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Genotoxicity prediction of common pesticides through QSAR based bioinformatics

Shashi Aggrawal, Pragya Chaturvedi

Abstract— Pesticides are widely used in agricultural production to prevent or control pests, diseases, weeds, and other plant pathogens. In prediction of genotoxicity , the use of in silico prediction methods such as QSAR (Quantitative Structural Activity Relationship) model is required or encouraged in order to increase efficiency and minimize the reliance on animal testing .In present study prediction of 100 insecticides, 40 fungicides and 40 herbicides were done with the help of T.E.S.T.(Toxicity Estimation software Tool, 4.1 version). In our present study 20 insecticides ,8 fungicides and 7 herbicides were showing positive mutagenicity and that there are 4 insecticides whose experimental mutagenicity were positive and predicted mutagenicity negative. And other 3 insecticides were showing experimental value negative and predicted value positive.

Index terms— QSAR, Genotoxicity, Pesticides, Mutagenicity

1 INTRODUCTION

Toxicity is a science that examines the adverse effects of chemicals on organisms. In silico, a phrase coined as an analogy to the familiar phrases in vivo and in vitro, is an expression used to denote "performed on computer or via computer simulation. "In silico toxicology" means "anything that we can do with a computer in toxicology." In silico or computational toxicology is an area of very active development and great potential. In silico toxicology is difficult to define exactly, as today practically all toxicological research and risk assessment have major in silico components. The United States Environmental Protection Agency (US EPA) defines in silico toxicology as the "integration of modern computing and information technology with molecular biology to improve agency prioritization of data requirements and risk assessment of chemicals" (US EPA, 2003).

We live in a world of chemicals. More than 60 million chemical compounds were known to exist as of 26 May 2011. Fortunately we are exposed to only a fraction of these during our lifetime. These include inadvertent exposures, e.g., pesticide residues and products of chemical industries, and deliberate exposures, e.g., cosmetics and drugs. Toxicology as a science and regulatory tool has the goal of ensuring the safety of humans, animals, and the environment. Assessment or risks of all categories of chemicals foreign to the body (xenobiotics) is still mainly based on animal experimentation. However, developments in knowledge of general pathophysiology, cellular pathways, genetics, and computer-supported modeling, have resulted in a better understanding of the molecular mechanisms of xenobiotic action and plant pathogens, weeds, molluscs, birds, mammals, fish nematodes (round worm) and microbes etc. A pesticide toxicity (Boobis et al. ,2002: Nigsch et al.,2009).

A pesticide is a substance or mixture of substances intended for preventing , destroying , repelling or lessening the damage of any pest. The pest can be insects, may be chemical in nature , biological agent, antimicrobial or disinfectant.

The main intention of the introduction of pesticides was to prevent and control insect pests and diseases in the field crops and of course, initially the use of pesticides reduced pest attack and paved way for increasing the crop yield as expected. Simultaneously, increased use of chemical pesticides has resulted in contaminating the environment and the long-term implications on the society are found to be many. Knowingly or unknowingly, now the farmers are addicted to using agrochemicals indiscriminately and excessively to make the situation from bad to worse not only in India but also in other parts of world as well (Conway, 1984).

In India pests cause crop loss of more than RS 6000 crores annually, of which 33 per cent are by weeds, 26 per cent by

diseases, 20 per cent by insects, 10 per cent by birds and rodents and the remaining, 11 per cent is due to other reasons. The magnitude of the problem would grow further as more and more (newer) pests and diseases likely to attack crops and the need to use pesticides in different forms will be necessitated in the years to come (Rajendran 2003).

Quantitative Structure Activity Relationships (QSARs) are mathematical models that are used to predict measures of toxicity from physical characteristics of the structure of chemicals (known as molecular descriptors). Acute toxicities (such as the concentration which causes half of fish to die) are one example of toxicity measures which may be predicted from QSARs (US EPA 2012(http://www.epa.gov/nrmrl/std/cppb/war/sim_war.htm).).

