Review Article

Scientific framework of homeopathy: Evidence-based Homeopathy

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ABSTRACT

Paper aims at considering all important aspects of the scientific framework of homeopathic practice, looking at the levels of scientific evidence of each aspect in an objective way, through an extensive review of literature. Levels of evidence considered are: I) existence of meta-analyses and/or systematic positive reviews of literature; IIa) multiple positive randomized controlled trials (RCTs); IIb) some positive RCTs; IIIa) positive multiple cohorts studies; IIIb) positive studies with some cohorts; IV) opinion of experts (clinical and daily practice cases). Conclusions are clear: homeopathy must stay within the framework of medical practice, and it is even a necessity for public health.

Keywords: Evidence-Based medicine, Homeopathy, Scientific framework, Literature review

Introduction

The World Health Organization (WHO) concluded, in a report of 2005 on traditional medicine (TM) in several countries [1], that TM maintains its popularity worldwide. In addition, during the last 10 years, the use of complementary and alternative medicine (CAM) has increased in several countries. The safety of the products employed in CAM, their quality control and evaluation in terms of efficacy are priorities to political authorities as well as the population.

More particularly, the WHO asked questions to its 191 members. 141 countries (74%) answered. 32% of them have developed health policies including TM/CAM; 56% stated that policies regarding TM/CAM are “under construction”. Only 5 countries effected regularization before 1990. Moreover, 28% of countries have a national program specific for TM/CAM and 58% have established a national committee in charge of TM/CAM.

In most cases, these committees are located in Health Departments. Finally, 43% of countries have named a committee of experts for TM/CAM. Harmony lacks among countries. Major difficulties include: absence of a standardized educational program for TM/CAM and lack of experts. Countries ask the WHO for support and advice in order to develop national policies for the regularization of TM/CAM.

In Europe, the report “Concerted Action for Complementary and Alternative Medicine Assessment in the Cancer Field” [2], observed the same tendency regarding the increase in the use of CAM. In the United States of America, the Consortium of the Academic Health Centers [3] integrates CAM in 30 university medical centers. As in the United Kingdom, the concept of “integrated” medicine predominates; all possible treatments must be offered to patients. This stance is based on the results of intensive scientific research on CAM. Until this moments, results for homeopathy are very hopeful.

Recent publications show the benefit of homeopathy in hospital care, as well as in emergency services for patients in critical state [4-6]. Authors suggest the development of algorithms including homeopathy, allowing quick and adequate reactions for these patients.

The aim of the present paper is to review the scientific framework of current homeopathic practice worldwide. Scientific accuracy is appraised according to the level of evidence available for each aspect. Levels of evidence considered are: I) existence of meta-analyses and/or systematic positive reviews of literature; IIa) multiple positive randomized controlled trials (RCTs); IIb) some positive RCTs; IIIa) positive multiple cohorts studies; IIIb) positive studies with some cohorts; IV) opinion of experts (clinical and daily practice cases).
**Meta-analyses: Systematic review**

The “gold-standard”, universally accepted for the evaluation of the efficacy of medicines, is the meta-analysis, or systematic audit of RCTs. Since 1991, 6 comprehensive reviews regarding homeopathy were published. The conclusion of them all was that homeopathy has a positive and specific effect greater than placebo. (Table 1)

### Table 1. Comprehensive systematic reviews on homeopathic trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Studies</th>
<th>Results</th>
</tr>
</thead>
</table>
| Kleijnen et al., 1991 [7]     | 105 studies with interpretable results. Meta-analysis based on validated criteria | - 77% of studies show positive result of homeopathy  
- regarding quality of trials, results are most favorable for homeopathy  
- “there is valid argument for further evaluation of homeopathy” |
| Boissel et al., 1996 [8]      | 15 studies. Inclusion only of highest quality studies.                  | - Combined p-values for the 15 studies is significant (p=0.0002)  
- Little evidence for non-published negative results.  
- “it is evident that homeopathy is more efficient than placebo” |
| Linde et al., 1997 [9]        | 89 studies                                                              | - Odds ratio combined 2.45 (95% CI, 2.05-2.93) in favor of homeopathy  
- Odds ratio for the best 26 studies was 1.66  
- “it is not possible that the clinical effects of homeopathy are due completely to placebo” |
| Linde & Melchart, 1998 [10]   | 32 studies; inclusion only of individualized homeopathy                | - Individualized homeopathy is more efficient than placebo; value of combined coefficient = 1.62 (95% CI, 1.17-2.23)  
- Further research is justified |
| Cucherat et al, 2000 [11]     | 16 trials, representing 17 comparisons to placebo (based on Boissel et al.) | - Several studies have positive results; more trials with positive results than expected by chance alone  
- Publication bias is unlikely  
- More clinical trials are needed |
| Shang et al., 2005 [12]       | 110 trials included, but conclusions taken from a few post hoc selected studies (n=8, 7%) | - Quality of studies is on average better than studies with conventional remedies  
- No significant effect exist with homeopathic medicines  
- The authors conclusion is based on an amalgamation of biases (selection, post hoc criteria and heterogeneity) [16] |
The fact that some meta-analyses have shown positive evidence for homeopathy is remarkable, as meta-analyses are far from appropriate when trials are extremely heterogeneous (as in homeopathy), not only regarding results, but also the interventions and health conditions under study, as well as when a therapeutic system works in some but not all indications.

