Homeopathy (2010) 99, 25–36

doi:10.1016/j.homp.2009.11.008, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Repetitions of fundamental research models for homeopathically prepared dilutions beyond 10^{-23}: a bibliometric study

PC Endler[1], K Thieves[1], C Reich[1,*], P Matthiessen[2], L Bonamin[3], C Scherr[4] and S Baumgartner[4,5]

[1]*Interuniversity College for Health and Development Graz/Castle of Seggau, Austria*
[2]*Centre for Integrative Medicine, University of Witten/Herdecke, Germany*
[3]*Universidade Paulista, Sao Paulo, Brazil*
[4]*Hiscia Institute, Society for Cancer Research, Arlesheim, Switzerland*
[5]*Institute of Complementary Medicine KIKOM, University of Bern, Switzerland*

Introduction: **Repeatability of experiments is an important criterion of modern research and a major challenge for homeopathic basic research. There is no recent overview about basic research studies in high homeopathic potencies that have been subjected to laboratory-internal, multicenter or independent repetition trials.**
Methods: **We considered biochemical, immunological, botanical, cell biological and zoological studies on high potencies, i.e. beyond a dilution of 10^{-23}. Main sources of information were reviews, personal contact with members of the homeopathic basic research community, and the MEDLINE and HOMBREX databases. Studies were extracted from the publications and grouped into models. Studies were further sorted according to repetition type (laboratory-internal, multicenter, or independent) and results achieved.**
Results: **A total of 107 studies were found. Of these, 30 were initial studies. In the attempt to reproduce one of these initial studies, 53 follow-up studies yielded comparable effects (35 laboratory-internal, 8 multicenter, 10 independent repetitions), eight studies showed a consistent, yet different result from the initial study (2 laboratory-internal, 2 multicenter, 4 independent repetitions), and 16 studies yielded no effects (5 laboratory-internal, 2 multicenter, 9 independent repetitions). When all repetitive studies are considered, 69% reported effects comparable to that of the initial study, 10% different effects, and 21% no effects. Independently performed repetition studies reported 44% comparable effects, 17% different effects, and 39% no effects.**
Conclusions: **We identified 24 experimental models in basic research on high homeopathic potencies, which were repeatedly investigated. 22 models were reproduced with comparable results, 6 models with different results, and repetition showed no results for 15 models. Independent reproductions with either comparable or different results were found for seven models. We encourage further repetition trials of published studies, in order to learn more about the model systems used and in order to test their repeatability.** *Homeopathy* (2010) **99**, 25–36.

Keywords: review; basic research; homeopathy; potentisation; ultra high dilutions

*Correspondence: Interuniversity College for Health and Development Graz/Castle of Seggau, Petrifelderstr. 4, A-8042 Graz, Austria.
E-mail: college@inter-uni.net

Introduction

Repeatability of experiments is one of the main features of deterministic systems. Scientists therefore routinely investigate experimental reproducibility to identify such systems. One of the main questions of basic research into homeopathic preparations is whether the effects of the latter are deterministic in their very nature or not.[1,2]

This publication therefore tries to give an overview of fundamental biochemical and biological studies that used high homeopathic potencies, and that have been subjected to laboratory-internal, multicenter or independent repetition trials. In other words, physicochemical or clinical studies were not included, nor studies on dilutions below 10^{-23}, nor studies in relation to which no attempt of repetition has been found in literature.

With regard to their importance for scientific research in ultra high dilutions and homeopathy, *internal* repetitions (from the same laboratory or working group), multicenter trials (as a rule centrally organized multicenter approaches with team authorship publications) and *external* repetitions (i.e. an independent researcher in an independent laboratory with an independent publication) were considered. To perform this overview classification, a certain broadness of clusters concerning methodological details of the studies concerned was necessary (see below Methods).

Methods

Literature search

Sources of information were reviews,[1–11] personal contact with members of the homeopathic basic research community, and the MEDLINE (www.pubmed.gov) and HOMBREX (www.carstens-stiftung.de) databases. Allowed literature sources were publications (in peer-reviewed and not peer-reviewed journals, book chapters and books) and theses. Although we have done all that is practical to identify relevant studies, the annotated bibliography presented here does not claim to be exhaustive.

Inclusion criteria

We included biochemical, immunological, botanical, cell biological and zoological studies on high potencies, i.e. ≥12c or 24x. Studies published after 1940 had to report evaluation of results by statistical methods (minimum requirement: mean or median, number [*n*] of samples, standard deviation or standard error, OR number *n* of samples, level of significance of a statistical test). Results reported, i.e. differences between potency and control group, were statistically significant or not significant.

To be included the experiment had to have been repeated. Repetition was formally defined by identifying either at least two publications with independent authorship (dealing with the same experimental model, see below), or at least one publication reporting on a multicenter trial (independent experiments in different locations/laboratories, organized by one study coordinator), or at least two publications by the same initial working group, including a follow-up trial of an initial publication (internal repetition).

Furthermore, a repetition was defined by the use of one and the same experimental model (e.g. algae Chlorella) and one and the same potentized substance (e.g. copper sulfate). Within these clusters, however, some differences were accepted both in the model (e.g. the use of *Chlorella vulgaris* or *Chlorella pyrenoidosa*), in the potency level (e.g. 25x or 30x) and potency type (centesimal (c) or decimal (x)) and in the nature of the control (e.g. unsuccussed, succussed, potentized, or type not mentioned).

One and the same publication could refer to the results of more than one study. Specifically for multi-centre trials, the number of studies corresponds to the number of independent experiments in different locations/laboratories. We extracted all studies from the included publications and grouped them into experimental models (see above). Studies were further sorted according to results achieved (consistent/different/none) as well as repetition type (within-laboratory/multicenter/independent).

Studies were sorted according to the results achieved as follows:

1. *Initial* studies that have meanwhile led to follow-up studies.
2. Repeated studies referring to (1), the results of which were *consistent* with (1), i.e. where a *comparable* effect (in the same direction, e.g. enhancing growth) was found.
3. Repeated studies referring to (1), the results of which were statistically significant, but *different* from (1), i.e. when effects were *different* in direction (e.g. decreasing instead of increasing).
4. Repeated studies referring to (1), the results of which were not statistically significant, i.e. where *no* effect was found.

Study types 1–4 were furthermore classified according to repetition type:

A. Studies that have essentially been performed by one researcher or one working group ('initial working group studies'). When the name of that person could not be identified from the publication, the first author's name was mentioned. This category also includes repetitions by one and the same researcher and successive repetitions by different researchers in one and the same laboratory.
B. Multicenter studies, i.e. studies that were centrally organized, but carried out by various researchers in different laboratories, normally leading to a team authorship publication.
C. Independent repetitions, i.e. studies that were carried out in an independent laboratory, organized independently from the initial laboratory.

