Effects of homeopathic high dilutions on plants: literature review

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Abstract

Background: Among the non-conventional assumptions of homeopathy, the use of medicines in high dilutions (HD) is a cause for objections and skepticism among the scientific community, trained within the dose-dependency paradigm of classic pharmacology. Research aiming at evidencing the effects of homeopathic HD has resource to several experimental models (*in vitro*, plants and animals). Aim: To describe the results of studies with high methodological quality that demonstrated positive effects of homeopathic HD on plants. Methods: Taking reviews published until 2015 as reference source, we updated the information through addition of data from recent studies included in database PubMed. Results: From 167 experimental studies analyzed, 48 met the minimum criteria of methodological quality, from which 29 detected specific effects of homeopathic high dilutions on plants through comparison to adequate controls. Conclusions: Despite the substandard methodological quality of most experiments, studies with systematic use of negative controls and reproducibility demonstrated significant indisputable effects of homeopathic HD on plants.

Keywords

Homeopathy; High dilutions; Agriculture; Plants; Phytopathological models; Review

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Introduction

Since homeopathic treatment is grounded on non-conventional assumptions (therapeutic similitude, pathogenetic investigation of medicines on healthy individuals and use of highly diluted and agitated medicines selected according to the full set of characteristic symptoms and signs of patients) its acceptance is resisted by the medical and scientific community, which ignores its specificities and the evidences that support it [1,2]. Used to large and increasing doses that have contrary and palliative action relative to the manifestations of disease, doctors and investigators do not consider the application of a treatment based on infinitesimal or minimal doses of medicines that cause similar disorders to the ones to be cured. This even though they do consider the advances of research in immunotherapy and nanotherapy, based on grounds similars to the ones of homeopathy.

Among the homeopathic assumptions, use of serially diluted and agitated medicines (potencies, high dilutions – HD) with concentration less than 1 gram-molecule (above Avogadro's number, 6.02×10^{-23}) is the reason for the greatest criticism among skeptics, who adhere to the dose-dependent model of modern pharmacology. Denying any plausible effect to homeopathic HD in living beings [3,4], critics attribute the patent improvements induced by homeopathic treatment to the patient-doctor relationship and placebo effect.

To evidence the efficacy of homeopathic medicines in the treatment of diseases and the effectiveness of HD in biological systems, clinical and experimental studies are conducted with human beings, animals, plants, cell cultures, etc. In the present review we describe scientific evidences for the effect of homeopathic HD on plants found in the past decades.

By comparison to other types of studies, research on plants has countless advantages such as: large sample size; large datasets; short duration; low cost; absence of placebo effect; and absence of the ethical issues that apply to animal and human research. However, there are some disadvantages too: systematic pathogenetic trials of medicines have not been conducted with plants that would result in a homeopathic materia medica specific for plants, necessary for the selection of individualized medicines for each plant species and disease type, as we have asserted all along the past decade [5-8]. Then, some relevant parameters or artifact cannot be controlled, which interfere with the development and health of plants and hinder the reproducibility of experiments.

Studies assessing the effect of homeopathic HD on plants are known since 1926 [9]; the first literature review was published in 1984 [10]. Several reviews described the effects of homeopathic medicines on plants [11-16] and analyzed the factors related with improvement of the methodological quality of experiments and corresponding publications (detailed description of experiments, randomization, blinding, control group, statistical analysis of results, systematic use of negative controls and reproducibility, among others).

It should be noticed that systematic use of negative controls (placebo group not subjected to any other intervention) is the ideal method to ensure the stability of a system, exclude false-positive results and assess the specific effect of HD [16]. Reproducibility excludes false-positive results, thus ensuring the scientific quality of experiments [14-17]. As a result of the efforts to improve the methodological quality of studies, the number of articles on homeopathic fundamental research in peer-reviewed journals considerably increased in the past 2 decades [18], being an indirect indicator of improvement in the experiments.

