

STATEMENT

Where Does Homeopathy Fit in Pharmacy Practice?

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Homeopathy has been the cause of much debate in the scientific literature with respect to the plausibility and efficacy of homeopathic preparations and practice. Nonetheless, many consumers, pharmacists, physicians, and other health care providers continue to use or practice homeopathic medicine and advocate its safety and efficacy. As drug experts, pharmacists are expected to be able to counsel their patients on how to safely and effectively use medications, which technically includes homeopathic products. Yet many pharmacists feel that the homeopathic system of medicine is based on unscientific theories that lack supporting evidence. Since consumers continue to use homeopathic products, it is necessary for pharmacists to have a basic knowledge of homeopathy and to be able to counsel patients about its general use, the current state of the evidence and its use in conjunction with other medications.

Keywords: homeopathy, pharmacist, education, complimentary and alternative medicine

INTRODUCTION

Homeopathy has been the cause of much debate in the scientific literature with respect to the plausibility and efficacy of homeopathic preparations and practice.¹⁻⁵ This is a system of medicine that has been in widespread use for the last 200 years, the theory of which is diametrically opposed to modern pharmaceutical knowledge and theories.⁶⁻⁸ Nonetheless, many consumers, pharmacists, physicians and other health care providers continue to use and practice homeopathic medicine and advocate its safety and efficacy. Regulated under federal Food and Drug Acts in Canada and the United States, homeopathic preparations are recognized as drugs in both countries, which presents a unique conundrum for pharmacists.^{3,9} As drug experts, pharmacists are expected to be able to counsel their patients on how to safely and effectively use medications, which technically include homeopathic products. Yet many pharmacists feel that the homeopathic system of medicine is based on unscientific theories without supporting evidence, and therefore should not be promoted by pharmacists in any way. If a consensus could be reached on whether homeopathy really provides a health benefit, then the answer to the question, “should pharmacists know about homeopathic medicine?” would become clear.

In this article we aim to answer this question, first by examining the scientific literature in regards to homeop-

athy. Why pharmacists should know about homeopathy is then outlined. The paper concludes with a brief outline of what pharmacists should know about homeopathy to help them counsel patients.

The information presented is based on articles found using Scholar’s Portal search engine, which includes MEDLINE. Search terms used were *homeopathy, homeopathic, medicine, dilution, ultra, basophil, degranulation, crystal, growth, oscillatory, zoning, potentization, meta-analysis, pharmacists, and education*. An attempt was made to systematically gather all English language articles available in the extensive University of Toronto library system or publicly available online. The reference lists of articles obtained from the original search were then assessed for additional relevant articles.

Homeopathy is based on 3 premises: the law of similars; individualized therapy based on broadly defined symptoms; and the use of very small doses.^{3,6-8} The law of similars is the theory that a plant, animal, or mineral substance that causes a particular set of symptoms in a healthy person, when administered in a homeopathic dosage form to a sick person exhibiting those symptoms, will cure them. The practice of individualized therapy based on symptoms is grounded on the premise that every patient has a unique personality and symptom pattern of illness, meaning that the same biomedical disease manifests in subtly different ways in each person. Thus, each homeopathic remedy must be chosen by a homeopathic practitioner, so that it most closely addresses each unique variation. The use of very small doses is important because often the substances used to make the remedy are toxic at undiluted concentrations. The diluting process

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involves *succussion*, vigorous shaking of the original substance with alcohol or water, which activates and “potentizes” the remedy. Homeopathic products are often diluted so much that conventional pharmacology tells us that no molecules of the original solute remain in the finished product.

The fundamental tenets of homeopathy are completely different from modern medicine, pharmacology, and chemistry.¹⁰ Main sources of contention include: the implausibility of homeopathic principles; the lack of a proven or plausible mechanism of action for homeopathy; and mixed results from randomized, controlled trials on homeopathic preparations. These conflicts, coupled with the existence of some high-quality trials that did not show a benefit with homeopathy have caused many pharmacists to conclude that homeopathy is nothing more than quackery.^{1,10-13}

PHYSICAL EXPERIMENTS IN DILUTION RESEARCH

The supposed implausibility of homeopathy, which is based on the argument that very dilute substances (diluted beyond Avogadro’s number) cannot have biological activity, has been investigated by a number of scientists. Basic science research appears to suggest that the use of extremely dilute solutions may not be as implausible as has been claimed.