Results

Table 1 classifies the identified investigations according to the results achieved (comparable, different, no effect) and the type of repetition (internal, multicenter, independent). Basically, a total of 24 *models* were concerned[12–98]. In 85 *publications*,[12–60,62–95,97,98] a total of 107 *studies* were found: one publication could refer to the results of more than one study. Two further publications[61,96] provided additional details to other publications.[62,95]

Table 1 Repeated fundamental research studies into homeopathically prepared dilutions beyond 10^{-23}. Studies were classified according the results achieved (comparable, different, no effect) and the type of replication (internal, multicenter, independent trial). Multicenter studies were listed separately for the centres involved. The name of the researcher is mentioned when it could be identified from the publication, otherwise the first author's name is referred to

Model no.	*Workgroup*	*1: Initial study*	*2: Repetition*	*3: Repetition*	*4: Repetition*
			Comparable effect	*Different effect*	*Zero effect*
1. Biochemistry: enzyme diastase & mercury chloride					
A	Primary	Persson[12]			
B	Multicenter				
C	Independent			Boyd[82]	Bluth[88]
Summary: increase or decrease of enzyme reaction in 2 out of 3 studies					
2. Biochemistry: enzyme acid phosphatase & ubiqinone					
A	Primary	Harisch[13]	Harisch[36]		
B	Multicenter				
C	Independent				
Summary: decrease of enzyme reaction in both studies					
3. Biochemistry: enzyme acid phosphatase & cAMP					
A	Primary	Harisch[14]	Harisch[37]		
B	Multicenter				
C	Independent				
Summary: decrease of enzyme reaction in both studies					
4. Biochemistry: enzyme alpha amylase & mercury chloride					
A	Primary	Sukul[15]			
B	Multicenter				
C	Independent				Bluth[88]
Summary: increase of enzyme reaction in the initial study only					
5. Cultured mammalian cells: neuroblastoma cells & tumour necrosis factor alpha					
A	Primary	Carmine[16]			
B	Multicenter				
C	Independent				Herberth[89]
Summary: increase of H_20_2 production in the initial study only					
6. Plants: algae chlorella & copper sulphate					
A	Primary	Graviou[17]			
B	Multicenter				
C	Independent				Moss[90]
Summary: growth stimulation of poisoned algae in the initial study only					
7. Plants: wheat seedlings & silver nitrate					
A	Primary	Kolisko[18]			
B	Multicenter		Pongratz[39] Nograsek[39]		Endler[39]
C	Independent		Pongratz[38]		
Summary: increase of stalk growth in 4 out of 5 studies					
8. Plants: arsenic poisoned wheat seedlings & *Arsenicum album*					
A	Primary	Betti[19]	Brizzi[40,41] Nani[42]		
B	Multicenter				
C	Independent			Binder[83] Lahnstein[84]	Lahnstein[84]
Summary: Betti/Brizzi/Nani: stimulation of growth and germination rate, decrease of variance; Binder/Lahnstein: decrease of growth and germination rate, increase of variance					
9. Plants: dwarf peas & gibberellic acid					
A	Primary	Baumgartner[20]	Baumgartner[43]	Baumgartner[43]	Baumgartner[43]
B	Multicenter				
C	Independent				
Summary: growth increase for certain harvest lots					
10. Plants: wheat seedlings & gibberellic acid					
A	Primary	Pfleger[21]	Hofäcker[44] Reich[45]		
B	Multicenter			Reischl[86] Thieves[85]	
C	Independent				
Summary: decrease of stalk growth in autumn, increase in winter experiments					
11. Isolated immune cells: basophils & antiserum against IgE					
A	Primary	Davenas[22]	Benveniste[46]		
B	Multicenter				
C	Independent				Ovelgönne[91] Hirst[92]
Summary: reduction of degranulation in 2 out of 4 studies					

(*continued on next page*)

Table 1 (*continued*)

Model no.	*Workgroup*	*1: Initial study*	*2: Repetition*	*3: Repetition*	*4: Repetition*
			Comparable effect	*Different effect*	*Zero effect*
12. Isolated immune cells: basophils & *Apis mellifica*					
A	Primary	Poitevin[23]	Poitevin[47] Benveniste[46]		
B	Multicenter				
C	Independent				
Summary: reduction of degranulation in all studies					
13. Isolated immune cells: basophils & histamine					
A	Primary	St. Laudy[24]	St. Laudy[48–52]	St. Laudy[87]	
B	Multicenter		St. Laudy[53] Ennis[53] Mannaioni[53]		Wiegant[53]
C	Independent		Brown[54] Lorenz[55,56] Chirumbolo[57]	Lorenz[56]	Guggisberg[98]
Summary: inhibition of degranulation in 13 out of 17 studies					
14. Isolated immune cells: lymphocytes & *Phytolacca americana*					
A	Primary	Colas[25]			
B	Multicenter				
C	Independent				Bildet[93]
Summary: decrease of lymphocyte reaction in the initial study only					
15. Isolated immune cells: lymphocytes & N-methyl-N'-nitro-N-nitrosoguanidine					
A	Primary	Francis[26]			Anderson[94]
B	Multicenter				
C	Independent				
Summary: decrease of lymphocyte reaction in the first study only					
16. Isolated organs: rat intestine contraction & Atropa belladonna or atropine sulfate					
A	Primary	Cristea[27]			
B	Multicenter				
C	Independent		Schmidt[58] Radau[59] Michael[60]		
Summary: increase or decrease of contraction at different potency levels in all studies					
17. Animals: amphibian metamorphosis & thyroxin or *Thyroidinum*					
A	Primary		Welles[63] Pongratz[63] Suanjak[63]		Weber[63]
B	Multicenter	Endler[28] Pongratz[28] van Wijk[28]	Zausner[62] Pongratz[62] Lassnig[62]		
C	Independent		Guedes[64]		
Summary: decrease of metamorphosis speed in 10 out of 11 studies					
18. Animals: amphibian metamorphosis & thyroxin sealed in glass vials					
A	Primary		Hermann[65]		Dieterle[95]
B	Multicenter	Endler[30] Waltl/Gehrer[30] Pongratz[30] Vinattieri[30] Hilgers[30]			
C	Independent				
Summary: decrease of metamorphosis speed in 6 out of 7 studies					
19. Animals: frog climbing activity & thyroxin					
A	Primary	Endler[29]	Pongratz[66]		
B	Multicenter				
C	Independent				
Summary: decrease of climbing activity in both studies					
20. Animals: arsenic trioxide poisoned mice & *Arsenicum album*					
A	Primary	Mitra[31]	Mitra[67] Datta[68] Kundu[69] Mallick[70] Banerjee[71–73]		
B	Multicenter				
C	Independent				
Summary: stimulation of damage repair in all studies					

Table 1 (*continued*)

Model no.	*Workgroup*	*1: Initial study*	*2: Repetition*	*3: Repetition*	*4: Repetition*
			Comparable effect	*Different effect*	*Zero effect*
21. Animals: mercury poisoned mice & mercury					
A	Primary	Larue[32]	Cal[76] Larue[74,75]		
B	Multicenter				
C	Independent				
Summary: protection effect in all studies					
22. Animals: carbon tetrachloride poisoned mice & *Phosphorus*					
A	Primary	Bildet[33]			
B	Multicenter				
C	Independent		Andresen[77]		
Summary: protection effect in both studies					
23. Animals: lead poisoned rats & *Plumbum metallicum*					
A	Primary	Fisher[34]			Fisher[97]
B	Multicenter				
C	Independent				
Summary: increase of excretion in 1 study, no effect in the other study					
24. Animals: thrombus formation in rats & acetyl salicylic acid					
A	Primary	Doutremepuich[35]	Belougne-Malfatti[78] Aguejouf[79] Eizayaga[80] Doutremepuich[81]		
B	Multicenter				
C	Independent				
Summary: increase in thrombus formation in all studies					

Initial studies

The following basic research models to study the effects of high dilutions that have subsequently led to reproduction studies were identified.

