Commentaries

Implementation of Bioavailability in Standard Setting and Risk Assessment?

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Background

Biological availability is a key word that is often encountered in current publications on the fate of pollutants in ecosystems and their effects on individual species, populations, and ecosystem levels. Despite several years of research within the area of bioavailability, its implementation in standard setting and (site-specific) risk assessment is still hampered by a lack of knowledge on the fundamental processes constituting bioavailability, and the lack of generalized procedures to translate results of bioavailability research into procedures suited for risk assessment and standard setting.

Assessing the Biological Availability of Substances

Bioavailability implies that within a given timeframe just a (small?) fraction of the total amount of a chemical substance present, for instance, in the water column or the soil, can actually be taken up (or made available for uptake) by living organisms and micro-organisms, and subsequently induce adverse effects. An example is specified in **Fig. 1**.

As a matter of course, the ultimate way of assessing the biological availability of substances, is by actually measuring the amount of chemicals accumulated within organisms, preferably at the site of toxic action. This would either re-

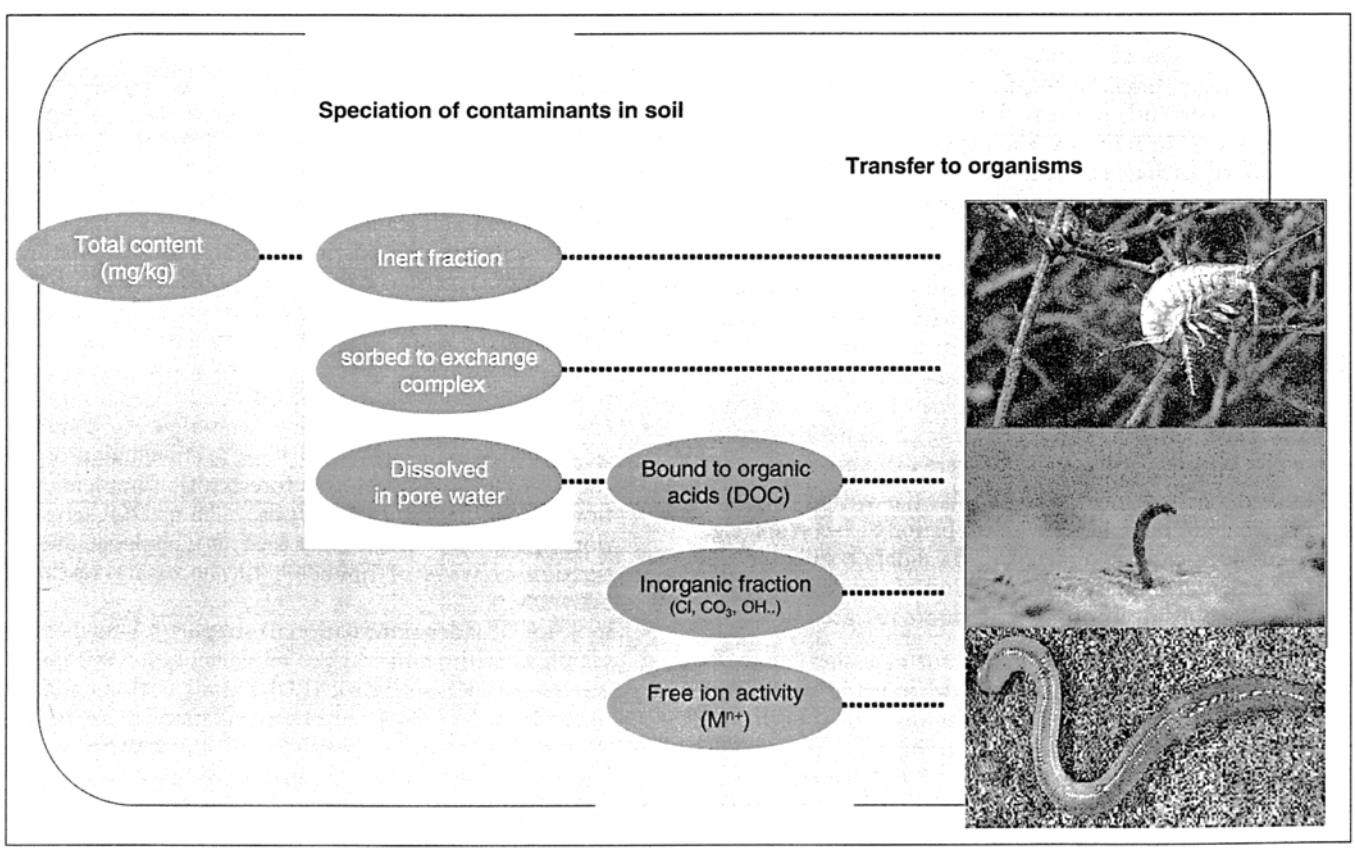

Fig. 1: Schematic overview of the various metal fractions in soil

quire the dispatching of individual species to determine the total amount of chemical present within the organism, or measuring internal contents by means like sampling of blood or fat. From an ethical point of view, this is often not desirable. Furthermore, there may be physiological mechanisms that may affect either the uptake or the level in the (micro)-organism, which could limit the interpretation of the concentration within a (micro)organism. From a pragmatic point of view, it is not always feasible to determine levels of contaminants in organisms on a regular basis. As a matter of course, there is no infinite pool of fish in our rivers and streams, or an infinite pool of earthworms in soil. Therefore, assessing internal concentrations and effects is costly and time-consuming, and no unified methodologies are available to do so. Also, many factors that differ considerably in time and space may affect bioavailability in the field. This is why measurements in the field often do not provide a good insight in THE bioavailable fraction. In view of these limitations, there is a quest for chemical methodologies that can be used to mimic the biological availability of substances. Considerable progress has been made over the last decade in this area.

Methodologies for Assessing Bioavailability

Legislators, on the other hand, have been challenged to adequately anticipate the scientific progress made within the area of bioavailability. To meet this challenge, a small group of Dutch co-workers at RIZA and RIVM prepared a workshop on this theme jointly with experts from other research institutes, industry and universities. The workshop was held in September 2001 and organized under the umbrella of the Dutch Steering Group that is responsible for setting the Dutch Environmental Quality Standards for chemicals. The main aim of the workshop was to judge the various methodologies that are currently in use to measure or estimate biological availability, in terms of usefulness for risk assessment and standard setting. The first requirement for possible implementation was that the methodology proposed had to be judged by the experts as being sound from a scientific point of view. Thereupon, the proposed methodologies had to be useful for risk assessment and standard setting from a pragmatic point of view, and the costs and benefits of implementation (as compared to the current situation) had to be clear. Methodologies passing the criteria set were subdivided in three categories on the basis of the time period in which the experts expected that the methodology could be implemented. The following categories were distinguished:

