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The *in vitro* evidence for an effect of high homeopathic potencies—A systematic review of the literature

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Neutrophiles;
Lymphocytes;
In vitro

Summary
Objective: Systematic assessment of the *in vitro* research on high potency effects.
Method: Publications of experiments were collected through databases, experts, previous reviews, citation tracking. Inclusion criteria: stepwise agitated dilutions $<10^{-23}$; cells or molecules from human or animal. Experiments were assessed with the modified SAPEH score.
Results: From 75 publications, 67 experiments (1/3 of them replications) were evaluated. Nearly 3/4 of them found a high potency effect, and 2/3 of those 18 that scored 6 points or more and controlled contamination. Nearly 3/4 of all replications were positive. Design and experimental models of the reviewed experiments were inhomogenous, most were performed on basophiles.
Conclusions: Even experiments with a high methodological standard could demonstrate an effect of high potencies. No positive result was stable enough to be reproduced by all investigators. A general adoption of successed controls, randomization and blinding would strengthen the evidence of future experiments.

Introduction

Homeopathic remedies are prepared ('potentized' or 'dynamized') in steps of alternately diluting and successing a homeopathic stock[1] (historically known as 'mother tincture'). After several steps,

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the remedies reach calculatory dilutions beyond Avogadro's number, implying a non-molecular action of remedies with specific healing properties. Research in this field arranges around three core problems[2]: (1) What are the therapeutic effects of homeopathic remedies? (2) What are the specific characteristics of potencies? (3) Through what mechanism(s) do they influence the organism? Relating to (1) and (3), *in vitro* research searches for effects of potentized remedies on molecular or cellular systems. Reducing complexity this way allows a higher degree of standardization than clinical research, and may eventually provide model systems to reveal the mode of action of high dilutions devoid of pharmacologically active molecules.

Previous reviews of the field have been either descriptions of individual experiments without systematic evaluation[3–7], investigations of only the independence of replications[8], or do not present details and rationales of their scoring procedure.[9] Other restrictions had been set on publications language[3,4,6] or research area,[7,8] so that a both broad and systematic assessment with transparent criteria does not exist. In this evaluation we therefore systematically assessed the *in vitro* research on effects of high potencies of a stock preparation by using a score system. Additionally, we tried to identify experimental models that provide reproducible results or promising approaches that should be replicated.

Methods

Inclusion criteria and data sources

We searched for written publications of *in vitro* investigations on high potencies. *In vitro* was defined as 'concerning cellular or subcellular entities in isolation from a living organism'. This included cells (also from cultures) or molecules, but not isolated organs. All systems had to be of human or animal origin. Pathological materials such as cancer cells or cells from allergic donators were accepted. Pretreatment before cell extraction, such as intoxication or sensitization, was allowed, but the application of homeopathic preparations had to be *in vitro* only. Tested remedies had to include high potencies that imply a calculatory dilution of at least 10^{-23} (e.g. $\geq$D23, $\geq$C12). Remedy mixtures ('complex remedies') were allowed. No other restrictions were imposed; all publication languages were included.

References from the Basic Research Database of the Karl and Veronica Carstens-Foundation, D-Essen,[10,11] were collected until December 2005 by searching for 'homöopathie + basic research + experimental + *in vitro*' in each of the following fields: immunology, toxicology, pharmacology, neurology, biochemistry. Medline® was searched for publications of the years 1966 until December 2005 using MeSH and full text terms in various spellings. Searched was for 'homeopathy' combined with each of the following terms: '*in vitro*'; 'cell culture'; 'tissue culture'; 'cells, cultured'; 'granulocyte'; 'lymphocyte'; 'macrophage'; 'neutrophil'; 'basophil'; 'enzyme'; 'biomolecule'; 'immunocompetent'. Amed® (Allied and Alternative Medicine) was searched from 1985 to December 2005 using the same search as in Medline. Previous reviews,[3–6,8,9] and all obtained publications were screened for further references. In addition, we asked experts for information.

Data extraction

From the identified references, those too short for a sensible scoring were excluded, among them were all abstracts. From publications that were mostly or fully identical or obviously referring to identical experiments only the most detailed description was included. One author (MB) extracted data and scored the experiments except his own paper[12] that was scored by another author (SB) who did not participate in this work, the data were discussed with a second author (CMW). For each experiment the following data were extracted: publication, objective, technique, findings, substance tested, control or comparison, and solvent of potentizing, together with additional information of interest. All identified publications were classified by system: non-cellular systems (enzymes), or cellular systems of the categories cultured cells, erythrocytes, basophile granulocytes, neutrophile granulocytes, and lymphocytes/mononuclear cells (including experiments with both neutrophiles and lymphocytes).