One study, namely GRECHO’s [13] occupies excessive place and exerts considerable influence on the results of all 6 audits, especially in Shang et al.’s (1/7 = >15%), where *Opium* and *Raphanus* were administered to stimulate intestine activity after surgery. Both remedies were compared to placebo and no positive result was obtained. However, individuality – a basic principle of homeopathy – was not taken into account.

The major problem in this type of analysis is linked to the initial hypothesis: “homeopathy is not better than placebo”. Recently, the zero-hypothesis was reformulated as “homeopathy functioned not better than placebo in a specific case”. This hypothesis indeed corresponds to systematic conventional research and as such, cannot be contested.

It also represents a solution to the problem of heterogeneity in medical conditions. 17 systematic reviews or meta-analysis focusing RCTs of homeopathy in 15 specific areas were performed. This critical approach was explained by Jonas, Kaptchuk and Linde [14]. Results are described in Table 2.

### Table 2. Levels of evidence of 17 systematic reviews of RCTs of homeopathy in 15 specific areas

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Childhood diarrhea and seasonal allergic rhinitis [14]. Allergic rhinitis [15], post-operative ileus (16), rheumatoid arthritis [17], protection against toxic substances [18]</td>
</tr>
<tr>
<td>IIa</td>
<td>Asthma [19], fibrositis [20], influenza [21], muscular pain [22], otitis media [23], several pains [24], side effects of radiotherapy [25], strains [26], NET infections [27].</td>
</tr>
<tr>
<td>IIb</td>
<td>Anxiety [28], hyperactivity disorders [29,30], irritable bowel [31], migraine [32], knee osteoarthritis [33], premenstrual syndrome [34], pain association to unwanted postpartum lactation [35], prevention of nausea and vomiting associated to chemotherapy [36], septicemia [37] and analgesia post-tonsillectomy [38].</td>
</tr>
</tbody>
</table>

While this approach corresponds to the common criteria of conventional medicine, it is very limited in and does not analyze the actual daily practice of a homeopathic GP. Further phases are needed, as general practice involves more than searching for the treatment of a specific disease, it seeks for a global amelioration of the health of the patient. Therefore, a GP applies a broader frame than the treatment of a disease, to take into account other factors (diet, psychological state, activity, environment, etc.) RCTs results have only a very limited influence on the practical choice of a treatment for a specific patient. RCTs are conducted in “ideal artificial situations”, far from the particular context of the individual patient. The methods of evaluation must take this reality into account.

**Results of “echo studies”**

‘ECHO’ are surveys looking at Economic, Clinic and Humanistic Outcomes. In the literature, 19 publications using validated scores for quality of life (QOL) are found to evaluate the efficacy of homeopathic medicines, totaling 19,804 patients. **Evidence level IIIa** is obtained in all ECHO-studies, all diagnoses merged. (Table 3)
### Table 3. ECHO studies in homeopathy

