

## Preface

---

Type-2 diabetes mellitus has become a significant health problem in both developed and developing countries. Worldwide prevalence of diabetes mellitus is expected to increase from 382 million people in 2013 to 592 million by 2035. Type-2 diabetes has been associated with various co-morbidities including central nervous system (CNS) disorders such as depression, anxiety, cognitive dysfunctions, and neuropathic pain and inflammation. Numerous structural, behavioural, and biochemical alterations of the CNS are observed in diabetic patients and in rodent models of diabetes. Treating these problems however remains a challenging field in medical science. Unfortunately, most of the currently available psychoactive drugs do not meet the therapeutic demands of diabetic patients and many of them are even contraindicated for patients with diabetes. Ayurvedic methods of treating psychiatric disorders such as depression, anxiety and memory impairments are gentle, natural and effective. Ayurveda offers a more effective treatment for psychiatric disorders without side effects and the real possibility of prevention. Ayurvedic methods not only increase the balance in the body, they also progressively raise the overall level of inner contentment. *Andrographis paniculata* (Burm. F.) Wall. Ex Nees is a traditionally known Ayurvedic medicinal plant of Acanthaceae family, and andrographolide (labdane diterpinoid) is quantitatively the major bioactive secondary metabolite of the plant identified to date. Although some leads have been taken by researchers to investigate the well-known effects of *Andrographis paniculata* extract and its secondary metabolites on liver functions, systemic inflammations as well as therapeutically indicated for management of common cold and relief from Flu-like symptoms. Extensive preclinical as well as clinical efforts made during past few decades have identified broad spectrums of therapeutically interesting pharmacological properties of diverse types of *Andrographis paniculata* extracts, andrographolide and other structurally unique bioactive constituents of such extracts. However, little attention was paid on its potential effects on CNS, till date there is no comprehensive scientifically validated study available for co-morbid brain disorders, rather only few

scattered and less systematic evaluation studies are explored in past two decades about the effect of this plant having CNS modulating activities. Although, several publications have mentioned that *Andrographis paniculata* is an adaptogenic herb, classified as Rasayana herb in Ayurveda, and it is often included as an active ingredient in numerous currently commercialized Ayurvedic formulations. Many Ayurvedic Rasayana herbs have been reported to possess anti-depressant, anxiolytic, cognitive function improving and diverse other CNS-function modulating activities. Keeping in mind, the encouraging leads and the limited data regarding the use of *Andrographis paniculata* in treating neurological disorders, present study was conducted to fully exploit the potential of *Andrographis paniculata* in this promising area. The present research work encompasses neuropsychopharmacological studies of standardised hydro-methanolic extract of *Andrographis paniculata* and isolated pure andrographolide in nondiabetic rodents, on co-morbid CNS disorders generally associated with type-2 diabetes as well as neurological effects during stressful conditions using validated behavioural models of rodents followed by elucidation of mechanism(s) of observed action(s) through biochemical estimations. In addition to neuropsychopharmacological studies, cell-line toxicity and molecular studies were also performed in order to establish molecular mechanism(s). Observations made during such efforts strongly suggest that like other well-known adaptogenic Rasayana herbs, *Andrographis paniculata* extract and its major active secondary metabolite andrographolide could as well be a therapeutic option for combating mental health problems commonly associated with diverse non-communicable diseases. However, further efforts to identify the roles of diverse other known bioactive secondary metabolites of the plant are necessary for understanding its Ayurvedic pharmacology.

