

Homeopathy and Nanopharmacology: A Review of the Conventional Medical Literature

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ABSTRACT

Homeopathic medicine is a controversial system of medicine that has been used worldwide for 200 years. Drawing from research in the material sciences and in nano-scale technologies, discussion about viable means by which homeopathic nanodoses can create physiological responses and influence gene expression is provided. This review of controlled clinical trials only discusses studies that were published in conventional medical and scientific peer-review journals. A critical review of five leading meta-analyses is provided. The meta-analyses that are most critical of homeopathy are found to have significant flaws in their methodology and analysis. The most recent meta-analysis showed that there are a small number of clinical trials with a low risk of bias that verify efficacy. The impressive safety profile of homeopathic medicines is reviewed with a special acknowledgement for it representing the epitome the Hippocratic command to “first, do no harm.”

Keywords: Homeopathy; Homeopathic medicine; Nanomedicine; Nanopharmacology; Nanodoses; Genetic expression; Homeopathic meta-analysis; Evidence based medicine

INTRODUCTION

Diamond and graphite are both made of pure carbon, but a diamond is considered the hardest mineral in the world, while graphite is one of the softest. Likewise, gold is that shiny, golden noble metal that doesn't tarnish, melts at 1,948 degrees (F), and is non-magnetic. And yet, in nanosizes as small as 10 nm, the gold particles absorb green light and thus appears red, its melting temperature decreases considerably, and gold is no longer noble but at 2-3 nm exhibits significant magnetic properties. The point to the above facts is that the properties and effects of an agent is not simply its chemistry, but also its dose [1]. In fact, nanodoses of specific agents can have significant effects and even dramatically different effects than larger doses of the same agent. The United States' nano.gov website well describes how and why nanoscale materials play a much larger role in material properties and interaction than normally assumed, “Nanoscale materials have far larger surface areas than similar masses of larger-scale materials. As surface area per mass of a material increases, a greater amount of the material can come into contact with surrounding materials, thus affecting reactivity. The Nano.gov site continues, “Nanotechnology is not simply working at ever smaller dimensions; rather, working at the nanoscale enables scientists to utilize the unique physical,

chemical, mechanical, and optical properties of materials that naturally occur at that scale.”

LITERATURE REVIEW

...“Over millennia, nature has perfected the art of biology at the nanoscale. Many of the inner workings of cells naturally occur at the nanoscale. For example, hemoglobin, the protein that carries oxygen through the body, is 5.5 nanometers in diameter. A strand of DNA, one of the building blocks of human life, is only about 2 nanometers in diameter.” Homeopathic medicine is that controversial system of medicine that utilizes nanodoses of various medicinal agents. Skeptics of homeopathy insist that many homeopathic medicines are diluted so much that there are literally no molecules remaining in solution, though recent research has disproven this assertion and that nanoparticles of the original medicinal agents persist in solution even when diluted 1:100 two hundred times. Homeopathic medicine is a medical and pharmacological specialty that has been utilized in virtually every country in the world for the past 200 years. Homeopathy has been widely used by medical doctors and numerous other health and medical professionals as a complement and as an alternative to conventional medical care to treat a wide variety of physical, emotional, and mental health

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complaints, and it is been used in self-treatment by the general public for minor, self-limiting complaints. The World Health Organization considers homeopathy to be a part of “traditional medicine. Historically, conventional scientists have claimed that homeopathic medicines are “implausible” because the doses of the homeopathic medicinal agents are so small that it is reasonable to wonder if and how they can have physiological effects. However, such seemingly valid concerns may be outdated in the light and development of greater understanding of nanodoses of medicinal agents (discussed later in this article). Skeptics of homeopathy also have claimed that there is no reliable body of clinical evidence to prove that homeopathy is effective for any specific condition. However, this assertion is entirely dependent upon how one defines “reliable” (discussion of this topic will be provided in the section, “A Review of Meta-analyses and Clinical Usage of Homeopathic Medicines”) [2].

This article will first summarize the relatively new body of evidence that helps to better understand how the exceedingly small doses of medicines used in homeopathy can have relevant physiological effects and health impacts. This article will then evaluate clinical evidence with the gold standard of randomized double-blind and placebo controlled trials, but this writing will also evaluate other types of evidence, including evidence from basic sciences research, epidemiological and observational studies, historical evidence, and evidence from respected scientists and physicians.

Virtually every study referenced in this article will be to conventional medical and scientific journals, even many of the most respected medical and scientific journals known today. The exceptions to references to research in non-conventional medical journals (i.e. in homeopathic and/or complementary and alternative medicine journals) will be when a high-impact medical journal or science news magazine provides a review of a study or when extremely high profile physicians or scientists report on their experiences with homeopathic medicine [3].

