Experimental Evidence Supports New Perspectives in Homeopathy

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Abstract

The contentious debate between homeopathy and orthodox medicine has been due to the fact that homeopathy is founded on a heuristic philosophy that is not justified by contemporary scientific evidence. In this context, however, two pillars of the method, that is, serial dilution and succussion, are poorly understood in orthodox pharmacology. The experimental data collected in the last 10 years, by means of electronic microscopy, electron diffraction and DNA arrays investigations, are consistent with the presence of nanoparticles (nanoassociates) in homeopathic medicines and seem to provide a coherent view of the essence of the homeopathy discipline, superseding all previous speculative interpretations. An acceptance of this new evidence is here suggested to remove, in principle, the barrier that separates the conventional and homeopathic therapeutic methods, and to offer new and important perspectives on future health care.

Introduction

Homeopathy is a therapeutic modality that finds its roots in heuristic philosophy: in its historical development neither the chemical nature of the homeopathic medicine nor the reason for its postulated efficacy at biological level was considered. The paucity of the experimental data in the orthodox sense, together with a skepticism toward the scientific meaning of infinitesimally diluted drugs, leads orthodox medicine to condemn the foundations of homeopathy, which are strictly related to the serial dilution of the medicine coupled with succussion, that is, a vigorous shaking procedure of the resulting solution. The meaning of either the serial dilution or the succussion procedure is not well understood in the framework of orthodox pharmacology. However, since the method predicts that very diluted solutions are therapeutically active as well, even if they challenge the doctrine of matter quantization defined by Avogadro’s number, the theoretical plausibility of homeopathy is deemed to be questionable, despite the fact that this health-care approach is being used by more than 500 million people worldwide. In addition, it is worth mentioning that all the theoretical claims that have been formulated in the past for supporting the therapy must be considered as scientifically unsubstantiated, since they are inconsistent with the currently accepted paradigms of chemistry, physics, pharmacology and toxicology, and therefore are detrimental for the discipline.

If the answers of the homeopathy world to these criticisms may appear hesitant, not convincing and sometimes stuttering, it is important to underline also that the dismissive sentences that ridicule this healing system in terms of theoretical implausibility have been expressed without any appropriate experimental support and find their basis in the speculative opinions of their self-referenced authors. But what is more astonishing, and often underestimated, is that in the recent past several research groups have independently obtained a set of experimental data which, although limited, provide a coherent view of the discipline. This aspect, which should be central in a serious scientific context, is largely under-rated compared with the attention devoted to the formulation of mere opinions and speculations. In addition, a large part of the homeopathy world, including both producers and prescribers, when not
indifferent, is surprisingly reluctant to embrace the new perspective offered by this experimental evidence, and, consequently, the possibility of paving the way for a consolidation of the discipline finds in this attitude a further obstacle. It should be stressed, however, that this position, which succeeds in burying the newness and maintaining an unproductive perspective, is fostering attempts at monopolizing the paradigm of biomedicine toward the supremacy of totalitarian thought in medical therapies—in other words toward the legitimacy of a mono-paradigmatic reductionism, whose resultant is always totalitarian ideology.¹

The aim of this contribution is to show how these experimental findings, when considered as a whole, lead to a well-defined interpretation of the therapeutic method and infer a new scientific consistency to it, whose effectiveness has been more fully discussed elsewhere.²,³ Importantly, the message suggested here does not support the idea that if homeopathy is going to move forward, it has to reinvent itself. The true message is that these experimental data can provide a platform that may justify an examination of the rational evolution of the discipline. In this sense, the attempt is different from that of comparable contributions that have been published in the recent past.⁴–⁸

**Relevant Experimental Points**

In this contribution, to address the problem with appropriate arguments, it is necessary first to define the nature of homeopathic medicines from a physical–chemical point of view and subsequently to investigate if the “drug” affects a biological substrate. Indeed, the therapeutic use of the medicine can be suggested, though not necessarily justified, only if the latter investigation produces significant positive results. In addition, as will be later discussed, when such experimental support is attained, this argument may constitute the conception of a new justified health-care perspective which has profound social impact.