<table>
<thead>
<tr>
<th>Condition/Study</th>
<th>N</th>
<th>Design QOL</th>
<th>Test group</th>
<th>Control group</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker-Witt., et al. [48,49]</td>
<td>2851</td>
<td>Prospective observational MOS SF-36</td>
<td>homeopathy</td>
<td>-</td>
<td>Significant and relevant improvement of SF-36</td>
</tr>
<tr>
<td>Bordet et al. [50] Menopause flushes, 6 months</td>
<td>438</td>
<td>Prospective observational. Multicentric (99 MD) Not validated double QOL score</td>
<td>homeopathy</td>
<td>-</td>
<td>Significant and relevant improvement on both QOL scores (daytime / sleep)</td>
</tr>
<tr>
<td>Dias-Brunini [51] Asthma – pediatrics 6 months</td>
<td>51</td>
<td>Prospective observational AUQEI QOL score applied to children.</td>
<td>homeopathy</td>
<td>-</td>
<td>QOL score from 42.27 to 54.94, significant statistical increase.</td>
</tr>
<tr>
<td>Goossens et al [52] Hay fever</td>
<td>74</td>
<td>Prospective observational non comparative. RQLQ QOL</td>
<td>homeopathy</td>
<td>-</td>
<td>Significant improvement after 3 and 4 weeks.</td>
</tr>
<tr>
<td>Guthlin et al [53] All conditions &lt;4 years</td>
<td>951</td>
<td>Prospective observational MOS SF-36</td>
<td>homeopathy</td>
<td>-</td>
<td>Number of patients too small for valid results.</td>
</tr>
<tr>
<td>Guthlin et al [54] All conditions &lt;4 years</td>
<td>750</td>
<td>Prospective observational MOS SF-36</td>
<td>homeopathy</td>
<td>-</td>
<td>QOL improved in most dimensions highly significantly</td>
</tr>
<tr>
<td>Jong et al [55] Respiratory and ear complaints 7-14-28 days, final results.</td>
<td>2055</td>
<td>Prospective observational. HSQ-12; HSQ-5</td>
<td>homeopathy</td>
<td>conventional</td>
<td>No significant differences in duration of illness, response to treatment, patient satisfaction and adverse effects.</td>
</tr>
<tr>
<td>Riley et al [56] Respiratory and ear complaints 14-28 days</td>
<td>456</td>
<td>Prospective observational. HSQ-12; HSQ-5</td>
<td>homeopathy</td>
<td>conventional</td>
<td>Homeopathy at least as effective as conventional medical care (64.3% &gt;=56.6%). Adverse effects 7.8% versus 22.3%</td>
</tr>
<tr>
<td>Hochstrasse [57] pregnancy &lt;9 months</td>
<td>205</td>
<td>Prospective observational comparative. SEIQoL</td>
<td>homeopathy</td>
<td>conventional</td>
<td>Lower QOL in the homeopathic group (2 different populations, comparison impossible)</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Duration</td>
<td>Outcome Measures</td>
<td>Comparator</td>
<td>Results</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Muscari-Tomaio et al [58] Headache 6 months</td>
<td>Prospective observational</td>
<td>MOS SF-36 homeopathy</td>
<td>-</td>
<td>Mean and median scores of all QOL dimensions rose. Strongest results in “bodily pain” and “vitality” parameters p&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Spence et al [59] Wide range of Chronic conditions</td>
<td>Prospective observational</td>
<td>homeopathy</td>
<td>-</td>
<td>Positive health changes in routine homeopathic hospital practice</td>
<td></td>
</tr>
<tr>
<td>Strosser et al [60] Vertigo 6 weeks</td>
<td>Double-blind comparative MOS SF-36 homeopathy (VertigoHeel®) conventional (betahistins)</td>
<td>-</td>
<td>Significant amelioration of physical and mental health with homeopathy. Equivalent efficacy in the 2 groups</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thompson et al [61] Cancer 5 consultations later</td>
<td>Prospective observation EORTC QLQ-30 QOL score</td>
<td>homeopathy</td>
<td>-</td>
<td>Improvement in 75% patients</td>
<td></td>
</tr>
<tr>
<td>Thompson et al [62] Management of oestrogen withdrawal in women with breast cancer</td>
<td>Prospective observational</td>
<td>homeopathy</td>
<td>-</td>
<td>Significant improvement in anxiety, depression and QOL</td>
<td></td>
</tr>
<tr>
<td>Anelli et al [63] All conditions 6 months</td>
<td>Prospective observational MOS SF-36 &amp; DUKE QOL scores homeopathy</td>
<td>-</td>
<td>QOL score differences: Allergy +7.987; General problems +10.198; Bowels +8.189; Muscles &amp; bones +0.764; Stress, anxiety, sadness +6.041; Nose, ears +4.677; Skin +6.395. Small but statistically significant improvement.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weber et al [64] Acute sinusitis</td>
<td>Non-randomized clinical trial HCG-5 QOL score homeopathy + herbal therapy conventional</td>
<td>-</td>
<td>Equally effective (or ineffective)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White et al [65] Asthma-pediatrics</td>
<td>Randomized placebo controlled QOL subscale of Childhood Asthma Questionnaire homeopathy + conventional placebo+ conventional</td>
<td>-</td>
<td>No statistically significant changes in QOL score, small improvement in severity. NB: very high initial QOL score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Witt et al [66] All conditions 3,12,24 months</td>
<td>Prospective multicentre cohort QOL score homeopathy</td>
<td>-</td>
<td>Marked and sustained improvement</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A first group of studies compared QOL-scores before and after treatment; control is the same group before treatment. Improvements are statistically and clinically significant, all diagnoses merged. Some diagnoses were especially analyzed: asthma in children, headache, cancer, anxiety and depression after suspension of estrogenic treatment due to breast cancer, allergy, general problems, intestinal disorders, anxiety disorder, depression and skin problems. These are also the most common diagnoses in general practice.