How homeopathic medicines may work

Before discussing the evidence base for homeopathic medicines, it is important to acknowledge that modern medical science still doesn't know how many of their most commonly prescribed drugs work. For instance, despite the fact that acetaminophen is one of the most popularly prescribed over-the-counter drugs for pain and fever, it is still unknown precisely how it works. Lithium is one of the most commonly prescribed psychiatric drugs over the past 50+ years, and yet, the specific biochemical mechanism of lithium action in stabilizing mood is unknown. Metformin is a first-line medication for the treatment of type 2 diabetes and it has been used in medical care for almost 100 years, and yet, its mechanism of action is incompletely understood. Even drugs for general anesthesia do not have an adequately understood mechanism by which they work. Despite the billions and even hundreds of billions of dollars of sales of each of these drugs, this lack of adequate understanding about how these drugs work doesn't stop physicians from prescribing them or patients from wanting to take them. This acknowledged humility about present-day ignorance about the action of modern drugs is mentioned here because some skeptics assert

that the precise mechanism of action of homeopathic medicines is unknown, and they therefore assert that it should be unethical for health and medical professionals to prescribe homeopathic medicines, and further, these medicines should not be sold by pharmacies. Homeopaths may not yet understand the precise mechanism of each individual homeopathic medicine, but new and compelling basic sciences research has uncovered reasonable and plausible explanations for how homeopathic nanodoses can have surprisingly remarkable and tangible physiological effects and health benefits. Skeptics of homeopathy claim that once a medicinal agent is diluted of 1:10 twenty-four times or 1:100 twelve times, that, according to an important premise in chemistry called Avogadro's number, there shouldn't have any remaining molecules of the original medicinal agent. Therefore, these skeptics assert that any homeopathic medicine greater than 24X or 12C would in all probability have no remaining molecules of the medicine. However, such criticisms show oversimplistic thinking by skeptics. Conventional pharmaceutical research has found that when one places a medicinal agent in a glass bottle that has double-distilled water (this is the “pharmaceutical grade water” that is used in homeopathic manufacturing) and then is vigorously shaken, the medicinal agent and the bubbles and the “nanobubbles” that get created from the turbulence strike again against the side walls of the glass bottle, and 6ppm of silica fragments fall from the glass into the water. Then, according to Rustum Roy, PhD (the late head of a highly respected material sciences laboratory at Penn State University) and William A. Tiller, PhD (the former head of Stanford's Department of Material Sciences), the vigorous shaking process used in homeopathy increases the water pressure in the glass bottle substantially. When these nanobubbles implode, they release heat and pressure that creates physical conditions that are different from normal water at rest. It should be noted that homeopathic medicines are not only made in glass but in porcelain (during the trituration process of making non-water soluble medicines) and occasionally in plastic [4]. These different containers also release nanoparticles from its constituent parts to which a medicinal agent can adsorb to the increased surface areas (be it glass that would release silicon quantum dots and silicates that can form silica nanoparticles or be it plastic that would release carbon quantum dots and larger carbon nanoparticles). Research on nanoparticles has confirmed substances placed in water solutions become embedded with the nanoparticle materials of the container. Homeopathic medicines are usually made in a double-distilled water, and then, they are placed on lactose (or sucrose), though certain non-water soluble minerals are triturated and diluted directly with lactose. A study in conventional nanopharmacology published in *Angewandte Chemie* (a journal of the German Chemical Society) found that lactose serves as a “Trojan horse” in that it serves as an effective intracellular delivery system for quantum dots. An essential question remains: how can exceedingly small doses of a substance have profound physiological effects? MIT physicist Seth Lloyd asserts, “Nature is the great nano-technologist. The chemical machinery that powers biological systems consists of complicated molecules structured at the nanoscale and sub-nanoscale. At these small scales, the dynamics of the chemical machinery is governed by the law of quantum mechanics. The obvious explanation for how nanodoses can have profound

physiological effects stems from evidence that shows that small nanoparticles can readily cross cell membranes and translocate around the body via blood and lymph and can pass through the blood-brain barrier with much greater ease than larger doses. One of the strongest statements in this article was the confirmation that four of the five leading previous systematic reviews of homeopathic research found a benefit from homeopathic treatment over that of placebo [4].

“Five systematic reviews have examined the RCT research literature on homeopathy as a whole, including the broad spectrum of medical conditions that have been researched and by all forms of homeopathy: four of these ‘global’ systematic reviews reached the conclusion that, with important caveats, the homeopathic intervention probably differs from placebo. The most significant observation of this review of homeopathic clinical research is that there is a difference between homeopathy and placebo, despite what skeptics and the certain media tend to assume and assert [5].

The governments of Switzerland, Australia, and England have each funded reviews on homeopathic medicine, though each came to different conclusions, including two different reviews funded by the government of Switzerland, one finding no benefits from homeopathic treatment and one finding numerous benefits from homeopathic treatment. An analysis of all of these reviews will help provide perspective on each evaluation of scientific evidence [6].

