Integrative Medicine Newsletter
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Mission
Be a change agent, through research and education, to achieve full integration of evidence-based complementary and alternative medicine into conventional healthcare so all people can enjoy optimum wellness.

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Bridges to Healthy Living
Holistic health expo, demos, dinner, and auction to raise funds for holistic health research for human cancer and chronic diseases.

Save the date!
September 5th, 2014
4pm to 9pm (4pm – VIP admission, 5pm – General admission)
Club Tico, 1599 City Park Drive, Fort Collins

Optimum Wellness for All through Integrative Medicine
From the Executive Director’s desk

AlterMed Research Foundation is very pleased to present this August issue of the AlterMed Integrative Medicine Newsletter. In this issue, the researchers AlterMed has funded in the last year have provided background and status on Mindfulness Based Stress Reduction (MBSR) Bibliotherapy and Evidence-Based Research on the Nanoparticle Nature of Homeopathic Medicines. I hope you will find their state of the art research informative and interesting. The benefit of the MBSR bibliotherapy study, if found to be effective, is to make MBSR more readily accessible to patients. On the study of homeopathic medicines, since over 500 million users use it worldwide, it is important that we better understand the characteristics so we can perhaps use the new findings as a stepping stone to understanding whether a plausible mechanism exists on how something with high dilution could have more potency. If you have any input regarding this Newsletter, please contact editor@AlterMedResearch.org

To enable AlterMed to raise more funding to support evidence-based research in complementary and alternative medicine, I invite you to join AlterMed in supporting our September 5th, Bridges to Healthy Living Fundraising Event. This event is a holistic expo with demos of healthy living approaches along with a healthy dinner and auctions. We invite exhibitors to join us from these six areas of healthy living (DARCIE: Diet, Activity, Relaxation, Coping positively to life stresses, Interconnectedness, and Environmental impact awareness on health).

Today our health care expenditures are about 18% of GDP. Chronic disease treatment accounts for over 75% of this cost and the rising rates of overweight and obesity and their contribution to chronic illnesses is of great concern to policy makers. Based on the latest science, proper diet and exercise are key elements in preventing and treating diabetes, heart diseases, and other chronic illnesses. Whether or not one is a holistic health advocate, we must first tend to the fundamentals of good health like diet/nutrition, exercise, and relaxation. In addition to the fundamentals of lifestyle medicine, mind-body medicine for stress reduction and environmental impact on health should not be overlooked.
I have had the privilege to take an MBSR program this year. I was reminded of the importance of being mindful (be in the here and now, aware but without judgment) of our bodily sensations with body scans/yoga/meditation/breathing, of our daily routines, of our emotions, and of our communications. Emerging research is showing that mindfulness meditation can reduce chronic inflammation conditions. An example of this research is being conducted by Melissa Rosenkranz, PhD, funded in part by AlterMed. As far as our environment, we need to be aware of herbicides, insecticides, and other pollutants with possible links to increased health risks.

Whether you are remote or reside in or close to Fort Collins, I hope you consider either joining us locally at the September 5th Bridges to Healthy Living Fundraising Event or donate online to enable AlterMed to fund more evidence-based complementary and alternative medicine research to further this exciting field so all people can enjoy optimum wellness.

Bridges To Healthy Living 2014 Flyer:

Thank you for your support of AlterMed Research Foundation. Enjoy the August issue of our Newsletter.

Kerri Diamant
Executive Director
AlterMed Research Foundation
Effectiveness of Mindfulness-Based Stress Reduction Bibliotherapy: Description and Update of a Current Investigation

Holly Hazlett-Stevens, PhD and Yelena Oren, MA
University of Nevada, Reno

Chronic stress can compromise physical and emotional health in a myriad of ways. A well-known mind-body approach to stress reduction, Mindfulness-Based Stress Reduction (MBSR), was developed by Jon Kabat-Zinn over 30 years ago, and much research now supports its effectiveness for a wide range of medical and psychological conditions. The traditional group intervention format of MBSR requires 30 hours of instruction by a provider with specialized training to teach mindfulness meditation and movement practices, potentially leaving MBSR unavailable to many who may benefit. Fortunately, a workbook teaching these practices in a self-help bibliotherapy format was recently published by two highly experienced senior MBSR teachers, possibly allowing for wider dissemination of this potentially effective intervention. In this article, we will describe our current investigation underway to examine the effectiveness of this MBSR workbook in a randomized control trial comparing the intervention group to a wait-list no-intervention control group. If the MBSR workbook intervention is accepted and utilized by participants in its self-help format, and if it appears effective in reducing self-reported stress and related symptoms, this bibliotherapy may offer a cost-effective alternative to the traditional group format in settings where traditional MBSR might not be available to all patients.