A second group used an external control group, treated with conventional medicine. Results show that homeopathy is as efficient as conventional medicine in general practice. Respiratory problems, chronic NET problems and problems during pregnancy were considered.

A third group used QOL-score during a RCT. In vertigo, homeopathy was as efficient as conventional medicine, but in a study on asthma, initial QOL was so high, that no significant difference could be found after treatment.

Studies about treatment cost-efficiency are mostly requested by authorities. Here also a evidence level IIIa was obtained for all analysed aspects. The reason for this interest is multiple. The cost of the conventional medicine is more and more a problem for certain patients. The survival of social security systems is threatened by these enormous costs.

Available data (15 studies – 9,932 patients) show that reduction of the total costs is possible while maintaining global efficacy when using homeopathy. (Table 4)

### Table 4. Cost-efficiency of homeopathic treatment

<table>
<thead>
<tr>
<th>Condition/Study</th>
<th>N</th>
<th>Design Economic Survey</th>
<th>Test group</th>
<th>Control group</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker-Witt, et al [67] Different chronic conditions</td>
<td>493</td>
<td>Prospective, comparative cohort.</td>
<td>homeopathy; patients could opt for concomitant conventional therapy</td>
<td>patients could opt for conventional therapy</td>
<td>Patients seeking homeopathic treatment had a better outcome overall compared to patients on conventional treatment.</td>
</tr>
<tr>
<td>Chaufferrin [68]</td>
<td></td>
<td>Compilation of nationally available data (secondary sources)</td>
<td>homeopathy</td>
<td>-</td>
<td>Homeopathic medication prices per unit lower than allopathic (number of prescriptions unknown, though). Fewer reimbursements for homeopathic doctors, only 1 % of reimbursement of French national health insurance system</td>
</tr>
<tr>
<td>Frei et al [69] Acute otitis media</td>
<td>230</td>
<td>Prospective, uncontrolled interventional</td>
<td>homeopathy</td>
<td>-</td>
<td>72% resolved within 12 hours, 28% were given antibiotics. Conventional treatment was 14% more expensive (109 SFR vs. 94,6 SFR)</td>
</tr>
<tr>
<td>Frenkel et al [70] Atopic and allergic disorders</td>
<td>48</td>
<td>Prospective, uncontrolled interventional</td>
<td>homeopathy primarily + conventional treatment</td>
<td>-</td>
<td>Before intervention on average 3.1 different conventional drugs/patient after 1.6 (p=0.001). Before intervention 31 used conventional drugs (costs on average $40) after intervention 35 (costs on average $16).</td>
</tr>
<tr>
<td>Study</td>
<td>Conditions</td>
<td>Study Design</td>
<td>Treatment</td>
<td>Control</td>
<td>Findings</td>
</tr>
<tr>
<td>-------</td>
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</tr>
<tr>
<td>Güthlin et al [53]</td>
<td>Different chronic conditions</td>
<td>Prospective, uncontrolled observational</td>
<td>homeopathy</td>
<td>-</td>
<td>Significant changes in quality of life, less sick leave.</td>
</tr>
<tr>
<td>Van Haselen et al [71]</td>
<td>Rheumatoid arthritis</td>
<td>Retrospective (n=89) acupuncture (n=4)</td>
<td>homeopathy</td>
<td>-</td>
<td>32% reduced conventional drugs. Total costs for 89 patients was 7,129 GBP (including medication, staff time and diagnostic procedures – 29% of costs for consultation, 22% for conventional drugs)</td>
</tr>
<tr>
<td>Jain [72]</td>
<td>Reduced costs by homeopathic prescription</td>
<td>Prospective uncontrolled observational</td>
<td>homeopathy</td>
<td>-</td>
<td>Savings by homeopathic treatment calculated by deducting costs for homeopathic medication from conventional medication (hypothetical) for same diagnosis and same duration amounted to 60.40 Pound Sterling</td>
</tr>
<tr>
<td>Rossi et al [73]</td>
<td>Respiratory diseases</td>
<td>Retrospective observational</td>
<td>homeopathy</td>
<td>conventional</td>
<td>Reduction in use of conventional remedies, 40% costs saved</td>
</tr>
<tr>
<td>Schafer et al [74]</td>
<td>Allergic disorders</td>
<td>Population-based nested case control</td>
<td>alternative medicine</td>
<td>no alternative medicine</td>
<td>26.5% used CAM – patients were significantly younger and better educated. CAM mostly provided by MDs, average costs for single and entire treatment of 4 and 205 euro. CAM users scored efficacy of conventional therapy lower than non user (p&lt;0.001)</td>
</tr>
<tr>
<td>Sevar [75]</td>
<td>All conditions</td>
<td>Prospective cohort</td>
<td>homeopathy</td>
<td>-</td>
<td>Conventional drug saving of £39.90/patient/year</td>
</tr>
<tr>
<td>Taïeb et al [76]</td>
<td>Chronic allergic rhinitis</td>
<td>Prospective, comparative cohort</td>
<td>homeopathy (H)</td>
<td>conventional (C)</td>
<td>At 3 months SF-12 score on physical dimension H 51.8; C 47.9 (p&lt;0.05). Lowering of cost of care for patients from 45.74€ for C to 27€ for H; for social security system 50% for patients using H.</td>
</tr>
<tr>
<td>Trichard et al [77]</td>
<td>Anxiety disorders</td>
<td>Prospective, comparative cohort</td>
<td>homeopathy</td>
<td>conventional</td>
<td>Homeopathy produced equivalent result but less overall costs reimbursed by national health system</td>
</tr>
<tr>
<td>Trichard et al [78]</td>
<td>Acute rhinopharyngitis</td>
<td>Prospective, comparative cohort</td>
<td>homeopathy</td>
<td>conventional (antibiotics)</td>
<td>Comparable overall costs, but less sick leave in the homeopathic group</td>
</tr>
</tbody>
</table>
Once again, a first group of studies compares the same cohort of patients before and after the study. The control group is the group itself before treatment. Financial savings with homeopathy are statistically and clinically significant for all diagnoses merged. Some diagnoses are especially analyzed, such as otitis media, atopic eczema and allergy, rheumatoid arthritis and anxiety disorders.

