



Complementary Medicine meets Oncology
Merano 11-13 settembre 2008

Clinical and Laboratory evidence in homeopathy

Paolo Bellavite, Salvatore Chirumbolo, Paolo Magnani
Dipartimento di Scienze Morfologico-Biomediche, Università di Verona
paolo.bellavite@univr.it



TERAPIE COMPLEMENTARI NELLA CURA PALLIATIVA IN PAZIENTI ONCOLOGICI

“Le medicine complementari sono divenute un importante aspetto dell’assistenza a malati di cancro. “

“Si sono trovati risultati promettenti per alcuni trattamenti ed in particolare per agopuntura, terapia con enzimi, omeopatia, ipnosi terapeutica e varie tecniche di rilassamento.”

“Purtroppo, gli autori della rassegna giudicano le evidenze raccolte come non convincenti (“not compelling”) per ciascuna di queste terapie.”

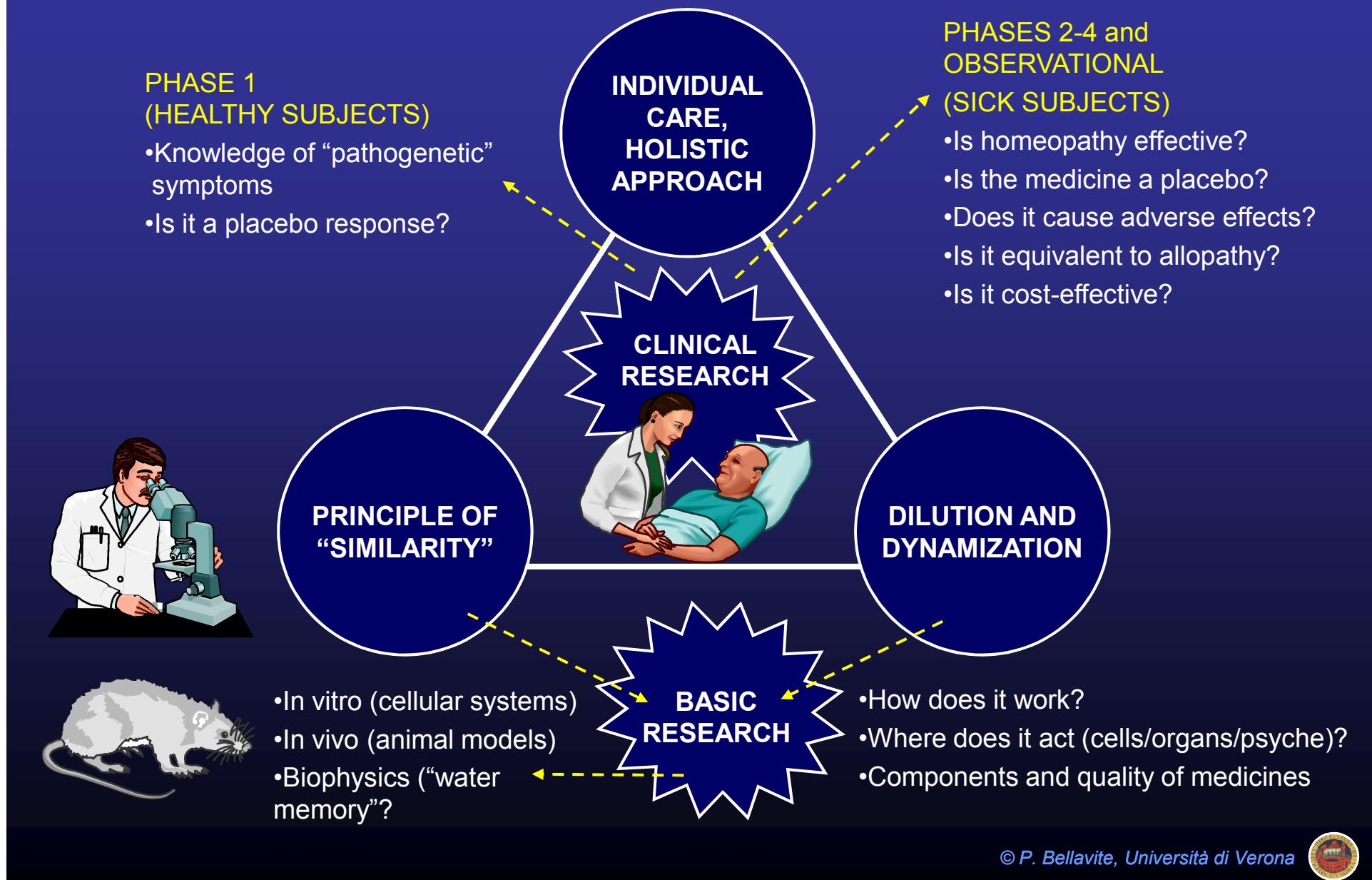
CONCLUSIONI: Questi risultati sottolineano l’esistenza di qualche potenziale utilità delle medicine complementari nell’assistenza palliativa ai malati di cancro. Allo stesso tempo, essi dimostrano l’urgente necessità di ulteriore e più rigorosa ricerca nel settore.



