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CONFERENCE REPORT

Basic research in homeopathy and ultra-high dilutions: what progress is being made?

This report summarises the latest research developments in the field of high dilutions and homeopathy, as presented at the GIRI symposium of the leading international organisation of scientists in this field, in Florence, Italy in September 2012. The scientific community's early scepticism concerning the possible biological and pharmacological activity of highly diluted solutions, is giving way to a more open-minded attitude that no longer obstructs critical and experimental investigations in this emerging field of biomedicine. *Homeopathy* (2013) **102**, 151–154.

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Introduction

Twenty-four years after the controversial findings published by the Benveniste[1,2] group, and despite the many scientific articles published in international journals since then, the idea that 'ultra-low doses' and ultra high dilutions (UHDs) such as those found in homeopathic remedies can exhibit biological and pharmacological activity continues to be regarded as 'unbelievable' by so-called academic science.[3–5] This scepticism ignores the burgeoning popularity of homeopathic treatments and their high levels of patient satisfaction, essentially centres on the fact that UHDs are made by repeated dilutions that lead them to contain extremely low or even undetectable amounts of the active substance. Although the mechanism of action of UHDs is not yet fully understood, knowledge in this 'pioneering' field is rapidly advancing, with significant implications not just for pharmacology but also for biology, physics and agricultural and environmental science.

The XXVI Annual Symposium of GIRI (Groupe International de Recherche sur I'Infinitésimal – International Research Group on Very Low Dose and High Dilution Effects), held in Florence, Italy on 20–22 September as part of ECIM 2012 (5th European Congress for Integrative Medicine), was organised by our research groups based at the Universities of Bologna and Verona, Italy. The symposium documented the latest advances in this field through numerous presentations of the highest scientific quality, the most significant of which are summarised in this short report. Essentially, the international basic research being done in this field revolves around three main topic areas: 1) physicochemical properties of UHD and role of dynamisation, 2) homeopathy and plants: *in vitro*, *in planta* and field studies, 3) other laboratory methods.

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Physicochemical properties of UHDs and role of dynamisation

The first session opened with an introductory report[6] illustrating how the physicochemical properties of UHDs (prepared by an iterated process of dilution and dynamisation) are closely correlated with those of water obtained by iterative filtration through sintered glass filters (IFW), or by repeated wetting and drying of the Nafion polymer (INW). The parameters studied were: electrical conductivity, heat of mixing with acid and base solutions, and pH. The results obtained from the three different experimental protocols all share the common element of a variation in the supramolecular structure of the water solvent, allowing them all to be attributed to a single working hypothesis: the formation of dissipative structures.

This hypothesis is based on the fact that water is a complex liquid capable of self-organising in response to mechanical and/or electromagnetic perturbations even of slight magnitude, to form aqueous nanostructures. In the liquid phase, these structures are capable of remaining in a far-from-equilibrium state by dissipating radiant energy drawn from the environment, while in the solid phase (after the associated water is removed by evaporation) they can indefinitely retain their properties without dissipating. When a sufficient amount of water becomes available, such nanostructures can exploit radiant energy from the environment to return to their preceding state.

The existence of aqueous nanostructures in the solid phase at ambient temperature and pressure is a novel and entirely unexpected phenomenon, which is however encountered on a daily basis in clinical practice: whenever homeopathic globules are dissolved in the patient's mouth, the aggregates revert to the liquid phase, recovering their

ability to dissipate radiant energy, remaining in a far-from-equilibrium state. In this condition, they are able to exert their therapeutic action as dissipative structures.

The physicochemical properties of UHDs have been further analysed by other methods: UV spectroscopy appears to be better suited for investigating homeopathic preparations than visible spectrum or near-infrared spectroscopy;[7] the crystallogenesis of organic liquids can become a valid diagnostic tool in homeopathy[8] and the droplet crystallisation method, presented here for the first time, can yield eloquent images highlighting the efficacy of UHDs, applied in this case to stressed wheat seeds.[9] It has also been suggested that UHDs might share a common epigenetic mechanism with EMIT (ElectroMagnetic Information Transfer): water aggregates with an electric dipole moment might act as mediators of specific weak bioelectromagnetic signals on target stem cells, altering their proliferation, differentiation, apoptosis or adaptive responses.[10] The concluding paper of the session summarised the current state of knowledge concerning the 'homeopathic phenomenon'.[11]