QSAR toxicity predictions may be used to screen untested compounds in order to establish priorities for expensive and time-consuming traditional bioassays designed to establish toxicity levels. When conditions do not permit traditional bioassays, QSARs are an alternative to bioassays for estimating toxicity (US EPA 2012) (http://www.epa.gov/nrmrl/std/cppb/war/sim_war.htm**).**

The QSAR models used for regulatory purposes should be associated with the following purposes.

1-To defined end points

2-An unambiguous algorithm

3-Appropriate measures of goodness-of-fit robustness and predictability

4-A mechanistic interpretation if possible.

Generally ,the prime aim in developing QSAR is so that it can be used for predicting purposes. It is therefore important that the statistics given with the QSAR give an indication of its predictability.

2 MATERIALS AND METHODS

2.1 Materials – Tools and Databases

2.1.1 Toxicity Estimation Software Tool (T.E.S.T. Version 4.1):

The Toxicity Estimation Software Tool (T.E.S.T.) has been developed to allow users to easily estimate toxicity using a variety of QSAR methodologies. T.E.S.T allows a user to estimate toxicity without requiring any external programs. Users can input a chemical to be evaluated by drawing it in an included chemical sketcher window, entering a structure text file or importing it from an included database of structures. Once a chemical has been entered, its toxicity can be estimated using one of several advanced QSAR methodologies. The program does not require molecular descriptors from external software packages (the required descriptors are calculated within T.E.S.T.) (US EPA 2012).

2.1.2 Pubchem:

PubChem is a database of chemical molecules and their activities against biological assays. The system is intained by the National Center for Biotechnology Information (NCBI), a component of the National Library of Medicine, which is part of the United States National Institutes of Health (NIH). PubChem can be accessed for free through a web user interface. Millions of compound structures and descriptive datasets can be freely downloaded via FTP. PubChem contains substance descriptions and small molecules with fewer than 1000 atoms and 1000 bonds. More than 80 database vendors contribute to the growing PubChem database.

2.2 Methodology

A list of common pesticides is prepared and there structure files are derived from the database. QSAR methodology is used to determine the mutagenicity of these 180 pesticides. Positive mutagens are selected and studied further and results are discussed.

3 RESULTS AND DISCUSSION

Prediction of Mutagenicity of 100 Insecticides was done with the help of T.E.S.T. (4.1 software). During this analysis we observed that out of 100 insecticides, experimental value of 20 insecticides were found to be positive mutagenic. So there is a strong need to check their genotoxic levels in vitro and in vivo. Other 40 insecticides are negative mutagenic agent.

We also observed that there are 4 insecticides whose experimental mutagenicity were positive and predicted mutagenicity negative. And other 3 insecticides were showing experimental value negative and predicted value positive.

We also observed that out of 100 insecticides mutagenicity of 60 insecticides were not available.

Out of 100 insecticides 27 insecticides are showing positive mutagenicity. These are Parathion, Carbofuron, Nailed, oxydemeton- methyl, Allethrin, Bensulide, Methidathion, Isoprocarb, Chlorpyriphos- methyl, Dioxicarb, Tetramethrin, Fenoxicarb, Imidacloprid, Thiamethoxam, Deguelin, Thiacloprid, Alatamiprid, Clothianidin, Transfluthrin, Nitenpyram, Mthomyl, Dicrotophos, Polyketide (23 Predicted).

Four insecticides Diclorvos, Dimethoate, Phenothrin and Monocrotophos are showing experimental value positive and predicted value negative.

Out of 40 fungicides, 8 predicted positive mutagenic fungicides are Myclobutanil, Captan, Difolaton, Etridizole, Fenbuconazole, Cyprodinil, Boscalid, Pyrachlostxobin and experimental positive mutagenic fungicides are Thiram, Dizomet, Carbendazim and Thiophanote- methyl.

In analysed 40 herbicides , 9 herbicides are positive mutagenic. These are Naptalan, Bensulide, Napropamide, Ethalfluralin, Sathosodim, Imazethaphyr and Tralkoxydim (7 predicted herbicides). 2 Experimental positive herbicides are Diuron and Trifluralin.

