From cancer to a common cold, one of the frequently encountered denominators in various diseases is **INFLAMMATION**. Thus, inflammation is known to play a direct or an indirect role in the aetiology of many chronic diseases. Chronic inflammation results from various factors which seriously undermines the health and longevity of the population in general with no age, race, social class, national or geographic boundaries. A plethora of diseases such as allergies, alzheimer's, asthma, arthritis, autoimmune diseases, cancer, colitis, diabetes, gastritis, heart disease, hepatitis, myocarditis, nephritis, neuritis, osteoporosis, prostatitis, and sinusitis, either arise or associated to an "inflammatory cascade."

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the backbone of rheumatic disease management. However, their use is marred by serious adverse effects, the most important being gastric injury leading to ulceration and renal damage. Several strategies have been adopted to surmount these shortcomings. The most promising approach seemed to be the design and development of NSAIDs specifically inhibiting the inducible isoform of cyclooxygenase (COX-2). However, selective COX-2 inhibitors suffer from cardiovascular side effects and necessitate the continuing efforts to obtain drugs that specifically inhibit COX-2 without inherent toxicity. Therefore, activity retention of traditional NSAIDs, while being able to circumvent their main drawbacks would provide a safe therapeutic alternative for the management of chronic inflammation and pain.

The research work encompasses the design, pharmacological evaluation and molecular modelling studies of some novel 5,6-diphenyl-1,2,4-triazine-3(2*H*)-ones bearing five membered heterocyclic moieties as a relatively safe potential COX-2 inhibitors. The present work utilises the concept of molecular hybridisation approach wherein a 5,6-Diphenyl-1,2,4-triazine-3(2*H*)-one moiety was tethered to a 1,3,4-oxadiazole or its bioisosteric equivalent of 1,3,4-thiadiazole or a 1,2,4-triazole ring system *via* a linker.

The designed molecules were synthesised, characterised and evaluated against various conventional anti-inflammatory bioassay models including the assessment of their COX-2 inhibitory potential. The relevant gastrointestinal, hepatic, renal and cardiac safety parameters of promising compounds were

evaluated against appropriate standard drugs. Further, computational studies were performed to access the possible binding mode of the potential compounds at the COX-2 active site followed by an *in silico* prediction of the pharmacokinetic properties. To this date, the research work has led to the publication of two research papers and two international presentations. Suggestions and comments on the part of the readers are always welcome.

The entire thesis has been divided into eight chapters as follows:

Chapter-1: The first chapter offers an introductory section which deals with a brief account of modern drug discovery and includes basic information about inflammation and its management followed by a short historical background of NSAIDs and the structure and functions of the cyclooxygenase (COX) enzymes.

Chapter-2: This chapter focused on detailed literature survey on anti-inflammatory and analgesic activity including the selective COX-2 inhibitory potential of the 1,2,4-triazine; 1,3,4-oxadiazole/thiadiazole and the 1,2,4-triazole ring systems.

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

Chapter-4: This chapter describes the experimental procedure used in the synthesis, characterisation, protocols for *in vitro* and *in vivo* pharmacological evaluation and modelling studies.

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 section includes the references as a source of information to carry out the research work.

Chapter-8: An appendix consisting of the NMR (^{1}H and ^{13}C) spectra of the representative compounds followed by a list of published papers and presentations at international conferences.