



# ADVANCES IN HOMEOPATHY RESEARCH

## | Evidence-based homeopathy

### | Fundamental research

- Physicochemical properties
- *In vitro* and *in vivo* biological activities

### | Clinical research

- Meta-analyses
- Randomized controlled trials
- Real-life observational studies

Boost of neuroblastoma cells differentiation, with Gelsemium 5 C - Lejri I, et al. 2022



***"H**omeopathy, a medicine founded over two centuries ago, continues to attract growing interest among healthcare professionals and the general population alike. Although it is based on specific principles such as “the law of similitude”, the individualization of treatment and the use of active ingredients (diluted and succussed stocks), homeopathy does not escape the demands of modern science.*

*Research in homeopathy, whether fundamental or clinical, plays an essential role in gaining a better understanding of its mechanisms of action, evaluating its effects and ensuring high standards in its practice. Driven by its ongoing commitment to science, our laboratory has been working with international research teams and learned societies for many years.*

*This brochure provides an overview of recent advances, the methodologies used and the challenges of research in this field. It highlights the fact that homeopathy is more than ever a medicine based on science, offering practitioners a safe, effective therapeutic tool as part of a patient-centered approach."*

# FUNDAMENTAL RESEARCH IN HOMEOPATHY

The aim of **fundamental research** is to study the physicochemical characteristics and biological actions of homeopathic solutions, and to develop hypotheses to understand their mechanisms of action.

The research is **current, multidisciplinary and high-quality** and involves international researchers working on experimental models (plant, cell and animal). Around a hundred studies replicated in 28 different experimental models were identified in a literature review spanning more than 20 years.<sup>1</sup>

This research is conducted in **international academic or private centers** such as:

- The **Homeopathy Research Institute**, the international coordinator and reference for homeopathy research: <https://www.hri-research.org/fr/>.
- A research unit **in Brazil** including around 15 university laboratories.
- The University of Bern **in Switzerland**, which regularly publishes scientific articles on plant models.
- Scientific and university research centers **in France**: the University of Reims Champagne-Ardenne, INSERM in Strasbourg, etc.

# Physicochemical properties of homeopathic solutions

**Physics and chemistry research** studies the specific properties of homeopathic solutions, particularly highly diluted, succussed preparations.

**72%** demonstrate **measurable and specific properties of homeopathic solutions.**<sup>2-4</sup>

Recent systematic reviews by Tournier *et al.* show **significant research developments in this field** in recent years, proposing **hypotheses on homeopathy's mechanisms of action.**<sup>2-4</sup>



These results were obtained using cutting-edge technology such as:<sup>2-4</sup>

- NMR.
- UV-Vis-IR optical spectroscopy.



Klein *et al.*, 2018



Tournier *et al.*, 2019



Tournier *et al.*, 2021

| **IR:** Infrared; **NMR:** Nuclear Magnetic Resonance; **UV:** Ultraviolet

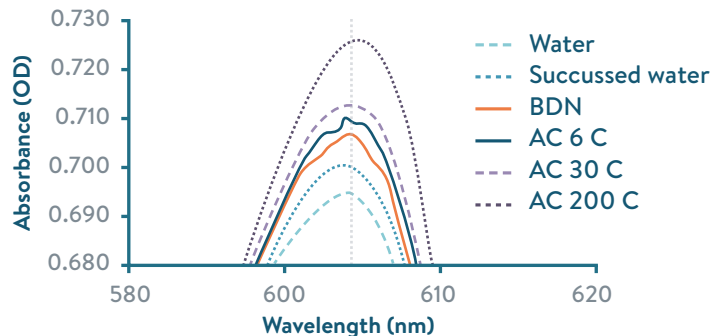
These data presented cannot be extrapolated under any circumstances for clinical use in humans.

# Physicochemical properties of homeopathic solutions

The analysis of homeopathic solutions using physics or chemistry techniques (NMR, conductometry, solvatochromism) reveals specific **physicochemical properties** and the **importance of succussion**.

## Specific physicochemical properties<sup>5</sup>

Modification of absorbance as a function of the homeopathic solution in solvatochromic dye BDN.<sup>5</sup>



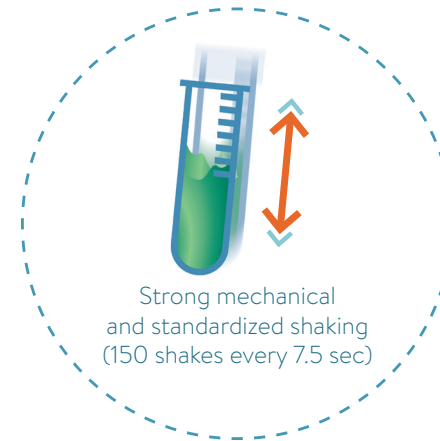
Adapted from Bonamin et al., 2020<sup>5</sup>

A homeopathic solution has **specific physicochemical properties according to its level of dilution.**



Bonamin et al., 2020

## Importance of succussion



- **Key stage** in the homeopathic solution manufacturing process.<sup>6</sup>
- **Essential** for distinguishing homeopathic solutions from neutral solutions or simply diluted solutions.<sup>7</sup>

- Succussion is key for an ultra-highly diluted solution to express a biological activity. **A simply diluted solution does not have the same biological activity as a diluted and succussed solution.**<sup>8</sup>

| **AC:** *Antimonium crudum*; **BDN:** dimethylaminonaphthalene

# Biological action of homeopathic solutions

Fundamental research in homeopathy uses a variety of **study models**:



**Plant**



**Cell**



**Animal**

***In vitro* and *in vivo* models have demonstrated the biological action of homeopathy in different areas**, including:

- Action on the immune response (see page 8).
- Action on the nervous system's biological parameters (see page 9).