Research on the effects of diluted substances has been ongoing in 2 main areas: (1) how very dilute solutions act and interact on a molecular level; and (2) how dilute solutions might interact with biological tissue. An example of the former is a 2003 meta-analysis of experiments,¹⁴ each examining the ability of homeopathic preparations to alter physical properties of solvents. Of the 44 papers reviewed, 38 claimed to have found positive results for homeopathy, meaning that the dilutions were active in some way. However, of these 38 positive experiments, only 6 were considered to be of high methodological quality. The authors of the review suggest that the high number of positive trials may reflect a publication bias against publishing negative trials. The authors also caution that most of the trials were performed without adequate controls, randomization, blinding, and/or statistical analysis.

Several hypotheses of how dilute solutions might retain properties of the mother tincture have emerged, including clathrates (also known as I_E crystals and ice-like crystals); the unique structure of water; hormesis; subtle energy that is retained in the solution and transmitted; and electromagnetic frequency. For example, Anagnostatos et al proposed a model involving small

water clusters, known as *clathrates*, that can explain and predict how medicinal properties of homeopathic dilutions can be transferred to a “vehicle” solvent.^{15,16} Clathrates can reproduce themselves during the dilution process, similar to the way crystals grow. This model may also explain the oscillatory effectiveness seen in the serial dilutions process in Davenas et al¹⁷ as crystal growth is also oscillatory.^{15,16,18}

When graphed, peaks and valleys (oscillations) of effects were found as the dilutions were increased. Davenas et al conjectured that the succussion step in the dilution process subtly changes the structure of the water, causing the water to imitate the native molecules.¹⁷ Besides this, several other hypotheses centering on the physical properties of water and alcohol, the “vehicles” of homeopathic preparations, have also been proposed.^{17,19}

In another example, chemists Kurt Geckler and Shashadhar Samal found that particles dissolved in a polar solvent clustered into aggregates 5 to 10 times bigger than those in the original solutions as the solution was diluted, rather than dispersed, as conventional wisdom would dictate.²⁰ Thus, diluting a homeopathic remedy may increase the size of the particles until they become biologically active. This phenomenon cannot apply to ultra-high dilutions, but it does offer a clue as to why less dilute remedies may work. Furthermore, these findings show that water has properties that are still not understood, a claim posited by many homeopaths.²⁰

Another example is *hormesis*, also known as the Arndt-Shulz Law, which refers the stimulatory effects caused by small amounts of potentially toxic substances.²¹ In 1982 Stebbing reported on how this principle is seen in the growth and recovery of a range of taxa. This theory is also supported by several other studies.²² In 1995, Matsumoto²² related hormesis to homeopathy, by pointing out the similarities between their postulated mechanism of actions.

A full review of all the hypothesized mechanisms of action for homeopathy currently being investigated is outside the scope of this paper. In short, physical experiments have demonstrated a variety of possible mechanisms for the transmission and preservation of therapeutic properties in highly diluted solutions. Taken together, these findings may lead to a mechanism for how homeopathic medications act and interact on a molecular level.

BIOLOGICAL EXPERIMENTS IN DILUTION RESEARCH

Basic science research on the biological effects of highly diluted solutions has yielded mixed results. For example, in 1988, Davenas et al¹⁷ reported that extremely

dilute solutions of anti-IgE (10^2 to 10^{120}) caused basophils to degranulate, releasing histamine at rates of 40%-60%. This *in vitro* study has been successfully replicated several times,²³⁻²⁶ most recently in 2004 by Belon et al²⁷ in a rigorous, blinded, multi-center approach carried out by 3 independent laboratories. The results showed that extreme dilutions of histamine-inhibited basophil activation models behave in a reproducible fashion. However, it should be noted that other studies of equal quality have not been able to reproduce these findings.²⁸⁻³⁰

Another example is a series of studies that found that the administration of an oral dose of a homeopathic preparation of arsenic trioxide protected mice from the detrimental changes in proteins, enzymes, DNA, and RNA caused by one injection of arsenic trioxide of 1mg/kg bodyweight, corroborating the 1997 findings of Weigant et al.³¹⁻³⁷

Overall, the results from studies assessing the ability of very dilute solutions to have biological effects are mixed. Although, high quality research shows that homeopathic preparations do have measurable effects on biological systems; to date, studies have not successfully settled the original dilemma concerning a mechanism of action for very dilute solutions. The lack of knowledge of a proven mechanism of action is the Achilles heel of homeopathic clinical research. Clinical studies showing positive results are still received with doubt due to the lack of an elucidated mechanism of action. Clearly this is an area where additional research is warranted.