A second group uses an external control group using conventional treatment. The results of these studies confirm that homeopathic treatment in general practice allows savings under all conditions. Some data were especially analyzed, such as seasonal allergic rhinitis, asthma, atopic eczema, food related allergy, chronic allergic rhinitis, anxiety disorders and acute rhinopharyngitis.

**Internal Evidence Heuristic**

Homeopathy acts following the principle of similarity: symptoms are treated with a medicine able to cause similar symptoms in a healthy person. This principle must be observed in clinical and basic studies.

**Pure experiments or ‘provings’**

In order to know the effects of homeopathic medicines, experiments are conducted on healthy individuals. This procedure was initiated by S. Hahnemann more than two centuries ago and has never stopped since. In our days, provings are standardized and performed as a rule with a placebo control [82].

Therefore, the homeopathic materia medica has some level of evidence, and the higher the level of evidence, the higher the probability that the remedy will heal the patient. On the other hand, the more “significant” symptoms the patient has in common with the medicine, the more remarkable and complete will be the effect of the latter. The analysis of published provings indicates evidence level IIb [83].

At the 63rd World Congress of LMHI, 2008, a number of provings was presented. Provings, methods and results are described in Table 5.

**Clinical verification of homeopathic symptoms**

Symptoms obtained through pure experimentation must be confirmed by clinical results. Traditionally, experts in homeopathy were considered references for clinical verification? This corresponds to evidence level IV. Expert advice is very common in medicine. The “ideal value” of cholesterol, e.g. corresponds to this same level of evidence.

Two statistical techniques may be applied to retrospective analysis:

1. To consider exclusively indisputable results of homeopathic prescriptions, i.e. failures or spectacularly positive results. Analysis involves searching for a possible link between outcome and the symptoms of the patient selected for the choice of the remedy. This method is very close to the traditional analysis by experts. Results establish a strong connection between the results of pure experimentation and clinical efficacy of the prescription [95]. At the end of the process, a table of characteristic symptoms (or groups of symptoms) composing the characteristic picture of the homeopathic medicine may be established and verified [96].