The use of **standardized models** demonstrates the **reproducibility** of results and **confirms the biological action of homeopathic solutions**, for example through 20 years of experiments conducted in the duckweed plant model (see page 12) or, more recently, in a strawberry plant model (see page 13).



## **Did you know?**

- 77% of biological experiments show reproducible effects on various animal, cell and plant models.<sup>9</sup>
- 95% of controlled studies in plant models show significant effects compared with the control.<sup>10</sup>

# BIOLOGICAL ACTION OF A HOMEOPATHIC SOLUTION OF *ANTIMONIUM CRUDUM* ON IMMUNE RESPONSE MODULATION

## ►► Preliminary *in vivo* study in a mouse model<sup>11</sup>



**Objective:** *In vivo* evaluation of the activity of *Antimonium crudum* 30 C in mice infected with leishmaniasis.



**Result:** Mice treated with *Antimonium crudum* 30 C show a decrease in the infiltration of inflammatory cells at the site of parasite inoculation compared to the control. This decrease is particularly marked during the chronic phase.

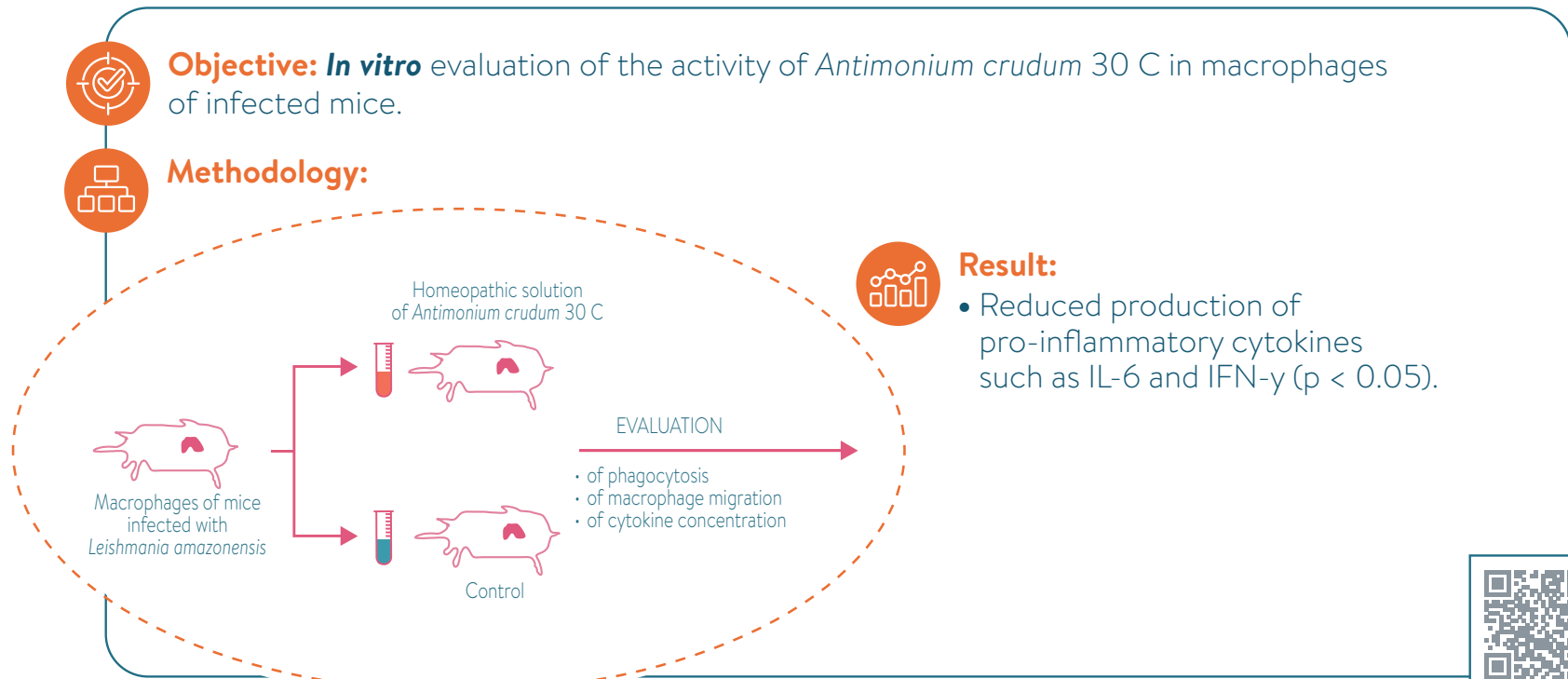
## ►► *In vitro* confirmation in an immune cell model<sup>12</sup>



**Objective:** *In vitro* evaluation of the activity of *Antimonium crudum* 30 C in macrophages of infected mice.



**Methodology:**



IL-6: Interleukin-6; IFN- $\gamma$ : Interferon gamma

De Santana et al., 2017

# RESEARCH PROGRAM ON THE BIOLOGICAL ACTION OF HOMEOPATHIC SOLUTIONS OF *GELSEMIUM*



This research program is carried out by two independent centers in collaboration with Boiron:

- Biopathology of myelin, neuroprotection and therapeutic strategies department, INSERM U1119 in Strasbourg, France.
- Neurobiology laboratory for brain ageing, mental health and molecular and cognitive neurosciences, University of Basel, Switzerland.

