

# RESEARCH ADVANCES IN HOMEOPATHY

## Fundamental research

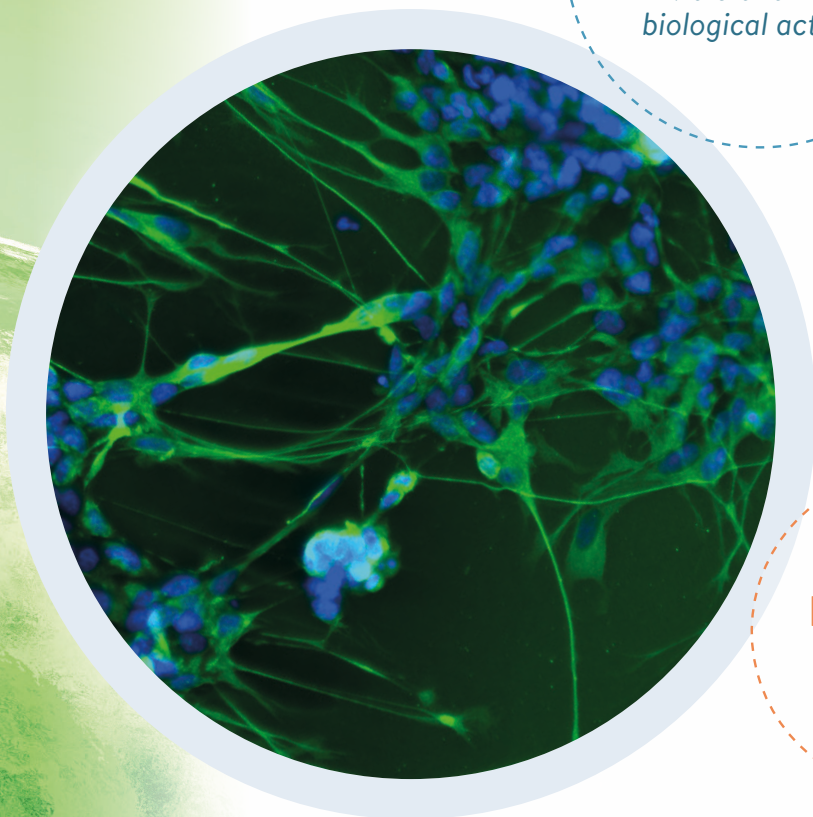
*In vitro and in vivo  
biological activity*

