

Danish Pharmaceutical Society
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Experimental research in homeopathic
medicine: *In vitro* assessments and
production control

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Open scientific questions regarding homeopathic potentization

- > Homeopathic potentization (succussion and stepwise dilution) is a pharmaceutical procedure regulated by law (§ 55 German Pharmaceuticals Act; regulations in the European Pharmacopoeia)
- > No generally accepted theory to explain specific effects of homeopathically potentized substances in high dilution levels
 - Inverse Avogadro number ($\approx 24x$, 12c)
 - Ubiquitariness (purity potentization medium)
- > Partially undefined concentrations for low potencies
 - Lacking solubility of water-insoluble substances
 - Adsorption at vessel walls
 - Dissolution out of vessels (e.g. Si, Ca, Mg...)

Basic Research in Homeopathy

- > The HomBrex database holds more than 1000 publications:
<http://www.carstens-stiftung.de/hombrex/>
- > But there are only few (5–10%) basic research investigations with high methodical quality
 - using adequate controls (succussed, potentized)
 - randomized & blinded
 - with several independent experiments (including independent production lots)
 - with systematic negative control experiments
 - with adequate statistics
- > Only about 50 high-quality publications – but with evidence for specific effects of highly diluted potentized substances

Homeopathic basic research phenomena

- > Jonas et al. 2006 Integr Cancer Ther: Male rats were injected with MAT-LyLu (prostate tumor) cells and exposed to several homeopathic remedies
- > There was a **23% reduction in tumor incidence** versus controls, and for animals with tumors, there was a **38% reduction in tumor volume** in homeopathically treated animals versus controls
- > **No effects** on cell viability or gene expression were observed when MAT-LyLu cells were exposed *in vitro* to the same homeopathic remedies
- > Saha et al. 2013 BMC Compl Alt Med: similar results with Swiss albino mice injected with EAC (Ehrlich's ascites carcinoma) cells
- > Thus it seems that the biological mode of action of homeopathic remedies is not primarily targeted at cellular level, but rather on a superordinate organizational level

Evaluation of experimental models to study homeopathic preparations

- > Since 1996: Basic Research Dept. at the Institute of Complementary Medicine of the University of Bern
- > Aim: investigations with several experimental laboratory models to
 - Assess and characterize any effects of homeopathic remedies
 - Develop reliable and reproducible models
 - Investigate pharmaceutical questions (e.g. sterilization methods, stability against external influences such as cell phone radiation)
 - Determine the physical mode of action
- > Evaluation of 17 experimental models

Evaluation of experimental models to study homeopathic preparations

Model

UV-Spektroskopie

NMR Relaxation Time Measurements

PBMC (Lymphocytes)

Jurkat cells

Basophils

Fibroblasts

Saccharom. cerevisiae / Schizosacchar. pombe (yeasts)

Saccharom. cerevisiae / Arsenic

Lemna gibba (duckweed)

Lemna gibba / Arsenic

Lemna gibba / Ca deficiency

Pisum sativum (dwarf peas)

Lepidium sativum / Biocrystallization

Triticum aestivum / Arsenic

Malus domestica / Dysaphis plantaginea

Malus domestica / Venturia inaequalis

Arabidopsis thaliana / Pseudomonas syringae

Effect size

Cancer cell lines: $\approx 0\%$

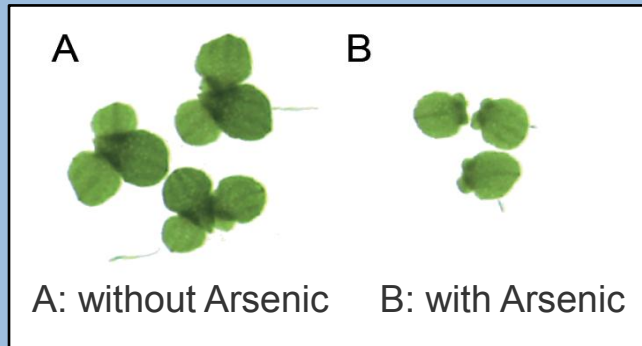
Micro-organisms: $< 1\%$

Plants: up to 10%

Plant-Pathogen-
Systems: up to 20%

Adaptation of ecotoxicological assay with *Lemna gibba* (duckweed)

