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Editorial Open Access

Hormetic Curves: Superposition of Declining Deleterious and Activation Processes

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Hormesis phenomenon first described almost a century ago for sometime was virtually forgotten, but recently recalled and got new inspiration [1]. Despite enormous efforts have been applied, our knowledge on molecular mechanisms is still rather limited. Recently I have published the paper with analysis of components and molecular mechanisms potentially responsible for the hormetic effects and interested reads are invited to learn the problem in details [2]. General ideas on the hormetic effects are given at the Figure 1. Obviously, activation part of the hormetic relationships (curve 1) is under hot debates. The area limited by upper portion of curve 1 and horizontal dashed line is usually called "activation" area. However, it is not correct from theoretical point of view. In reality, curve 1 is a superposition reflecting two different processes such as deleterious one which in most experiments demonstrate dose/concentration promoted decline (curve 2) and other one reflecting "activatory" processes (curve 3). In this case, the activation portion of total hormetic curve 3 may be calculated by subtracting parameters of curve 2 from ones of curve 1. So, received curve 3 shows the only activation process of the endpoint at different doses/concentrations.

The question is: how experimentally factorize total curve 1? To respond the question, it is desirable to know the mechanism(s) responsible for observable activation. To date, in some cases potential mechanisms involved in net provision of total hormetic curve have been deciphered. For example it is believed that in animals regulatory Nrf2/Keap1 system may be responsible for the resulting behavior of the system [3]. Interestingly, this system was found to be a master regulator of animal adaptive response to oxidative stress and one induced by electrophyles [4]. In budding yeast *Saccharomyces cerevisiae* we found that hormetic effect of adaptogenic medicinal herb *Rhodiola rosea* could be realized via protein Yap1, a master regulator of yeast adaptive response to oxidative stress [5].

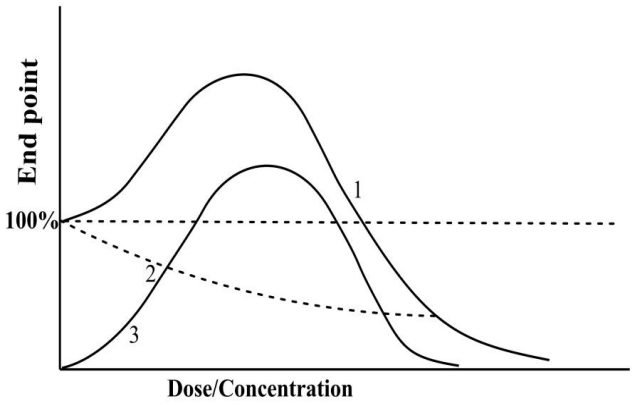

Figure 1: The area limited by upper portion of curve 1 and horizontal dashed line is usually called "activation" area. However, it is not correct from theoretical point of view. In reality, curve 1 is a superposition reflecting two different processes such as deleterious one which in most experiments demonstrate dose/concentration promoted decline (curve 2) and other one reflecting "activatory" processes (curve 3).

There are several potential ways to identify regulatory pathways involved in realization of hormetic effects. Here I will highlight only two of them, which look the most straightforward. The first one, if we know or least predict potentially involved pathway and there is a more or less specific inhibitor, the pathway may be inhibited. If this inhibitor abolishes activation part of the curve 1 (virtually it that finally transforms curve 1 in curve 2) one may expect involvement of the pathway under inspection. On the other hand, if that is not the case, there is a real chance, that the questioned regulatory pathway is not involved. The second approach is provided by ability to manipulate with genetic material. It is possible now to inactivate specific gene(s) and prevent production of certain proteins, including regulatory ones. Using these sort of specific knock-outs one may inspect certain regulatory pathways. If some effector causes hormetic effect in the organism, but in its knock-outed counterpart does not do this, it is possible to expect involvement of the pathway of interest in realization of hormetic effects. One more approach is ideologically close to these two listed ones. If it is suggested that gene expression may be responsible for hormetic effect, it is possible to use inhibitors of mRNA and/or protein biosynthesis. With prokaryotes usually chloramphenycol (chlornitromycin) is used to inhibit bacterial protein synthesis, whereas rifamycins are used to inhibit bacterial RNA synthesis. With eukaryotes, inhibitor of RNA synthesis actynomicin D and inhibitor of protein biosynthesis cycloheximide are used, respectively. The described strategies may be used also in certain combinations to get more reliable response to question of interest.

Overall, the described above analysis may not be only used for deciphering of molecular mechanisms involved in development of hormetic phenomenon. It also may have predictive power. Results from this sort of studies, similar strategy can be applied to investigate effects of hormetins with unknown mechanisms of action. That can be useful at studies in Biochemistry and Pharmacology of potential drugs most of which may have hormetic character of influencing of biological systems.

References

1. Calabrese EJ, Baldwin LA (1998) Hormesis as a biological hypothesis. Environ Health Perspec 106: 357-362.

2. Lushchak V.I. Dissection of the hormetic curve: analysis of components and mechanisms. Dose-Response, 2014. In press. DOI: 10.2203/dose-response.13-051.

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3. Calabrese V, Cornelius C, Dinkova-Kostova AT, Calabrese EJ, Mattson MP. Cellular stress responses, the hormesis paradigm, and vitagenes: novel targets for therapeutic intervention in neurodegenerative disorders. Antioxid Redox Signal. 2010;13(11):1763-811.

4. Lushchak VI. Adaptive response to oxidative stress: Bacteria, fungi, plants and animals. Comp Biochem Physiol C Toxicol Pharmacol. 2011 Mar;153(2):175-90.

5. Bayliak MM, Burdyliuk NI, Izers'ka L.I., Lushchak V.I. (2014) Concentration-dependent effects of Rhodiola rosea on longterm survival and stress resistance of yeast Saccharomyces cerevisiae: the involvement of Yap1 and Msn2/4 regulatory proteins, Dose-Response 12: 93-109.