Science of the Total Environment 643 (2018) 435–450

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

# Assessment of river sediment toxicity: Combining empirical zebrafish embryotoxicity testing with *in silico* toxicity characterization

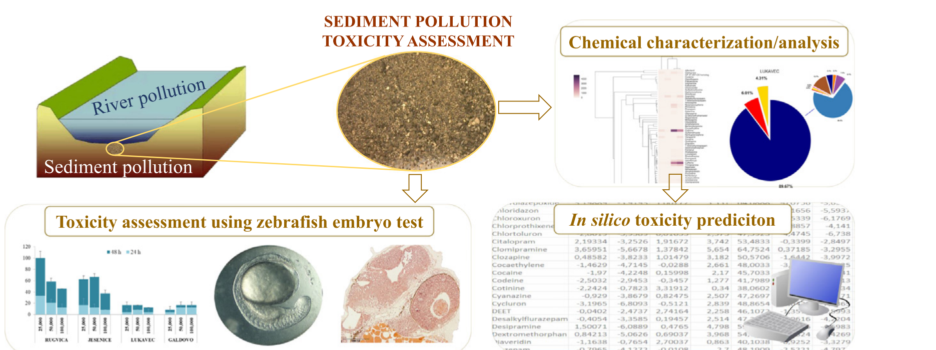
Sanja Babić [a,b], Josip Barišić [a,b], Draženka Stipaničev [c], Siniša Repec [c], Mario Lovrić [d,e], Olga Malev [f,g], Dalma Martinović-Weigelt [h], Rozelindra Čož-Rakovac [a,b], Göran Klobučar [f,*]

[a] Laboratory for Biotechnology in Aquaculture, Division of Materials Chemistry, Ruđer Bošković Institute, Bijenička cesta 54, Zagreb, Croatia
[b] Centre of Excellence for Marine Bioprospecting-BioProCro, Ruđer Bošković Institute, Bijenička cesta 54, Zagreb, Croatia
[c] Croatian Waters, Central Water Management Laboratory, Ulica grada Vukovara 220, Zagreb, Croatia
[d] Know-Center, Inffeldgasse 13/6, A-8010 Graz, Austria
[e] NMR Centre, Ruđer Bošković Institute, Bijenička cesta 54, Zagreb, Croatia
[f] Division of Zoology, Department of Biology, Faculty of Science, University of Zagreb, Rooseveltov trg 6, Zagreb, Croatia
[g] Department for Translational Medicine, Children's Hospital Srebrnjak, Srebrnjak 100, Zagreb, Croatia
[h] University of St. Thomas, Department of Biology, Mail OWS 390, 2115 Summit Ave, Saint Paul, MN 55105, USA

## HIGHLIGHTS

- Pharmaceuticals are a major component of river sediment pollution.
- ZET and histopathological analysis are good indicators of sediment toxic potential.
- *In silico* sediment toxicity predictions should include OCs with low or high log $K_{ow}$.

## GRAPHICAL ABSTRACT




## ARTICLE INFO

*Article history:*
Received 19 March 2018
Received in revised form 29 May 2018
Accepted 10 June 2018
Available online xxxx

Editor: Henner Hollert

*Keywords:*
Toxicity prediction
*Danio rerio*
Pharmaceuticals
Pesticides
QSAR
Histopathology

## ABSTRACT

Quantitative chemical analyses of 428 organic contaminants (OCs) indicated the presence of 313 OCs in the sediment extracts from Sava River, Croatia. Pharmaceuticals were present in higher concentrations than pesticides thus confirming their increasing threat to freshwater ecosystems. Toxicity evaluation of the sediment extracts from four locations (Jesenice, Rugvica, Galdovo and Lukavec) using zebrafish embryotoxicity test (ZET) accompanied with semi-quantitative histopathological analyses exhibited correlation with cumulative number and concentrations of OCs at the investigated sites (10.05, 15.22, 1.25, and 9.13 μg/g respectively). Toxicity of sediment extracts and sediment was predicted using toxic unit (TU) approach and persistence, bioaccumulation and toxicity (PBT) ranking. Additionally, influential OCs and genes were identified by graph mining of the prior knowledge informed, site-specific chemical-gene interaction models. Predicted toxicity of sediment extracts ($TU_{ext}$) was similar to the results obtained by ZET and associated histopathology with Rugvica sediment being the most toxic, followed by Jesenice, Lukavec and Galdovo. Sediment TU ($TU_{sed}$) favoured OCs with low octanol-water partition coefficients like herbicide glyphosate and antibiotics ciprofloxacin and sulfamethazine thus indicating locations containing higher concentrations of these OCs (Galdovo and Rugvica) as the most toxic. Results

* Corresponding author.
*E-mail address:* gklobuca@biol.pmf.hr (G. Klobučar).

https://doi.org/10.1016/j.scitotenv.2018.06.124

suggest that comprehensive *in silico* sediment toxicity predictions advocate providing equal attention to organic contaminants with either very low or very high log $K_{ow}$.



## 1. Introduction

A wide variety of organic contaminants (OCs) enters the aquatic environment through a myriad of the point sources (*e.g.*, wastewater treatment plants, domestic, industrial or hospital effluents, municipal landfills) and the non-point sources, such as agricultural or urban runoff, contributing to ever more complex chemical eco-exposome (Li, 2014; Pal et al., 2010). In the recent years particular attention has been given to OCs of emerging concern; these typically include pharmaceuticals, personal care products, illicit drugs, pesticides and industrial chemicals with poorly characterized hazards and increasing input (Arp, 2012; Vodyanitskii and Yakovlev, 2016).

