Homeopathy (2011) 100, 275–287

doi:10.1016/j.homp.2011.05.008, available online at http://www.sciencedirect.com

RESEARCH REVIEW

Use of homeopathic preparations in experimental studies with abiotically stressed plants

Tim Jäger[1,2,*], Claudia Scherr[3], Devika Shah[3], Vera Majewsky[1,4], Lucietta Betti[5], Grazia Trebbi[5], Leoni Bonamin[6], Ana Paula Simões-Wüst[7], Ursula Wolf[1], Meinhard Simon[8], Peter Heusser[9] and Stephan Baumgartner[1,3,9]

[1]*Institute of Complementary Medicine KIKOM, University of Bern, Switzerland*
[2]*Research Institute of Organic Agriculture, Frick, Switzerland*
[3]*Society for Cancer Research, Hiscia Institute, Arlesheim, Switzerland*
[4]*Clinic for Animal Reproduction, Freie Universität Berlin, Germany*
[5]*Department of Agro-Environmental Science and Technology, University of Bologna, Italy*
[6]*Laboratory of Cell and Molecular Biology, University Paulista, São Paulo, Brazil*
[7]*Paracelsus Hospital Richterswil, Switzerland*
[8]*Institute for Chemistry and Biology of the Marine Environment, University of Oldenburg, Germany*
[9]*Center for Integrative Medicine, University of Witten/Herdecke, Germany*

Background: **Experimental research on the effects of homeopathic treatments on impaired plants was last reviewed in 1990.**
Objectives: **To compile a systematic review of the existing literature on basic research in homeopathy with abiotically stressed plants using predefined criteria.**
Methods: **The literature search was carried out on publications that reported experiments on homeopathy using abiotically stressed whole plants, seeds, plant parts and cells from 1920 to 2010. Outcomes had to be measured by established procedures and statistically evaluated. Using of a Manuscript Information Score (MIS) we identified those publications that provided sufficient information for proper interpretation (MIS ≥ 5). A further evaluation was based on the use of adequate controls to investigate specific effects of homeopathic preparations and on the use of systematic negative control experiments.**
Results: **A total of 34 publications with abiotically stressed plants was identified, published between 1965 and 2010. The 34 publications described a total of 37 experimental studies. Twenty-two studies included statistics, 13 had a MIS ≥ 5, 8 were identified with adequate controls and 4 with negative control experiments. Significant and reproducible effects with decimal and centesimal potencies were found, including dilution levels beyond Avogadro's number. One experimental model was independently assessed by another research team and yielded inverted results compared to the original trial.**
Conclusions: **Abiotically stressed plant models seem to be a useful approach to investigate homeopathic basic research questions, but more experimentation and especially more independent replication trials are needed. Systematic negative control experiments should be implemented on a routine basis to exclude false-positive results.** *Homeopathy* (2011) **100**, 275–287.

Keywords: Review; Basic research; Homeopathy; Potentisation; Impaired plants; Noxa

Introduction

The question of the most adequate test systems in homeopathic basic research is still open. There are three major fields in homeopathic basic research with plants: experimental models with healthy plants, plants infected by viruses or

*Correspondence: Tim Jäger, Institute of Complementary Medicine KIKOM, University of Bern, Bern, Switzerland.
E-mail: tim.jaeger@kikom.ch
Received 4 January 2011; revised 20 April 2011; accepted 11 May 2011

bacteria (phytopathological models), and plants impaired by abiotic stress. A recent review of studies with healthy plants was published by Majewsky *et al.*[1] Betti *et al.*[2] published a corresponding review of phytopathological models. The research field with plants impaired by abiotical stress was last reviewed by Scofield[3] and Majerus.[4] Both reviews were of qualitative and narrative nature and did not use predefined criteria to assess study quality. Similar to Majewsky *et al.*[1] and Betti *et al.*[2] we used a predefined Manuscript Information Score (MIS) to include only publications that provided enough information to be interpreted properly. Furthermore, we focused on studies which investigated specific effects of homeopathic remedies, i.e. effects related to the substance potentised, by using adequate controls (succussed or potentised potentisation medium, see below). Thus the aim of this systematic review is an evaluation of the current state of research by focusing on investigations, which used advanced experimental methods and detailed descriptions, also to support development of future experimental designs.

Methods

The major part of the literature was gathered by searching basic research articles by year, mostly by checking bibliographies of basic research articles, by manually searching in scientific journals, and by information from colleagues. Additionally, the HomBRex Database[5] (maintained by the Karl und Veronica Carstens-Stiftung, Essen, Germany) and standard online literature databases (e.g. MEDLINE® or PubMed®) were used with several combined search terms like 'plants + homeopathy', 'plants + potentised' etc.

Publications reporting experiments that investigated effects of homeopathic medicines on impaired plants, which had been stressed abiotically on purpose, were relevant for this systematic review, i.e. plants had been stressed with physical or chemical interventions, excluding biological agents. The review included experiments with whole plants, parts of plants, plant cells and plant seeds. Studies with bacteria- or virus-infected plants or healthy plants were excluded. Outcome parameters had to be measured by established procedures, e.g. length, weight, leaf area or secondary metabolites. Unconventional methods such as Gas Discharge Visualisation as measurement techniques were not considered in this review. English, French, German, Italian and Portuguese publications from 1920 to 2010 were analysed using the reviewing procedure described by Majewsky *et al.*,[1] which comprises several steps: statistics, a MIS, the question of adequate controls (in Majewsky *et al.*[1] and Betti *et al.*[2] called 'Study Methods Evaluation Procedure' (SMEP)) and furthermore a sub-selection of studies with negative control experiments. Publications reporting on more than one experiment were subdivided in studies. This review complements the reviews of Majewsky *et al.*[1] and Betti *et al.*[2] that included either healthy plants or phytopathological models and field trials.

Statistics: Publications that did not use a statistical evaluation of the results (at minimum descriptive statistics: mean/median, number *n* and standard deviation or standard error) were excluded.

MIS: The MIS was used to include only publications with sufficient information to be interpreted properly (Table 1). In the MIS, a maximum of 10 points were given for 5 category groups. A minimum of 5 points was necessary for a study to be included in the review.

Adequate controls: We aimed at identifying the studies, which used adequate controls to investigate specific effects of homeopathic preparations. We distinguished six different types of controls: Succussed potentisation medium (i.e. succussed only once), potentised potentisation medium (e.g. water or water ethanol mixture diluted and succussed in the same way as the potentised test substances), unsuccussed potentisation medium, diluted test substance, positive control, no treatment. To be included in the further reviewing process, samples with succussed or potentised potentisation medium had to be part of the experiment. Use of the other four types of controls may generate false-positive results when it comes to identifying treatment effects that are due to specific properties of the homeopathic substance potentised.[6]

Table 1 Assessment of the manuscript information content by the MIS. A maximum of 10 points were given for 5 category groups. A minimum of 5 points was necessary for the study to be included in the review

MIS	*Fully described*	*Partly described*	*Not mentioned*
Score	*2 Points*	*1 Points*	*0 Points*
Experimental set-up	Detailed information is given: way of treatment of plants, growth period, time of measurements, etc.	Only some details are described or few information about the set-up is given	No information is given about the experimental set-up
Materials	All materials used in the experiment are described with trade name, etc.	Some materials used in the experiments are described or mentioned	No information is given about the materials used
Measuring instruments	Measuring instruments are described in detail, operation mode, trade name, type, etc.	Measuring instruments are only mentioned	There is no information about measuring instruments in the paper
Potentisation	Potentisation technique, date and time of potentisation and potentisation medium are described in detail	Some information about potentisation technique is given	No information about potentisation, only the potentised test substance is mentioned
Controls	Detailed information, e.g.: sterile distilled water from the same batch of distilled water	Some information about the sort of control is given: e.g.: water control	Controls are not mentioned or not done

Systematic negative control experiments: Finally we selected studies with systematic negative control experiments. These are experiments with the identical set-up as in potency experiments, but using only one control substance for all samples (e.g. distilled water) to verify the stability of the chosen experimental set-up.

