GSJ: Volume 7, Issue 8, August 2019
ISSN 2320-9186

Global Scientific JOURNALS

GSJ: Volume 7, Issue 8, August 2019, Online: ISSN 2320-9186
www.globalscientificjournal.com

TOXICOLOGICAL STUDIES OF NEW HYDRAZONE DERIVED FROM ISONIAZID

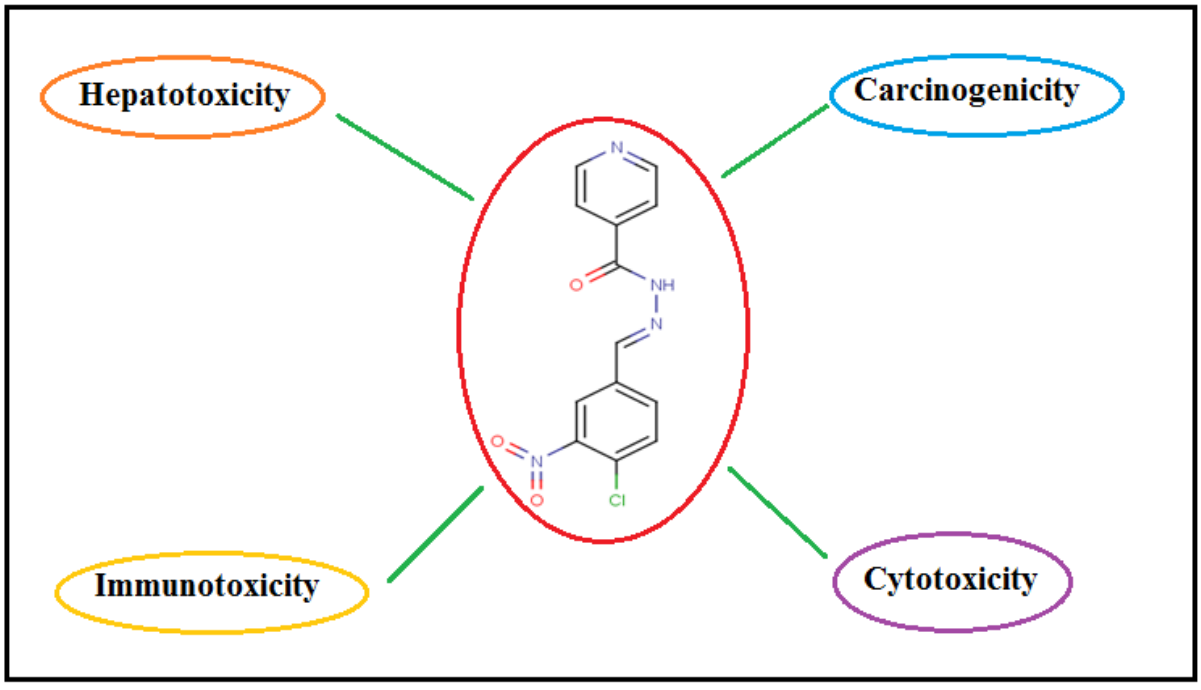
Kamel Mokhnache, Hanane Khither, Soraya Madoui, El-khamsa Soltani, Noureddine Charef

Laboratory of Applied Biochemistry, University, Setif-1, Algeria

Abstract

In this study, a new hydrazone was investigated for their adverse effects, such as carcinogenicity, hepatotoxicity, immunotoxicity and cytotoxicity using online software program (ProToxII).

Graphical abstract



Carcinogenicity prediction

One of the strategies for human health protection is the study and evaluation of chemicals carcinogenicity [89]. For this reason, the prediction of carcinogenicity has been discussed for

GSJ: Volume 7, Issue 8, August 2019
ISSN 2320-9186

a long time [90]. In order to predict the carcinogenicity of **INH** and its derivative, results displayed in **Table 1**, reveal the carcinogenicity of **INH** with high active probability of 93%, whereas **H** exhibited inactive action with probability of 50%. From these results, it's remarkable the reduction in the carcinogenicity when INH reacts with our carbonyl compounds. For **H**, predicted results indicate the absence of the carcinogenicity. This indicates the importance of the condensation reaction of carbonyl compounds with INH. These results suggest that **INH** derivatives could be no or low carcinogens. From these results, it's clear that we introduce important modifications in the anti-tubercular drug **INH** structure.

Table 1. Carcinogenicity prediction of **INH**, and **H**

Compounds	Prediction	Probability %
INH	**Active**	81
H	**Inactive**	50

Hepatotoxicity prediction

Drug induced hepatotoxicity is a fundamental problem in human health and drug development [91]. This adverse effect could be introduced directly by the drug or by their reactive metabolites [92]. Several studies indicated that **INH** metabolites are responsible for its hepatotoxicity [93]. Our results from hepatotoxicity prediction of the drug **INH** and its derivative, demonstrate the high hepatotoxic effect of this drug with probability of 93%, whereas the derivative **H** has low toxic effects, with probabilities of 51 %. These results indicate reduction in the hepatotoxic effect of **INH** from 93% to 51% in **H**, with a considerable difference of 42% . These results are given in **Table 2**.

