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

BOIRON®

"Homeopathy, 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 strains), 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 scientific evidence, 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.[1]

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 Champagne-Ardennes, 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.**[2-4]

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.**[2-4]

These results were obtained using cutting-edge technology such as:[2-4]

- 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

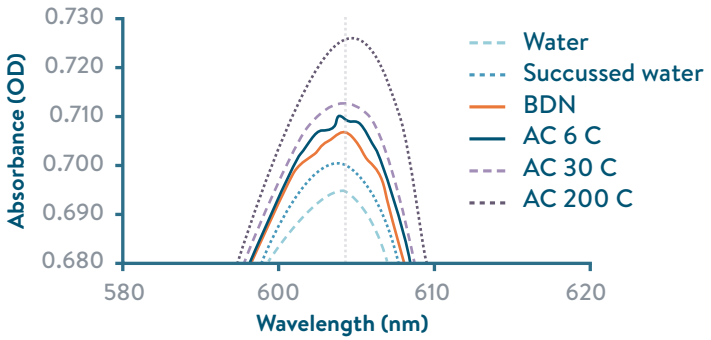
The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

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[5]

Modification of absorbance as a function of the homeopathic solution in solvatochromic dye BDN.[5]

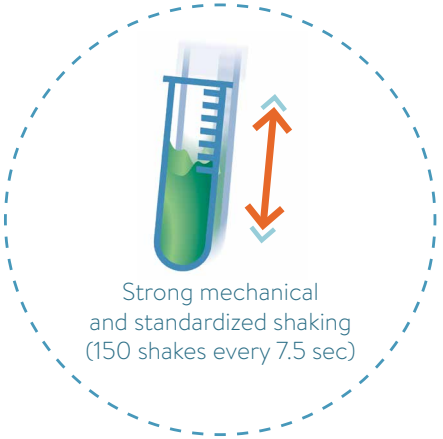


Adapted from Bonamin *et al.*, 2020[5]

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.[6]
- **Essential** for distinguishing homeopathic solutions from neutral solutions or simply diluted solutions.[7]

- A **simply diluted solution does not have the same biological activity as a succussed solution** at any dilution stage.[8]

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

The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

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 have reproducible effects on various animal, cell and plant models.[9]
- 95% of controlled studies in plant models show significant effects compared with the control.[10]

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

Preliminary *in vivo* study in a mouse model[11]

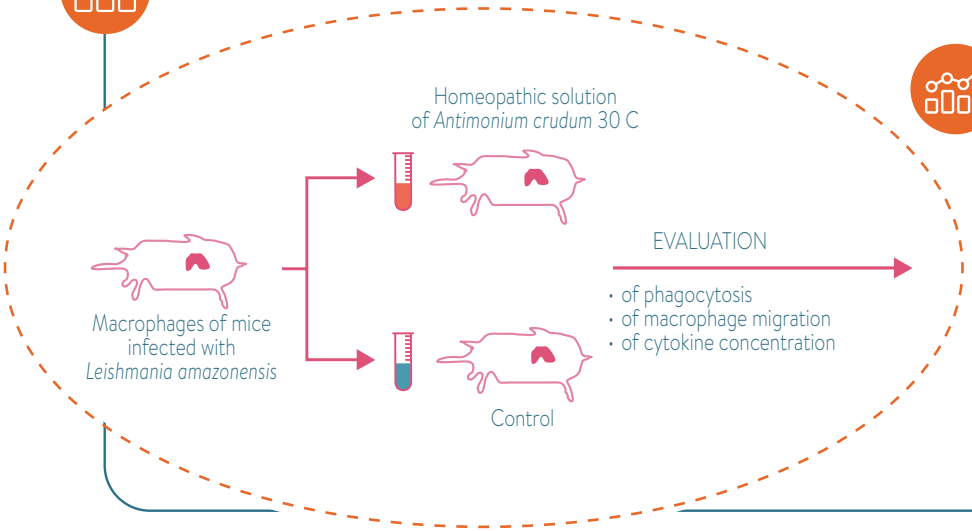
Objective: *In vivo* evaluation of the activity of *Antimonium crudum* 30 C in mice infected with leishmaniasis.

Results: Reduced size of infection-induced lesions and associated inflammatory response modulation compared with control ($p < 0.05$).

