, scopolamine, and haloperidol) induced neurological disorders with the following objectives.

- To perform physico-chemical analysis of *H. hookerianum* and phytochemical analysis of ethanolic extract of *H. hookerianum* (EEHh) and its acid hydrolyzed glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh).
- To analyze the neuropsychopharmacological (anxiolytic, antidepressant, antiamnesic and antiparkinson) like effects of ethanolic extract of *H. hookerianum* (EEHh) and its acid hydrolyzed glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh).
1.4. Work design

The working pattern of this study was tested by various experiments which was divided into following chapters:

- Physico-chemical analysis of *H. hookerianum*, phytochemical analysis of ethanolic extract of *H. hookerianum* (EEHh), separation of enriched glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh) from EEHh and *in vitro* antioxidant potential of EEHh and GFHh
- Anxiolytic like activity of ethanolic extract of *H. hookerianum* (EEHh) and glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh) in stress induced Swiss Albino mice.
- Antidepressant like effect of ethanolic extract of *H. hookerianum* (EEHh) and glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh) in reserpine induced Swiss Albino mice.
- Antiamnesic like effect of ethanolic extract of *H. hookerianum* (EEHh) and glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh) in scopolamine induced Swiss Albino mice.
- Antiparkinson like effect of ethanolic extract of *H. hookerianum* (EEHh) and glycosidic flavonoid enriched extract of *H. hookerianum* (GFHh) in haloperidol induced Swiss Albino mice.