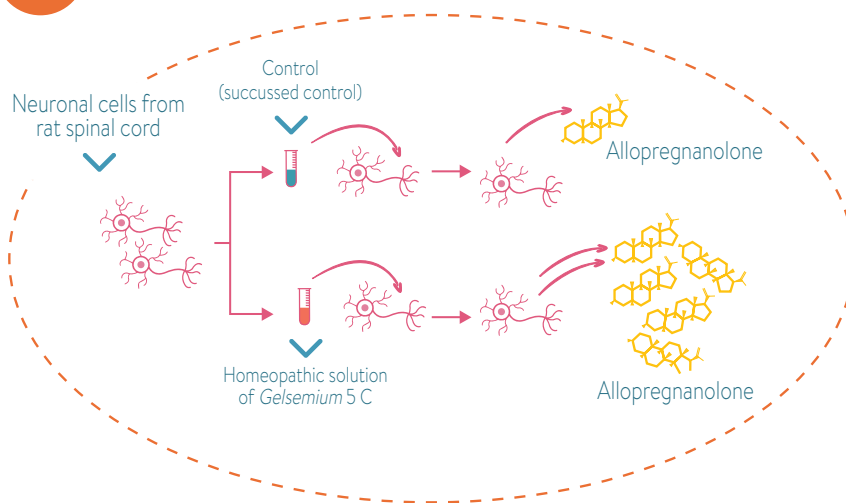
## »» **In vitro study in a rat neuronal cell model<sup>13</sup>**



**Objective:** Evaluation of the biological action of *Gelsemium* 5 C.



**Methodology:**



**Result:**



Venard et al., 2011

**x5**

**Allopregnanolone\*** secretion is increased fivefold with *Gelsemium* 5 C versus control ( $p < 0.001$ ).

\* a neurosteroid involved in managing anxiety.

These data presented cannot be extrapolated under any circumstances for clinical use in humans.

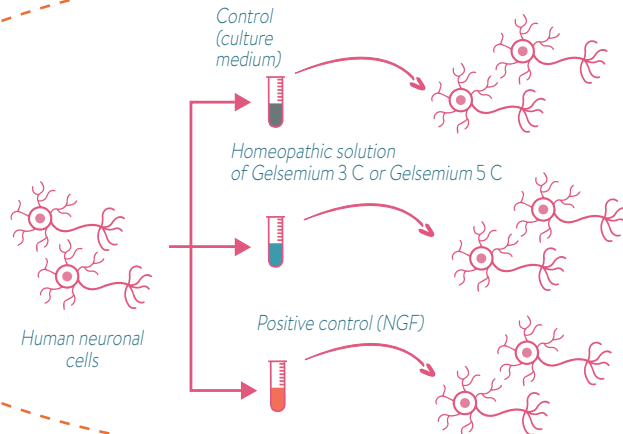
# »» In vitro study on the metabolism of human neuronal cells in physiological conditions<sup>14</sup>



**Objective:** Evaluate the effect of *Gelsemium 3 C* and *Gelsemium 5 C* on mitochondrial functions and neurite outgrowth.



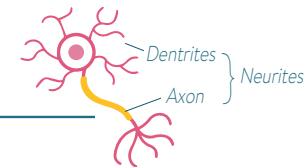
**Methodology:**



**Results:**

*Gelsemium 3 C* and *Gelsemium 5 C* significantly stimulate :

- ATP production,  $p < 0.01$ .
- Mitochondrial functions,  $p < 0.05$ .
- Neurite outgrowth and complexity (dendrites + axons),  $p < 0.01$ .



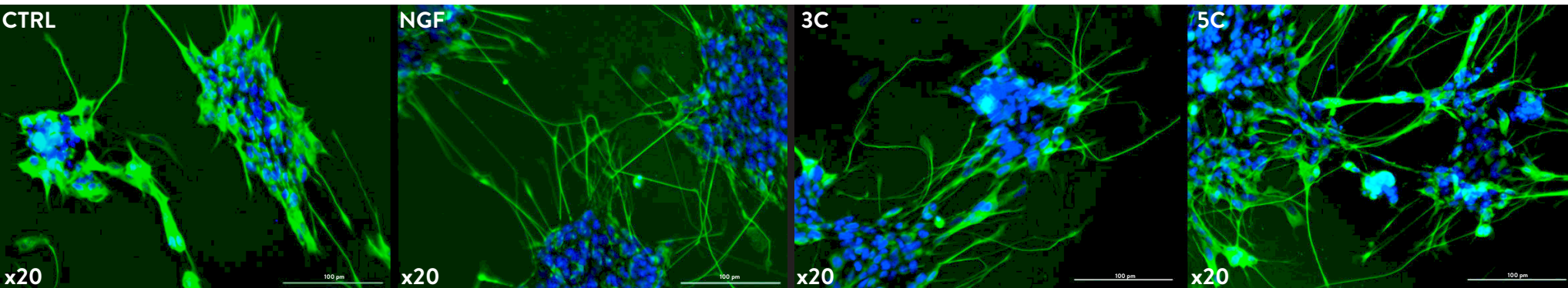
Lejri et al., 2022

Control - culture medium

Positive control

*Gelsemium 3 C*

*Gelsemium 5 C*



Photographs taken from the publication showing neurite outgrowth and complexity under different experimental conditions.