In the 3 main reviews that analyzed the use of homeopathic medicines in plants [11-13] the experimental results were clustered into 3 groups: a) models using healthy plants [11] useful to investigate issues related with homeopathic potencies and to perform homeopathic pathogenetic trials; b) phytopathological models [12] which are ideal to study the use of homeopathy for management of plant diseases and pests, which is allowed for and used in organic agriculture (agrohomeopathy) [12]; and c) models using plants subjected to abiotic stress (mineral toxicity, salinity, pH, etc.) [13] in which HD of the same stressors are used to re-establish the plants' health.

As mentioned above, the lack of a homeopathic materia medica specific for plants including a large number of signs and symptoms in different species does not allow for the application of the therapeutic similitude principle, and consequently for individualized treatment of diseases and other disorders of plants. In addition to empirical application of homeopathic medicines to various plant disorders, studies evidence the efficacy of biotherapy or isotherapy (therapeutic identity principle) for management of diseases and mineral and chemical imbalance through administration of HD of the biotic (viruses, fungi, bacteria, insects, pests, etc.) and abiotic (toxic agents, NaCl, etc.) stressors that cause such disorders to neutralize them [16-20].

The main aim of the present review was to describe studies that evidenced effects of homeopathic HD on plants, which were clustered in tables according to the 3-group classification mentioned above. Then, based on criteria for methodological quality, we described the most significant experiments and lines of research, including some pursued in Brazil.

Materials and methods

The sources for information on the studies included in the present review were the aforementioned reviews [11-16]. The experiments with the highest methodological quality (Manuscript Information Score – MIS $\geq$ 5) published from 1979 onward were selected. Since the 3 previous reviews analyzed articles published from 1920 to 2015, to update the dataset we added studies published from 2015 to 2017 located through a search in database PubMed using keywords "homeopathy" AND "plant"; "homeopathy" and "agriculture". We also described some Brazilian initiatives for homeopathic research on plants.

Results

The articles that met the inclusion criterion (MIS $\geq$ 5) were clustered into 3 main groups (healthy plants, phytopathological and abiotic stress). The corresponding data were synthesized and described in individual tables.

Table 1. Main studies on the effect of homeopathic high dilutions on healthy plants

Author; year	Species	Aim	Parameters	Treatment	Control	Frequency and mode of application	Effects
Endler et al., 2015 [21]	Wheat	Effect of gibberellic acid in HD on seedling growth in autumn vs. winter-spring	Stalk length	Gibberellic acid 30x	Water; potentized water	Treatments applied to Petri dishes containing seeds	In all autumn experiments gibberellic acid 30x reduced** seedling growth. Results for winter-spring were inconsistent
Majewsky et al., 2014 [22]	Gibbous duckweed (*Lemna gibba*)	Effect of gibberellic acid in HD on seedling growth	Growth rate	Gibberellic acid 14x to 30x	Water; potentized water	Seedlings were kept in Becker glass with nutritive solution and 1 treatment	Increase** of the growth rate with some HD; the plant developmental stage seems to influence response to treatment
Hribar-Marko et al., 2013 [23]	Wheat	Whether seed pre-treatment with gibberellic acid in molecular dose increases the effect of gibberellic acid in HD on seedling growth	Seedling length	Seeds were pre-treated with gibberellic acid in molecular dose (10^{-5}, 10^{-4}, 10^{-3}); treatment with gibberellic acid 30x	Water; potentized water	Application of 2 ml of pre-treatment in Petri dishes containing seed; 4 h later, application of 4 ml of treatments	In the group pre-treated with water gibberellic acid 30x reduced** seedling growth. In the groups given gibberellic acid in molecular dose, the lower the concentration the greater the effect of HD to reduce seedling growth
Kiefer et al., 2012 [24]	Wheat	Effect of gibberellic acid in HD on seed germination	Winter wheat seeds	Gibberellic acid 30x	Water; potentized water	Treatments applied to Petri dishes containing seeds	Gibberellic acid 30x reduced** the germination rate in the 2009-2010 experiments; no difference in 2011. This divergence might be due to poorer seed viability and season of the year
Endler et al., 2011 [25]	Wheat	Effect of gibberellic acid in HD on seedling growth in different seasons of the year	Seedling length	Gibberellic acid 30x	Water; potentized water	Treatments were applied to Petri dishes containing seeds	Gibberellic acid 30x reduced** seedling growth. Best effect in autumn. Causes for difference

