Basic research on homeopathic principles

Paolo Bellavite, Marta Marzotto, Debora Olioso, Clara Bonafini

University of Verona
Buon giorno! Good morning! 早安！

We thank for research grants:
- Boiron Laboratoires
- Italian Research Ministry

Verona Integrative Medicine Research Group (y. 2015)

Clara Bonafini  Marta Marzotto  Debora Olioso
Basic research on homeopathic principles

Summary

1. Introduction (motivation)
2. Studies in animal and plant models
3. In vitro laboratory studies
4. Perspectives
any unpublished trials and to get further details of the published ones. We used strict criteria to select the best trials and based our main conclusions on the results of these. The amount of positive evidence even among the best studies came as a surprise to us. Based on this evidence we would be ready to accept that homoeopathy can be efficacious, if only the mechanism of action were more plausible. The way in which the belief of people changes after the presentation of empirical evidence depends on their prior beliefs and on the quality of the evidence. Thus, people who

The two major PRINCIPLES to be investigated

- The same substance or similar substances can have opposite (inverse) effects in different conditions:
  a) doses or
  b) sensitivity of the target system

- Pharmacological power of the original substance is retained (or even enhanced?) in serial dilutions with succussion
Basic research on homeopathic principles

1. Introduction (motivation)
2. Studies in animal and plant models
3. In vitro laboratory studies
4. Perspectives
## EXAMPLES OF STUDIES IN WHOLE ORGANISMS (ANIMALS AND PLANTS)

<table>
<thead>
<tr>
<th>System</th>
<th>Agent</th>
<th>“Conventional” effect</th>
<th>“Homeopathic” effect</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat, Guinea pig</td>
<td>Histamine Lung Histamine Apis mell.</td>
<td>Pro-inflammatory agent</td>
<td>Histamine (30x), Lung histamine (18c) and Apis mellifica (7c/10c) reduce inflammation symptoms</td>
<td>Bastide 1975, Poitevin 1988, Bildet 1990, Conforti 1993</td>
</tr>
<tr>
<td>Rat, Mouse</td>
<td>Arsenic</td>
<td>Whole body and liver toxicity</td>
<td>Ars. high dilutions (7c-30c) protect from intoxication</td>
<td>Lapp 1955; Wurmser 1955; Cazin 1987-1991; Banerjee, P, Khuda-Bukhsh 1998-2000</td>
</tr>
<tr>
<td>Rat</td>
<td>Nux vomica</td>
<td>Neuroinhibition (strychnine)</td>
<td>Reduces alcohol-induced sleeping time</td>
<td>Sukul et al., 1999</td>
</tr>
<tr>
<td>Rat</td>
<td>Aspirin</td>
<td>Antithrombotic</td>
<td>Aspirin 10(^{-30}) g/kg (15c) has pro-thrombotic effects</td>
<td>Beulogne-Malfatti, Doutremepuich, Eizayag et al. 1998-2012</td>
</tr>
<tr>
<td>Rat</td>
<td>Phosphorus</td>
<td>Hepatotoxicity</td>
<td>Phosphorus high dilutions (30x) protects from toxic hepatitis</td>
<td>Bildet 1984, Guillemain 1987, Palmerini 1993</td>
</tr>
<tr>
<td>Rat, Mouse</td>
<td>Gelsemium s.</td>
<td>Toxic and convulsivant</td>
<td>Anxiolytic effect (2c-30c) of Gelsemium s.</td>
<td>Magnani 2010, Venard 2011, Bellavite 2012</td>
</tr>
<tr>
<td>Wheat</td>
<td>Arsenic</td>
<td>Cell toxicity</td>
<td>Ars. high dilutions (45x) stimulate vitality</td>
<td>Betti et al. 1997-2014</td>
</tr>
</tbody>
</table>

Madleine Bastide (1935-2007)

1975 ➢ Homeopathic dilutions (7C-9C) of bee venom (Apis mellifica and Apium virus, have a **protective and curative effect on X-ray induced erythema in albino guinea pig** (Bastide1975, Bildet1989, 1990)

1988 ➢ High dilutions of *Apis mellifica* inhibit basophil degranulation (histamine release) (Poitevin et al., 1988)

1993 ➢ Our group studied the effects of homeopathic preparations of *Apis mellifica* (and *Histamin*) on rat paw edema induced by the injection of inflammatory doses of histamine. High dilutions of up to 30D had a **small but significant inhibitory effect on the development of edema** (Conforti et al., 1993).