| **ATP:** Adenosine Triphosphate; **NGF:** Nerve Growth Factor

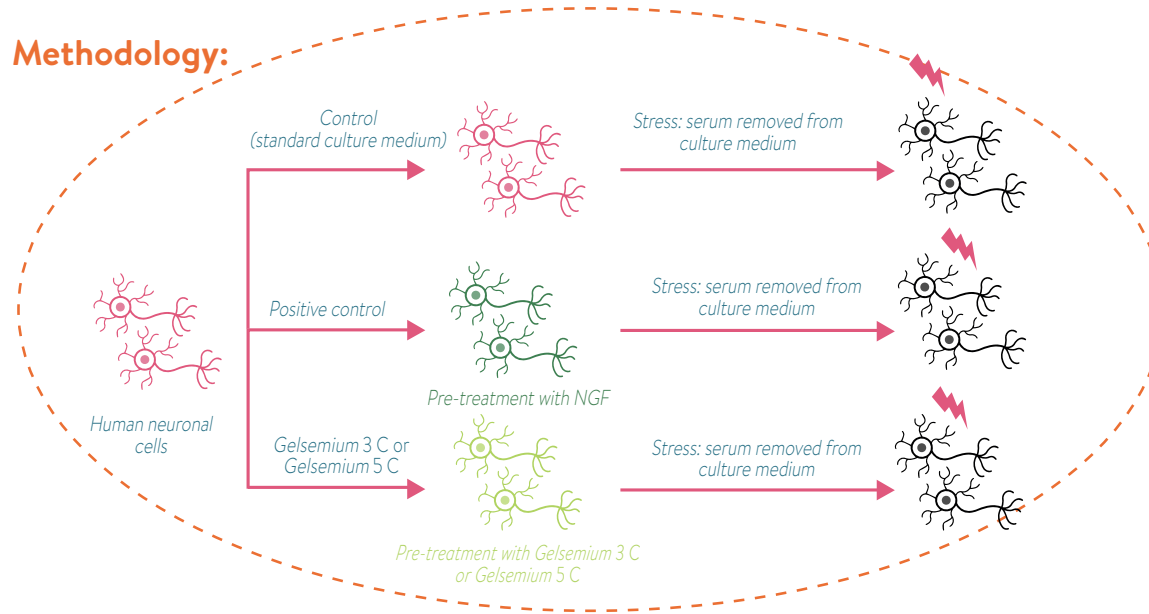
# »» In vitro study on the metabolism of human neuronal cells in stress conditions<sup>15</sup>



**Objective:** Evaluation of the protective effect of *Gelsemium 3 C* and *Gelsemium 5 C* against cellular stress.



**Methodology:**



Lejri et al., 2025



**Results:**

*Gelsemium 3 C* and *Gelsemium 5 C* significantly protect ( $p < 0.05$ ) cells against stress induced by serum deprivation:

- Preservation of mitochondrial structure.
- Improved ATP production.
- Reduced free radical production.

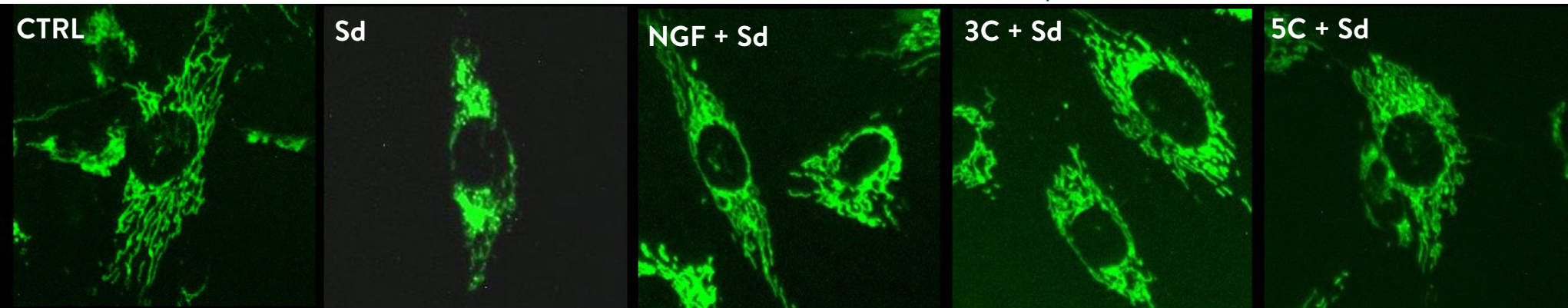
Control - standard culture medium

Control - culture serum-free medium

NGF pre-treatment

*Gelsemium 3 C* pre-treatment

*Gelsemium 5 C* pre-treatment



Photographs taken from the publication showing the mitochondrial network structure under different experimental conditions.

These data presented cannot be extrapolated under any circumstances for clinical use in humans.

# BIOLOGICAL ACTIVITY OF HOMEOPATHY ON PLANT MODELS

Experiments conducted at the University of Bern (Switzerland) resulting in around fifty publications in leading scientific journals.