- Biochemistry.[12–15]
- Cultured cells.[16]
- Plants.[17–21]
- Isolated immune cells.[22–26]
- Isolated organs.[27]
- Whole animals.[28–35]

Repeated studies yielding comparable effects

Some of these experimental models were independently investigated by different researchers, with comparable results (see Table 1):

- Biochemistry
  - Results on potentized ubiqinone[13] were confirmed by the same working group.[36]
  - Results on potentized cAMP[14] were confirmed by the same working group.[37]
- Plants
  - Results on potentized silver nitrate[18] were confirmed by others.[38,39]
  - Results on potentized arsenic[19] were confirmed by the same working group.[40–42]
  - Results on potentized gibberellic acid and dwarf peas[20] were confirmed the same working group[43] for one specific seed lot.
  - Results on potentized gibberellic acid and wheat[21] were confirmed by the same working group.[44,45]
- Isolated immune cells
  - Results on potentized antiserum against IgE[22] were confirmed by the same working group.[46]
  - Results on potentized *Apis mellifica*[23] were confirmed by the same working group.[46,47]
  - Results on potentized histamine[24] were confirmed by the same working group and by others.[48–57]
- Isolated organs
  - Results on potentized atropa belladonna/atropine sulfate[27] were confirmed by others.[58–60]
- Animals
  - Consistent multicenter results on potentized thyroxin and frog metamorphosis were obtained[28] and subsequently confirmed by the same working group with potentized thyroxin[61–63] and by others with potentized thyroidinum.[64]
  - Consistent multicenter results on potentized thyroxin sealed in glass vials were obtained[30] and confirmed by the same working group.[65]
  - Results on potentized thyroxin and frog climbing activity[29] were confirmed by the same working group.[66]
  - Results on potentized arsenic[31] were confirmed by the same working group.[67–73]
  - Results on potentized mercury[32] were confirmed by the same working group.[74–76]
  - Results on potentized phosphorus[33] were confirmed by others.[77]
  - Results on potentized acetyl salicylic acid[35] were confirmed by the same working group.[78–81]

Repeated studies resulting in different effects

Other intents of reproduction led to interesting, statistically significant, but modified results:

- Biochemistry
  - A different result[82] was found on potentized mercury cloride compared to Persson *et al.*[12]

- Plants
  - A different result[83,84] was found compared to Betti *et al*.[19] on potentized arsenic for meta-analysis of all experiments.
  - A different result[43] was found on potentized gibberellic acid compared to Baumgartner *et al*.[20] for one specific seed lot of dwarf peas.
  - A different result[85,86] was found on potentized gibberellic acid compared to Pfleger[21] for wheat growth at different times of the year.
- Isolated immune cells
  - A different result[56,87] was found on potentized histamine compared to Sainte-Laudy *et al*.[24]

Repeated studies yielding no effect

Further studies did not reveal any significant effects:

- Biochemistry
  - Effects of potentized mercury chloride on the enzyme diastase[88] compared to Persson *et al*.[12]
  - Effects of potentized mercury chloride on amylase[88] compared to Sukul *et al*.[15]
- Cultured cells
  - Effects of potentized tumour necrosis factor[89] compared to Carmine.[16]
- Plants
  - Effects of potentized copper sulfate[90] compared to Graviou *et al*.[17]
  - Effects of potentized silver nitrate (one researcher in a multicentre trial[39]) compared to Kolisko.[18]
  - Effects of potentized arsenic[84] compared to Betti *et al*.[19] for single experimental series.
  - Effects of potentized gibberellic acid[43] compared to Baumgartner *et al*.[20] for two specific seed lots.
- Isolated immune cells
  - Effects of potentized antiserum against IgE[91,92] compared to Davenas *et al*.[22]
  - Effects of potentized histamine[53,98] compared to Sainte-Laudy *et al*.[24]
  - Effects of potentized phytolacca[93] compared to Colas *et al*.[25]
  - Effects of potentized nitrosoguanidine[94] compared to Francis *et al*.[26]
- Animals
  - Effects of potentized thyroxine (one researcher in a multicentre trial)[63] compared to Endler *et al*.[28]
  - Effects of potentized thyroxine sealed in glass vials[95,96] compared to Endler *et al*.[30]
  - Effects of potentized *Plumbum*[97] compared to Fisher.[34]

Table 2 summarises the various outcomes at the level of studies. A total of 107 studies were found. Of these, 30 were initial publications, 22 performed by one working group, and 8 performed in a multicenter setting. In attempts to reproduce one of these initial studies, 53 follow-up studies yielded comparable effects, namely 35 performed as a repetition by the same initial working group, 8 performed as a repetition in a multicenter setting in contact with the researcher from the initial study and 10 as a repetition in a fully independent setting. Eight studies showed a consistent, yet different result from the initial study, 2 performed as a repetition by the same initial working group, 2 performed as a repetition in a multicenter setting in contact with the researcher from the initial study and 4 as a repetition in a fully independent setting. In attempts to reproduce one of the 30 initial studies, 16 studies showed no effect, 5 performed as a repetition by the same initial working group, 2 performed as a repetition in a multicenter setting in contact with the researcher from the initial study and 9 as a repetition in a fully independent setting.

When all repeated (but not initial) studies are considered (77), 69% reported an effect comparable to that of the initial study, 10% a different effect and 21% no effect.

When only the independent repetitive studies are taken into account, only 44% reported an effect comparable to that of the initial study, 17% a different effect, but 39% no effect. Multicenter studies showed 67% comparable, 17% different and 17% no effects, whereas initial researcher or working group studies showed 83% comparable, 5% different and 12% no effects (Figure 1).

Table 3 sums up the outcomes with regard to Table 1 at the level of models. A total of 24 models have been used. There have been reported comparable results with regard to 22 models, different results with regard to 6 models, and no effects with regard to 15 models. These numbers mirror the fact that certain models yielded diverse results in repetition trials (e.g. comparable and different effects).

Discussion

Initial studies

All initial studies collected in this publication have been tracked by follow-up studies. Thus, the models concerned have been more profoundly researched than a considerable number of other models. This gives them a special weight in the frame of scientific exploration. However many studies in the field have *not* been subjected to repetition so far, although they may be worthy candidates for follow-up.

