

## REVIEW

# High-dilution effects revisited. 1. Physicochemical aspects



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**Several lines of evidence suggest that homeopathic high dilutions (HDs) can effectively have a pharmacological action, and so cannot be considered merely placebos. However, until now there has been no unified explanation for these observations within the dominant paradigm of the dose–response effect. Here the possible scenarios for the physicochemical nature of HDs are reviewed. A number of theoretical and experimental approaches, including quantum physics, conductometric and spectroscopic measurements, thermoluminescence, and model simulations investigated the peculiar features of diluted/succussed solutions. The heterogeneous composition of water could be affected by interactive phenomena such as coherence, epitaxy and formation of colloidal nanobubbles containing gaseous inclusions of oxygen, nitrogen, carbon dioxide, silica and, possibly, the original material of the remedy. It is likely that the molecules of active substance act as nucleation centres, amplifying the formation of supramolecular structures and imparting order to the solvent. Three major models for how this happens are currently being investigated: the water clusters or clathrates, the coherent domains postulated by quantum electrodynamics, and the formation of nanoparticles from the original solute plus solvent components. Other theoretical approaches based on quantum entanglement and on fractal-type self-organization of water clusters are more speculative and hypothetical. The problem of the physicochemical nature of HDs is still far from to be clarified but current evidence strongly supports the notion that the structuring of water and its solutes at the nanoscale can play a key role.** *Homeopathy* (2013) **103**, 4–21.

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## Introduction

Central to the controversy surrounding homeopathy is the need of a plausible mechanism of action for the very high dilutions (HDs) often used in homeopathy.<sup>1,2</sup> The idea of using extremely low doses of diluted and succussed substances was originally proposed by Hahnemann in the eighteenth century: “*The homeopathic system of medicine develops for its special use, to a*

*hitherto unheard degree, the inner spirit-like medicinal powers of the crude substances by means of a process peculiar to it and which has hitherto never been tried, whereby only they all become immeasurably and penetratingly efficacious (...). This process is called dynamizing, potentizing (development of medicinal power) and the products are dynamizations or potencies in different degrees.*” (Organon, par. 269, 295).<sup>3</sup> These paradoxical claims have always elicited great skepticism,<sup>4</sup> because homeopathic medicines undergo a process of serial dilution whereby the final remedy contains extremely low (often non-measurable) amounts of the active substance. However, not only has homeopathy ‘survived’ these attacks, becoming an increasingly popular medical discipline in western countries, but the study of drugs in HDs is today a rising new interdisciplinary field with more and more

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publications in mainstream scientific journals.<sup>5</sup> Currently, we have reached a stage of research where the investigation of HDs can no longer be presumed to be ‘implausible’,<sup>6,7</sup> as there exists a solid body of interdisciplinary work in favor of such effects which were initially described by homeopathic tradition.