Two reviewers independently evaluated all publications. Any differences in assessment were resolved by discussion.

Results

A total of 34 publications were identified[7–40] (Figure 1). Auquière *et al.*[8] described three different experiments, Boiron and Marin[15] two different experiments in one publication. These publications were subdivided into three and two 'studies', respectively. Thus a total number of 37 studies form the basis of this review.

The first publication using impaired plants was released by Boiron[12], whilst the latest was published by Jäger *et al.*[30] Out of the 37 experimental studies described in the 34 publications, 15 either did not use a statistical analysis to evaluate the results or did not mention the statistics in the publication.[8,14–18,25,28,29,33–37] Twenty-two studies with statistics (published from 1965 to 2010) remained within the reviewing procedure.[7–13,19–24,26,27,30–32,38–40] Thirteen of these 22 studies contained sufficient information for a detailed interpretation, i.e. these studies achieved 5 or more points in the MIS (Table 2). Five of these 13 studies mentioned unsuccussed potentisation medium as control, but evaluated the results by comparison with other potency levels of the same test substance.[7–10,31] Eight studies included succussed or potentised controls and therefore adequate controls to identify specific effects of the tested homeopathic remedies[8,11,20–22,30,32,40] (Tables 3a, b). In 4 of these 8 studies systematic negative control experiments were conducted.[11,20,30,32]

Studies with sufficient information

Thirteen studies contained sufficient information for a detailed interpretation, i.e. these studies achieved 5 or more points in the MIS (Table 2). In the following, we give an overview about the key features of the experiments performed.

Plants: The most frequently used experimental plant model was the wheat seedling model. The influence of homeopathic potencies on the germination and the growth of seedlings were investigated in 10 of 13 studies with wheat seeds.[7,8,10,11,20–22,31,32] One study each was conducted with cress seeds,[40] with duckweed[30] and with white mustard.[9]

Noxa: In 6 studies with wheat seeds the noxa was arsenic trioxide (As_2O_3).[10,11,20–22,32] In one study with wheat seeds, three stressors were applied: sodium chloride (NaCl), copper chloride ($CuCl_2$), potassium dichromate ($K_2Cr_2O_7$).[31] Lysine ($C_6H_{14}N_2O_2$)[8] and copper sulphate ($CuSO_4$)[7,9] were used in two studies each. In the model with cress seeds sodium chloride (NaCl)[40] was used, and duckweeds were stressed with arsenic(V) ($AsHNa_2O_4 \times 7H_2O$).[30]

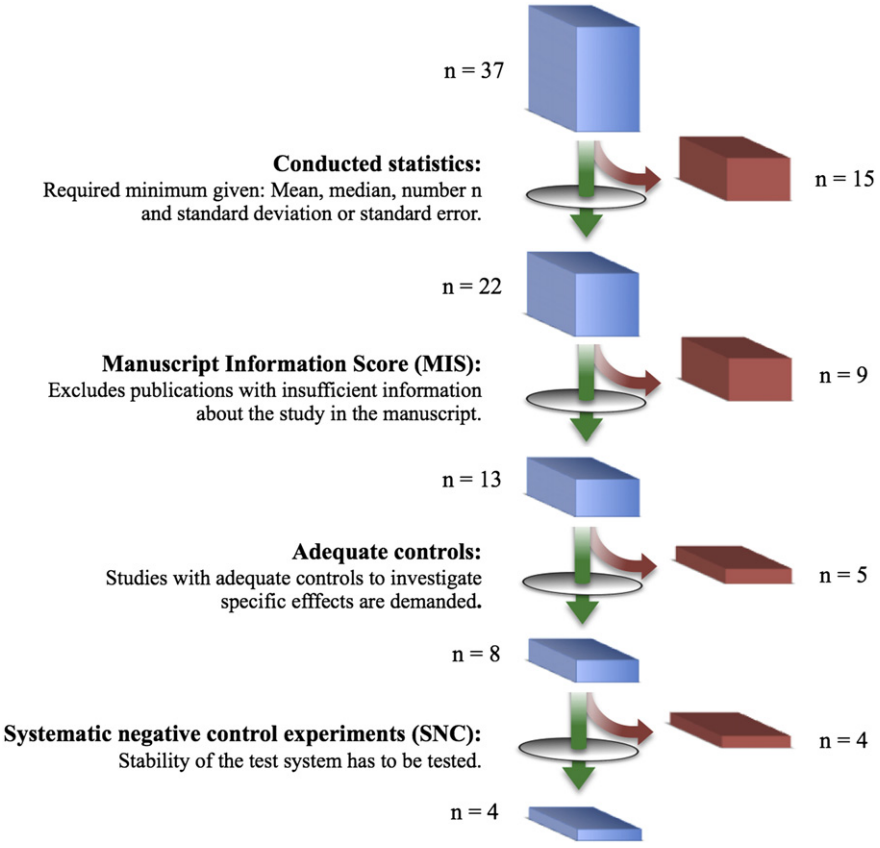

Figure 1 Flow diagram of the review. A total of 34 publications described a total of 37 experimental studies that were included in the review process.

Table 2 All 13 studies with MIS ≥ 5. One publication[8] was subdivided in multiple studies, because several experiments were described in one publication