Table 2 Numerical summary of Table 1, at the level of studies. The number of studies fitting in a given category was counted

		Initial study	*Repetition*	*Repetition*	*Repetition*
			Comparable effect	*Different effect*	*Zero effect*
A	Initial working group studies	22	35	2	5
B	Multicenter studies	8	8	2	2
C	Independent repetitions	0	10	4	9
A + B + C		**30**	**53**	**8**	**16**

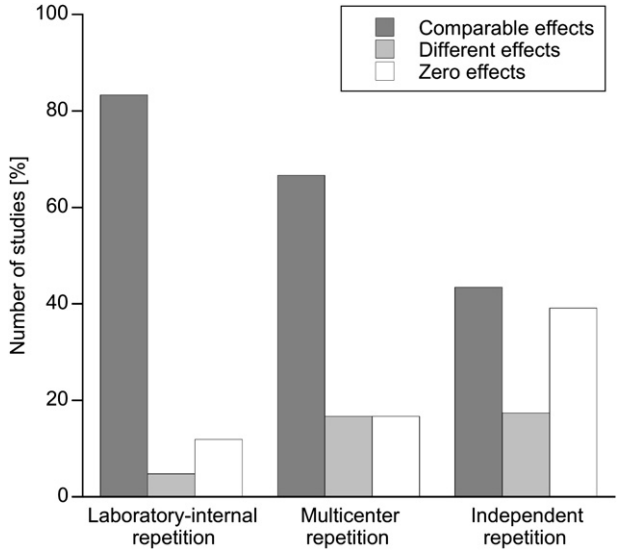

Figure 1 Numerical summary of Table 1, at the level of studies. The number of studies fitting in a given category was counted and referred to the sum of the repetition type category (set to 100%).

All but the two oldest publications align with certain standards of information given on their subject (minimum requirement: mean or median, number n of samples, standard deviation or standard error, OR number n of samples, level of significance). One will agree that these standards are not too high, i.e. that we are not referring to 'Gold Standard' publications only.[99,100] Some models that have not been included by reasons mentioned above may be interesting candidates for follow-up studies when fulfilling the required quality standards.

Repeated studies

Often, but not always, repeated studies contributed more detailed information on procedures and effects than the initial publications did.

Repeated studies with comparable results: According to the current paradigm of science, a follow-up study leading to results *comparable* to the results of the initial study is indicative of a deterministic behaviour of the investigated experimental system. In other words, the hypothesis that the results of the initial study are repeatable has been successfully tested and one may in principle proceed towards a full deterministic theory. In case the results obtained in the different studies are quantitatively unequal, further research will be necessary to identify the factors responsible for the size of the effects.

Repeated studies with different results: When both the initial and the follow-up study yield statistically convincing results, but opposed to each other, we have classified them as (interesting, yet) *different* results. Such effects can, of course, be found not only in homeopathic basic research. First thing any researcher confronted with different results has to do is to scrutinize the details of the methodological set-up of the study (e.g. different materials may have been used, there may be circadian or seasonal shifts etc.). Thus there may be unidentified and therefore unknown factors leading to effect inversions. Identification of these parameters will substantially contribute to scientific progress. Possible reasons for problems with reproducibility are discussed in detail elsewhere.[2]

It may well be that ''even the most painstaking research in homeopathy is subject to greater uncertainty than are many conventional fields of research. This is presumably due to the complexity of the nonlinear stimulus-response relationships that underlie homeopathic effects''.[4,101,102] Furthermore, homeopathy (like other regulatory methods) provides a certain background to classify and understand inverse effects. The notion of 'ortho-taxic' and 'anti-taxic' effects has been suggested by P. Fisher.[29] Inverse effects are known among homeopathic therapists e.g. as ''initial aggravation''.

Repeated studies yielding no effect: Repeated studies that show no difference between the treatment and the control groups may be due to a variety of reasons.

Irreproducibility of results can be due to the fact that the results of the initial studies were artefacts (meaning false-positive results). Artefacts can be due to contamination, systematic drifts or stochastic noise of the experimental set-up, which are wrongly interpreted as treatment effects. Correspondingly, results of earlier studies cannot be reproduced by follow-up studies with better methodology.

Repetition studies may be statistically underpowered, i.e. the number of investigated experimental subjects may be too low to properly identify effects as observed in the initial study. The same reasons discussed above for effect inversions may also lead to no effects: uncontrolled relevant parameters, inappropriate outcome measures, or inherent irreproducibility of the system. As already mentioned above, a detailed discussion of these possible reasons for problems with reproducibility can be found elsewhere.[2]

Which of all these, or other, possible reasons for irreproducibility may apply in a specific situation, cannot be determined in a simple way. Carefully repeated experiments of

Table 3 Numerical summary of Table 1, at the level of models. The number of models fitting in a given category was counted

		Initial model	*Repetition*	*Repetition*	*Repetition*
			Comparable effect	*Different effect*	*Zero effect*
A	Initial working group studies	22	14	2	5
B	Multicenter studies	2	3	1	2
C	Independent repetitions	0	5	3	8
A + B + C		**24**	**22**	**6**	**15**

the primary working group and by the follow-up study groups are necessary to contribute to scientific progress. When repetition experiments consistently yield negative results, the corresponding model might be excluded from further research. In any case, repeated studies yielding effect should lead to scrutinizing closely the details of the methodological set-up of the studies and of their written presentation.

So far, we know of three model systems where at least one relevant parameter crucial for successful repetition has been identified. In the amphibian metamorphosis model system developed by Endler *et al*.,[28] only animals from high-land biotopes consistently respond to a treatment with homeopathically potentized thyroxin,[63] presumably due to a higher endogenous level of thyroxin or higher susceptibility to thyroxin. In the dwarf pea model of Baumgartner *et al*.,[20] seed quality (supposedly premature harvest) was identified as relevant trigger factor for a response to a treatment with homeopathic preparations of gibberellic acid.[43] In the mice model of Larue and Cal,[32,74–76] annual chronobiological rhythms modulate the protective effect of an isopathic treatment with mercury.

Independent repeated studies leading to comparable or different results: We identified five models that have been reproduced by at least one independent research team with comparable results:

1. Growth of wheat seedlings after treatment with potencies of silver nitrate,
2. Human basophil degranulation after treatment with potencies of histamine,
3. Amphibian metamorphosis after treatment with potencies of thyroxin or thyroidinum,
4. Experimental hepatitis of the rat due to poisoning with carbon tetrachloride after treatment with phosphorus,
5. Contraction of rat intestine *in vitro* after treatment with potencies of Atropa belladonna or atropine sulfate.

However, when comparing the studies in detail one must conclude that no independent repetition trial yielded exactly the same results as the initial study, and methods always differed to a smaller or larger extent. For the wheat bioassay, Kolisko[18] grew grains in flowerpots or glass tubes watered at different potencies levels, while Pongratz[38] used glass dishes filled with blinded samples. In the human basophil degranulation test, effective potency levels differed in all independent follow-up studies.[54,57] Lorenz *et al*.[55,56] furthermore investigated decimal (instead of centesimal) potencies. The amphibian metamorphosis study of Guedes *et al*.[64] used potencies prepared from thyroid glands instead of pure thyroxin as in the experiments of Endler *et al*.[28] In the model of experimental hepatitis, Bildet[33] worked with *Phosphorus* 15c, whilst Andresen[77] investigated the effect of *Phosphorus* 30x; outcome parameters (biochemical analysis, histology) also differed. Concerning *in vitro* rat intestine contraction, Cristea *et al*.[27] investigated centesimal *Belladonna* potencies using duodenum fragments, whilst Schmidt *et al*.[58] investigated decimal *Belladonna* potencies using fundus/corpus- as well as ileum fragments; Radau[59] and Michael[60] studied decimal atropine sulfate potencies with ileum fragments only.