Background: Decades of research have documented the damaging effects of chronic stress across multiple physiological systems, including cardiovascular, endocrine, and immune systems. The American Institute of Stress recently estimated that 77% of Americans regularly experience physical symptoms caused by stress and labeled stress as ‘America’s number 1 health problem.’ While a variety of stress management approaches have been developed over the past several decades, one particular approach has garnered substantial research support for a variety of medical and psychological conditions: Mindfulness-Based Stress Reduction (MBSR). First developed by Jon Kabat-Zinn in 1979 after observing many University of Massachusetts (UMass) Medical School patients suffer the deleterious effects of stress, MBSR is now typically an eight-week program where patients gain first-hand experience applying mindfulness, characterized by an open present-moment awareness to the immediate stressors of daily life, pain, and illness [8].
What is mindfulness meditation?
The roots of mindfulness meditation are found in the more than 2500-year-old tradition of Buddhism. However, as Jon Kabat-Zinn observed, these meditation practices can be taught in a manner acceptable to the average American medical patient and is sensitive to his or her mainstream American cultural background. Dr. Kabat-Zinn developed a systematic curriculum designed to teach the essence of mindfulness meditation and movement practices in a straightforward way which patients could apply in their daily lives. Dr. Kabat-Zinn originally designed this stress reduction program for medical patients coping with the stress associated with chronic pain as well as for patients whose difficulties coping with stressful life circumstances were adversely impacting their physical health. He defined mindfulness as ‘the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment to moment’ [7, p. 145]. From this perspective, many of us spend much of our time on autopilot mode, without truly being aware of what we are doing. Events happening around us, our thoughts, feelings, and body sensations can often trigger old habits of thinking and reacting, leading to stress. We are often unaware of these moment-to-moment patterns of thoughts, body sensations, feelings, and behavioral reactions. Therefore, we remain stuck in our usual stress reactivity mode. As we become better aware of our thoughts, feelings, and body sensations, we open up to the possibility of greater freedom and choice. We no longer have to repeat the same old patterns of reacting. Instead of just reacting automatically, we become better able to choose our responses and therefore act wisely and deliberately.

Research support for MBSR
As early outcome research at UMass documented the long-term benefits of MBSR for chronic pain patients [6,9], subsequent research documented benefits of MBSR for other chronic medical conditions such as fibromyalgia (long-term body pain and joint tenderness), cancer, chronic low back pain, rheumatoid arthritis, chronic fatigue syndrome, and heart disease [1]. The most extensive review and meta-analysis of MBSR treatment effects was the Campbell Systematic Review [5]. This review analyzed 31 randomized controlled trials with a total of 1,942 enrolled participants. No adverse effects were described in any of the reviewed studies.
The authors found ‘moderate- to high-quality evidence of a consistent and moderately large effect of MBSR on health and quality of life.’ In other words, this means MBSR was having a measurably positive effect on health and quality of life. MBSR now appears in the Substance and Mental Health Services Administration (SAMHSA) National Registry of Evidence-based Programs and Practices (NREPP) as an intervention that has been scientifically evaluated.

Some intriguing examples of MBSR outcome research can be found within the cancer literature. Large-scale analyses from ten MBSR investigations focusing on cancer patient groups showed a medium treatment effect for mental health symptoms [10]. MBSR also appeared to improve normal bodily functions in cancer patients. In a sample of 42 early stage breast and prostate cancer patients [3], MBSR yielded significant improvements in quality of life, stress symptoms, and sleep quality. This intervention also improved immune function. The study showed that disease-fighting immune cells called T-cells produced higher levels of a wound-healing molecule called Interleukin-4. In addition, these cells also produced lower levels of an inflammation-promoting molecule called Interferon gamma.

