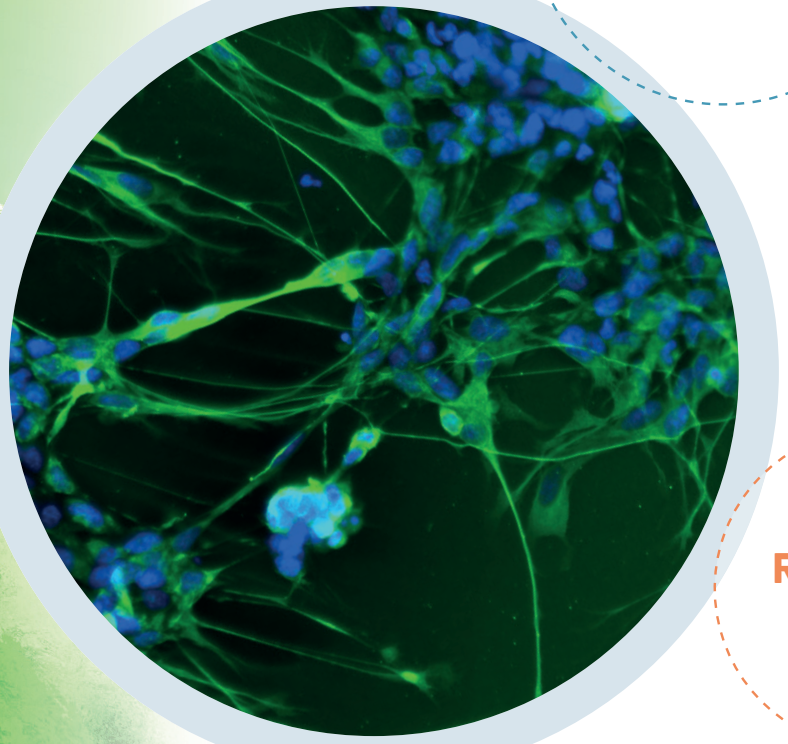
RESEARCH ADVANCE IN HOMEOPATHY



Fundamental research

In vitro and in vivo biological activity

EVIDENCE-BASED HOMEOPATHY

Clinical research

Randomized controlled trials & Meta-analyses

Real-world studies

BOIRON®

Research in homeopathy is evolving and is key to ensure its integration into medical practice and the healthcare system.

Our laboratory is involved next to research teams and learned societies for many years. We are comitted to medical science. Our international scientific approach aims to inform on research advance regarding our therapeutic solutions and particularly on homeopathy in complete transparency.

In this brochure, you will see ample scientific-based evidence that shows how effective, safe, and useful homeopathy is as patient-centric treatment approach.

BASIC RESEARCH IN HOMEOPATHY

Basic research aims at assessing biological action of homeopathy and its physicochemical features as well as elucidating its mechanism of action.

It's an **ongoing multidisciplinary research of good methodological quality**, involving high level researchers who are working on different experimental models (cellular, plant and animal). A scientific litterature review conducted over 20 years identified a hundred studies replicated in 28 different experimental models. [1]

This research is carried out by international academic or private centers, such as :

- The **Homeopathy Research Institute**, an international association coordinating research in homeopathy: https://www.hri-research.org/fr/
- A research center in **Brazil** with about fifteen university laboratories
- Bern University in **Switzerland,** which has published 48 scientific papers on plant models
- Scientific public research in **France** at Champagne-Ardennes University and INSERM in Strasbourg...

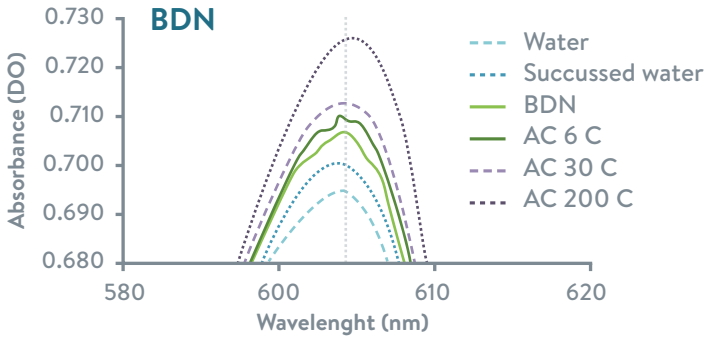
INSERM : Institut national de la santé et de la recherche médicale (National Institute of Health and Medical Research)

Physicochemical properties of homeopathic solutions

Analyses of homeopathic solutions made by physical or chemical techniques (NMR, conductometry, solvatochromism) have revealed specific **physicochemical properties** with **significant part of succussion**.

