

## Letter to the Editor

### Hormesis may provide a central concept for homeopathy development

Several toxicological studies have stressed that the interaction between a living organism and a large number of xenobiotics is characterised by a biphasic dose–response behaviour (Calabrese, 2005a, 2005b). Indeed, a stimulatory response is observed when low doses are used, whereas an inhibitory effect is observed when the xenobiotic dose is increased. Although this was observed more than a century ago, the phenomenon was later defined as “hormesis” (Southam and Ehrlich, 1943). The stimulatory response is often modest and difficult to detect so the phenomenon was not significantly considered by the scientific community. However, the large amount of data collected to date seems to suggest that hormesis represents a general biological phenomenon, thus deserving high consideration. In practice, it represents a revolutionary breakthrough of the biological and medical thought dictating that, as stressed by Calabrese and coworkers in the recent past (Calabrese and Baldwin, 2003), toxicology and pharmacology should rethink its central beliefs.

The lack of consideration of the hormetic behaviour resides in the difficulty of obtaining mechanistic explanation at molecular level and, as stated always by Calabrese, by the fact that this hypothesis might offer some support to homeopathy. The latter statement was strongly criticised by Oberbaum et al. (2005) on the pages of this Journal. According to these authors, an homeopathic remedy cannot infer a general benefit; it is highly specific and enduring for a given patient. In addition, homeopathy may involve the use of solutions containing a submolecular amount of the remedy, whereas hormesis always concerns the effects of low but detectable amounts of substances. Finally, the homeopathic remedy is effective only if a well-defined preparative procedure is followed. All the above considerations deserve some discussion.

The hormetic behaviour can be described as the adaptive response of a biological complex system in equilibrium once perturbed by an external agent. In practice, it is an intrinsic property of a self organised system. There exists an obvious parallelism with the principles of physical dynamics and chemical thermodynamics. When a system is moved away from its equilibrium state following the change of an external parameter, the system reacts to counter the external perturbation. Hormesis follows the same paradigm, thus allowing a unified view of the behaviour of any physical, chemical or biological system lying in a pseudoequilibrium stationary state. In a few words, it can be said that the living system not only

reacts in order to quench the perturbation, but it also prepares itself for further interaction by strengthening its defence–repair mechanisms. Following Toussaint et al. (2001), this enhancement of efficiency is associated with the stimulation of the whole set of cells by triggering a rate enhancement of the generation of the ATP. As free energy is made available, product elimination processes are favoured and other repair processes may occur, thus inducing a general benefit to the whole system.

The operational concept of homeopathic therapy is linked to the induction of a subtle interference inside an ill organism with the aim of removing the disease by stimulating the self recovery process. This interference is induced by the homeopathic remedy which in turn is prescribed following the law of similars. The evolution of this therapy since its two-century old original formulation has produced three different medical thoughts: unicism (classical homeopathy), pluralism (clinic homeopathy) and complexism. These different methodological approaches are believed to be characterised by similar therapeutic efficiency. It is worth mentioning that this evolution has partially removed the central concept of the law of similars as a necessary condition. In fact, pluralism and complexism dictate that there are substances which are not peculiar to one person but are claimed to induce general benefits to everybody by stimulating the self recovery processes. It is for these substances the hormesis paradigm fits like a glove. For these reasons, as suggested by Calabrese (2005a, 2005b), it seems desirable that studies concerning the hormetic phenomenon must be developed with the aim of achieving a new perspective in toxicology and pharmacology.

In this sense, it is strongly suggested that in the homeopathic research framework is necessary to develop separate investigations depending on the dilution of the homeopathic drug. As shown by Oberbaum et al. (2001), the use of solutions containing a molecular amount of the drug in the range shown to be effective for hormesis may allow the formulation of general protocols. In addition, valuable information on the mechanistic details may be gained with pharmacological methods by using an appropriate choice of agonist–antagonist systems or high-resolution receptor microautoradiography (Stumpf, 2005). This general perspective is much more difficult to conceive for solutions containing submolecular amounts of the drugs.

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Simonetta Bernardini  
*Società Italiana di Omeopatia e Medicina Integrata*  
(S.I.O.M.I.), Via Cornalia, Milano

Andrea Dei  
*Dipartimento di Chimica, Università di Firenze,*  
*Via della Lastruccia 3, 50019 Sesto Fiorentino-Firenze, Italy*  
E-mail address: andrea.dei@unifi.it.  
Corresponding author.

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