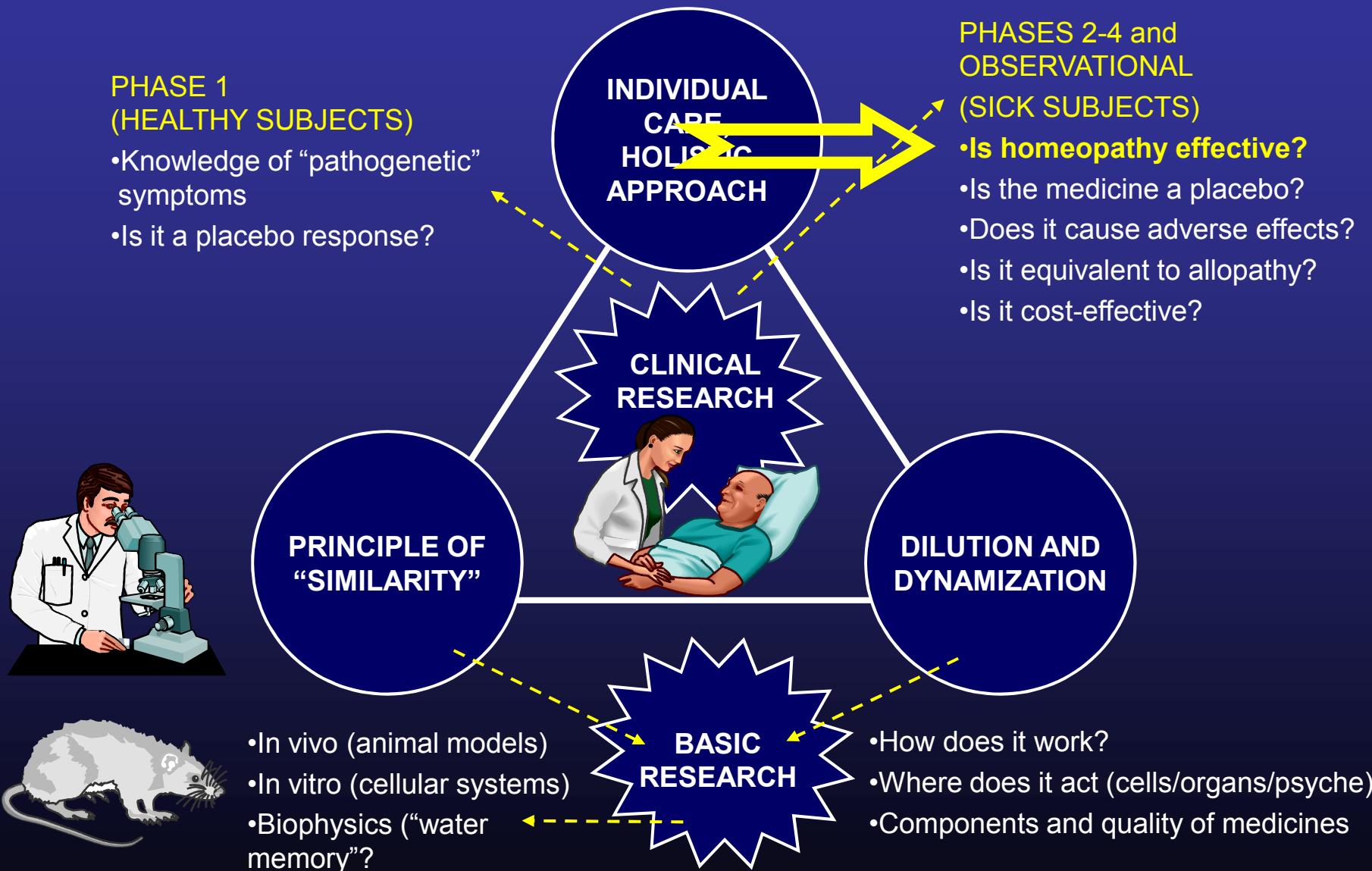
E. Ernst
Cancer 2001;91:2181-2185



Scientific investigation of homeopathy



Scientific investigation of the main homeopathic principles





“Ma l’omeopatia cura il cancro?”

Da un certo punto di vista, quello rigoroso della “medicina basata sulle prove di efficacia”, si dovrebbe rispondere “certamente no”

Infatti, nessun paziente affetto da tumore, allo stato attuale delle conoscenze, può confidare in una cura omeopatica per risolvere il suo problema.

Non ci sono sufficienti evidenze, mancano delle precise meta-analisi (valutazioni soppesate della letteratura) fatte da esperti del settore e pubblicate su riviste attendibili.

(Milazzo, Russell, and Ernst 2006, Ernst 2007).





Esistono, piuttosto, alcune analisi epidemiologiche che dimostrano come i pazienti, che “confidano” nelle terapie alternative per curare il cancro, vadano spesso incontro a un ritardo nella terapia efficace e/o abbiano una minore sopravvivenza globale

(Malik et al 2003, Chang et al., 2006)



A scenic view of a valley with mountains in the background. The foreground shows green hills and a winding road. In the middle ground, a small town or village is nestled in the valley. The background features a range of mountains under a cloudy sky.

L'omeopatia potrebbe intervenire quindi come approccio complementare:

- Stomatite da chemio
 - Dermatite da radioterapia
 - Vomito e nauseae causate da chemioterapia
 - “Salute generale”, “qualità della vita”
-
- Infezioni respiratorie
 - Otiti
 - Cefalea





Controlled clinical trials of homeopathy in cancer

Patients	Intervention	Outcome	Reference
82 patients with radiotherapy side effects	1. Cobaltum C30 2. Causticum C30 3. Placebo	Compared with placebo, the reaction profile score was lower In treated groups.	(Kulkarni, Nagarkar, and Burde 1988) <i>Hahnemann Homeopath.Sand.</i> 12:20-23.
30 young patients with chemotherapy-induced stomatitis	Traumeel S (Arnica compositum)* complex medication (oral rinse)/placebo	Significant differences favouring verum group were observed In terms of reduction in symptoms.	(Oberbaum et al. 2001). <i>Cancer</i> 92 (3):684-690.
66 patients with dermatitis during radiotherapy for breast cancer	Belladonna 7CH and X-ray 15CH /placebo	A trend towards a better activity of the homoeopathic medicine compared to placebo. Significant difference only during recovery	(Balzarini et al. 2000) <i>Br.Homeopath.J</i> 89 (1):8-12.
80 patients with breast cancer	Cocculin **/placebo	Decrease of the nausea episodes from 87.5% (placebo) to 61.5% (verum) (Preliminary data)	(Genre et al., 2003)
Menopausal symptoms in 83 breast cancer survivors	1: Individualized homeopathy 2: Individualized homeopathy plus complex remedy*** 3: Placebo	No significant differences of symptom score. Significant improvement in general health score in both homeopathy groups.	(Jacobs et al. 2005) <i>J.Altern.Complement Med.</i> 11 (1):21-27.
53 breast cancer survivors with Estrogen withdrawal Symptoms	Individualized homeopathy+verum/ Individualized homeopathy+placebo	Improvements in both groups, no significant differences	(Thompson et al. 2005) <i>J.Altern.Complement Med.</i> 11 (1):13-20.