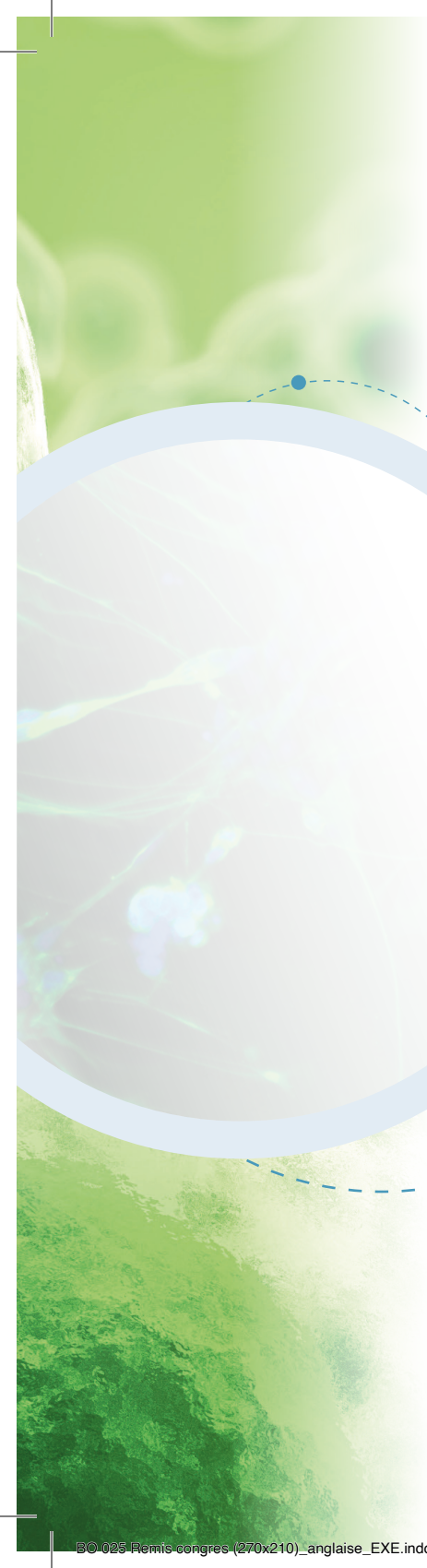
## EVIDENCE-BASED HOMEOPATHY

## Clinical research

*Randomized controlled trials  
&  
Meta-analyses*

## Real-world studies





**R**esearch in homeopathy is evolving and is key to ensuring its integration into medical practice and the healthcare system.

*Our laboratory has been collaborating with research teams and professional and academic organizations for many years. We are committed to medical science. Our international scientific approach aims to inform on research advancements 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 a 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 literature review conducted over 20 years identified a hundred studies replicated in 28 different experimental models.<sup>1</sup>

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

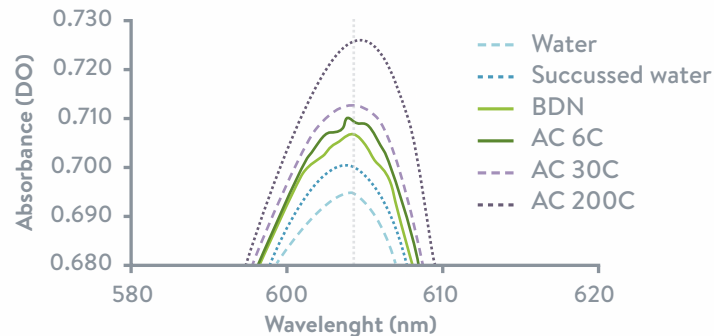
- The **Homeopathy Research Institute**, an international association coordinating research in homeopathy: <https://www.hri-research.org/fr/>
- A research center in **Brazil** with about fifteen university laboratories
- Bern University in **Switzerland**, which has published 48 scientific papers on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

# 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<sup>2-4</sup>

Change in absorbance depending on homeopathic solution in solvatochromic dye.<sup>5</sup>



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

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



Bonamin *et al.*, 2020

## Succussion significance



- **Key step** in the manufacturing process of homeopathic solutions.<sup>6</sup>
- **Essential** to differentiate homeopathic solutions from neutral or simply diluted solutions.<sup>7</sup>

- A **simply diluted solution does not have the same biological action** as a solution succussed at each stage of dilution.<sup>8</sup>

**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).

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

## ►►► *In vivo* preliminary study on a murine model <sup>9</sup>



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



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

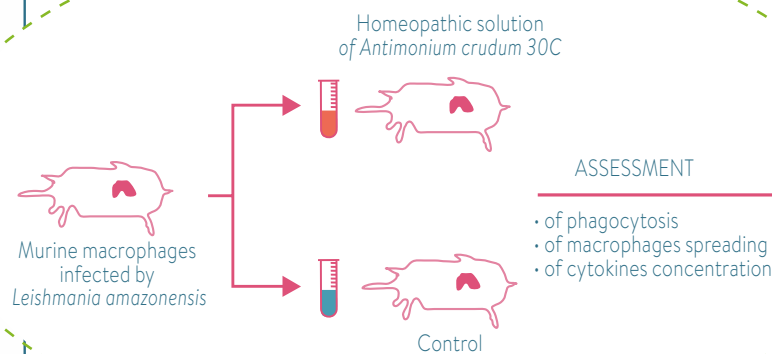
## ►►► Validation on an *in vitro* immune cell model <sup>10</sup>



**Goal:** *in vitro* assessment of *Antimonium crudum* 30C 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 independent 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