Specific physicochemical properties [2-4]

Change in absorbance depending on homeopathic solution in solvatochromic dye.[5]



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

Each dilution of homeopathic solution has its **own physicochemical properties**

Bonamin *et al.*, 2020

Succussion significance

Strong mechanical and standardized shaking (150 shakes every 7.5 seconds)

- **Key step** in the manufacturing process of homeopathic solutions.[6]
- **Essential** to differentiate homeopathic solutions from neutral or simply diluted solutions.[7]

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

AC: *Antimonium crudum*; **BDN:** dimethylamino naphthalenone; **NMR:** Nuclear magnetic resonance.

Biological action of homeopathic solutions

Basic research in homeopathy is settled on a variety of **experimental models**:

Animals **Plants** **Cells**

In vitro and in vivo models have shown biological action of homeopathy in different fields, such as:

- Action on immune response (see page 7),
- Action on biological parameters of nervous system (see page 8).

The use of **standardized models** have demonstrated the reproducibility of results and have confirmed the biological action of homeopathic solutions, for example the 20 years of experimentations on the duckweed plant model (see page 9).

The data presented can, under no circumstances, be extrapolated to any clinical use in humans that would require additional studies.

Biological action of *Antimonium crudum* homeopathic solution on immune response modulation

In vivo preliminary study on a murine model [9]

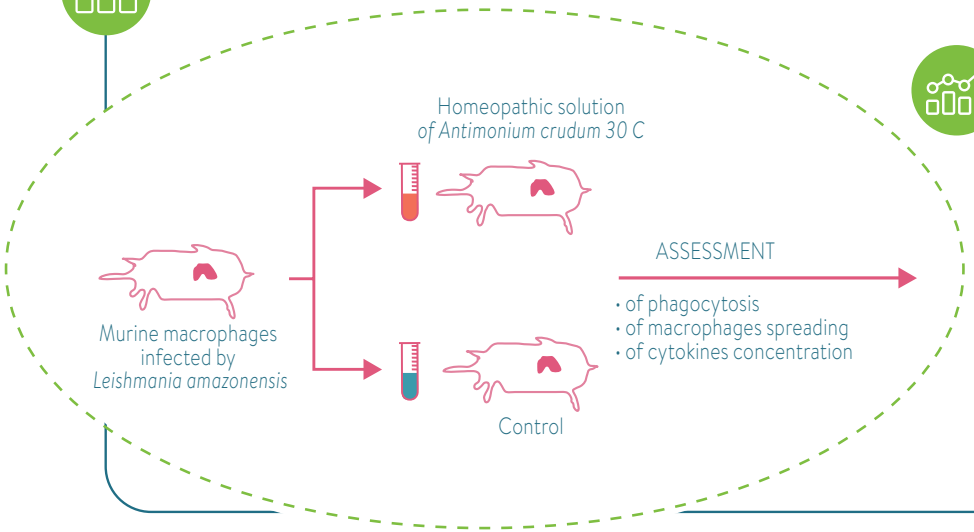
Goal: Assess ***in vivo*** *Antimonium crudum* 30 C activity on mice infected by leishmania.

Results: Immune response modulation and size reduction of injuries induced by the infection compared to control ($p<0.05$).

Validation on an *in vitro* immune cell model [10]

Goal: ***in vitro*** assessment of *Antimonium crudum* 30 C activity on murine infected macrophages.

Methods:



Results:

- Decrease of chemokine MCP-1 production, reflecting macrophages spreading ($p<0.05$).
- Decrease of proinflammatory cytokines production, such as IL-6, necessary to parasite survival ($p<0.05$).

de Santana *et al.*, 2017

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

The data presented can, under no circumstances, be extrapolated to any clinical use in humans that would require additional studies.