1. Immediate implementation possible (i.e. within <1 year).
2. Implementation possible within a period of 1–3 years (e.g. scientific research completed, field validation still needed).
3. Implementation only after a period of time exceeding 3 years (promising approach, but more research needed).

For each pre-selected methodology for assessing bioavailability, all relevant information was included in a so-called fact sheet. During the workshop, an analysis of each fact sheet was prepared containing the strengths, opportunities and weaknesses (SWOT-analysis) (see Box 1 for an illustration). On the basis of the SWOT-analysis, a final judgement was made as to whether the method had the potential of being suited for risk assessment and standard setting, whereas the timeframe for implementation was assessed in case of a positive outcome.

An overview of the methods selected, as well as the outcome of the SWOT-analysis during the workshop, is given in **Table 1** (see **Appendix**). As may be concluded from this table, one topic was considered to be suited for direct implementation (normalization for elementary carbon), six topics were scaled for implementation within 1–3 years and further research is needed for seven topics. Two of the topics with a time scale of 1–3 years deal with biomimetic simulation techniques for organic compounds, while one topic is related to directly measuring dissolved and total concentrations of organic pollutants in water. The remaining topics within this category account for the strong interaction of copper with DOC, and the inclusion of simulation methods for bioavailable metal fractions in soils and sediments. The latter methods are related and it is proposed that both methods be considered simultaneously when further investigating their applicability. Furthermore, it is recommended that further work be linked to these methods for two of the topics needing research for >3 years before implementation (DGT and subsequent or parallel extractions). The excess value of the proposed methodologies, as compared to the methods currently applied within risk assessment and standard setting, is related to the fact that the proposed methodologies have the potential of avoiding an unnecessary overestimation of the risk associated with the presence of contaminants in ecosystems.

Conclusions

On the basis of the discussion of the fact sheets during the workshop, it is advised to:

- implement the proposed method for normalization of levels of organic compounds on the basis of elementary carbon present in the substrate towards (Dutch) standard sediment and standard soil;
- decide to modify the existing standards for local natural background levels, as a short-term solution to substitute for the current practices in the Netherlands of normalization on the basis of so-called standard soil or sediment. This provided that a trajectory for the incorporation of bioavailability is initiated;
- establish clusters of research groups that are commissioned to prepare proposals for an implementation of the six topics for which it is foreseen that implementation is possible within 1–3 years, such as DOC-correction for copper in water (**Box 1**). This included an investigation of ways of financing the necessary research activities;
- look for broader (international) support for further research activities and ways of implementation within an international framework (EU) for all options with a timeframe >3 years. The recommendations of the workshop might be one of the criteria for the selection of research proposals within the area of bioavailability;
- stay alert on new developments within the broad area of bioavailability and continue looking for ways of implementing the most promising new insights.