In vitro confirmation in an immune cell model[12]

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

Methodology:



Results:

- Reduced production of chemokine MCP-1, reflecting macrophage migration ($p < 0.05$).
- Reduced production of pro-inflammatory cytokines such as IL-6, essential to the parasite's survival ($p < 0.05$).

De Santana *et al.*, 2017

IL-6: Interleukin-6; **MCP-1:** *Monocyte Chemoattractant Protein*-1

The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

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

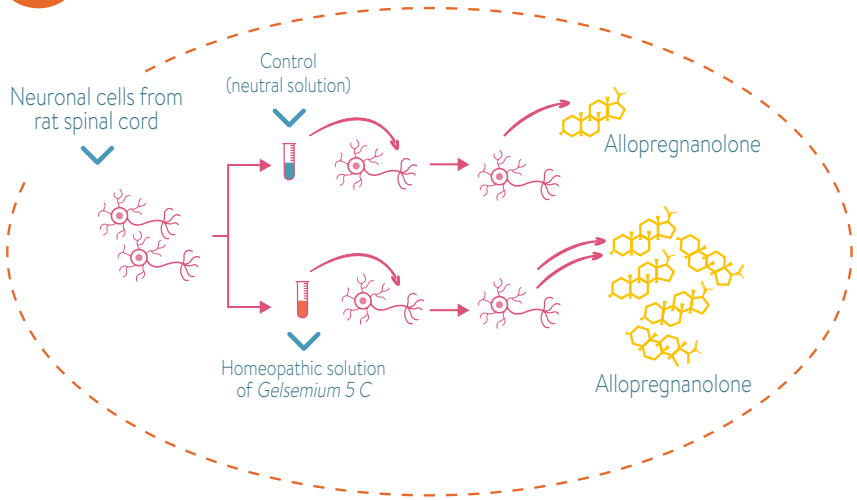
This research program is carried out by two independent centers in collaboration with Boiron:

- 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 confirmation in a rat neuronal cell model[13]

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 *vs* control ($p < 0.001$).

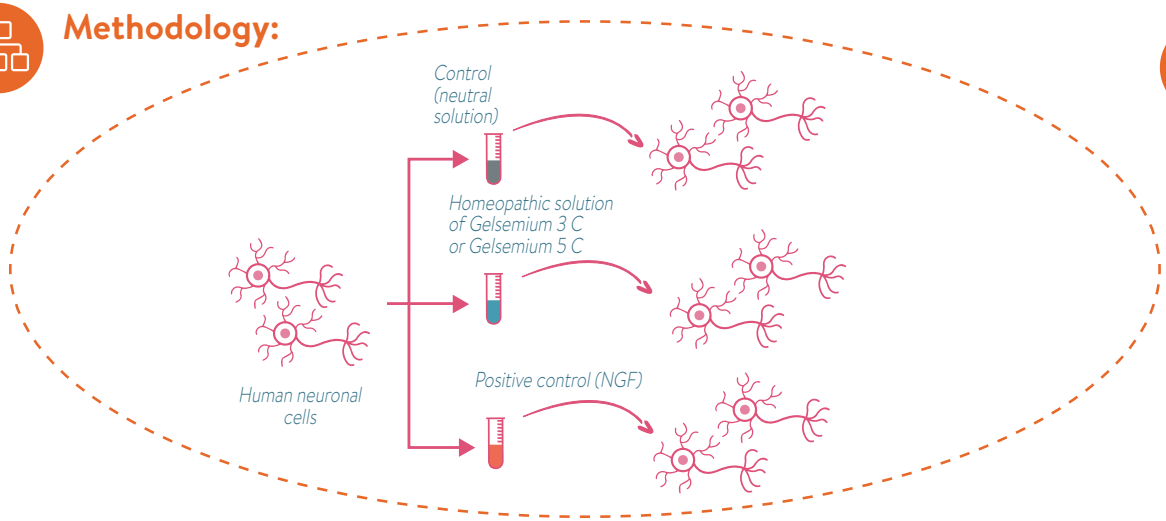
* a neurosteroid involved in managing anxiety

The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

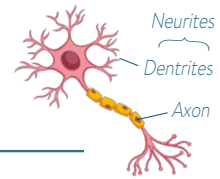
In vitro study on the metabolism of human neuronal cells in physiological conditions[14]

