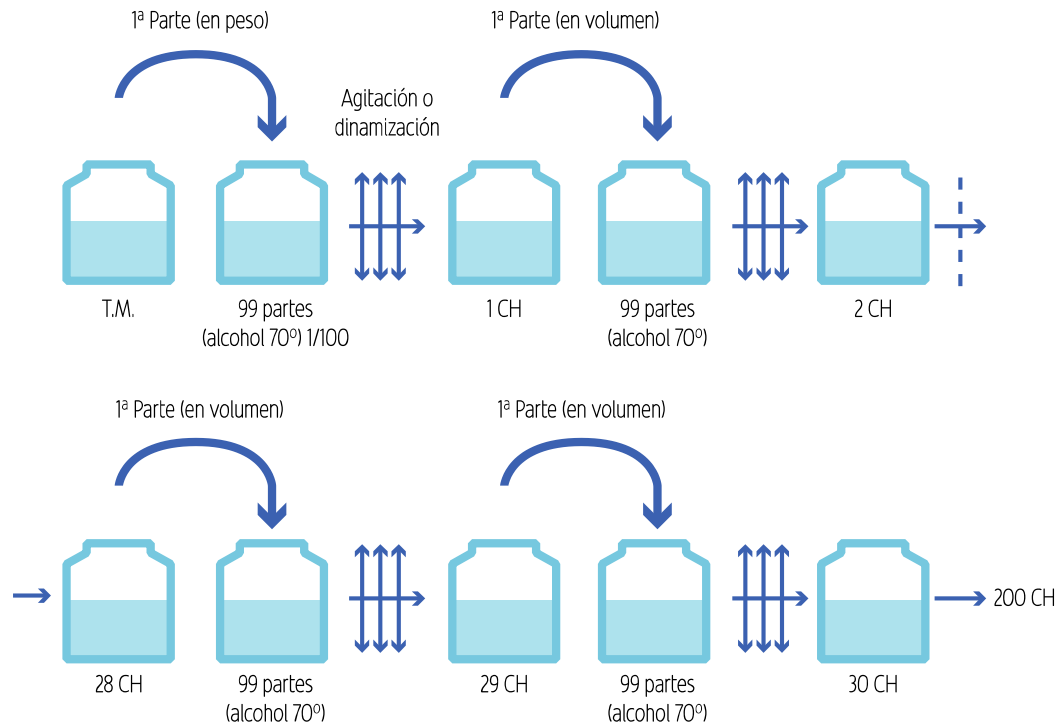
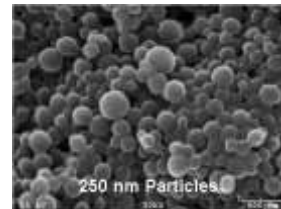
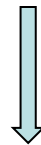
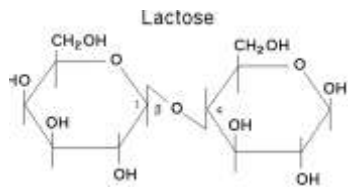


Aspectos fisicoquímicos

Método de Hahnemann

Frascos separados





Constante de Avogadro

<12C

>12C

Rango molecular

ultradiluciones

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Quality Assessment of Physical Research in Homeopathy

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and STEFAN N. WILLICH, M.D., M.P.H.¹

- Physical experiments have demonstrated structural changes of water in ultramolecular homeopathic preparations
- Methods used include:
 - low temperature thermoluminescence
 - flux calorimetry
 - conductometry
 - Raman and Ultra Violet spectroscopy
 - NMR (Nuclear Magnetic Resonance)
- However: studies low quality

REVIEW

High-dilution effects revisited. 1.
 Physicochemical aspects

Paolo Bellavite^{1,*,} Marta Marzotto¹, Debora Ofioso¹, Elisabetta Moratti¹ and Anita Conforti²

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Table 3 Physicochemical aspects of HDs as applied to homeopathy