## ►► Preliminary *in vivo* study in a plant model<sup>16</sup>



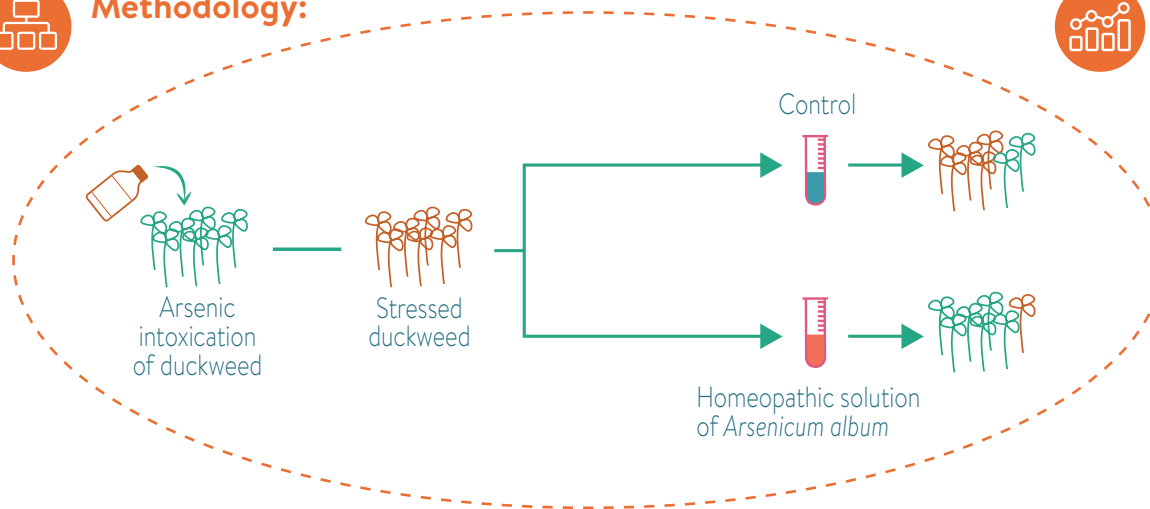
**Objective:** Evaluation of the biological activity of a highly diluted (17 to 33 D) homeopathic solution of *Arsenicum album* on the growth of duckweed previously stressed with arsenic.



**Methodology:**



**Results:** A homeopathic solution of *Arsenicum album* protects duckweed from arsenic poisoning, restoring its growth ( $p < 0.05$ ).



Jäger et al., 2010

## ►► Validation of reproducibility and robustness of results<sup>17</sup>



**Methodology:**

Replication of the Jäger et al. 2010 study in 2 sets of 5 experiments.



**Results:**

The results **confirm the robustness of the method** and are in line with the conclusions of the initial experiment (significant difference with the control group,  $p < 0.0001$ ).



Ücker et al., 2022

# BIOLOGICAL ACTIVITY OF HOMEOPATHY ON PLANT MODELS

Experiments conducted by Leonardo Faedo's team at the University of Santa Catarina in Brazil.

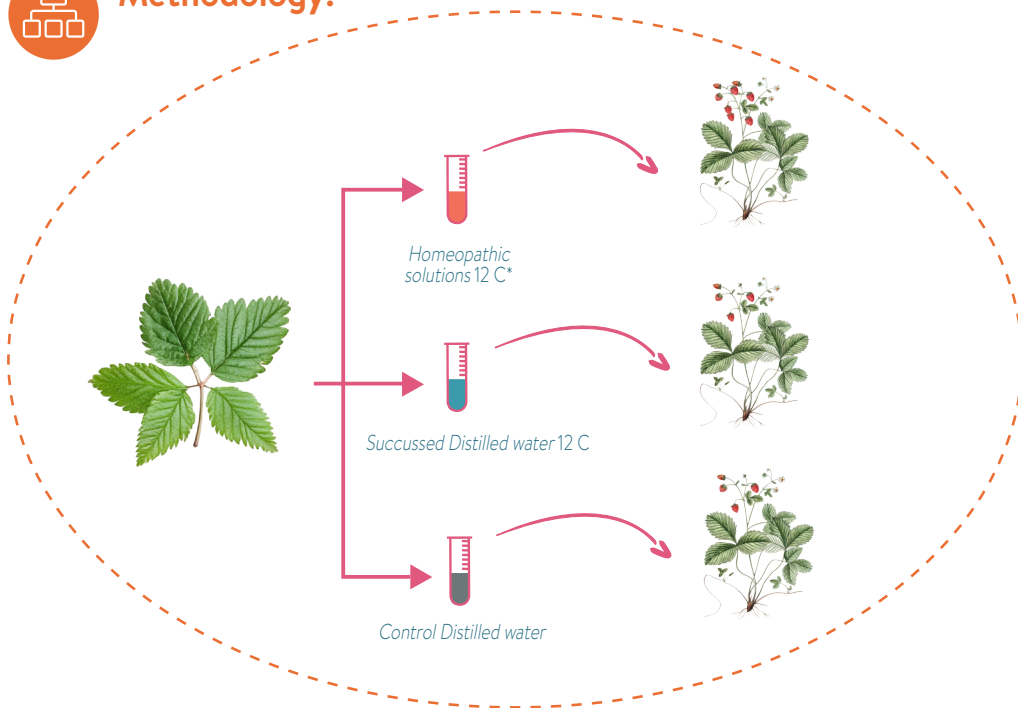
## Study in a strawberry plant model<sup>18</sup>



**Objective:** Evaluation of homeopathic solutions for the natural biostimulation of strawberry plants: study of the impact on production, plant growth, fruit quality and incidence of diseases and parasites.



### Methodology:



### Results:

- Plant growth and crop yield compared to control ( $p < 0.05$ ):
  - *Sulphur* 12 C
  - *Phosphorus* 12 C
  - *Kali carbonicum* 12 C
- Reduction of the incidence of severity of pest and disease compared to control ( $p < 0.05$ ):
  - *Sulphur* 12 C
  - *Silicea terra* 12 C
- Development of root system compared to control ( $p < 0.05$ ):
  - *Silicea terra* 12 C
  - *Calcarea carbonica* 12 C
- No significant difference between Succussed Distilled water 12 C to control.