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

Methodology:

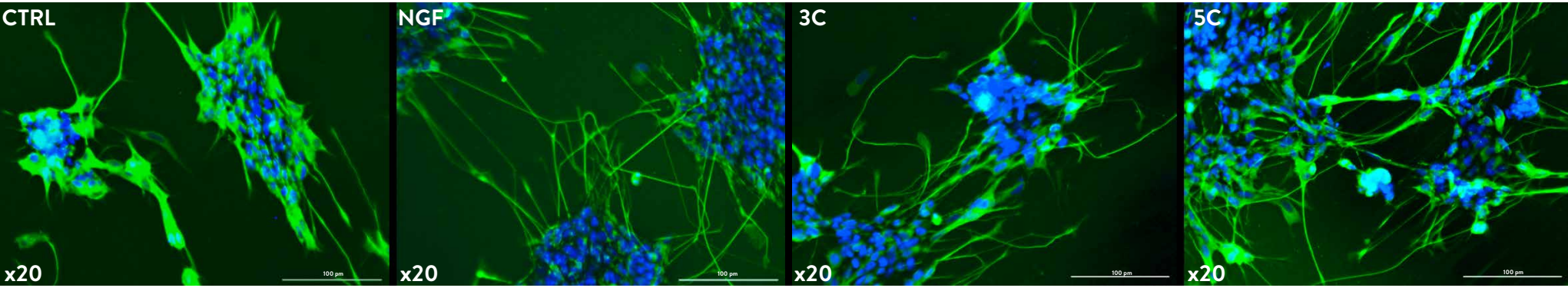


Results:
Gelsemium significantly stimulates:
- ATP production, $p < 0.05$.
- Mitochondrial functions, $p < 0.01$.
- Neurite outgrowth (dendrites + axons), $p < 0.01$.



Lejri *et al.*, 2022

Control | **Positive control** | **Gelsemium 3 C** | **Gelsemium 5 C**



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

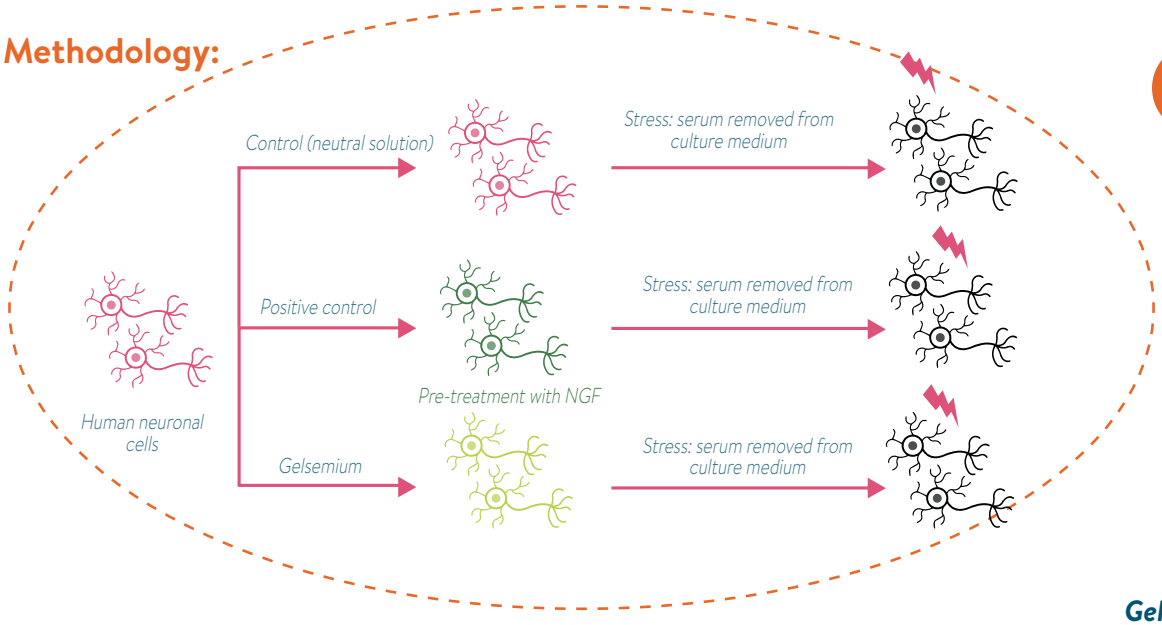
ATP: Adenosine Triphosphate; **NGF**: Neuronal Growth Factor

The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

In vitro study on the metabolism of human neuronal cells in stress conditions[15]

Objective: Evaluation of the protective effect of *Gelsemium* against cellular stress.