<i>Mechanism</i>	<i>Meaning</i>	<i>Implications</i>	<i>Notes</i>
'Vicinal' water	Well-ordered water molecules organized by solutes, macromolecules and surfaces	Partial explanation of ultra-low dose effects (information transmission at molecular distances)	Experimentally proven in non-homeopathic models
Increase of electrical conductance	Structuration of water, increasing with time	Hypothetical explanation of structural 'memory' of water solutions; information transmission through water	Experimentally proven in HDs, waiting independent confirmation
Changes in NMR parameters (T1/T2 relaxation time)	Presence of nanosized structures	Explanation of structural 'memory' of diluted water solutions	Not confirmed by all laboratories
Thermoluminescence peaks in HDs	Presence of supramolecular structures in HDs	Explanation of structural 'memory' of diluted water solutions	Confirmed by independent laboratories
Spectroscopic studies (UV, IR)	Proof of changes in hydrogen bonding	Explanation of structural 'memory' of diluted water solutions	Quantitatively small effects
Magnetic field effects on water	Suggests 'non-molecular' information transfer in water solutions	Possible effects of 'dynamization' by physical means. Problems of storage due to inactivation by magnetic fields	Little experimental evidence
Water 'clathrates'	Presence of nanocavities in water	Hypothetical explanation of structural 'memory' of water solutions	Theoretical hypotheses. Never isolated from homeopathic HDs
Water clusters	Demonstration of nanoheterogeneity of water solutions; possibly due to self-organization of clusters	Hypothetical explanation of structural 'memory' of water solutions	Major evidence from theory, little experimental proof of cluster stability. Never isolated from homeopathic HDs
CDs	Two phases of condensed matter	Explanation of dynamic (frequency-based) 'memory' of condensed matter	Strong support from QED theory, little or no direct experimental proof
Nanoparticles	Aggregates of water molecules with gas, salts and minerals (silica)	Hypothetical explanation of structural 'memory' of water solutions.	Strong experimental evidence of nanoparticles in various science fields, little application to homeopathic HDs
Nanoparticles in the presence of lactose	Remaining material in subsequent dilutions	Possible role of container material Explanation of HDs effects by permanence of original substance. Proof of trituration effects	Little experimental proof, unusual technique of dilution (sampling from top layers of liquid)
Quantum entanglement	Non-local connections between remedy, patient and doctor	Highly hypothetical explanation of clinical homeopathic effects	Need of a hypothetical 'weak' quantum theory, highly speculative
Fractal-like clusters	Nanoparticulate clusters in fractal shapes of variable dimensions during subsequent dilution/succussions	Hypothetical explanation of increase of activity on dilution/ dynamization and alternating active/inactive dilution in laboratory models	Highly speculative, waiting experimental proof