The first swiss study

The first study that the Swiss government funded is described below, while the second study is described next. Typical of the neutrality that Switzerland is known to embody, the Swiss government funded analyses of homeopathy from both skeptics and from advocates, and predictably enough, each came to different conclusions. Initially, the team of skeptics of homeopathy published their results. It is remarkable to note that these researchers found 21 of the homeopathic studies fit their definition of "high quality" clinical research but only nine of the conventional studies did so. One would have thought that the researchers would then compare these "high quality" trials. However, this result would have shown that there IS a difference between homeopathic treatment and a placebo in a variety of ailments, and a review in a highly respected journal specializing in clinical research analysis confirmed this fact Using large numbers of subjects is certainly possible in homeopathy, but it is simply less frequent, due to the high costs of such clinical trials and due to the fact that the profit margin for the sale of unpatentable homeopathic medicines does not even approach that of conventional drugs. Also, it is a lot easier using conventional medicine than homeopathic medicine in studies because it is generally necessary to evaluate a person's overall syndrome, not just any localized disease, when prescribing homeopathic medicines. One of the interesting characteristics of this study was that the authors did not evaluate safety issues of treatment. Therefore, it is not surprising that at least three of the conventional medical treatments that were found to be "effective" initially were later found to be dangerous enough that the drugs were withdrawn from medical use [7].

The second and more comprehensive swiss study

The Swiss government's provisional reimbursement for select alternative treatments ended in 2005, but as a result of the new study described below, the Swiss government's health insurance program began once again to reimburse for homeopathy and certain alternative treatments. Then, due to a national referendum in which more than two-thirds of Swiss voters supported the inclusion of homeopathic and select alternative medicines in their national health care insurance program, the field of complementary and alternative medicine became integrated in this government's constitution. The government of Switzerland funded a "health technology assessment" from a group of professors from Switzerland and Germany. This group published their findings in a book and in an article published in a peer-review medical journal. This report evaluated the studies conducted, both in terms of quality of design and execution (called "internal validity") and how appropriate each was for the way that homeopathy is commonly practiced (called "external validity"). The subject of external validity is of special concern because some scientists and physicians conduct research on homeopathy with little or no understanding of this system of medicine (some studies tested a homeopathic medicine that is rarely used for the condition tested, while others utilized medicines not commonly indicated for specific patients). When such studies inevitably showed that the homeopathic medicine did not "work," it is reasonable to ask if studies were conducted specifically to disprove homeopathy or if the study was an exploratory trial that sought to evaluate the results of a new treatment (exploratory trials of this nature are not meant to prove or disprove the system of homeopathy but only to evaluate that specific treatment for a person with a specific condition). After evaluating the pre-clinical basic research as well as the high quality clinical studies, this Swiss report claimed that homeopathic high-potencies seem to induce regulatory effects (e.g., balancing or normalizing effects) and specific changes in cells or living organisms. The report also determined that 20 of the 22 systematic reviews of clinical research testing homeopathic medicines detected at least a trend in favor of homeopathic treatment [8].

The second Swiss report found a particularly strong body of evidence to support the homeopathic treatment of Upper Respiratory Tract Infections and Respiratory Allergies. Citing 29 studies in "Upper Respiratory Tract Infections/Allergic Reactions," the report found 24 studies with a positive result in favor of homeopathy. Further, six out of seven controlled clinical trials that compared homeopathic treatment with conventional medical treatment found homeopathy to be more effective than conventional medical interventions (the one other trial found homeopathic treatment to be equivalent to conventional medical treatment). Distinct from conventional drug treatment, these results from homeopathic treatment came without the side effects. When reviewing only the randomized placebo controlled trials, 12 out of 16 studies showed a positive result in favor of homeopathy. After the Swiss government's sponsorship of the above two studies of homeopathy, the government granted provisional reimbursement to homeopathy between 2012 and 2017. Then, in 2017, the Swiss government

made the determination to include homeopathic treatment as a reimbursable medical expense [9].

The Australian report on homeopathy

In March 2015, the Australian National Health and Medical Research Council (NHMRC) published an Information Paper on homeopathy, which is commonly referred to as “The Australian Report [10].