Research program on biological action of *Gelsemium sempervirens* in homeopathic solutions

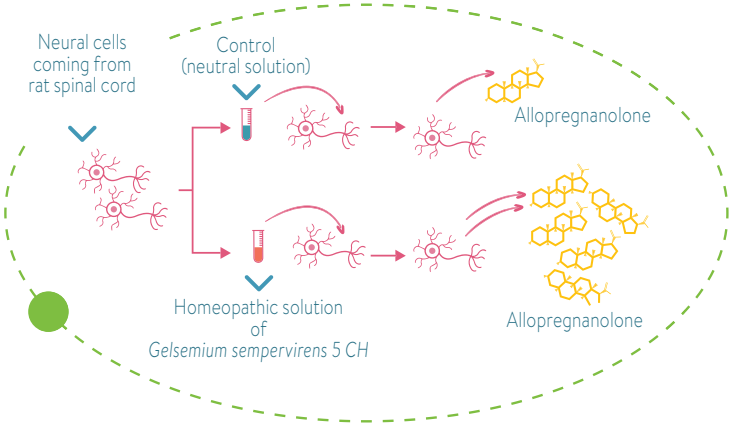
A Boiron research program was carried out with independant centers:

- The unit of "Biopathologie de la myéline, neuroprotection et stratégies thérapeutiques" laboratory in Strasbourg (INSERM), France
- The "neurobiologie du vieillissement du cerveau et de la santé mentale, neurosciences moléculaires et cognitives" laboratory in Basel Switzerland

In vitro study on one neural cell model [11]

Goal: ***In vitro*** assessment of *Gelsemium sempervirens* 5 C action on rat neural cells.

Methods:



Results:

x5

Allopregnanolone* secretion increased by 5 with *Gelsemium sempervirens* 5 C vs control ($p<0.001$)

* A neurosteroid involved in anxiety control

In vitro following research in neurology [12]

Gelsemium sempervirens 5 C solution **increased neuron size and number by stimulating mitochondrial function.**

Lejri *et al.*, 2022

The data presented can, under no circumstances, be extrapolated to any clinical use in humans that would require additional studies.

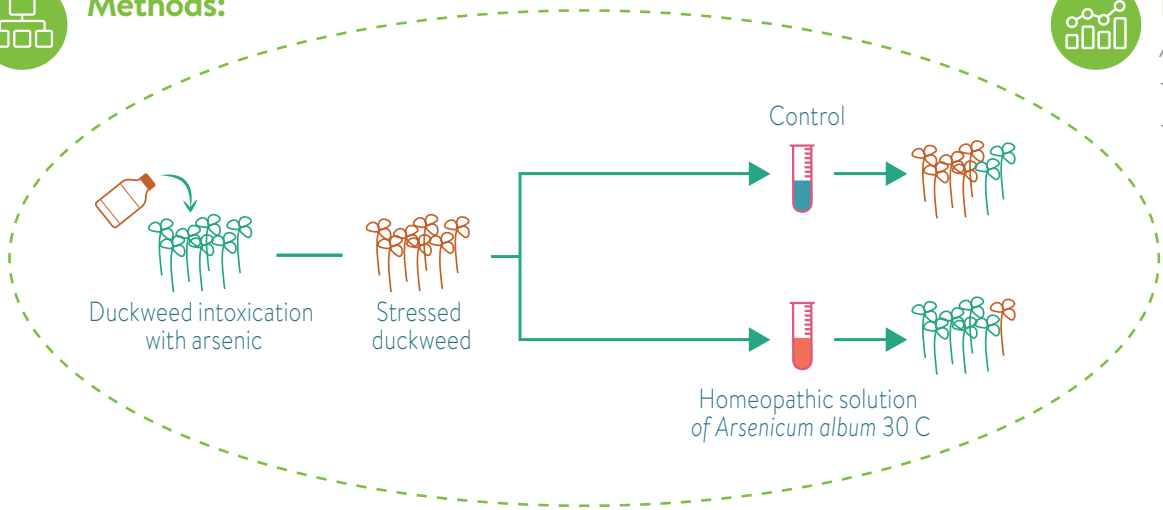
Biological activity of homeopathy on a plant model

- Experiments completed at Bern University leading to almost 50 papers in reference newspapers.

Preliminary *in vitro* study on a plant model [13]

Goal: Biological activity assessment of highly diluted *Arsenicum album* homeopathic solution (from 17 C to 33 C) on duckweed growth stressed by arsenic.

Methods:



Results: Homeopathic solution of *Arsenicum album* protected duckweed from arsenic intoxication, restoring their growth ($p<0.001$).

Validation of reproductibility and robustness of results [14]

Methods:
Replication of initial study with 2 sets of 5 experiments each.

Results:
Results **confirmed method robustness** and were in accordance with initial experiment (significative difference compared to control group, $p = 0.00001$).

Ücker et al., 2022

The data presented can, under no circumstances, be extrapolated to any clinical use in humans that would require additional studies.