2004 ➢ We described a **small inhibiting effect of *Apis mellifica*** (4 D, oral drops) in the carrageenan-induced edema in rats.

2014 ➢ Bigagli and coworkers (2014) showed with microarray techniques that *Apis mellifica* TM modifies **expression of hundreds of genes** in human prostate epithelial cells; dynamized dilutions (3C, 5C and 7C) still exert significant effects on genes involved in inflammation and oxidative stress.
Thyroxine/tadpoles studies (1990-2015!)

Christian Endler

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Arsenic/plant studies (1994-2015!)

Lucietta Betti

«AGRO-HOMEOPATHY»?
INVERSE EFFECTS OF ASPIRIN (1990-2013...!)© P. Bellavite, Università di Verona

Dr Christian Doutremepuich

Dr Francisco Eizayaga

High dose (500 mg)
Low dose (50-100 mg)

Ultra-low dose (5CH)
High dilution (15-30CH)

Anti-thrombotic

Pro-thrombotic

(Pro-haemorrhagic)

Adverse effect

Homeopathic use?

(Anti-haemorrhagic)
Our studies in mice behavioral models (2007-2012)

1. **First series (ECAM J 2009):**
   - 8 replication experiments with *Gelsemium s. 5C*
   - 3 replication experiments with *Gelsemium s. 7C*
   - 2 replication experiments with *Gelsemium s. 30C*
   Positive control: 8 replications with Diazepam

2. **Second series (Psychopharmacology 2010):**
   - 6 replication experiments with *Gelsemium s. 4C, 5C, 7C, 9C, 30C*
   Positive control: 5 replications with Buspirone
   - 1 replication with Diazepam

3. **Pooled data analysis of the two series With Gelsemium s. (ECAM J. 2012)**

4. **Other Drugs:**
   - 4 replication experiments with *Aconitum 5C, 7C, 9C, 30C*
   - 5 replications with *Ignatia 4C, 5C, 7C, 9C, 30C*

Note: each replication experiment lasts about 4 weeks
Homeopathic research team in mice models (2007-2012)

Paolo Bellavite
Paolo Magnani
Elisabetta Zanolin
Marta Marzotto
Anita Conforti

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Behavourial models used

Open Field

A. MOVEMENT IN WHOLE FIELD
(total distance travelled, index of general function)

B. TIME SPENT IN CENTRAL AREA
(index of exploration attitude, anxiolytic-like effect)

- Double blind
- Ethological models
- No stress or pain to animals

Light-Dark choice

C. TIME SPENT IN LIT AREA
(no aversion to light, anxiolytic-like effect)

D. LIGHT-DARK transitions
(anxiolytic-like effect exploration attitude and movement)

Dark chamber
Lit arena

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**POOLED DATA ANALYSIS (14 complete experiments)**
Evidence-Based Complementary and Altern. Med., 2012

**A. GENERAL MOVEMENT**
(total distance travelled, movement and possibly sedation)

**B. TIME SPENT IN CENTRAL AREA**
(index of exploration attitude)

---

**Open field**

![Graphs showing EFFECT (% of control placebo)](image)

- **EFFECT (% of control placebo)**
  - Control (placebo), Diazepam, Buspirone, Gels 4C, Gels 6C, Gels 1C, Gels 9C, Gels 30C

---

*<0.05
**<0.01
***<0.001
POOLED DATA ANALYSIS (14 complete experiments)
Evidence-Based Complementary and Altern. Med., 2012

Notes:
7c,9c,30c > 4c, 5c
No «inversion of effects» (good thing)
No hormesis
Striking non-linearity

B. TIME SPENT IN CENTRAL AREA
(index of exploration attitude)

C. TIME SPENT IN LIT AREA
(anxiolytic-like effect)

D. LIGHT-DARK transitions
(anxiolytic-like effect and movement)

EFFECT (% of control placebo)

Roles:
Light
Dark

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Gelsemium sempervirens Activity on Neurosteroid Allopregnanolone Formation in the Spinal Cord and Limbic System of Rats

Adapted from: Christine Venard et al., ECAM-2011

***P < 0.001 as compared to gelsemine; **P < 0.01, ***P < 0.001 as compared to G. sempervirens (ANOVA followed by Bonferroni’s test).
Gelsemium s. in mice: KEY-NOTES