What homeopathy offers to reducing the opiate crisis

The opiate epidemic was inevitable to anyone who understands what real healing is...and isn't. Although these drugs may provide blessed temporary relief of pain, these drugs inhibit real healing. The clinical trial found that 50% of patients prescribed a homeopathic medicine experienced a 25% or greater improvement in tender point pain on examination, as compared to only 15% of those who were given a placebo experienced a similar improvement ($P=0.008$). After four months, the homeopathic patients rated the “helpfulness of the treatment” significantly greater than did those who were given a placebo ($P=0.004$). One special additional feature of this clinical trial was that the first dose of medicine was given by olfaction (by smell) and that both groups were monitored with EEG. The researchers found that there were significant and identifiable differences in the EEG readings in patients who were given the real homeopathic medicine as compared to those given the placebo. The researchers included in this clinical trial 30 patients who seemed to fit the symptoms of Rhus toxicodendron, and they were given a homeopathic dose of this medicine, 6C (this dose is considered a “low potency,” that is, it is a dose that generally does not have long-term effects). The researchers found that there was a significant degree of improvement in the reduction of pain and tender points and improved sleep when the subjects were taking the homeopathic medicine, as compared to when the subjects were taking a placebo. The results of this trial were highly significant ($P<0.005$). This MSD study was a nationwide observational cohort of a representative sample of general practitioners (GP) and their patients in France. This study was designed and conducted by a prestigious group of professors from McGill University, University of Paris, Pasteur Institute, University of Bordeaux, and London School of Hygiene and Tropical Medicine. Some of the musculoskeletal disorders of patients who were included in this study were: Osteoarthritis, rheumatism, fibromyalgia, muscle spasms, tendinitis, rotary cuff syndrome, ankylosing spondylitis, intervertebral disc disorders, neck pain, torticollis, and spinal stenosis. Even though the homeopathic patients with chronic MSD used 49.8% less NSAIDs and patients with acute MDS used 38.4% less NSAIDs than those under conventional medical care, the homeopathic patients showed a similar clinical progression when less exposed to NSAID in comparison to patients seen in CM practice, with fewer NSAID-related adverse events and no loss of therapeutic opportunity. These results are further impressive because a greater number of homeopathic patients had chronic MSD at the beginning of the study [11].

What homeopathy offers to people with infectious diseases: alternatives to the over-use of antibiotics?

It is widely known and accepted that modern-day antibiotics have been over-utilized, thus leading to their reduced efficacy and resulting in disruptive internal ecologies that create dysbiosis and digestive disease. As comedian Professor Irwin Corey once said, “If we don't change our direction soon, we'll end up where we are going [12].

Treating infectious disease by attacking the microbe is only one potential treatment of this type of disease. Another viable treatment is to augment a person's immune and defense system, thereby influencing “host response.” Homeopathic medicine is a non-antimicrobial treatment method for which there is historical and scientific evidence to support it as a reasonable and viable treatment. It should be noted that using homeopathic medicines during infectious disease epidemics is a lot easier than other serious or chronic diseases. Homeopaths have found that during infectious disease epidemics large numbers in England, the House of Commons requested a report about the various methods of treating the cholera epidemic in 1854. When the report was published, the statistics from homeopathic hospitals were not included. The House of Lords asked for an explanation, and it was admitted that if the homeopathic figures were to be included in the report, it would “skew the results.” The Chairman of the report further admitted that including the results from homeopathic treatment “would give an unjustifiable sanction to an empirical practice alike opposed to the maintenance of truth and to the progress of science. In 2013, a EP13 survey using a nationwide population-based study of a representative sample of 825 GPs and their patients in France (2007–2008) was conducted. General practitioner doctors (GP) recruitment was stratified by self-declared homeopathic prescribing preferences. Adults and children with confirmed URTI (upper respiratory tract infection) were asked to participate in a standardized telephone interview at inclusion, at one-, three- and at twelve-month follow up. The study results compared medication consumption, URTI symptoms' resolution and potentially-associated infections (sinusitis or otitis media/externa) as reported by patients. Analyses included calibration to account for non-respondents and groups were compared using multivariate analyses adjusting for baseline differences with a propensity score. Patients who chose to consult GPs certified in homeopathy used less antibiotics and antipyretic/anti-inflammatory drugs for URTI than those seen by GPs prescribing conventional medications. No difference was observed in patients consulting GPs within mixed-practice.

What homeopathy offers to pediatric health?

Treating infants and children demands and commands clinicians to honor the “first, do no harm” priorities. At an 1883 meeting of the American Medical Association, one doctor complained, “Too many wives of conventional physicians are going to homeopathic physicians. And to make matters worse, they are taking their children to homeopaths too. Below are several studies published in leading conventional medical journals that show benefits from homeopathic treatment. Each of these trials are worthy of replication and need replication in

order for these studies to be taken more seriously. Relevant clinical results were found in the treatment of the following childhood ailments for which conventional medicine provides only partial benefits, often with both minor and major risks of treatment: upper respiratory tract infections, otitis media (middle ear infections), eczema, bedwetting, and attention deficit and hyperactivity disorder.

CONCLUSION

This study majorly focussed on homeopathy art of biology at the nanoscale. Many of the workings are still undre process which are ongoing in the nanoscale.

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