ABSTRACT

Five membered heterocyclic compounds and their derivatives have gained much attraction of synthetic chemists because of valuable biological activities. The broad spectrum of biological activities of 1,3,4-oxadiazole prompted us to synthesize its different 2,5-disubstituted-1,3,4-oxadiazole derivatives along with some sulfamoyl derivatives and to evaluate them for their various biological activities. It was assumed that 2,5-disubstituted-1,3,4-oxadiazole ring along with the potential acetamide/ butanamide functionality might boost up the pharmacological activities of the molecules. Also various solvent extracts of *Cassia suratensis* were taken to check out the different contents and their antioxidant, antibacterial and antifungal activities. Under the title, the research work includes the synthesis of some new 1,3,4-oxadiazole & sulfonamide derivatives of 2-amino-4-chloroanisole and the extraction, isolation, characterization & activity analysis of *Cassia suratensis*.

In organic synthesis, five schemes were processed. First scheme includes the synthesis of 5-substituted-1,3,4-oxadiazol-2-thiols from corresponding carboxylic acids after successive conversion into ethyl esters and hydrazides.

The seventeen carboxylic acids (**1a-q**) were converted into corresponding ethyl esters through esterification with ethanol in the presence of small amount of conc. H_2SO_4 as catalyst. The products were isolated through solvent extraction using ether & water after the addition of sodium carbonate base. Base was added to convert unreacted carboxylic acid & H_2SO_4 into salt which were dissolved in aqueous layer. Ethyl esters (**2a-q**) were further converted into carbohydrazides (**3a-q**) by stirring with hydrazine in methanol. The seventeen 1,3,4-Oxadiazoles (**4a-q**) were synthesized by refluxing carbohydrazides with CS_2/KOH (Scheme-1). The synthesized 5-substituted-1,3,4-Oxadiazol-2-thiols were collected after acidifying the medium. This step ensures the good yield but excess of acid should be obviated.

Out of these seventeen 1,3,4-oxadiazoles, twelve were processed for the synthesis of acetamide derivatives (Scheme-2). The first step of this scheme includes the synthesis of an electrophile, **5**, by the stirring of 2-amino-4-chloroanisole with 2-bromoacetylbromide in aqueous basic medium and second step comprises the synthesis

of corresponding 5-substituted-1,3,4-oxadiazol-2-yl-*N*-(2-methoxy-5-chlorophenyl)-2-sulfanyl acetamides (**6a-l**) by the stirring of 5-substituted-1,3,4-oxadiazol-2-thiols with **5** in the presence of NaH/DMF. The products were obtained after the addition of water.

Eleven 5-substituted-1,3,4-Oxadiazol-2-thiols were utilized for the synthesis of butanamide derivatives (Scheme-3). This scheme also includes the formation of an electrophile, **7**, by stirring of 2-amino-4-chloroanisole with 4-bromobutyrylbromide in aqueous basic medium and then the mixing followed by stirring of **7** with eleven 5-substituted-1,3,4-oxadiazol-2-thiols in NaH/DMF.

2-Amino-4-chloroanisole was reacted with different thirteen sulfonyl chlorides, **9-21**, in an aqueous basic media to synthesize different sulfonamides (**22-34**) which were further *N*-substituted by alkyl/aralkyl groups in the presence of NaH & DMF (Scheme-4 & Scheme-5) to synthesize the derivatives (**22a-e**, **23a-b** to **34a-b**). The products, **22-34**, were collected after the addition of dil. HCl but excess of it is avoided. The products synthesized in the polar aprotic solvent DMF were collected after the addition of distilled water.

Scheme-1 & scheme-2 derivatives were screened against AChE, BChE & LOX enzyme and showed relatively better inhibitory potential; scheme-3 derivatives screened against LOX enzyme and found to be moderate inhibitor of enzyme; scheme-4 derivatives screened against AChE, BChE, LOX enzyme & DPPH and exhibited good potential while scheme-5 derivatives were screened against certain bacterial strains.

In natural product extraction, first the extraction by methanol, *n*-hexane, chloroform, ethylacetate and *n*-butanol respectively was performed and these extracted layers were subjected to the tests for the detection of secondary metabolites. Further the antibacterial (using *Bacillus subtilis* & *Micrococus luteus*), antifungal (using *Aspergillus nigar* & *Rizopus microspores*) and antioxidants activities were executed for the different extracted layers. The results were presented in the form of %age inhibition & IC_{50} values.

The 1,3,4-oxadiazole derivatives having acetamide functionality, **6a-l**, and sulfamoyl derivatives, **22d** & **22e**, were found to be better inhibitors of acetylcholinesterase enzyme (AChE). The sulfamoyl derivatives, **22b**, **22c**, & **22e**, are better inhibitors of butyrylcholinesterase enzyme (BChE). Both the enzymes are involved in Alzeimer's Plaques. The 1,3,4-oxadiazole derivatives bearing butanamide moiety, **8a-**

e, 8m, 8o-q, inhibited the lipoxygenase enzyme (LOX) efficiently which plays an important role in inflammatory diseases. The sulfamoyl derivatives, **33, 24a & 30b,** presented the better activity against the Gram bacteria including Gram positive and Gram negative bacterial strains taken into account. These strains are known to involve in certain diseases. The evaluation of different fractions of *Cassia suratensis* for antibacterial activity resulted methanolic and chloroform extracts better against *B. subtillus* but methanolic and ethyl acetate extracts against *M. luteus*. The antifungal activity was evaluated against *A. niger* and *R. microspore*, three extracts including methanolic, chloroform and ethyl acetate were found to be better inhibitor. All the fractions with 15% solution were found to present better antioxidant activities.