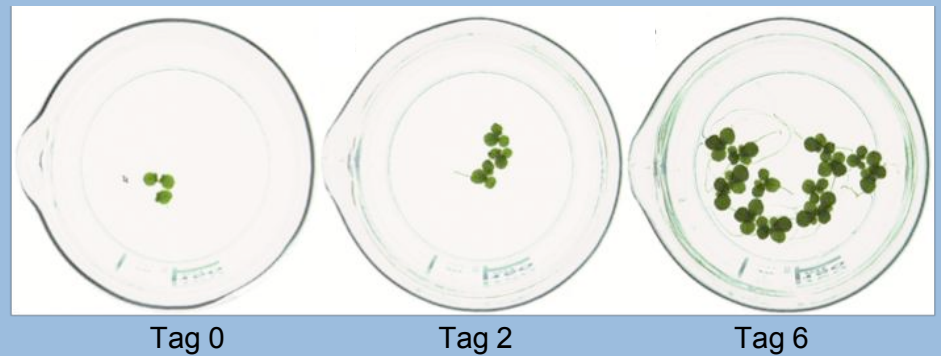
- > Homeopathic treatment (*Ars-alb*) of duckweed poisoned with arsenic



Duckweed without Arsenic impairment



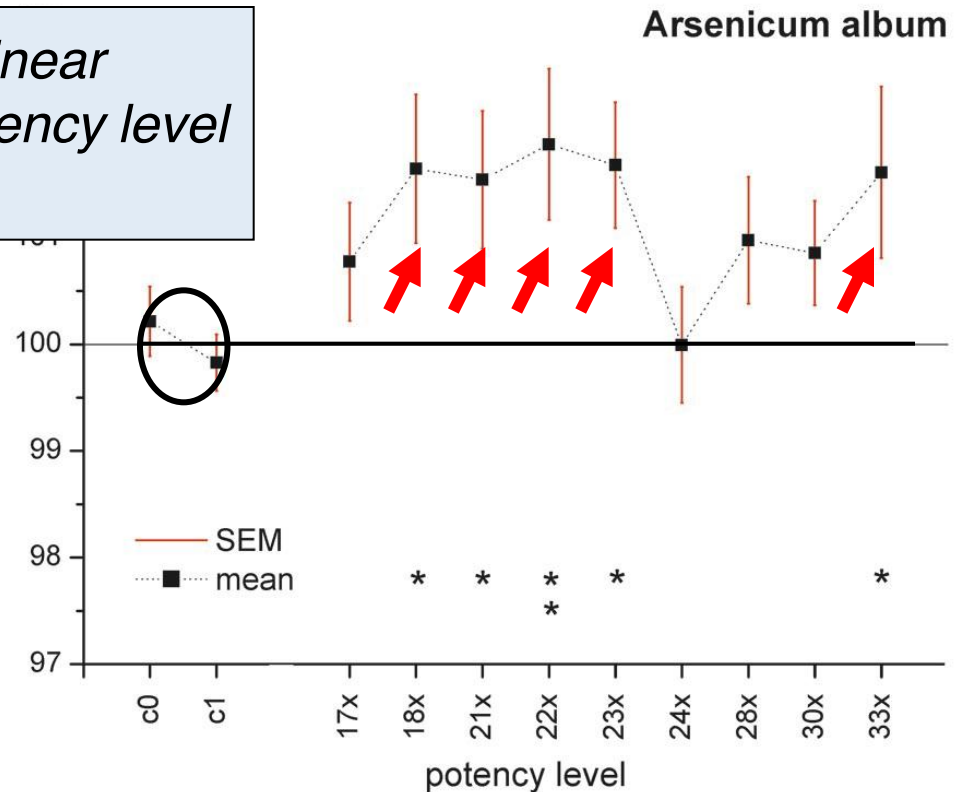
Arsenic-impaired Duckweed



Adaptation of ecotoxicological assay with *Lemna gibba* (duckweed)

- > Homeopathic treatment (*Ars-alb*) of duckweed poisoned with arsenic

Discontinuous and non-linear relationship between potency level and effect size



Jäger et al. 2010
ScientificWorldJournal 10:
2112-2129

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 - > Evaluation of 17 experimental models
 - > All publications available in full text online on ResearchGate.net
- > **Key result: Effects of homeopathic preparations increase with increasing complexity of the experimental system**

How to understand effects of homeopathic preparations?

