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Biomedical Significance of Hormesis

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Abstract: Hormesis is a two-phase dose response with specific quantitative characteristics for the amplitude and width of stimulation. It is highly generalized and independent of the biological model, endpoint, causative agent, biological organization level, and mechanism. Hormesis can be triggered by direct stimulation or by over-compensation for disruption of homeostasis. Induction of hormesis by low-level stressors not only rapidly regulates adaptive processes to repair damage, but also protects the adapted system from damage due to the next difficult dose (toxic) in a defined temporal window. The remarkable consistency of the amplitude of the hormetic reaction gives a quantitative description of the biological plasticity of the hormesis. Knowledge of hormesis has particular potential biomedical significance in slowing or slowing down normal aging processes and the development of severe diseases.

Key words: Hormesis, ageing process, diseases, curcumin, aerobic exercises

Introduction

The two-phase dose-response specific to the hormetic event can be triggered by many stressful conditions or by toxic substances, including nutrients. Recent evidence suggests that vitamins, minerals, and phytochemicals can provide healthy benefits that act in a hormone-like manner by modulating stress response pathways, leading to the concept of hormesis in the field of nutrition allows full application. All natural or synthetic compounds that exhibit this property are called hormetins.

Importantly, activation of hormonal mechanisms in different animal models prolongs life and delays the onset of age-related functional impairments. For example, multiple signs of a calorie-restricted animal stress response indicating life expectancy and hypothalamic-pituitary-adrenal activation. Thus, this type of nutritional intervention produces a moderate amount of stress that is capable of triggering a hormonal reaction, thereby increasing the body's ability to cope with many different ailments. However, it should be noted that the beneficial effects of calorie restriction are not universal but specific to the species, and different mouse strains may have opposite effects, ranging from longer life to shorter lifespan, a greater genetic background in disease control. indicates that it may play a role in stress response.

Curcumin induced hormetic effect

Curcumin (diferuloilmethane), a component of yellow powder made from the roots of *Curcuma longa* or *Zingiberaceae* (known as turmeric), is widely used not only to color and flavor food, but also as a pharmaceutical agent. Curcumin exhibits anti-inflammatory, anticancer, anti-aging and

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antioxidant activity, as well as efficacy in wound healing. It is worth noting that curcumin is a hormonal agent (hormetin) because it is a stimulant at low doses and an inhibitor at high doses. Hormesis by curcumin may also have a specific function at low doses (i.e., antioxidant effects) and another function at high doses (i.e., induction of autophagy and cell death). Recent findings suggest that curcumin responds to cells in a two-phase dose, with lower doses having a stronger effect than higher doses; (Nazanin Sadat Aghili Moghaddam 1, 2019) For example, mitogen-activated protein kinase signaling pathway activation or antioxidant activity. This suggests that many of the effects induced by curcumin are dose-dependent, and some effects may be greater at lower doses, indicating a hormetic response. Despite the consistent occurrence of hormetic reactions of curcumin in many biomedical models, epidemiological and clinical trials are needed to assess the dose effects of curcumin in humans. Fortunately, more than a hundred clinical trials with curcumin and curcumin derivatives are ongoing.

Aerobic exercises

Regular aerobic exercise has many benefits to human physiology, possibly serving as a hormetic stressor that leads to positive adaptation over time. It has long been known that aerobic exercise causes intestinal permeability at different intensities and duration, which is a characteristic feature of many pathologies of the gastrointestinal tract and metabolic diseases. Given the health benefits of exercise, it is unlikely that bowel permeability resulting from exercise outweighs positive adaptations. Indeed, a growing body of evidence suggests that adopting exercise regimens that last weeks and months will improve bowel permeability (Bryant H Keirns 1, 2020). The nutrient-sensing mechanisms of carbohydrates, amino acids, and lipids control the specific pathways required to adapt to different metabolic conditions. The role of nutrient-related biosynthesis of hormesis in achieving metabolic homeostasis in the body is significant. Overload of nutrients impairs basic metabolic cell functions and interferes with hormonally regulated inter-organ and intracellular communication, which can eventually lead to metabolic disorders. Hyperglycemia and high levels of saturated free fatty acids lead to overproduction of oxygen free radicals in tissues and cells. This phenomenon, observed in patients with type 1 and type 2 diabetes, is associated with impaired glucose tolerance and the development of the etiology of peripheral complications (Brownlee*, 2010). However, low levels of the same free radicals trigger hormonal reactions that protect cells from the harmful effects of the same radicals. Type 2 diabetes is characterized by subclinical systemic inflammation and impaired regulation of blood glucose levels. Interestingly, impairment of glycemic control occurs in the early stages of this disease despite significant insulin secretion. In the pathogenesis of type 2 diabetes, dysfunction of several organs (including pancreatic islets, liver, skeletal muscle, adipose tissue, intestines, hypothalamus, and immune system) has been identified. However, lifestyle factors that affect diabetes do not necessarily lead to disease in all affected people. Hence, there must be protective mechanisms that can stop the harmful effects of these risk factors. Hormesis describes the next event of exposure to a mild stressor, which is resistance to otherwise harmful, intensified stress conditions. This review discusses the emerging concept that the effectiveness of an adaptive (hormetic) response to lifestyle harmful factors determines the level of protection against the transition to type 2 diabetes. Further analysis of these protective hormone reactions at the molecular level will help identify new

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targets for prophylactic or therapeutic intervention in patients with type 2 diabetes or specific disease. Hormesis is a phenomenon by which a stressor (i.e., toxins, herbicides, etc.) stimulates the cellular stress response, including secondary metabolites production, in order to help organisms to establish adaptive responses. Hormetins of biotic origin (i.e., biostimulants or biological control compounds), in certain doses might enhance plant performance, however, in excessive doses they are commonly deleterious (Mattson, 2008). Biostimulants or biological control compounds of biotic origin are called “elicitors” that have widely been studied as inducers of plant tolerance to biotic and abiotic stresses. The plant response toward elicitors is reminiscent of hormetic responses toward toxins in several organisms. Thus, controlled management of hormetic responses in plants using these types of compounds is expected to be an important tool to increase nutraceutical quality of plant food and trying to minimize negative effects on yields.

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