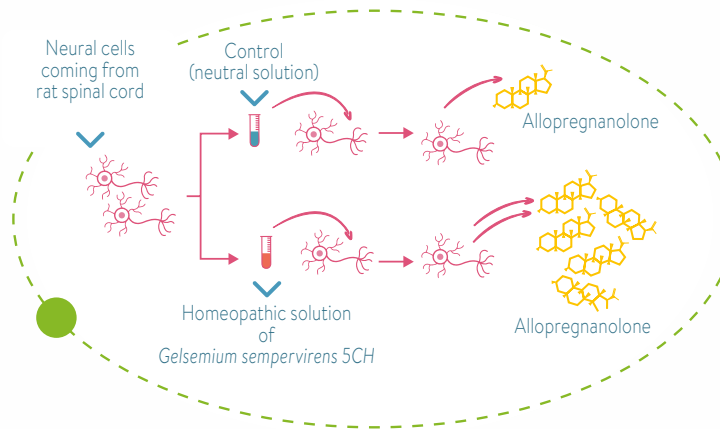
### ►►► *In vitro* study on one neural cell model<sup>11</sup>



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



**Methods:**



**Results:**

►►► **x5**

**Allopregnanolone\*** secretion increased by 5 with *Gelsemium sempervirens* 5C vs control ( $p < 0.001$ ), stimulating GABAergic neurons.

\* A neurosteroid involved in anxiety control

### ►►► *In vitro* following research in neurology<sup>12</sup>

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



Lejri et al., 2022



## Biological activity of homeopathy on a plant model

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

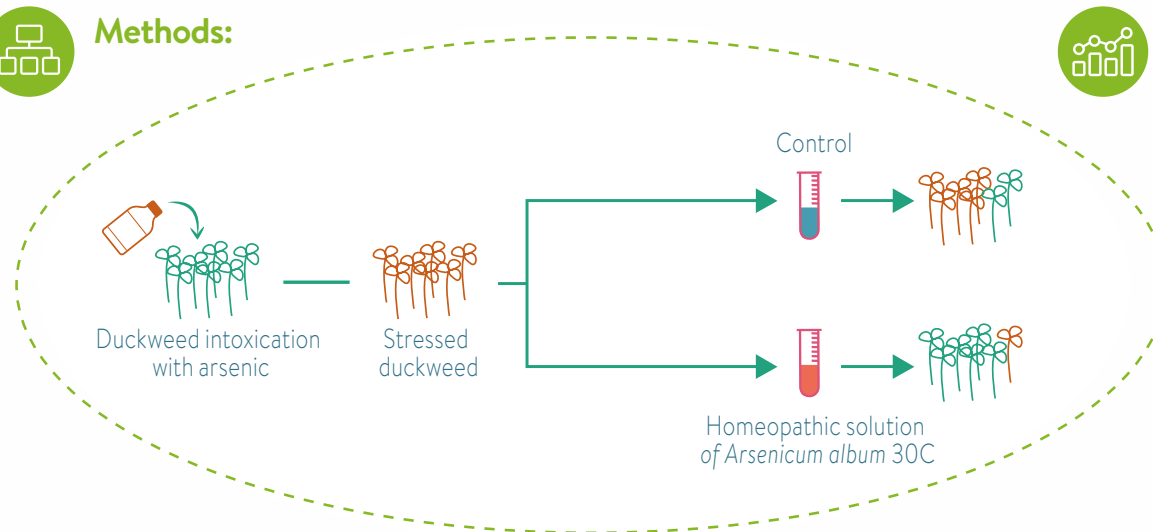
### ►► Preliminary *in vitro* study on a plant model <sup>13</sup>



**Goal:** Biological activity assessment of highly diluted *Arsenicum album* homeopathic solution (from 17C to 33C) 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 reproducibility and robustness of results <sup>14</sup>



**Methods:**

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



**Results:**

Results **confirmed method robustness** and were in accordance with initial experiment (significant 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 100 diseases<sup>15</sup> 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 <sup>16</sup>