							might be poorer seed viability, season of the year and temperature
Pfleger et al., 2011 [26]	Wheat	Effect of gibberellic acid in HD on seedling growth	Seedling length	Gibberellic acid 30x	Water; potentized water	Treatments were applied to Petri dishes containing seeds	Gibberellic acid reduced** seedling growth
Santos et al., 2011 [27]	*Verbena gratissima*	Effect of *Phosphorus* on plant growth and essential oil concentration	Growth parameters and essential oil content	*Phosphorus* 5cH, 6cH, 9cH, 12cH, 15cH, 18cH, 21cH, 24cH, 27cH, 30cH	Water; hydroalcoholic solution	Treatments applied 3 times per week, 100 ml per vase, along 3 months	Some HD, especially 9cH, increased** plant height and branch and leave dry mass; increased essential oil production
Scherr et al., 2009 [28]	Gibbous duckweed (*Lemna gibba*)	Influence of HD	Growth rate	Gibberellic acid, *Argentum nitricum*, kinetin and *Lemna minor*	Water; potentized water	Plants selected per similar number of leaves and size; kept in Becker glass with treatments	Gibberellic acid 15d, 17x, 18x, 23x and 24x reduced** growth rate
Sukul et al., 2009 [29]	Lady's finger	Influence of plant regulators (CCC, chlorocholine chloride; MH, maleic hydrazide) on plant development	Growth and physiologic-al variables	CCC 30c, CCC 200c, CCC (with copper nanoparticles) 30c and MH 30	Potentized hydroalcoholic solution	Leave spraying of treatment diluted 1:550, twice per day, 2 days	All treatments increased** plant growth, chlorophyll content, protein and water amount in leaves; CCC30c with copper nanoparticles was more effective than CCC30c
Baumgartner et al., 2008 [30]	Dwarf pea	Effect of gibberellic acid in HD on seedling growth	Shoot length	Gibberellic acid 17x and 18x	Water; potentized water	Seeds immersed into treatments 24 h	Gibberellic acid 17x enhanced** growth of seeds harvested in 1997
Sukul et al., 2008 [31]	Pigeon pea	Effects on plant growth	Growth and physiological variables	CCC 30c, CCC 200c, CCC (with copper nanoparticles) 30c and MH 30	Potentized hydroalcoholic solution	Leave spraying of treatment diluted 1:550, 8 days	All treatments increased** plant growth, chlorophyll, protein and sugar content