Strategies involved either cellular or cell-free systems, the former from healthy or from pathological donators. Indirect effects in which the potency modified the action of a stimulus on the target system were set apart from direct effects where the homeopathic preparation acted on the target system directly.

Replications were recognized when they investigated the same experimental setup (cell, enzyme, stimulant, noxa, ...) with the same homeopathic remedy in high (but not necessarily identical) potency. They were operationally defined as 'independent' if the publication had a different first author and less than half of their authors had published experiments with this model before.[8] Finally,

Table 1 The modified SAPEH (score for assessment of physical experiments on homeopathy)

Item	Points	Criteria
Objectives[P]	1	Explicit statement what problem or hypothesis was investigated
Controls[M]		
Declared	1	Stated use of controls
Adequate	+1	Succussed or correspondingly potentized solvent
Inadequate	−1	Not checking contamination, e.g. unsuccussed
Blinding[M]	1	Blinding of experimenter/tester
Randomization[M]	1	State of the art samples randomization
Consistency[M]	1	Similar results in two or more experiments or test series
Experiment standardization[S]		
Medium	1	Use of a buffer or buffered medium if necessary
Incubation	1	Standardized temperature and incubation time
Statistics[M]	1	Statistical analysis declared or described
Results[P]	1	Comprehensible presentation of results

[P]Presentation, [M]Methodology, [S]Standardization: quality constructs built into the score. Modifications check for buffer and incubation.

it was noted whether the publications stated or implied that the findings supported the existence of effects of high potencies for at least one of the tested potencies, or, in multicenter trials, at least one laboratory.

Modified SAPEH assessment

To provide a transparent and differentiated insight into the strengths and weaknesses of the assessed research, we applied a modified version of the Score for Assessment of Physical Experiments on Homeopathy (SAPEH, Table 1). SAPEH had been developed to assess the quality of physical research in homeopathy.[13] It is based on three quality constructs — methodology, experiment standardization, presentation — that divide into 8 items, checking for 10 criteria. Each item scores 1 point for an affirmative answer, except controls and experiment standardization with 2 points each.

The methodology items check that the experimental design uses techniques to control factors that may cause bias (e.g. systematic or random errors). Mentioning controls scores 1 point that is subtracted again if their nature allows for chemical differences to the potencies. Identical composition is assumed if controls have undergone a similar contaminant-affecting preparation (succussion or potentizing)[13] as the test potencies. It would earn 2 controls points, accepted are all meaningful descriptions such as ''produced like the verum'' or ''succussed (shaken, vortexed, sonicated, ...) medium''. Further methodology items cover blinding (preventing handling differences and bias effects), randomization (to prevent systematical errors), consistency (internal replications, ensuring test system stability), and the use of statistics.

Experiment standardization was adapted to the *in vitro* field, instead of the somewhat unspecific original criteria 'external factors' and 'experimental setup' that can affect results, the item now checks for the use of a buffer or buffered medium, and for standardized temperature and incubation time.

The remaining communication about the experiment is covered by presentation of objectives and results, which have to be reasonably detailed and understandable.

The modified SAPEH should be read at item level to assess an experiment. The total SAPEH score and its subscores support only rough global impressions and should always be accompanied by score details. For the purposes of the present study, 6 or 7 points with controls of equal contamination would indicate a reasonable control for bias, and >7 points (including 2 for controls) would strengthen this.

Results

Literature

We identified and obtained 75 publications[12,14–87] that fulfilled inclusion criteria, among them one sufficiently detailed correspondence.[45] Seventeen redundant publications were identified (Fig. 1): Three doctoral theses[12,33,35] were included that cover and extend the content of eight omitted papers: 71–75, 76; 77, and 78, respectively. Two summaries[79,87] of otherwise included experiments were ignored. From another summary[62] those parts

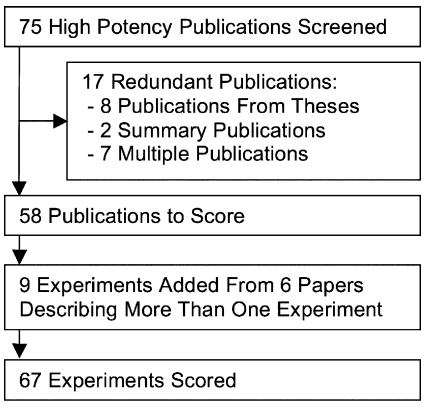

Figure 1 Publications and experiments.

were excluded that were less detailed than earlier papers.[56,57] Where the analyzed data set of an earlier publication[58] seemed to be not identical to the summary data[88] we scored both. Of publications with seemingly identical content, the first listed in each of the following groups was included: 31/80; 41/81; 66/83; 67/82; 68/84/85; 36/86.

