Fakulta rybářství
a ochrany vod
Faculty of Fisheries
and Protection
of Waters

Jihočeská univerzita
v Českých Budějovicích
University of South Bohemia
in České Budějovice
Czech Republic

Confidential

Review of USB FFPW PhD Thesis

First name(s), surname, titles of the PhD student: M.Sc. Olga Koba	**First name(s), surname, titles of supervisor:** Assoc. Prof. Dipl.-Ing. Roman Grabic, Ph.D.
Title of PhD thesis: Applications of advanced instrumentation for analysis of environmental pollutants	

REVIEWER:

Surname: Fick	**Institution:** Department of Chemistry
Name: Jerker	
Titles: Assoc. Prof.	**E-mail**: jerker.fick@umu.se
Please describe your professional relationship to the PhD student: No collaboration with the PhD student	**Please describe your field of expertise:** Analytical chemistry, fate and effects of pharmaceuticals in the environment

QUESTIONNAIRE

Originality, scientific importance, perspectives and impacts of results presented in the PhD thesis for basic and/or applied research

The thesis " Application of advanced instrumentation for analysis of environmental pollutants" by M.Sc. Olga Koba focus on the fate of emerging environment contaminants and uses advanced analytical instrumentation and techniques. M.Sc. Koba apply the state-of-the-art techniques of high resolution mass spectrometry and the new generation of triple quadrupoles in her thesis. The thesis includes method development for identification and quantification of metabolites in different tissues and studies of the fate and transport of pharmaceuticals in various environmental matrices.

This thesis addresses a highly relevant group pf pollutant in a very comprehensive and novel set of studies and present a number of highly interesting conclusions and findings. State-of-the–art methods are used throughout and the thesis also includes additional method development.

This thesis have helped increase the knowledge of the fate of PPCPs in soil, sediment and aquatic biota, Several metabolites and transformation products, as well as additional method development, are also presented. Results presented are highly original and of high scientific importance.

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Elaboration of the PhD thesis, objectives of the work and deliverables

This thesis reads well, with a logical and clear structure that is easy to follow. All chapters are in a logical order and the introduction and methods sections are appropriate. The general introduction gives a nice and comprehensive overview. All experiments and samplings were conducted using appropriate methods and the analyses were made with appropriate, novel and excellent analytical protocols. The thesis follows the guidelines and the included publications are all published in the top 5 percentile of the journals in the field.

References are relevant and cover the addressed field, and the abstract provides a clear and to-the-point version of the results and methodology.

All publications provide more knowledge regarding the fate of PPCP by using advanced novel instruments, whicg shows that they correspond well to the objectives of the thesis.

OVERALL COMMENTARY ON THE PhD THESIS

This thesis is based on a general introduction, three published papers and one submitted manuscript. All three published papers are in high-ranked journals and M.Sc. Koba is first author on all 4. I have some minor comments,

General Introduction

Page 5 Chap 1 General introduction, spelling error in the title...

Page 5 "It has been shown that most of recently used technologies for wastewater treatment could not solve elimination" This sentece is a bit misleading, there are several tertiary novel treatment technlogies that are capable of removing up to 99% of the PPCPs, e.g. ozonolysis.

Page 6 Also include ethinyl estradiol in the discussion of PPCPs included on the watch list.

Nice selection of relevant references, good overview of the field.

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Koba, O., Steinbach, C., Kroupova, H.K., Grabicova, K., Randak, T., Grabic, R., 2016. Investigation of diltiazem metabolism in fish using a hybrid quadrupole/orbital trap mass spectrometer. Rapid Communications in Mass Spectrometry 30: 1153-1162.

Excellent publication that uses state-of-the-art analytical instrumentation and software to determine the structures of the most relevant transformation products of diltiazem. Good rationale for choosing diltiazem and it's metabolites. Relevant method for both measuring and elucidating the structures.

Koba, O., Golovko, O., Kodešová, R., Fér, M., Grabic, R., 2017. Antibiotics degradation in soil: A case of clindamycin, trimethoprim, sulfamethoxazole and their transformation products. Environmental Pollution 220: 1251-1263.

Koba, O., Golovko, O., Kodešová, R., Klement, A., Grabic, R. 2016. Transformation of atenolol, metoprolol, and carbamazepine in soils: The identification, quantification, and stability of the transformation products and further implications for the environment. Environmental Pollution 218: 574-585.

Two papers that provide a comprhensive study of the degradation of PPCPs in soil, also using state-of-the-art instrumentation. These papers provide insight in how soil composition influence degradation and present an significant step forward in our knowledge of the fate of PPCPs in soil.

Koba O., Grabicova K., Cerveny D., Turek J., Kolarova J., Randak T., Zlabek V., Grabic R. Determination of pharmaceuticals and their metabolites that partition between water and sediments as a further potential exposure for aquatic organisms. Journal of Hazardous Materials (submitted)

This manuscript reads well but I would encourage an additional overview of the language since there are several spelling and grammatical errors present in the text. This manuscripts focuses on the fate of PPCPs in a three-compartment system.

Conclusion;
I consider this a strong thesis with several novel application of state-of-the-art analytical techniques that increases our knowledge about the fate of PPCPs considerably.