*Low potencies combination of Arnica, Calendula, Millefolium, Chamomilla, Symphytum, Belladonna, Aconitum, Bellis perennis, Hypericum, Echinacea angustifolia, Echinacea purpurea, Hamamelis, Mercurius sol. and Hepar sulfuris.

**Combination of Coccus, Tabacum, Nux vomica, Petroleum (all 4CH)

*** combination remedy was "Hyland's menopause," which contains amyl nitrate, sanguinaria canadensis, and lachesis.





INFECTIONS OF UPPER AIRWAYS AND EAR-NOSE-THROAT DISEASES

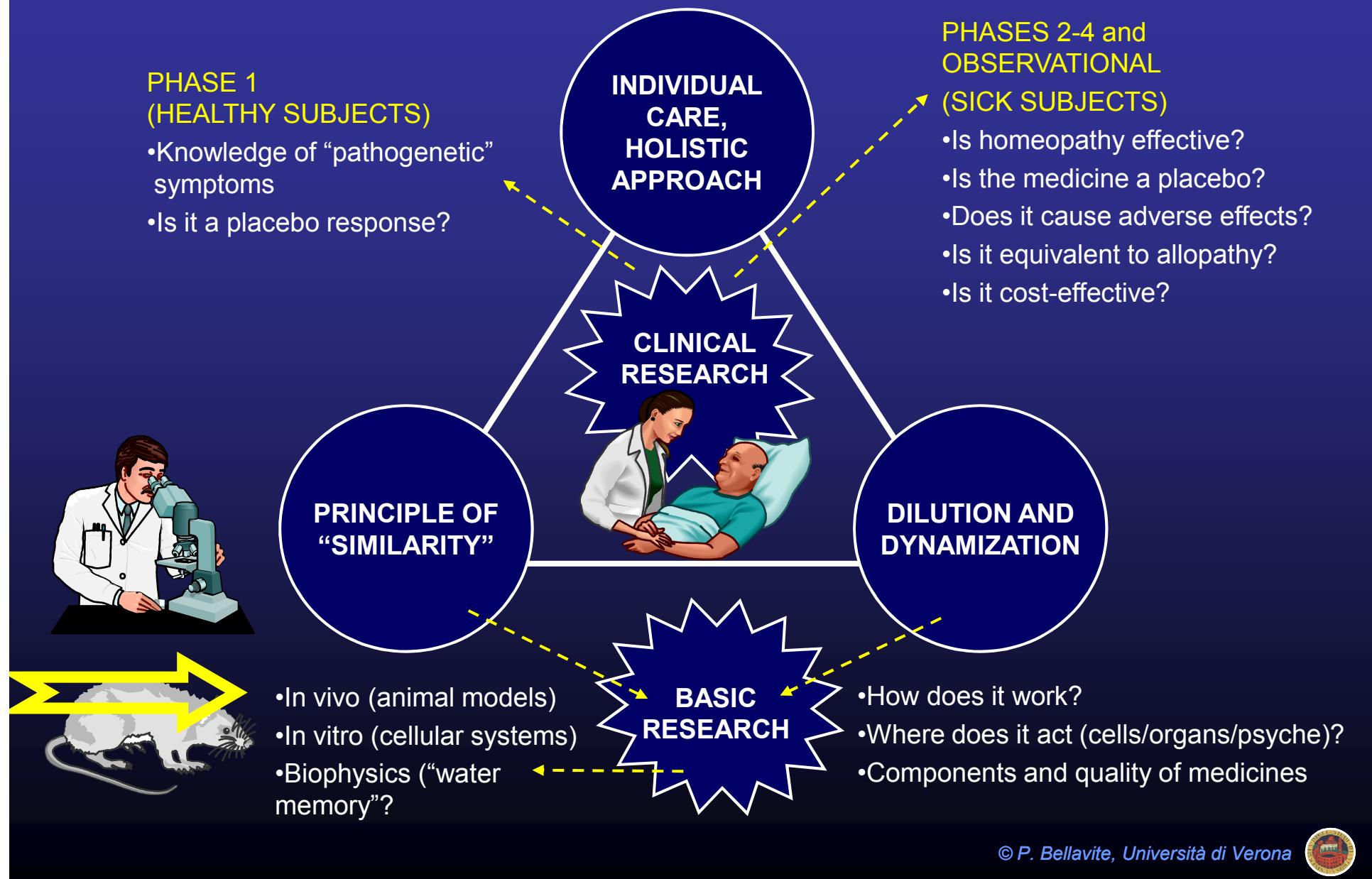
Bellavite et al., Evidence-Based Complementary and Alternative Medicine, 2006

bold= randomized controlled trial or meta-analysis covering the topic;
italics=non randomized controlled trial; normal case= uncontrolled, observational and retrospective studies; underlined=indexed journals.

Level of Evidence	Individualized Homeopathy	Complex formulations and low potencies of single remedies
Good Scientific Evidence	OTITIS (58), (59), (63), (64), (65)	<i>Euphorbium compositum</i> for rhinitis-sinusitis (52), (55), (56) , (68)
Unclear scientific evidence	UPPER RESPIRATORY TRACT INFECTIONS In favor: (64), (69) ; no effect: (61), (70), (71) .	<i>Eupatorium</i> (48) Homeopathic complex formulations <i>L52</i> (49) , <i>Drosera</i> (50) , <i>Grippheel</i> (51), (67)



Scientific investigation of the main homeopathic principles





Effects of homeopathic treatment on animal models of cancerogenesis (part 1)

