

also hampers further development and optimisation of homeopathic therapy. Therefore, development of a deeper understanding of the two basic tenets of homeopathy is of ultimate importance.

Only few basic research projects seem to have been performed to investigate the simile principle. The fundamental pioneering work of van Wijk and Wiegant so far has not been taken up by any other research team. Determination of the areas of applicability of the simile principle is an important task, as is the elucidation of the mode of action.

Comparably more research has been carried out to investigate the potentiation procedure. However, I currently do not know any laboratory model that reproducibly yields specific effects of highly diluted homeopathic potencies in different laboratories, and I do not know any theory that would satisfyingly explain any such specific effects of ultramolecular potencies. Thus I think that the following two main topics have to be addressed in the next years: development of optimal laboratory models to identify specificity and reproducibility of homeopathic effects, and identification of the long-sought-for mode of action of highly diluted potencies.

Are there any experimental laboratory systems that reliably yield reproducible evidence for specific effects of homeopathic potencies? To resolve this question, it will be necessary to investigate various model systems in parallel in different laboratories to determine any necessary and sufficient conditions for successful reproducibility; until now, according to my knowledge, corresponding parameters could be identified for three model systems only. Optimisation of the laboratory models does involve the choice of the test organism in a defined physiological state, an adapted potentised substance in an adequate potency level applied in an optimal route and dosage as well as optimal outcome measures. Furthermore, it will be necessary to develop model systems that not only demonstrate empirical effects of single homeopathic remedies, but also differentiate effects of different potentised substances. Thus, model systems have to be simple and cost-effective to enable easy implementation in other laboratories, and to allow multiple parameters to be tested in parallel (e.g. different substances and/or potency levels). Finally, stability of any experimental system used must be demonstrated by systematic negative control (SNC) experiments on a routine basis.

Identification of the mode of action of highly diluted homeopathic remedies is the ultimate goal of homeopathic basic research. This involves determination of the general type of interaction present between homeopathic potency and test organism: local material-like, force-like, or non-local entanglement-like. This not only implies precise investigations of homeopathic preparations by sophisticated physicochemical methods, but also experimental approaches to test Hahnemann's premise of force-like effects of homeopathic potencies. Furthermore, the general nature of the effects of homeopathic potencies has to be determined: reproducibly deterministic, chaotic or inherently indeterminate. Solid experimental data regarding these questions

will enable development of a precise theoretical framework, ultimately resulting in a thorough understanding of homeopathic effects.

Integrative nanomedicine: homeopathic remedies as source and silica nanoparticles acting as danger signals for nonlinear complex adaptive systems

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The alleged “implausibility” of homeopathic medicines is a foundation for attacks on homeopathy. Skeptics insist that homeopathic medicines are too dilute to contain any residual material from their mineral, plant, or animal sources or exert effects. Nonetheless, multiple studies on cells, animals, plants, and human subjects have demonstrated biological effects of remedies.

Research laboratories have shown that 6 different metal remedies and 3 different plant remedies contain persistent remedy source nanoparticles (NPs) from low to high potencies beyond Avogadro's number for bulk form materials. Multiple laboratories also have documented the ability of succussion in glass containers to release measurable amounts of silicon and silica into solution. Chikramane et al. (2012) showed that succussion can generate heterogeneous accumulation and layers of remedy source nanoparticles that lead to physical transfer carryover of nanoparticles from container to container during the “serial dilution” procedures, even though bulk form source materials may be diluted away. In addition, Das et al. (2013) demonstrated that homeopathic plant mother tinctures can biosynthesize silver nanoparticles from precursors, just as plant extracts can biosynthesize silica nanoparticles from silica precursors.

Nanoparticles could explain many puzzling observations and variability from study to study in homeopathic research. Elia et al. have found aging-related effects in homeopathically-prepared remedies in terms of heat release and electrical conductivity changes after storage — observations that overlap nanoparticle phenomena of aging and Ostwald ripening. Some homeopathically-prepared materials, e.g., specific bacteria nanoparticulates, also emit detectable electromagnetic signals after certain dilution-succussion processes. Certain spectroscopy studies showed unique patterns for homeopathically-prepared remedies compared with control solvents (succussed and nonsuccussed). Some investigators have also interpreted findings from proving studies as indications of quantum mechanical properties of remedies. NPs have enhanced bioavailability, adsorptive capabilities, adjuvant reactivity, electromagnetic, optical, thermal, biochemical, and quantum properties compared with their bulk forms.