Two papers[48,50] overlapped in content, the more detailed later one was included, whereas from the earlier publication we included only one additional experiment. Of two articles about the same research, two experiments were reviewed from the earlier publication[14] and one additional experiment from the other.[15] From one paper[37] one already published experiment was ignored in favor of the earlier publication.[34] Multiple experiments in a single publication[12,19,37,42,62,70] were scored individually, resulting in 67 experiments from 58 publications. Table 2 (published in online version at http://www.sciencedirect.com/as supplementary data) lists the details, together with some contextual information to provide a broader overview.

The included publications had appeared mostly in journal articles ($n = 46$), 25 of them were of

Table 3 Modified SAPEH scores and classifications of reviewed experiments

Language[a]	Strategy[b]	Replications	Criterion[c] =>	Objectives	Controls[d]	Blinding	Randomiz'n	Consist'y	Standardiz'n	Statistics	Results Pres.	Subscores			mod. SAPEH	Results[e]
			Quality Construct[c] =>	P	M	M	M	M	S	M	P	P	M	S	Σ	
			Maximum Points[c] =>	1	2	1	1	1	2	1	1	2	6	2	10	
			Non-Cellular Systems													
G	d/cf		Persson and Ginsberg, 1932	1	0*	0	0	1	1	0	1	2	1	1	4	+
G	d/cf		Persson, 1933	1	0*	0	0	1	1	0	1	2	1	1	4	+
G	d/cf		Persson, 1938	1	0*	0	0	0	1	0	1	2	0	1	3	+
E	d/cf		Boyd and Brit, 1954	1	2	1	1	1	1	1	1	2	6	1	9	+
F	d/cf		Kraus et al., 1981	1	0*	1	0	1	2	0	1	2	2	2	6	+
E	d/cf		Jussal et al., 1984 / Belladonna	0	0	0	0	0	2	0	0	0	0	2	2	+
E	d/cf		~ / Arsenicum	0	0*	0	0	1	0	0	0	0	1	0	1	+
E	d/cf		Petit et al., 1989	1	0*	0	0	1	2	0	1	2	1	2	5	–
E	d/cf		Shabir et al., 1996	1	0*	0	0	1	2	1	1	2	2	2	6	+
G	d/cf		Harisch and Dittmann, 1997	1	0*	1	0	1	2	1	1	2	3	2	7	+
G	d/cf		Harisch and Dittmann, 1998	1	0*	0	0	1	2	1	1	2	2	2	6	+
G	d/cf		Harisch and Dittmann, 1999 (Ubiqinone)	1	0*	1	0	1	2	1	1	2	3	2	7	+
G	d/cf		Harisch and Dittmann, 1999 (cAMP)	1	0*	1	0	1	2	1	1	2	3	2	7	+
G	d/cf		Dittmann et al., 2000	1	0*	1	0	0	2	1	1	2	2	2	6	+
E	d/cf		Sukul et al., 2002	1	2	0	0	0	2	1	1	2	3	2	7	+
E	d/cf		Batello, 2002	1	0*	0	0	1	2	1	1	2	2	2	6	+
G	d/cf		Bluth, 2005 / Amylase	1	2	0	0	1	2	1	1	2	4	2	8	–
G	d/cf		~ / Diastase	1	2	1	1	0	1	1	1	2	5	1	8	–
			Cultured Cells													
E	d/c/p		Mansvelt and Amons, 1975	1	0*	0	1	1	2	1	1	2	3	2	7	–
F	i/c/p		Aubin et al., 1980	1	0*	0	0	1	2	0	0	1	1	2	4	–
F	i/c/h		Boiron et al., 1981	1	2	0	0	1	2	1	0	1	4	2	7	–
G	d/c/p		Kandefer-Szerszen et al., 1993	1	2	0	0	1	2	0	1	2	3	2	7	+
F	i/c/p		Delbancut, 1994	1	2	0	0	1	2	1	1	2	4	2	8	+
G	d/c/h		Pison et al., 1995	1	2	0	0	1	1	1	1	2	4	1	7	–
G	i/c/p		Then, 1995	1	0*	1	0	1	2	1	1	2	3	2	7	–
E	d/c/p		Carmine, 1997	1	2	0	0	1	1	1	1	2	4	1	7	+
G	i/c/h		Herberth and Pison, 1999 / TNF	1	0*	0	0	1	1	1	1	2	2	1	5	–
G	i/c/h		~ / Leucocytes	1	0*	0	0	1	1	1	1	2	2	1	5	–
G	i/c/h		~ / Alveolar Cells	1	0	0	0	0	0	0	0	1	0	0	1	–
E	i/c/h		Jonas et al., 2001	1	2	0	0	1	2	1	1	2	4	2	8	+
E	i/c/p		Marotta et al., 2002	1	2	0	1	1	2	1	1	2	5	2	9	+
			Erythrocytes													
E	d/c/h		Sukul et al., 2003 / Erythrocytes	1	2	0	0	0	1	1	0	1	3	1	5	+
E	i/c/h		~ / Ethanol Intoxication	1	2	0	0	0	1	1	0	1	3	1	5	+