- Reproducible and significant effects in behavioral models in mice, concerning a subset of “symptoms”:
  - aversion to open space
  - amelioration with movement
  - feeling in a danger
  - aversion to light

- No adverse effects on general locomotion (an effect shown by buspirone in chronic treatment)

- NON-LINEARITY (various activity peaks) with increasing potencies, BUT in general different potencies have the same trend of effects (important for practical purposes). 7c-9c-30c higher effects than 4c and 5c

- Hypotheses of action mechanism: stimulation of glycine receptors and thus neurosteroid synthesis with consequent increase of GABA inhibitory effects (Venard et al 2011). More recently we also showed an effect on prokinectidine receptors (Olioso et al. 2014)
Confirmation of the “similia principle”: homeopathic dilutions counteract toxicity of ponderal doses (e.g. Arsenic, Phosphorus)

Confirmation in animals of some symptoms reported by Materia Medica (e.g. Gelsemium, Apis, Histaminum)

Hope of possible applications in agro-homeopathy

Consistent evidence that high dilutions (even beyond Avogadro) have reproducible effects different from control solutions: end of “placebo story”
End of “placebo story”? 

HOMEOPATHY IS NOT A PLACEBO! 

HOMEOPATHY CAUSES ADVERSE EFFECTS!
Basic research on homeopathic principles

1. Introduction (motivation)
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3. In vitro laboratory studies
4. Perspectives
## EXAMPLES OF INVERSE EFFECTS IN LABORATORY SYSTEMS

<table>
<thead>
<tr>
<th>System</th>
<th>Agent</th>
<th>First effect</th>
<th>Inverse effect</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast</td>
<td>Heavy Metals</td>
<td>Block growth</td>
<td>Low doses increase growth</td>
<td>Schulz 1988, Martius 1923, Stebbing 1982</td>
</tr>
<tr>
<td>Neurons</td>
<td>Naloxone</td>
<td>Antagonizes morphine</td>
<td>Low doses enhance the effect of morphine</td>
<td>Crain 1995</td>
</tr>
<tr>
<td>Neurons</td>
<td>β-amyloid</td>
<td>Toxic for mature cells</td>
<td>Promotes growth of young cells</td>
<td>Yankner 1990, Puzzo 2008</td>
</tr>
<tr>
<td>Epithelial and</td>
<td>Oxidants</td>
<td>Short-term/high doses decrease viability</td>
<td>Long-term/low doses increase viability</td>
<td>Da Silva 1996, Jenkins 1995</td>
</tr>
<tr>
<td>Tumor cells</td>
<td>Interferons</td>
<td>Activation of resting cells</td>
<td>Inhibition of pre-activated cells</td>
<td>Adams 1992</td>
</tr>
<tr>
<td>Macrophages</td>
<td>Endotoxins</td>
<td>Inhibit functions</td>
<td>Stimulate platelet adhesion</td>
<td>Andrioli-Bellavite 1997</td>
</tr>
<tr>
<td>Platelets</td>
<td>Diclofenac</td>
<td>Stimulate adherence</td>
<td>Low doses inhibit adherence</td>
<td>Bellavite 1993-1997</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>Bacterial</td>
<td>Metabolic inhibition</td>
<td>Metabolic priming and stimulation</td>
<td>Chirumbolo and Bellavite 1997</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Podophyllum</td>
<td>Metabolic inhibition</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Post-conditioning Hormesis: beneficial effects of low doses of a toxic substance

The influence of a step-down arsenite treatment on the induction of hsp68-mRNA.

**STIMULATION OF SELF-RECOVERY BY LOW DOSES OF ARSENITE IN ARSENITE-INTOXICATED CELLS.**

(F.A.C. WIEGANT, R. VAN WĲK et al.)

<table>
<thead>
<tr>
<th>treatment (µM Arsenite)</th>
<th>HSP 68</th>
<th>GAPDH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>time</td>
<td>time</td>
</tr>
<tr>
<td></td>
<td>-1</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
POSSIBLE MODELS EXPLAINING INVERSE EFFECTS (= SIMILIA PRINCIPLE) AT A CELLULAR LEVEL

- Detoxification enzymes (gene expression and enzyme activation)
- Heat shock proteins (stress proteins, chaperonins)
- Various receptors (different affinity and different coupling with signal transduction pathways)
- Gating theory (signal transduction)
- “Hormesis” (includes all the previous mechanisms): YES for low dilutions (ponderal doses); doubts for high dilutions.