CLINICAL STUDIES OF HOMEOPATHY

A growing body of scientific studies have investigated the clinical efficacy of homeopathy. See Table 1 for a summary of systematic reviews of homeopathic clinical trials. In the last 3 decades, a number of high-quality, randomized, blinded, placebo-controlled homeopathic studies have reported that homeopathically prepared products are more effective than placebo for a variety of conditions such as acute hayfever (mixed grass pollen 30C), rheumatoid arthritis (individualized remedies), primary fibromyalgia (rhus toxicodendron 6X), allergic asthma (isopathy to principle allergen), influenza syndrome (oscillococcinum 200C), childhood diarrhea (individualized remedies), and primary fibromyalgia (individualized remedies).³⁸⁻⁴³ (Note: C means that the homeopathic product was diluted 1:100, eg, 30C means it was diluted 30 times at a factor of 1:100; 200 C means it was diluted 200 times at a factor of 1:100. X means the homeopathic product was diluted 1:10, eg, a 6X product was diluted 6 times at a ratio of 1:10 each time.)

Of these, most compelling are the 2 randomized, double-blind, placebo-controlled, studies that were reproduced. In 1986 Reilly et al found that a homeopathic medicine consisting of 30C¹ of mixed grass pollen performed significantly better than placebo at eliminating hayfever.⁴³ Outcome measures were Visual Analogue Scales (VAS) of overall symptom intensity and the use of pharmaceutical antihistamines (the placebo group used significantly more). Reilly et al replicated these results in a later study done in 1994 in which a homeopathically prepared 30C remedy from the patients' principle allergen was used.⁴² The results showed that the homeopathic group did significantly better than the placebo group, based on improvement in VAS score.

In 1989, Fisher et al found that a homeopathic rhus toxicodendron 6X performed significantly better than placebo at reducing the number of tender spots and pain, and improving sleep in patients with primary fibromyalgia.³⁹ In 2004, Bell et al reproduced the positive results yielded by Fisher et al.³⁹ All participants in the study had physician-confirmed fibromyalgia.⁴⁴ Patients randomized to the homeopathic group were given individualized remedies. Those treated homeopathically all showed significantly greater improvements in tender point count and tender point pain, quality of life, global health, and a trend towards less depression compared to those on placebo.

Several meta-analyses have also concluded that homeopathic treatment is significantly better than placebo (Table 1).⁴⁵⁻⁴⁷ The first was carried out in 1991 by Kleijnen et al.⁴⁵ They identified 107 published papers that scientifically evaluated the efficacy of homeopathically prepared treatments. Of these studies, 81 reported positive effects for homeopathy, with 9 of the 11 highest quality trials showing positive results.

A second, extremely rigorous, meta-analysis was conducted in 1997 by Linde et al in an attempt to ascertain whether or not the clinical effects of homeopathy are due to placebo effects.⁴⁶ They evaluated 186 clinical trials that tested the efficacy of homeopathically prepared treatments. Of these, 89 reported sufficient data to be included in the main meta-analysis. After controlling for publication bias, and quality of evidence, their results showed that homeopathy performed significantly better (combined odds ratio was 2.45 in favour of homeopathy) than placebo, with a confidence interval of 95%.⁴⁶ Additional scrutiny, including methodological revisions by the authors themselves in a subsequent paper, confirmed these findings.⁴⁸⁻⁵⁰

In contrast to findings by Kleijnen and Linde, a 2005 meta-analysis by Shang et al that was published in *Lancet* found that the efficacy of homeopathic treatment was no different than placebo.⁵¹ However, this study has been