Table 3 (*Continued*)

			Basophile Granulocytes												
F	i/c/p		Murrieta et al., 1985	1	0*	0	0	0	2	1	1	2	1	2	5	–
F	i/c/p		Poitevin et al., 1985	1	0*	0	0	1	2	1	1	2	2	2	6	+
F	i/c/p		Sainte-Laudy and Belon, 1986 / Histamine	1	2	0	0	1	1	0	1	2	3	1	6	+
F	i/c/p		~ / PAF	1	0	0	0	0	1	0	1	2	0	1	3	+
E	i/c/p		Belon, 1987	1	0*	0	0	1**	2	1	1	2	1	2	5	+
E	d/c/h	●	Davenas et al., 1988	1	0*	1	1	1	2	1	1	2	4	2	8	+
E	d/c/p	●	Metzger and Dreskin, 1988	1	0*	1	0	1	2	0	1	2	2	2	6	–
E	i/c/h	●	Poitevin et al., 1988	1	0*	1	0	1	2	1	1	2	3	2	7	+
F	i/c/p	●	Ruff et al., 1988	1	0*	1	0	0	2	1	0	1	2	2	5	+
E	i/c/p	●	Sainte-Laudy, 1989	1	0*	0	0	1	2	1	1	2	2	2	6	+
F	d/c/h	●	Benveniste et al., 1991	1	2	1	0	1	2	1	1	2	5	2	9	+
E	i/c/p	●	Sainte-Laudy et al., 1991	1	0*	0	0	1	2	1	1	2	2	2	6	+
E	i/c/h	●	Sainte-Laudy and Belon, 1991	1	2	1	1	1	2	1	0	1	6	2	9	+
E	d/c/h	●	Övelgönne et al., 1992	1	0*	1	1	1	2	1	1	2	4	2	8	–
E	d/c/h	●	Hirst et al., 1993	1	2	1	1	1	2	1	1	2	6	2	10	–
E	i/c/h	●	Sainte-Laudy and Belon, 1993	1	0*	1	1	1	2	1	1	2	4	2	8	+
E	i/c/h	●	Sainte-Laudy and Belon, 1996	1	0*	0	0	1	2	1	1	2	2	2	6	+
E	i/c/h	●	Sainte-Laudy and Belon, 1997	1	0*	0	0	1	2	1	1	2	2	2	6	+
E	i/c/h	●	Belon et al., 1999	1	2	1	1	1	2	1	1	2	6	2	10	+
E	i/c/h	●	Brown and Ennis, 2001	1	0*	0	0	1	2	1	1	2	2	2	6	+
E	i/c/h	●	Sainte-Laudy, 2001	1	2	0	0	1	2	1	0	1	4	2	7	+
E	i/c/h	●	Lorenz et al., 2003 (Solvents)	1	0*	1	1	1	2	1	1	2	4	2	8	+
E	i/c/h	●	Lorenz et al., 2003 (Protocols)	1	0*	1	0	1	2	0	1	2	2	2	6	+
E	i/c/h	●	Belon et al., 2004 / Flow cytometry (#2)	1	0*	0	0	1	2	1	1	2	2	2	6	+
E	i/c/h	●	~ / Histamine release (#3A)	1	0*	0	0	1	2	1	0	1	2	2	5	+
E	i/c/h	●	~ / H2 Antagonist (#3B)	1	0*	0	0	1	2	1	0	1	2	2	5	+
E	i/c/h	●	~ / Histidine (#3C)	0	0*	0	0	1	2	1	0	0	2	2	4	+
E	i/c/h	●	Guggisberg et al., 2005	1	2	1	1	1	2	1	1	2	6	2	10	–
			Neutrophile Granulocytes												
G	d/c/h		Fanselow, 1984	1	0*	0	0	1	1	1	1	2	2	1	5	–
E	i/c/h		Chirumbolo et al., 1993	1	0*	0	0	1	2	1	1	2	2	2	6	+
			Lymphocytes												
F	i/c/h	●	Bildet et al., 1984	1	0*	1	0	1	0	1	1	2	3	0	5	–
F	i/c/h	●	Colas et al., 1984	1	0*	0	0	1	2	0	1	2	1	2	5	+
E	i/c/p		Chirila et al., 1992	1	2	0	0	1	2	0	0	1	3	2	6	+
E	d/c/p		Gibson and Gibson, 1996	1	0*	0	0	1	1	1	1	2	2	1	5	+