Scherr et al., 2007 [32]	Gibbous duckweed (*Lemna gibba*)	Effects of HD on growth rate	Growth rate	*Argentum nitricum*, copper sulfate, gibberellic acid, 3-indol acetic acid, kinetin, lactose, *Lemna minor*, methyl jasmonate, metoxuron, *Phosphorus*, potassium nitrate and *Sulphur* 14x-30x	Water; potentized water	Homogeneous plants (number of leaves and size) were placed in Becker glass with nutritive solution; then 46.2 ml of treatments were added	*Argentum nitricum* 24x, 28x, 29; kinetin 14x, 16x, 20x, 26x, 27x, 30x; *Phosphorus* 21x, 25x, 29d influenced** growth rate all along the assessment period
Baumgartner et al., 2004 [33]	Dwarf pea	Effect of plant hormones in HD on seedling growth	Seedling length	Gibberellic acid, kinetin, auxin, abscisic acid 12x to 30x	Water; potentized water	Seeds immersed 24 hours into treatments and placed to germinate	Gibberellic acid 13x, 15x, 17x, 23x; kinetin 19x increased** seedling growth
Chapman 2004 [34]	Lettuce	Effect of homeopathic medicines on plant growth	Plant size and weight	*Sulphur* and *Silicea* in HD	Potentized water	Treatments applied with plants on soil	*Silicea* and *Sulphur* 1LM influenced** plant development
Andrade et al., 2001 [35]	*Justicia pectoralis* Jacq	Effect of HD on *J. pectoralis* growth, coumarin production and electromagnetic field	Growth variables, coumarin yield, electromagnetic field	J. pectoralis, coumarin, guaco, *Phosphorus*, *Sulphur*, *Arnica montana*, humic acid 3cH	70% ethanol; 70% ethanol 3cH	Weekly spraying (9) of 2.65 ml/plant of solution (10 drops/l water)	J. pectoralis, humic acid, *Arnica* *Sulphur* and *Phosphorus* 3cH increased** coumarin yield
Brizzi et al., 2000 [36]	Wheat	Effect of *Arsenicum album* on seed germination	Number of non-germinated seeds	*Arsenicum album* (As_2O_3) 23x to 45x	Water; potentized water	Treatments were applied to Petri dishes containing seeds	HD 30d, 35x, 40x, 42x, 45x enhanced** a seed germination
Betti et al., 1994 [37]	Wheat	Effect of *Arsenicum album* on germination	Germination rate	*Arsenicum album* (As_2O_3) 23x, 25x, 30x, 35x, 40x, 45x	Water; water 30x	Treatments were applied to Petri dishes containing seeds	HDs 40x and 45x increased** seed germination
Pongratz & Endler, 1994 [38]	Wheat	Effect of silver nitrate in HD on germination and seedling development	Seedling size; germination rate	Silver nitrate 24x	Water; dynamized water	Seeds immersed in treatments	Silver nitrate 24x enhanced seedling development
Endler & Pongratz, 1991 [39]	African violet	Effect of indole butyric acid on plant development	Rooting and new leave development	Indole butyric acid 33x	Potentized water	Plant immersion	Enhanced rooting

Pongratz, 1990 [40]	Wheat	Effect of silver nitrate on germination and seedling development	Seedling length; germination rate	Silver nitrate 24x	Potentized water	Seed immersion	Increased** seedling development
Noiret & Claude, 1979 [41]	Wheat	Effect of copper sulfate in HD on germination and seedling growth	Dry and fresh weight	$CuSO_4$ 5c, 7c and 9c	Water; potentized water	Seed immersion	Reduction** of analyzed variables

** Statistically significant difference

Table 2. Main studies on the effect of homeopathic high dilutions on phytopathological models

Author; year	Species	Aims	Parameters	Treatment	Controls	Frequency and mode of application	Effects
Shah-Rossi et al., 2009 [42]	*Arabidopsis thaliana*	Effect of HD on plants infected with *Pseudomonas syringae*	Infection rate of leaves	30 substances 30x	Water; potentized water	Plants fully plunged upside-down for 30 sec into 20 ml of treatments; 1.5 ml of dipping solution dropped onto center of each plant rosette from which leaked into soil, the remainder was added to irrigation solution	Biplantol reduced infection**
Datta, 2006 [43]	Mulberry	Effect of *Cina maritima* on root-knot disease of mulberry	Growth and infection variables	*Cina* 200c and *Cina* MT before and after inoculation	90% hydroalcoholic solution	Plants were sprayed 4 times, every 3 days, with 10 ml of treatment; *Cina* MT diluted 1:40 and Cina 200c 1:20	Treatments increased** length and fresh weight of branches and roots, number of leaves/plant and foliar area; and reduced** gall number/plant; treatment before inoculation was more efficacious

Sukul et al., 2006 [44]	Lady's finger	Effect of homeopathic medicines on plants infected with nematode *Meloidogyne incognita*	Root gall number and nematode population	*Cina* 30c, Santonin 30c	Water; hydroalcoholic solution 30c	Spraying for 10 days, starting 7 days after inoculation. Each plant received 5-10 ml of treatment diluted in water 1:1000	Treatments reduced** root gall number and nematode population; and increased soil population
Betti et al., 2003 [45]	Tobacco	Effect of As_2O_3 on tobacco plants inoculated tobacco mosaic virus	Hypersensitivity lesions	As_2O_3 5x, 45x, 5cH and 45cH	Water; potentized water	10 disks of the 3rd or 4th inoculated leave from each plant were placed in Petri dishes with 15 ml of treatments	Decimal HD, 45x in particular, reduced** the number of hypersensitivity lesions
Sukul et al., 2001 [46]	Tomato	Effect of *Cina maritma* in HD on *Meloidogyne incognita*	Root gall number and nematode population	*Cina* 200c and 1000c	Globules impregnated with 90% hydroalcoholic solution	Leave spraying of 10 ml/plant of treatments (7.2 mg globules/ml distilled water), once per day, 10 days	*Cina* 200c reduced** gall number/plant; both HD reduced** the root nematode population
Sukul & Sukul 1999 [47]	Cowpea	Effect of *Cina maritma* on *Meloidogyne incognita*	Gall number; nematode population	*Cina* 1000c	Globules impregnated with 90% hydroalcoholic solution	Leave spraying	Reduction of gall number and root and soil nematode population

