Abstract

Central nervous system disorders are the psychological or behavioral pattern that occur in an individual and are thought to cause distress or disability that is not expected as part of normal development. Central nervous system disorders are characterized by alterations in thinking; mood or behavior (or some combination thereof) associated with significant distress and impaired functioning over an extended period of time. Drugs that influence brain function have long been essential to medical practice. Because of the importance of brain in normal physiological and psychological functions, the actions of centrally acting drugs are diverse. Drugs acting on CNS induce anesthesia, relieve pain and fever, prevent or modify seizures, induce sleep, reduce anxiety and ameliorate symptoms of major mental illness.

Currently, importance of natural products is being revitalized to alleviate various health discrepancies. Phytochemicals in diet could provide protection against several threats like free radical formation, degenerative disorders and lifestyle related diseases but still role of array of active ingredients should be unveiled.

In today’s life, stress, strain, sedentary life style, obesity, lack of physical work and environmental pollution are becoming crucial factors in the genesis and progression of variety of CNS diseases and disorders ranging from depression, mania, anxiety, psychosis, epileptic seizures, dementia, Parkinson’s and Alzheimer’s diseases. Various neurotransmitters play important role in brain functions. Serotonin and noradrenaline influence mental behavior patterns. Dopamine is involved in movements while acetylcholine in memory and learning. These substances are fundamental to normal brain functions. For this reason they have been center of neuroscientific study for many years. In the process of the study, new understanding has been gained of the neurochemistry of several important mental health disorders, especially schizophrenia, depression, anxiety as well as epilepsy.

Despite several advances in the health care system, numerous new diseases have emerged. Considering the inherent weakness and limitations, allopathy by itself could not tackle the plethora of problem posed by emergence of new diseases. Many newer drugs which have developed recently represent a real progress in the treatment of non responders and refractory patients. However, the problem of adverse effects has also not been circumvented completely. Hence, search should continue to develop newer, more effective and safer neuroprotective agents for the treatment of various CNS disorders. In search for new therapeutic agents for the treatment of CNS disorders, medicinal plant research, worldwide has progressed constantly, demonstrating the pharmacological effectiveness of different plant species in a variety of animal models.

Several medicinal plants are known to posses neuroprotective properties in ancient system of medicine and may be used clinically. However there is paucity of scientific data regarding their effects on nervous system disorders, therefore the present study was undertaken to carry out likely psychotropic and anxiolytic potential of Amaranthus spinosus, Brassica nigra and Annona squamosa extracts and selected fractions of most potential extract.
The leaves of *Amaranthus spinosus* and seeds of *Brassica nigra* successively extracted with different solvent to obtain extracts (ASL-PE, ASL-CH, ASL-AC, ASL-ME, BNS-PE, BNS-CH, BNS-AC, BNS-ET) while *Annona squamosa* fruit pulp extracted with methanol using maceration process to obtain methanol extract (ASP-ME). Further *Amaranthus spinosus* methanol extract and *Brassica nigra* ethanol extract were exhaustively fractionate with the help of soxhlet apparatus to obtain various fraction (ASL-PEF, ASL-CHF, ASL-ACF, ASL-EAF, BNS-PEF, BNS-CHF, BNS-ACF, BNS-EAF); and were subjected to chemical identification.

Preliminary physical phytochemical tests showed presence of flavonoids, alkaloids, glycosides, tannins, and saponins in most of extracts of *Annona squamosa* and extracts of *Brassica nigra* while flavonoids, glycosides, tannins, and saponins in methanol extract of *Amaranthus spinosus*. Further, tests for presence of phytoconstituents in fractions of *Brassica nigra* and of *Amaranthus spinosus* was carried out.

Presence of phytoconstituents was ratified with the help of TLC fingerprinting profile of extracts and of fractions shown presence of flavonoids, saponins, as well as tannins while HPLC fingerprinting confirmed presence of bioactive phytoconstituents showing same retention time as that of standard caffeic acid (3.875), gallic acid (3.830), quercetin (5.760) and rutin (3.820) and standardized using spectrophotometric methods. Fingerprinting profile of plant extracts and fractions confirmed presence of flavonoids as well as polyphenols.

Test extracts and fractions were screened for pharmacological profile using both *in vitro* and *in vivo* methods. Antioxidant profile (*in vitro*) was screened in terms of DPPH scavenging (% DPPH scavenging and % RRI of DPPH) and compared with standard antioxidant ascorbic acid.

All the extracts and fractions were exhibited reduction of pink colored free radical 2, 2-diphenyl-1-picrylhydrazyl (DPPH) to the yellow-colored diphenyl picryl hydrazine at varied extents which was measured as absorbance and calculated as percent inhibition. The percent DPPH scavenging activity possessed by standard antioxidant ascorbic acid, extracts and fractions at the concentration (150 and 40 µg/ml) respectively. ASL-ME BNS-ET, ASP-ME, ASL-EAF and BNS-ACF exhibited better antioxidant activity than the other ASL, BNS, ASP, ASL-ME and BNS-ET extracts and fractions.

Evaluation of % RRI of DPPH helps to measure the ability of test extracts and fractions to scavenge radicals at different time interval suggesting the ability of ASL-ME, BNS-ET, ASP-ME, ASL-EAF and BNS-ACF to scavenge the free radical and protecting biological component from invading action for longer duration as compared to other extracts.

The acute and sub-acute toxicity studies of methanol extract of *Amaranthus spinosus*, ethanol extract of *Brassica nigra* and methanol extract of *Annona squamosa* were performed according to OECD guidelines and LD₅₀ was determined. Further various behavioral, physiological, hematological, biochemical and morphological parameters were studied. The acute and sub-
acute oral administration of *Amaranthus spinosus*, *Brassica nigra* and *Annona squamosa* did not induce significant alterations in almost all biochemical, hematological and morphological parameters. Thus the methanol extract of *Amaranthus spinosus*, ethanol extract of *Brassica nigra* and methanol extract of *Annona squamosa* was found to be safe in acute and sub-acute toxicities in experimental animals.

The effect of extracts and fractions was studied on various *in vitro* preparations to assess its effect on various receptors and neurotransmitters. The result of the *in vitro* test indicates that extracts and fractions inhibited dopamine and serotonin induced contractions and potentiated acetylcholine-induced contractions.

Based on the results of the *in vitro* studies, the effect of extracts and fractions was studied in several behavioral animal models like elevated plus maze and light/dark paradigm for its anxiolytic property, forced swim test (FST), tail suspension test (TST) for anti-depressant effect, PTZ induced convulsion for its anticonvulsant potential, Haloperidol-induced catalepsy along with lithium sulphate-induced head twitch for its antipsychotic activity and foot shock-induced aggression for anti-aggression activity for neuropharmacological properties.

Earlier reports of chemical constituents and their pharmacology suggest that the plants containing flavonoids, alkaloids, saponins, tannins possess activity against many CNS disorders. It is possible that the presence of these chemical constituents may be responsible for diverse neuropharmacological effects of *Brassica nigra*, *Amaranthus spinosus* and *Annona squamosa*.

The plant *Brassica nigra*, *Amaranthus spinosus* and *Annona squamosa* showed a promising neuropharmacological and neuroprotective potential in various experimental models. The activity data generated in this study could help to explore these plants and set a new therapeutic strategy in the treatment of various central nervous system disorders. The results obtained in this study could also help to set a new research goals and strategies in the area of neuropharmacology and plant drug research. Further, there is a need to separate and identify individual chemical constituents; and to study their mechanism of action at molecular level.