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



**Methods:**

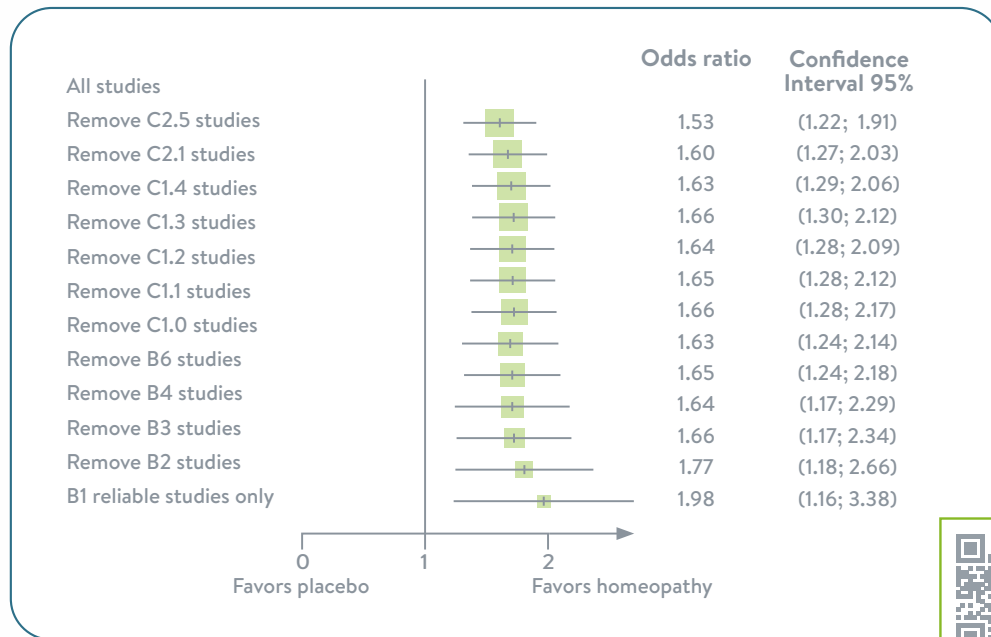
- Meta-analysis gathering **22 randomized controlled clinical trials** in every disease on **a population of 1.275 patients.**
- Global statistical analysis achieved by following criteria of Cochrane method.



**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<sup>5</sup>



Mathie et al., 2014

# Homeopathy interest in public health for patient care: EPI3 program<sup>17-20</sup>



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

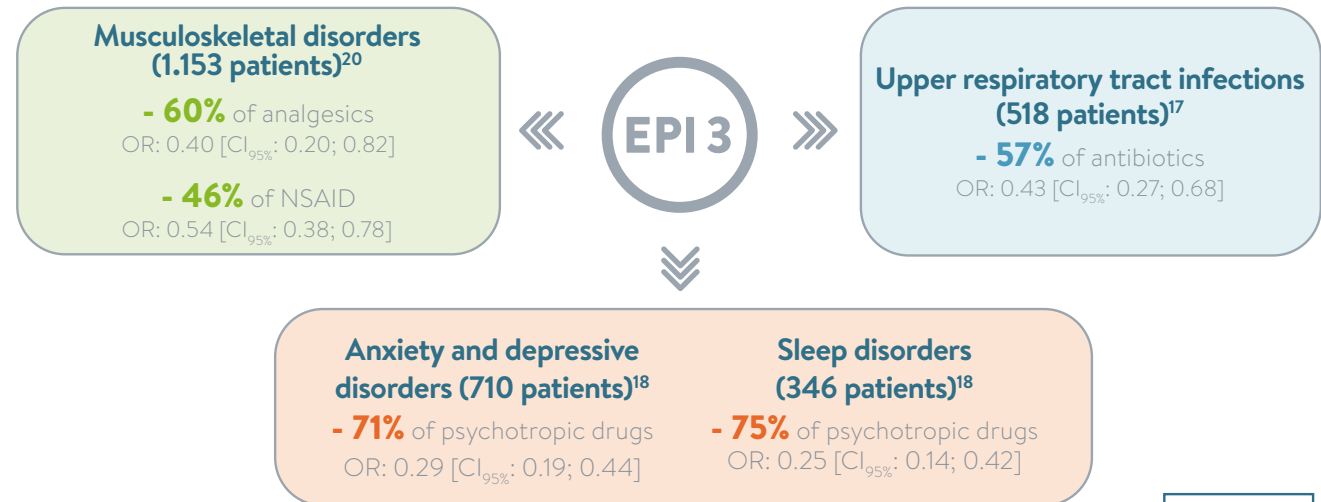


**Methods:** Wide pharmacoepidemiological program including 8,559 patients and 825 general practitioners and assessing homeopathic medical practice interest in **3 common reasons for consultation in primary care.**



## 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:



Link to the 12 EPI3 publications



# 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 <sup>21</sup>

#### Randomized, double-blind placebo-controlled clinical trial



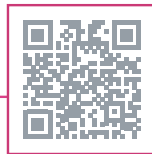
##### Methods:

- 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:**  
Significant 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:**  
Significant improvement of 3.2 points compared to placebo ( $p = 0.014$ ).



