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REVIEW ARTICLE

EVIDENCE-BASED TOXICOLOGY: WHERE DOES IT GO?

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Summary

Evidence-Based Toxicology (EBT) was established in 2005 as a tool for toxicological risk assessment and causal link on the basis of the parallel relationship between the toxicological test method evaluation and the Evidence-Based Diagnostic Testing Assessment (EBM). The introduction of evidence-based principles can provide new tools that are necessary to validate toxicological testing methods. EBT should contribute to testing strategies to address toxicology problems in the 21st century. Practice has shown that the underlying concepts of EBT, such as the use of systematic reviews to capture and consider all available information, improve the results of toxicological assessment conducted by different groups and organizations. New challenges are emerging before toxicology, such as safety assessments of new agrochemicals, pharmaceuticals and nanomaterials, and EBT can provide important results for their application in practice.

Key words: Evidence-based toxicology (EBT); causation; environmental health

INTRODUCTION

The experience of recent years with the ambiguous results of toxicological studies of significant chemical substances has convinced the scientific community that new ways of assessing are needed to keep pace with recent advances in the development of toxicological testing methods that use better scientific understanding through modern biochemistry and molecular biology. By analogy to evidence-based medicine (EBM) (Eddy, 2005), the umbrella term evidence-based toxicology (EBT) has been constituted (Stephens et al., 2013). The EBT aims to summarize all approaches to better implement the above principles based on evidence in toxicology in general and in toxicological decision-making in particular. The main reason for the development of new evidence-based toxicological approaches was to improve their predictive value and to increase the performance of toxicological testing methods (Hoffmann and Hartung, 2005).

The goal of the EBT is to unify all approaches to better implementation of the above evidence-based principles in toxicology in general and in toxicological decision-making in particular. The aim of the EBT is to improve the evaluation of the results of toxicological test methods (Hoffmann and Hartung, 2005). The EBT can be seen as a process of transparent, rigorous and objective assessment of all available scientific evidence that can contribute to addressing toxicological issues (Hoffmann and Hartung, 2006). The critical point of evidence-based approach for each discipline is the adoption of unbiased and transparent methods during the collection, evaluation and gathering of evidence. Toxicology is no exception.

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The EBT strives for an objective assessment of all available scientific evidence to answer toxicological questions. It must therefore study all the adverse effects of chemical, physical or biological agents on living organisms and the environment (Mandrioli and Silbergeld, 2016). This article aims to show one of the way in which the toxicology of the 21st century is going.

FROM NTP TO EBT

Program NTP (National Toxicology Program) was established in 1978 by Joseph A. Califano. NTP is headquartered at the National Institute of Environmental Health Sciences (NIEHS). NIEHS develops and validates test methods, coordinates toxicological testing programs, and develops approaches and data to strengthen scientific knowledge about potentially hazardous substances. During the 40 years of existence, NIEHS has become the world leader in providing scientific information.

The last decade of the 20th century and the turn of the 21st century have brought dramatic technological advances. This has been reflected in new materials, new chemicals and new pharmaceuticals, but also in new and more dangerous drugs. A huge leap was made by molecular biology and computer science. It is necessary to include these new scientific technologies in the research and testing strategies of toxicology and to expand the scientific knowledge on the link between the mechanism of toxic effect and the disease. The idea of the NTP for the 21st century is to shift toxicology from predominantly observer science to predictive model-specific models. The NTP is to create a framework that will support the further development of toxicology.

DOUBTS

Guzelian et al. (2005) proposed that toxicological risks for humans can only be determined on the basis of human evidence, not on the basis of animal experiments. Ruden and Hansson (2008) believe that looking for a link between EBT and EBM is incorrect. They point out that the criteria for the use of scientific data in the EBM refer to evidence of therapeutic effects, whereas in the EBT these criteria concern evidence of adverse effects. The EBM concept is based on clinical medicine, which retrospectively evaluates evidence of the effectiveness of the approach, while in the case of toxicology it is not possible or at least very difficult (Hartung, 2010, Stephens et al., 2016). While until the 1980s, the field of medicine was dominated by authority-based opinions, expressed by consensus groups of experts relying on their education, training, experience, wisdom, prestige, intuition, skill and improvisation, today is asked to rigorous evaluation of causal relationships and applying these criteria to the published knowledge.

IN SILICO TOXICOLOGY

One of the current toxicology methods that conform to the EBT concept are the *in silico* methods. It has high productivity, but less accuracy. These methods are of great interest to both academic staff and private sector businesses. They are being increasingly evaluated and applied by regulators. *In silico* toxicology methods can complement and strengthen evidence for some regulatory review processes and improve risk management by supporting more informed decisions on prioritization for further toxicological tests in product research and development (Valerio, 2011).