Animal	Disease Model	Intervention	Results	Ref
Mice	Cytogenetical damage induced by exposures to ultrasonication	Actinomycin D or Arnica 30/placebo	AMD had genotoxic effects of its own. Sonicated mice fed with Arnica 30 showed appreciably reduced genotoxicity	(Chakrabarti, Biswas, and Khuda-Bukhsh 2001) Indian J.Exp.Biol. 39 (12):1235-1242.
Mice	p-dimethylaminoazobenzene (p-DAB)-induced hepatocarcinogenesis	Two potencies of Chelidonium (Ch-30, Ch-200)	Feeding of Chelidonium reduced genotoxic effects to a significant extent ($p < 0.05$ to $p < 0.001$).	(Biswas and Khuda-Bukhsh 2002) BMC.Complement Altern.Med 2:4.
Mice	p-DAB-induced hepatocarcinogenesis	Chelidonium-30 (Ch-30) and Chelidonium-200 (Ch-200),	Both Ch-30 and Ch-200 also modulated favourably some toxicity marker enzymes	(Biswas and Khuda-Bukhsh 2004) Indian J.Exp.Biol. 42 (7):698-714.
Mice	Genotoxic Effects Produced by Mercuric Chloride	Mercurius Solubilis(Merc Sol-30 and Merc Sol-200)	Less chromosome aberrations in the drug-fed series. The amelioration by Merc Sol-200 appeared to be slightly more pronounced.	(Datta, Biswas, and Khuda-Bukhsh 2004) Evid.Based.Complement Alternat.Med 1 (3):291-300.
Mice	p-DAB-induced hepatocarcinogenesis	Carcinosin 200, fed alone and in combination with Chelidonium 200	Carcinosin 200 and Chelidonium 200 when administered alone show considerable ameliorative effect on cytogenetical endpoints and toxicity biomarkers	(Biswas et al. 2005) J Altern.Complement Med 11 (5):839-854.
Mice	Sarcoma 180	Canova, a homeopathic complex medicine*	Delay in the development, increased infiltration by lymphoid cells with active treatment. Increased number of leukocytes and lymphocytes.	(Sato et al. 2005) Homeopathy 94 (1):26-32.

*The formula of Canova is composed of 19x Thuya occidentalis, 18x Bryonia alba, 11x Aconitum napellus, 19x Arsenicum album and 18x Lachesis muta (Viperidae) venom, all extracted and diluted in 70% alcohol, in equal parts.

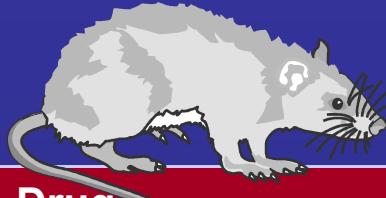




Effects of homeopathic treatment on animal models of cancerogenesis (part 2)

Animal	Disease Model	Intervention	Results	Ref
Rats	Prostate cancer (rats injected with MAT-LyLu cells)	<i>Thuja occ.</i> 1000c, <i>Conium mac.</i> 1000c, <i>Sabal serr.</i> 200c, <i>Carcinosin</i> 1000c from MAT-LyLu cells	23% reduction in tumor incidence ($P < .0001$), and 38% reduction in tumor volume ($P < .02$). Tumors showed a 19% increase in apoptotic cell death ($P < .05$).	(Jonas et al. 2006) Integr.Cancer Ther. 5 (4):343-349.
Mice	p-DAB-induced hepatocarcinogenesis	<i>Lycopodium</i> 30c and 200C	Protection from chromosome aberrations and toxicity biomarkers	(Pathak et al. 2006 and 2007) Mol.Cell Biochem. 285 (1-2):121-131. Forsch.Komplementarmed. 14 (3):148-156.
Mice	Dalton's lymphoma ascites, Ehrlich ascites carcinoma (EAC)	<i>Ruta graveolens</i> (low potencies and 200C)	Increase the lifespan of tumour bearing animals	(Preethi, Kuttan, and Kuttan 2006) Asian Pacific J Cancer Prev 7:439-443.
Mice	Genotoxicity induced by repeated injections of arsenic trioxide	<i>Arsenicum album</i> 200 alcohol (Alcohol-200)	Drug fed mice showed reduced toxicity at statistically significant levels in respect of all the parameters studied	(Banerjee et al. 2007) J Vet.Med.A Physiol Pathol.Clin.Med. 54 (7):370-376.
Rats	N'-nitrosodiethylamine (NDEA) induced hepatocellular carcinoma and sarcomas	<i>Ruta</i> , <i>Hydrastis</i> , <i>Lycopodium</i> and <i>Thuja</i> (200C), <i>Phosphorus</i> 1M	Homeopathic drugs retarded the tumor growth and reduced the marker enzymes (<i>Ruta</i> 200c of liver tumor, <i>Ruta</i> 200c and <i>phosphorus</i> 1M of sarcomas)	(Kumar et al. 2007) Asian Pac.J Cancer Prev. 8 (1):98-102.
Mice	Human prostate xenografts cancer growth	<i>Sabal serrulata</i> , <i>Thuja occidentalis</i> , and <i>Conium maculatum</i>	Xenograft size was significantly reduced in <i>Sabal serrulata</i> -treated mice compared to untreated controls ($P=.012$). No effect was observed on breast tumor growth.	(MacLaughlin et al. 2006) Integr.Cancer Ther. 5 (4):362-372.
Mice	Hepatocarcinogenesis through P-DAB and Phenobarbital	<i>Natrum Sulphuricum</i> 200 (Nat Sulph-200)	Less number of liver tumors and of chromosome aberrations reduced toxicity parameters	(Bhattacharjee, Pathak, and Khuda-Bukhsh 2007) eCAM Advance a.