References in www.paolobellavite.it
And recent papers in Journal «Homeopathy»
FROM LOW DOSES TO HIGH DILUTIONS: THE MOLAR LAW

- Dilutions of 1 Mol/L substance beyond 12CH or 24D do not contain (in theory) any molecule of the original substance.
- Since the initial concentration of active principles is usually much lower than 1 Mol/L, it can be assumed that a potency of 10 CH or 20D corresponds to the limit indicated by Avogadro’s constant: $6.02 \times 10^{23}$.)

Example: *Gelsemium* TM = $6.5 \times 10^{-4}$ Mol/l of gelsemine

*Gelsemium* 5c = $6.5 \times 10^{-14}$ Mol/l of gelsemine

*Gelsemium* 10c = $6.5 \times 10^{-24}$ Mol/l of gelsemine
### EXAMPLES OF HIGH DILUTION EFFECTS “IN VITRO”

<table>
<thead>
<tr>
<th>System</th>
<th>Agent</th>
<th>Dilution</th>
<th>Effect</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human basophils</td>
<td>Apis, Histamine</td>
<td>12CH-16CH 10^{-24} → 10^{-32}</td>
<td>Inhibition of activation markers</td>
<td>Poitevin 1988, Belon 1999-2009 (and Verona Group)</td>
</tr>
<tr>
<td>Human basophils</td>
<td>Adrenaline</td>
<td>12CH-16CH 10^{-24} → 10^{-32}</td>
<td>Inhibition of activation markers</td>
<td>Mannaioni et al. 2010</td>
</tr>
<tr>
<td>Cicken embryo</td>
<td>Bursin</td>
<td>15 CH (10^{-27} g)</td>
<td>Immunomodulatory and endocrine activity</td>
<td>Bastide, Youbicier-Simo 1993-97</td>
</tr>
<tr>
<td>Human neutrophils</td>
<td>Phosphorus</td>
<td>12 D to 30 D</td>
<td>Inhibition of superoxide production</td>
<td>Chirumbolo and Bellavite 1993</td>
</tr>
<tr>
<td>Rat neurons</td>
<td>Glutamate</td>
<td>10^{-18} → 10^{-30}</td>
<td>Protection from glutamate toxicity</td>
<td>Jonas et al., 2001</td>
</tr>
<tr>
<td>Neurocytes</td>
<td>Cycloheximide</td>
<td>10^{-27}</td>
<td>Increases viability</td>
<td>Marotta 2002</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Arsenicum</td>
<td>30CH</td>
<td>Protects from toxicity</td>
<td>Das et al 2011, De et al 2012</td>
</tr>
<tr>
<td>Neurocytes</td>
<td>Gelsemium s.</td>
<td>2-30 CH</td>
<td>Prevalent gene down-regulation</td>
<td>Marzotto 2014, Olioso 2014</td>
</tr>
<tr>
<td>Colon cancer cells</td>
<td>Ruta grav.</td>
<td>MT-30CH</td>
<td>Decrease viability, apoptotic gene expression</td>
<td>Arora and Tandon 2015</td>
</tr>
</tbody>
</table>
One of the first «homeopathic» papers in top journals


Figure 1  Basophil degranulation induced by $1.66 \times 10^{-9}$ M (final concentration) anti-IgE antibody in the presence of serial dilutions of Apis mel from 1 to 20 Apis mel. Control degranulations in the presence of HEPES-buffered Tyrode’s alone or the dilution corresponding to 9 Apis mel without adding Apis mel in the starting solution were 47.1 ± 1.0% and 46.5 ± 1.6% respectively (mean ± s.e. mean, n = 4). Control numbers were pooled in the figure (-----, mean ± s.e. mean, n = 8). * P < 0.02.
Inhibition of human basophil degranulation by successive histamine dilutions: Results of a European multi-centre trial

P. Belon¹, J. Cumps², M. Ennis³, P.F. Mannaioni ⁴, J. Sainte-Laudy⁵, M. Roberfroid⁶ and F.A.C. Wiegant⁷

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⁶ Laboratoire de biotoxicologie, UCL 7369, 73 avenue Emmanuel Mounier, B-1220 Brussels, Belgium
⁷ University of Utrecht, Department of Molecular Cell Biology, P.O. Box 80.056, NL-3508 TB Utrecht, The Netherlands