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Methodology</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichard et al [79]</td>
<td>5,549</td>
<td>Cross-sectional descriptive survey</td>
<td>Homeopathy</td>
<td>-</td>
<td>Only costs for medication included – average overall cost 6.78€ of which 3.78€ were reimbursed</td>
</tr>
<tr>
<td>Wassenhoven et al [80]</td>
<td>782</td>
<td>Observational unselected; comparison to nationally available data (secondary sources)</td>
<td>Homeopathy</td>
<td>-</td>
<td>Following homeopathic treatment, significant reduction in consultations to other specialists and generalists; cost of treatment €370 to €287. The largest cost savings made by the patients with the worst ratings of their physical condition prior to homeopathic treatment</td>
</tr>
<tr>
<td>Witt et al [81]</td>
<td>135</td>
<td>Prospective, comparative cohort</td>
<td>Homeopathy</td>
<td>Conventional</td>
<td>Comparable efficacy, less costs in homeopathic group</td>
</tr>
</tbody>
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</tr>
</tbody>
</table>
2. To apply Bayes’ theorem to the same clinical database. All values are expressed as prevalence and compared to the remainder of the population (Likelihood ratio or probability factor as the link between a medicine’s symptom and the observed clinical results). This method may be applied in both retrospective [69] and prospective [70] designs. These statistical treatments allow to attain evidence level IIIb. Clinical verification of homeopathic symptoms represents internal validation of the principles of homeopathy and its results will be able to be used to improve daily practice in the near future. A description of the latest reports on clinical verification is presented in Table 6.

<table>
<thead>
<tr>
<th>Remedy</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogenium peroxidatum [84]</td>
<td>Double-blind, randomized,</td>
<td>16 provers presented several symptoms clinically verified in humans and animals.</td>
</tr>
<tr>
<td>Lactroductus mactans tredecimguttatus [85]</td>
<td>Open</td>
<td>8 provers manifested groups of symptoms clinically verifies</td>
</tr>
<tr>
<td>Potentilla anserine [86]</td>
<td>Multi-centric, prospective,</td>
<td>10 provers manifested 27 groups of symptoms</td>
</tr>
<tr>
<td></td>
<td>double blind.</td>
<td></td>
</tr>
<tr>
<td>Neptunium muriaticum [87]</td>
<td>Placebo-controlled</td>
<td>19 provers manifested 315 symptoms distributed into 12 groups.</td>
</tr>
<tr>
<td>Helleborus niger [88]</td>
<td>Third confirmation, multi-</td>
<td>4 groups of symptoms are regularly recorded.</td>
</tr>
<tr>
<td></td>
<td>centric, international.</td>
<td></td>
</tr>
<tr>
<td>Sutherlandia frutescens [89]</td>
<td>Double-blind, placebo-</td>
<td>24 provers manifested 15 symptoms correlated to the traditional use of the pant.</td>
</tr>
<tr>
<td></td>
<td>controlled.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>controlled.</td>
<td></td>
</tr>
<tr>
<td>Lobelia cardinalis [91]</td>
<td>Open design</td>
<td>7 provers revealed 32 symptoms</td>
</tr>
<tr>
<td>Gallium aparine [92]</td>
<td>Open design</td>
<td>8 provers manifested 18 groups of symptoms</td>
</tr>
<tr>
<td>Ytterbium nitricum [93]</td>
<td>Open design</td>
<td>13 provers manifested 32 symptoms</td>
</tr>
<tr>
<td>Hecla lava [94]</td>
<td>Multi-centric, international</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Provings presented at 63rd World Congress of LMHI

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of subjects</th>
<th>of Design</th>
<th>Number of symptoms</th>
<th>Number of remedies</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Wassenhoven [95]</td>
<td>2148</td>
<td>LR R</td>
<td>&gt;230</td>
<td>100</td>
<td>Symptoms; similarity; globality</td>
</tr>
<tr>
<td>CCRH [96]</td>
<td>3032</td>
<td>TM</td>
<td>?</td>
<td>1</td>
<td>Symptoms</td>
</tr>
<tr>
<td>Rutten et al [99]</td>
<td>4094</td>
<td>LR P</td>
<td>6</td>
<td>75</td>
<td>Similarity</td>
</tr>
<tr>
<td>Araújo [100]</td>
<td>5</td>
<td>TM</td>
<td>?</td>
<td>1</td>
<td>16 groups of symptoms; Similarity (constitution)</td>
</tr>
<tr>
<td>Gnaiger et al [101]</td>
<td>25</td>
<td>TM</td>
<td>?</td>
<td>1</td>
<td>6 groups of symptoms; Similarity</td>
</tr>
</tbody>
</table>