Author	*Plant*	*Noxa*	*Potentised test substances*	*Tested potency levels*	*Effective potency levels**	*Controls*[†]	*Independent treatment lots*[‡]*/ experiments [n]*	*Methods*[§]	*Control of system stability*
Auquière and Moens[7]	Wheat (*Triticum aestivum* L.), cv. 'Hardi'	Copper sulphate ($CuSO_4$)	Copper sulphate ($CuSO_4$)	5c	5c	U	?/25	Not reported	Not mentioned
Auquière *et al.*[9]	White mustard (*Sinapis alba* L.), cv. 'Dialba'	Copper sulphate ($CuSO_4$)	Copper sulphate ($CuSO_4$)	14x	14x	U	2/40	Not reported	Not mentioned
Auquière *et al.* I[8]	Wheat (*Triticum aestivum* L.), cv. 'Tallent'	Lysine ($C_6H_{14}N_2O_2$)	Lysine ($C_6H_{14}N_2O_2$)	8c, 16c	8c, 16c	U	?/20	r	Not mentioned
Auquière *et al.* II[8]	Wheat (*Triticum aestivum* L.), cv. 'Tallent'	Lysine ($C_6H_{14}N_2O_2$)	Lysine ($C_6H_{14}N_2O_2$)	8c	–	U; P	?/5	r	Not mentioned
Betti *et al.*[10]	Wheat (*Triticum aestivum* L.[¶]), cv. 'MEC'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	45x	45x	U	1/1	b; r (reported in Brizzi *et al.*[21])	Not mentioned
Binder *et al.*[11]	Wheat (*Triticum aestivum* L.), cv. 'Pandas' and 'MEC'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	45x	45x	U; P	8/8	b; r	Partially done
Brizzi *et al.*[22]	Wheat (*Triticum aestivum* L.[¶]), cv. 'MEC'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	30x, 40x, 42x, 45x	30x, 40x, 42x, 45x	U; P; D	?/?	b	Not mentioned
Brizzi *et al.*[21]	Wheat (*Triticum aestivum* L.), cv. 'MEC'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	5x, 15x, 25x, 35x, 45x	45x	U; P; D	1/9	b; r	Not mentioned
Brizzi *et al.*[20]	Wheat (*Triticum aestivum* L.), cv. 'Pandas'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	45x	45x	U; P	1/16	b; r	Partially done
Jäger *et al.*[30]	Duckweed (*Lemna gibba* L.)	Arsenic(V) ($AsHNa_2O_4 \times 7H_2O$)	Arsenic trioxide (As_2O_3), nosode, gibberellic acid	17x, 18x, 21x, 22x, 23x, 24x, 28x, 30x, 33x	18x, 21x, 22x, 23x, 33x	U; S	15/15	b; r	Done
Kovac *et al.*[31]	Winter wheat, cv. 'Innwalder'	Sodium chloride (NaCl), Copper chloride ($CuCl_2$), Potassium dichromate ($K_2Cr_2O_7$)	Sodium chloride (NaCl), Copper chloride ($CuCl_2$), Potassium dichromate ($K_2Cr_2O_7$)	10x−30x	Not reported	U	6/6	Not blinded	Not mentioned
Lahnstein *et al.*[32]	Wheat (*Triticum aestivum* L.), cv. 'Pandas'	Arsenic trioxide (As_2O_3)	Arsenic trioxide (As_2O_3)	45x	45x[‖]	U; P	9/9	b; r	Partially done
Tighe[40]	Cress (*Lepidium sativum* L.)	Sodium chloride (NaCl)	Sodium chloride (NaCl)	12c, 18c, 24c	12c, 24c	U; P	1/3	b; r	Not mentioned

* Effective potency levels: list of all potency levels which were significantly effective in any of the measured parameters.
† Controls: U = Unsuccussed potentisation medium; S = Successed potentisation medium; P = Potentised potentisation medium; D = Diluted test substance.
‡ Independent Treatment Lots = number of independent potency treatment production lots.
§ Methods: b = Blinding; r = Randomisation.
‖ Significant only in meta-analysis with all experiments of Binder *et al.*[11]
¶ In original publications *Triticum durum* L.

Table 3a All 8 studies (with MIS ≥ 5) using adequate controls to investigate specific effects of homeopathic preparations

Author	*Plant*	*Noxa*	*Treatment with noxa**	*Treatment with test substances**	*Measured parameters*	*Rate of impairment†*	*Test substance*
Auquière *et al.* II[8]	Wheat (*Triticum aestivum* L.), cv. 'Tallent'	Lysine ($C_6H_{14}N_2O_2$)	B: impairment of germinating seedlings during 48 h of precultivation in 1% lysine, followed by rinsing in distilled water twice	D: Watering after 48 h of precultivation	Shoot length, fresh weight, dry weight	Length: −(30–50)%	Lysine ($C_6H_{14}N_2O_2$)
Binder *et al.*[11]	Wheat (*Triticum aestivum* L.), cv. 'Pandas' and 'MEC'	Arsenic trioxide (As_2O_3)	B: impairment of non-germinated seeds for 30 min (0.1%, 0.12% As_2O_3), followed by rinsing in tap water for 60 min	D: Watering at the beginning of the experiment	Shoot length	Length: −15%	Arsenic trioxide (As_2O_3)
Brizzi *et al.*[22]	Wheat (*Triticum aestivum* L.‡), cv. 'MEC'	Arsenic trioxide (As_2O_3)	B: impairment of non-germinated seeds for 30 min (0.1% As_2O_3), followed by rinsing in tap water for 60 min	D: Watering at the beginning of the experiment	Germination rate	Germination rate: −14% (non-stressed: 5%)	Arsenic trioxide (As_2O_3)
Brizzi *et al.*[21]	Wheat (*Triticum aestivum* L.), cv. 'MEC'	Arsenic trioxide (As_2O_3)	B: impairment of non-germinated seeds for 30 min (0.1% As_2O_3), followed by rinsing in tap water for 60 min	D: Watering at the beginning of the experiment	Shoot length	Not mentioned	Arsenic trioxide (As_2O_3)
Brizzi *et al.*[20]	Wheat (*Triticum aestivum* L.), cv. 'Pandas'	Arsenic trioxide (As_2O_3)	B: impairment of non-germinated seeds for 30 min (0.1% As_2O_3), followed by rinsing in tap water for 60 min	D: Watering at the beginning of the experiment	Germination rate	Not mentioned	Arsenic trioxide (As_2O_3)
Jäger *et al.*[30]	Duckweed (*Lemna gibba* L.)	Arsenic(V) ($AsHNa_2O_4 \times 7H_2O$)	B: impairment of growing plants for 48 h (158 mg/l $AsHNa_2O_4 \times 7H_2O$)	D: Watering at the beginning of the experiment	Frond area, frond number	Area-related growth: −56%	Arsenic trioxide (As_2O_3), nosode, gibberellic acid
Lahnstein *et al.*[32]	Wheat (*Triticum aestivum* L.), cv. 'Pandas'	Arsenic trioxide (As_2O_3)	B: impairment of non-germinated seeds for 30 min (0.1%, 0.16% As_2O_3), followed by rinsing in tap water for 60 min	D: Watering at the beginning of the experiment	Germination rate, shoot length	Length: −50%; germination rate: −30%	Arsenic trioxide (As_2O_3)
Tighe[40]	Cress (*Lepidium sativum* L.)	Sodium chloride (NaCl)	B: impairment of non-germinated seeds for 16 h (1% NaCl)	D: Watering at the beginning of the experiment	Germination rate, root and shoot length	Length: −61%	Natrum Mur = sodium chloride (NaCl)

* Treatment: B = Before cultivation; D = During cultivation.
† Rate of impairment: impaired organisms in relation to healthy organism.
‡ In original publications *Triticum durum* L.