- > Organism (specific form, pattern, behaviour)
 - > Organs (specific functions)
 - > Cells
 - > Matter (atoms, compounds)
-
- ↑ Conventional Medicine
- ↓ Homeopathic Medicine
- Complementary Medicine
- > Conventional Medicine in general uses a bottom-up approach
 - > Complementary Medicine in general uses a top-down approach
 - > Complementary Medicine (phytomedicine, homeopathy) uses complementary medicines (whole extracts), partially processed with complementary pharmaceutical methods (e.g. potentization)

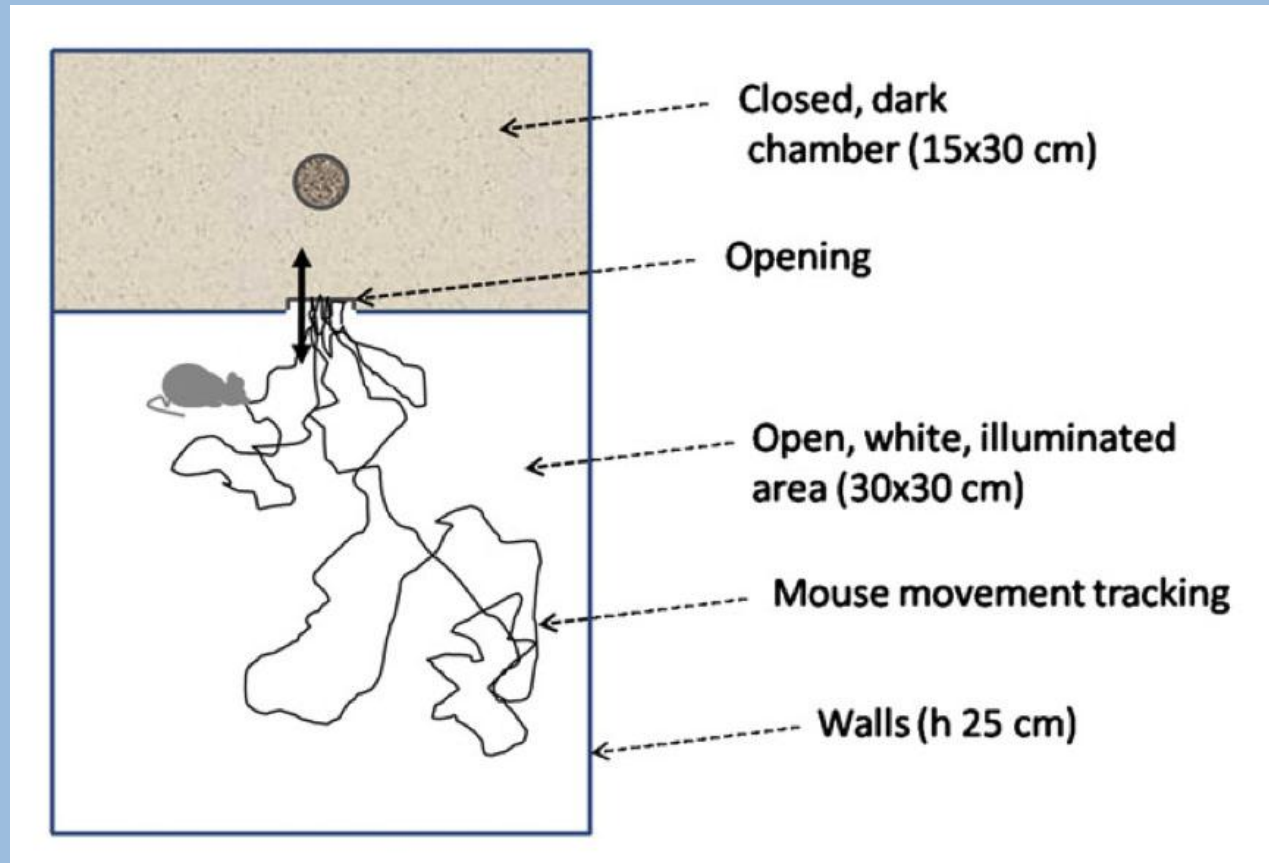
> **Complementary Medicine needs complementary (top-down) scientific methods to be properly investigated**

What are “complementary” (top-down) scientific methods?