Michael *et al.*, 2019

### DEPRESSION <sup>22</sup>

#### Randomized controlled pragmatic trial



##### Methods:

- 566 patients followed for 12 months
- Divided in two cohorts (usual care  $\pm$  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 maintained at 12 months.**



Viksveen *et al.*, 2017

## In mental disorders

### ATTENTION DEFICIT AND HYPERACTIVITY DISORDER<sup>23</sup>

#### Meta analysis



##### Methods:

- Analysis of 6 clinical trials comparing individualized homeopathy to placebo or reference treatment



##### Results:

- All studies but one were randomized and showed **low-to-moderate risk of bias**
- **Significant improvement of ADHD in homeopathy group:**  
vs reference treatment group ( $p < 0.001$ )  
vs placebo group ( $p = 0.03$ )



Gaertner K et al., 2022

### SLEEP AND ANXIETY<sup>24</sup>

#### Double blind randomized control trial



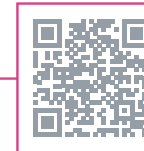
##### Methods:

- 614 patients included, 4 weeks follow-up
- Protocol: *Passiflora composita* during 4 weeks
- Primary endpoint: Anxiety assessment by general practitioners (Score HAM-A) and by patients (STAI questionnaire)
- Secondary endpoint: Sleep assessment by patients (JSS questionnaire)



##### Results:

- **42.1% decrease of anxiety (HAM-A)** ( $p < 0.001$ )
- **13.6% decrease of anxiety (STAI)** ( $p < 0.001$ )
- **29.4% decrease of sleep disorders** ( $p < 0.001$ )



Villet et al., 2016

## In oncological supportive care

### QUALITY OF LIFE ASSESSMENT

#### »»» Prospective observational study<sup>25</sup>



##### 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).
- **Significant decrease of fatigue symptoms in homeopathy group (p<0.001).**



Rostock *et al.*, 2011

#### »»» Pharmacoepidemiological study<sup>26</sup>



##### 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<sub>95%</sub>: 0.79; 0.85]
- ↳ **17%** antidiarrheals: OR= 0.82  
[CI<sub>95%</sub>: 0.79; 0.85]
- ↳ **10%** antiemetics: OR= 0.90  
[CI<sub>95%</sub>: 0.87; 0.93]



Medioni *et al.*, 2023

### PATIENT PERCEPTION<sup>27</sup>



##### Methods:

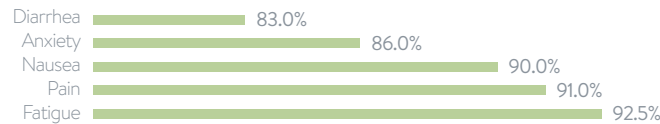
Observational study of 535 cancer patients treated in 5 centers



##### Results:

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

- Significant improvement of disabling symptoms:



Adapted from Bagot *et al.*, 2021<sup>25</sup>



Bagot *et al.*, 2021

CI: Confidence Interval; OR: Odds Ratio.

## In oncological supportive care

### JOINT PAIN LINKED TO AROMATASE INHIBITORS<sup>28</sup>

#### »»» Prospective observational study



##### Methods:

- 40 patients included, 3 month follow-up
- Protocol: *Ruta graveolens* 5C and *Rhus toxicodendron* 9C during 3 months
- Primary endpoint: score for pain and stiffness, impact of pain on sleep, analgesic consumption



##### Results:

- **Decrease of joint pain score** in favor of homeopathy group (-1.3 in Homeopathy vs +3.4 in control group;  $p=0.0001$ )
- **Decrease of number of pain sites, frequency and intensity of pain** whereas increase of all three parameters in control group
- **Less analgesic consumption** in homeopathy group vs control group ( $p=0,0076$ )