Table 3b All 8 studies (with MIS ≥ 5) using adequate controls to investigate specific effects of homeopathic preparations

Author	*Potentisation*[†]	*Tested potency levels*	*Effective potency levels*[§]	*Controls*[‡]	*Statistical tools and tests*	*Independent treatment lots/ experiments [n]*	*Methods*[*]	*Control of system stability*
Auquière *et al.* II[8]	Multiple-vessel method	8c	–	U; P	ANOVA F-tests	?/5	r	Not mentioned
Binder *et al.*[11]	H: multiple-vessel method, 100 ml polyethylene vessels, 70 beats against a firm base	45x	45x	U; P	ANOVA, LSD-test, Levene test, Kolmogorov–Smirnov, chi-square test, Kruskal–Wallis-ANOVA test, Mann–Whitney-U-test	8/8	b; r	Done (not in complete extent)
Brizzi *et al.*[22]	H: 70 vigorous impacts after each dilution stage (between 23x and 45x, freshly made for each experiment)	30x, 40x, 42x, 45x	30x, 40x, 42x, 45x	U; P; D	χ^2-Test, Poisson test, Bonferroni correction, odds ratio	?/?	b; r	Not mentioned
Brizzi *et al.*[21]	M: using a specially designed succussion machine which vertically shakes 100 ml volumes (in polyethylene bottles filled to 90%) at 70 times per min with an oscillation amplitude of 24 cm. Each potency was succussed for 1 min	5x, 15x, 25x, 35x, 45x	45x	U; P; D	Indices of location, dispersion, skewness; parametric statistics (mean, M, standard deviation, SD); quantile-based statistics (median, Md, and mean absolute deviation, MAD); Mann–Whitney two-sample comparison and the Kruskal–Wallis non-parametric analysis of variance for independent samples; Levene test; Siegel–Tukey test; t-test	1/9	b; r	Not mentioned
Brizzi *et al.*[20]	M: using a specially designed succussion machine that vertically shakes 1000 ml volumes (in polyethylene bottles filled to 90% of capacity) at a rate of 70 times per min with an oscillation amplitude of 24 cm; each potency was succussed for 1 min	45x	45x	U; P	Global Poisson test, median, standard deviation, mean absolute deviation from the median, Wilcoxon–Mann–Whitney rank sum test, Bravais–Pearson linear coefficient of correlation	1/16	b; r	Done (not in complete extent)
Jäger *et al.*[30]	H: multiple-vessel method using 500 ml (<6x: 250 ml) Erlenmeyer flasks filled with 350 ml (<6x: 150 ml) fluid. The flasks were agitated once upside-down to generate a vortex. After calming down of the vortex, the flask was shaken a second time producing a chaotic agitation in water. These two steps were repeated ten times	17x, 18x, 21x, 22x, 23x, 24x, 28x, 30x, 33x	18x, 21x, 22x, 23x, 33x	U; S	2-Way analysis of variance F-test, protected Fisher's LSD, Levene's test, quantile–quantile plots	15/15	b; r	Done
Lahnstein *et al.*[32]	H: multiple-vessel method, 100 ml polyethylene vessels, starting from the mother tincture (As_2O_3 1‰ solution), 70 beats against a firm base	45x	45x[‖]	U; P	Standard deviation, ANOVA, LSD-test, chi-square test, Kruskal–Wallis-ANOVA, Mann–Whitney-U-test	9/9	b; r	Done (not in complete extent)

Tighe[40]	H: prepared and supplied by Ainsworth's Homeopathic Pharmacy	12c, 18c, 24c	12c, 24c	U; P	Means, medians, ranges, skew, standard error of skew and standard deviations for variable Length; ANOVA followed up with post-hoc tests, Pearson Chi-square test; Fisher's exact test	1/3	b; r	Not mentioned

* Methods: b = Blinding; r = Randomisation experiments.
† Potentisation: H = Hand succussion; M = Machine succussion.
†† Controls: U = Unsuccussed potentisation medium; S = Succussed potentisation medium; P = Potentised potentisation medium; D = Diluted test substance.
§ Effective potency levels: list of all potency levels which were significant effective in any of the measured parameters.
‖ Significant only in meta-analysis with all experiments of Binder *et al.*[11]

Test substances: Considering the choice of the homeopathic test substances all but one study used an isopathic approach, i.e. the substance that was used to stress the organisms was applied in potentised form as homeopathic preparation. Only Jäger *et al.*[30] tested a *similar* remedy (potencies of arsenic trioxide (As_2O_3) after applying arsenic(V) ($AsHNa_2O_4 \times 7H_2O$) as stressor), and in addition a nosode preparation and potentised gibberellic acid.

Tested potency levels: Decimal potency levels from 5x to 45x and centesimal potency levels from 5c to 24c were tested. In 6 studies 45x was tested among other potency levels,[10,11,20–22,32] in 4 of these solely 45x.[10,11,20,32]

Effective potency levels: Effects were reported with decimal potency levels ranging from 14x to 45x, centesimal potency levels ranged from 5c to 24c.

Controls: In all studies unsuccussed water was used as control. In 5 studies only unsuccussed water was used.[7–10,31] One study used in addition successed water,[30] 7 studies used potentised water in addition.[8,11,20–22,32,40]

Independent treatment lots/experiments: Four of 13 studies comprised only one independent homeopathic treatment production lot meaning that all experiments were conducted with homeopathic preparations from one batch.[10,20,21,40] Five studies used as many treatment lots (production batches) as experiments.[10,11,30–32] In 4 studies the number of independent treatment lots was not clearly identifiable in the manuscript.[7,8,22] In the other studies one treatment lot was used for up to 20 experiments. The number of conducted experiments within a single study ranges from 1 to 40 (Table 2).

Blinding and randomisation: Seven of 13 studies were carried out under blind and randomized conditions.[10,11,20,21,30,32,40] One study was blinded only.[22] In two studies, the samples of the experiments were distributed at random, but the researchers were not blinded to the treatments.[8] Two of the 13 studies did not mention blinding or randomisation[7,9] and one study mentioned only the not blinded conditions[31] (see Table 2).

Systematic negative control experiments: Four studies described systematic negative control experiments to control any disturbing influences from inhomogeneous laboratory conditions (Table 4), three of them partly.

Studies with sufficient information and adequate controls

Eight studies with sufficient information available (MIS $\geq$ 5) had adequate controls to identify specific effects of homeopathic preparations. Seven studies were published in peer-reviewed Journals, one study was compiled as thesis.[40] All studies were randomized, and all but one study[8] were blinded (Table 3b). In these 8 studies, 3 different plants (wheat, cress and duckweed) were used and 5 potentised test substances were investigated (Table 5). In 7 studies impaired seedlings (wheat and cress) were used as test-organisms,[8,11,20–22,32,40] in 1 study impaired water plants (duckweed).[30] In 5 studies the same experimental design was used: wheat seedlings and arsenic trioxide as noxa.[11,20–22,32] In one study wheat seedlings and lysine as noxa were used,[8] in one further study impaired cress seedling

Table 4 All 4 studies with systematic control experiments

Author	*Main experiments*	*Systematic negative control experiments*	*Methods**	*Controls†*
Binder *et al.*[11]	8 Experiments	2 Experiments	b; r	U; P
Brizzi *et al.*[20]	16 Experiments	5 Experiments	b; r	U; P
Jäger *et al.*[30]	3 × 5 Experiments	5 Experiments (analysed with 4 different randomized allocations)	b; r	U; S
Lahnstein *et al.*[32] (meta-analysis)	17 Experiments	5 Experiments	b; r	U; P

* Methods: b = Blinding; r = Randomisation experiments.
† Controls: U = Unsuccussed potentisation medium; S = Succussed potentisation medium; P = Potentised potentisation medium.

and sodium chloride as noxa.[40] In the experimental design with adult plants, intoxicated duckweed and arsenic (V) were used.[30] In all studies plants were intoxicated before beginning of the experiment, with a rate of impairment between 14% and 61% (Table 3a). All plants were watered with homeopathic preparations after intoxication, duckweed continuously floating in homeopathic preparations/nutrient solution (50%/50%) during the experiment. In 4 studies the outcome was germination rate,[20,22,32,40] in 5 studies length of plants[8,11,21,32,40] and in one study each frond (leaf) area and frond number,[30] and fresh and dry weight.[8] In addition to mean values, standard deviation and data distribution shape were also used as outcome measure.

