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Review

Growth, bioluminescence and shoal behavior hormetic responses to inorganic and/or organic chemicals: A review

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ABSTRACT

A biphasic dose response, termed hormesis, is characterized by beneficial effects of a chemical at a low dose and harmful effects at a high dose. This biphasic dose response phenomenon has the potential to strongly alter toxicology in a broad range. The present review focuses on the progress of research into hormetic responses in terms of growth (in plants, birds, algae and humans), bioluminescence, and shoal behavior as end points. The paper describes how both inorganic and organic chemicals at a low dose show stimulatory responses while at higher doses are inhibitory. The article highlights how factors such as symbiosis, density-dependent factors, time, and contrasting environmental factors (availability of nutrients, temperature, light, etc.) affect both the range and amplitude of hormetic responses. Furthermore, the possible underlying mechanisms are also discussed and we suggest that, for every end point, different hormetic mechanisms may exist. The occurrences of varying interacting receptor systems or receptor systems affecting the assessment of hormesis for each endpoint are discussed. The present review suggests that a hormetic model should be adopted for toxicological evaluations instead of the older threshold and linear non-threshold models.

Contents

1. Introduction

Moderate levels of organic and inorganic chemicals promote biological end points such as cell viability and proliferation, growth, bioluminescence, shoal behavior, life span and reproduction, whereas excessive levels are debilitating (Cedergreen et al., 2004, 2005a; He et al., 2007; Kurta and Palestis, 2010; Lefcort et al., 2008; Shen et al., 2009; Silva et al., 2012). Toxicology is the study of chemical toxic effects on the ecosystem or environment (Gallo and Doull, 1996), but many chemicals as a factor of dose have opposite effects. For example, antibiotics such as streptomycin, penicillin and erythromycin at low doses stimulate bacterial growth and are inhibitory at higher doses. Additionally, it has been documented that mild chemical stress can enhance the growth and respiration of yeast, but intense stress shows inhibitory effects (Cabral et al., 2003; Mattson, 2008). Similarly, the generalized phenomenon of positive effects at a low dose and negative effects at a high dose has been published by many authors for different chemicals and is now

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known as the Arndt–Schulz Law. Six centuries ago, Paracelsus explained that dose is important and the effect of noxious chemicals in medicine depends on the dosage. These examples of small quantities having positive effects in contrast to large quantities are commonly termed hormesis (Calabrese and Baldwin, 2002). The hormesis concept claims that when the dose of a toxic chemical being studied is reduced, the response of the end point being measured does not simply get smaller and smaller, drifting into background noise, but may actually reverse course and alter to a contradictory response. Hormesis proponents consider it extremely generalizable according to the chemical/physical agent, end point selection and measurement. Hormesis is apparent in both toxicology and biology (Calabrese, 2008, 2011).

Toxic chemical and biological dose responses show relationships that usually come in two classes. The first is the threshold model, the most extensively used and central model in toxicology, which can influence several aspects of research. The second, the linear non-threshold model (LNT), shows increased biological effect with higher concentrations, typically seen with carcinogenic compounds (Davis and Svendsgaard, 1990). However, neither the threshold model nor the linear non-threshold model is completely reliable, because various responses affected by dose cannot be explained by these models. Recently, over the past decade, the hormetic dose response model has attracted considerable interest as it describes positive effects at a low dose and negative effects at a high dose (Fig. 1).

For a variety of chemicals such as heavy metals, cyanide, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, pesticides, organic arsenic compounds and some antibiotics, and different biological systems (animals, plants, and microorganisms), the hormetic model is quite common (Calabrese and Baldwin, 2001, 2003; Rodricks, 2003). A typical dose–response curve shape depends on the end point of interest, which may be either U-shaped or inverted U-shaped. The shape of the dose–response curve is an inverted U-shape if longevity or growth is the endpoint; if disease is the endpoint, it would be U-shaped and J-shaped. The new hormetic model challenges both the threshold model and the LNT model, and suggests that lower doses enhance quantitative and qualitative changes in the response assessed. That is, as the dose of a carcinogenic compounds decreases, it attains a position where the toxic chemical really might lessen the threat of cancer compared to the control group. Although hormesis is a very commonly observed phenomenon, the presumption of a biphasic response has been crippled by a less understood and accurate underlying vigorous mechanism and the partial correlation between in vitro and in vivo studies (Bae et al., 2008).