Homeopathic medicine and animal (murine) cancer models

Drug	Effect	Group and reference
Arnica 30CH	Reduces sonication-induced Genotoxicity	{CHAKRABARTI2001} University of Kalyani, Nadia, India
Chelidonium 30CH and 200CH, alone or with Carcinosin 200CH	Reduces p-DAB-induced tumors incidence, genotoxicity and improves Biomarkers	{BISWAS2002} {BISWAS2004} {BISWAS2005} University of Kalyani, Nadia, India
Mercurius Sol 30CH and 200CH	Reduces mercury-induced genotoxicity	{DATTA2004} University of Kalyani, Nadia, India
Lycopodium 30CH and 200CH	Reduces p-DAB-induced tumors incidence, genotoxicity and improves Biomarkers	{PATHAK2006} {PATHAK2007} University of Kalyani, Nadia, India
Natrum sulf. 200CH	Reduces p-DAB-induced tumors incidence, genotoxicity and improves Biomarkers	{BHATTACHARJEE2007} University of Kalyani, Nadia, India
Canova complex (Thuja , Bryonia , Aconitum , Arsenicum , Lachesis)	Inhibit development of sarcomas-180	{SATO2005} Universidade do Vale do Itajai, Brazil
Thuja 1000CH, Conium 1000CH, Sabal S. 200CH Carcinosin 1000CH	Reduces prostate cancer incidence and tumor volume	{JONAS2006A} Samueli Institute, Alexandria, VA, USA
Sabal S. 200CH	Reduces prostate cancer incidence and tumor volume	{MACLAUGHLIN2006} Georgetown University, Washington, DC
Ruta , Hydrastis , Lycopodium , Thuja 200CH, Phosphorus 1000CH	Inhibits liver tumor development (Ruta max effect in one paper and reported as the only remedy in another)	{KUMAR2007} {PREETHI2006} Cancer Research Centre, Kerala State, India



Omeopatia in modelli animali di cancerogenesi

Esistono almeno 13 pubblicazioni sperimentali fatte su modelli murini, con risultati positivi, tutte nella letteratura scientifica. Risulta che alcuni medicinali:

Sabal serrulata (pancreas)

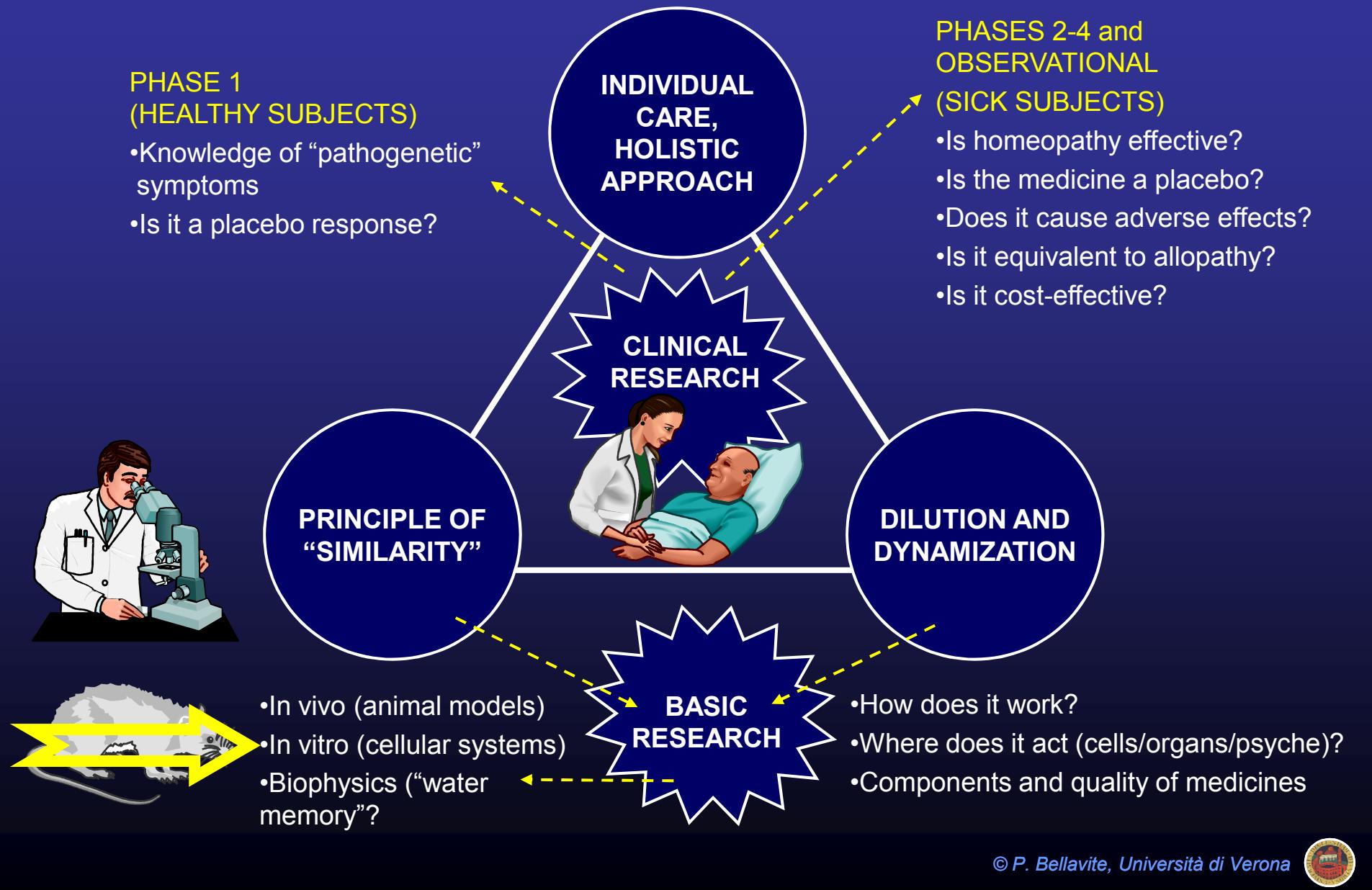
Thuja, Carcinosin, Ruta, Chelidonium, Lycopodium (fegato, sarcomi)

producono effetti significativi di rallentamento della crescita in tumori indotti sperimentalmente.

Ovviamente, ciò non significa che le stesse medicine possano essere usate nell'uomo con qualche possibilità di successo, in assenza di studi dimostrativi, ma aprono nuove possibilità per la ricerca.