Table 1. Meta-analyses of Homeopathic Clinical Trials

Author and Year	Number of Studies Examined	Inclusion Criteria	Outcome
Kleijnen et al, 1991 ⁴⁵	107 homeopathic trials	Papers that attempted to scientifically evaluate the effectiveness of a variety of homeopathic treatments	81 papers reported positive effects, however, overall quality of the studies was low
Linde et al, 1997 ⁴⁶	Found 189 homeopathic trials, of which 119 met inclusion criteria, of which 89 had sufficient data for meta analysis	All studies were placebo-controlled, human trials that explicitly reported randomization and/or double-blind allocation of treatment. Studies also had to be formally written and published, and provide sufficient data on the outcome.	74 papers showed positive results. The overall odds ratio was 2.45 in favour of homeopathy. However, the authors reported that most of the trials were of low quality.
Linde et al, 1999 ⁵⁰	89 (re-analysis of the results from 1997 ⁴⁶)	The results of studies meeting criteria of methodological quality were compared with those that did not.	The odds ratio decreased, relative to the quality of the studies, indicating publication bias. However, the results still show that homeopathy performed better than placebo.
Cucherat et al, 2000 ⁴⁷	Found 118 homeopathic trials, however, only 16 met inclusion criteria	Trials had to be randomized, placebo-controlled, and evaluate the efficacy of a homeopathic treatment for a disease diluted beyond 3C. Prevention trials were not included.	The <i>p</i> value of 17 comparisons of the 16 trials was computed to be significant at <i>p</i> = 0.000036. The sensitivity value tended towards non-significance at <i>p</i> = 0.08. Overall, homeopathy performed better than placebo; however, most of the trials were of low quality.
Shang et al, 2005 ⁵¹	Found 110 independent homeopathic trials, however, excluded all except 8	Inclusion criteria was not specified for selection of 8 trials	Based on the odds ratio of 8 trials (0.88), authors concluded that the clinical effects of homeopathy are placebo effects.

highly criticized for being methodologically flawed on many levels.⁵²⁻⁶¹ Of particular concern, the researchers eliminated 102 of 110 homeopathic trials and based their conclusions on only the 8 largest high-quality trials without clearly identifying the criteria by which these trials were selected or the identity of these trials. Odds ratios calculated before the exclusions (on all 110 trials) do not support their ultimate conclusion that homeopathic interventions are no better than placebo.

Overall, enough clinical evidence exists to warrant further research. Future research should attempt to identify which specific homeopathic medicines are effective for which constellation of symptoms. In addition, comparisons with conventional treatments are needed to iden-

tify if there are any indications for which homeopathy may have superior efficacy.

REGULATION

Research on the efficacy of homeopathy is clearly not conclusive; however, the way homeopathic medicines are regulated supports the notion that this is a topic about which pharmacists should be knowledgeable because a key part of their practice is the provision of information about drugs.^{3,10,62} In the United States, since 1938, all homeopathic medicines included in the Homeopathic Pharmacopoeia have been regulated as drugs under the *Food, Drug, and Cosmetic Act*.⁶³ However, they are exempt from a 1962 amendment requiring that all new drugs

provide clinical trial data supporting safety and efficacy to the Food and Drug Administration (FDA) before the drug can enter the market.

Prior to January 2004 in Canada, homeopathic medicines were regulated as drugs under the Canada *Food and Drugs Act* and were issued drug identification numbers (DIN) by Health Canada. Since then, these products have been moved to the Natural Health Product Regulations. Natural Health Products are still technically drugs at the level of the Act. Rather than DIN numbers, since 2004, they have been issued DIN-HMs, which are drug identification numbers for homeopathic medicines.⁶⁴

Taken together, it is clear that North American regulatory bodies view homeopathic products as drugs. According to many pharmacist codes of ethics, pharmacists have a professional mandate to be knowledgeable about substances regulated as drugs in order to most effectively counsel their patrons—regardless of their personal feelings on the matter, (eg, Ontario⁶⁵), thereby strengthening the argument for pharmacists to know about homeopathy.

IMPACT ON PHARMACY PRACTICE

Patients Want Pharmacists' Advice

In a 2005 Canadian survey conducted by the Canadian Natural Health Products Directorate, 71% of citizens reported using at least one natural health product at some point in their lives. Of this 71%, 5% reported using homeopathic medicines.⁶⁶ In the same survey, 43% of respondents said they completely trusted pharmacists for advice on natural health products, and 27% said they prefer to purchase natural health products from pharmacies. These numbers show that although many consumers do not turn to pharmacists for advice on natural health products such as homeopathy, a significant number expect pharmacists to be knowledgeable. These data corroborate the estimates of homeopathic use based on sales reports.^{3,67,68} Further, the results of this survey underscore the role of pharmacists as trusted and accessible community health advisors, preferentially sought out by the public.

From 1990 to 2000, sales of homeopathic products in the United States rose 1000%⁶⁹ and are expected to continue growing steadily each year. Americans spend over \$165 million annually on these products.^{6,67} In 1994, 69% of chain drugstores and 3000 independent pharmacies in the US stocked homeopathic medicine.³ US statistics are similar to those in Canada, suggesting increasing use of homeopathy in both countries.