According to the tenets of the method, it is important to highlight that the succussion procedure is a necessary and fundamental component of the correct preparation of a homeopathic remedy. However, it is important not to attribute a “dynamicist” character to this procedure, as postulated by Hahnemann and unfortunately accepted and justified so far by several homeopathy supporters, but a materialistic one. Although the Hahnemann formulation can be considered in agreement with the vitalistic philosophy of that historical period, it is obvious that the presumed dynamicist character of the procedure (i.e., energy transfer translated into information by isothermal shaking) strongly conflicts with basic thermodynamics. The concept of entropy as a measure of information was introduced many years later than the Hahnemann hypothesis.

Nevertheless, the succussion procedure of the remedy solution in glass has been found to play a determining role, since the alleged therapeutic efficacy of the medicine vanishes if the procedure is performed by isolating the glass surface of the recipient with paraffin or if a plastic vial is used.⁹,¹⁰ On the other hand, once powdered glass is added to solutions prepared in plastic vials, the lost therapeutic effects reappear. This means that there is a relationship between the efficacy of the drug and the presence of hydroxosilicate oligomers, whose transfer from the glass container to the drug solution is facilitated by the mechanical stress. The concentration of these hydroxo species is not relevant (in the range of 10⁻⁵ to 10⁻⁴ M), and potentiometric studies suggest that the dominant species in water is the monomeric Si[OH]₄ for a concentration lower than 10⁻³ M.¹¹ However, the possibility of formation of polysilicate species in low-donor solvents such as water–ethanol mixtures has to be considered even in a sub-micromolar concentration range.¹²,¹³ Therefore, these results suggest that the presence of poly(hydroxo) silicate species is necessary for the therapeutic efficacy of the homeopathic remedy. Conversely, the suggested possibility that these chemical species could be involved in some therapeutic information carrying process (the so-called silica hypothesis)¹⁴ does not appear worthy of further development according to the limitation of structural properties of the poly(hydroxo) silicates themselves. A hypothesis about the role of succussion in the preparation of homeopathic medicines has recently been reported and discussed.¹⁵

The role of hydroxosilicate oligomers is somewhat simpler. In the recent past, Bellare’s research group has shown by means of electron diffraction (ED) and transmission electron microscopy (TEM)—and contrary to any previous belief—that when homeopathic medicines containing metal nanoparticles or metal salts are progressively diluted and succussed, their highly diluted solutions contain an unexpected amount of the original substance (some pg/ml).¹⁶–¹⁸ According to these authors, this is due to the formation of an enriched monolayer of nanoparticles or nanoassociates of the remedy on the surface due to froth flotation induced by succussion. The chemical nature of the nanoassociates is supported by experimental data analysis.

The formation of nanoassociates is nothing new, since this event represents a well-known problem in orthodox pharmacology and may profoundly affect the bioavailability, pharmacodynamics and reactivity properties of a drug molecule.⁴,¹⁹–²¹ Conversely, if this phenomenon can be easily justified for natural organic products as a consequence of the balance between solute–solute and solute–solvent interactions, it is difficult to understand in the case of simple inorganic salts unless the donor power of the solvent (in Bellare’s case, water/ethanol 90/95% mixtures) favors the formation of clusters of ionic counterparts.¹⁵,¹⁸ The formation of nanoparticles is associated with a solvent c Hathare and gas nanobubbles,²²,²³ and the resulting system in a homeopathic remedy is stabilized by the poly(hydroxo)metasilicate oligomers, acting as nanoassociate coatings. Therefore, the role of succussion can be explained in terms of a process favoring the occurrence of a simple Lewis acid–base adduct formation involving these hydroxosilicate species.