- > Scientific methods that assess
 - Shapes, patterns, forms (of entire living organisms or within experiments)
 - Behaviour of organisms / functional relationships

Animal behavior test with homeopathic remedies

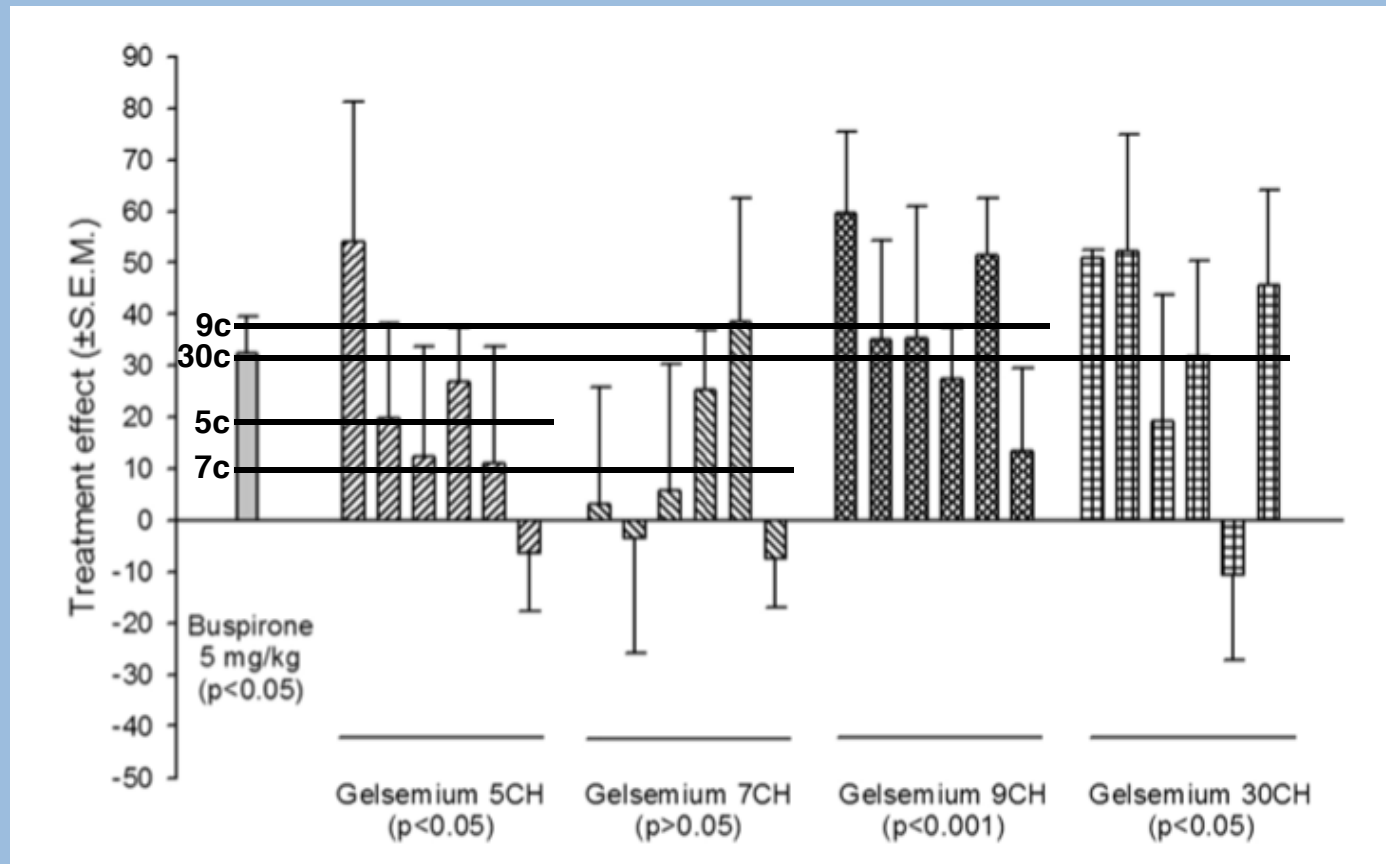
> LD exploration test with mice



Bellavite et al. 2009
Homeopathy 98: 208-227

Animal behavior test with homeopathic remedies

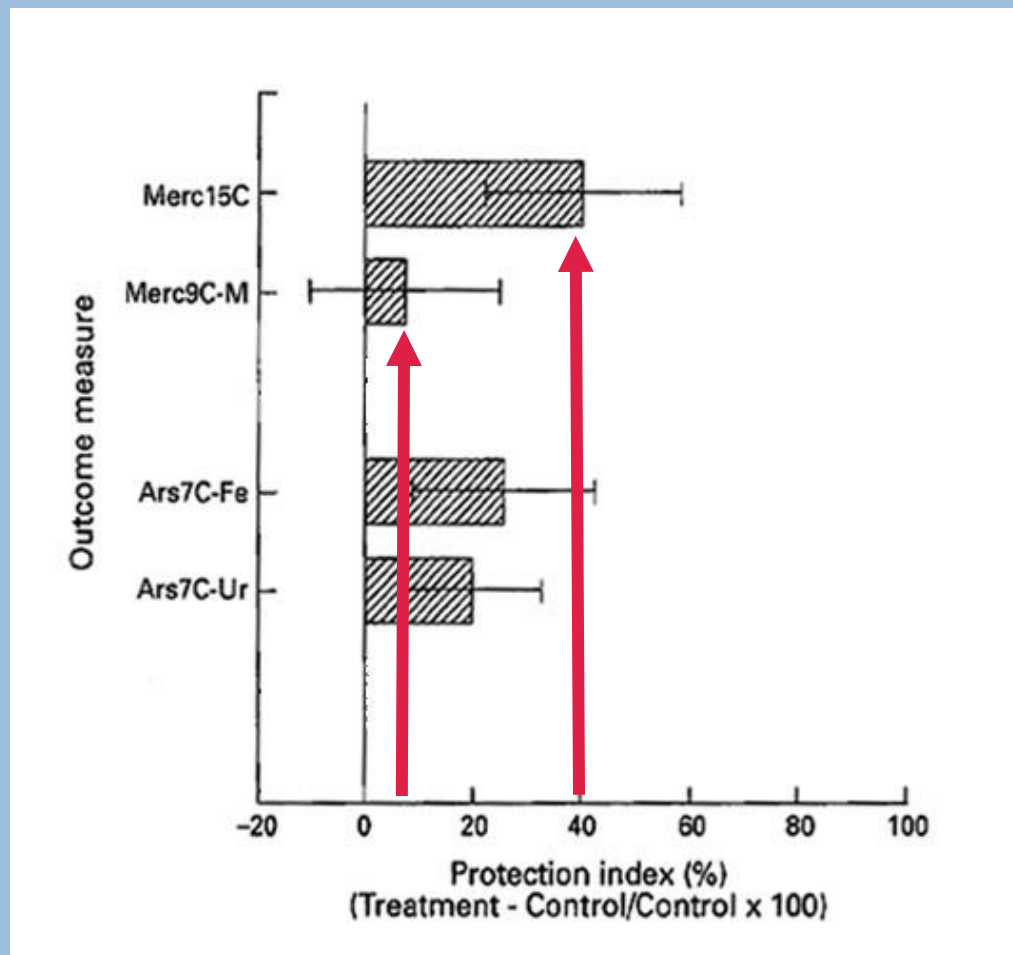
> LD exploration test with mice, treated with Gelsemium



Bellavite et al. 2009
 Homeopathy 98: 208-227

Meta-analysis regarding detoxication with homeopathic preparations

- > Mortality reduction after application of Mercury 15c or 9c for mice poisoned with mercury
- > Increase of arsenic excretion (in stool or urine) after application of arsenic 7c in rats poisoned with arsenic
- > Meta-analysis of Linde et al.: Hum Exp Toxicol 1994