Among the 40% of cancer patients who had higher levels of a stress hormone called cortisol, MBSR intervention was observed to decrease cortisol levels [4]. Among the total number of cancer patients, a decreased in systolic blood pressure was observed following MBSR. Furthermore, patients were able to maintain a healthy blood pressure until their one-year follow up [2]. In addition, patients receiving MBSR intervention also had lower levels of inflammation-promoting molecules in their bodies over the course of the follow-up year.

**Limitations of the eight-week MBSR curriculum**

This intensive group intervention program typically requires up to 30 hours of instruction, consisting of eight 2.5-hour-long weekly sessions and one day-long extended practice session. During these sessions, a trained instructor teaches a series of formal and informal mindfulness meditation techniques and mindfulness movement practices such as gentle stretching, yoga and walking. MBSR was developed as an intervention to meet public health needs; however, there are a series of obstacles people often face in gaining access to MBSR training.
MBSR classes are typically offered in the evenings and might not be accessible for individuals with variable and/or non-standard work schedules. MBSR instruction requires rigorous, specialized professional training. Instructors are required to maintain their own intensive mindfulness meditation practice, limiting the number of trained teachers who can deliver the intervention, especially in small cities or rural areas. Furthermore, the typical cost of the entire MBSR program ($400) might be cost-prohibitive to many individuals, especially when not covered by an insurance provider.

A new approach
Fortunately, the original MBSR program was adapted into a self-help bibliotherapy format. A Mindfulness-Based Stress Reduction Workbook, a book authored by senior MBSR instructors Bob Stahl, Ph.D. and Elisha Goldstein, Ph.D., was published by New Harbinger in 2010. This workbook consists of an introduction, 11 chapters, and a CD with audio recordings of guided meditations. The chapters contain information describing the nature of mindfulness and the mind-body connection, as well as the autonomic nervous system and how mindfulness plays a role in stress-reduction. Formal mindfulness meditation practices from the original MBSR program are introduced in the text and are guided by audio recordings. Informal practices and the application of mindfulness in interpersonal relationships are also discussed.

Research Investigation in Progress
The purpose of our current investigation is to examine whether the self-help bibliotherapy format provides a feasible and acceptable alternative to the full MBSR group intervention for undergraduate and graduate university students as well as for nursing and medical students. We are very grateful to the AlterMed Research Foundation for supporting our research. We are in the process of recruiting students enrolled at the University of Nevada, Reno who are interested in participating in a study to improve their health and well-being. After completing a variety of health-related and psychological questionnaires, students who chose to participate are then randomized to a bibliotherapy intervention condition or to a no-intervention control condition. If randomly assigned to the bibliotherapy intervention, students receive this workbook and the accompanying guided practice recordings free of charge. For ten weeks, they are advised to read a specific portion of the workbook; complete all associated journal writing exercises; and perform formal and informal mindfulness meditation and movement practices.
Each week these students also complete a series of questionnaires pertaining to their use of the workbook as well as a few standardized measures of psychosocial functioning. At the end of the intervention period, the students repeat the same battery of health-related and psychological questionnaires. Students who are randomly assigned to the no-intervention condition take the same battery of tests at the end of the study.

We have currently enrolled 22 students in this study: five are graduate students and 17 are undergraduate students. We have also received formal approval to expand our recruitment to nursing and medical students. Two enrolled participants have completed the study at this time, and twelve more are near completion. So far, our attrition rate is lower than expected at 10%. We look forward to finishing up our proposed data collection of 90 students over the course of this fall, at which time we will begin examining and analyzing the data. We are curious to know whether busy college and health care students would be willing to take the time to learn MBSR on their own without the support and structure of the traditional MBSR group intervention format. If so, we will also investigate whether this alternative format yields the expected emotional, psychological, and health-related stress reduction benefits.

Summary and Conclusion
Chronic stress compromises the functioning of the cardiovascular, endocrine, and immune systems. In addition, it also poses a negative influence on our psychology and quality of life.