Methodology:

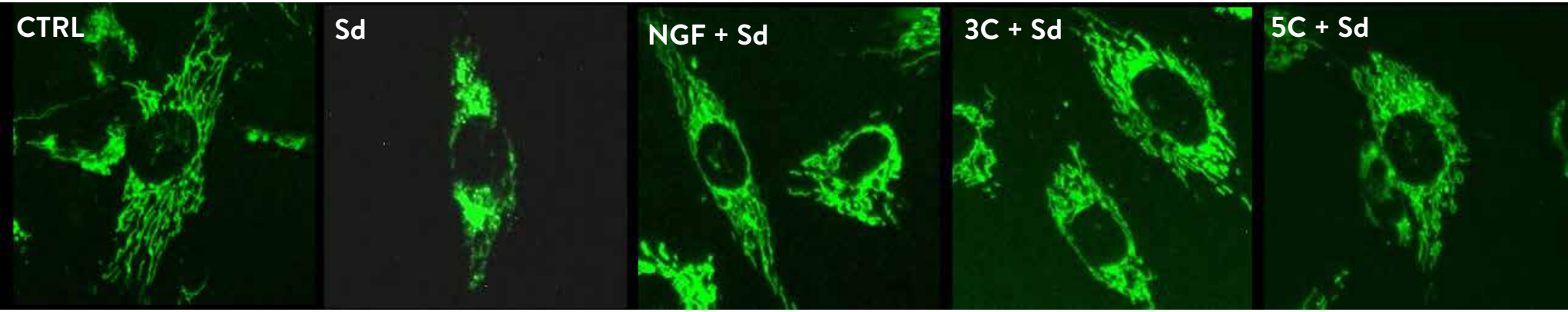


Results: *Gelsemium* significantly protects ($p < 0.05$) cells against stress induced by serum deprivation:

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

Lejri *et al.*, 2025

Control - standard medium	Control - 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.

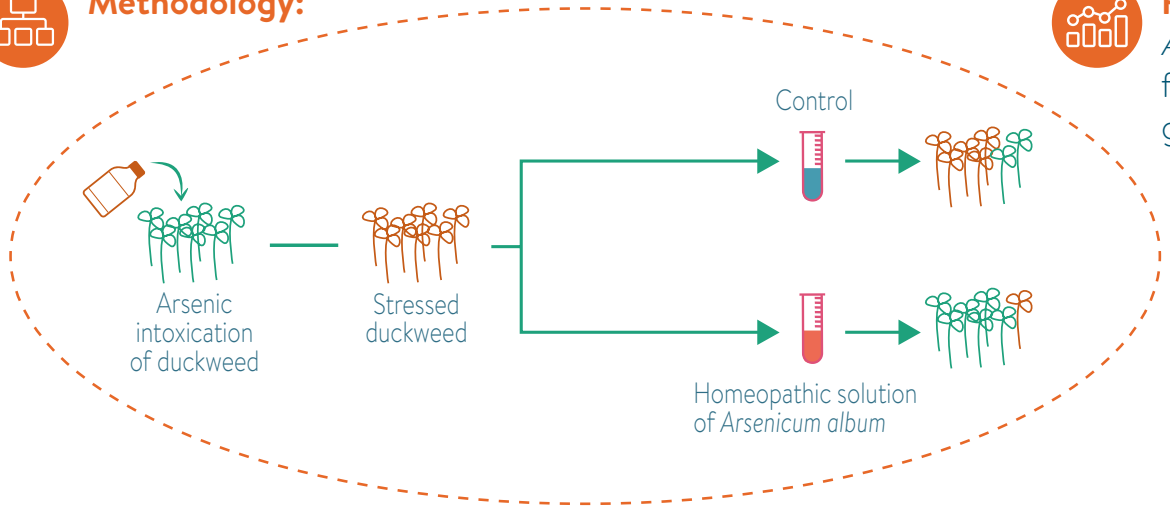
BIOLOGICAL ACTIVITY OF HOMEOPATHY ON PLANT MODELS

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[16]

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[17]

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, $p = 0.00001$).