Box 1: Summary SWOT Table 'DOC-correction for copper in water'

Contents. Standards (like Maximum Permissible Concentration, Target Value) for copper in surface water are deduced from laboratory tests in which the metal has been added as a highly soluble copper salt. Due to very low dissolved organic carbon (DOC) concentrations in the test medium, the copper ions generally have a maximum availability for uptake by organisms. Standards that are deduced from laboratory tests, in which exposure is expressed on the basis of actually measured total copper concentrations in the aqueous phase, therefore truly reflect bioavailable metal fractions. Under field conditions, it is evident that a significant fraction of the copper present in surface water is bound to DOC. Hence, toxicity of copper in surface waters will be less than predicted on the basis of laboratory testing and current standards will not take this effect into account.

For copper, and other metals for which a binding to DOC is of relevance, it is proposed for:

- Standards for dissolved metal: to either correct monitoring data for the fraction of metal bound to DOC before comparing the data to the current risk limits, or to adjust the current standards for dissolved metal by expressing the standards in terms of DOC-levels of the surface water.
- Standards for total metal: to modify the current risk limits by taking the modifying effects of binding to DOC into account.

Framework. Site-specific risk assessment of copper in surface water.

Assumptions

- Uptake of copper by biota proceeds via the aqueous phase, while the biological availability of the metal fraction bound to DOC is negligible for all aquatic organisms.
- Binding of metals to DOC is independent of other water parameters (zoals pH, alkalinity). Should this basic assumption not be met, then ranges for pH and alkalinity should be given within which the DOC-correction proposed here is applicable. Recently developed Biotic Ligand Models may be useful for this purpose.
- The (average) complexation constant K ('average' because we are dealing with many Cu-complexes) for the binding of Cu to DOC is constant over the year and independent of the composition of the DOC.

Evaluation. Maximum Permissible Concentrations (MPCs) for copper (and zinc) are systematically exceeded in Dutch surface waters: in many cases by more than a factor of 3. Binding to DOC appears to be relevant at least for copper. It is expected that hardly any exceeding of standards will occur after correction for binding to DOC. It is expected that the inclusion of binding to DOC will result in an MPC for copper in the Rhine and Meuse rivers (3 mg DOC per liter) of 3.2 µg/l, instead of the current value of 1.5 µg/l.

Limitations

- DOC-levels in surface waters are not routinely measured.
- Binding to DOC is relevant for a limited number of metals.
- Values of the metal-specific (average) complexation constant K for the binding of metal to DOC have not been determined for most metals. Data from empirical field surveys is only available for copper.
- Lack of knowledge of the dependence of K on other water parameters like pH and alkalinity may be a limiting factor.
- The impact of complexation to DOC on toxicity has only been shown for copper during acute toxicity tests with Daphnia. More data for other trophic levels is needed.
- A basic assumption is that copper uptake takes place merely via the aqueous phase. More data is needed to substantiate this assumption.
- Empirical data collected in the field shows that binding to DOC is substantially 'different' in acid surface waters (pH <6), although it should be noted that alkalinity in these 'acid' waters was low as well.

Applicability. For copper, it seems possible to take binding to DOC into account. Currently, research aimed at assessing the impact of DOC-binding on copper toxicity for other water organisms than Daphnids (fish and algae) is about to be completed. Implementation will probably take 1–3 years. Insufficient information is available for other metals.

The fact sheets and the main findings and recommendations of the workshop are reported in a joint RIZA/RIVM report (in Dutch), which is available upon request (RIZA-report 2002.003, RIVM-report 607220006/2002).

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Appendix

Table 1: Overview of the fact sheets on the basis of the time frames indicated

Fact Sheet	Suited for either adjustment of standards, or implementation in generic or site-specific risk assessment	Final judgement (Yes, Yes provided that..., No provided that..., No)	Further remarks and possible or necessary follow-up
Time frame: <1 year			
Normalization for elementary carbon	Adjustment of standards and generic risk assessment	– Yes. – Modification of a method for measuring organic carbon that, in contrast to the current methods, produces a univocal measurement of the organic carbon content of sediments or arable soils. The method is being used internationally. – Implementation of the method would result in a (slight) modification of current standards since the current standards are based on organic **matter** contents.	– It is recommended to implement the method proposed in generic risk assessment.

