ABSTRACT

In this dissertation, conditions were optimized to synthesize novel and more potent pyrazole derivatives from celecoxib, a well-known drug used to treat inflammation. The aim was to find future candidates that can be used in replacement with celecoxib because of the potential side effects of this drug. Three synthetic routes were established using easily available raw materials and easy to produce derivatives having high purity as well as experimental yield.

In the first part of this study, 4-methyl group of celecoxib pharmacophore (**3**) was selectively oxidized. The product 4-{1-[4-(aminosulfonyl)phenyl]-3-(trifluoromethyl)-1*H*-pyrazol-5-yl}benzoic acid (**306**) was esterified, followed by its hadrazinolysis to get 4-[5-(4-hydrazinocarbonyl-phenyl)-3-trifluoromethyl-pyrazol-1-yl]-benzenesulfonamide (**308**) which was further reacted with different reagents to produce the target pyrazoles. Substituted pyrazoles **309-326** were prepared by condensation of carbohydrazide (**308**) with different aromatic aldehydes.

Keeping in view the potential biological activities of 1,2,4-triaozle and different pyarozles, the synergism of both the heterocyclic moieties in a single nucleus was introduced in the second part of this study. Compound **308** was converted to 4-(5-(4-(4-amino-5-mercapto-4*H*-1,2,4-triazol-3-yl)phenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (**327**) by reaction with carbon disulphide in alkaline ethanol followed by its hydrazinolysis, the product obtained was subsequently reacted with a number of benzaldehyde derivatives to afford the title compounds **328-340**. In the third part of this study, chalcones prepared from substituted acetophenone and benzaldehyde derivatives were allowed to react with carbohydrazide (**308**) in acidified ethanol to produce the compounds **341-352**. All the compounds were characterized by FT-IR, ^{1}HNMR, mass and elemental analyses along with the single crystal X-ray crystallography of few compounds.

The synthesized compounds were evaluated for their anti-inflammatory, ulcerogenic, anti-bacterial and anti-oxidant activities. Most of the compounds were found active against inflammation when Paw Oedema Model on albino Wistar rats. Few of the compounds (**313, 314, 322, 329-331, 333-340**) showed even greater anti-inflammation effect than the reference drug celecoxib along with no ulcerogenic effect. Similarly, many of these compounds were observed to be good anti-bacterial when tested against gram positive and gram negative bacteria. Many of the tested compounds also showed good anti-oxidant activity when compared with standard butylated hydroxytoluene (BHT) with few of them showing greater anti-oxidant potential than BHT.