INTRODUCTION

Inflammation in one form or the other is at the root of the common ailments ranging from traumatic disorder, fever associated with infection to major life threatening diseases like myocardial infarction or brain hemorrhage or infarct. In addition, inflammation underlies different kinds of arthritis, disorders of bones, tendons, and joints causing minor stiffness or even grave disability and deformity.

Recently, it is estimated that more than 800 million people worldwide are suffering from one or other types of arthritis leading to loss of several million working man-days.

In England in the mid-eighteenth century, Reverend Edmund Stone described in a letter to the president of Royal Society "an account of the success of the bark of the willow in the cure of agues" (fever). Leroux in 1829 isolated the active ingredient of bark as salicin, a bitter glycoside, and demonstrated its anti-pyretic effect. Sodium salicylate was first used for the treatment of rheumatic fever and as an anti-pyretic effect. Sodium salicylate was first used for the treatment of rheumatic fever and as anti-pyretic in 1875, and of its usefulness in the treatment of gout, soon followed. The enormous success of this drug prompted Hoffman to prepare acetyl salicylic acid. After the demonstration of its antiinflammatory effects, this compound was introduced into medicine in 1899 by Dreser under the name of aspirin. By the early years of this century the chief therapeutic benefits of aspirin were known. Towards the delete of the nineteenth century other drugs were discovered that shared some or all these therapeutic effects.

Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids are widely used with success to combat inflammation with its accompanying pain and fever. However, these agents have high incidence of serious side effects like gastrointestinal ulceration, gastric mucosal damage, impairment of platelet function, bleeding disorders. Also NSAIDs are unable to check disease
progression in chronic inflammatory setting. To overcome these limitations search is on going throughout the world to find newer effective and safe anti-inflammatory drugs.

The intensive work in the field of NSAIDs for more than a century has witnessed progressive change in conception, design and development of structure of ideal drugs. The purely emperical methods of earlier days have been replaced by more natural multidisciplinary approaches involving biochemistry, biophysics, enzymology, immunology, biochemical pharmacology, molecular modeling, combinatorial chemistry etc. In earlier stages of medicinal research, the screening of natural products in many instances provided the principle sources of lead material. This still remains one of the few important aspects of discovery of the new drugs. Synthesis of inhibitors of enzymes, which are implicated in the genesis of the disease and metabolites have also been utilized for the identification of lead compounds.

Inspite of considerable progress in the field of anti-inflammatory drugs, there is no single drug available, which can be termed as ideal in terms of risk-benefit ratio. Hence, it is worthwhile to search new NSIADs exhibiting superiority over already existing NSAIDs.

The discovery of a novel drug in this field is mainly the outcome of random synthesis followed by screening of the new compounds. Thus, overwhelming bulk development of novel drug encompasses molecular modification of the currently known agents. The work delineated in the present study is based on this approach.

Currently used NSAIDs belong to wide variety of chemical classes such as pyrazole derivatives (like celecoxib), pyrazolone derivatives (like phenylbutazone, anthranilic acid derivatives (like mefenamic acid), indole derivatives (like indomethacin), naphthalene derivatives (like naproxen), propionic acid derivatives (like ibuprofen) etc. The present work supplements that NSAIDs by synthesizing additional improved derivatives belonging to chemical classes like indoles, phenothiazines, naphthalenes, quinazolinones,
anthranilic acids, azetidinones, thiazolidinones, oxadiazoles etc. evaluating them for their anti-inflammatory and other biological activities. The newly synthesized compounds are as follows-

**SCHEME-I**

3-Chloroacetyl-2-(4-chlorophenyl) indole; 3-(2’-aminothiazol-4’-yl)-2-(4-chlorophenyl) indole; 3-(2’-aminoaxazol-4’-yl)-2-(4-chlorophenyl) indole; N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl)thiazol-2-amine; N-(substituted benzylidene)-4-(2-(4-chlorophenyl)-1H-indol-3-yl) oxazole-2-amine; N-((substituted phenyl)((E)-(substituted phenyl) diazenyl) methylene-4-(2-(4-chlorophenyl)-1H-indol-3-yl) thiazol-2-amine; N-((substituted phenyl)((E)-(substituted phenyl)diazenyl) methylene-4-(2-(4-chlorophenyl)-1H-indole-3-yl)-4,5-dihydrooxazol-2-amine;