MBSR systematically teaches several forms of mindfulness meditation and movement practices, and much research supports this stress reduction approach for many medical conditions, including cancer, as well as for mental health conditions and for health enhancement among healthy individuals. However, the intensive group intervention format of MBSR may not be accessible to all individuals who might benefit from learning these practices. We therefore are currently conducting a randomized controlled investigation of a self-help bibliotherapy version of MBSR among university and health care students to examine whether this different format provides a viable alternative. Enrollment for this investigation is well underway, and data collection is expected to conclude on schedule later this year in the fall. If our results look promising, future research would examine this alternative for patients who desire stress reduction benefits but cannot access traditional MBSR for a variety of reasons.
References


The Nanoparticle Nature of Homeopathic Medicines: current status and future research
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Homeopathy is an over 200-year old system of alternative medicine used worldwide. The nature of its medicines has spurred debate since it began. Recent studies suggest that, contrary to the position of skeptics, homeopathic medicines may contain different sizes and shapes of tiny particles, called nanoparticles. Additionally, they may also contain an element called silica. On the basis of their minute size, nanoparticles acquire some remarkable electromagnetic, optical, and even quantum mechanical properties that larger particles do not possess. This paper summarizes some of the scientific evidence in this exciting new area of nanomedicine and explains the current plan for systematic, blinded, placebo-controlled ‘test tube’ studies on nanoparticles in homeopathic medicines, funded by the AlterMed Research Foundation this year.

Background: Homeopathy is an over 200-year old system of alternative medicine used worldwide by over 500 million people [1]. This system uses natural plant, mineral, and animal source materials in low, usually nontoxic doses to treat people with chronic and acute illnesses ranging from cancer and autoimmune diseases to infections [2,3]. Homeopathy relies on the adaptive ability of the body to heal itself as a whole indivisible network through a chain of internal changes over time when stimulated by a biological signal. Homeopathic medicines serve as a biological signal [4], possibly through biochemical, electromagnetic, optical (light) or quantum physics (atom-like) mechanisms. A number of homeopathic medicines have been shown to kill abnormal cells in test tube studies using cancer cells and animals with cancer [5-9]. Homeopathic manufacturers make their medicines using the same materials and methods developed 200 years ago by the German physician-chemist Samuel Hahnemann, MD, PhD. These methods include grinding plant, mineral, or animal-derived material (the source material) in pure dry milk sugar (lactose) and then diluting and vigorously mixing in a water or alcohol-water solution within a glass container.
Classically, Hahnemann also used real corks from oak tree bark, not rubber or plastic, to seal his glass bottles.

Traditionally, Hahnemann would take a small part of the last bottle’s solution and put it into a new bottle of mostly fresh solution. The number of times this transfer of solution occurred was measured using dilutions. Homoeopathists describe their medicines in terms of potencies on the basis of the number of dilutions. The dilution ratios of medicine-to-solvent are either 1/100 (C potency) or 1/10 (X potency).

As homeopathic manufacturers make higher potency medicines (more steps beyond 24X or 12C), they often use what they call a Korsakovian method of making the medicines. In this method, they pour off 90% or 99% of the diluent from the original solution and add fresh diluent into the same piece of glassware over and over again for the next round. Regardless of how the serial dilutions are done, the solution is vigorously agitated (succussed) multiple times after every dilution step.

Over the years, homeopathy has faced a notable amount of skepticism. In theory, past a certain limit (24X or 12C), no molecules of the source materials should remain in the medicine. Proponents believe that these higher homeopathic ‘potencies’ nonetheless capture the specific subtle information or perhaps ‘energetic properties’ of the source material. Skeptics typically focus on the dilutions and ignore the grinding, mixing, and agitation processes, as well as the lactose, ethanol, glassware, and cork materials used. Ignoring these important subtleties in homeopathic manufacturing may have led to an erroneous assumption that these homeopathic medications have nothing in them.

Skeptics still argue that the dilutions would remove any trace amounts of the source materials and leave nothing but plain water (or an alcohol-water solution). Then homeopathic medicines would be considered merely elaborate placebos (sugar pills) without the ability to treat various diseases. They base their beliefs on the assumption that homeopathic medicines are like bulk form conventional drugs that do not work at all. A deeper understanding of homeopathy is therefore necessary for a more scientifically aware community and widespread utilization of homeopathic medicines.

The nanoparticle discovery in homeopathic medicines
Despite much skepticism, previous controlled research studies have shown that homeopathic medicines retain the unique signal and biological activity of their source material, even though no source molecules theoretically persisted above 24X or 12C potencies [10-12]. Until recently, no one knew how these observations could occur.
Studies using tools such as electron microscopes have shown that homeopathic medicines contain nanoparticles (NPs) - a tiny form of source material [13-17], silica from glassware [18], and perhaps other materials originating from the use of lactose, ethanol, glassware, and cork stoppers. For perspective, nanoparticles range in size from 1-100 nanometers, while a single human hair is roughly 90,000 nanometers wide.