Pharmacists' Response

Pharmacists have built their reputations on providing accurate unbiased information to patients about all

drugs.⁷⁰ In order to maintain this positive consumer perspective, pharmacists will have to remain abreast of the latest trends in the medications that their patrons are using and requesting information on. By educating themselves about homeopathy, pharmacists will be in the best possible position to maintain their good reputation for providing comprehensive, unbiased advice to patients about their therapy options, and to safeguard patient health.^{2,3,71-76}

An American Pharmaceutical Association survey in 2000 (n=589) reported that the majority of pharmacists expressed an interest in receiving more homeopathic instruction for 2 primary reasons: 31% wanted to improve personal knowledge, 7.3% wanted to make accurate recommendations to their patients and 47.3% were interested in more instruction for both reasons.⁶⁹ Notably, 42% responded “probably yes” when asked if they would participate in homeopathic educational programs. These numbers show that a significant number of pharmacists recognize a need for knowledge about homeopathy.

THE OTHER SIDE OF THE ARGUMENT

Critics imply that pharmacists should *not* know about homeopathy because learning it and being able to counsel patients on it means pharmacists are implicitly validating it. This is something that could hurt their reputation as evidence-based health practitioners, as the scientific literature has shown mixed results regarding the efficacy/effectiveness of homeopathic products and treatments.

Second, in theory, most pharmacists would not recommend homeopathy as effective medicine because it has generally not been proven to be effective for specific conditions and many feel it does not work.^{1,10-12,70,77-79} Ethically, pharmacists with these beliefs and opinions could not actually *recommend* the use of homeopathic products; rather, only provide information to patients on homeopathic principles and the current state of the scientific evidence, or refer the patient to a homeopathic practitioner. In practice, pharmacists who do not support homeopathy would inevitably urge their patients to try a therapy that has a better scientific evidence base.

Finally, some have suggested that pharmacists' ethical mandate to dispense only “good medicine” precludes them from even stocking homeopathic products.^{10,13,65} According to conventional medical paradigms, good medicine would be only that which has a significant body of peer-reviewed scientific evidence supporting it as a viable therapy, meaning that pharmacists would never recommend homeopathy, given its dubious scientific support. As such, they would have no need to know about it. In these scenarios, the only thing pharmacists would need to say to patients about homeopathy is “It does not

work. . .try something else,” rendering any time the pharmacist spent on in-depth learning about the discipline wasted.

What Should Pharmacists Know About Homeopathy?

It does not appear to make sense for pharmacists to attempt to learn about homeopathic medicine in detail. However, we argue that some basic knowledge is required for pharmacists to meet their duty of care. It is recommended that pharmacists learn the 3 main principles of homeopathy, as outlined above; the law of similars, individualized therapy based on symptoms, and the use of very small doses.^{3,6-8} Pharmacists should also be aware that the data assessing the efficacy of homeopathy are mixed—there are rigorous, reproducible studies that show homeopathy is effective,^{39,42-44} and equally scientifically sound studies that show it is not.^{28-30,80-82} A similar situation exists with respect to *in vivo* studies of homeopathic products used to treat plants and animals.^{83,84} Pharmacists should also be aware that there is currently no plausible mechanism of action postulated for homeopathy; even homeopathic doctors do not claim to know how it works.¹¹ Furthermore, pharmacists should be aware that, unless the product is contaminated, there are generally no direct adverse health effects or drug interactions associated with using homeopathics.^{7,8,68} However, an aggravation may sometimes occur, meaning that the symptoms worsen before they resolve. This is seen as a positive effect by homeopaths because it indicates that the body’s own healing mechanism is engaging.⁶ Finally, pharmacists should be aware that patients may alter or discontinue using conventional medications if they perceive that their health is improving due to homeopathy.

With these items in mind, pharmacists should be able to differentiate between homeopathic and non-homeopathic dietary supplements; assist the patient in evaluating the scientific homeopathic literature before selecting a product, and identify patients who should not be self-medicating with homeopathic drugs and need referrals to a homeopathic practitioner or medical doctor.⁸

CONCLUSIONS

Pharmacists must be aware of the scientific literature and decide for themselves if the data are sufficient for them to endorse the use of homeopathic preparations in their practices. To fulfill their obligations to their patients and their profession, pharmacists should at least have a basic understanding of homeopathic principles and the nature of remedies. The fact that homeopathic medicines are regulated as drugs in both Canada and the United States underscores the importance of this.^{63,64} As acces-

sible, critical, science-based health care professionals, pharmacists should evaluate the research on homeopathy without bias, and then convey the facts to their patients and other health professionals.

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American Journal of Pharmaceutical Education 2007; 71 (1) Article 07.

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