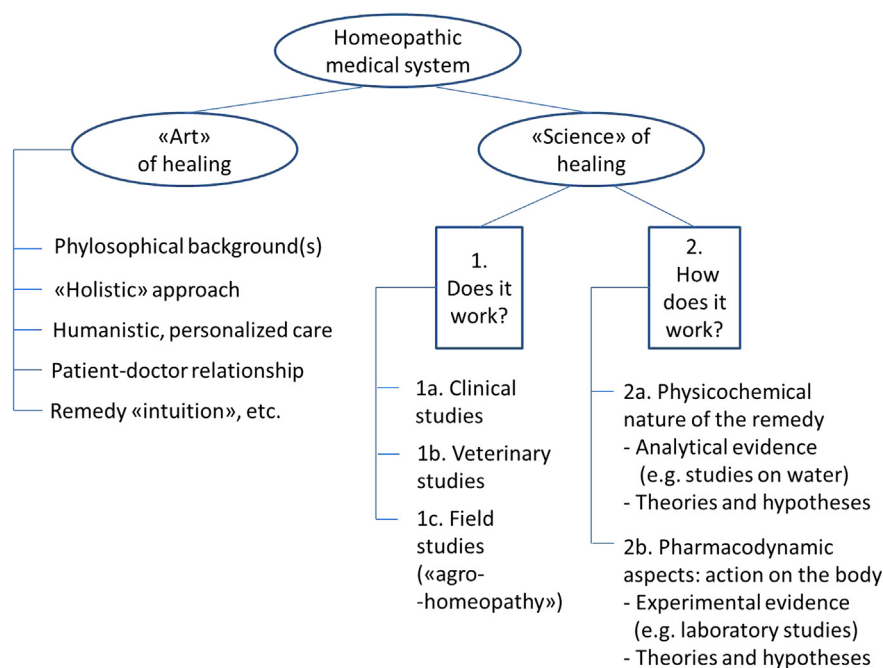
Homeopathy is a complex method of diagnosis and of healing, which has various aspects dealing with peculiar traditional and philosophical background and other aspects dealing with the scientific and rational bases of medicine (Figure 1). These latter are exploited by rigorous scientific research, whose commitments may be divided in two main topics: (1) clinical, veterinary and field research, trying to answer to the question: “does homeopathy work?”, i.e. the problem of efficacy and effectiveness; (2) basic research, trying to answer to the question: “how does it work?”, i.e. the problem of the nature of the remedy and its putative action mechanisms. These great questions may be investigated utilizing different experimental models, made either of human subjects, of animals, of cells and of chemical solutions. The literature in all these fields is rapidly growing. Point 2a of the scheme presented in Figure 1 is the object of this review, while point 2b is the object of a subsequent work.

Even if the clinical evidence of homeopathic remedies’ efficacy is still a matter of discussion for a number of methodological problems,<sup>1,2,8–11</sup> the results from laboratory models<sup>12–18</sup> suggest that highly diluted drugs are endowed with authentic pharmacological activity and are not mere ‘placebos’. That said, there is still a need for more consistent and detailed experimental evidence, in both clinical and laboratory settings, and for working hypotheses that can help us construct unified and consistent theories

explaining the physicochemical nature of HDs and how they exert an action on living organisms. Since this paper deals with physicochemical studies and theories which may be difficult to readers unfamiliar with the specific terminology of the various disciplines, we have provided in Table 1 a glossary of terms, with their definitions.

Homeopathic drugs are used in a wide range of dilutions/dynamizations (also referred to as potencies). The low dilutions – i.e. between 3C and 5C which, depending on the concentration of active principles in the Mother Tincture (MT), correspond to concentrations between  $10^{-6}$  and  $10^{-10}$  mol/L (moles/litre) – can act ‘conventionally’ upon specific molecular and biochemical targets by simply exploiting the high sensitivity of biological systems. Activity of higher dilutions (extremely low doses) – i.e. between 6C and 10C, corresponding to approximately  $10^{-12}$  mol/L (picomoles) to  $10^{-18}$  mol/L (attomoles) – has been often reported in the scientific literature, even in work unrelatedly to studies on homeopathic drugs.

We evaluated through Pubmed the size of the body of knowledge concerning ultra-low doses and related topics. The extreme lower limit of a molecular concentration is the yoctomole, that is  $10^{-24}$  moles/L, corresponding to approximately one molecule per litre of solution. This means a probability of 1/1000 of finding a single molecule in 1 ml of solution. We searched Pubmed using a number of keywords of molar concentrations from picomole(s) to yoctomole(s) and other entries (Table 2). This simple evaluation showed that there are hundreds of scientific papers where ultra-low doses of substances have been analytically measured and/or their effects have been ascertained. As expected, the number of non-homeopathic papers on HDs tends to zero near the Avogadro–Loschmidt constant



**Figure 1** Schematic representation of the main areas of investigation of homeopathic medicine. As every field of medicine, homeopathy is characterized by aspects which belong to the ‘art’ of healing and by aspects which are belong to scientific domains. The two wings are not necessarily in contrast and should be taken into account for a whole evaluation of the medical system.

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