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ORIGINAL PAPER

Enhancement of adaptive biological effects by nanotechnology preparation methods in homeopathic medicines

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Multiple studies have demonstrated that traditional homeopathic manufacturing reagents and processes can generate remedy source and silica nanoparticles (NPs). Homeopathically-made NPs would initiate adaptive changes in an organism as a complex adaptive system (CAS) or network. Adaptive changes would emerge from several different endogenous amplification processes that respond to exogenous danger or threat signals that manufactured nanomaterials convey, including (1) stochastic resonance (SR) in sensory neural systems and (2) time-dependent sensitization (TDS)/oscillation. SR is nonlinear coherent amplification of a weak signal by the superposition of a larger magnitude white noise containing within it the same frequencies of the weak signal. TDS is progressive response magnitude amplification and oscillatory reversal in response direction to a given low dose at physiological limits with the passage of time.

Hormesis is an overarching adaptive phenomenon that reflects the observed nonlinear adaptive dose–response relationship. Remedies would act as enhanced micro- and nanoscale forms of their source material via direct local ligand-receptor interactions at very low potencies and/or by triggering systemic adaptive network dynamical effects via their NP-based electromagnetic, optical, and quantum mechanical properties at higher potencies. Manufacturing parameters including dilution modify sizes, shapes, and surface charges of nanoparticles, thereby causing differences in physico-chemical properties and biological effects. Based on surface area, size, shape, and charge, nanoparticles adsorb a complex pattern of serum proteins, forming a protein corona on contact that constitutes a unique biological identity. The protein corona may capture individualized dysfunctional biological mediator information of the organism onto the surfaces of the salient, i.e., resonant, remedy nanostructures.

SR would amplify this weak signal from the salient remedy NPs with protein corona adsorbed, leading to sensitized nonlinear dynamical modulation of gene expression and associated changes in biological signaling pathways. When the system reaches its physiological limits during a homeopathic aggravation or the natural disease state, the amplified remedy signal triggers a nonlinear reversal in dynamical direction back towards health. *Homeopathy* (2015) **104**, 123–138.

Keywords: Nanoparticles; Homeopathy; Top down; Bottom up; Nanotechnology; Complex adaptive system; Nonlinear dynamics; Stochastic resonance; Time dependent sensitization; Hormesis

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Introduction and Overview

The purpose of this paper is to discuss how traditional homeopathic manufacturing reagents and processes could generate the ability of a given potency to initiate nonlinear adaptive changes in an organism as a complex adaptive system (CAS) or network. As previously proposed,[1–4] the homeopathic medicine (HM) would be a heterogeneous mixture of nano-sized particles (NPs, small particles that measure 1–100 nanometers along at least one dimension) of the source material, with or without the nonspecific presence of nanosilica released during succussions of solutions in borosilicate glassware.[5] Other materials in solution also readily adsorb to, dope or seed silica NPs, thereby creating unique surface 'defects' and modifying their properties.[6–12]

The smallest nanoparticles, termed quantum dots, range in size from 1 to 10 nanometers or so and exhibit quantum mechanical properties as a function of the very small size trapping of a large proportion of the atoms and their associated electrons, close to the particle surface.[13–17] Nanoparticles in general are more bioavailable and biologically-active forms of their source material.[18,19] Quantum dots and other very small nanomaterials can readily cross cell membranes.[13,20,21] Their small size facilitates olfactory, oral, or dermal administration by allowing passive entry into cells and translocation via blood and lymph, including crossing the blood–brain barrier in experimental cancer treatments.[22]

At least six different laboratories have now found some type of nanoparticle or nanostructure in homeopathically-prepared materials.[1,23–27] Multiple laboratories have also identified silicates from glassware in succussed solutions.[5,23,26,28–30] Two of those laboratories have shown biological interactions of proteins in solution with these agitation-released silica materials in vitro.[5,28] Nanoparticle characterization methods included transmission electron microscopy, scanning electron microscopy, and dynamic light scattering.

Nanomedicine researchers have shown marked reductions of dose size and/or repetitions of nanoscale forms versus conventional bulk (larger) forms of a given agent by orders of magnitude, ranging from 10 to 1000 times lower for direct pharmacological effects.[31–34] Lowering dose requirements for therapeutic effects also means that some NPs are toxic at significantly lower doses than ordinary bulk forms of the same material[35–37] and that the cut-off level for no-observed-adverse-effects (NOAEL), i.e., where hormesis usually occurs, nonlinear low-dose responses would also be correspondingly reduced.[4,38–41] Despite their low concentrations in HMs, e.g., in the parts per million and parts per billion range, perhaps even lower,[1,5,42] the enhanced highly reactive large surface areas of NPs still leave them chemically[43,44] and/or biologically[36,45] highly active.

With NPs, however, effects are never just a matter of material composition or dose alone. Different sugars used during manufacturing can lead to different sizes of the manufactured NPs.[41] Lactose but not other sugar coatings, enhances uptake of silver NPs into cancer cells.[47] Nanosilica coating on other NPs can stabilize them.[48] Particle size, shape, and surface charge,[13,49–51] as well as the set of serum proteins that attach or adsorb onto the nanoparticle surfaces in the body to form a unique protein corona,[46,52] play a major role as well.[53–56] The protein corona confers a unique biological identity apart from the physical chemical identity onto nanoparticles that get into living systems (Figure 1).

Cartwright reported in a recent conference paper on HMs that the silanol groups (silicon with an alcohol –OH hydroxyl group)[57] on the walls of the glassware in which succussions occur may play a key role in carrying the homeopathic information into higher potencies.[58] Variations in hydoxyl density on NP surfaces affect how a major serum protein like fibrinogen attaches to silica nanoparticles (NPs) as part of the protein corona at physiological concentrations.[59] Ions in solutions also affect the final NP product.[60] Thus, even subtly different manufacturing procedures would lead to variations in the chemistry and protein corona biology of specific remedy nanostructures. In turn, the interaction of the remedy NPs with the specific biology of the individual recipient would lead to the individualized physiological responses that characteristically unfold during homeopathic treatment.

Understanding HMs as various types of nanostructures with unique surface properties enables a meaningful synthesis for a larger understanding of the biology of homeopathic effects. For instance, the patterns of proteins attached to the surfaces of NPs like silica nanoparticles can determine the nature of biological effects on monocytes and macrophages in serum.[61,62] Previous studies on homeopathically-prepared combination remedies like Canova (various potencies of Aconite, Arsenicum, Bryonia, Lachesis, and Thuja in 1% ethanol) or individual remedies like Belladonna or Echinacea demonstrated that HMs can mobilize macrophages,[63–66] which in turn can activate lymphocytes to exert anti-cancer effects.[67]

Nanoparticles of materials such as silica (silicon dioxide) and titanium dioxide also activate intracellular defenses involving the inflammasome set of proteins.[68] When the inflammasome cascade is activated, cytokines are released. Studies on other combination homeopathically-prepared remedies have shown that HMs can also induce cytokine release.[69] Cytokines are part of the endogenous neuro-immune-inflammatory network that carries biological signals from cell to cell, as well as from local tissues to brain.[70,71]

It is important to step back from the conventional assumptions of mainstream medicine that require therapeutic agents to always act as structural ligands that fit into specific local receptors. Biology is increasingly understood as a nanoscale process with electromagnetic[72,73] and quantum mechanical aspects[74] in a self-organized living CAS or network. By definition, a CAS is ever-responsive to environmental change.[75,76]

Exogenous nanoparticles and nanostructures speak to the biology of the organism as a whole CAS with nonlinear dynamics. One aspect of the adaptive network communication