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FINAL RECOMMENDATION

- [X] **PhD Thesis can be recommended for defence**
- [ ] **PhD Thesis can be recommended with reservations for defence**
- [ ] **PhD Thesis can not be recommended for defence**

Umeå 20/6 -17

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Date and place

Jerker Fick

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Name and signature

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Title of PhD thesis: Applications of advanced instrumentation for analysis of environmental pollutants	

REVIEWER:

Surname: Brooks	**Institution:** Baylor University
Name: Bryan	
Titles: Distinguished Professor and Director	**E-mail:** Bryan_Brooks@baylor.edu
Please describe your professional relationship to the PhD student: None	**Please describe your field of expertise:** Environmental toxicology and chemistry, hazard and risk assessment, environmental public health

QUESTIONNAIRE

Originality, scientific importance, perspectives and impacts of results presented in the PhD thesis for basic and/or applied research

Evaluate competitiveness of the PhD thesis in the international context and compare its level with the current state of the art in the field **(extent ¼ – ½ page)**:

More people now live in cities than ever before. By 2050 70% of people live in urban areas. Global projections of population growth and urbanization present challenges to sustainable management of environmental quality. Such challenges are even more profound in and around megacities of developing countries. Thus, minimizing adverse influences of urbanization on aquatic ecosystems remains a critical environmental protection goal. The Koba thesis aims to advance analytical approaches for environmental contaminants, including inputs of pharmaceuticals and personal care products from urban centers. In fact, these substances, which are considered contaminants of emerging concern, are indicators of an increasingly urban water cycle. Due to the timeliness of the subject material and the efforts undertaken findings should be relevant to international researchers investigaging urbanization influences on surface water and other environmental influences. The thesis represents a novel, timely and important contribution. I find the thesis acceptable but have a number of questions and comments.

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Elaboration of the PhD thesis, objectives of the work and deliverables

Evaluate the overall level of elaboration of the PhD thesis (structuring of the main text, comprehensibility, logicality of the chapters and their ordering) and the originality of the selected approaches to solve the objectives; evaluate publications and whether the results described correspond to objectives of the PhD thesis **(extent ¼ – ½ page)**:

The thesis is constructed with a short introduction chapter then proceeds with chapters 2 and 3 including three papers pubished in reputable international peer-reviewed jouranls (*Rapid Communications in Mass Spectrometry* and *Environmental Pollution*). Chapter 4 presents a paper in review. These are original contributions, which engaged timely topics. Thus, it remains critical to developed advanced Submitting a thesis for defense with three published articles with one in review is advantaged and compares positively with others working international in her field of environmental chemistry.

Though simply copying and pasting pdf images of pubished papers directly into a thesis document is not common in other PhD theses and dissertations I have reviewed, I found the specific papers to be original, interesting and useful contributions. The structure and ordering of these publications aligns with the objectives of the PhD theses (as stated in chapter 1).

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OVERALL COMMENTARY ON THE PhD THESIS

Please write comments in extent of 1-2 pages:

How does your thesis research link to global megatrends? By 2050 70% of people will reside in urban areas, yet 80% of the global sewage production remains untreated, and these waste streams are being reused for variouos purposes, including habitats for aquatic life and terrestrial agriculture and aquaculture. During the next few decades global food production must increase globally by 50% and by 200% in developing countries. It is in these regions where human populations are concentrating use of resources, including chemicals, while access to chemicals in commerce, including medicines, is occuring faster than environmental management systems and public health interventions can be implemented.

What are the United Nations Sustainable Development Goals? How does your work link to specific Sustainable Development Goals?

What evidence exists that diltiazem accumulates in aquatic life? How can we translate observations of diltiazem or other residues in fish to identify whether accumluation is high enough to warrant concern?

cott et al (2016) identified diltiazem to accumulate in fish from urban estuaries of the Gulf of exico in Texas. Specifically, fish plasma levels of diltizem approached and in some cases exceeded man therapeutic doses. Please identify

t is known about comparative metabolism of pharmaceuticals in general and drug ansformation specifically by fish and other aquatic organisms?

vitro S9 substrate depletion assay is being developed as an OECD method for sformation assessments. Previous work by Connors et al (2013), which was not cited in 2, employed this S9 substrate depletion technique for several pharmaceuticals known to ansformed by general or specific CYP450 isoenzymes in humans. Connors et al (2013) d diltiazem biotransformation by rainbow trout was extremely limited in vitro. How does lings compare to your work? What reasons can explain such differences between your hese previous observations?

ee examined transformation of antibiotics in soil; chapter four examined partitioning to lease describe partitioning of organic chemicals to soil and sediments. What modeling re used to predict partitioning of organic chemicals to soils and sediments?

mechanisms influence antibiotic and other pharmaceutical partitioning processes in ents? Are historic modeling tools adequate for pharmaceutical partitioning to soil Why, or why not?

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nted in the PhD thesis

vel with the current state of

ve in urban areas. Global
sustainable management
and around megacities of
ion on aquatic ecosystems
aims to advance analytical
aceuticals and personal care
considered contaminants of
. Due to the timeliness of the
e relevant to international
ter and other environmental
contribution. I find the thesis

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What factors influence bioconcentration of pharmaceuticals in aquatic organisms?

Over 80% of all pharmaceuticals in commerce are acids and based. Please describe how, specifically, pH influences uptake of ionizables by fish and other aquatic organisms.
To what extend does dietary exposure influence pharmaceutical bioaccumulation by fish?

What evidence exists to support trophic magnification of drugs in aquatic systems?

Specific comments to chapter 1:
Figure 1 caption: PMTTs?

Table 1. Occurence information and remove efficiency data presented are not comprehensive. I recommend indicating these details are representative (if they are) or redeveloping.

FINAL RECOMMENDATION

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- [ ] **PhD Thesis can not be recommended for defence**

23 June 2017 — Bryan W. Brooks

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Date and place — Name and signature