Ücker et al., 2022

The data presented can, under no circumstances, be extrapolated to any clinical use in humans.

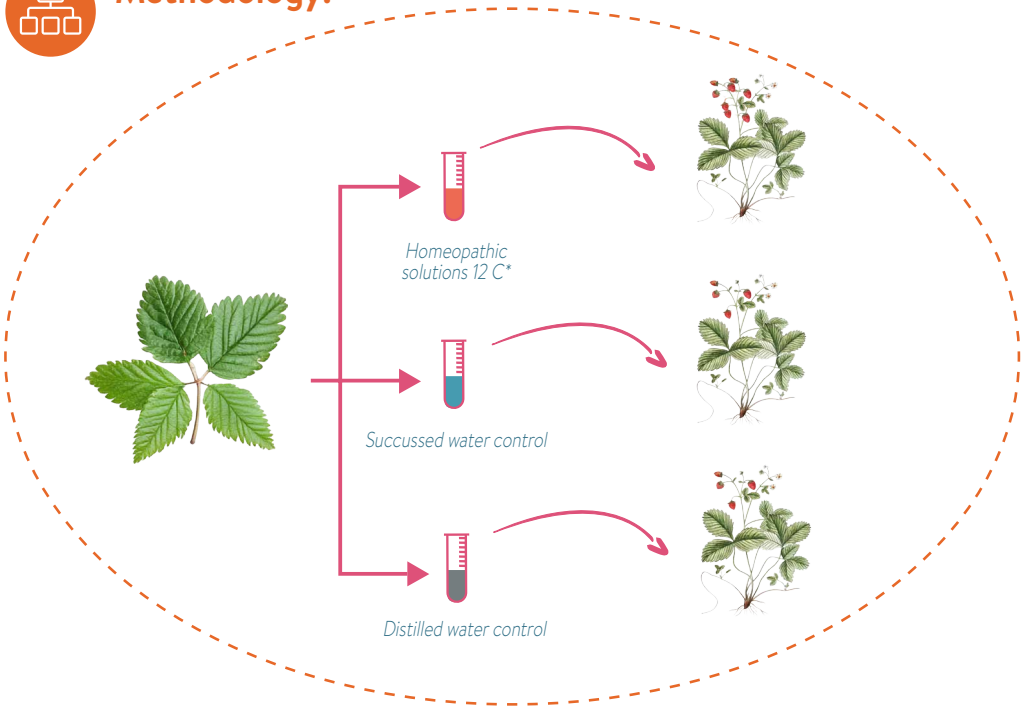
BIOLOGICAL ACTIVITY OF HOMEOPATHY ON PLANT MODELS

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

Study in a strawberry plant model[18]

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 disease and parasites.

Methodology:



Results: Significant increase in the following parameters depending on the strains used* ($p < 0.05$):

- Fruit production up to 5 times greater than that of the controls.
- Plant vitality.
- Disease resistance with reduced use of pesticides.
- Fruit pulp firmness up to 1.7 times higher than the controls.

** Calcarea carbonica 12 C, Kali carbonicum 12 C, Mercurius solubilis 12 C, Natrun muriaticun 12 C, Phosphorus 12 C, Sulphur 12 C, Silicea terra 12 C.*

Faedo *et al.*, 2024

The data presented can, under no circumstances, be extrapolated to any 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.[19]

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 *vs* placebo[20]