Table 6. Latest reports on clinical verification of homeopathic symptoms
Homeopathic Medicines have specific activity

In the present time, the proof for the action of high dilutions has reached evidence level IIa, in some instances, level I. Several university-based researchers had surveyed literature on this subject, upon European Committee for Homeopathy request [108]. New references are added for 2005-2008.

The least expensive model, easy to perform and to reproduce, probably is "acetylcholine-induced contraction of rat ileum". This is a validated experimental model [109], initially applied to homeopathic preparations by Cristea [110]. SüB, from the Institute of Pharmacy of Leipzig university used this model to test the transition of homeopathic Atropinum sulphuricum 60D from the original liquid form to tablets [111]. Monohydrate α-lactose tablets impregnated with high dilution of Atropinum showed systematic efficacy as opposed to anhydrous α-lactose tablets. This means that the quality of tablets can be tested before pharmaceutical commercialization (constant reproducibility). This simple model shows beyond any doubt that high diluted homeopathic medicines are active.

It took some time before another experimental model could be accepted by the scientific community. Initial development was in 1991, but only in 2004 results were accepted for publication by Inflammation Research, a peer-reviewed scientific journal [112]. Roberfroid and Cumps, from the Department of Pharmacy of Louvain university, led a multi-centric European survey involving 4 laboratories, showing the clear inhibition of human
basophils degranulation by high dilutions of histamine [113,114].

There is research in high dilutions since the 1950s, but the number and quality of publications has increased in the last decade. Articles showing the efficacy of high dilutions were published in peer-reviewed journals [115-117] as well as their efficacy on pharmacological models [118-127].

The oldest model used, subject of several international publications is the toxicological (arsenic, phosphor, mercury, cadmium, cisplatin, glutamate, sulphate, copper sulphate, etc.) This model is still in use and is currently the subject of cooperative research between the universities of Bern and Bologna on the effect of homeopathic preparations of arsenic trioxide in plants. This research group, under the coordination of Dr. Lucietta Betti, has recently published the results of some experiments [128-132].

A systematic review of in vitro evidence for high dilutions has been published in 2007 [133]. Conclusions state that experiments with high methodological standards were able to demonstrate effects. No positive result was as stable as to be reproduced by all researchers; among those that were replicated by independent researchers: the effect of mercury bichloride on hydrolases and, especially, of histamine on basophils degranulation, as mentioned above.

Several audits of these publications are available and justify evidence level I [133, 135, 136]. 75 publications were evaluated by a German team, 105 articles were analyzed in a second audit examining the protective effect against toxics (isopathic model). 70% of the articles are of indisputable quality and show the positive effect of the homeopathic preparations employed. In a third audit, 76 of the 162 analyzed studies were rated as “highest quality”, effects are significant and reproducible.

New results, since 2005, include Alecu et al. [136,137], dos Santos et al. [138] and those presented at 63rd World Congress of LMHI, 2008 [139,140].

### Homeopathy in veterinary practive

Advantages of the results of veterinary practice are several: environment where animals live may be considered stable and very similar for all animals considered; studies on large animal cohorts are easier to conduct than in humans; double-blind designs are easier to achieve.

The number of surveys is still small, but for two clinical diagnoses sufficient studies have been published and reproduced, so that evidence level I might be attained in the near future. These two areas are infertility in cows [141-143] and mastitis in cows [144,145]. Both problems have important consequences for public health as antibiotics (usually prescribed for mastitis) enter the food chain and milk, therefore, must be destroyed, with the corresponding economic consequences. Moreover, homeopathic treatment is the only one authorized in Europe in organic breeding.

Other results come from another farming area: chickens are very sensitive to stress, and pick each other, which results in important production losses [146]. The same is observed in turkeys, very sensitive to hematomas caused during transportation. This problem can be reduced 30% with homeopathic treatment. Regulation of sexual hormones in sows is also significant [147], homeopathy can offer a solution without risks for consumers.

More recent works have been reported between 2006-2008 [148-162].

