PREFACE

The thesis evaluates the pharmacological effect of drugs in the comorbid condition of type-2 diabetes mellitus (T2DM) and post-traumatic stress disorder (PTSD) in the experimental animals. Diabetes mellitus is the leading metabolic epidemic and is prevalent in developed and developing countries. However, a majority of the patients belong to the T2DM class. Co-morbid mental disorders may have effect on medical outcomes of patients who have diabetes which gains critical attention now-a-days. Recently, it has been reported that an exponential growth in T2DM is observed among young work force due to changes in life style. Further, it has been documented that the psycho-social disorder due to a chronic low level stress, increases the prevalence of T2DM apart from other predisposing factors. The PTSD constitutes second largest population among diabetic biome. The pandemic is a specific anxiety disorder with estimated lifetime prevalence of about 7–25 % in the general population (depending on gender of victim, type of trauma and study methodology) and of 15–31 % in war veteran samples. PTSD patients may be particularly vulnerable to T2DM. Behavioral perspective study speculates the fact that PTSD can be related to the unhealthy lifestyle that lead to obesity and diabetes, such as smoking, lack of exercise, over-eating and alcohol consumption. Further, it has been reported that PTSD is associated with increased risk of diabetes. Therefore, it can be presumed that there exist a strong association between T2DM and PTSD.

T2DM is a complex, chronic metabolic disorder predominantly associated with insulin resistance in several tissues including liver, pancreas and brain. There are several energy signaling pathways such as TGF-β/Smad3, phophatidylinositol-3-kinase (PI3K)/Akt, AMP-activated protein kinase (AMPK) and many more which are responsible for insulin resistance in the tissues. Further, it has been reported that mitochondria and this signaling pathway are

interlinked in several disorders. Recent data documents that PI3K/Akt signaling pathway is strongly associated in the pathobiology of PTSD, indicating the fact the PI3K/Akt signaling pathway may be common to the pathophysiology of T2DM and PTSD. Moreover, this signaling pathway is not clearly elaborated in either of these conditions. It is documented that gamma-amino butyric acid (GABA)-A receptor activity is interlinked with the insulin sensitivity in the diabetic condition, but how this receptor modulates this signaling pathway is still a challenge in the pharmacotherapy of T2DM. Recent data suggests that PI3K/Akt signaling pathway interacts with serotonergic system in several stress conditions including PTSD. However, the detailed mechanism is yet to be explained in the pathophysiology of such co-occurring condition of T2DM and PTSD.

Taking into consideration the golden rule in therapeutics that treatment of the cause is better than the effect, we hypothesize that mitochondria whose function is altered both in PTSD and T2DM is the common substrate, whose modulation can result in effective treatment of such co-occurring condition. Hence, the following chapters were structured for the thesis to achieve a conclusion in the pharmacological investigation of drugs in the comorbid condition of T2DM and PTSD in the experimental animals. The first chapter describes a brief introduction to the thesis work with a layout of working hypothesis. The subsequent nine chapters constitute the introduction, materials and methods, results and discussion based on specific objectives of the thesis. The eleventh chapter provides a summary to the whole experimental work followed by bibliography of the thesis as twelfth chapter. A brief explanation to the following chapters is as follows: