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Toxicological Studies and Biodegradability Prediction of Isonicotinylhydrazide

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Abstract: The antitubercular drug isonicotinylhydrazide (Isoniazid) was selected for toxicological and biodegradation studies. In silico ecotoxicological and biodegradability predictions were carried out online computer software programs such as Pro Tox, Pred-skin, Endocrine Disruptor Knowledge Base (EDKB) and UM-BBD. In silico predictions, results showed high toxicity of this drug; hepatoxicity with probability of 93%, carcinogenicity; 81% and without nephrotoxic effect. For biodegradability prediction, the results indicate the ability of microorganism to degrade the drug with no-toxic resultant products. We conclude the possibility to using the drug with high precautions from environment and human health.
Keywords: toxicological, biodegradability, microorganisms, online software programs.

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Methods

Online software programs

ProTox web server was used for toxicity prediction method. The University of Minnesota Biocatalysis/Biodegradation Database (UM-BBD, http://umbbd.msi.umn.edu/) was used for predict microbial biocatalytic reactions and biodegradation pathways.

Results and Discussion

Toxicological studies

Results displayed in Table 1, showed high toxicity of Isoniazid; hepatoxicity with probability of 93%, carcinogenicity; 81% and without nephrotoxic effect.

Table 1. Toicity evaluation of isoniazid

Toxicity	Prediction	Probability %
Hepatotoxicity	Active	93
Carcinogenicity	Active	81
Nephrotoxicity	Inactive	-

Bioderadability prediction

Numerous chemicals used in human-life are supposed to be pollutants [1], when were accumulated in environment, interacted with biological system caused mortal interactions.

Thus, obliged to create processes for decrease these pollutants and guard living organism. Among of these processes; the biodegradability [2], the ability of soil bacteria to decompose organic matter by extracellular enzymes production., led to facilitate and accelerate the mineralization process [3].

Several studies, confirmed the accompaniment of both increasing of microorganisms and the rate of mineralization when the organic matter introduced in the soil [4]. Recently, the progress in computational studies led to developed different rules of biotransformation of organic groups from UM-BBD data.

Results displayed in Figure 1; represents various pathways of isoniazid biodegradation and the resultants products. We can summarize isoniazid biodegradation in the following steps by different pathways:

In first time, isoniazid was biodegraded to five compounds (2 to 6), with oxidative and reductive reactions of bacterial enzymes such as monooxigenases, dioxigenases, hydrolases and nitroreductases.

bt0042: From Nitrobenzene to Catechol [5] by dioxygenase (2), bt0067: From secondary Amide to Carboxylate + primary Amine [6] by hydrolase (3, 4, 7, 13,17, 24, 25,35), bt0078: From Nitrobenzenoid to Hydroxylaminobenzenoid [8] by nitroreductase (5), bt0080: From Nitroaromatic to Aminoaromatic [9] by NAD (P) H nitroreductase (6).

After these steps, each one of these compounds was transformed to several compounds until obtain degradation final compounds with the following reactios pathways:

bt0037: From Hydroxylaminobenzene to 2-Aminophenol [10] by hydroxylaminobenzene mutase (15, 16), bt0035: from aromatic Hydroxylamine to aromatic Amine [10] by reductase (14), bt0042: from 1-Nitro-2-unsubstituted aromatic to *vic*-Dihydroxyaromatic [10] by nitrobenzene reductase (7), bt0051: from isonicotinate to pyridine [11] by isonicotinate decarboxylase (12), bt0005: from *vic*-unsubstituted Aromatic to *vic*-Dihydroxyaromatic [12] by dioxygenase (11), bt0065: from1-Amino-2-unsubstituted aromatic to *vic*-Dihydroxyaromatic [13] by dioxygenase (7), bt0078: from Nitrobenzenoid to Hydroxylaminobenzenoid [14] by nitroreductase (13)., bt0254: from *vic*-Dihydroxyaromatic to intradiol ring cleavage [15] by dioxygenase (8,17). bt0351: from *vic*-Dihydroxybenzenoid to 2-Oxopent-4-enoate derivative + Carboxylate [16] (9, 10, 24), bt348: from [2-halo]Maleylacetate derivative to Succinate (18,19, 27), bt0377: from 3-Hydroxy-2-methylpyridine-5-carboxylate derivative to 2-(Acetamidomethylene)succinate derivative [17] by oxygenase, bt0318: from Carbamate to Amine [18] (31), bt0373 fromFrom 3,4-Dehydroadipyl-CoA to Succinyl-CoA and Acetyl-CoA [66] (33),bt0388: from 2-Aminophenol derivative to *vic*-Dihydroxybenzenoid [19] (7, 26, 35),bt0391: From 3 Formiminopyruvate to 3-Formylpyruvate [22] by hydrolase (34), bt0021: From *cis*-2-Hydroxypenta-2,4-dienoate to 4-Hydroxy-2-oxovalerate [21] by hydratase (32), bt0022: Halomethyl derivative to 1-Methylalcohol derivative [23] (28), bt0082: from 2-Ketocarboxylate to Carboxylate [24] by oxidase (29).The results indicate neutral (yellow color) and likely transformations (green color), with no-toxic resultant products.