In 7 studies the potentisation was by the multiple-vessel (Hahnemannian) method,[8,11,20–22,30,32] in 2 mechanically[20,21] and in 5 manually.[8,11,22,30,32] In one study a company manufactured the homeopathic preparations and no information was given about the nature of the potentisation process.[40] In one study, potentisation vessels were made of glass,[30] in four studies they were made of polyethylene.[11,20,21,32] In 3 studies it was not mentioned what material was used for the potentisation vessels.[8,22,40] Methods of succussion were similar in 5 studies (70 vigorous impacts after each dilution step).[11,20–22,32] In 3 of these 5 studies succussion was performed manually,[11,22,32] in two cases by a machine.[20,21]

The 4 different noxa-plant models of the studies with sufficient information and adequate controls

Arsenic trioxide wheat seedling model: The wheat (*Triticum durum* L.) seedling model stressed with arsenic trioxide (Figure 2) and treated with the homeopathic preparation arsenic trioxide 45x, is the most frequently investigated model with impaired plants. This isopathic approach was introduced in 1997 by an Italian team. The homeopathic treatment led to an increase in shoot growth after 7 days cultivation *in vitro*, compared to an unpotentised water control.[10]

By measuring the germination rate in another experiment 3 potency levels of arsenic trioxide (40x, 42x, 45x) repeatedly showed a significant stimulation effect compared to potentised controls. The potency level 30x showed contradictory stimulating and inhibiting effects. Even potencies of water yielded significant results compared to unpotentised controls, non-potentised high dilutions of arsenic trioxide never significantly affected the germination rate.[22]

The finding of increased shoot length from 1997 was reproduced in an independent trial, carried out at a different place with a different experimental team 8 years later. In this study, all experiments were conducted with *Triticum aestivum* L. Potencies of arsenic trioxide (45x) and water (45x) induced an increase in growth and/or a decrease of variability. Non-potentised high dilutions of arsenic trioxide did not induce relevant results.[21]

External reproducibility of this model was studied in another laboratory by a Swiss-German research team. Investigations were carried out with two different lots of wheat cultivars in two experimental series with 4 experiments each. In both series statistically significant effects of arsenic trioxide (45x) were revealed, but inverted in direction compared to the original trial[10]: shoot length was reduced after 7 days (both series pooled).[11]

These results stimulated the Swiss-German team to search for possible reasons for this effect inversion. Three parameters, which could have induced the effect inversion, were investigated: 1. Geographical location (or an unknown factor associated with the original laboratory); 2. Main experimenter; 3. Seed sensitivity towards arsenic. They performed 3 further series of independent reproduction trials to empirically test these hypotheses. First, the experimenter of the preceding study of the Swiss-German research team reconsidered an experimental series in the Italian laboratory. Another experimenter of the Swiss-German research team conducted two further series in the Swiss laboratory with the same wheat cultivar as in the two series of the previous study.[11] All three series revealed no significant effects of arsenic trioxide (45x).[32] The meta-analysis of all 5 series (17 experiments) performed[11,32] yielded a statistically significant shoot growth decrease with isopathic arsenic trioxide (45x) treatment. This effect was quantitatively similar across all 5 series of experiments. The investigated factors (geographical location, experimenter, seed sensitivity to arsenic poisoning) did not seem to be responsible for the effect inversion.

Summarising, the Italian group observed an increase in shoot length and germination rate, and a decrease in standard deviation, while the Swiss-German group observed a decrease in shoot length and germination rate, and an increase in standard deviation.

The latest experiments with the arsenic trioxide wheat seedling model were carried out by the Italian team to evaluate effects of temperature and aging on the efficacy of arsenic trioxide (45x) on Pandas wheat cultivar seeds. The

Table 5 Overview of the potentised substances tested in the 8 experiments (Table 3a, b) using adequate controls to identify specific effects

Potentised substances	*No. of studies*	*Noxa*	*Plants*	*Tested potency levels*	*Effects reported by author*	*Effect**
Arsenic trioxide (As_2O_3)	6[11,20–22,30,32]	Arsenic trioxide (As_2O_3); arsenic(V) ($AsHNa_2O_4 \times 7H_2O$)	Wheat (*Triticum aestivum* L.); Duckweed (*Lemna gibba* L.)	5x, 15x, 17x, 18x, 21x, 22x, 23x, 24x, 25x, 28x, 30x, 33x, 35x, 42x, 45x	18x, 21x, 22x, 23x, 30x, 33x, 40x, 42x, 45x	I, D
Gibberellic acid	1[30]	Arsenic(V) ($AsHNa_2O_4 \times 7H_2O$)	Duckweed (*Lemna gibba* L.)	17x, 18x, 21x, 22x, 23x, 24x, 28x, 30x, 33x	–	–
Lysine ($C_6H_{14}N_2O_2$)	1[8]	Lysine ($C_6H_{14}N_2O_2$)	Wheat (*Triticum aestivum* L.), cv. 'Tallent'	8c	–	–
Nosode	1[30]	Arsenic(V) ($AsHNa_2O_4 \times 7H_2O$)	Duckweed (*Lemna gibba* L.)	17x, 18x, 21x, 22x, 23x, 24x, 28x, 30x, 33x	–	–
Sodium chloride (NaCl)	1[40]	Sodium chloride (NaCl)	Cress (*Lepidium sativum* L.)	12c, 18c, 24c	12c, 24c	I

* I = Increase; D = Decrease; – = no effect.