Different concentrations of ethanol, variations in pH, temperature, and glassware, as well as dilution sampling and succussions (or sonication, vortexing) will lead to different sizes, shapes, surface charges, and properties of the resultant nanostructures. Even minor variations in the latter variables could contribute variability to remedy actions.

This talk discusses implications of the homeopathic nanoparticulate findings for a biological signaling model of the homeopathic remedy nanostructures in initiating a cascade of endogenously amplified adaptations and cross-adaptations across the organism as a whole.

Homeopathic remedy manufacturing probably generates NPs by a crude “top-down” mechanical grinding in lactose and/or succussions in room temperature ethanolic solutions within borosilicate glass containers. Silica nanostructures could serve as remedy source NP drug delivery vehicles and nonspecific biological amplifiers. Nanoparticles induce self-organized adaptive changes in the organism at nontoxic doses (hormesis), serving as salient, low level danger signals to the biological stress response networks. Release of exosomes and activation of stress response effectors, including heat shock proteins, inflammasomes, cytokines and neuroendocrine networks, would initiate and progressively amplify beneficial compensatory reactions. Thus, homeopathy may represent the earliest practical development of “integrative nanomedicine” for using pulsed doses of nanoparticles from natural source materials safely and effectively in treating a wide range of acute and chronic clinical conditions.

Modulation of chronic inflammation response to *Leishmania (L.) amazonensis* by Thymulin 5CH in mice

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In previous studies, we observed that thymulin 5CH could modulate the chronic inflammation response to BCG in an experimental infection, by increasing peritoneal B1 stem cells differentiation into phagocytes and improving bacilli phagocytosis efficiency into the infection site. Herein, the same protocol was used to study the effects of thymulin 5CH in a protozoan experimental infection. Male Balb/c mice were orally treated with thymulin 5CH or vehicle during 60 days after the subcutaneous inoculation of 2×10^5 units of *Leishmania (L.) amazonensis* into the footpad. Then, washing inflammatory cell suspension

from peritoneal cavity and spleen were harvested to be identified and quantified by flow cytometry and the tissue of infection site, as well as the local lymph node were harvested for histological examination and quantification. Treated mice presented increase in B1 stem cells percentage in peritoneal washing fluid and in spleen ($p=0.0001$), in relation to other cell types, and more organized and exuberant inflammation response in the infection site, with decrease in the number of parasites per field ($p=0.05$). No difference was seen in local lymph node histology. The results show that thymulin 5CH is able to improve B1 stem cell activation and *Leishmania (L.) amazonensis* phagocytosis efficiency in mice, similarly to that observed previously in BCG experimental infection.

Homeoprophylaxis: evidence from basic research and practical applications

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Homeo-Prophylaxis (HP), has been one of the more questioned application of homeopathy despite it also could be considered one of the most revolutionary uses in terms of benefits for health quality. Although the protection effects and impact (effectiveness and efficacy) are frequently difficult to demonstrate, the lack of scientific research, among other factors, hinder the acceptance and implementation of HP but also limits the possibility of running proper clinical studies. In order to breakdown this close circle, in vitro experiment, animal's models and clinical evaluation should be combined with the current knowledge and evaluation methodologies of the immune system.

A summary of unpublished results from basic research experiments on the effects of homoeopathically diluted biological material as prophylactic formulations on in vitro and animal models will be presented. According to the results, an approach to underlying immune mechanisms could be proposed and discussed.

Results from 5 years follow up of large scale Leptospirosis HP intervention will be complemented and analysed. Further clinical evaluation of HP on other epidemic diseases at large scale could be presented.

A integral analysis of evidence coming from experimental model and clinical testing suggest that HP could be consider in fact as a very promising and potent tool to face infectious diseases in the context of current global situation.