[a] Publications languages: E = English, F = French, G = German.
[b] Research strategy: d/cf = direct effect on cell-free system; d/c/h = direct effect on cells from healthy probands; d/c/p = direct effects on cells from pathological donators; i/c/h = indirect effects on cells from healthy probands; i/c/p = indirect effects on cells from pathological donators.
[c] For criteria, quality constructs (P = Presentation, M = Methodology, S = Standardization) and score points see text and Table 1.
[d] 0* = (+1−1), see text.
[e] Findings support the existence of a high potency effect (+) or not (−) (stated or implied).
** Only for histamine part.

the mainstream: organs of conventional medicine ($n = 12$), sciences in general ($n = 7$), or biological medicine ($n = 6$). The other 21 articles appeared in periodicals of homeopathy in general ($n = 15$), homeopathic research ($n = 3$), or complementary and alternative medicine ($n = 3$). The remaining 12 publications were dissertations ($n = 7$, including 1 comparable thesis for a homeopathy diploma (28)), congress presentations ($n = 3$), and books ($n = 2$). Most authors had published in English (57%), followed by German (25%) and French (18%).

Experiments

The investigated systems were mostly basophile granulocytes (42%), non-cellular systems (27%), and cultured cells (19%). Seldom lymphocytes (6%), erythrocytes (3%), or neutrophiles (3%) were chosen. Measuring indirect effects on healthy proband cells was the most favoured approach (37%), followed by direct effects on cell-free systems (27%), indirect effects on cells from pathological sources (19%), direct effects on cells from healthy (10%) and pathological (8%) donators. Table 3 lists the classifications of the assessed experiments.

Presentation was sufficiently good for most (79%) experiments (Table 3); 16% lacked a clear description of either objectives or results and 4% of both. Randomization was only reported for 18% and blinding for 33% of the experiments. For most investigations at least one successful replication was stated (83%), 31% checked contamination with succussed controls, in 4% no use of controls was stated. Statistical evaluation was common (76%). In 73% of the experiments buffer and incubation were standardized, in 22% only one of these was mentioned,

and in 4% none. The overall modified SAPEH mean was 6.1 (S.D. $\pm$1.9, median 6.0). Most experiments were done with basophiles models, here also the most positive results were found.

From the 67 assessed experiments, 73% stated an effect of high potencies. So did 68% of the 18 experiments with succussed controls and a modified SAPEH score of at least 6 points. Eight of these 19 experiments have not been replicated. Of all scored experiments, 33% were replications. Positive results were reported for 73% of the replications, and for 18% of those with 6 or more points and succussed controls. Replications were most often performed with flow cytometry on basophiles, here mostly by independent teams and with positive results except one.[63] All attempts to replicate effects on hydrolase activity were independent and successful but one.[12] The action of anti-IgE potencies on basophiles was only reproduced by the same team.

Discussion

We systematically assessed *in vitro* experiments on high potencies with the modified SAPEH score. The designs of the 67 evaluated experiments were very inhomogenous. We observed an uneven distribution of the investigated systems, ranging from two unrelated experiments each with neutrophile granulocytes or erythrocytes to 28 with basophiles (15 of them being replications). One third of the experiments were replications of earlier research. Nearly 3/4 of the identified experiments found a high potency effect. Even if only those experiments that tried best to exclude bias were considered (SAPEH score of 6 points or more and succussed controls), a positive effect was still demonstrated in more than 2/3 of the experiments. Although it seems unlikely, we could not be totally sure that the results of these experiments are unbiased.