Farmacodinamia

mecanismos de acción

Dinamizaciones bajas o moderadas <12C

Table 1 Aspects of homeopathic pharmacodynamics

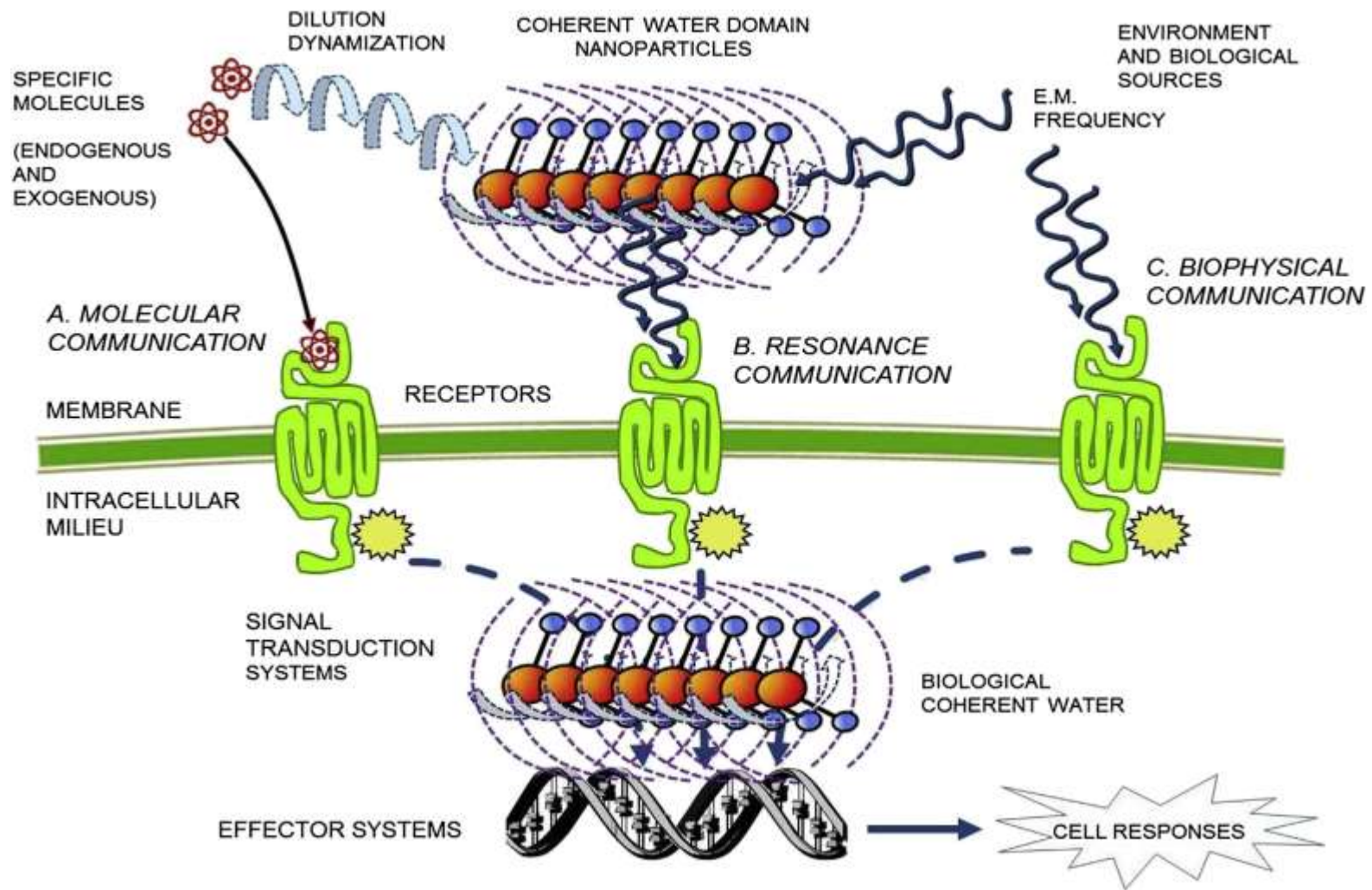
<i>Aspect</i>	<i>Medium potencies (ultra-low doses)</i>	
Nature of the medicine ^a		Very low concentrations of active molecules Nanoparticles
Biological targets	Local	Molecular interactions: - Cell receptors - Enzyme activation/regulation - Gene expression
	Systemic	Neuroimmunologic networks
Amplification mechanisms		Cell responsiveness: - Receptor priming - Signal transduction - Stochastic resonance Enzyme activity: - Allosteric activation - Silica nanostructures
Information transfer		Molecular interactions Water chains
Inversion of effects (the 'Simile')		Hormesis Dual receptors Gating by cAMP Hsps Paradoxical pharmacology

Bellavite et al 2014

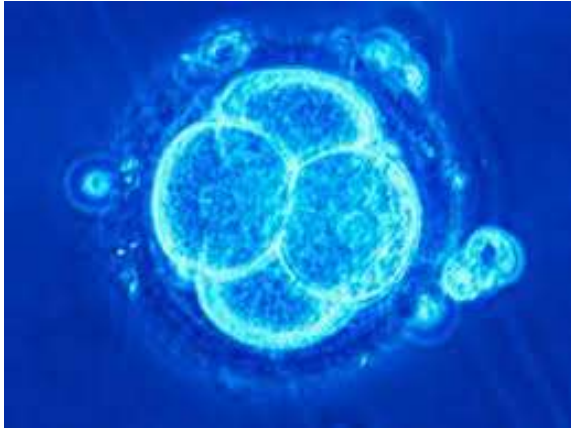
Efectos inversos: Hormesis, farmacología paradójica