Figure 2 Wheat seedlings stressed with arsenic trioxide (here the inner plastic bag is pulled out of the paper envelope).

number of non-germinated seeds was measured after 96 h. A possible temperature effect was investigated by heating each homeopathic treatment in a water bath for 30 min at 20°C, 40°C or 70°C, or for 5 min at 100°C. To investigate a possible aging effect, experimental data (collected over a period of nearly five months) were divided into early and late experiments. It was observed that the efficacy of the homeopathic preparation was comparable at 20 and 40°C, increased at 70°C and decreased at 100°C. Regarding aging, a difference was found between early experiments, with no significant efficacy, and late experiments, in which homeopathic preparations revealed a significant effect *versus* control, except at 100°C. Variability was reduced for homeopathic preparations at 20°C *versus* control.[20]

Lysine wheat seedling model: Lysine was chosen because it enters the seeds rapidly and is easily metabolisable.[4] After stressing wheat with lysine in an isopathic approach the effect of a centesimal potency of lysine (8c) was investigated on the impact of shoot length, fresh weight and dry weight. No effects were observed compared to analogously potentised water 8c.[8]

Sodium chloride cress seedling model: This trial was conducted with cress seeds (*Lepidium sativum* L.) stressed by watering in sodium chloride solution for 16 h. After impairment seeds were treated with sodium chloride (12c, 18c and 24c). After 96 h of incubation the germination rate and length of seedlings were assessed (Figure 3). Germination decreased through potency levels 12c and 24c ($p = 0.033$). The 18c treatment showed no significant effect on germination. As far as seedling growth is concerned, the treatment

Figure 3 Cress seedlings (*Lepidium sativum* L.) stressed with sodium chloride.

with 12c and 24c showed a trend to inhibition (statistically not significant).[40]

Arsenic(V) duckweed model: This study evaluated the effects of homeopathically potentised arsenic trioxide, nosode (prepared of stressed duckweed) and gibberellic acid with duckweed (*Lemna gibba* L.) stressed for 48 h with arsenic(V) (Figure 4). These three homeopathic preparations were selected after a screening of 11 different test substances.[41] The test substances were applied in nine potency levels (17x, 18x, 21x−24x, 28x, 30x, 33x), which were pooled for statistical analysis. Growth rates of frond area and number were determined for three different time intervals (day 0−2, 2−6, 0−6). Additionally to the five independent experiments evaluated for each test substance, five systematic negative control experiments were analysed to investigate the stability of the experimental set-up. They did not yield any significant effects, thereby providing evidence that the experimental set-up was stable and did not produce false-positive results. The test system exhibited a low coefficient of variation ($\approx 1\%$). Growth rates for day 0−2 were not influenced by any homeopathic preparation. Growth rates for day 2−6 increased after application of potentised arsenic trioxide regarding both frond area ($p < 0.001$) and frond number ($p < 0.001$), and by application of potentised nosode (frond area growth rate only, $p < 0.01$). Potencies of gibberellic acid did not influence duckweed growth rate.[30]

Figure 4 Duckweed (*Lemna gibba* L.) stressed with arsenic(V).

Discussion

Approximately two-thirds (60%) of all publications found had performed at least basic statistics and were included in this review. Almost two-thirds (59%) of these studies contained sufficient information to be interpreted properly and also about two-thirds (62%) thereof included adequate controls to investigate specific effects of homeopathic preparations. Half of these studies implemented systematic negative control experiments to verify the stability of the test system.

There is a noticeable correlation between publication date and elaborateness. All studies which did not report sufficient statistics, were carried out before 1983. At about the same time (1981) the first study with a MIS ≥ 5 was performed.[7] Except for one study,[23] all studies published after 1983 had an MIS ≥ 5. The 7 most recent studies and one earlier study[8] included adequate controls to investigate the specific effect of homeopathic preparations (since 2000). Systematic negative control experiments were first published in 2005.[11]

From these studies with adequate controls, only one study − the lysine wheat seedling model[8] − did not show significant effects of homeopathic preparations. The sodium chloride cress seedling model and the arsenic(V) duckweed model showed growth increasing effects, whereas the arsenic trioxide wheat seedling model showed increasing and decreasing effects. The reasons for effect inversions in the arsenic trioxide wheat seedling model are not clear yet. Three parameters were investigated, which were suspected to cause the inversion: 1. Geographical location; 2. Main experimenter; 3. Seed sensitivity towards arsenic. No correlations were found. Other parameters, for example ambient conditions or differing of single potency levels should be investigated in future.

Based on the assumption that a characteristic feature of homeopathic preparations is to induce equilibrating effects, test systems with impaired organisms can be hypothesised to yield more stable as well as more pronounced effects after

application of homeopathic preparations compared to test systems using healthy organisms. Apart from one study,[8] where no specific effects of the homeopathic treatment were observed, one other plant study showed more pronounced effects with stressed organisms compared to healthy organisms.[42] In consequence of the equilibrating character of homeopathic preparations on test systems with impaired plants, one may expect that all active potency levels act in the same direction, e.g. growth promoting in a system where the stress induces a growth reduction. This opens the possibility of pooling data from several different potency levels in the statistical evaluation which in turn might yield more stable effects due to the broader observational basis.

A major problem in test systems with stressed organisms is the increased variance of outcome parameters due to the impairment of the organisms. The arsenic trioxide wheat seedling model particularly exhibits a high standard deviation.[8,31,32] This may be due to the fact that arsenic trioxide is an unstable arsenic species, dependent on various ambient conditions such as oxygen content.[41] Furthermore, there is no obvious method to select a homogeneous subpopulation of comparably impaired wheat seeds after arsenic poisoning. This is in contrast to the duckweed model, where a selection of organisms with a comparable degree of damage is feasibly due to phenomenological distinguishable features like colour, texture or shape. Furthermore wheat seedlings are prone to a re-diffusion of arsenic by contact with the endosperm. This may be prevented by the choice of another seed, e.g. white mustard (*Sinapis alba* L.) as test organism.[8] Hence, when using impaired organisms a high degree of standardisation is very important, to achieve a standard deviation as low as possible. A possibly negative aspect of a high stabilisation might be a reduction of the effect size. However, in basic research the magnitude of the effect size is less important than in applied science. In basic science a small standard deviation is crucial to get as reproducible results as possible.

When developing a homeopathic test system with impaired organisms, the choice of the test organism may play an important role. Whilst k-strategists predominantly aim at a qualitative adaptation of the organisms, r-strategists (such as duckweed) aim at increasing the quantity of offspring.[43] A consequent drawback for a test system using r-strategists might be the fast production of new plant material, which is not impaired anymore as soon as the external stress is removed. Homeopathic medicines might have a greater effect on k-strategists by supporting qualitative stress adaptation than on r-strategists by increasing offspring production. However, the advantage of r-strategists is the shorter experimental duration and the faster accomplishment of multiple repetition experiments. Germination, in turn, is an exceptional period in lifetime of plants. Growth, which is depending on storage substance, is very fast in this period. Thus the choice of the developmental phase of the organism (germination, growth etc.), the choice of the stressor as well as its application in time and the time points of observation have to be carefully adjusted.

In the development of an experimental set-up with stressed organisms, the choice of the stressor is difficult due to a wide range of inorganic toxins, organic toxins, radiation or lack of nutrients for example. In addition to stressor and plant species, the most appropriate outcome parameter must be found. The impairment rate again is closely related to the outcome parameter. For instance *S. alba* stressed with copper sulphate showed a 25% reduction in fresh weight and a 88% reduction in chlorophyll content, which is furthermore strongly related to light conditions.[9] Stem growth of wheat seedlings stressed with arsenic trioxide was inhibited by 60%, whilst roots were inhibited by 30%. Only stem length showed an effect of homeopathic preparations.[10] Furthermore the applicability of outcome parameters depends on their regulation capacity, the potential to react to external stimuli. For example, a very low standard deviation of an outcome parameter could be caused by a prefinal state of organisms that may prevent a reaction to homeopathic preparations. It might therefore be interesting in future studies to compare various outcome parameters, since the response to homeopathic preparations may manifest in various parts or different metabolism pathways of the organism under observation.

