Microbial prediction of metabolism of toluene in the environment

Yana Koleva, Yordanka Tasheva

Abstract: *The aim of this work is to predict the possible microbial metabolism of toluene by a software of (Q)SAR Application Toolbox. The toluene was metabolically activated in the microorganisms and their protein and DNA binding was estimated. Observed and predicted microbial pathways were observed. Observed and predicted metabolites have different mechanisms of protein binding.*

Key words: *toluene, microbial prediction, environment*

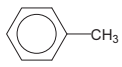
INTRODUCTION

The aim of this work is to predict the possible microbial metabolism of toluene by a software of (Q)SAR Application Toolbox. It`s predicted that toluene was metabolically activated in the microorganisms and their protein and DNA binding.Toluene is generated solely through manufacturing processes of petroleum and is released to the environment by human activities. Exposures to toluene at high levels would usually be expected only in the case of accidents or spills, especially in enclosed spaces. But the content of toluene in reformulated gasoline significantly increases the possibility of the general public being exposed to toluene at low levels. Opportunities for exposure will closely parallel those for other organic hydrocarbon gasoline additives such as benzene. In addition to inhalation risks while fueling motor vehicles and direct exposures from vehicle emissions, toluene will be emitted to the ambient air, primarily from precombustion volatilization. This can then lead to low-level background exposure potentials over a large geographical area. Toluene has a very unpleasant odor that most people can smell before any harmful effects would occur, but others might feel irritation of the nose or throat before noticing the smell. Adverse health effects are not expected to result from the environmental concentrations of toluene to which most people would be exposed.

MATERIALS AND METHODS

Compounds. Petroleum toluene and its microbial metabolites were investigated which are presented in Table 1.

Table 1. Petroleum toluene

CAS Number	Name of compound	Structure of compound
108-88-3	Toluene	

OECD (Q)SAR Application Toolbox. (Quantitative) Structure-Activity Relationships [(Q)SARs] are methods for estimating properties of a chemical from its molecular structure and have the potential to provide information on the hazards of chemicals, while reducing time, monetary costs and animal testing currently needed. To facilitate practical application of (Q)SAR approaches in regulatory contexts by governments and industry and to improve their regulatory acceptance, the OECD (Q)SAR project has developed various outcomes such as the principles for the validation of (Q)SAR models, guidance documents as well as the QSAR Toolbox (OECD (Q)SARs Application Toolbox).

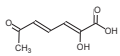
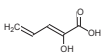
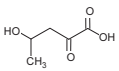
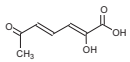
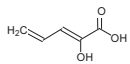
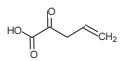
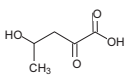
Metabolic pathways documented for 200 organic chemicals in different mammals are stored in a database format that allows easy computer-aided access to the metabolism information. The collection includes chemicals of different classes, with variety of

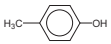
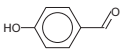
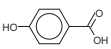
functionalities such aliphatic hydrocarbons, alicyclic rings, furans, halogenated hydrocarbons, aromatic hydrocarbons and haloaromatics, amines, nitro-derivatives, and multifunctional compounds. *In vivo* and *in vitro* (predominantly, with liver microsomes as experimental systems) studies were used to analyze the metabolic fate of chemicals. Different sources, including monographs, scientific articles and public websites were used to compile the databasewhich are described in [1,2].

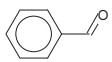
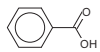
RESULTS AND DISCUSSION

The results of protein and DNA binding of the probable microbial metabolites (observed and predicted) of toluene are presented in Table 2.

Table 2. Probable metabolic activation of toluene, protein and DNA binding by (Q)SAR Application Toolbox

Compound/ CAS number	Observed Microbial Metabolism by (Q)SAR Application Toolbox (Protein and DNA binding)	Microbial Metabolism Simulator by (Q)SAR Application Toolbox (Protein and DNA binding)
Toluene 108-88-3	15 metabolites;  1) Protein binding – No binding; DNA binding – No binding;  2) Protein binding – No binding; DNA binding – No binding;  3) Protein binding – Michael-type nucleophilic addition; DNA binding – No binding;  4) Protein binding – No binding; DNA binding – No binding;  5) Protein binding – No binding; DNA binding – No binding;	8 metabolites;  1) Protein binding – No binding; DNA binding – No binding;  2) Protein binding – Michael-type nucleophilic addition; DNA binding – No binding;  3) Protein binding – No binding; DNA binding – No binding;  4) Protein binding – No binding; DNA binding – No binding;  5)

	 6) Protein binding – Schiff base formation; DNA binding – No binding;  7) Protein binding – No binding; DNA binding – No binding;  8) Protein binding – No binding; DNA binding – No binding;  9) Protein binding – No binding; DNA binding – No binding;  10) Protein binding – No binding; DNA binding – No binding;  11) Protein binding – No binding; DNA binding – No binding;  12) Protein binding – No binding; DNA binding – No binding;  13) Protein binding – No binding;	Protein binding – No binding; DNA binding – No binding;  6) Protein binding – No binding; DNA binding – No binding;  7) Protein binding – Schiff base formation; DNA binding – No binding;  8) Protein binding – No binding; DNA binding – No binding;

	DNA binding – No binding;  14) Protein binding – No binding; DNA binding – No binding;  15) Protein binding – No binding; DNA binding – No binding;	

The microbial metabolites of the parent structure (toluene) were predicted for the possible side effects which can cause in protein and DNA binding. This was done theoretically by a software ((Q)SAR Application Toolbox) – observed and predicted microbial metabolism.

CONCLUSION

It were investigated the observed and predicted microbial metabolism of petroleum toluene. It`s established that the microbial metabolities of the investigated arene structure. It was predicted the possible side effects which petroleum toluene can cause in protein and DNA binding.

Acknowledgement

This work was funded by the University "Prof. Dr. Assen Zlatarov"-Burgas (project No.: 297/2013).

REFERENCES

[1] OECD(Q)SARs Application Toolbox: http://www.oecd.org/document/23/0,3343,en_2649_34379_33957015_1_1_1_1,00.html.

[2]. Mekenyan, O.G., Dimitrov, S.D., Pavlov, T.S., Veith, G.D. 2004: A systematic approach to simulating metabolism in computational toxicology. I. The TIMES heuristic modeling framework. Current Pharmaceutical Design, 10: 1273-1293.

About the authors:

Assoc. Prof. PhD Yana Koleva, department: “Physical and organic chemistry”, University “Prof. Dr. Assen Zlatarov” – Burgas, phone: 056/716278, email: yanuriana@abv.bg

This paper has been reviewed