\* Strains studied individually  
*Calcarea carbonica* 12 C, *Kali carbonicum* 12 C,  
*Mercurius solubilis* 12 C, *Natrum muriaticum* 12 C,  
*Phosphorus* 12 C, *Sulphur* 12 C, *Silicea terra* 12 C.



Faedo et al., 2024

These data presented cannot be extrapolated under any circumstances for clinical use in humans.



# CLINICAL RESEARCH IN HOMEOPATHY

**Clinical research** aims to demonstrate the benefit provided by individualized homeopathic treatment, which considers each individual to be unique, as well as the specific efficacy and safety of each medicine.

**Interventional research** in homeopathy includes 286 randomized controlled trials, 166 of which were double blind, carried out on homeopathic medicines in around a hundred clinical situations and providing tangible proof of efficacy.<sup>19</sup>

**The joint analysis of clinical trials** has enabled **meta-analyses to be created**, providing an additional level of proof.

**"Real-life" observational studies** offer an evaluation methodology that is particularly suited to homeopathy as they take into account its specific characteristics such as **individualized treatment** and measuring a benefit for **all patient profiles**, including vulnerable populations.

# Efficacy of individualized homeopathic treatments versus placebo<sup>20</sup>



**Objective:** Evaluation of the clinical benefit of individualized homeopathic treatment versus placebo.



**Methodology:**

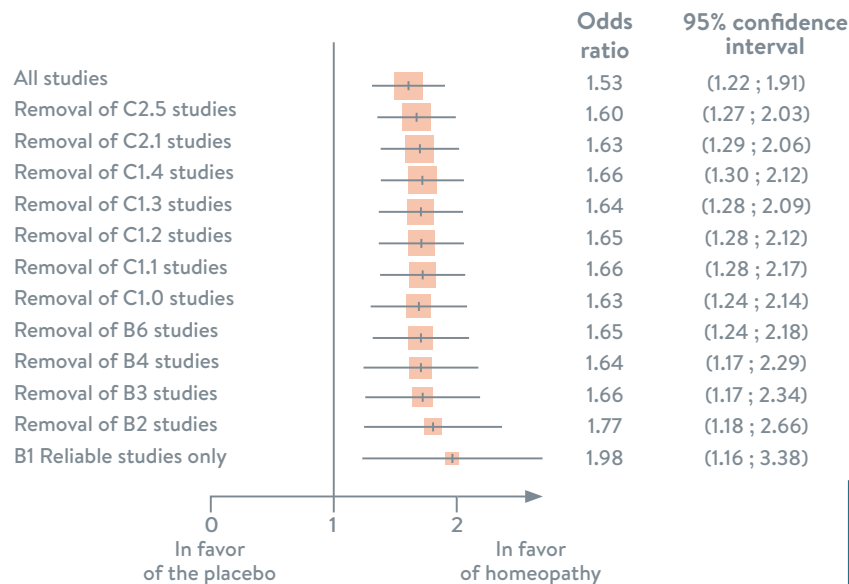
- **Meta-analysis** compiling the results of **22 randomized controlled trials**, in all clinical situations.
- Global statistical analysis carried out according to Cochrane methodology criteria.



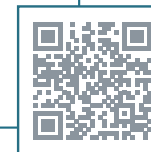
**Results:**

- Homeopathic medicines, when prescribed during individualised treatment, are **1.5 to 2 times** more likely to have a beneficial effect than placebo.
- More criteria were of high methodologic quality, more results seemed to be in favor of homeopathy compared to placebo.

**Sensitivity analysis showing the progressive effect on the combined odds ratios of the studies by progressively removing studies classified by risk of bias.**



Adapted from Mathie et al., 2014



Mathie et al., 2014

# Efficacy of homeopathic treatments *versus* placebo<sup>21</sup>



## Objective:

Evaluation of the efficacy of homeopathic treatments *versus* placebo, for all indications.



## Methodology:

Systematic literature review evaluating 6 meta-analyses published between 1997 and 2017 relating to randomized controlled trials evaluating homeopathy *versus* placebo for all indications (gastroenterology, gynecology, obstetrics, respiratory infections, neurology, etc.).



## Results:

**5 out of 6 meta-analyses** demonstrate the **significant efficacy of homeopathy** compared with a placebo, with particularly robust results for individualized homeopathy (OR = 1.53 [CI<sub>95%</sub>: 1.22 ; 1.91]).



Hamre et al., 2023

This publication highlights the superiority of homeopathy over the placebo:

“*Contrary to what is commonly stated, meta-analyses of randomized controlled trials available in homeopathy, regardless of indication, demonstrate significantly better positive effects than the placebo.*”

| OR: Odds Ratio; CI: Confidence Interval

# Public health benefit of medical care by a homeopathic general practitioner compared with conventional medical care: EPI 3 program<sup>22-25</sup>



**Objective:** • Evaluate the public health benefit of medical care by a homeopathic general practitioner compared with conventional medical care.  
• Describe and compare patients according to whether their doctor practices conventional or homeopathic medicine.



**Methodology:** This program includes a **cross-sectional study** (8,559 patients, 825 general practitioners) and **three cohort studies of conditions** representing the **main reasons for consulting a general practitioner:**

- Upper respiratory tract infections.
- Musculoskeletal pain.
- Sleep disorders/Anxiety-depression.