OTHER PATH IS NOT POSSIBLE

The EBT initiative is motivated by growing concerns about whether toxicological decisions based on current tests are correct. Toxicology, despite all scientific and technical progress, is still based on traditional assessment methodologies that have not changed almost anywhere. As a result, the safety assessment is largely based on tests of little known relevance and reliability. Effective and relevant safety assessments in toxicology, however, critically depend on progress in basic scientific research and should adapt continuously to advances in knowledge (Hartung et al., 2017). Concerns mainly center on the transparency and consistency of data interpretation and the integration of various data sets.

In 2011, Johns Hopkins Bloomberg School of Public Health established a nonprofit organization Evidence-based Toxicology Collaboration (EBTC) aiming at improving public health outcomes and limiting the impact of humans on the environment by introducing an evidence-based approach to security science (von Aulock, 2013). The EBTC was based on the idea that adopting the principles of transparency and objectivity would enable regulators to take

more informed decisions on the effects of chemicals on human health and the environment for all stakeholders. The EBTC intends to achieve this gathering under the auspices of the EBTC all workers to apply evidence-based approaches that include safety decisions and have serious consequences for public health (Wikoff and Miller, 2018).

CONCLUSIONS

Even though the EBT concept has been already established in 2006, not a few things had happened since then. At present, systematic reviews are rarely published in toxicology by regulatory agencies, international organizations, or academic scientists. It is evident that the adoption of the EBT-based approach will require significant improvement in the toxicological strategy. The EBT must provide a transparent, objective and scientifically valid evidence assessment in order to generate conclusive decisions. If people do not trust environmental protection, decisions on food safety and medicines and consumer protection and the truth of information that informs them will not trust government activities or participate in civic discourse. To achieve this goal, individual national organizations need to join forces, create a unified concept, share tasks, and work hard on them. In the Czech Republic, the Research Institute of Organic Syntheses is a coordinating workplace - Center for Ecology, Toxicology and Analytics (CETA). This Institute performs analytical, physico-chemical, ecotoxicological and toxicological testing of chemicals and products, wastes and environmental components including sampling. Many universities in the Czech Republic also deal with issues of chemical safety, which in their research projects process materials and information concerning chemicals, preparations and handling in the broadest sense. It is based on both Czech and European regulations and processes information on methods for the detection and evaluation of their hazardous properties.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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REFERENCES

1. Eddy DM. Evidence-Based Medicine: A Unified Approach. Health Aff. 2005;24(1):9–17.
2. Guzelian PS, Victoroff MS, Halmes NC, James RC, Guzelian CP. Evidence-based toxicology: a comprehensive framework for causation. Hum Exp Toxicol. 2005;24(4):161-201.
3. Hartung T. Evidence-based toxicology - the toolbox of validation for the 21st century? ALTEX. 2010;27(4):253-263.
4. Hartung T, Fitzgerald RE, Jennings P, Mirams GR, Peitsch MC, Rostami-Hodjegan A, Shah I, Wilks MF, Sturla SJ. (2017). Systems toxicology: Real world applications and opportunities. Chem Res Toxicol. 2017;30(4),870-882.
5. Hoffmann S, Hartung T. Diagnosis: toxic! Trying to apply approaches of clinical diagnostics and prevalence in toxicology considerations. Toxicol Sci. 2005;85:422–428.
6. Hoffmann S, Hartung T. Toward an evidence-based toxicology. Hum Exp Toxicol. 2006;25(9):497–513.
7. Mandrioli D, Silbergeld E. Evidence from toxicology: the most essential science for the prevention. Environ Health Perspect. 2016;124:6–11.
8. Rudén C, Hansson SO. Evidence-based toxicology: "sound science" in new disguise. Int J Occup Environ Health. 2008;14(4):299-306.
9. Stephens M, Andersen M, Becker RA, Betts K et al. (2013). Evidence-based toxicology for the 21st century: Opportunities and challenges. ALTEX. 2013;30(1):74–104.
10. Stephens ML, Betts K, Beck NB, Cogliano V, Dickersin K, Fitzpatrick S, Freeman J, Gray G, Hartung T, McPartland J, Rooney AA, Scherer RW, Verloo D, Hoffmann S. The Emergence of Systematic Review in Toxicology. Toxicol Sci. 2016;152(1):10-16.
11. Valerio LG, Jr. In silico models and databases as FDA critical path initiative toolkits. Jum Genomics 2011;5(3):200-207.
12. Von Aulock S. Evidence-Based Toxicology Collaboration (EBTC). Editorial. ALTEX. 2013;30(1):1.
13. Wikoff DS, Miller GW. Systematic Reviews in Toxicology. Toxicological Sciences, 2018;163(2),335–337.