4 CONCLUSION

The work was untaken to determine the genotoxic effect of common pesticides (insecticides ,fungicides and herbicides). QSAR have long been used for predicting wide range of endpoints. In present analysis we found that out of 180 pesticides (100 insecticides, 40 fungicides and 40 herbicides), 20 insecticides, 8 fungicides and 7 herbicides were found to be positive mutagenic. Now we conclude that the pesticides which were showing potent values, have strong need to test in vivo or in vitro.

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REFERENCES

[1] J.S. Bridle, "Probabilistic Interpretation of Feedforward Classification Network Outputs, with Relationships to Statistical Pattern Recognition," *Neurocomputing – Algorithms, Architectures and Applications,* F. Fogelman-Soulie and J. Herault, eds., NATO ASI Series F68, Berlin: Springer-Verlag, pp. 227-236, 1989. (Book style with paper title and editor)

[2] W.-K. Chen, *Linear Networks and Systems.* Belmont, Calif.: Wadsworth, pp. 123-135, 1993. (Book style)

[3] H. Poor, "A Hypertext History of Multiuser Dimensions," *MUD History,* http://www.ccs.neu.edu/home/pb/mud-history.html. 1986. (URL link *include year)

[4] K. Elissa, "An Overview of Decision Theory," unpublished. (Unplublished manuscript)

[5] R. Nicole, "The Last Word on Decision Theory," *J. Computer Vision,* submitted for publication. (Pending publication)

[6] C. J. Kaufman, Rocky Mountain Research Laboratories, Boulder, Colo., personal communication, 1992. (Personal communication)

[7] D.S. Coming and O.G. Staadt, "Velocity-Aligned Discrete Oriented Polytopes for Dynamic Collision Detection," *IEEE Trans. Visualization and Computer Graphics*, vol. 14, no. 1, pp. 1-12, Jan/Feb 2008, doi:10.1109/TVCG.2007.70405. (IEEE Transactions)

[8] S.P. Bingulac, "On the Compatibility of Adaptive Controllers," *Proc.*

- Dr. Shashi Agrawal is currently working as lecturer,Deptt. Of zoology , D.A.V. college , Kanpur, India , PH-919335014995. E-mail: agrawals1111@yahoo.in
- Pragya Chaturvedi is currently pursuing Doctoral research in Biotechnology from KIIT University, India , PH-91-7897890030. E-mail: mbi_pragya@yahoo.com

Fourth Ann. Allerton Conf. Circuits and Systems Theory, pp. 8-16, 1994. (Conference proceedings)

[9] H. Goto, Y. Hasegawa, and M. Tanaka, "Efficient Scheduling Focusing on the Duality of MPL Representation," *Proc. IEEE Symp. Computational Intelligence in Scheduling (SCIS '07)*, pp. 57-64, Apr. 2007, doi:10.1109/SCIS.2007.367670**.** (Conference proceedings)

[10] J. Williams, "Narrow-Band Analyzer," PhD dissertation, Dept. of Electrical Eng., Harvard Univ., Cambridge, Mass., 1993. (Thesis or dissertation)

[11] E.E. Reber, R.L. Michell, and C.J. Carter, "Oxygen Absorption in the Earth's Atmosphere," Technical Report TR-0200 (420-46)-3, Aerospace Corp., Los Angeles, Calif., Nov. 1988. (Technical report with report number)

[12] L. Hubert and P. Arabie, "Comparing Partitions," *J. Classification,* vol. 2, no. 4, pp. 193-218, Apr. 1985. (Journal or magazine citation)

[13] R.J. Vidmar, "On the Use of Atmospheric Plasmas as Electromagnetic Reflectors," *IEEE Trans. Plasma Science*, vol. 21, no. 3, pp. 876-880, available at http://www.halcyon.com/pub/journals/21ps03-vidmar, Aug. 1992. (URL for Transaction, journal, or magzine)

[14] J.M.P. Martinez, R.B. Llavori, M.J.A. Cabo, and T.B. Pedersen, "Integrating Data Warehouses with Web Data: A Survey," *IEEE Trans. Knowledge and Data Eng.*, preprint, 21 Dec. 2007, doi:10.1109/TKDE.2007.190746.(PrePrint)