Karp *et al.*, 2016

### MASTECTOMY AND BREAST RECONSTRUCTION<sup>29</sup>

#### »»» Double blind randomized control trial



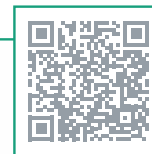
##### Methods:

- 55 patients who underwent mastectomy and immediate breast reconstruction for cancer or risk reduction
- Protocol: *Bellis perennis* 30C and *Arnica montana* 30C before surgery until drain removal
- Primary endpoint: drain removal time



##### Results:

- **The drain removal time is 2.4 days shorter** in the homeopathy group than for the placebo group ( $p<0.05$ )
- On days 3 and 7 postoperatively, there was no significant difference between the two groups with regard to postoperative pain, quality of recovery, hemoglobin or cortisol levels



Lotan *et al.*, 2016



## In gynecology

### PREMENSTRUAL SYNDROME <sup>30</sup>

»» Randomized, double-blind placebo-controlled clinical trial



#### Methods:

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



#### Results:

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



Yakir *et al.*, 2019

### DYSMENORRHEA <sup>31</sup>

»» 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 Multidimensional Scoring System Measure (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

## In gynecology

### ENDOMETRIOSIS SUPPORTIVE CARE<sup>32</sup>

#### »» Double blind randomized control trial vs placebo



##### Methods:

- 50 patients included, treated with potentized estrogen
- Primary endpoint: Evaluation of the endometriosis associated pelvic pain severity score (EAPP) by visual analogue scale which include dysmenorrhea, non cyclic pelvic and cyclic intestinal pain.



##### Results:

- **Decrease of the overall score of 12.8 points** in the homeopathy group ( $p < 0.001$ )
- No significant decrease in the placebo group



Teixeira et al., 2017

### HOT FLUSHES DURING MENOPAUSE<sup>33</sup>

#### »» Randomized control trial vs placebo: pilot study



##### Methods:

- 40 patients included, treated with *Capsicum frutescens* followed up during 4 weeks
- Primary endpoint: Evaluation of the endometriosis associated pelvic pain severity score (EAPP) by visual analogue scale which include dysmenorrhea, non cyclic pelvic pain and cyclic intestinal pain.
- Secondary endpoint: insomnia and irritability



##### Results:

- **Significant improvement** in the intensity of hot flushes in the treated group compared to the placebo group ( $p < 0.001$ ).
- **Decrease** of insomnia and irritability ( $p = 0.001$ )



Andrade et al., 2019

## In gynecology

### BREAST PAIN RELATED TO LACTATION<sup>34</sup>

#### Randomized control trial vs placebo: pilot study



##### Methods:

- 71 patients included, treated with *Apis mellifica* 9C and *Bryonia* 9C followed up during 10 days
- Primary endpoint: Breast pain evaluated with visual analogue scale during 4 days



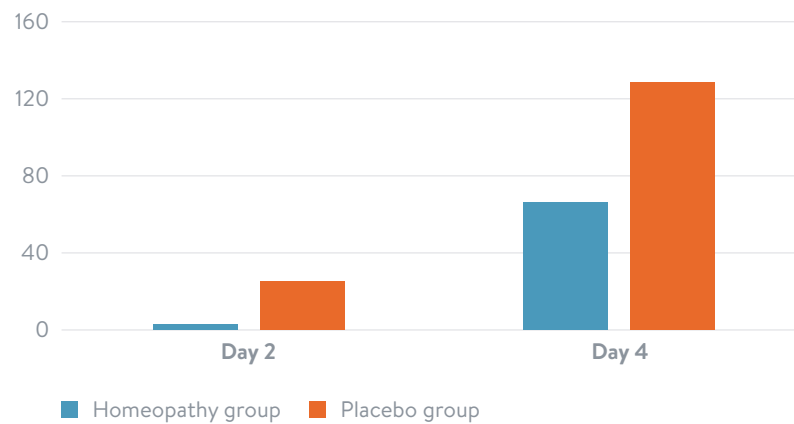
##### Results:

**Significant decrease** of breast pain in homeopathy group compared to placebo group at day 2 ( $p < 0.02$ ) and day 4 ( $p < 0.01$ )



Berrebi et al., 2001

##### Global pain score



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