We furthermore identified three models that have been reproduced by at least one independent research team, but with differing results:

1. Hydrolysis of starch with malt diastase, treated with potencies of mercury chloride,
2. Growth and germination rate of arsenic poisoned wheat after treatment with potencies of arsenic,
3. Human basophil degranulation after treatment with potencies of histamine.

When comparing the studies in detail one has to conclude that methods differed to a smaller or larger extent, precluding straightforward interpretation. In the malt diastase model, Persson and Ginsberg[12] investigated every 5th decimal potency between 10x and 60x, and observed varying (decreasing/increasing) responses as a function of dilution level; in contrast, Boyd[82] used a 1:200 dilution ratio and always observed stimulation by the potency levels 26 up to 31. Methods of the repetition trials of Binder *et al*.[83] and Lahnstein *et al*.[84] concerning growth and germination rate of arsenic poisoned wheat were quite close to the original trial,[19] however also here, differences in wheat seed lots used preclude formal comparability. Lorenz *et al*.[56] got varied results for different solvents.

The multicenter approach

When all repetitive (but not the initial) studies are considered, 69% report an effect comparable to that of the initial study, 10% a different effect and 21% no effect. This relation is fairly well reflected by multicenter studies, i.e. studies that were centrally organized, but carried out by various researchers in different laboratories, namely 66% comparable, 17% different and 17% no effects. Thus, multicenter studies seem to be an adequate tool to investigate basic high potency models.

On the other hand, initial researcher or working group studies show 83% comparable, 5% different and 12% no effects and may include methodological influences that could not be made explicit in the publications, even together with possible researcher effects.[4]

The situation is also different when only the independent repetition studies are taken into account (44% comparable, 17% different, 39% no effect). Some of these may lack detailed laboratory know-how transfer that can be better obtained when a training phase in the initial laboratory precedes the attempt to repeat a study.

Conclusion

We found 24 experimental models in basic research on high homeopathic potencies, which were repeatedly investigated. 22 models were reproduced with comparable results, 6 models with different results, and repetition showed no results for 15 models. Seven models were independently reproduced with either comparable or different results.

Thus, 10 years after the last comparable systematic literature collection[9] we conclude that the question of independent reproduction in homeopathic basic research has considerably improved. Vickers[9] in 1999 was not able to identify a single experimental model that had been successfully be reproduced by an independent research team, we are now able to identify seven models yielding comparable or significant but different results.

We strongly encourage further repetitions of published studies, in order to learn more about the model systems used, to identify crucial parameters influencing experimental outcome, and to test repeatability of results. To allow this, research methods, as well as presentations of methods and results should align with minimum standards, e.g. the guidelines for studies in homeopathy,[99,100] either in the publication or in a readily available background website. Like in other fields of science, a training phase in the initial laboratory may precede the attempt to repeat a study.

Acknowledgements

Special thanks are due to Tim Jäger, Vera Majewsky and Johannes Endler for their input. We gratefully acknowledge the supply of articles by the libraries of the Karl und Veronica Carstens foundation (Daniela Hacke) and the Deutsche Homöopathie Union (Susanne Rehm) as well as the support provided by Dr Peithner Laboratories, Vienna.

Note

The authors will be grateful for comments and further information on relevant studies that fit the inclusion criteria of the bibliography. It may be of interest to the research community to further refine this publication from an annotated bibliography into a fully detailed review.

References

1 Baumgartner S. Reproductions and reproducibility in homeopathy: dogma or tool? *J Altern Complement Med* 2005; **11**(5): 771–772.

2 Baumgartner S. The state of basic research on homeopathy. In: Albrecht H, Witt C (eds). New Directions in Homeopathy Research – Advice From an Interdisciplinary Conference. Essen: KVC-Verlag, 2009, p. 107–130.

3 Albrecht H, van Wijk R, Dittloff S. A new database on basic research in homeopathy. *Homeopathy* 2002; **91**: 162–165.

4 Endler PC. *Homeopathy Research – An Expedition Report. Edition Interuniversity College, Graz 2003/Expedition Homöopathieforschung – Ein altes Heilsystem Wird Plausibel*. Vienna: Maudrich Verlag, 1998, p 52.

5 Endler PC. Fundamental research into high dilution effects. A classification of non-clinical research topics. In: Schulte J, Endler PC (eds). Fundamental Research in Ultra High Dilution and Homoeopathy. Dordrecht: Kluwer Academic Publishers, 1998.

6 Forschung im Dienste der Gesundheit (Projektträgerschaft). *Unkonventionelle Medizinische Richtungen. Bestandsaufnahme zur Forschungssituation*. Bonn: Wirtschaftsverlag, Verlag für neue Wissenschaft, 1992.

7 Göldner C., Review und Evaluierung von neuen, mit homöopathischen Zubereitungen durchgeführten toxikologischen Experimenten. Thesis, University of Graz 2006.

8 Linde K, Jonas WB, Melchart D, Worku F, Wagner H, Eitel F. Critical review and meta-analysis of serial agitated dilutions in experimental toxicology. *Hum Exp Toxicol* 1994; **13**: 481–482.

9 Vickers AJ. Independent replication of pre-clinical research in homoeopathy: a systematic review. *Res Compl Med/Forsch Komplementärmed* 1999; **6**: 311–320.

10 Walach H, Jones WB, Ives J, Wijk RV, Weingartner O. Research on homeopathy: state of the art. *J Altern Complement Med* 2005; **11**: 813–829.

11 Witt CM, Bluth M, Albrecht H, Weisshuhn TE, Baumgartner S, Willich SN. The in vitro evidence for an effect of high homeopathic potencies-a system review of the literature. *Complement Ther Med* 2007; **15**: 128–138.

12 Persson WM, Ginsberg AS. Die Einwirkung von Mikrodosen homöopathischer Arzneimittel (chemischer oder pflanzlicher) auf die Fermente Urease und Diastase. [The action of microdoses of homeopathic remedies (of chemicals and plants) on the enzymes urease and diastase]. *Dt Z Hom* 1932; **11**: 97–106.

13 Harisch G, Dittmann J. Untersuchungen zur Wirkung von Ubichinon Injeel und Injeel forte mit zellfreien Systemen. [Investigations of the effect of Ubichinon Injeel and Injeel forte with cell-free systems]. *Biol Med* 1997; **26**: 99–104.

14 Harisch G, Dittmann J. Unterschiedlicher Einfluß von cAMP-Potenzen und cAMP-Verdünnungen am Beispiel verschiedener Enzymsysteme. [Different influence of potencies and dilutions of cAMP exemplified on several enzyme systems]. *Biol Med* 1998; **27**: 55–62.

15 Sukul NC, Sukul A, Sinhababu SP. Potentized mercuric chloride and mercuric iodide enhance alpha-amylase activity in vitro. *Homeopathy* 2002; **91**: 217–220.