Biocrystallisation as an example for a complementary scientific method

- > Crystallisation of copperchloride with added organic extract on flat circular glass plates under defined conditions
- > Visual evaluation (ISO criteria) or computer-based texture or structure analysis to assess the patterns / shapes formed



Without organic additive



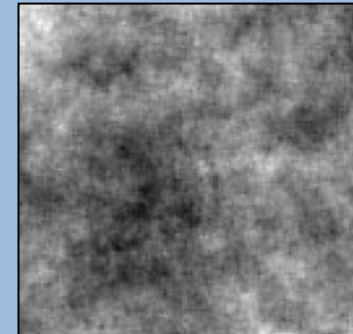
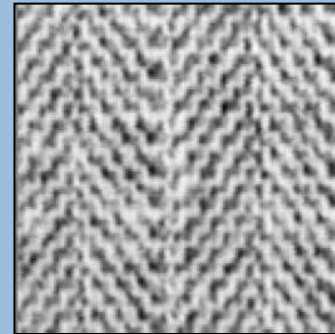
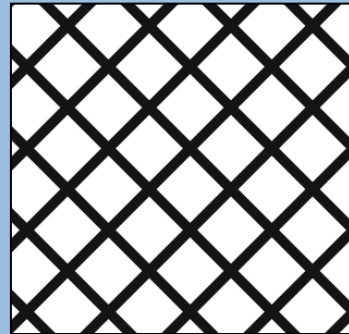
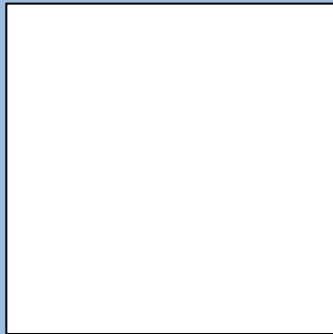
barley flour extract



extract from cress seedlings

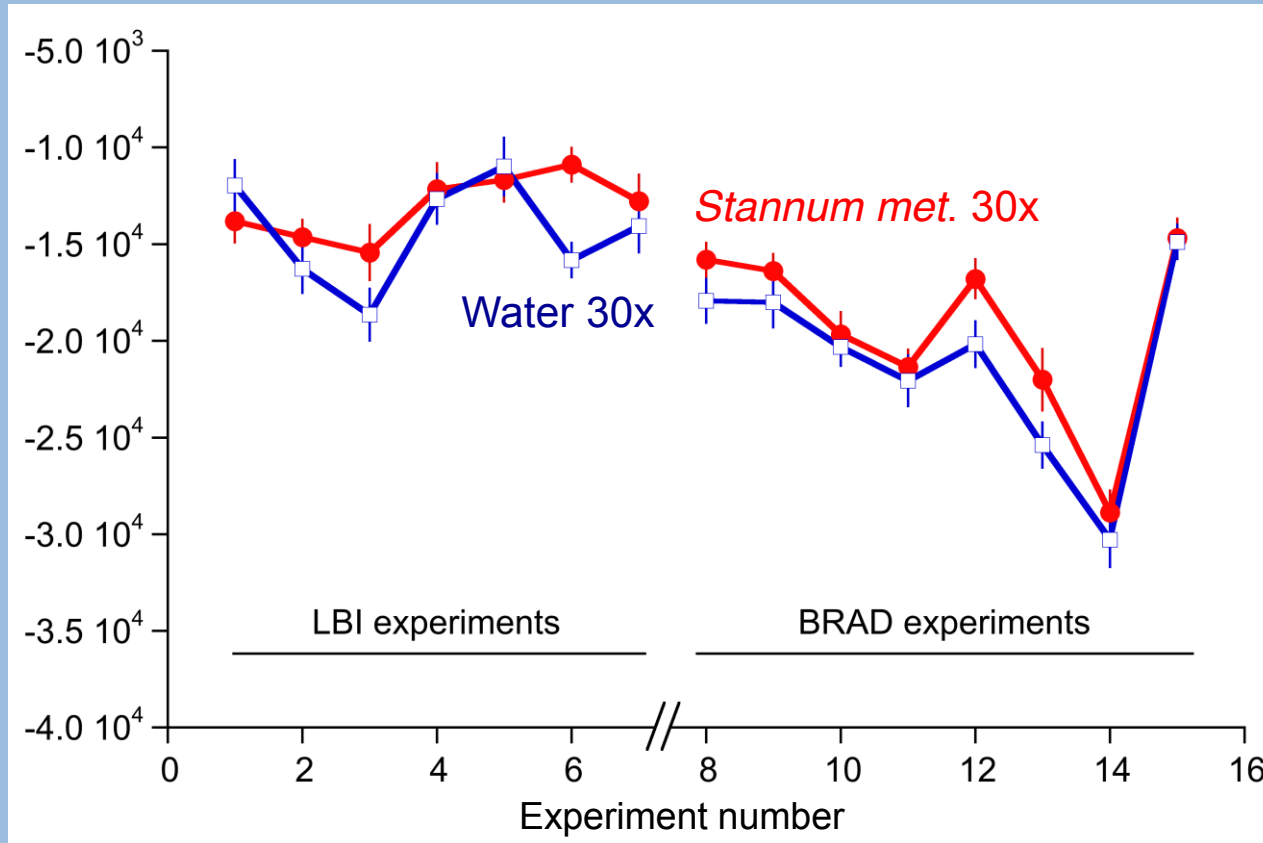
Biocrystallisation as an example for a complementary scientific method

