INTRODUCTION

Recent epidemiological studies have revealed that roughly more than 800 million people of the world are suffering from different types of arthritis leading to the loss of several million working man-days.

For the alleviation of inflammation both acute and chronic as well as for the treatment of inflammatory diseases, many drugs like Indomethacin, Sulindac, ibuprofen, naproxen, piroxicam, nabumetone etc. are in use. The corticosteroids have high anti-inflammatory activity and provide significant relief in many types of inflammation. But they have major disadvantage of equally harmful side-effects. Narcotic analgesics which are highly effective in relieving pain, lack the property to suppress inflammation. Thus the only drugs that are commonly used in inflammatory disorders are non-steroidal anti-inflammatory agents (NSAIDs) which have comparatively less side effects. These agents are a heterogenous group of compounds which have a carboxy group in their structure and are therefore acidic in nature. The important acidic non-steroidal compounds are aspirin, indomethacin, mefenamic acid, flufenamic acid, naproxen, sulindac, tolimetin, ibuprofen, Naproxen etc. Most of these acidic compounds are organic acids and non-selectively inhibit the COX-1 and COX-2 enzymes. Due to their modest selectivity of inhibition of COX-1, they exhibit these drugs possessed serious inherent side-effects like gastric haemorrhage, perforation, bone marrow depression and particularly gastric ulcer. On the contrary the recently developed non-steroidal, non acidic or weakly acidic anti-inflammatory agents like nabumetone are preferentially COX-2 isoform inhibitor. Since COX-2 is not normally present in tissues but is induced at the site of inflammation, the COX-2 inhibitors selectively inhibit the inflammation and are devoid of producing gastric ulceration which is due to suppression of COX-1, therefore they possess substantially lower incidence of gastric ulcer.

Inspite of considerable progress in the field of anti-inflammatory drug, there is no single drug available which can be termed as ideal. Since currently available drugs show variable response in different individuals and possess serious side effects like gastric haemorrhage, perforation, bone marrow depression and gastric ulcer. The search for the better drug for the treatment of inflammation is the need of the day.
More than a century have witnessed progressive changes in the conception, design and development of structures of ideal non-steroidal anti-inflammatory drugs. The purely empirical methods of earlier days have been replaced by more rational multidisciplinary approaches involving biochemistry, enzymology, biophysics and biochemical pharmacology etc. In the earlier stages of medical research, the screening of natural products in many instances provided the principal sources of the lead material. This still remains one of the few important sources of drug-discovery. 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 compound.

The other main route generating the lead compound is a mechanistic refinement of preparing structural analogues of the prototype acting drugs. Therefore, the understanding of chemoreceptor processes could enable a chemist to build a molecular model that could fit the active domain of the drug receptor. Unfortunately the attempts to purify the active region of a receptor and indeed the chemical nature of the receptor have remained unresolved till today in inflammation disorders like arthritis, gout etc. It, therefore, implies that the discovery of a novel drug structure in this field is mainly the outcome of synthesis followed by screening of the new compounds. Thus, overwhelming bulk of development of novel drug encompasses molecular modification of the currently known agents. The work delineated in the present study is based on the approach. In the present work, the following types of compounds have been synthesized and evaluated for their anti-inflammatory activity. The work delineated in the present study is based on this approach. Number of indoles, napthalenes, pyrazolines, thiadizoles, thiazolidinones and azetidinones etc. have been synthesized and evaluated for the anti-inflammatory and analgesic activities which are summarized as follows:

**SCHEME-I :** N-((5-[(aryl)methylene]amino]-1,3,4-thiadiazol-2-y1)methyl) [1,3,4] thia diazino[6,5-b]indol-3-amine, 2-aryl-3-{(5-[(1,3,4] thia dia zin o[6,5-b]indol-3-ylamino)methyl]-1,3,4-thi adiazol-2-y1}-1,3-thiazolidin-4-one, and 3-chloro-4-aryl-1-{5-{{[1,3,4]thia dia zin o[6,5-b]indol-3-ylamino]methyl]-1,3,4-thia diazol-2-y1]azetidin-2-one.

**SCHEME-II :** 5-Bromo-3-chloroacetylarnino indole, 5-bromo-3-hydrazino-acetylamine indole, 5-bromo-3-[(substituted phenyl) methylene aminoamido-methylene amino]indole, 5-Bromo-3-(4'-oxo-2'-substituted aryl-1'-thiazolinyl)-
amidoaminomethylenes indoles, 5-bromo-3-[2-{3'-chloro-2'-oxo-4'-(substituted phenyl)-1'-azetidinyl}amido aminomethylene] indole.

**SCHEME-III**: β-(Carbethoxymethyl)aminonaphthalene, β-(Thiosemicarbazidocarbonyl- methyl) aminonaphthalene, β-(2'-Amino-1',3',4'-thiadiazole-5'-yl) methylamino napthalene β[2'-(Benzylideneamino-1',3',4'-thiadiazole-5'-yl methyl]amino napthalenes, β-[2'-(2''-Substitutedaryl-4''-thiothiazolide-3'-yl-)1',3',4' thiadiazol-5''-ylmethyl]amino napthalenes, and β[2'-(3''-Chloro-2''-substituted aryl-4''-oxo-azetidin-1''-yl)-1',3',4'thiadiazole-5''-ylmethyl]amino napthalenes.

**SCHEME-IV**: 5-Substitutedbenzylideneamino-1,3,4,- thiadiazole-2-thiols, 5-substituted- benzylideneamino-2- thioacethyl- methyl-1,3,4-thiadiazoles, 5-substituted benzylideneamino-2-(thiosemicarbazidomethyl-thio)-1,3,4-thiadiazoles, 5-substitutedbenzylideneamino-2-[5'-amino-1',3',4'-thiadiazole-2'-ynithiethyl]-1,3,4-thiadiazoles, 5-substitutedbenzylidene amino-2-[5''-(substituted benzylideneamino-1',3',4'- thiadiazol-2'-yl)-thiophenyl]-1,3,4-thiadiazoles, 5-[4'-oxy-3'-chloro-2'-substitutedphenyl-azetidin-1'-yl]-2-[{5''-(4''-oxy-3'' chloro-2''- arylazetidin-1''-yl)-1''',3''',4''''-thiadiazol -2''-yl}thiophenyl]-1,3,4-thiadiazoles.

**SCHEME-V**: 5-Methoxy-3-substituted chalconylindoles, 5-Methoxy-3-[1-acetyl-5-(substitutedphenyl)-2'-pyrazolin-3-yl]indoles, 5-Methoxy-3-[1-acetyl-5-(substitutedphenyl)-4-phenylazopyrazolin-3-yl]indoles, and 5-Methoxy-1'- [acetylmethylamino{substitutedphenyl-5''-(substitutedphenyl)-4-phenylazo}-2-pyrazoline-3'-yl]-indoles.

**SCHEME-VI**: β-(2-Arylideneamino thiazol-4-yl) amino- β'-methoxy naphthalenes, β-[2-(3''-chloro-2''-oxo-4''-substitutedaryl-1''-azetidinyl]thiazol-4''-yl]amino- β'-methoxy naphthalenes and β-[2-(1',3'-disubstituted phenyl-3'-substituted arylformazan-4'-yl]thiazol-4-yl]amino-β'-methoxynaphthalenes.