Homeopathy and plants: *in vitro*, *in planta* and field studies

Homeopathic treatments have also been applied to plants. A historical overview of this research area, from the pioneering work of Lili Kolisko in 1923 to the most recent studies,[12] divided the experimental findings into two groups: those that assess the effects of UHDs on germination/growth of different crops (generally conducted on healthy plants or on plants subjected to abiotic stress) and those that study the applicability of these treatments to the control of phytopathology (generally conducted on artificially infected plants).

This in-depth review of the available publications[13–15] was a somewhat critical picture: the majority of studies lack scientific validity due to inadequate experimental protocols or the absence of proper statistical analysis.

To bolster the credibility of experiments on UHDs, a field that is so widely criticised by conventional science, the presentation stressed the importance of building international collaboration networks between research groups to conduct multicentre studies on selected plant models with shared experimental protocols that permit the application of powerful statistical tests such as meta-analysis.

Another point emphasised was the necessity for a rigorous statistical approach in homeopathic research, with the Poisson distribution proposed as a suitable test for various biological models and especially for those on seed germination, where the assessed experimental variable is the number of non-germinated seeds.[16]

The next contributions illustrated the results obtained with isopathic models, where the same substance is used in a measurable dose for the 'stress' and in diluted and dynamised form for the 'cure'. The first model presented concerned the growth of wheat seedlings:[17] the initial hypothesis, that pre-treating the seeds with high concentrations of gibberellic acid could enhance the inhibitory effect produced by the same plant hormone in UHD doses, as had been observed in previous experiments,[18,19] was not confirmed by the experimental results.

Another isopathic model was presented by an Indian research group:[20] seeds of *Vigna unguiculata* were pre-treated with *Natrum muriaticum* and then stressed with NaCl. The pre-treatment produced an increase in seed germination compared to the stressed controls, and the biochemical analysis of the seedlings showed an increase in certain physiological parameters (total protein content, chlorophyll, rubisco and sugars). This model sparked great interest among the symposium participants because the problem of lack of water (comparable to a saline stress) is of the utmost topical relevance and calls for eco-friendly solutions such as UHD treatments.

Finally in this session, a presentation was given of the findings of a comparative study of two plant models: the so-called 'fat duckweed' (*Lemna gibba*), an autotrophic multicellular organism, and the *Saccharomyces cerevisiae* yeast, a heterotrophic single-celled organism. A variety of substances were tested, with the most significant results obtained using a known concentration of arsenic as a preliminary stressor followed by treatment with *Arsenicum album* in decimal scale. The results confirm the original hypothesis according to which UHDs exert a stronger effect on more complex organisms, in this case on *L. gibba*.[21]

Other laboratory models

The final session of the symposium, devoted to laboratory models, summarised the findings of three recent reviews on the use of plants for basic research in homeopathy.[22] Few of the 157 publications identified and analysed meet the quality criteria set out in the recently published guidelines,[23,24] this presentation emphasised the need to conduct independent replications of experiments and use systematic negative controls to exclude false-positives and negatives.

A subsequent presentation showed how UHDs can be identified and distinguished by their UV absorption spectra, as well as on the basis of their effects on animals, plants, isolated organs and enzymes *in vitro*.[25] Another presentation reported the interesting results obtained by application of modern molecular biology techniques: this work, conducted by the University of Verona group,[26] showed that *Gelsemium sempervirens*, a homeopathic remedy whose 'anxiolytic-like' activity has been previously demonstrated in animal models, also exerts effects on neurons *in vitro*, including at doses such that the molecules are practically absent. The extraordinarily interesting aspect of this research is that the microarray method, applied to the human genome, has identified a small set of genes (around 50 out of 45,000) that are especially sensitive to the homeopathic remedy in UHDs. Recent experimental findings both *in vitro* and *in vivo*[27] support the hypothesis that gene regulation explains the molecular mechanism of activity of UHDs. The last presentation of this session focussed on results obtained by treating murine granuloma with