** Statistically significant difference. MT: mother tincture

Table 3. Main studies on the effect of homeopathic high dilutions on plants subjected to abiotic stress

Author; year	Species	Aims	Parameters	Treatment	Controls	Frequency and mode of application	Effects
Brizzi et al., 2011 [48]	Wheat	Effect of *Arsenicum album* 45x on germination of seeds previously exposed to As_2O_3	Germination rate	*Arsenicum album* 45x	Distilled water; distilled water 45x	Seeds were exposed to As_2O_3 30 min and rinsed (60 min) with water before treatments, heated 30 min at 20, 40, 70 and 100ºC (5 min)	*Arsenicum* 45x enhanced** seed germination; efficacy was not changed by heating up to 40ºC, but decreased at 100ºC

Jager et al., 2011 [49]	*Lemna gibba*	11 substances in HD on plant growth following exposure to As_2O_3	Number and foliar area; leave color	*Arsenicum album,* nosode, gibberellic acid, arsenic and other substances in various dilutions	Water; succussed water	Exposure to As_2O_3 48 h (intoxication), then plants were transferred to other containers with the treatments	*Arsenicum album* and nosode increased** the growth rate of plants
Jager et al., 2010 [50]	*Lemna gibba*	Effect of 3 substances in HD on plant growth after exposure to As_2O_3	Foliar area	*Arsenicum album,* nosode and gibberellic acid in various dilutions	Water; potentized water	Exposure to As_2O_3 48 h (intoxication), then plants were transferred to other containers with treatments	*Arsenicum album* and nosode increased** the growth rate of plants
Lahn-stein et al., 2009 [51]	Wheat	Effect of *Arsenicum album* in HD on germination of seeds exposed to As_2O_3 and seedling growth	Shoot growth	*Arsenicum album* 45x	Distilled water; distilled water 45x	Seeds exposed to As_2O_3 30 min, rinsed with water (60 min) and applied 3.3 ml of treatment	Reduction** of seedling growth
Binder et al., 2005 [52]	Wheat	Effect of *Arsenicum album* on seeds exposed to As_2O_3	Seedling growth	*Arsenicum album* 45x	Distilled water; water 45x	Seeds exposed to 0.1% As_2O_3 30 min, rinsed with water (60 min); treatments were placed in Petri dishes containing seeds	Reduction** of seedling growth
Brizzi et al., 2005 [53]	Wheat	Effect of As_2O_3 in HD on growth of plants exposed to sublethal dose of As_2O_3	Seedling length	As_2O_3 5x, 15x, 25x, 35x and 45x	Distilled water; potentized distilled water; diluted, not agitated As_2O_3	Seeds exposed to As_2O_3 30 min, rinsed with water (60 min) and applied 3.2 ml of treatments	As_2O_3 45x increased** seedling growth
Brizzi et al., 2000 [54]	Wheat	Effect of *Arsenicum album* on germination of seeds exposed to As_2O_3	Germination rate	As_2O_3 30x, 40x, 42x, 45x	Distilled water; potentized distilled water; diluted, not agitated As_2O_3	Seeds exposed to 0.1% As_2O_3 30 min, rinsed with water (60 min); treatments were placed in Petri dishes containing seeds	$As_2O_3$40x, 42x and 45x enhanced** germination of seeds exposed or not to As_2O_3; diluted As_2O_3 had no effect on germination
Betti et al., 1997 [55]	Wheat	Effect *Arsenicum album* 45x on seeds exposed to As_2O_3	Shoot and root growth	*Arsenicum album* 45x	Distilled water	Single application of 3.2 ml of treatments per container	24% increase** of shoot growth

