PREFACE

An epileptic seizure is a transient occurrence of symptoms due to abnormal excessive or synchronous neuronal activity in the brain. According to the WHO, epilepsy affects around 50 million people worldwide and majority of the epileptic patient are found in the developing regions. It is the most common brain disorder worldwide with no age, racial, social class, national or geographic boundaries. Understanding the causes of epilepsy is essential both for the management and discovery of target–specific anticonvulsant drugs. Anticonvulsant drug therapy is the primary line of treatment to control epileptic seizure.

Pathological disturbances related to glutamatergic neurotransmission results in excitotoxicity and generate epileptic seizures. The decade long understanding of the structure and function of excitatory glutamatergic neurotransmission have paved the way for the developments of a number of prospective anticonvulsants. Among the primary glutamate receptors exemplified by NMDA, AMPA and KA receptors, it has been reported that drugs acting as an AMPA receptor antagonist showed promising anticonvulsant activity

The research work encompasses the design, synthesis, pharmacological evaluation and molecular modelling study of quinazolin–4(3*H*)–ones as potential anticonvulsant agents. The work was based around the idea that the receptors involved in glutamatergic neurotransmission are responsible for fast excitatory neurotransmission and molecules that block the excitation mediated by glutamate receptors provide protection against seizures. Therefore, the designed molecules were tested against various conventional seizure models including an attempt to evaluate their activity against AMPA induced seizure. The computational studies have been carried out to predict the pharmacokinetic parameters and probable binding mode of the designed molecules at the AMPA receptor site. To date, this work has led to the publication of a review article, two research papers and two presentations. Suggestions and comments on the part of the readers are always welcome. The entire thesis has been divided into seven chapters as follows:

Chapter-1: The first chapter offers an introductory part which deals with a brief account on modern drug discovery and includes basic information about epilepsy and its management.

Chapter-2: This chapter is focused on detailed literature survey of AMPA receptor antagonist with particular emphasis on the anticonvulsant activity of quinazoline derivatives.

Chapter-3: This chapter summarizes the research objectives, the overall rationale for carrying out this research and plan of work as embodied in this thesis.

Chapter-4: This chapter describes the experimental procedure used in the synthesis, characterization, pharmacological evaluation and modelling study.

Chapter-5: This chapter covers the results and discussion part of the research work.

Chapter-6: This chapter outlines the summary and conclusion.

Chapter-7: This chapter includes the references as a source of information to carry out the research work followed by a list of published papers, presentations in national and international conferences and a brief personal profile of the research scholar.