Table 3 Examples of inverse effects in animal models

<i>System</i>	<i>Agent</i>	<i>First effect</i>	<i>Inverse effect</i>
Tadpoles (frogs) ^{20,21,182,183} Rat blood ^{184–186}	Thyroxine Acetylsalicylic acid	Stimulates metamorphosis Inhibit platelet aggregation and haemostasis	HDs inhibit metamorphosis Very low doses have thrombogenic activity
Dog heart ¹⁸⁷	Ischemia	Causes infarction	Ischemic preconditioning protects from infarction
Mice kidney ¹⁸⁸	Free radicals	Toxicity	Pre-treatment with low doses protect from toxicity
Mouse prostate ¹⁸⁹ Mouse and rat immune system ^{190,191} Mice ¹⁹²	Estrogens Protein antigens Morphine	Inhibit growth Induce allergy autoimmune disease Antinociceptive effects	Low doses promote growth Oral administration protects and cures autoimmunity Extremely low doses enhance pain sensitivity
Rat arthritis ¹⁹³ Mice ^{194,195} Rat, guinea pig ^{196–201} Rat liver ^{202,203} Rat immune system ^{204–206}	Naloxone Naloxone Histamine and/or bee venom Carbon tetrachloride Mycobacteria in adjuvant	Hyperalgesia Antagonizes morphine Inflammation, oedema Toxicity Induce arthritis when injected intra-paw	Low doses have antinociceptive effects Analgesic effects in ULDs Low doses and HDs reduce inflammation Low doses protect from liver toxicity Intraperitoneal low doses cure arthritis
Mice, guinea pig, rats ^{207–211}	Arsenic	Liver toxicity, genotoxicity	Protection by ULDs of arsenic and increase of arsenic elimination
Rat ^{212,213}	Carcinogens (acetaminofluorene, phenobarbital) <i>Bacillus antracis</i>	Induce cancer	Low doses protect from cancer
Rat ²¹⁴ Mice ²¹⁵	<i>Gelsemium sempervirens</i>	Severe inflammation and death Causes severe weakness, dizziness, convulsions	Low doses of bacillus extract protect from toxicity HDs are anxiolytic and increase exploration movement



Extracto de Bellavite et al 2014



Estudios en modelos celulares

Evidencias en experimentación
“básica”



The *in vitro* evidence for an effect of high homeopathic potencies—A systematic review of the literature

Claudia M. Witt^{a,□}, Michael Bluth^b, Henning Albrecht^c,
Thorolf E.R. Weißhuhn^a, Stephan Baumgartner^d, Stefan N. Willich^a

Metaanálisis de 67 estudios *in vitro* en 75 publicaciones acerca de las diluciones homeopáticas:

- La mayoría muestran un efecto de las altas potencias
- El efecto persiste en los estudios de más alto estándar metodológico (mas restrictivos)
- Alta heterogenicidad de los estudios
- Efectos positivos en $\frac{3}{4}$ de todos los estudios replicados

Estudios en modelos celulares

- **Estudios con más replicaciones**

- Efecto inhibitorio de las ultradiluciones de histamina en la activación de los basófilos
- Efecto inhibidor de las ultradiluciones de Tiroxina en el grado de metamorfosis de anfibios
- Efecto protector de las ultradiluciones de arsénico sobre el efecto tóxico inducido por dosis ponderales de trióxido de arsénico sobre el crecimiento del trigo

Estudios en modelos celulares "in vivo"

- efecto **proagregante** plaquetario **aspirina** ultradiluida al método homeopático
 - opuesto al efecto antiagregante inducido a dosis ponderales (Lalanne, 1990, Eizayaga, 2007) y está mediado a través de la enzima COX2 (Aguejoug, 2008).
- modulación de la **expresión** de citoquinas en **células inmunológicas**
 - parte de los efectos de la homeopatía se median a través de células del sistema inmunológico (Fimiani, 2000; Ramachandran, 2007; De Oliveira, 2008; Smit, 2008)
- Gelsemium, ansiolítico. Cocculus, antiestrés
- **Activación epigenética**
 - Modulación expresión genómica en E coli y Saccharomyces expuestas a arsénico
 - Zhong Xi Yi Jie He Xue Bao. 2011
 - Zhong Xi Yi Jie He Xue Bao. 2012
 - Gelsemium, transcripción neuronal
 - Marzotto M, Oliosio D, Brizzi M, Tononi P, Cristofolletti M, Bellavite P. Extreme sensitivity of gene expression in human SH-SY5Y neurocytes to ultra-low doses of Gelsemium sempervirens. BMC Complement Altern Med 2014; 14:104.
 - Oliosio D, Marzotto M, Moratti E, Brizzi M, Bellavite P. Effect of Gelsemium sempervirens L. on pathway-focused gene expression profiling in neuronal cells. J Ethnopharmacol 2014; 153(2):535-9.

