Indian Journal of Chemistry
Vol. 51B, March 2012, pp. 493-497

Synthesis and anticancer activity of 3,5-diaryl-1,2,4-oxadiazole derivatives

Mrityunjoy Kundu*[a], Jagadish Singh[b], Brijesh Singh[a], Tirtha Ghosh[b], B C Maiti[c] & T K Maity[b]

[a]Institute of Pharmaceutical Sciences, Guru Ghasidas University, Bilaspur 495 009, India

[b]Department of Pharmaceutical Technology, Jadavpur University, Kolkata 700 032, India

[c]Indian Institute of Chemical Biology, Jadavpur, Kolkata 700 032, India

E-mail: nrityunjoy79@yahoo.com

Received 5 February 2010; accepted (revised) 1 December 2011

3,5-Diaryl-1,2,4-oxadiazole derivatives are synthesized by condensation reaction of amidoximes with aromatic acid chloride. Amidoximes are obtained from aromatic nitriles and acid chlorides from corresponding aromatic monocarboxylic acid derivatives. There are broad possibilities of preparing several such compounds in this series by using different aromatic nitriles as well as different aromatic monocarboxylic acid derivatives. The synthesized compounds are evaluated for their anticancer activity by using mice specific Ehrlich Ascites Carcinoma cell (EAC cells) in Swiss albino mice model. Synthesized compounds (dose 25 mg/kg body weight) show significant reduction of tumor cell count as well as tumor weight. Life span of the treated mice also increases. The standard drug used for the study is 5-fluorouracil (5 mg/kg body weight).

Keywords: Amidoxime, 1,2,4-oxadiazole, acid chloride, EAC cells

Drug discovery and development is a multi-disciplinary, creative, innovative and highly regulated process. Finding a successful lead has been a great challenge in pharmaceutical research. It is also important to take into account the formulation development. Lead candidates are those with promising characteristics for development into new drugs. Finding of a 'lead' is not only the current focus but rather it has also to be optimized. Optimization of 'lead' refers to the process used to manipulate the compound to improve its chemical stability, potency and biological or therapeutic effectiveness.

Nitrogen containing heterocyclic ring systems have a huge potential to become successful drug candidates which was proven in the recent past. 1,2,4-Oxadiazole is a five membered heterocyclic moiety with three hetero atoms, out of which two are nitrogen atoms and one is an oxygen atom. 1,2,4-Oxadiazole is an asymmetric system of oxadiazole series. Therefore, position isomer is possible in case of non identical 3,5-disubstituted 1,2,4-oxadiazole. A number of reports have highlighted the synthetic chemistry and use, and most of the investigation reports give promising results which are statistically significant. A series of activities are already shown by this candidate. These include novel ligands for the imaging of β-amyloid plaques in AD (Alzeimer's disease)[1], antiparasitic[2], anthelmintic[3], diuretic[4,5], anti-inflammatory[6,7], a novel apoptosis inducer with tumor-selective properties[8,9], antimicrobial[10], hypoglycemic[11], skeletal muscle relaxant[12], hypertensive activity[13] and anti-HIV[14].

There are broad possibilities for the synthesis of new compounds offering highly effective bioisosteric agents with ester and amide groups, which is related to the high stability of the 1,2,4-oxadiazole ring with respect to metabolism in the entire physiological *p*H and temperature range. Being bioisosteric with ester and amide groups and having significant biological activity, 1,2,4-oxadiazoles have been extensively studied with a view to their use in pharmaceutical chemistry[15-18]. Synthesis of some 3,5-disubstituted 1,2,4-oxadiazole and their derivatives have been carried out using the synthetic procedure based on the ring closure reactions of appropriate amidoxime with substituted acid chloride. Unless the substituents are very bulky, the oxadiazoles are volatile in nature and rather unstable. However, the 3,5-diaryl-substituted derivatives are more stable. The 3,5-disubstituted-1,2,4-oxadiazoles are white crystalline compound which