CLINICAL RESEARCH IN HOMEOPATHY

Clinical research aims to demonstrate the beneficial effects provided by individualized patient care, which considers each person's uniqueness, as well as the effectiveness and safety specific to each drug.

Interventional research in homeopathy has included at least 250 randomized clinical trials, conducted on homeopathic drugs in almost one hundred diseases[15] and has brought tangible evidence of efficacy.

Conjoint analysis of clinical trials have allowed for meta-analyses, adding another level of proof.

Observational studies, conducted in **real life,** are particularly well-suited to the specificities of homeopathy, allowing for **individualized treatment** and benefit measurement for **all patient profiles,** including frail populations.

Individualized homeopathic treatment *vs* placebo [16]

Goal: Assessment of clinical efficacy of individualized homeopathic treatment *vs* placebo.

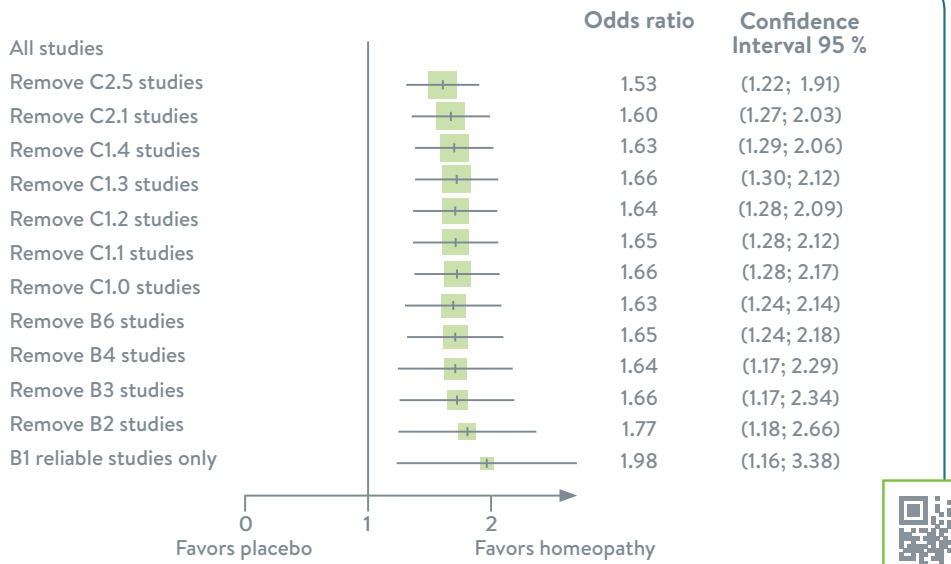
Methods:

- Meta-analysis gathering **22 randomized controlled clinical trials** in every disease on **a population of 1.275 patients.**
- Global statistical analysis achieved by following criteria of Cochrane method.

Results:

- Individualized homeopathic treatment **increased by 1.5 to 2 fold beneficial effect** *vs* placebo ($p<0.02$).
- More criteria were of high methodologic quality, more results seemed to be in favor of homeopathy compared to placebo.

Sensitivity analysis, showing progressive effect on pooled odds ratio of removing data by trials' risk-of-bias rating.



Adapted from Mathie *et al.*, 2014[5]

Mathie *et al.*, 2014

Homeopathy interest in public health for patient care: EPI3 program [17-20]

Goal: Assessment of homeopathic medical practice interest by general practitioners who prescribed either mostly homeopathy or conventional-only medicines.

Methods: Wide phamacoepidemiological program including 8,000 patients and 825 general practioners and assessing homeopathic medical practice interest in **3 common reasons for consultation in primary care.**

Results:

- **Clinical course of patients followed by a homeopathic general practitioner was similar to other patients**, without a reduction in quality of life.
- **Decrease in the consumption of conventional medicines:**

Musculoskeletal disorders (1.153 patients)[20]

- 60% of analgesics
OR: 0.40 [$CI_{95\%}$: 0.20; 0.82]

- 46% of NSAID
OR: 0.54 [$CI_{95\%}$: 0.38; 0.78]

EPI 3

Upper respiratory tract infections (518 patients)[17]

- 57% of antibiotics
OR: 0.43 [$CI_{95\%}$: 0.27; 0.68]

Anxious and depressive disorders (710 patients)[18]

- 71% of psychotropic drugs
OR: 0.29 [$CI_{95\%}$: 0.19; 0.44]