Comprobación de los efectos de la homeopatía en voluntarios sanos

Homeopathic pathogenetic trials produce more specific than non-specific symptoms: results from two double-blind placebo controlled trials

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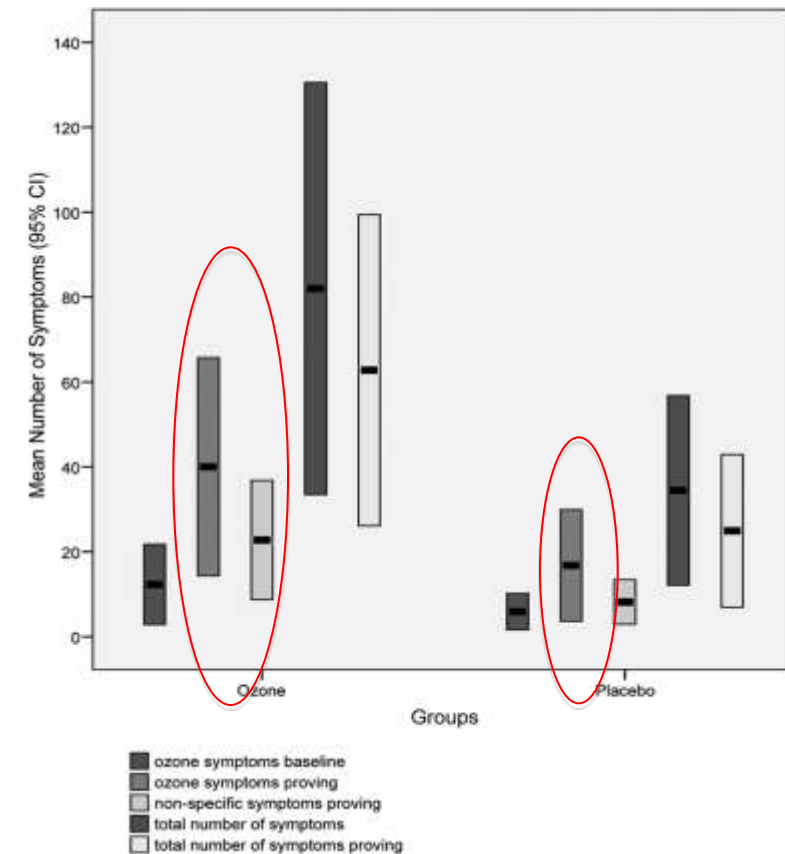
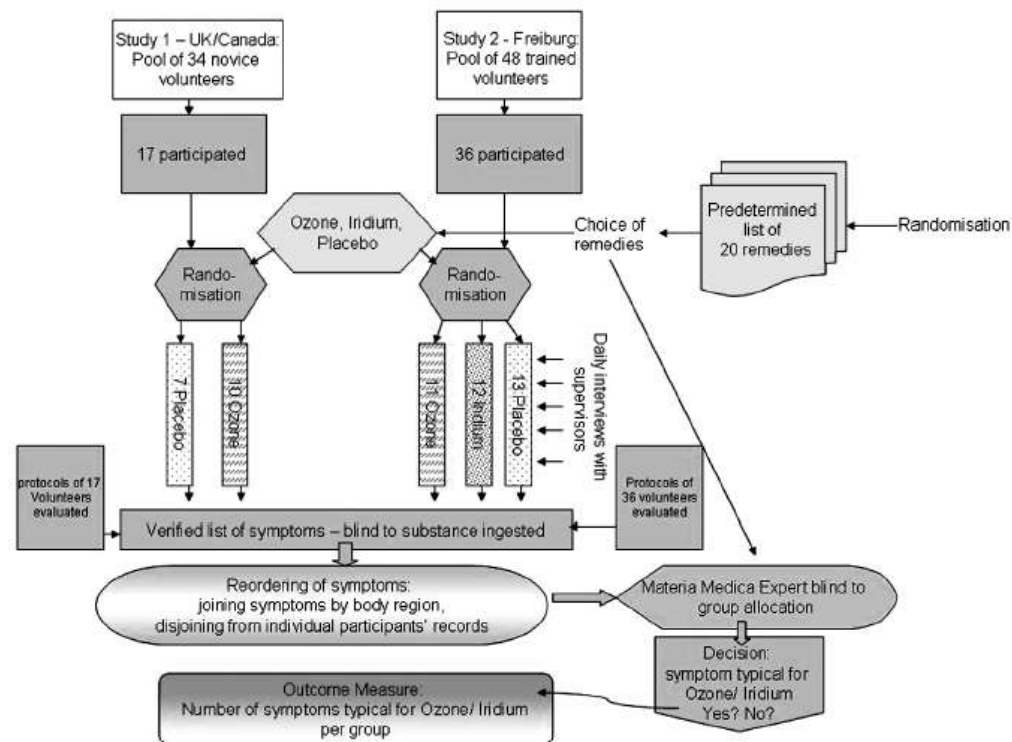