The choice of the homeopathic test substances for plants is a substantial problem for all models with healthy and impaired plants due to the lack of a Materia Medica for plants. But by stressing plants new approaches develop, primarily the isopathic application, which might be a good starting point for tuning the experimental parameters in order to

Table 6 Experimental parameters in experiments with homeopathic preparations, which might interact with the effect size of the homeopathic treatment

Homeopathic medicine
◦ Selection of homeopathic medicine
◦ Point in time of application
◦ Application rate (dose)
◦ Mode of production, e.g. trituration or dilution
◦ Potency level
◦ Potentisation method
◦ Quality of prime substance
◦ Quality of potentisation medium
◦ Influences during potentisation
Organisms/noxa
◦ Kind of organism, e.g. r/k-strategist, organisational level
◦ Kind of noxa, e.g. radiation, inorganic or organic substances
◦ Kind of impairment, e.g. cytotoxic, genotoxic
◦ Degree of damage − fitness of organisms
◦ Mode of impairment, e.g. concentration, point in time
Test system
◦ Growth conditions, e.g. light, nutrients, temperature, rhythms
◦ Point in time of measurement
◦ Measuring parameter
◦ Variance
◦ Sensitivity
◦ Specificity
Special considerations for experiments with homeopathic medicines
◦ Crossover effects, e.g. by agitation of potentised medicines, shielding, distance
◦ Attenuation of efficacy, e.g. through UV-radiation, electromagnetic fields, pressure
◦ Modulation of efficacy, e.g. constellation, impact of plastic material
◦ Confining factors during experiments, e.g. sterile filtration
◦ Influence of experimenter

maximize the effect size. After optimization of the experimental parameters, a screening of multiple test substances could be performed to identify homeopathic test substance with stronger effects. The origin and production method of test substances should also be considered. For example, homeopathic arsenic trioxide as used in the isopathic studies identified in this review was always prepared from a 0.1% aqueous solution as mother tincture, which was further potentised in water. Usually homeopathic Arsenicum album is first triturated in lactose (up to 3c or 6x) and only afterwards potentised in liquid form.

The application of stressors in test systems with impaired plants leads to a lot of experimental parameters that require optimization, and due to their interactions to even more degrees of freedom with consequent necessities of tuning all parameters in order to maximize the effect size. There are several parameters concerning the homeopathic medicines like the selection of preparations or the time point of application, several parameters exists also for the organisms, the noxa, and the test system itself, especially for experiments with homeopathic medicines, like the crossover effect for instance (Table 6). The development of experiments with impaired organisms may be useful to stabilise a test system, but it takes a larger effort to optimize all parameters to reduce the inherent increase of standard deviation.

Conclusion

Homeopathic basic research models using impaired plants are usually short term, allowing large numbers of experimental replications, and eliminate disadvantages such as the placebo effect or ethical concerns. They provide the opportunity of studying the presumed characteristic equilibrating (regulative) effects of homeopathic medicines, and at the same time the stress applied may allow to stabilise the test system. Major attention has to be given to a high degree of standardisation to achieve a standard deviation as low as possible.

Results of the studies included in this review support the notion that the impaired plant models are useful tools to investigate the controversial specific efficacy of homeopathic preparations. Furthermore, this type of basic research model may be used for investigations of the mode of action and may develop into a method to study the stability of homeopathic preparations against external influences and to compare different production methods.

It is necessary to further improve the quality of the experimental design, by blinding, randomisation, adequate statistical analysis and appropriate controls to identify specific remedy effects and to enable replication. Furthermore, the use of systematic negative control experiments is strongly recommended to control system stability.

Acknowledgments

The authors thank Silvia Ivemeyer for helpful comments. We thank the library staff of the Boiron library (Sainte-Foy-lès-Lyon, France) and of the Karl und Veronica Carstens-Stiftung (Essen, Germany) as well as the literature service of the Deutsche Homöopathie Union DHU (Karlsruhe, Germany) for help in identifying articles and for providing several article reprints. This investigation was funded by Weleda AG (Arlesheim, Switzerland) and Dr. Hauschka Stiftung (Bad Boll/Eckwälden, Germany). The sponsor had no influence whatsoever upon design, conduct and evaluation of the investigation, the decision to publish and the contents of the manuscript.

Conflict of interest

Neither the authors nor their affiliates have any conflicts of interest to declare. No competing financial interests exist.

References

1 Majewsky V, Arlt S, Shah D, *et al*. Use of homeopathic preparations in experimental studies with healthy plants. *Homeopathy* 2009; **98**(4): 228−243.
2 Betti L, Trebbi G, Majewsky V, *et al*. Use of homeopathic preparations in phytopathological models and in field trials: a critical review. *Homeopathy* 2009; **98**(4): 244−266.
3 Scofield M. Homeopathy − and its potential role in agriculture − a critical review. *Biol Agric Hortic* 1984; **2**: 1−50.
4 Majerus M. Kritische Begutachtung der wissenschaftlichen Beweisführung in der homöopathischen Grundlagenforschung. Thesis, Tierärztliche Hochschule Hannover, Germany, 1990.
5 Albrecht H, van Wijk R, Dittloff F. A new database on basic research in homeopathy. *Homeopathy* 2002; **91**: 162−165.
6 Baumgartner S, Heusser P, Thurneysen A. Methodological standards and problems in preclinical homeopathic potency research. *Forsch Komplementärmed* 1998; **5**(1): 27−32.
7 Auquière JP, Moens P. Recherches de l'action de dilutions homéopathiques sur les végéteaux: I. Action du $CuSO_4$ 5CH sur blé intoxiqué au $CuSO_4$ 1 ‰. *J Pharm Belg* 1981; **36**(5): 303−320.
8 Auquière JP, Moens P, Linster T, Speileux M. Recherche de l'action de dilutions homéopathiques sur les végétaux. Unpublished report, Louvain-la-Neuve, 1988.
9 Auquière JP, Moens P, Martin PL. Recherche de l'action de dilutions homéopathiques sur les végéteaux: II. Action du $CuSO_4$ 14DH sur la Moutarde blanche (*Sinapis alba* L. var. dialba) intoxiquée au $CuSO_4$ 0.1 et 0.2 ‰. *J Pharm Belg* 1982; **37**(2): 117−134.
10 Betti L, Brizzi M, Nani D, Peruzzi M. Effect of high dilutions of Arsenicum album on wheat seedlings from seed poisoned with the same substance. *Br Hom J* 1997; **86**(April): 86−89.
11 Binder M, Baumgartner S, Thurneysen A. The effects of a 45x potency of Arsenicum album on wheat seedling growth − a reproduction trial. *Forsch Komplementarmed Klass Naturheilkd* 2005; **12**(5): 284−291.
12 Boiron J. Action d'une dilution hahnemannienne arsenicale sur la croissance du blé intoxiqué à l'arsenic. *Ann Homéopath Fr* 1965; **7**(4): 253−258.
13 Boiron J. Action de dilutions 5CH-7CH et 15CH de Sulfate de Cuivre sur la respiration de *Salvinia natans*. In: L.M.H.I.: 28th Congress of the International Homeopathic Medical League, Wien, 1973, pp 597−602.
14 Boiron J, Abecassis J, Reynaud J. Etude de l'action d'une 15CH de sulfate de cuivre sur la germination de grains de blé subintoxiqués par cette substance. *Ann Homéopath Fr* 1978; **20**(4): 293−302.
15 Boiron J, Marin A. Action des doses infinitésimales (15CH) d'une substance sur la cinétique d'élimination de cette même substance

au cours de la culture de graines préalablemtent intoxiquées. *Ann Homéopath Fr* 1967; **9**(2): 121−130.