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

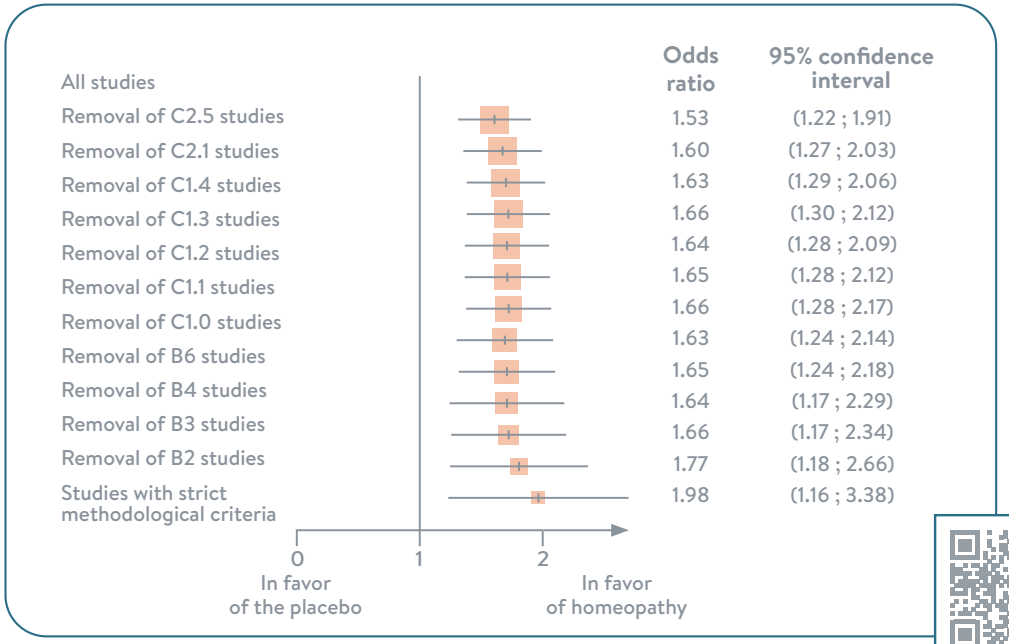
Methodology:

- **Meta-analysis** compiling the results of **22 randomized controlled trials**, in all clinical situations and involving **a total of 1275 patients**.
- Global statistical analysis carried out according to Cochrane methodology criteria.

Results:

Individualized homeopathic treatments have a 1 to 2 times higher probability of having a beneficial effect than the placebo ($p < 0.02$).

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[5]

Mathie *et al.*, 2014

Efficacy of homeopathic treatments *vs* placebo[21]

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 [$CI_{95\%}$: 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 treatment by a homeopathic general practitioner compared with conventional treatment: EPI 3 program[22-25]

Objective: • Evaluate the public health benefit of treatment by a homeopathic general practitioner compared with conventional treatment.
• 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 opportunity (no significant difference in terms of clinical progression complications).
• **Two to three times lower consumption of conventional medicines** in patients treated by a homeopathic general practitioner compared with treatment by a conventional general practitioner.

Musculoskeletal pain (1,153 patients)[25]
- 60% analgesics
OR = 0.40 [$CI_{95\%}$: 0.20 ; 0.82]
- 46% NSAIDs
OR = 0.54 [$CI_{95\%}$: 0.38 ; 0.78]

EPI 3

Upper respiratory tract infections (518 patients)[22]
- 57% antibiotics
OR = 0.43 [$CI_{95\%}$: 0.27 ; 0.68]

Anxiety and depressive disorders (710 patients)[23]
- 71% psychotropic drugs
OR = 0.29 [$CI_{95\%}$: 0.19 ; 0.44]

Sleep disorders (346 patients)[24]
- 75% psychotropic drugs
OR = 0.25 [$CI_{95\%}$: 0.14 ; 0.42]

NSAID: Non-Steroidal Anti-Inflammatory Drug

Critical review of the EPI 3 study[26]

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 by assessing its methodological quality.

Methodology:
Review of the 9 main articles written by the study researchers based on best practices in observational research.

Results:
Confirmation of the methodological quality of the EPI 3 study:

- Rigorous selection of doctors and patients included in the study.
- Analyzed data is good quality.
- 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 treatment meets the specific needs of patients, with lower use of conventional medicines, a comparable clinical benefit and no loss of opportunity.

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[27]

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 compared with the placebo group ($p = 0.014$).

Michael *et al.*, 2019

DEPRESSION[28]

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[29]

Objective: Measure the impact of individualized homeopathic treatment in addition to conventional treatment on cancer patients' quality of life.

Methodology:
639 patients split into 2 groups:

- Conventional cancer treatments and individualized homeopathic treatment (259 patients).
- Conventional treatments only (380 patients).

Results:

- **Significant improvement ($p < 0.05$) in quality of life in the homeopathy group at 12 months** compared with the beginning of the study for all the studied parameters.
- **4.9-point improvement in the overall quality of life score** in the homeopathy group *vs* control.
- **Significant reduction in fatigue** in the homeopathy group at 12 months ($p < 0.01$).