16 Carmine TC. Effects of high potencies of tumour necrosis factor alpha on H_20_2 production in cultured neuroblastoma cells by enhanced luminol-dependent chemiluminescence (ECL): a possible system for investigating the biological significance of homeopathic high potencies. *Br Homeopath J* 1997; **86**: 67–72.

17 Graviou E, Biron MA. Action d'une 15e CH de sulfate de cuivre sur la culture des *Chlorella vulgaris*. *Ann Hom Fr* 1971; **7**: 539–548.

18 Kolisko L. *Physiologischer und physikalischer Nachweis der Wirksamkeit kleinster Entitäten bei sieben Metallen*. Dornach: Goetheanum Verlag, 1926.

19 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 Homeopath J* 1997; **86**: 86–89.

20 Baumgartner S, Thurneysen A, Heusser P. Growth stimulation of dwarf peas (*Pisum sativum* L.) through homeopathic potencies of plant growth substances. *Forschende Komplementärmedizin und Klassische Naturheilkunde* 2004; **11**: 281–292.

21 Pfleger A. Weizenkeimung unter dem Einfluss von homöopathisch zubereitetem Gibberellin (D30). Thesis (MSc), Interuniversitäres Kolleg, Graz 2008.

22 Davenas E, Beauvais F, Amara J, *et al*. Human basophil degranulation triggered by very dilute antiserum against IgE. *Nature* 1988; **333**: 816–818.

23 Poitevin B, Aubin M, Benveniste J. Approche d'une analyse quantitative de l'effet d'apis mellifica sur la dégranulation des basophiles humains in vitro. *Innovation et Technologie en biologie et medecine* 1986; **7**(1): 64–68.

24 Sainte-Laudy J, Belon P. Biological activity of ultra low doses. II. Effect of ultra low doses of histamine on human basophil degranulation triggered by anti-IgE. In: Doutremepuich C (ed). Ultra Low Doses. London, Washington: Taylor & Francis, 1991, p. 139–144.

25 Colas H, Aubin M, Picard P, Lebecq JC, Bastide JM. Inhibition du test de transformation lymphoblastique (TTL) à la phytohémagglutinine (PHA) par Phytolacca americana en dilutions

homéopathiques. [Inhibition of lymphoblast transformation test (LTT) by phythemagglutinine (PHA) through Phytolacca americana in homeopathic dilutions]. *Hom Franc* 1984; **72**: 219–224.

26 Francis AJ, Anderson D, Fisher P. Further studies of the 'adaptive' repair response in human lymphocytes after treatment with MNNG (Abstract). *Environ Meloc Mutagen* 1990; **15**(S17): 69.

27 Cristea A, Nicula S, Darie V. Pharmacodynamic effects of very high dilutions of belladonna on the isolated rat duodenum. In: Bastide M (ed). Signals and Images. Dordrecht: Kluwer Academic Publishers, 1997, p. 161–170.

28 Endler PC, Pongratz W, van Wijk R, Kastberger G, Haidvogl M. Effects of highly diluted succussed thyroxin on metamorphosis of highland frogs. *Berlin J Res Hom* 1991; **1**: 151–160.

29 Endler PC, Pongratz W, Kastberger G, Wiegant FAC, Haidvogel M. Climbing activity in frogs and the effect of highly diluted succussed thyroxine. *Br Homeopath J* 1991; **80**: 194–200.

30 Endler PC, Pongratz W, Smith CW, Schulte J. Non-molecular information transfer from thyroxin to frogs with regard to 'homoeopathic' toxicology. *Vet Hum Toxicol* 1995; **37**(3): 259–260.

31 Mitra K, Kundu SN, Khuda-Bukhsh AR. Efficacy of a potentized homeopathic drug (Arsenicum Album-30) in reducing toxic effects produced by arsenic trioxide in mice: I. On rate of accumulation of arsenic in certain organs. *Complement Ther Med* 1998; **6**: 178–184.

32 Larue F, Cal JC, Tetau M, Buisard AM, Guillemain J, Cambar J. Mise en evidence de l'effet Protecteur de differentes dilutions de mercurius corrosivus. *Cahiers de Biothérapie* 1985; **88**: 71–74.

33 Bildet J. Etude de l'action de différentes dilutions homéopathiques de phosphore blanc (Phosphorus) sur l'hépatite toxique du rat. Thèse, Université de Bordeaux II, 1975.

34 Fisher P. The treatment of experimental lead intoxication in rats by penicillinamine and plumbum met. *Proceedings of the 35th congress of the Liga Medicorum Homeopathica Internationalis, Brighton* 1982;320–332.

35 Doutremepuich C, Aguejouf O, Pintigny D, Sertillanges MN, De Seze O. Thrombogenic properties of ulta-low-dose of acetylsalicylic acid in a vessel model of laser-induced thrombus formation. *Thromb Res* 1994; **76**: 225–229.

36 Harisch G, Dittmann J. Aktivitätsbestimmungen der sauren Phosphatase in Gegenwart von Ubichinon-Einzelpotenzen und Ubichinon-Potenzmischungen. [Determination of activity of acid phosphatase in presence of single potencies and potency mixtures of ubiquinone]. *Biol Med* 1999; **28**: 188–194.

37 Harisch G, Dittmann J. Aktivitätsbestimmung der sauren Phosphatase in Gegenwart von cAMP-Einzelpotenzen und cAMP-Potenzmischungen. [Determination of acitivity of acid phosphatase in presence of single potencies and potency mistures of cAMP]. *Biol Med* 1999; **28**: 4–8.

38 Pongratz W, Endler PC. Reappraisal of a classical botanical experiment in ultra high dilution research. In: Endler PC, Schulte J (eds). Ultra High Dilution: Physiology and Physics. Dordrecht: Kluwer Academic Publishers, 1994, p. 121–128.

39 Pongratz W, Nograsek A, Endler PC. Highly diluted agitated silver nitrate and wheat seedling development. Effect kinetics of a process of successive agitation phases. In: Schulte J, Endler PC (eds). Fundamental Research in Ultra High Dilution and Homeopathy. Dortrecht: Kluwer Academic Publishers, 1998, p. 155–187.

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

41 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. *Res Compl Med/Forsch Komplementärmed* 2005; **12**: 277–283.

42 Nani D, Brizzi M, Lazzarato L, Betti L. The role of variability in evaluating ultra high dilution effects: considerations based on plant model experiments. *Forschende Komplementärmedizin* 2007; **14**(5): 301–305.

43 Baumgartner S, Shah D, Schaller J, Kämpfer U, Thurneysen A, Heusser P. Reproducibility of dwarf pea shoot growth stimulation by homeopathic potencies of gibberellic acid. *Complement Ther Med* 2008; **16**: 183–191.

44 Hofäcker J. Der Einfluss der Intervalldauer bei der Herstellung ultrahochverdünnter homöopathischer Präparate (homöopathische Hochpotenzen). Thesis (MSc), Interuniversitäres Kolleg, Graz 2008.

45 Reich C. Über den Umgang mit hochpotenzierten Lösungen, Untersuchungen am Saatgutmodell. Thesis (MSc), Interuniversitäres Kolleg, Graz 2009.