It turns out that grinding insoluble drugs or other materials like eggshells for hours can break down the bulk form into nanoparticles [19-23]. Agitating dissolved materials like salts can also produce nanoparticles [24]. As a general guideline, the duration and intensity of grinding or agitation determines the size of the resulting particles. Granted, these particles may be inconsistent in terms of their size and shape in comparison to what modern nanotechnologists can produce; however, they are still nanoparticles.

At the nanometer scale, the increased potency of NPs means that one can use extremely small quantities and still get chemical or biological effects [25,26]. In fact, NPs are so reactive on their surfaces that modern nanotechnologists add other materials like lactose to stabilize them and to improve their ability to enter cancer cells [27,28,33]. Making natural materials into nanoparticles using silica as the carrier can also boost the anti-cancer effects of traditional medicines and natural antioxidants like Curcumin [29,30].

The ordinary forms, or bulk forms, of the source material are still present in lower homeopathic potencies than one might find in a health food store, up to 23X and 11C. Past these potencies, the ordinary bulk forms of the source materials may be diluted out; however, experiments show that the nano scale forms are not removed [31].

The agitation process releases measurable amounts of silica from the inside walls of the glassware, a finding that has been repeated in multiple independent laboratories around the world. Silica, especially nanosilica, biologically amplifies effects of accompanying materials with which it enters the body. Nanosilica alone stimulates the cellular defense systems. We know from homeopathic studies that experiments performed using agitated controls sometimes produce greater medicinal effects than those performed using non-agitated controls [32]. Could these observations be due to nanosilica in the agitated controls? In other words, are the agitated controls truly inert ‘placebos’, or are they biologically active?
It is possible to specifically tune the optical (light) and electronic effects of smaller sized nanosilica by ‘doping’ it with small amounts of ‘filler’ nanomaterial. It is hypothesized the doping process might occur during homeopathic manufacturing. Herbal plant extracts can also biologically synthesize new nanoparticles from their building blocks, e.g., for silver, gold, or silica. The plants have biologically active traces of their own material on the surfaces of the nanoparticles and can form their own nanoparticles as well. This may even have implications for corks in aged wines.

Nanoparticles are not really fully ‘dissolved’ in a scientific sense. Rather, many homeopathic solutions are actually what chemists call a colloid. A colloid contains tiny particles dispersed or suspended, but not dissolved, within a liquid (such as alcohol or alcohol-water solutions). Milk is a common example of a colloid. Unlike the water structures that many homeopathic researchers have previously thought might carry the homeopathic signal, nanostructures can persist with their biochemical and biological activity intact even after being dried out [34-37]. If a homeopathic medicine is made in water or a water-alcohol ethanol solution, it is often dried onto small sugar pellets for easier storage and administration.

How could low doses of nanoparticles have biological effects?

There are several overlapping processes by which the body itself could amplify the size of the response to such a tiny dose of tiny nanoparticles. First, even at low potencies, the nano scale forms are simply taken up better and used more effectively by the body. A large amount of research outside homeopathy is focused on creating nano forms of cancer treatment drugs and herbs to take advantage of their lower dose and fewer side effects.

In addition, even at very low concentrations, nanoparticles can be more reactive than at higher concentrations. At low doses, nanoparticles can take advantage of the body’s ability to detect small yet meaningful signals and amplify their response. This process occurs all the time in the sensory systems of people and animals. For example, a tiny noise at night or a certain odor at very low concentrations can inform an animal that a predator is nearby. This signal activates the body’s stress response systems to flee the area or confront the predator. The weak signal in the example (a tiny noise) is actually amplified and converted into a larger signal (the body’s stress response). This phenomenon is known as stochastic resonance. Stochastic resonance is how complex biological networks can react with large responses to small but relevant changes in the environment.
We believe that stochastic resonance is just the start of an adaptive chain of events in the person, animal, or cell that the right nanoparticles can set into motion. Our bodies are bombarded with nanoparticles of various types at all times. What matters is whether or not they signal an individually meaningful threat or danger signal. If those nanoparticles are particularly relevant to the individual, the body responds vigorously. Sometimes, at a low enough dose, these types of signals trigger a reversal of the ongoing response of the individual organism. This is termed hormesis.