Table 2. Hepatotoxicity prediction of **INH**, and **H**

Compounds	Prediction	Probability %
INH	**Active**	93
H	**Active**	51

Immunotoxicity prediction

GSJ: Volume 7, Issue 8, August 2019
ISSN 2320-9186

Immunotoxicity, defined as the adverse effects of xenobiotics (immunotoxicants) on the immune system includes two main types: immunosuppression (decreased immuno competence) and inappropriate immunostimulation [96]. From the obtained results (**Table 3**), **H** has high immunotoxic effect with probability of 80%. This adverse effect could be due to the chemical structure of **H** and the presence of nitro group and chlorine atom attached to the aromatic ring, similar to *p*-chloronitrobenzene structure that reduces the numbers of NK, T, and B cells in spleen of mice and induces an increase of macrophage and nucleated erythrocyte numbers [97].

Table 3. Immunotoicity prediction of **INH** and **H**

Compounds	Prediction	Probability %
INH	**Inactive**	98
H	**Active**	80

Cytotoxicity prediction

In drug development, the cytotoxicity was estimated by the concentration of a drug that induces the death of half of cells in culture (LC_{50}) [98]. This type of toxicity was widely employed for testing the pharmaceutical formulations developed for gastrointestinal absorption and permeability of drugs [99]. The drug **INH** and its derivative **H** was investigated for the cytotoxicity prediction; results in **Table 4** reveal the absence of cytotoxic effect of this compound with inactivity percentage of 93.79 %.

Table 4. Cytotoxicity prediction of **INH**, and **H**

Compounds	Prediction	Probability %
INH	**Inactive**	93
H	**Inactive**	79

REFERENCES

[89] R. Benigni, Predicting the carcinogenicity of chemicals with alternative approaches: recent advances, *Expert opinion on drug metabolism & toxicology* 10 (2014) 1199–1208.

GSJ: Volume 7, Issue 8, August 2019
ISSN 2320-9186

[90] M. Casalegno, G. Sello, Carcinogenicity prediction of noncongeneric chemicals by augmented top priority fragment classification, *Computational biology and chemistry*. 61 (2016) 145–154.

[91] C.Y. Liew, Y.C. Lim, C.W. Yap, Mixed learning algorithms and features ensemble in hepatotoxicity prediction, *Journal* of *computer-aided molecular* design .25 (2011) 855–871.

[92] B.K Gunawan, N. Kaplowitz. Mechanisms of Drug-Induced Liver Disease, *Clinics in liver disease*. 11 (2007) 459–475.

[93] A. Chowdhury, A. Santra, K. Bhattacharjee, S. Ghatak, D. R. Saha, G.K. Dhali, Mitochondrial oxidative stress and permeability transition in isoniazid and rifampicin induced liver injury in mice, *Journal of hepatology*. 45 (2006) 117–26.

[94] Z. Ji, N.S. Ball, M. J. LeBaron, Global Regulatory Requirements for Mutagenicity Assessment in the Registration of Industrial Chemicals, *Environmental and molecular mutagenesis***.** 58 (2017) 345–353.

[95] V. Leiro, A. Fernandez-Villar, D. Valverde, L. Constenla, R. Vazquez, L. Pineiro, A. Gonzalez-Quintela, Influence of glutathione S -transferaseM1and T1homozygous null mutations on the risk of antituberculosis drug-induced hepatotoxicity in a Caucasian population, *Liver International*. 28 (2008) 835–839.

[96] A.K. Schrey, J. Nickel-Seeber, M.N. Drwal, P. Zwicker, N. Schultze, B. Haertel, R. Preissner, Computational prediction of immune cell cytotoxicity. *Food and chemical toxicology*. 107 (2017) 150–166.

[97] Q. Li, M. Minami, T. Hanaoka, Y. Yamamura, Acute immunotoxicity of p-chloronitrobenzene in mice: II. Effect of *p*-chloronitrobenzene on the immunophenotype of murine splenocytes determined by flow cytometry, *Toxicology*. 137 (1999) 35–45.

[98] M. Zhang, D. Aguilera, C. Das, H. Vasquez, P. Zage, V. Gopalakrishnan, J. Wolff, Measuring Cytotoxicity: A New Perspective on LC50, *Anticancer research***.** 27(2007) 35–38.

[99] P. Bu, S. Narayanan, D. Dalrymple, X. Cheng, A.T.M. Serajuddin, Cytotoxicity assessment of lipid-based self-emulsifying drug delivery system with Caco-2 cell model: Cremophor EL as the surfactant, *European journal of pharmaceutical sciences***.** 91 (2016) 162–171.