**SCHEME -II**

2-Chloro-10-chloroacetyl phenothiazone; 2-chloro-10- (2-aminothiazol-4-yl)- phenothiazone; 2-chloro-10- (2-aminoaxazol-4-yl)-phenothiazone; 2-chloro-10-[2-(substituted benzylidene)-aminothiazol-4-yl]- phenothiazines; 2-chloro-10-[2-(substituted benzylidene)-aminoaxazol-4-yl]-phenothiazines; 2-chloro-10-[2-{3’-chloro-2’-oxo-4’-(substituted phenyl)-1’-azetidinyl}-thiazol-4-yl]- phenothiazines; 2-chloro-10-[2-{3’-chloro-2’-oxo-4’-(substituted phenyl)-1’- azetidinyl} oxazol-4-yl]-phenothiazines.

**SCHEME -III**

7-Methoxy-β-(chloroacetyl)amino naphthalene; 7-methoxy-β-(2-aminothiazol-4-yl)amino naphthalene; 7-methoxy-β-[2-(2-substitutedindole)-aminothiazol-4-yl]-amino naphthalenes; 7-methoxy-β-[2-(1’di/mono substituted phenyl-3’-2 substituted indole formazan -4’-yl)-thiazol-4-yl]-amino naphthalenes; 7-methoxy-β-[2-(3’-chloro-2’-oxo-4’-2-substitutedindole-1’-azetidinyl)-thiazol-4-yl]-aminonaphthalenes.
SCHEME -IV
2-Ethyl-6-bromo-benzoxazin-4-one ; 3-anilino-2-ethyl-6-bromo-quinazolin-4-one; 3-(N-chloroacetyl)-anilino-2-ethyl-6-bromo-quinazolin-4-one; 4-phenyl-6-dihydro-2-ethyl-10-bromo-[1',2',4']-triazino-quinazolin-5-one; 5-chloro-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazoline; 5-hydrazone-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazoline; 5-substituted-arylidene-hydrazone-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazolines; 5-(3'-methyl-2''-oxo-5''-substituted arylidene-4''-thiazolidinyl)-amino-4-phenyl-2-ethyl-10-bromo-[1',2',4']-triazino-quinazolines.

SCHEME -V
5-Bromoanthranilic acid; 5-Bromo-N- ethylacetoanthranilic acid; 5-Bromo-N-(semicarbazido-carbonyl-methyl) anthranilic acid; 5-Bromo-N-(2'-amino-1',3',4'-oxadiazol-5'-yl-methyl)-anthranilic acid; 5-bromo-N-(2'-aminoacetyl-1',3',4',-oxadiazol-5'-yl-methyl)-anthranilic acid; 5-bromo-N-[2'-amino-(2-substituted indolidene)-acetyl-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids; 5-bromo-N-[2'-amino-{1''-acetyl-5''-(2-substituted indolyl)-2''-pyrazolin-3''-yl}-1',3',4'-oxadiazol-5'-yl-methyl]-anthranilic acids ; N-ethylacetoanthranilic acid; N-(thiosemicarbazido-carbonyl-methyl)-anthranilic acid; N-(2'-amino-1',3',4'-thiadiazol-5'-yl-methyl)-anthranilic acid; N-(2'-aminoacetyl-1',3',4'-thiadiazol -5-yl-methyl)-anthranilic acid; N-[2'-amino-(2-substituted-indolidene)-acetyl-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids; N-[2'-amino-{1''-acetyl-5''-(2-substituted indolyl)-2''-pyrazolin-3''-yl}-1',3',4'-thiadiazol-5'-yl-methyl]-anthranilic acids.