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Editorial

Hormesis in Biology and Pharmacology

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Two models of dose-response relationships between dose, concentration or intensity of any effector and response of living organisms are commonly applied in biology and pharmacology [1-8]. In the simplest first linear model, the registered parameter shows a linear increase with increase of dose, concentration, or intensity of the effector (Figure 1A) and in some cases this linear model is also called linear non-threshold model [9]. The latter is important in order to discriminate it from the second widely applied "threshold model" when the response cannot be linearly extrapolated to "zero" level of the effector (Figure 1B). In both cases (Figure 1A and 1B), the α-angles can vary widely and depend on many factors including the model type, specific conditions used and the properties of effectors as well as do the distance "a" in Figure 1B. The latter is called the "lag phase" and may reflect the operation of defense mechanisms that prevent an immediate response by organisms. Biological and pharmacological effects depend on the cumulative effects of single acts of interaction between the effector and the biological subject.

However, in many cases the dose-response relationships do not follow neither linear (Figure 1A), nor threshold (Figure 1B) models. In those cases it shows changes in opposite directions over zones of low and high levels of the effectors. These relationships where low levels of the effector trigger responses opposite to high ones have been called "hormetic", from the Greek hórmēsis meaning "rapid motion, eagerness" (or the ancient Greek hormáein "to set in motion, impel, urge on"). Two main types of these dependences were found. One is called J-shaped (Figure 1C) and the other is inversed U-shaped (Figure 1D) [3,9]. I also propose that the inversed U-shaped hormetic relationship may be more correctly named inversed J-shaped, because it is asymmetric and is cut off at the "zero" point of the abscissa. The relationship between the level of the effector and the biological response that it elicits is a cornerstone of basic and applied disciplines such as biochemistry, physiology, pharmacology, and toxicology. Obvious importance of detail analysis and understanding of dose-response relationships may be illustrated by the existence of specialized scientific journal dedicated to this phenomenon [10]. Search in scientific databases on the hormesis field resulted in 1061 papers in Pubmed found with this keyword on January 14, 2014, and in Scopus for the same date it was mentioned in 1855 documents.

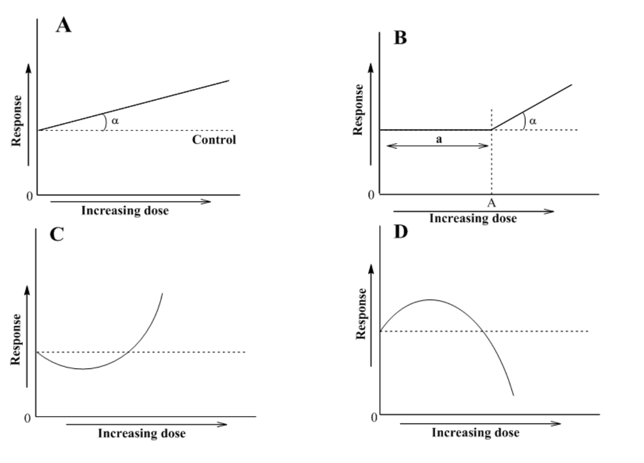

Figure 1: Dose-response relationships: (A) the linear model, (B) the threshold (linear) model, (C) the J-shaped model, and (D) the inverted U-shaped model, or inverted J-shaped model. The dashed line shows initial level of the response being measured (endpoint).

The hormetic relationship was first described more than a century ago [Scultz 1888, cited after 2]. However, due to various reasons it was largely ignored until last decades when it was re-analyzed in details by E. Calabrese and colleagues [1,2]. It is important to note that hormetic effects may be found for broad range of effectors such physical (temperature, irradiation, illumination), chemical (different compounds including drugs), and physiological (physical exercise, hypoxia and hyperoxia, starvation and overfeeding). For convenience all this factors, inducing hormetic effects have been called "hormetins". The registered endpoints also may represent diverse biological parameters such as survival time and efficiency, fecundity, organism mass and length, stress resistance, blood pressure, enzyme activity, protein and hormone levels, energy reserves, etc. Depending on the endpoint selected, dose-response curves can differ for the same organism or under the same conditions.

Last years, attention of researchers is focused on deciphering of molecular mechanisms responsible for development of hormetic relationships [11-13]. It seems that this phenomenon can be based on the induction of nonspecific response of the organisms on stressful conditions without principal difference which sort of stressor is applied. General feature of the hormesis is associated with capability of the organisms to increase their potential to resist stress which may result in improved vital characteristics.

Hormetic concept provides many important clues to biology and pharmacology. However, currently it faces the problems with low reproducibility of the results and their low predictability because the observed effects often depend on many parameters particularly on the physiological state of the organisms. These problems may be solved in several ways. The first, disclosing of molecular mechanisms responsible for hormetic effects may make this field more predictable and reliable. The second, active introduction of mathematical approaches to characterize hormetic curves may help to develop quantitative tools. The third, evaluation of dynamics of the hormetic effects may provide solid basis for pharmacokinetic investigations and application of the hormetic approaches to modern medicine. Finally, careful selection of

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the parameters of interest, their dynamics can be used at treatment of diverse pathologies in targeted and individual manner.

References

1. Calabrese EJ, McCarthy ME, Kenyon E (1987) The occurrence of chemically induced hormesis. Health Phys 52: 531-541.
2. Calabrese EJ, Baldwin LA (1998) Hormesis as a biological hypothesis. Environ Health Perspect 106: 357-362.
3. Calabrese EJ (2008) Hormesis and medicine. Br J Clin Pharmacol 66: 594-617.
4. Calabrese EJ (2013) Biphasic dose responses in biology, toxicology and medicine: accounting for their generalizability and quantitative features. Environ Pollut 182: 452-460.
5. Calabrese EJ (2013) Hormesis: Toxicological foundations and role in aging research. Exp Gerontol 48: 99-102.
6. Ristow M, Schmeisser S (2011) Extending life span by increasing oxidative stress. Free Radic Biol Med 51: 327-336
7. López-Martínez G, Hahn DA (2012) Short-term anoxic conditioning hormesis boosts antioxidant defenses, lowers oxidative damage following irradiation and enhances male sexual performance in the Caribbean fruit fly, Anastrepha suspensa. J Exp Biol 215: 2150-2161
8. Demirovic D, Rattan SI (2013) Establishing cellular stress response profiles as biomarkers of homeodynamics, health and hormesis. Exp Gerontol 48: 94-98
9. Hadley C (2003) What doesn't kill you makes you stronger. A new model for risk assessment may not only revolutionize the field of toxicology, but also have vast implications for risk assessment. EMBO Rep 4: 924-926
10. http://www.dose-response.com
11. Cornelius C, Perrotta R, Graziano A, Calabrese EJ, Calabrese V (2013) Stress responses, vitagenes and hormesis as critical determinants in aging and longevity: Mitochondria as a "chi". Immun Ageing 10: 15.
12. Bayliak MM, Burdyliuk NI, Izers'ka LI, Lushchak VI (2013) Concentration-dependent effects of Rhodiola rosea on long-term survival and stress resistance of yeast Saccharomyces cerevisiae: the involvement of Yap1 and Msn2/4 regulatory proteins. Dose-Response. DOI: 10.2203/dose-response.13-013.
13. Lushchak VI (2014) Dissection of the hormetic curve: analysis of components and mechanisms. Dose-Response. Submitted for publication.