Sleep disorders (346 patients)[18]

- 75% of psychotropic drugs
OR: 0.25 [$CI_{95\%}$: 0.14; 0.42]

CI: Confidence Interval; **NSAID:** Non-Steroidal Anti-Inflammatory Drugs; **OR:** Odds Ratio

Beneficial effect of individualized homeopathy in different therapeutic areas

- Strong bodies of evidence combining scientific data of randomized controlled trials with observational data are now well established in the following disorders:

In mental disorders

INSOMNIA [21]

Randomized, double-blind placebo-controlled clinical trial

Methods:
- 60 patients followed for 3 months
- Primary endpoint: patient-administered sleep diary
- Secondary endpoint: Insomnia Severity Index (ISI)

Results:
- **Improvement of quality and duration of sleep:** Significative improvement of 5/6 outcomes of sleep diary in homeopathy group *vs* 1/6 outcomes in placebo group ($p<0.01$).
- **Improvement of insomnia score:** Significative improvement of 3.2 points compared to placebo ($p=0.014$).

Michael *et al.*, 2019

DEPRESSION [22]

Randomized controlled pragmatic trial

Methods:
- 566 patients followed for 12 months
- Divided in two cohorts (usual care ± homeopathy)
- Primary endpoint: Patient Health Questionnaire (PHQ-9)
- Secondary endpoint: Generalized Anxiety Disorder (GAD-7)

Results:
- **Improvement at 6 months of:** **depression score** of 2.6 points ($p=0.018$) anxiety score of 2.8 points ($p=0.004$).
- **Results maintened at 12 months.**

Viksveen *et al.*, 2017

In oncological supportive care

QUALITY OF LIFE ASSESSMENT

Prospective observational study [23]

Methods:

- 639 patients suffering from cancer allocated in two cohorts (usual care ± homeopathy)

Results:

- **Improvement of quality of life at 12 months :** +8.5 points in homeopathy group *vs* +3.5 points in the conventional-strict group (p<0.001).
- **Significative decrease of fatigue smptoms in homeopathy group (p<0.001).**

Rostock *et al.*, 2011

Pharmacoepidemiological study [24]

Methods:

- Retrospective study based on the French National Healthcare Data System
- **98,000 patients** underwent a mastectomy for breast cancer
- Five-year follow-up

Results: decrease in the dispensing of conventional supportive care in patients receiving homeopathy

↘ **18%** corticosteroids:
OR= 0.82 [$CI_{95\%}$: 0.79; 0.85]

↘ **17%** antidiarrheals:
OR= 0.82 [$CI_{95\%}$: 0.79; 0.85]

↘ **10%** antiemetics:
OR= 0.90 [$CI_{95\%}$: 0.87; 0.93]

Medioni *et al.*, 2023

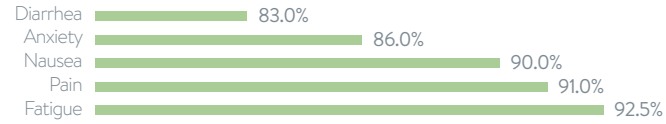
PATIENT PERCEPTION [25]

Methods:
Observational study of 535 cancer patients treated in 5 centers

Results:

- **1/3 of cancer patients** used homeopathy in oncological supportive care (31%).

- Significative improvement of disabling symptoms:



Adapted from Bagot *et al.*, 2021[25]

Bagot *et al.*, 2021

CI: Confidence Interval; **OR:** Odds Ratio.

In gynaecology

PREMENSTRUAL SYNDROME [26]

Randomized, double-blind placebo-controlled clinical trial

Methods:

- 105 patients included and followed for 3 months
- Primary endpoint: Mood Disorder Questionnaire (MDQ)

Results:

Significative decrease of premenstrual symptoms compared to placebo (35.3% *vs* 20.2%; p=0.043).

Yakir *et al.*, 2019

DYSMENORRHEA [27]

Randomized, double-blind placebo-controlled clinical trial

Methods:

- 128 patients included and followed for 3 months
- Primary endpoint: Numeric Rating Scale (NRS) to assess pain
- Secondary endpoint: Verbal Multidimentional Scoring System Mesure (VSSM) to assess associated symptoms intensity

Results:

- **Decrease of NRS** score of 1.4 points compared to placebo (p<0.001)
- **Improvement of associated symptoms** of 2.6 points compared to placebo (p=0.009)

Ghosh *et al.*, 2021

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