Scientific investigation of the main homeopathic principles



Effects of homeopathic preparations on human prostate cancer growth in cellular and animal models

B. W. MacLaughlin et al. Integr. Cancer Ther., 5 (2006) 362-372.

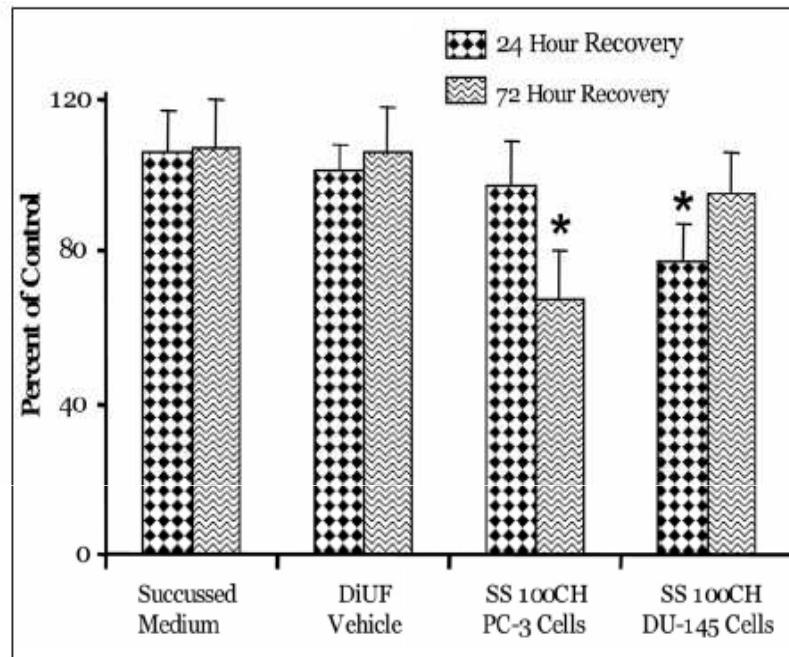


Figure 1 Antiproliferative effect of 100 CH *Sabal serrulata* (SS 100CH) on both human prostate cancer cell lines PC-3 and DU-145. Cells were treated with 1 dose (10 μ L) every 4 hours of *Sabal serrulata* and left to recover for either 24 or 72 hours. DiUF = succussed deionized ultrafiltered water; SS 100CH = *Sabal serrulata* 100 CH dilution. Crystal violet technique was used. Error bars represent \pm SD. PC-3, 72 hour and DU-145, 24 hour recovery are statistically significant, $P < .01$ (*) as assessed by Student's t test.

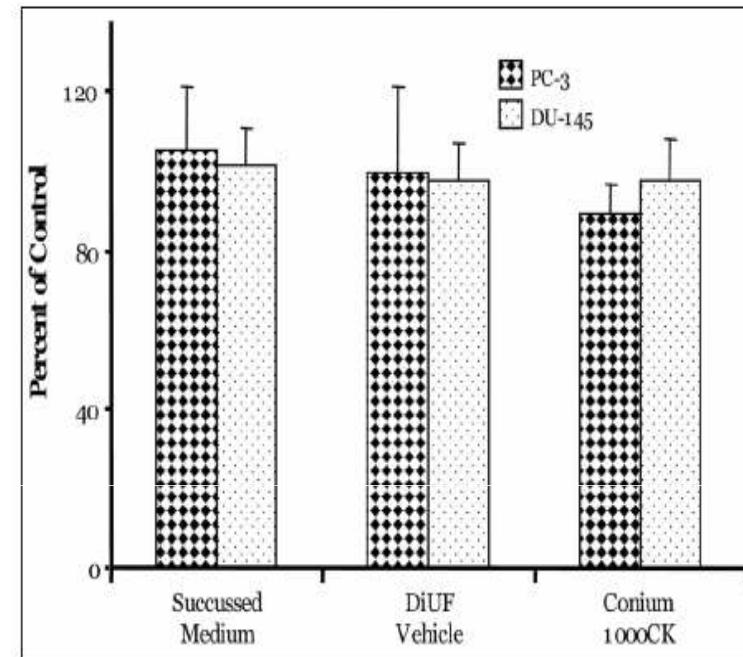


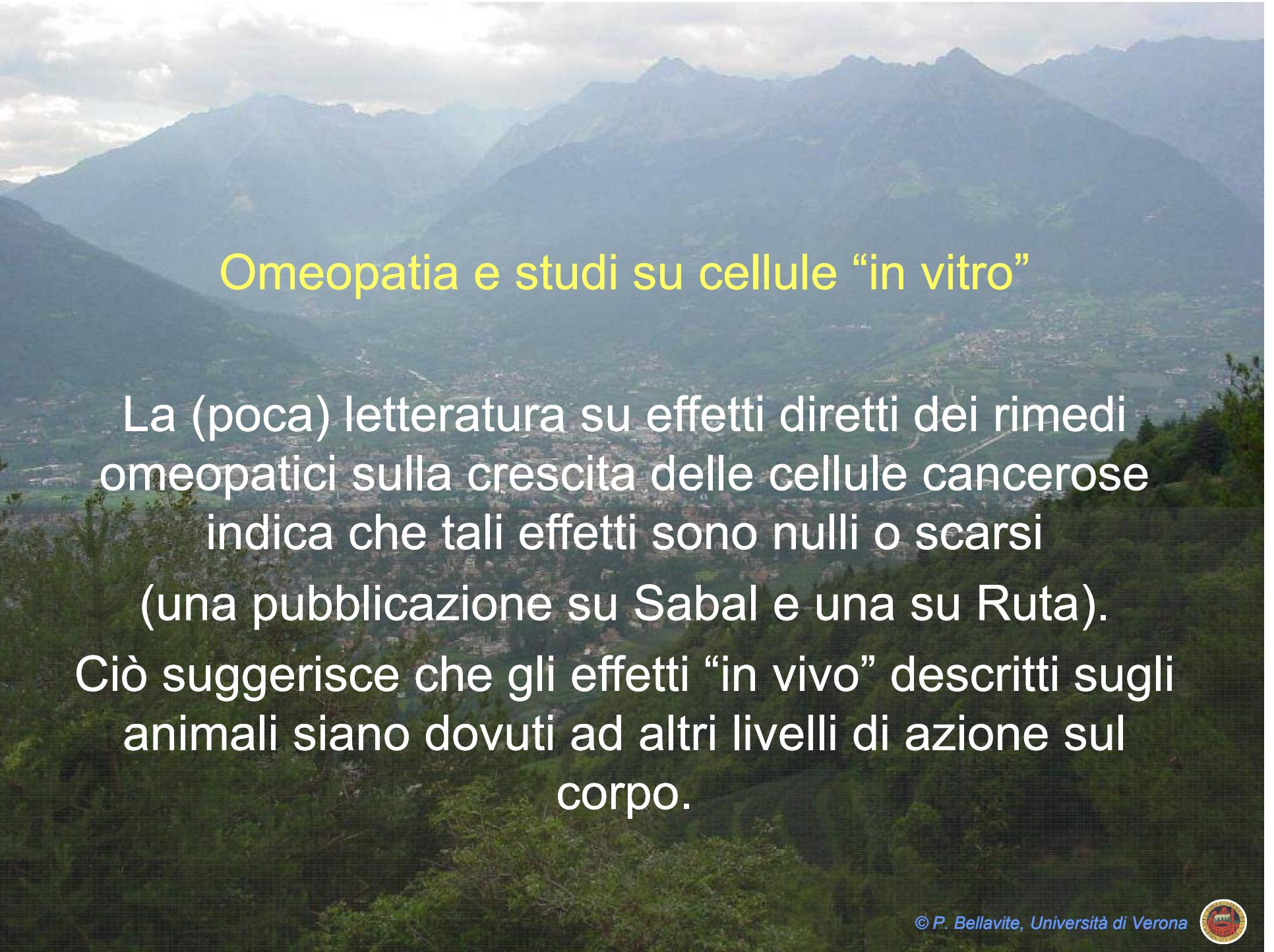
Figure 4 Effect of 1000 CK *Conium maculatum* on both human prostate cancer cell lines PC-3 and DU-145. They were treated with 1 dose every 4 hours and left to recover for 24 hours. MTT technique was used. DiUF = succussed deionized ultrafiltered water. Error bars represent \pm SD. No statistically significant effect was observed, $P > .05$.