### Individualized homeopathic research

When the individualizing approach of homeopathy is taken into account, the scientific framework is much broader than the expected. Homeopathic physicians are mostly focused on research on individualization, similarity and globality. This does not exclude research centered on specific diagnostic categories, and many indications are reaching evidence level IIIb. A few examples presented at 63rd World Congress of LMHI, 2008 are described in Table 7.

<table>
<thead>
<tr>
<th>Area</th>
<th>Diagnostic category</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy</td>
<td>Asthma</td>
<td>Flitchev et al.[163]; Kekata et al.[164]</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>Jurj [165]; Popowski[166]</td>
<td></td>
</tr>
<tr>
<td>Summer benign lucitis</td>
<td>Marijnen et al.[167]</td>
<td></td>
</tr>
</tbody>
</table>

### Table 7. Clinical research on specific diagnostic categories, LMHI, 2008.
<table>
<thead>
<tr>
<th>Dentistry</th>
<th>Extraction of third molar</th>
<th>Camacho et al.[168]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodontal disease</td>
<td></td>
<td>Clercq et al.[169]</td>
</tr>
<tr>
<td>Temporomandibular disorders</td>
<td></td>
<td>Tiba et al.[170]</td>
</tr>
<tr>
<td>Gynecology</td>
<td>Cervical dystocia</td>
<td>Chiche[171]</td>
</tr>
<tr>
<td></td>
<td>Flashes</td>
<td>Dungler et al.[172]; Masson et al.[173]</td>
</tr>
<tr>
<td></td>
<td>Recurrent vaginal mycoses</td>
<td>Honneger et al.[174]</td>
</tr>
<tr>
<td></td>
<td>Prolactinoma</td>
<td>Roca [175]</td>
</tr>
<tr>
<td></td>
<td>Uterine fibroid and ovarian cyst</td>
<td>Shangloo [176]</td>
</tr>
<tr>
<td></td>
<td>Breast lumps</td>
<td>Shukla [177]</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>Hypothyroidism</td>
<td>Grelle [178]</td>
</tr>
<tr>
<td></td>
<td>Chronic thyroiditis</td>
<td>Baroli [179]</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>Bronchiolitis</td>
<td>Arjoun et al. [180]</td>
</tr>
<tr>
<td></td>
<td>Chickenpox</td>
<td>Bahloul et al. [181]</td>
</tr>
<tr>
<td></td>
<td>Eye irritation</td>
<td>Fayard [182]</td>
</tr>
<tr>
<td></td>
<td>Long lasting fever of febrile origin</td>
<td>Rusev et al. [183]</td>
</tr>
<tr>
<td>Neurology</td>
<td>Muscular dystrophy</td>
<td>Bolognani et al.[184]</td>
</tr>
<tr>
<td></td>
<td>Progressive spinal amiotrophy</td>
<td>Bolognani et al. [185]</td>
</tr>
<tr>
<td></td>
<td>Attention deficit hyperactivity disorder</td>
<td>Bolognani et al. [186]; Mateescu [187]</td>
</tr>
<tr>
<td></td>
<td>Infantile cerebral palsy</td>
<td>Damaceno et al. [188]; Serpa et al.[189]</td>
</tr>
<tr>
<td></td>
<td>Migraine</td>
<td>Kivellos et al.[190]</td>
</tr>
<tr>
<td></td>
<td>Choreoathetosis</td>
<td>Martins et al.[191]</td>
</tr>
<tr>
<td></td>
<td>Parkinson’s disease</td>
<td>Mendes et al.[192]</td>
</tr>
<tr>
<td></td>
<td>Spastic conditions</td>
<td>Teixeira et al.[193]</td>
</tr>
<tr>
<td></td>
<td>Multiple sclerosis</td>
<td>Roberfroid et al.[194]</td>
</tr>
<tr>
<td>Oncology</td>
<td>Veterinary</td>
<td>Pevenage [195]</td>
</tr>
<tr>
<td>Toxicology</td>
<td>Arsenic poisoning</td>
<td>Khuda-Bukhsh [196]</td>
</tr>
</tbody>
</table>
Conclusions

Consideration of patients’ rights means that patients must be informed of all possible therapies that may improve his/her health, including homeopathy, even when hospitalized.

The evidence level of homeopathy in several conditions is sufficient to ground its use in the scientific framework of general medical practice. Basic and veterinary research confirm findings in humans. Internal evidence validated and confirms the effects of homeopathic medicines.

University research on homeopathy must be encouraged and supported by public health authorities.

Data presented in this review are indisputable. For this reason, homeopathy must be accepted within the scientific framework of medicine, especially in general medical practice.

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