16 Boiron J, Marin J. Action d'une 15CH de $CuSO_4$ sur la cinétique d'élimination de cette substance au cours de la culture "d'embryons" préalablement intoxiqués. *Ann Homéopath Fr* 1968; **10**(3): 219−226.

17 Boiron J, Marin M. Action d'une 15CH de sulfate de cuivre sur la culture de *Chlorella vulgaris*. *Ann Homéopath Fr* 1975; **17**(4): 367−372.

18 Boiron J, Reynaud J. Démonstration de l'activité de dilutions 5-7-9 et 15CH de Cuprum sulfuricum sur la Respiration de *Salvinia natans* L. *Ann Homéopath Fr* 1975; **17**: 499−507.

19 Brizzi M, Biondi C, Lazzarato L, Betti L. Analisi esplorativa dell'effetto di soluzioni ultramolecolari di triossido di Arsenico sullo sviluppo vegetativo in vitro di plantule di grano. *Statistica* 2002; **62**(3): 515−522.

20 Brizzi M, Elia V, Trebbi G, Nani D, Peruzzi M, Betti L. The efficacy of ultramolecular aqueous dilutions on a wheat germination model as a function of heat and aging-time. *eCAM* 2009.

21 Brizzi M, Lazzarato L, Nani D, Borghini F, Peruzzi M, Betti L. A biostatistical insight into the As_2O_3 high dilution effects on the rate and variability of wheat seedling growth. *Forsch Komplementarmed Klass Naturheilkd* 2005; **12**(5): 277−283.

22 Brizzi M, Nani D, Peruzzi M, Betti L. Statistical analysis of the effect of high dilutions of arsenic in large dataset from a wheat germination model. *Br Hom J* 2000; **89**: 63−67.

23 Carvalho LM, Casali VWD, Cecon PR, Lisboa SP, Souza MA. Effect of homeopathy on recovery of feverfew plants [*Tanacetum parthenium* (L.) Schultz Bip] under water stress. *Rev Bras Plantas Med* 2004; **6**: 20−27.

24 Flemming H. Potenzieren − ein Weg, die Gegenwirkung der Stoffe zu erschliessen? *Element Naturwiss* 1974; **20**(1): 26−32.

25 Graviou E. Action d'une 15 ème centésimale de $CuSO_4$ sur la respiration de pois intoxiqués au cuivre. *Ann Homéopath Fr* 1968; **10**(3): 227−228.

26 Graviou E. Moment, sens et intensité de l'action d'une haute dilution sur un materiél végétal préintoxiqué. *Ann Homéopath Fr* 1980; **22**(2): 145−162.

27 Graviou E. Dosage de l'action d'une 15CH de sulfate de cuivre Comparaison des résultats dans le temps. *Ann Homéopath Fr* 1981; **23**(3): 5−23.

28 Graviou E. Problème de l'optimum de succussions en fonction du moment de la préparation de dilutions cuivriques. *Homéopath Fr* 1982; **24**(1): 29−34.

29 Graviou E, Biron MA. Action d'une 15CH de sulfate de cuivre sur la culture de *Chlorella vulgaris*. *Ann Homéopath Fr* 1971; **13**(7): 539−548.

30 Jäger T, Scherr C, Simon M, Heusser P, Baumgartner S. Effects of homeopathic Arsenicum album, nosode, and gibberellic acid preparations on the growth rate of arsenic-impaired duckweed (*Lemna gibba* L.). *ScientificWorldJournal* 2010; **10**: 2112−2129.

31 Kovac H, Muhry F, Novic S, Moser M. Das Wachstum von Weizenkeimlingen nach Zugabe von toxischen Substanzen. *Mitt Inst Strukt Med Forsch* 1991; **3**: 43−63.

32 Lahnstein L, Binder M, Thurneysen A, *et al*. Isopathic treatment effects of Arsenicum album 45x on wheat seedling growth − further reproduction trials. *Homeopathy* 2009; **98**(4): 198−207.

33 Moss V, Roberts J, Simpson H. The effect of copper sulphate on the growth of the alga *Chlorella*. *Br Hom J* 1977; **LXVI**(3): 169−177.

34 Netien G. Action de doses infinitésimales de sulfate de cuivre sur des plantes préalablement intoxiquées par cette substance. *Ann Homéopath Fr* 1966; **4**: 130−136.

35 Netien G, Graviou E. Action d'une 15CH de sulfate de cuivre sur du materiel végétal préintoxiqué. Importance de la rythmologie pour cette étude. *Ann Homéopath Fr* 1979; **21**(4): 415−427.

36 Netien G, Graviou E, Marin A. Action de doses infinitésimales de sulfate de cuivre sur des plantes préalablement intoxiquées par cette substance. *Ann Homéopath Fr* 1965; **7**(4): 248−252.

37 Noiret R, Claude M. Etude enzymatique du grain de froment intoxiqué par $CuSO_4$ et traité par différentes dilutions hahnémanniennes de la même substance. *Rev Belg d'Hom* 1976; **IX**(1): 461−496.

38 Noiret R, Glaude M. Expérimentation des acides nucléiques ARN et ADN sur les graines de froment (inhibition de croissance et stimulation). *Rev Belg d'Hom* 1979; **11**(2): 71−82.

39 Projetti ML, Guillemain J, Tetau M. Effets curatifs et préventifs de dilutions homéopathiques de sulfate de cuivre appliquées à des racines de lentilles pré-ou post-intoxiquées. *Cah Biothér* 1985; **22**(88): 21−27.

40 Tighe M. Homeopathy on cress − a pre-clinical method development using a simple plant growth model. Thesis, University of Westminster, London, UK, 2005.

41 Jäger T, Scherr C, Simon M, Heusser P, Baumgartner S. Development of a test system for homeopathic preparations using impaired duckweed (*Lemna gibba* L.). *J Altern Complement Med* 2011; **17**(4): 315−323.

42 Betti L, Trebbi G, Zurla M, Nani D, Peruzzi M, Brizzi M. A review of three simple plant models and corresponding statistical tools for basic research in homeopathy. *ScientificWorldJournal* 2010; **10**: 2330−2347.

43 Begon M, Townsend C, Harper J. *Ecology: from individuals to ecosystems*. Malden, USA: Wiley-Blackwell, 2005.