Effects of homeopathic treatment on cell models of cancerogenesis



Cells	Laboratory test	Intervention	Results	Ref
Normal and leukemic lymphocytes	Cell viability	Pretreatment with either low concentrations (nM-microM) or high potencies (15-20c) of cadmium (Isopathic)	Increased cell viability in primary lymphocytes. Weaker effect in cancerous cells	(Walchli, Baumgartner, and Bastide 2006). J Altern. Complement Med. 12 (5):421-427.
Prostate tumor cells	Tumor cell viability and apoptosis gene expression	Thuja occidentalis 1000c, Conium maculatum 1000c, Sabal serrulata 200c	No effects on cell viability or gene expression	(Jonas et al. 2006) Integr.Cancer Ther. 5 (4):343-349.
Prostate and breast cancer cell lines	Tumor cell viability and apoptosis gene expression	Conium maculatum, Sabal serrulata, Thuja occidentalis, Asterias, Phytolacca, and Carcinosin in several potencies	No effects on cell viability or gene expression	(Thangapazham et al. 2006a) Integr.Cancer Ther. 5 (4):356-361.
Copenhagen rat tumor tissues	mRNA levels of the apoptotic genes or the cytokines in prostate tumor	Conium maculatum, Sabal serrulata, Thuja occidentalis, and a MAT LyLu Carcinosin nosode	No significant changes of any treatment	(Thangapazham et al. 2006b) Integr.Cancer Ther. 5 (4):350-355.
Human prostate cancer and breast cancer cell lines.	Cell proliferation	Sabal serrulata (saw palmetto) 100CH	33% decrease of prostate cell proliferation, no effect on breast cells.	(MacLaughlin et al. 2006) Integr.Cancer Ther. 5 (4):362-372.
Lymphoma ascites and other tumors	Cell growth	Ruta graveolens (phytotherapy and homeopathy 200C)	Cytocidal action of both preparations	(Preethi, Kuttan, and Kuttan 2006) Asian Pacific J Cancer Prev 7:439-443.





Omeopatia e studi su cellule “in vitro”

La (poca) letteratura su effetti diretti dei rimedi omeopatici sulla crescita delle cellule cancerose indica che tali effetti sono nulli o scarsi

(una pubblicazione su Sabal e una su Ruta).

Ciò suggerisce che gli effetti “in vivo” descritti sugli animali siano dovuti ad altri livelli di azione sul corpo.





Le prove sperimentali del “Simile”

Bellavite P. et al., (1997) *Medical Hypotheses* 49: 203-212.

Bellavite P. and Signorini A. (2002) *The Emerging Science of Homeopathy*. North Atlantic,
Berkeley
Bellavite P. (2005) *Il Medico Omeopata* IX (27): 41-56

