Perspective

Bias, complexity, and uncertainty in ecosystem risk assessment: pharmaceuticals, a new challenge in scale and perspective

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Abstract

Because thousands of pharmaceutical and industrial compounds are in use today and distributed into ecosystems via waste water, effective analysis of environmental risk needs to change as our understanding of the complexity of ecosystem services grows. Klaminder et al (2014 Environ. Res. Lett. 9 084003) now provide some important observations on a methodological bias in standardized ecotoxicological tests. First, the authors show that the formalized use of control species in risk assessment impacts how data is judged and valued. Reducing quantitative uncertainty may improve the rigor of toxicological assays, but may also increase the risk of missing likely ecosystem-scale impacts, essentially ‘throwing the baby out with the bathwater’. Second, we should recognize the importance of integrating nature, complexity, and dynamics across temporal and spatial scales in relation to the unintended consequences of pharmaceuticals and their partial degradation products in the environment. Since ecosystems and our broader life support system are composed of various stability states with dynamic cycles, feedback can destabilize a system as we know it. Complex systems have emergent properties with high degrees of uncertainty and ecosystem risk assessments must report not only toxicological risks but also ‘benefits’. In addition, risk assessment must expand its scale from the molecular and cellular to that of the ecosystem with real world conditions. The authors’ findings that exposure to Oxazepam led to increased survival and aggressiveness should inform changes in standardized testing methodology as well as improvements in regulatory policy.

Keywords: pharmaceuticals, risk assessment, complex systems, ecosystem, uncertainty

Exposure assessment is a major component of the risk assessment process and an integral part of managing environmental risks (Dunlap et al 2011, Loring and Duffy 2011). As the human population increases and knowledge about ecosystem function grows, both science and society have expanded their perspectives, recognizing the scale change in the expanded interaction between the growing human social economic system and the Earth’s ecosystems. Living in megacities and the growth of the global pharmaceutical industry have had an undeniable impact on human health over the last century. Both social and environmental systems are complex with many interconnected components and feedbacks from which emerge distinctive features and behaviors. These complex systems are characterized by self-organization, dynamic cycles, stability domains, and uncertainty (Chapin et al 2009). However, the implication that this uncertainty...
means risk assessment and environmental management is weak and needs to be simplified, regimented, and standardized is dangerously misleading (O’Brien 2000). Risk assessment needs to move to a more complex world view that includes both spatial and temporal scales as well as increasing organizational scales. In the last decade, new analysis models combining risk and benefit have been developed (Ginsberg and Teal 2009). Including the benefit component makes the associated monitoring and exposure assessment more challenging in terms of logistics, statistics, and economics. Many basic ecotoxicology questions regarding chronic population-wide exposure to mixtures of contaminants remain unanswered (Godduhn and Duffy 2003). Klaminder et al (2014) suggest that increased standardization may not be the right answer for ecosystem risk assessment because tests may be too narrow in scope and a toxicological bias in experimental design of controls may exist. Klaminder et al (2014) illustrate a conceptual problem when standardized methods systematically disregard assays with high mortality in the control groups, which often occurs in natural populations—especially fish.

In the last decade, environmental scientists struggled with interpreting complex data from endocrine disrupting compounds (Colborn et al 1996, Diamanti-Kandarakis et al 2009). Today, the field of ecotoxicology has widened to include pharmaceuticals, which as endocrine disruptors can be toxic at very low concentrations (Christen et al 2010). Until now, a bias against a therapeutic effect has not been very clearly demonstrated. Klaminder et al (2014) observe that ecotoxicological tests with mortalities greater than ten percent are generally discarded. Omitting naturally occurring low mortality rates reduces the likelihood of finding a positive survival effect. This standardized approach can overlook potential therapeutic effects, such as improved population growth. Unnaturally healthy controls may improve the statistics and reproducibility of the assay, but may be inappropriate as an ecopharmacological model in a similar way that young mice and rats were poor models for the Alzheimer’s brain. Klaminder et al (2014) using wild Eurasian perch fry, demonstrate that a low dose of Oxazepam, a benzodiazepine, reduces mortality and increases aggressive behavior. Their observation of Oxazepam’s effect during days 7–9 add to the validity of the specific therapeutic impacts pharmaceuticals can have on brain development. This type of effect would lead to a population growth of perch in the ecosystem, which might be good for perch but disastrous for the system.

Their second and perhaps more significant contribution encourages us to consider ecosystem functions and values, which will differ from those of an individual organism or species. Carson (1962) was among the first to alert us to the dangers of chemicals on the ecosystem. Later, Ehrlich (1968) alarmed us in his controversial book The Population Bomb that numbers do matter and over population is interrelated with resources and environment. As we enter the Anthropocene, we see that some aspects of his predictions may be more correct than previously believed.

While outcome predictions are inherently speculative, especially in complex systems, feedback to the ecosystem from pharmaceuticals on behavior and survival make risk assessment more complex than current toxicological ecosystem response models can account for. Even as scientific knowledge of a system improves, uncertainty will remain (Godduhn and Duffy 2003). Unfortunately, feedback does not wait for our recognition to operate, so precaution must become an important tool in managing human activity to ensure functional ecosystem services.

From historical waste sites to contemporary spills and non-point source pollution, there are many unintentional natural experiments occurring in which the inadvertent pharmacological effects of chemicals can be monitored in addition to traditional toxicological assays (Bowyer et al 2003, Manahan 2011, Godduhn et al 2013). The precautionary principle accounting for the irresolvable uncertainty of complex systems needs to be included so that recognition a system’s potential
destabilization is included in policy decisions. The logistical and spatial barriers to accomplishing a thorough ecosystem risk assessment can be reduced by using ‘citizen science’ to increase the availability of data, creating an ecosystem perspective. This approach will allow a longitudinal design to support the sustainability goal for the health and welfare of future generations.

Summary

People have been making risk assessments based on observations for much longer than government organizations have existed. A systematic and strict disciplinarian paradigm has developed out of a delicate mix of science, statutes, management policy and economics. The steps of risk assessment for ubiquitous, low level mixtures of pharmaceutics that may cause multi-generational effects on a species and even its ecosystem may be confounded by historical biases associated with the method development. Klaminder et al (2014) has demonstrated a bias exists against therapeutic impacts on species behavior. As the authors suggest, the battery of ecotoxicological tests should include specific assays observing any therapeutic impacts of pharmaceuticals in urban waste effluents, similar to the development of endocrine disruptor assays in the 1990s. This could be a reasonable first step in overcoming and identifying any method biases.

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