Hormesis is a well-documented phenomenon in which higher and lower doses of a particular material can initiate changes in the organism in opposite directions [38,39]. Thus, a well-known chemotherapy drug called cycloheximide at low hormetic doses (below the cut-off for toxicity or conventional drug use) will actually protect, not kill, cancer cells. Similarly, aspirin, a conventional drug used for thinning the blood, will actually cause clots at extremely low doses. It therefore follows that if a plant, mineral or animal source material were to be used in homeopathy, which is generally recognized as very safe, you would need very low doses to get this hormetic effect.

Consequently, things that might be toxic at higher doses are instead therapeutic in very low doses, i.e., in homeopathic form and dose.

What Is Needed Scientifically?
Skeptics are not about to accept the data summarized in this article and stop their campaign to end homeopathy. They demand that independent laboratories repeat and improve upon the methodologies used in the original breakthrough studies. In science, healthy debate is a good thing – it stimulates us to think more analytically and to do well-controlled experiments to improve our understanding.

In the spirit of true scientific exploration and balance, nanotechnology may have important implications in homeopathy, perhaps enough to enable well-controlled research studies. These research studies will help us draw a distinction between the truth and what we currently perceive to be the truth. What is most important is that we are guided by the scientific data and not our desire to be right about a certain hypothesis or a theory.

There is still much to be learned about nanoparticles, specifically in the context of homeopathic medicines.
What if the historical homeopathic manufacturing methods were actually varying the size, shape, and number of nanoparticles? How might these nanoparticles act to kill cancer cells better, especially if used at higher potencies? Why do some homoeopaths in India use both low and high potency medicines together and report good clinical results in their advanced cancer patients?

Our network of research collaborators have embarked on an ambitious but necessary research program on the nanoparticle nature of homeopathic medicines. The grant support that we have received this year from the AlterMed Research Foundation has given us a way to begin. It has enabled us to start the essential and exciting work of making new discoveries in this centuries-old field and publishing our findings.

This new study proposes to use cutting-edge nanotechnology methods to analyze the optical properties of nanoparticles in different homeopathic medicines that are used to treat certain cancers and infections. Our laboratory testing will include several potencies (6C, 30C, 200C) and compare the potencies with their appropriate placebo controls. Previous research has shown that the natural source materials used for the test medicines, either as homeopathic medicines or modern manufactured nanoparticles, can kill cancer cells [9,40,41,8].

The technology chosen for this study has major advantages over other methods used by previous research groups in their testing. The two scientific technologies that this study will use to test the homeopathic medicine samples are called nanoparticle tracking analysis and ultraviolet visual spectroscopy. Nanoparticle tracking analysis uses lasers to track the spontaneous movements of individual nanoparticles in a drop of liquid in which they are suspended. This technique is able to accurately measure the sizes and concentrations of particles with greater accuracy. In addition, the method has a lower operating cost. The first phase of our project is currently in progress: we have just finished collecting data and are in the process of analyzing it.

The ultraviolet spectroscopy method analyzes at the optical (light) properties of our samples. This method has been previously shown to help scientists distinguish between homeopathic remedies of varied potency and age. In addition, the method will help determine the specific light-related patterns that a particular sample can generate. Currently, there are no previous studies that have analyzed homeopathic medicines using the aforementioned combination of methods.
To improve on previous basic science studies on nanoparticles in homeopathy, we are randomizing and blinding (i.e. we remain unaware of which bottles contain medicine and which contain control samples) the bottles of homeopathic medicines and controls when they are tested. We are including both agitated and non-agitated controls. The importance of this study is that it will help determine new key information about the types, stability, sizes, and concentrations of nanomaterials in homeopathic medicines and controls. Findings from the proposed new study could eventually help resolve the historical debate over the plausibility of homeopathy as an alternative treatment system with energy medicine features. Our study will also reveal crucial new information about how each aspect of homeopathic manufacturing that Hahnemann designed might contribute to making these medicines.

This work could someday lead to new advances for making homeopathic products already used by millions of consumers. Thanks to the grant award from the AlterMed Research Foundation, we are now on our way to making discoveries and advancing scientific knowledge in the field.

References