Figure 1 Participant flow and essential design features.

Homeopathic Pathogenetic Trials Produce Specific Symptoms Different from Placebo

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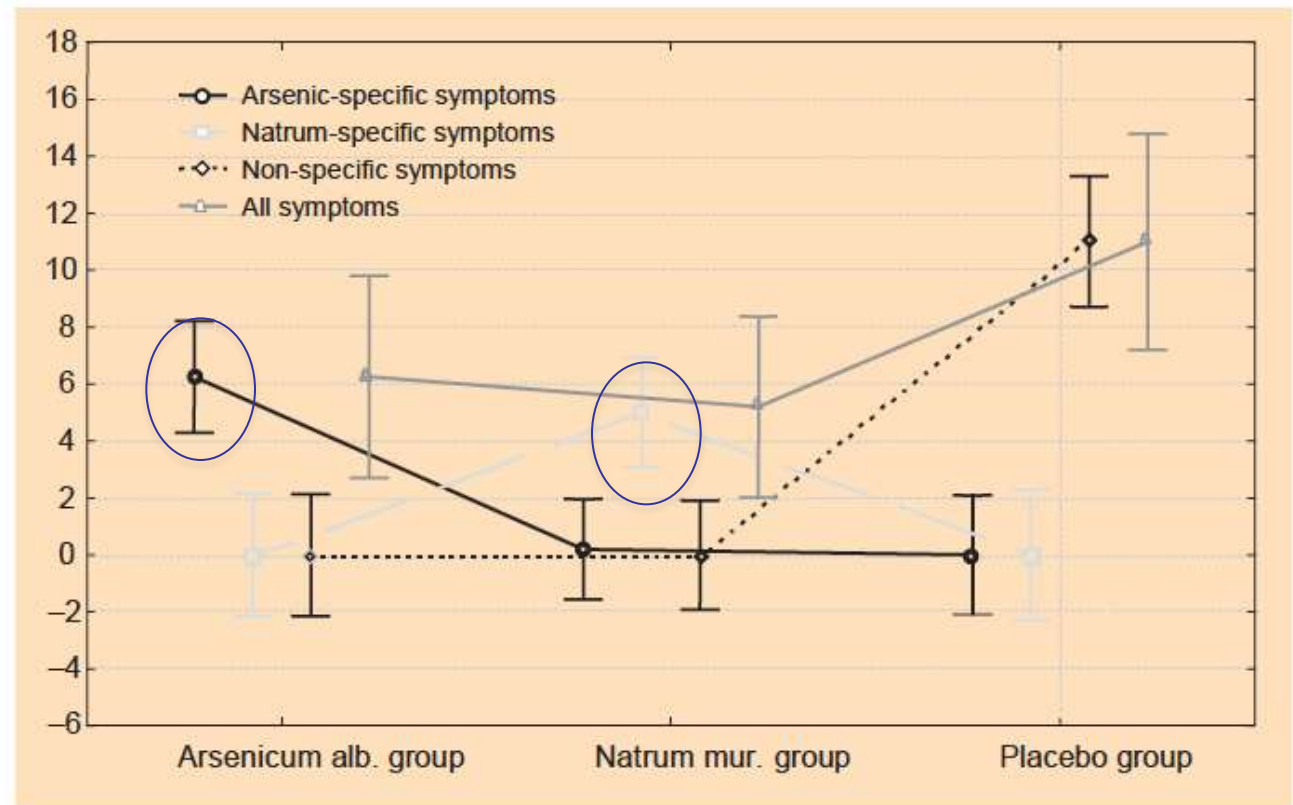


Fig. 1. Mean number of symptoms (vertical bars: 95% confidence intervals) specific for Arsenicum album or Natrum muriaticum, respectively, and non-specific symptoms in the three experimental groups.