- > Germination of cress (*Lepidium sativum* L.) in *Stannum met.* 30x or water 30x (2 x 3 experimental groups with 6 biocrystallisation replicates)
- > 7 and 8 experiments in 2 independent labs (Denmark, The Netherlands)
- > Computer-based texture analysis



Biocrystallisation as an example for a complementary scientific method

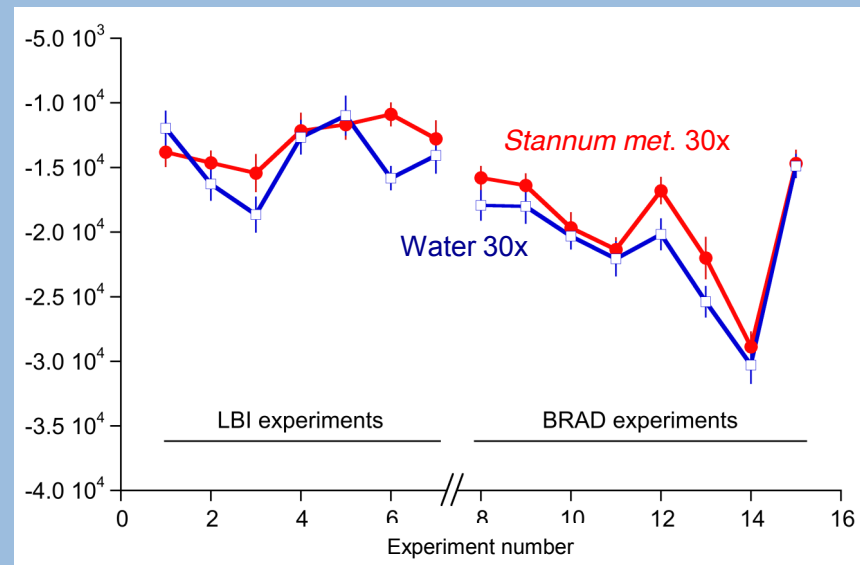
> Example: variable cluster_shade of texture analysis



Baumgartner et al. 2012
 eCAM, Article ID 125945

Biocrystallisation as an example for a complementary scientific method

- > Effect of *Stannum met.* 30x compared to water 30x on the texture of biocrystallograms is reproducible (within statistical power)
- > Follow-up trial (*Stannum met.* 30x vs. lactose 30x) to assess reproducibility as well as effects of autoclavation and cell-phone radiation on biological activity of *Stannum met.* 30x



Baumgartner et al. 2012
eCAM, Article ID 125945

Bioassays to assess homeopathic potentization: Summary

- > Results from laboratory trials support the notion that highly diluted potentized substances may exert specific effects
- > Effect size of homeopathic treatments seems to increase with increasing complexity of the bioassay
- > Homeopathic basic research needs top-down scientific methods (using entire organisms and complex/functional outcomes) to yield reproducible results
- > There are active and inactive potency levels (unknown pattern rules)