Sediments are the main sinks for the anthropogenic contaminants in the aquatic environments (Šrut et al., 2011). Chemicals are reintroduced to the water column *via* re-suspension and trophic transfer, and often represent a long-term source of pollution (Hollert et al., 2003; Schulze-Sylvester et al., 2016). Therefore, it is of great importance to assess and characterize the ecotoxicological risks posed by the contaminated aquatic sediments (Šrut et al., 2011). Complex nature of the sediments presents a challenge for development of environmental quality standards and the risk assessment, which are typically driven by the evaluation of the exposure and hazards associated with single chemicals (Brack et al., 2015; Schroeder et al., 2016). A shift from target-based analytical approaches to the broad spectrum chemical screening with highly sensitive analytical techniques (which allow for low-level detection in surface freshwater and sediments) has been recommended (Comtois-Marotte et al., 2017; Krauss et al., 2010). Broad spectrum screening of OCs confirmed the presence of emerging contaminants such as pharmaceuticals, disinfectants, illicit drugs and associated metabolites (ng/g concentration range) in the sediments of a variety of freshwaters worldwide (Ebele et al., 2017; da Silva et al., 2011).

Sava River has the largest river basin in the Southeast Europe, and is the largest tributary of the Danube River covering the total catchment area of approximately 97,700 $km^2$ hosting around 8,000,000 people. In the Croatian part of the Sava River basin (510 km), municipal and industrial wastewaters have been identified as the major point sources of pollution; a high percentage of municipal effluents remain untreated (Milačič et al., 2015). Monitoring activities of the Sava River (Croatia) have been restricted to the analyses of a comparatively small number of contaminants in the surface water and in the associated industrial and domestic wastewater effluents (Bielen et al., 2017; Senta et al., 2015; Terzić and Ahel, 2006; Terzić et al., 2008). Some of these monitoring studies performed a more extensive characterization of surface waters where the role of polar OCs in overall toxicity was emphasized (Smital et al., 2011; Terzić and Ahel, 2006). Evaluation of the sediment contamination with heavy metals and some organic chemicals was

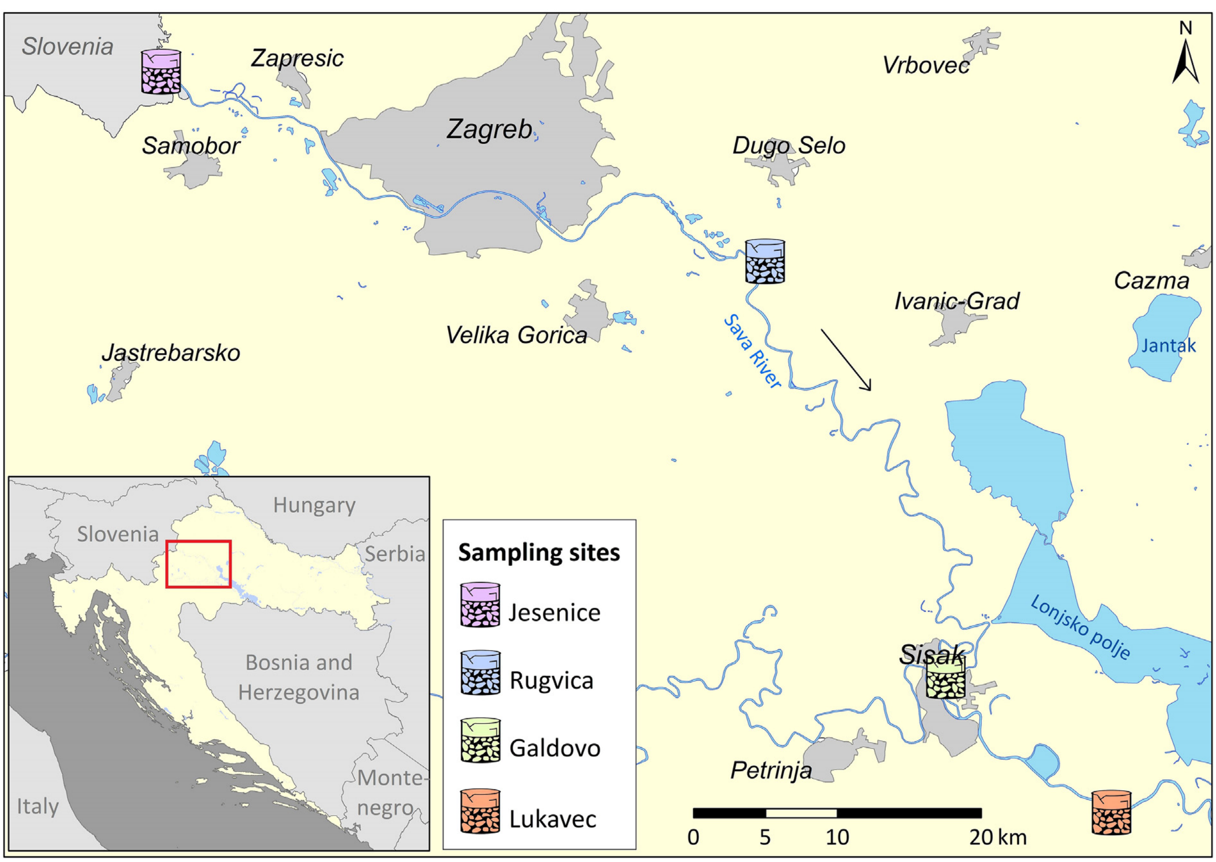



**Fig. 1.** A map of the sediment sampling locations - grey areas represent urban zones, arrow indicates flow direction of the Sava River. Map inset - location of Croatia and Sava River basin sampling locations (red rectangle). Generated with ArcGIS 10.1 software. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)