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Control (% degranulation)</th>
<th>Histamine (% degranulation)</th>
<th>Number</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45.8</td>
<td>36.5</td>
<td>123</td>
<td>0.0002</td>
</tr>
<tr>
<td>2</td>
<td>50.2</td>
<td>47.5</td>
<td>312</td>
<td>0.0065</td>
</tr>
<tr>
<td>3</td>
<td>51.6</td>
<td>47.4</td>
<td>183</td>
<td>0.024</td>
</tr>
<tr>
<td>4</td>
<td>47.8</td>
<td>35.7</td>
<td>154</td>
<td>≤ 0.0001</td>
</tr>
<tr>
<td>All</td>
<td>48.8</td>
<td>41.8</td>
<td>772</td>
<td>≤ 0.0001</td>
</tr>
</tbody>
</table>

Table 1. Comparison of percentage degranulation induced by anti-IgE (0.04 μg/ml) in the absence and presence of histamine dilutions (15th–19th centesimal dilutions).

Statistical comparisons were made using MANOVA.
Note:
No inversion of effects
No hormesis
Striking non-linearity
Gelsemium s. in a neuronal model

SH-SY5Y neurocytes-human neuroblastoma cells

Inverted microscope image

Confocal immunofluorescent image

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HRI – Roma 2015
Exposure to the Gelsemium s. 2CH promoted the significant down-expression of 49 genes while 7 genes were overexpressed

Many of these genes belong to:

• neuropeptide/receptor systems
• calcium signalling
• G-protein coupled transduction systems
• inflammatory pathways

HRI – Roma 2015
Effects of *Gelsemium* increasing dilutions/dynamizations on the expression of 49 Gels C2-down-regulated genes

<table>
<thead>
<tr>
<th>Gels 3c /Placebo 3c</th>
<th>N. Genes UP/DOWN</th>
<th>P (Fisher)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2↑</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>47↓</td>
<td></td>
</tr>
<tr>
<td>Gels 4c /Placebo 4c</td>
<td>3↑</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>42↓</td>
<td></td>
</tr>
<tr>
<td>Gels 5c /Placebo 5c</td>
<td>3↑</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>38↓</td>
<td></td>
</tr>
<tr>
<td>Gels 9c /Placebo 9c</td>
<td>9↑</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>30↓</td>
<td></td>
</tr>
<tr>
<td>Gels 30c /Placebo 30c</td>
<td>7↑</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>27↓</td>
<td></td>
</tr>
</tbody>
</table>

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**Recent evidence of Homeopathy and genome analysis**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Potencies</th>
<th>Cell type</th>
<th>Effect</th>
<th>REF</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Carcinosinum</em></td>
<td>MT, 30C, 200C</td>
<td>DLA cells</td>
<td>↑ specific gene expression (p53 pro-apoptotic)</td>
<td>(Sunila et al. 2009)</td>
</tr>
<tr>
<td><em>Arsenicum alb.</em></td>
<td>30C</td>
<td>Saccharomyces cerevisiae, E. coli</td>
<td>↑ Resistance to arsenicum toxicity ↓↑ expression of specific genes (apoptotic, stress response proteins)</td>
<td>(Das et al. 2011; De et al. 2012 of Khuda-B.group)</td>
</tr>
<tr>
<td><em>Carcinosinum, Hydrastis, Ruta or Thuja</em></td>
<td>200C</td>
<td>DLA cells</td>
<td>↑ Apoptosis , ↓↑ Gene expression (whole genome analysis)</td>
<td>(Preethi et al. 2012)</td>
</tr>
<tr>
<td><em>Gelsemium s.</em></td>
<td>2C, 3C, 5C, 9C, 30C</td>
<td>Human neurocytes SHSY5Y</td>
<td>7 genes ↑ 49 genes ↓ expression (whole genome analysis) ↓ gene expression (RT-Array, 2C)</td>
<td>(Marzotto et al. 2014; Olioso et al. 2014)</td>
</tr>
<tr>
<td><em>Apis mellifica</em></td>
<td>3C, 5C, 7C</td>
<td>Human prostate RWPE-1</td>
<td>↑↓ expression of different groups of genes (whole genome analysis)</td>
<td>(Bigaglì et al. 2014)</td>
</tr>
<tr>
<td><em>Rhus tox.</em></td>
<td>30X</td>
<td>Primary cultured mouse chondrocytes</td>
<td>↑ specific gene expression (COX-2), ↓ specific gene expression (collagen II; de-differentiation role)</td>
<td>(Huh et al. 2013)</td>
</tr>
<tr>
<td><em>Arsenicum alb.</em></td>
<td>45X</td>
<td>Arsenic-intoxicated wheat seeds</td>
<td>↑ Germination ↓ Gene expression levels</td>
<td>(Marotti et al. 2014)</td>
</tr>
<tr>
<td><em>Condurango</em></td>
<td>30C</td>
<td>H460-non-small-cell lung cancer cells</td>
<td>↓↑ expression of specific genes (apoptotic), ↑ Apoptosis, oxidative stress, mitochondrial depolarization</td>
<td>(Sikdar et al. 2014)</td>
</tr>
</tbody>
</table>
DNA gene expression is sensitive to:

→ Low energy information (Montagnier studies)
→ High homeopathic dilutions
→ Bioelectromagnetics
→ Water clusters

The rapid development of new high-throughput technology platforms provides a methodological basis for deep understanding the action mechanisms and targets of homeopathic remedies.

In future: Help in prescription??
Basic research on homeopathic principles

1. Introduction (motivation)
2. Studies in animal and plant models
3. In vitro laboratory studies
4. Perspectives
3 major certainties

- The inverse effects of high vs low doses in several cellular, plant and animal models (classic hormesis, Arndt-Schulz, initial value of Wilder)
- The effects of different substances in high dilutions (beyond Avogadro) described in many different models and many different laboratories: no placebo
- Action on cell receptors and on gene expression

3 major uncertainties

- The inter-experiment and inter-laboratory reproducibility, seasonal effects, etc. An “intrinsic” feature of high dilutions (non-linearity, chaos theory)?
- The nature of the “physical” state of the highly diluted solutions
- The transfer of information from triturations to liquid and from liquid to granules
Future tasks

- Further development of laboratory models for:
  a) **high dilutions/dynamizations** and
  b) **similia principle** (opposing effects in normal and stressed systems)

- Identification of **variables and critical factors in reproducibility**

- Evaluation of different **preparations** (liquid, granules, alcohol) and different dynamization procedures

- **Integration** of experimental models from molecules to humans for specific relevant remedies ("from bench to bedside")
Scientific research on high dilutions of Phosphorus

1975-84 ➢ Protective effect of high dilutions (7c and 15c) of phosphorus on CCl4-induced toxic hepatitis in the rat [Bildet et al. 1975; Bildet et al. 1984a; Bildet et al. 1984b].

1987 ➢ The mortality of rats treated with lethal doses of α-amanitine is significantly slowed by treatment with 15c dilutions of Phosphorus [Guillemain et al. 1987].

1993 ➢ Protective effect of Phosphorus 30c on fibrosis of the liver caused by chronic administration of CCl4 in rats [Palmerini et al. 1993]

1993 ➢ Phosphorus and Magnesia phosphorica (dilutions greater than 15x) decrease free radical production by human granulocytes [Chirumbolo et al. 1993]

2007 ➢ Phosphorus 1M reduces the incidence of 3-methylcholanthrene-induced sarcomas and also increase the life span of mice harboring the tumours [Kumar et al. 2007].

2008 ➢ In rats, Phosphorus 12x shows a protective action on the mortality by T. cruzi infection (Chagas disease) [de Almeida et al. 2008]

2011 ➢ Homeopathic Phosphorus (P) (9c) improved growth and yield of essential oil of Verbena gratissima, a plant native to Brazil [Santos et al. 2011]. No effects on Lemna gibba where Arsenicum acted [Jager et al. 2011]

2014 ➢ Phosphorus high dilutions (15c and 200c) was successfully used in 2 patients with fulminant hepatic failure from Amanita phalloides poisoning [Frass et al. 2014]
The research ways: Evidence and Plausibility

Homeopathy acceptance and progress

CLINICAL RESEARCH

«EVIDENCE»

PLAUSIBILITY

BASIC RESEARCH

«PLAUSIBILITY»
SAPERE AUDE! 
(DARE TO KNOW! - 必须知道的勇气！)

Orazio (Epistole I, 2, 40)