46 Benveniste J, Davenas E, Ducot B, Cornillet B, Poitevin B, Spira A. L'agitation de solutions hautement diluées n'indit pas d'activité biologique spécifique. [Agitating highly diluted solutions does not induce specific biological activity]. *C R Acad Sci Paris* 1991; **312**: 461–466.

47 Poitevin B, Davenas E, Benveniste J. In vitro immunological degranulation of human basophils is modulated by lung histamine and Apis mellifica. *Br J Clin Pharmacol* 1988; **25**(4): 439–444.

48 Sainte-Laudy J, Belon P. Inhibition of human basophil activation by high dilutions of histamine. *Agents Actions* 1993; **38**: 525–527.

49 Sainte-Laudy J, Belon P. Analysis of immunosuppressive activity of serial dilutions of histamine on human basophil activation by flow cytometry. *Inflamm Res* 1996; **45**: 33–34.

50 Sainte-Laudy J, Belon P. Application of flow cytometry to the analysis of the immunosuppressive effect of histamine dilutions on human basophil activation: effect of cimetidine. *Inflamm Res* 1997; **46**: 27–28.

51 Sainte-Laudy J, Belon P. Improvement of flow cytometric analysis of basophil activation inhibition by high histamine dilutions. A novel basophil specific marker: CD 203c. *Homeopathy* 2006; **95**(1): 3–8.

52 Sainte-Laudy J, Boujenaini N, Belon P. Confirmation of biological effects of high dilutions. Effects of submolecular concentrations of histamine and 1-, 3- and 4-methylhistamines on human basophil activation. *Inflamm Res* 2008; **57**(S1): S01–S02.

53 Belon P, Cumps J, Ennis M, *et al*. Histamine dilutions modulate basophile activation. *Inflamm Res* 2004; **53**: 181–188.

54 Brown V, Ennis M. Flow-cytometric analysis of basophil activation: inhibition by histamine at conventional and homeopathic concentrations. *Inflamm Res* 2001; **50**: 47–48.

55 Lorenz I, Schneider EM, Stolz P, Brack A, Strube J. Sensitive flow cytometric method to test basophil activation influenced by homeopathic histamine dilutions. *Forschende Komplementärmedizin und Klassische Naturheilkunde* 2003; **10**: 316–324.

56 Lorenz I, Schneider EM, Stolz P, Brack A, Strube J. Influence of the diluent on the effect of highly diluted histamine on basophil activation. *Homeopathy* 2003; **92**: 11–18.

57 Chirumbolo S., Brizzi M., Ortolani R., Vella A., Bellavite P. Inhibition of CD203c membrane up-regulation in human basophils by high dilutions of histamine: a controlled replication study. *Inflamm Res*; **58**: 755–764.

58 Schmidt F, Süss WG, Nieber K. In-vitro Testung von homöopathischen Verduennungen. *Biol Med* 2004; **1**: 32–37.

59 Radau K. Materialwissenschaftliche Untersuchungen an pharmazeutischen Hilfsstoffen und ihre Bedeutung für die Herstellung homöopathischer Arzneimittel. Thesis. Fakultät für Biowissenschaften, Pharmazie und Psychologie, Universität Leipzig; 2004.

60 Michael S. Untersuchungen zur Wirkung von homöopathischen Verdünnungen am isolierten Ileum der Ratte. Thesis. Institut für Pharmazie, Universität Leipzig; 2004.

61 Zausner-Lukitsch C. Auswirkungen von homöopathisch zubereitetem Thyroxin auf die Metamorphosegeschwindigkeit von Rana temporaria unter besonderer Berücksichtigung der Einzelhaltung und unterschiedlicher Methoden der Applikation. Thesis, Vienna University 2001.

62 Zausner C, Lassnig H, Endler PC, *et al*. Die Wirkung von homöopathisch zubereitetem Thyroxin auf die Metamorphose

von Hochlandamphibien. Ergebnisse einer multizentrischen Kontrollstudie. *Perfusion* 2002; **17**: 268–276.

63 Welles SU, Suanjak-Traidl E, Weber S, *et al*. Pretreatment with thyroxine (10e-8) and the effect of homeopathically prepared thyroxin (10e-30) on highland frogs – a multi-researcher study. *Res Compl Med/Forsch Komplementärmed* 2007; **14**: 353–357.

64 Guedes JRP, Ferreira CM, Guimaraes HMB, Saldiva PHN, Capelozzi VL. Homeopathically prepared dilution of *Rana catesbeiana* thyroid glands modifies its rate of metamorphosis. *Homeopathy* 2004; **93**: 132–137.

65 Hermann B. *Zur Wirkung von ‚homöopathisch' zubereitetem Thyroxin (10e-30) in Glasphiolen auf die Metamorphose vorstimulierter* Rana temporaria-*Larven*. Graz: Interuniversitäres Kolleg, 2005.

66 Endler PC, Pongratz W, Kastberger G, Wiegant FAC, Schulte. The effect of highly diluted agitated thyroxin on the climbing activity of frogs. *J Vet Hum Tox* 1994; **36**: 56–59.

67 Mitra K, Kundu SN, Khuda-Bukhsh AR. Efficacy of a potentized homeopathic drug (Arsenicum Album-30) in reducing toxic effects produced by arsenic trioxide in mice: II. On alterations of body weight, tissue weight and total protein. *Complement Ther Med* 1999; **7**: 24–34.

68 Datta S, Mallick P, Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum Album-30) in reducing genotoxic effects produced by arsenic trioxide in mice. *Complement Ther Med* 1999; **7**(2): 62–75. 7(3): 156-163.

69 Kundu SN, Mitra K, Khuda Bukhsh AR. Efficacy of a potentized homoeopathic drug (Arsenicum-album-30) in reducing cytotoxic effects produced by arsenic trioxide in mice. *Complement Ther Med* 2000; **8**(2): 76–81. 8 (3): 157-165.

70 Mallick P, Chakrabarti Mallick J, Guha B, Khuda-Bukhsh AR. Ameliorating effect of microdoses of a potentized homeopathic drug, arsenicum album, on arsenic-induced toxicity in mice. *BMC Complement Altern Med* 2003; **3**: 7.

71 Banerjee P, Biswas SJ, Belon P, Khuda-Bukhsh AR. A potentized homeopathic drug, Arsenicum Album 200, can ameliorate genotoxicity induced by repeated injections of arsenic trioxide in mice. *J Vet Med A Physiol Pathol Clin Med* Sep 2007; **54**(7): 370–376.

72 Banerjee P, Bhattacharyya SS, Pathak S, Naoual B, Belon P, Khuda-Bukhsh AR. Comparative efficacy of two microdoses of a potentized homeopathic drug, arsenicum album, to ameliorate toxicity included by repeated sublethal injections of arsenic trioxide in mice. *Pathobiology* 2008; **75**: 156–170.

73 Banerjee P., Bhattacharyya S.S., Pathak S., Boujedaini N., Belon P., Khuda-Bukhsh A.R. Evidences of protective potentials of microdoses of ultra-high diluted arsenic trioxide in mice receiving repeated injections of arsenic trioxide. *Evid Based Complement Alternat Med*. February 25, 2009; doi:10.1093/ecam/nen.090.