** Statistically significant difference

Discussion

Recent reviews on the effect of homeopathic HD on plants [11-13] performed until 2011 analyzed 167 experimental studies described in 157 articles. These reviews were performed by a same group of authors, who applied a specific scale (MIS) to assess the methodological quality of studies. Scores (0 to 2) were attributed to 5 items: experiment design; materials; measurement instruments; potentization techniques; and type of controls.

Relative to the 167 analyzed experimental studies, global assessment [16] showed that 84 (50%) included statistical analysis and 48 (29%) attained the minimum score required (MIS ≥ 5) for adequate interpretation of results. 29 studies (17%) used adequate controls to detect specific effects of homeopathic HD; these studies found significant effects with HD over Avogadro's number. 10 studies (6%) systematically used negative controls (placebo group).

Among 48 experimental studies with MIS ≥ 5, wheat was the species most often used (23 studies), followed by dwarf pea and gibbous duckweed (3 studies each). Homeopathic agents most frequently used were: silver nitrate (9 studies), arsenic (8 studies), gibberellic acid (6 studies) and *Cina maritima* (4 studies). Various HD were tested; linear relationship was not found between HD level and effect size. Some studies applied a broad range of HDs to one same experimental model; the results showed that some HDs were active, while others were not. In healthy plants, some HD enhanced germination, while others inhibited it, which evidences the biphasic effect of the various concentrations [16,36].

Analysis of the reviews [16] showed that among 86 studies conducted with healthy plants [11] 43 (50%) included statistical analysis; 29 (34%) had MIS ≥ 5; 15 (17%) used adequate controls; and 5 (6%) systematically employed negative controls [28,30,32,33]. Among 44 studies that tested phytopathological models [12] 19 (43%) included statistical analysis; 6 (7%) had MIS ≥ 5; 6 (7%) used adequate controls; and 1 (2%) systematically employed negative controls [42]. Among 37 studies with plants exposed to abiotic stress [13], 22 (68%) included statistical analysis; 13 (35%) had MIS ≥ 5; 8 (22%) used adequate controls; and 4 (11%) systematic use of negative controls [48,50-52].

To assess the reproducibility of homeopathic experiments in plants, which might confirm the validity of isolated results, recent reviews [14,15] clustered studies per line of research. Among the models with healthy plants, experiments belonging to lines of research 'wheat seedlings & silver nitrate' [9,38,40,56,57), 'dwarf pea and gibberellic acid' [30,33], 'wheat seedlings/stalk growth & gibberellic acid [21-23,25,26] and 'wheat seedlings/germination & gibberellic acid' [24,58] stand out. Among the models with plants exposed to abiotic stress and following treatment, experiments of 'intoxication of wheat seedlings with arsenic & *Arsenicum album*' [48,53-55,59] predominated.

In the first review of studies of HD on plants, in 1984, Scofield [10] called the attention to methodological flaws in study design and development among the analyzed experiments, including: inadequate sample size; no statistical analysis; no detailed description of methods (selection and preparation of medicines, dose, mode of application, etc.) or controls; no double-blinding; inadequate control and reproducibility of experiments; and inadequate outcome measures, among others.

In addition to the aforementioned flaws, easily corrected through rigorous observance of the assumptions of the scientific method, aspects intrinsic to homeopathy make systematization and improvement of experiments difficult, such as the complexity inherent to selection of individualized medicines and application of HD. However, analysis of the studies published in the past decades evidenced a qualitative leap in the research conducted with homeopathic HD in plants, including suggestions for improvement of the design, development and description of this type of experiments [17,60-64].