These conclusions have been further confirmed and developed by results obtained in other laboratories using different homeopathic products and investigation techniques.⁴,⁷,²⁴–²⁷ For that reason, these findings suggest a counter-intuitive conclusion: the serial dilution of a homeopathic medicine.
does not reach the point where no molecule of the homeopathic substance is left in solution, as generally claimed. When the amount of nanoparticles (nanoassociates) reaches a peculiar threshold, that is, when the population of the surface is not negligible with respect to the bulk, the established rules expected for a dilution process are not respected. The suggestion is consistent with the chemical expectation of $10^{12}$–$10^{14}$ molecules/cm$^2$ being present in a bi-dimensional system, as in a monolayer. In fact, the solution of a homeopathic remedy must be considered "non-homogeneous", or a "non-solution", because there is a gradient of concentration between the top and the bulk. In practice, since the serial dilution procedures are currently made using a micropipette to pick the required amount from the top of the apparent homogeneous solution, all the dilutions starting from 3C to 4C are only formal and not real. Of course, this must be considered a methodological "accident", but it greatly facilitates our understanding of extreme dilutions, especially those used as homeopathic medicines. It is also true that the procedures require well-defined standard methods for serial dilutions, as is currently the case in the homeopathic pharmacy industry. If this condition is not verified, the efficacy of a homeopathic medicine may become solely operator-dependent.

The persistence of the presence of active molecules in diluted homeopathic remedies provides significant help in the interpretation of experiments concerning their biological activity. As stressed at the beginning of this contribution, these experiments represent the key to the validation and general acceptance of the therapeutic method, since homeopathy has been developed without consideration for the necessity of establishing the reasons of its alleged efficacy at a biological level.

A notable number of experiments concerning the biological activity of homeopathic medicines has been reported in recent years, most of them being performed by means of DNA microarrays. This technique represents an important tool for clarifying the very heart of a biological network system once perturbed by interaction with a drug. The comparison of gene expression profiles of the perturbed and non-perturbed biological substrate provides significant information. Some of these investigations are experimentally supported by polymerase chain reaction analysis. All studies reported so far show that homeopathic medicines with different concentrations, including those with a formal presence of molecules well beyond Avogadro’s number (i.e., dilution factors larger than 12C), affect DNA gene expression profiles.

The majority of these studies have been performed by comparing the effect of the mother tincture of the remedy with that induced by a highly diluted solution of the same remedy. These studies therefore suggest that homeopathic medicines are biologically active, but they do not provide any information about the mechanism involved or the identity of what is responsible for it. However, some investigations performed by two independent groups have triggered new significant suggestions. These studies show that by treating the DNA microarrays with homeopathic remedies (Gelsemium sempervirens, Apis mellifica and Arnica montana) in different concentrations, including 15C and 30C, the response of the biological system decreases smoothly with increased dilution of the homeopathic medicine. As an example, it was found that the 30C samples show significantly less induced gene expression compared with the 3C ones (by 80–90%). More importantly, they reveal a concentration-dependent inversion of some gene expression as expected in the case of operative hormetic mechanisms. Since it is difficult to accept that all the mysterious mechanisms that have been proposed for justifying homeopathy in both the remote and the recent past—that is, water “memory”, epitaxy, resonance coherent domains, quantum entanglement and many more—should be affected by serial dilutions, it is reasonable to believe that the observed results are consistent with a remedy concentration which is different from that expected, in agreement with the conclusion achieved from ED and TEM investigations.

As a final consideration, it should be mentioned that in homeopathy the therapeutic efficacy of a remedy is postulated to change with concentration. In this concern, the experimental data are very limited. However, in agreement with the above expectation, the concentration-dependent inversion of gene expression has been seen to occur no less than three times for different gene-sets in a human prostate epithelial cell-line treated with copper(II) solutions, with concentrations ranging from $10^{-6}$ to $10^{-17}$ M. For natural products, no well-defined data are available. Since these products are generally mixtures of different constituents, which induce different reactions with the biological substrate, a possible explanation may be suggested by considering the different association affinities of the constituents. In this case, the ratio between the constituents is expected to be dependent on dilution. Nevertheless, detailed investigations are needed to explain the behaviour of any single homeopathic remedy.

The whole set of experimental data, therefore, seems to be consistent with a definition of homeopathy as “nano-dose pharmacology”, where material entities interact with the biological substrate in agreement with the classic view of orthodox pharmacology: to make things clear, the therapeutic consequence is the effect induced by adduct formation by the remedy and the appropriate biological receptor or by modulation of the allostatic stress response network induced by an appropriate xenobiotic. The observation of hormetic behavior of a perturbed biological system may therefore explain the Simile law, which constitutes the basis of the homeopathic method. Finally, these considerations highlight the chemical nature of the biological information induced by a homeopathic medicine, thus leading one to dismiss any other speculative and unfortunately frequently attempted hypothesis about the nature of the therapy.