74 Larue F, Cal JC, Guillemain J, Cambar J. Influence de la durée de prétraitement sur l'effet de mercurius corrosivus vis-a-vis de la toxicité induite par le chlorure mercurique chez la souris. *Homéopathie Française* 1986; **74**(5): 275–281.

75 Larue F, Cal JC, Guillemain J, Cambar J. Variations saisonnières et circadiennes de l'efficacité du prétraitement par mercurius corrosivur 15CH vis-à-vis de la toxicité induite par le chlorure mercurique. *Bulletin du Groupe d'Etude des Rhythmes Biologiques* 1986; **18**(1–2): 8–9.

76 Cal JC, Larue F, Guillemain J, Cambar J. Chronobiological approach of protective effect of *Mercurius corrosivus* against mercury-induced nephrotoxicity. *Ann Rev Chronopharmacol* 1986; **3**: 99–103.

77 Andresen M. Zytosolische und mitochondriale Effekte einer Intoxikation mit CCl_4 am Beispiel des Lebergewebes der Ratte. Einfluss von Phosphorus D6 und Phosphorus D30. Thesis, Tierärztliche Hochschule Hannover, 1985.

78 Belougne-Malfatti E, Aguejouf O, Doutremepuich F, Belon P, Doutrempuich C. Combination of two doses of acetyl salcylic acid: experimental study of arterial thrombosis. *Thromb Res* 1998; **90**: 215–221.

79 Aguejouf O, Malfatti E, Belon P, Doutremepuich C. Time related neutralization of two doses acetyl salicylic acid. *Thromb Res* 2000; **100**: 317–323.

80 Eizayaga FX, Aguejouf O, Belon P, Doutremepuich C. Platelet aggregation in portal hypertension and its modification by ultra-low doses of aspirin. *Pathophysiol Haemost Thromb* 2005; **34**: 29–34.

81 Doutremepuich C, Aguejouf O, Eizayaga FX, Desplat V. Reverse effect of aspirin: is the prothrombotic effect after aspirin discontinuation mediated by cyclooxygenase 2 inhibition? *Pathophysiol Haemost Thromb* 2007; **36**: 40–44.

82 Boyd WE. Biochemical and biological evidence of the activity of high potencies. *Br Homeopath J* 1954; **44**: 7–44.

83 Binder M, Baumgartner S, Thurneysen A. The effects of a 45x potency of *Arsenicum album* on wheat seedling growth – a reproduction trial. *Res Compl Med/Forsch Komplementärmed* 2005; **12**: 284–291.

84 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**: 189–207.

85 Thieves K. Einfluss von ‚homöopathisch zubereitetem Gibberellin (10–30) auf die Sprosslänge bei unterschiedlichen Gewichtsgrössen von Weizensaatgut. Thesis (MSc), Interuniversitäres Kolleg, Graz 2009.

86 Reischl T. Wirkung mentaler Projektion auf Ultrahochverdünnungen. Ein Weizenkeimungs-Gibberellin-Homöopathie-Experiment. Thesis (MSc), Interuniversitäres Kolleg, Graz 2009.

87 Sainte-Laudy J. Stimulatory effect of high dilutions of histamine on activation of human basophils induced by anti-IgE. *Inflamm Res* 2001; **50**: 63–64.

88 Bluth M. In-vitro-Forschung mit homöopathischen Potenzen. Ein systematischer Review und eigene Versuche mit zellfreien Systemen [In-vitro-research on homeopathic potencies. A systematic review and own experiments with cell-free systems]. Thesis. Berlin: Institut für Sozialmedizin, Epidemiologieund Gesundheitsökonomie; Charité-Universitätsmedizin 2005.

89 Herberth G., Pison U. Homöopathische Arzneimittel in zellbiologischen Systemen [Homeopathic remedies in cell-biological systems]. In: Albrecht H., Frühwald M., editors. Jahrbuch der Karl und Veronika Carstens-Stiftung, Band 5 (1998). Essen: 1999, p. 77–95.

90 Moss VA, Roberts JA, Simpson HKL. The effect of copper sulphate on the growth of the alga Chlorella. *Br Homeopath J* 1977; **66**: 169–176.

91 Ovelgönne JH, Bol AWJM, Hop WCJ, van Wijk R. Mechanical agitation of very dilute antiserum against IgE has no effect on basophil staining properties. *Experientia* 1992; **48**: 504–508.

92 Hirst SJ, Hayes NA, Burridge J, Pearce FL, Foreman JC. Human basophil degranulation is not triggered by very dilute antiserum against human IgE. *Nature* 1993; **366**: 525–527.

93 Bildet J, Dupont H, Aubin M, *et al*. Action in vitro de dilutions infinitesimales de Phytolacca americana sur la transformation lymphoblastiques (TTL) à la phytohémagglutininec. [In vitro action of infinitesimale dilutions of Phytolacca americana on the transformation of lymphoblasts by phytohemagglutinine]. *Hom Franc* 1984; **72**: 225–230.

94 Anderson D, Edwards AJ, Fisher P, Lovell DP. Statistical analysis of adaptive response in sister chromatid exchanges in human lymphocytes after treatment with very low and extremely low doses of N-methyl-N′-nitro-N-nitrosoguanidine using a study design to control variability. *Br Homeopath J* 1999; **88**: 7–16.

95 Endler PC, Heckmann C, Lauppert E, *et al*. The metamorphosis of amphibian and information of thyroxin storage via the bipolar fluid water. In: Schulte J, Endler PC (eds). Fundamental Research in Ultra High Dilution and Homoeopathy. Dordrecht: Kluwer Academic Publishers, 1998, p. 155–187.

96 Dieterle D. Überprüfung einer Hypothese zum indirekten Einfluß potenzierter Thyroxinlösungen auf die Metamorphosegeschwindigkeit von Rana temporaria. Thesis, University of Tubingen, 1999.

97 Fisher P, House I, Belon P, Turner P. The influence of the homeopathic remedy Plumbum metallicum on the excretion kinetics of lead in rats. *Hum Toxicol* 1987; **6**: 321–324.

98 Guggisberg AG, Baumgartner S, Tschopp CM, Heusser P. Replication study concerning the effects of homeopathic dilutions of histamine on human basophil degranulation in vitro. *Complement Ther Med* 2005; **13**: 91–100.

99 Stock-Schröer B, Albrecht H, Betti L, *et al*. Reporting Experiments in Homeopathic Basic Research (REHBaR) – description of the checklist development. *eCAM* 2009; 10.1093/ecam/nep170.

100 Stock-Schröer B, Albrecht H, Betti L, *et al*. Reporting Experiments in Homeopathic Basic Research (REHBaR) – a guideline for authors. *Homeopathy* 2009; **98**: 287–298.

101 Bell IR, Baldwin CM, Schwartz GE. Translating a nonlinear systems theory model for homeopathy into empirical tests. *Altern Ther Health Med* 2002; **8**(3): 58–66.

102 Bellavite P. Complexity science and homeopathy. A synthetic overview. *Homeopathy* 2003; **92**: 203–212.