Table 1: Overview of the fact sheets on the basis of the time frames indicated (cont'd)

Fact Sheet: Code and title	Suited for either adjustment of standards, or implementation in generic or site-specific risk assessment	Final judgement (Yes, Yes provided that..., No provided that..., No)	Further remarks and possible or necessary follow-up
Time frame: 1–3 years			
Passive sampling of hydrophobic organic micropollutants (with log K_{ow} 4–8) in the aquatic environment	Site-specific risk assessment	– Yes, provided that the methods are properly validated. – Yes, provided that the link with uptake and ecotoxicological effects is clarified.	– For all six topics, most of the fundamental research efforts have been completed. Consequences of implementation cannot yet be foreseen. – The first two topics should preferably be further processed jointly. – With regard to DOC-correction, it is necessary to take international developments, like the application of Biotic Ligand Models within the framework of the European Risk Assessment of metals, into account. It was also emphasized that new methods should not be restricted to copper, but should be applicable for 'all' metals. – The two extraction methods for metals are linked to each other as well as to three of the topics for which a time horizon of >3 years is foreseen. It is recommended not to limit further activities within the area of metal extraction to the two methods with a short time horizon, but to instead include the latter topics as well. The framework for subsequent or parallel extractions is recommended to be used as a guide for further work in this area. A time frame for the development of the overall framework of >3 years is foreseen.
Tenax-extraction	Site-specific risk assessment	– Yes, provided that the methods are properly validated. – Yes, provided that the link with uptake and ecotoxicological effects is clarified.	
The 0.43 M HNO_3 extractable metal content	Generic standard setting	– Yes, provided that: 1 – more insight is obtained using this method regarding differences between available background levels and available metal levels following metal addition to soils, and 2 – the link with uptake by biota and ecotoxicological effects is clarified.	
The 0.01 M $CaCl_2$ extractable metal fraction	Site-specific risk assessment	– Yes, provided that the underlying basic assumptions are validated (different organisms and plants, various soil types and various soil properties, as well as different emission sources). Application in combination with other extraction methods (like 0.43 M HNO_3). – 1 year when applied in combination with aquatic toxicity data. – >3 years when applied in combination with terrestrial toxicity data that is based upon 0.01 M $CaCl_2$-extraction.	
Measuring truly dissolved and total concentrations of pollutants in water	Generic risk assessment	– Yes, but only for highly hydrophobic organic micropollutants. – Applicability from a technical point of view: <1 year. – Applicability from a practical point of view: 1–3 years because of additional needs to tackle the threats.	

Table 1: Overview of the fact sheets on the basis of the time frames indicated (cont'd)

Fact Sheet: Code and title	Suited for either adjustment of standards, or implementation in generic or site-specific risk assessment	Final judgement (Yes, Yes provided that..., No provided that..., No)	Further remarks and possible or necessary follow-up
DOC-correction for copper in water	Site-specific risk assessment	– Yes. – 1–3 years, dependent upon collection of chronic toxicity data. Approach can also be used for other metals.	
Time frame: > 3 years			
Passive sampling for other micropollutants in the aquatic environment and for all compounds in the soil compartment.		– >3 years for other compounds in the aquatic environment and for **all** compounds in soil. – In all cases: provided that the link with uptake and ecotoxicological effects is laid.	– Active participation within broader research frameworks needed (like EU).
Distinction between soft and hard bodied species.	Site-specific risk assessment	– Yes, provided that (a lot of) additional research is carried out. – >3 years (probably even >5 years).	
Site-specific risk assessment and transfer functions	Site-specific risk assessment	– Yes, provided that transfer functions are linked to uptake and actually occurring effects. Otherwise, application for assessing remediation priorities of pollution sites. – >3 years: between 1–3 years needed for further development of transfer functions.	
Use of DGT (Diffusive Gradients in Thin films) to assess bioavailable fractions	Site-specific risk assessment	– Yes, but only for water and sediment and provided that the link with ecotoxicological effects is clarified (this is generally a difficulty for most simulation techniques for bioavailability). – >3 year.	
Subsequent or parallel extractions	Generic risk assessment	– Yes, provided that the link with ecotoxicological effects is fortified. – >3 year.	
Correction for local background concentrations only	Deriving criteria	– No, unless a trajectory for incorporation of bioavailability in risk assessment is started (temporary solution). – Implementation of the correction for local background levels, in itself, possible within <1 year.	
Two-step risk assessment of zinc in anaerobic sediments, incorporating AVS-corrections.	Site-specific risk assessment	– No, unless the benefits of the assessment are shown. Amongst others, relationship with ecotoxicity needs to be substantiated. – >3 years, mainly because of the need of substantiating the relationship with ecotoxicity.	