**Comprobación de los efectos de la
homeopatía en HUMANOS**

Estudios de Neuroimagen

Estudios con EEG

- ◎ Ensayos clínicos de alta calidad metodológica
- ◎ 4 estudios positivos en voluntarios sanos
- ◎ 1 estudio positivo en pacientes con insomnio
- ◎ 2 estudios positivos en pacientes con fibromialgia
- ◎ Necesidad de reproducción por grupos independientes

Multiweek Resting EEG Cordance Change Patterns from Repeated Olfactory Activation with Two Constitutionally Salient Homeopathic Remedies in Healthy Young Adults

Iris R. Bell, MD, PhD,¹⁻⁵ Amy Howerter, PhD,¹ Nicholas Jackson, MPH,^{1,5}
 Audrey J. Brooks, PhD,^{3,4} and Gary E. Schwartz, PhD²⁻⁴

TABLE 3. MEANS AND STANDARD ERROR VALUES
 OF POST-PRE CHANGE IN EEG CORDANCE FOR
 EACH FREQUENCY BAND BY REMEDY GROUP

Band	Visit	Remedy group	
		Sulphur	Pulsatilla
δ	1	0.15 (0.10)	0.15 (0.11) ^c
	2	0.23 (0.10)	0.10 (0.10) ^b
	3	0.13 (0.11)	0.32 (0.11) ^a
θ	1	-0.08 (0.15)	0.01 (0.17)
	2	-0.27 (0.16) ^{a,c}	0.21 (0.17) ^d
	3	0.08 (0.16) ^b	-0.02 (0.17)
α	1	-0.15 (0.05)	-0.07 (0.05) ^b
	2	-0.18 (0.05)	-0.07 (0.05) ^b
	3	-0.15 (0.05)	-0.23 (0.05) ^a
β	1	0.39 (0.17) ^{b,d}	-0.37 (0.18) ^{b,c}
	2	-0.04 (0.17) ^a	-0.06 (0.18) ^a
	3	0.22 (0.18) ^d	-0.35 (0.18) ^{c,e}

δ: Pulsatilla ^{a>b} $p < 0.02$; ^{a>c} $p < 0.07$.

θ: Sulphur ^{a>b} $p < 0.02$; Sulphur versus Pulsatilla ^{c>d} $p < 0.05$.

α: Pulsatilla ^{a<b} $p < 0.0005$.

β: Sulphur ^{a<b} $p < 0.04$; Pulsatilla ^{a>b} $p < 0.04$; ^{a>c} $p < 0.06$; Sulphur
 versus Pulsatilla ^{d>e} $p < 0.03$.

EEG, electroencephalographic.

- 97 adultos jóvenes sanos tipo constitucional consiste *Pulsatilla* o *Sulphur*.
- 3 sesiones semanales aleatorizadas EEG pre y post medicamento (6C, 12C o 30C) o placebo.
- análisis cordancia en reposo del área prefrontal (Fp1 y Fp2)
- **Este estudio demuestra efectos medibles mediante EEG específicos de *Sulphur* y *Pulsatilla* en adultos jóvenes**
- **confirma al EEG como herramienta eficaz en la demostración de los efectos fisiológicos de la homeopatía en el ser humano.**

Resumen

- El proceso de fabricación del medicamento homeopático induce **cambios fisicoquímicos** que pueden ser **objetivables** por técnicas como la termoluminiscencia y la RMN
- Los medicamentos homeopáticos inducen **efectos biológicos comprobables** tanto *in vitro* como *in vivo*
- Los medicamentos homeopáticos son capaces de inducir **efectos prototípicos en voluntarios sanos y sus efectos** pueden ser **diferenciados de los del placebo mediante EEG**
- Son **necesarios más estudios** y estudios confirmatorios