Publications on homeopathic research are widely scattered, often not entered into databases, and thus difficult to find. The database of the Karl and Veronica Carstens-Foundation was very helpful. In addition citation tracking and expert contacts enlarged the number of found publications. Presentations at conferences of either basic or clinical research are not too often followed up by journal articles (e.g. only half of the conventional randomized clinical trials[89])—the reason why we did not restrict our search to full articles. Publication bias that is very likely in the field of homeopathy[90] would cause a tendency to positive results. For example, unsuccessful pilot studies in search for a viable test system may not have been published. But the existence of more negative studies would not rebut those high-scoring works that demonstrated an effect of potentizing beyond Avogadro's number. Compared to a previous evaluation of physical research on high potencies[13] we found in the present review more *in vitro* investigations for the same time frame (until 2001, 53 experiments *in vitro* versus 37 in physics). We observed also a greater percentage of experiments scoring at least 6 points with succussed controls (26% versus 14%), more replications (25% versus 8%), and more publications in renowned periodicals.

Applying a score to assess publications systematically is not common in basic research on homeopathy. Although scores have limitations we decided for it because of the benefits of systematizing the synopsis and making the assessment criteria transparent. Most relevant works are well known which made blinded scoring or split assessments of methods and results impossible. We tried to achieve high internal consistency by having all scoring done by one investigator. This review is limited to the presentation of experiments in the literature, as common for reviews, presuming correctness and accuracy of the reports, but it can never be sufficiently detailed to set up reproductions. Because SAPEH was designed for quick and easy use, we accepted a limitation that lies in not accounting for the number of repetitions, which would have to be observed on several levels. The number of independently produced potencies, test runs per potency, samples per test run, variations in date or location, etc. would require a much more detailed score system.

From the mostly self-explaining SAPEH score the items blinding, standardization, and controls require some discussion. In order to identify results that were the most robust to bias and systematic errors[91] we included blinding as a criterion. Although probably rare, unconscious bias may creep in through processes that involve human interpretation or judgment, or minute differences in handling. The additional standardization through a buffered medium reduces the variability of results that otherwise might mask a difference between sample types.

To prove that high potencies have a specific effect they should only differ from controls in being a potentized stock preparation. Several types of controls or comparisons are available: stock preparation (original material of remedy preparation), unsuccussed solvent, succussed solvent, and another remedy (potency of different stock preparation). A stock preparation would entail gross chemical differences. Untreated solvent has recently been found to be different from a potency

in the concentration of contaminants that are introduced during the potentizing through interactions of solvent and container material.[92] In multi-container potencies (Hahnemann technique), trace element concentrations had reached with the first potency a level that remained constant in higher potencies.[39,92] This applied to potentization with standard parameters[93] that are commonly adopted in basic research. Differences between untreated and potentized[36,37] or simply sonicated[94] solvent have been observed in biological activity as well as physical measurements[95], they might be causally linked to contamination.[92,95]. Trace elements are the rationale for our emphasis on succussed — better: fully potentized — controls. Other contaminants make the fully identical preparation more desirable, like acetate, formate or lactate from the human skin, or methanol and acetone used for cleaning, all easily being introduced with ordinary handling.[96] A second remedy as control might in the lower (material) dilutions have its own interaction with container materials[97], making a solution of which the exact composition is unknown but which is likely to be different from the one of the first potency. Both thus would differ not only in their known initial stock preparation. Moreover, the effect of both potencies on the measurements might be identical which would invalidate a clearly 'negative' result to mean merely 'possibly negative, or possibly positive but differences cancelled out'. For the purposes of the present review we asked for the type of control that allowed the clearest conclusions.

Conclusions

The reviewed *in vitro* experiments with high homeopathic potencies were inhomogenous in design and quality. A surprisingly high number of different experimental approaches have been adopted. Two thirds of the experiments with higher scores and contaminant-checking controls demonstrated specific high potency effects. Some of them have also been successfully replicated, but no positive result could be reproduced in all attempts. Among those that have been replicated by independent investigators the action of mercuric bichloride on hydrolases and especially the action of histamine of the Anti-IgE triggered basophile granulocyte degranulation seemed to be the best reproducible. A publication bias in a highly controversial field like homeopathy is not unlikely. More replications should be done independently to establish models that are stable across laboratories and teams. A general adoption of succussed controls, randomization and blinding would strengthen the evidence of further experiments.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ctim.2007.01.011.

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