Various review papers on hormesis have been published on different end points, such as carcinogenicity (Fukushima et al., 2005), health nutrition hormesis (Hayes, 2006) and hormesis modeling (Calabrese and Blain, 2005), default dose–response models (Calabrese, 2004) and dose response revolution (Calabrese and Baldwin, 2003); some generalized reviews on U-shaped dose–responses in biology, toxicology, and public health are also available (Calabrese and Baldwin, 2001). However, in the last two decades, much of the attention has been focused on chemical hormesis using growth, bioluminescence (frequently used) and shoal behavior (less frequently used) as the end points to check hormetic effects of chemicals in plants, algae, birds, human cells, bacteria and fish. These end points not only provide a good picture of the ecological integrity of a system, but also provide an early warning of impending ecological change under chemical stress (Harwell, 1993; Lackey, 1994; Suter and Barnthouse, 1993). Using these end points means that one can easily figure out the potential beneficial or harmful effects of chemicals on organisms, their aggregate toxic effects, chemical bioavailability, and also characterize the nature of a beneficial or toxic effect, relatively simply and cheaply (Suter and Barnthouse, 1993). Such methods are reproducible, responsive, representative, robust and relevant and have practical applications in toxicity testing and ecological risk assessment (Spurgeon, 2002).

Several factors influencing the expression of these three aspects hormesis could be identified that may explain its unpredictability, and hamper its practical use to stimulate growth, bioluminescence and shoal behavior. Therefore, the present review highlights the potential of

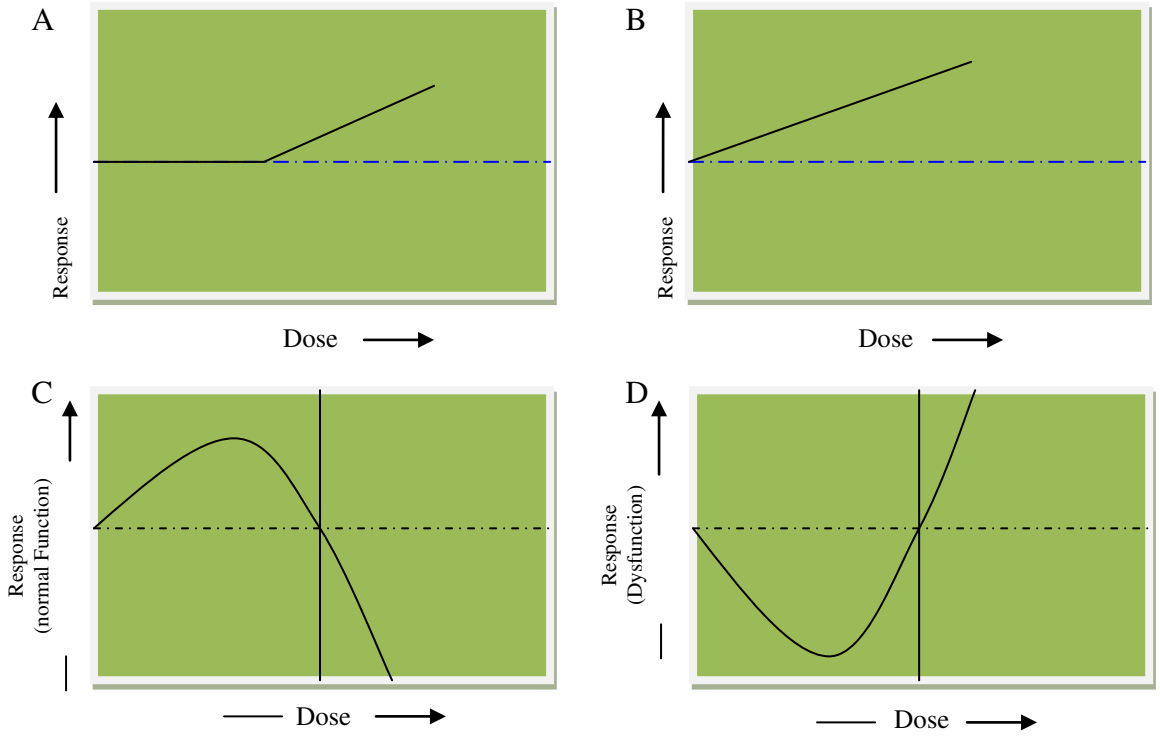

Fig. 1. Dose–response relationships described by (A) the threshold model, (B) the linear non-threshold model, (C) the inverted U-shaped hormetic model and (D) the J-shaped hormetic model.
Adapted from (Davis and Svendsgaard, 1990).