EPI 3 publications



## Results:

- **Clinical progression of patients treated by a homeopathic general practitioner similar to that of other patients**, with no loss of chance (no significant difference in terms of clinical progression complications).
- **Two to three times lower consumption of conventional medicines** in patients followed by a homeopathic general practitioner compared with treatment by a conventional general practitioner.

### Musculoskeletal pain (1,153 patients)<sup>25</sup>

- **60%** analgesics  
OR = 0.40 [CI<sub>95%</sub>: 0.20 ; 0.82]

- **46%** NSAIDs  
OR = 0.54 [CI<sub>95%</sub>: 0.38 ; 0.78]



### Upper respiratory tract infections (518 patients)<sup>22</sup>

- **57%** antibiotics  
OR = 0.43 [CI<sub>95%</sub>: 0.27 ; 0.68]

### Anxiety and depressive disorders (710 patients)<sup>23</sup>

- **71%** psychotropic drugs  
OR = 0.29 [CI<sub>95%</sub>: 0.19 ; 0.44]

### Sleep disorders (346 patients)<sup>24</sup>

- **75%** psychotropic drugs  
OR = 0.25 [CI<sub>95%</sub>: 0.14 ; 0.42]

**NSAID:** Non-Steroidal Anti-Inflammatory Drug

# Critical review of the EPI 3 study<sup>26</sup>

Conducted by Professor Yola Moride, an internationally recognized expert in pharmacoepidemiology with over 25 years' experience in conducting observational studies.



**Objective:** Confirm the validity of the conclusions of the EPI-3 study regarding the quality of evidence, methodological robustness, and generalization of results.



## **Methodology:**

Critical analysis of the methodological quality of the EPI3 study by comparing the nine articles published in the literature by the study researchers and good practices in pharmacoepidemiology.



## **Results:**

Confirmation of the methodological quality of the EPI 3 study:

- Rigorous selection of doctors and patients included in the study.
- Results measured using scales and validated instruments for the three pathologies of interest (musculoskeletal pain, sleep disorders, anxiety/depression and upper respiratory tract infections).
- Robust statistical analyses according to best practices in observational research.
- Representativeness of the results of the EPI 3 study and extrapolation to the French population.



Moride, 2022

**This critical review confirms that homeopathic medical care meets the specific needs of patients, with lower use of conventional medicines, a comparable clinical benefit and no loss of chance.**

# Benefits of homeopathic treatments in different therapeutic areas

Bodies of evidence combining scientific data from randomized controlled trials and observational data are now well established in the following clinical situations.

## Psychological disorders

### INSOMNIA<sup>27</sup>

#### Double-blind, randomized, placebo-controlled clinical trial



##### Methodology:

- 60 patients (30 patients in the homeopathy group and 30 patients in the placebo group) monitored for 3 months.
- Primary endpoint: sleep questionnaire based on 6 criteria (latency to fall asleep, minutes awake in the middle of the night, minutes awake too early, hours spent in bed, total sleep time in hours, sleep efficiency).
- Secondary endpoint: score from 0 (no insomnia) to 28 (severe insomnia) to measure insomnia severity (ISI).



##### Results:

##### Improved sleep time and quality:

Significant improvement in 5 criteria in the homeopathy group (no significant difference concerning minutes awake too early) compared with only 1 (sleep efficiency) in the placebo group ( $p < 0.01$ ).

##### Improved insomnia score:

Significant score reduction of 3.2 points in the insomnia severity score compared with the placebo group ( $p = 0.014$ ).



Michael et al., 2019

### DEPRESSION<sup>28</sup>

#### Pragmatic, randomized, controlled trial



##### Methodology:

- 566 patients monitored over twelve months.
- 185 patients in the usual treatment and homeopathy group and 381 in the control group (usual treatments only).
- Primary endpoint: patient health questionnaire (PHQ-9), scale of 0 to 27 (severe depression).
- Secondary endpoint: anxiety score (GAD-7), scale of 0 to 21 (severe anxiety).



##### Results:

- **Depression score at 6 months lower** by 2.6 points ( $p = 0.018$ ) and **anxiety score lower** by 2.8 points ( $p = 0.004$ ) in the homeopathy group.
- **Results maintained at 12 months.**



Viksveen et al., 2017

**GAD:** Generalized Anxiety Disorder;  
**ISI:** Insomnia Severity Index;  
**PHQ:** Patient Health Questionnaire

## In supportive care in oncology

Homeopathy does not treat cancer but is a valuable asset when used alongside other methods at each stage of the treatment journey to help patients better tolerate the side effects of the treatments and illness.

### »»» Prospective observational study<sup>29</sup>



**Objective:** Measure the impact of an individualized homeopathic treatment, in addition to conventional treatments, on the quality of life of cancer patients (breast, prostate, melanoma, etc...).



#### Methodology:

- 2 independent cohorts (639 patients in total) :
- Conventional cancer treatments and individualized homeopathic treatment (259 patients).
  - Conventional treatments only (380 patients).



#### Résultats :

##### Quality of life at 3 months:

- Group Homeopathy: Significant ( $p < 0.001$ ) and clinically relevant improvement in the global score of quality of life by 5.5 points, with enhancement in all 4 evaluated parameters: physical, social, emotional, and functional well-being.
- Group "Conventional treatment only": Significant ( $p < 0.05$ ) but not clinically relevant improvement in the overall quality of life score by 1.3 point, with enhancement in 2 evaluated parameters: social and emotional well-being.