Although systematic use of negative controls and reproducibility ought to be routine components of future studies with homeopathic HD on plants to ensure the system stability, exclude false-positive results and confirm the validity of results, some aspects might hinder their internal or external reproducibility, such as: relevant parameters that cannot be controlled; inadequate outcome measures; and inherent irreproducibility. Many false-positive results might be related to artifact, be the result of contamination, systematic deviation or random noise of the experimental design, while they are mistakenly interpreted as effects of treatment [14,15].

According to Baumgartner [17,60,65] the reproducibility of homeopathic experiments is a complex issue, as a function of the many factors involved, for which reason interactive approaches are needed.

As mentioned above, we need to stress once again the need for researchers to congregate around the production of a homeopathic materia medica specific for plants, a project launched in Brazil in 2003 [5-8,20,66,67]. The availability of such materia medica is an indispensable requirement for the selection of individualized medicines for treatment of the various plant disorders and diseases. This need recently reasserted by other authors [13,16,22], such materia medica would allow for the application of the classic therapeutic similitude principle based on the similarity between the signs and symptoms elicited by homeopathic medicines during homeopathic pathogenetic trials on plants and the signs and symptoms exhibited by the plant species to be treated. Except for isotherapy – which employs HD of pathogens to prevent and/or treat the harmful effects they themselves cause (analogously to immunization and immunotherapy in humans, respectively), the vast majority of medicines used for homeopathic treatment of plants is empirically and unspecifically selected (without description of the method of selection used), but analogically from the signs and symptoms described in the traditionally materia medica (result of pathogenetic trials of substances on human beings).

As a complementary suggestion and reproducing our work with modern drugs in the past decade (with the goal to use them based on the similarity between the adverse effects they induce and the signs and symptoms of patients, see *New homeopathic medicines: use of modern drugs according to the similitude principle*, www.newhomeopathicmedicines.com) [68-73] a homeopathic materia medica for plants might begin by the survey, systematization and organization of the signs and symptoms elicited in plants by the various substances commonly used in agricultural practice (mineral, pesticides, fertilizers, etc.) to be later complemented with classical homeopathic pathogenetic trials.

To illustrate the validity of this method, the study by Betti et al. [45] employed arsenic trioxide (As_2O_3) to reduce the severity of infection with the tobacco mosaic virus (TMV). The medicine was selected based on the classical therapeutic similitude principle, i.e., similarity of signs and symptoms, once the authors observed that application of As_2O_3 in toxic dose to tobacco leaves caused lesions similar to the ones of TMV-induced hypersensitivity. The results showed that homeopathic treatment with As_2O_3 in HD significantly increased the plant resistance to TMV, assessed based on the number of hypersensitivity lesions.

Betti's group also succeeded in reducing the symptoms caused by fungus *Alternaria brassicicola* to cauliflower with As_2O_3 35x. This medicine was selected based on a pathogenetic trial of 1mM As_2O_3 on cauliflower, which resulted in symptoms similar to the ones induced by the fungus [74].

Similar studies conducted in Brazil detected similarity between the pathogenetic signs and symptoms of eucalyptus oil on bean plants and the ones caused by fungus *Pseudocercospora griseola,* namely, the etiologic agent of angular leaf spot [66,75]. Studies on reduction of infection of bean plants with *P. griseola* are still incipient, but point to possible control of angular leaf spot with potentized eucalyptus oil [76] via activation of biochemical mechanisms of plant defense [77].

Conclusions

Effect of homeopathic HD on plants was demonstrated in various experimental models with satisfactory methodological quality. These studies systematically employed negative controls and exhibited reproducibility, with consequent reduction of the odds of false-positive results; thus the validity of the results is confirmed.

In addition to the confirmation of the effect of HD on various biological systems, the positive results of homeopathic experiments with plants lend support to the plausibility of homeopathic treatment for human diseases, as factors doctor-patient relationship and placebo effect – commonly mentioned by skeptics to account for the improvement observed in homeopathic clinical practice – are absent.

The methodological flaws of the older studies notwithstanding, the advances in homeopathic research on plants made in the past decades – as a function of the advantages proper to this experimental model and of an increasing interest in the use of homeopathy in agroecology - point to a promising field of research to elucidate the particularities of the mechanism of action of homeopathic HD and to broaden the scope of their therapeutic use.

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