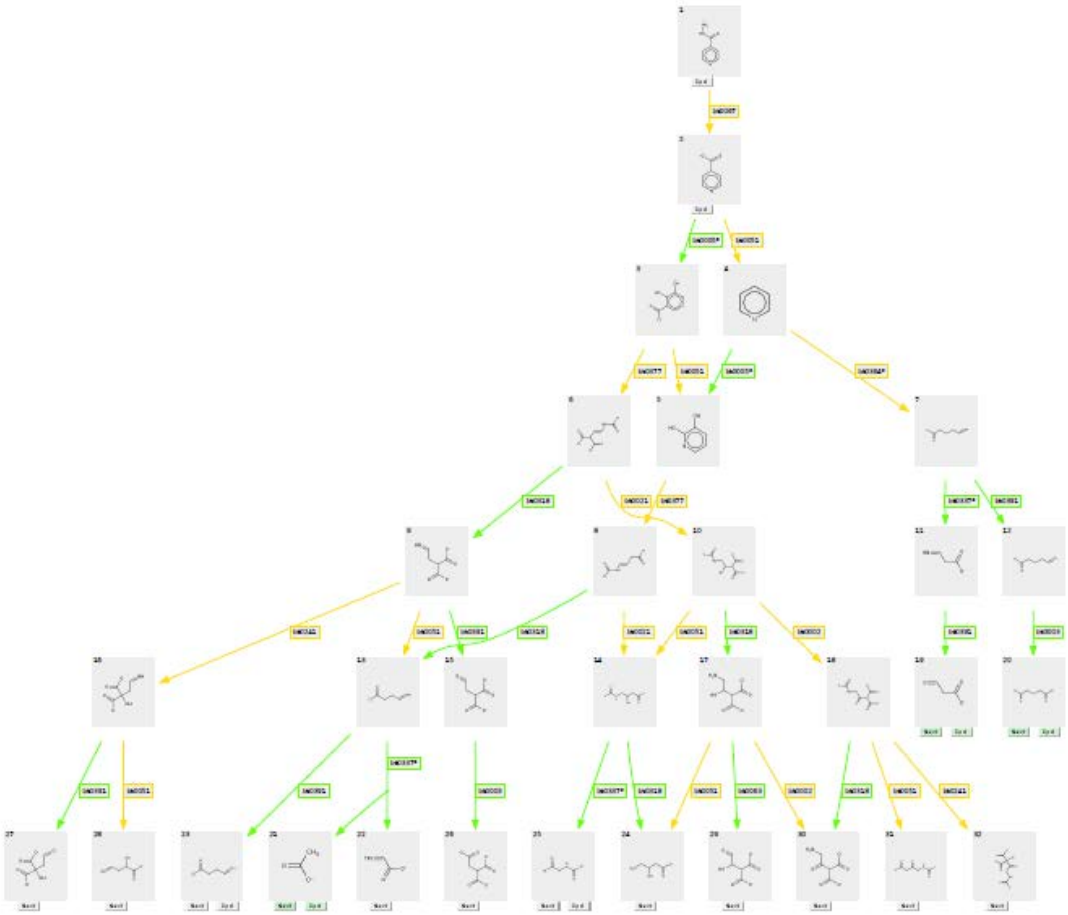

Figure 1. Biodegradation pathways of Isoniazid

Conclusion

Toxicological and biodegradability of the drug Isoniazid were evaluated by in silico predictions. Results showed that the drug able to degrade by microorganisms with different biotransformation reactions. The obtained results indicate the possibility to used drug with high precautions from environment and human health.

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