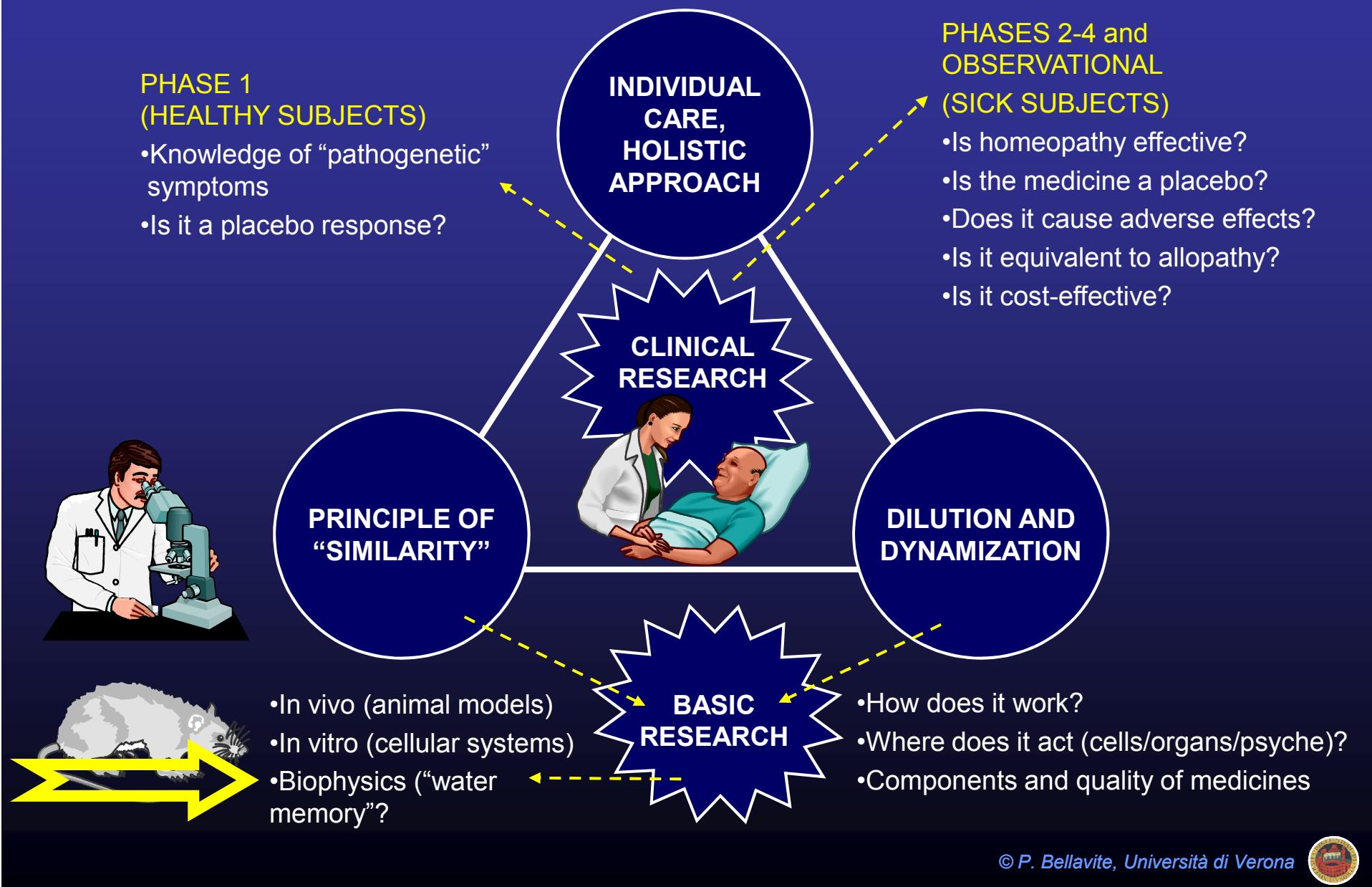
Bellavite et al.(2007) eCAM Journal doi: 10.1093/ecam/nel117

- **EFFETTI INVERSI SECONDO LA DOSE** (“ormesi”, reg. di Arndt-Schultz): sostanze o stimoli di varia natura possono causare effetti opposti al variare della dose
- **RUOLO DEL VALORE INIZIALE** (reg. di Wilder): l’effetto di un certo trattamento dipende dallo stato fisiologico del sistema ricevente, se a riposo o già stressato, se sano o malato, se in presenza di altri fattori concomitanti
- **EFFETTI PARADOSSALI DEI FARMACI** (“paradoxical pharmacology”, “rebound”): spesso i farmaci provocano effetto opposti nei trattamenti acuti e cronici
- **VIA DI INTRODUZIONE**: effetti diversi e persino opposti secondo la via di somministrazione, es. orale vs. parenterale (modelli immunologici)
- **METODO DI PREPARAZIONE**: l’effetto dipende dalla preparazione che determina la natura fisico-chimica del segnale, la sua biodisponibilità e l’interazione col bersaglio

<http://ecam.oxfordjournals.org>



Scientific investigation of the main homeopathic principles



EXAMPLES OF HIGH-DILUTION EXPERIMENTS



System	Agent	Dilution	Effect	Ref.
Human basophils	IgE	10^{-60}	Stimulation (not confirmed by others)	Davenas 1988
Human basophils	Histamine	10^{-24} → 10^{-32} (16CH)	Inhibition	Belon 1999-2006 et al (including Verona Group)
Cicken embryo	Bursin	15 CH 10^{-27} g	Immunomodulatory and endocrine activity	Youbicier-Simo 1993-97
Human neutrophils	Magnesium phos Phosphorus	12 x to 30 x	Inhibition of free radicals production	Chirumbolo 1993
Rat Hypothalamus	Sodium chloride	10^{-60}	Reduces firing rate in rats under high-salt diet	Sukul 1991-98
Mice nervous system	Nux vomica	30 CH	Reduction of alcohol-induced sleep time	Sukul 1999
Rat duodenum	Atropa belladonna	60 CH 200 CH	Increases Ach-induced spasm	Cristea 1991-98
Mouse blood	Acetylsalicylic acid	10^{-30}	Pro-thrombotic	Doutremepuich 1998
Mouse ears	Silica	10^{-60}	Speeds up wound healing	Oberbaum 1998
Wheat germination	Arsenic Silver nitrate	10^{-45} 26 D	Protect from toxicity Enhances growth	Betti 1997/2001 Pongratz 1998
Neurons	Cycloheximide	10^{-27}	Increases viability	Marotta 2002
Saccharomyces	Aroxystrobin Phosphorus	9-30 CH	Affect growth kinetics	Scherr 2006





Omeopatia e cancro – SOMMARIO

1. Mancanza di evidenze di efficacia nel modificare la storia naturale del tumore
2. Alcune evidenze di efficacia come terapia palliativa soprattutto nei sintomi da radio-chemioterapia
3. Discrete evidenze nelle infezioni ricorrenti delle prime vie aeree e nella cefalea (a prescindere dalla malattia di base)
4. Alcune evidenze di efficacia in modelli animali
5. Scarse evidenze di un effetto diretto sulle cellule cancerose
6. Buone evidenze che, in generale, l'omeopatia “NON è solo un placebo”
7. Perciò è necessario incentivare le ricerche!!!





Grazie per l'attenzione!!!

Vielen Danken für ihre Beachtung!!!