Rostock *et al.*, 2011

Retrospective observational study[30]

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 non-metastatic breast cancer.
- Evaluation of drug consumption alleviating the side effects of cancer treatment (indirect quality of life criterion).

Results: Six months after surgery, **significant reduction in dispensing of conventional supportive care drugs** in patients having received at least 3 homeopathic treatments (*vs* group not having received homeopathic treatment):

- ↘ **21%** immunostimulants:
  RR = 0.79 [$CI_{95\%}$: 0.74 ; 0.84].
- ↘ **18%** corticosteroids:
  RR = 0.82 [$CI_{95\%}$: 0.79 ; 0.85].
- ↘ **17%** antidiarrheals:
  RR = 0.83 [$CI_{95\%}$: 0.77 ; 0.88].
- ↘ **10 %** antiemetics:
  RR = 0.90 [$CI_{95\%}$: 0.87 ; 0.93].

Medioni *et al.*, 2023

RR: Relative Risk; **SNDS**: French Nationwide Healthcare Database

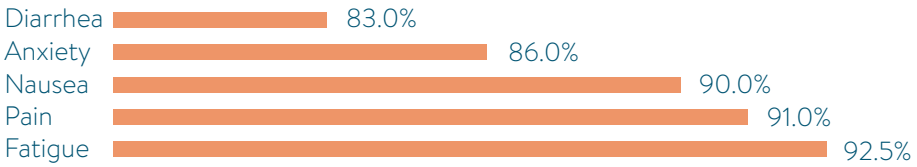
Descriptive study[31]

Objective: Evaluate the prevalence of the use of complementary medicines by cancer patients, analyze homeopathy-related data and compare it with data from 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

Bagot *et al.*, 2021

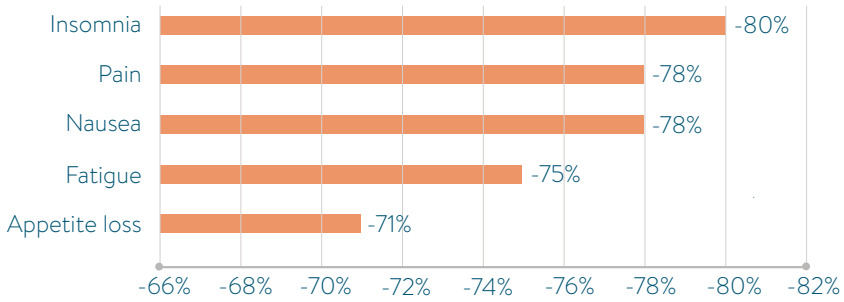
Double-blind, randomized, placebo-controlled trial[32]

Objective: Evaluate the effect on quality of life of individualized homeopathic treatment in addition to conventional cancer treatments in patients with advanced-stage non-small cell lung cancer.

Methodology: Study of 150 patients:

- Conventional cancer treatments and individualized homeopathic treatment (51 patients).
- Conventional cancer treatments and placebo, neutral pellets (47 patients).
- Conventional cancer treatments (52 patients).

Results: Homeopathy group *vs* placebo group: at 18 weeks, **significant improvement** ($p < 0.001$) **in quality of life** and all the studied parameters (physical functioning, social functioning, fatigue, nausea, dyspnea, insomnia, pain, diarrhea, appetite loss, constipation, etc.).



Adapted from Frass *et al.*, 2020

Frass *et al.*, 2020

In gynecology

PREMENSTRUAL SYNDROME[33]

Double-blind, randomized, placebo-controlled trial

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

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

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

Yakir *et al.*, 2019

DYSMENORRHEA[34]

Double-blind, randomized, placebo-controlled trial

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

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

Results:
- **Pain intensity score lower** by 1.4 points compared with the placebo group (4.9 ± 1.7 *vs* 6.3 ± 1.3 respectively, p < 0.001).
- **Associated symptoms score lower** by 2.6 points compared with the placebo group (13.8 ± 5.1 *vs* 16.4 ± 6.0 respectively, p = 0.009).

Ghosh *et al.*, 2021

MDQ: *Mood Disorder Questionnaire*; **NRS:** *Numeric Rating Scale*; **VMSS:** *Verbal Multidimensional Scoring System*

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