##### Fatigue assessment:

- Group Homeopathy: Significant reduction ( $p \leq 0.01$ ) in all 5 studied factors (general, physical, and mental fatigue, reduction in motivation and activity) at 3 and 12 months.
- Group "Conventional treatment only": Significant reduction ( $p \leq 0.05$ ) in only one factor (mental fatigue) at 3 months and in 3 factors (physical fatigue, reduction in motivation and activity) at 12 months.



Rostock et al., 2011

### »»» Descriptive study<sup>30</sup>



**Objective:** Assess the prevalence of the use of complementary medicines, particularly homeopathy, in cancer patients and compare the results with a similar study conducted in 2005\*.



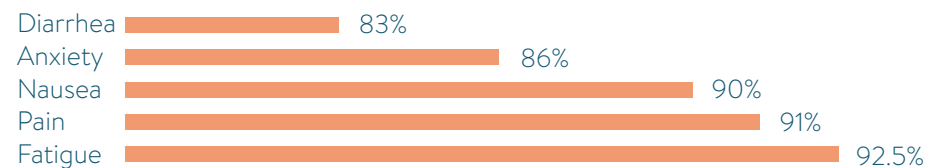
#### Methodology:

Study in 5 centers in Strasbourg (France) involving 535 patients receiving cancer treatment or monitoring.



#### Results:

- **1/3** of cancer patients (31%) use homeopathy in addition to conventional cancer treatments (+83% in 12 years).
- **83%** of patients are satisfied with this treatment.
- Significant improvement in disabling symptoms.



Adapted from Bagot et al., 2021

\*Simon L et al. Complementary and alternative medicines taken by cancer patients. Bull Cancer 2007, 94(5), 483-488.



Bagot et al., 2021

## Retrospective observational study<sup>31</sup>



**Objective:** Evaluate the benefit of homeopathy in supportive care on the quality of life of female patients with non-metastatic breast cancer.



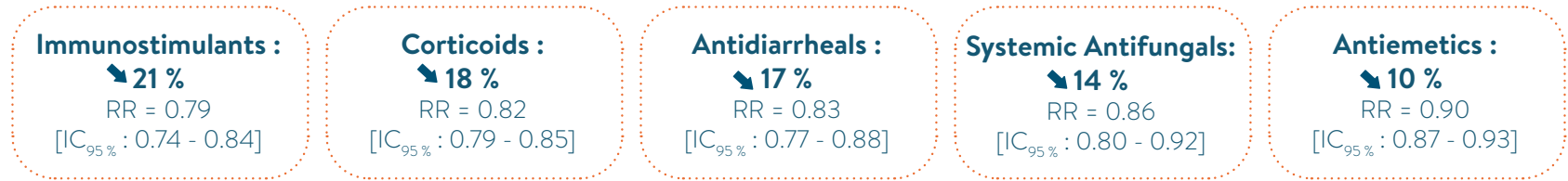
### Methodology:

- Retrospective cohort study based on SNDS data (French nationwide healthcare database).
- Inclusion of 98,009 female patients having undergone a total or partial mastectomy associated with a newly diagnosed, non-metastatic breast cancer.
- Evaluation of drug consumption alleviating the side effects of cancer treatment (indirect quality of life criterion).
- Evaluation of Homeopathy exposure (before and after the surgery).



### Results : Dispensing of conventional supportive care medications prescribed to alleviate the side effects of cancer treatments.

Six months after the surgery, there was a significant overall decrease in the dispensing of conventional supportive care medications in patients treated with at least 3 dispensing of homeopathy compared to the group that did not receive homeopathy (RR = 0.88; 95% CI = 0.87 – 0.89).



### Homeopathy exposure, before and after the surgery.



The dispensing of homeopathy (from one dispensation) is twice as high 6 months before and 6 months after the operation compared to previous use. The exposure to homeopathy remains at a high level during the first year after surgery and then stabilizes at a higher level than the period before cancer (14-15% versus 11%).



Medioni et al., 2023

## In gynecology

### PREMENSTRUAL SYNDROME<sup>32</sup>

»» Double-blind, randomized, placebo-controlled trial

**Objective:** Evaluate the efficacy of individualized homeopathy in women suffering from premenstrual syndrome.

**Methodology:**

- 105 female patients monitored for 3 months, including 49 in the homeopathy group and 56 in the placebo group.
- Primary endpoint: menstrual distress questionnaire (MDQ).

**Results:** Significant reduction in premenstrual symptoms compared with the placebo group (35% versus 20%;  $p = 0.043$ ).



Yakir et al., 2019

### DYSMENORRHEA<sup>33</sup>

»» Double-blind, randomized, placebo-controlled trial

**Objective:** Evaluate the efficacy of individualized homeopathy versus placebo to treat primary dysmenorrhea.

**Methodology:**

- 128 female patients monitored for 3 months, including 64 in the homeopathy group and 64 in the placebo group.
- Primary endpoint: measurement of pain intensity : NRS score on a score scale from 0 (no pain) to 10.
- Secondary endpoint: measurement of intensity of associated symptoms: VMSS score.

**Results:**

- Pain intensity score lower by 1.4 point compared with the placebo group ( $4.9 \pm 1.7$  versus  $6.3 \pm 1.3$  respectively,  $p < 0.001$ ).
- Associated symptoms score lower by 2.6 points compared with the placebo group ( $13.8 \pm 5.1$  versus  $16.4 \pm 6.0$  respectively,  $p = 0.009$ ).



Ghosh et al., 2021

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