**Conclusions and Perspectives**

From a general perspective, an acceptance of the above paradigm removes the wall separating the conventional and the homeopathic therapeutic methods. Indeed, there exists experimental evidence that highly diluted homeopathic medicines always contain a relevant amount of molecules. In addition, the same homeopathic preparations are able to induce biological responses, as shown by gene profile
investigations. It may be suggested therefore that these two sets of experimental data provide the basis for acceptance of this therapeutic modality. This until recently unexpected result enables the conclusion that homeopathy can be considered as micro-dose or nano-dose pharmacology in the orthodox sense: formulation of alternative mechanisms, which do not require the presence of molecules, is not necessary. It is also apparent, though much less important, that the same paradigm removes the debate occurring in the homeopathy world between “unicism”, “pluralism”, “complexism” and so on, which are reduced to simple operational approaches.

The conclusion that homeopathy can be defined as a kind of nanomedicine is in agreement with the suggestion made recently by Rajendran.5 This suggestion, which finds its roots in the presence of nanaoassociates in homeopathic medicines, has been criticized and some debatable points concerning the plausibility of such hypothesis have been pointed out.50,51 These criticisms are worthy of consideration and cannot be neglected. In addition, a recent study performed by Van Wassenhoven et al did not confirm the nanaoassociate hypothesis.52 However, it should be stressed that ED data provide unambiguous evidence about the chemical composition of nanaoassociates and—what is more important—the DNA-arrays investigations, which neither Rajendran nor his critics took into account, are consistent with a remedy concentration which is different from that expected, in agreement with the presence of nanaoassociates. Further support for this conclusion is clearly displayed in the results of the studies reported by Konovalov and Ryzhkina.22

There is no doubt that the experimental data we have considered in this contribution are limited, but, as mentioned above, they represent a coherent rational set. The attainment of a larger reliable platform of experimental data is both necessary and highly desirable, and some aspects of the proposed paradigm can be revised and improved with the aim of achieving a better definition. However, it seems reasonable to believe that the obtained experimental evidence overcomes a previously unavoidable limitation, enabling the development of convergent views about the future of the orthodox and homeopathic medical disciplines. These views are not only limited to the traditional improvement of healthcare modalities but also to the development of other perspectives, such as, for example, “anti-aging” medicine, which aims at disease prevention and at extension of human lifespan in a state of wellbeing. The development of proteomics and metabolomics is showing how all xenobiotics can be effective in determining the gene expression of DNA. In this sense, the use of therapies exploiting hormetic responses—or, more generally speaking, modulating the allostatic stress response network—may have a large social impact for minimizing the effects of harmful perturbations.53-55 In this sense, both the concepts pre-conditioning and post-conditioning hormesis may play a significant role in the medical practice of the future.54,55 The evidently successful homeopathic treatment of the Spanish influenza pandemic in 1918 constitutes a relevant example for supporting this view.36

Following this statement, the cultural heritage of two centuries of homeopathy must be considered not the final step of a static health-care approach, as many of the above-mentioned producers and prescribers have been considering it, but a valuable tool for dynamic health-care development.4,54,55 For these reasons, the view summarized in this contribution involves a relevant political perspective and should prompt institutions and pharmaceutical companies alike to develop appropriate research programs involving a profound change from the present standard thinking in considering public health and medical practices.

Conflict of Interest
None declared.

References
1 Matthiesen PF. Homeopathy and pluralism of theories in medicine arguments put forward to remove homeopathic products from pharmacies contradict actual scientific evidence and suggest deliberate misinformation. Am J Clin Exp Med 2019;7:42–46
5 Baumgartner S. The state of basic research on homeopathy. In: Witt C, Albrecht H, eds. New Directions in Homeopathy Research. Essen; KVC Verlag; 2009:107
8 Rajendran ES. Homeopathy seen as personalised nanomedicine. Homeopathy 2019;108:66–70
16 Chikramane PS, Suresh AK, Bellare JR, Kane SG. Extreme homeopathic dilutions retain starting materials: a nanoparticulate perspective. Homeopathy 2010;99:231–242

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