Ricottini L.



SUMMARY

Homeopathy, one of the inspiring backgrounds of Physiological Regulating Medicine, is founded on the "principle of similarity" and bases its treatment strategies on the use of correctly diluted and potentised substances according to the indications of the Homeopathic Pharmacopoeia.

However, the concept of dilution seems to contradict the conventional pharmaceutical principles. Nevertheless basic research and clinical studies have proved the scientific validity of homeopathy. The combination of those new homeopathic achievements, together with the realization of the importance of the delicate homeostatic mechanisms present in the human body has brought to the model of the Physiological Regulating Medicine. In particular, the therapeutic use of cytokines, hormones and neuropeptides, diluted and potentised according to fundamental homeopathic principles, offers new highly effective treatment options.

With our approach, we can offer, as well as an innovative treatment system, even more importantly, a key to reading the complexities of biological phenomena.

KEY WORDS

SIMILARITY CRITERION, DILUTION, POTENTISATION, HOMEOPATHISED HOR-MONES-CYTOKINES -NEUROPEPTIDES, COMPLEX BIOLOGICAL SYSTEMS, PHYSIOLOGICAL REGULATING MEDICINE

HOMEOPATHY,

FROM HOMEOPATHY TO PHYSIOLOGICAL REGULATING MEDICINE: HIGHLIGHTS

Even if Homeopathy may seem to be some kind of *folklore*, the Italian Research Group took inspiration from some of the principles of Classic Homeopathy, later updated by Dr. H.-H. Reckeweg (1905-1985) in his synthesis on Homotoxicology, to develop a new treatment strategy known as **Physiological Regulating Medicine** (PRM).

The Group's work started 10 years ago and was also inspired by the latest Immunology and Neuroendocrinology discoveries (PNEI).

In fact the work was founded principally on the intuition of the saxon Dr. C. F. S. Hahnemann, the founder of Homeopathy. But, as sometimes happens, the children outstripped the father, and so PRM, based on homeopathic ideas, is actually a completely different thing. It is a physiological regulating method based on scientific evidence and therefore a long way from the visions, sometimes based on "faith" of some classic homeopaths.

However, it seems important and certainly useful for understanding this new method that we analyze the foundations of the homeopathic thought on which is part of its basis.

Speaking of Homeopathy today, that is, the branch of medicine which treats "like with like" (in ancient Greek, the word *omeòs* means "like"), there seems to be a kind of resonance with commonly used treatment methods. We immediately think about anti-viral or anti-allergy vaccines.

However, the use of vaccines is based on the "principle of identity", in other words the cure is prepared using substances or materials which are the same as those which can cause the illness (aequalia aequalibus), thus establishing a direct relationship between the pathogenic agent and the therapeutic agent. In Homeopathy, this principle of identity gives way to the principle called the "criterion of similarity". But it is the second principle on which Homeopathy is based which, for many, is anomalous in the practice of medicine: the use, for therapeutic treatment purposes, of potentised and diluted substances - so diluted that often there is no trace of them any more in the final product. Inevitably, the use of such medicines, which may not even contain one molecule of the original substance, forces the modern doctor to look at his ideas on Pharmacology and to confront a conceptual challenge: to identify a possible mechanism of action in a homeopathic medicine, taking into account the clinical results and treatment successes documented in a growing number of protocol studies (Milani, 2002; Milani, 2008a).

In this respect, the effort made by the Italian PRM Group is notable.

After long, careful analysis of the existing vast homeopathic/ homotoxicological literature, the *Advisory Committee* selected the publications which conform to the criteria and scientific methods currently adopted (Homeopathy: the scientific proofs of efficacy. Guna Ed., Milano, 2002, 1st edition). In the light of what has been published it seems inevitable that we should be open to alternative hypotheses which also touch on physical phenomena since the effect of a homeopathic product cannot reasonably be correlated with mechanisms of a purely chemical type.

In recent years, well-known researchers and experts in the field of the exact sciences have come out in support of the idea that homeopathic medicine may be effective, providing valuable conceptual tools for the clinician.

In fact, it has been possible to establish correlations with the new discoveries about the chemical-physical properties of water (Del Giudice and Preparata, 1998; Elia and Niccoli, 1999), the applications of functional type electrodynamic diagnostics (Bellavite and Signorini, 1996) and finally the use of substances, for treatment purposes, obtained according to the principle of similarity and strongly diluted (Bellavite and Signorini, 1995).

These correlations seem to validate the effectiveness of homeopathic medicine and methods.

Let us analyze, so that we can re-read in a "modern" light, the two cardinal points of Homeopathy, which emerged from experimental studies carried out by the german Dr. C. F. Samuel Hahnemann (1796):

- the principle of similarity
- the use of dilution.

The treatment of like with like is an ancient principle existing in the history of medicine right from its beginnings. However, in homeopathic medicine, the principle of similarity becomes the theoretical nucleus of the entire treatment concept. Initially derived from empirical evidence, the principle of similarity is now based on some experimental evidence (Pennec and Aubin, 1984; Lazzarato et al., 2007) and, although some of its aspects have still to be investigated, the principle of similarity seems to be a possible key to reading the complexity of biological phenomena (Bellavite, 1998).

Let's start with the traditional concept, expressed in Hahnemann's own words (Organon of Medicine) so that we can understand better the idea of homeopathic similarity:

"One imitates nature which sometimes heals one chronic disturbance by adding another and uses for the illness that remedy which is able to provoke another artificial illness as similar as possible to the one which it wants to cure and which it is able to cure: similia similibus" (Hahnemann, 1842). "Choosing a remedy for a specific natural illness which is able to produce a very similar artificial illness, we can cure the more obstinate illness" (ibid.). "Every single case of illness is much more surely, radically, rapidly and definitively conquered and cured when the medicine (which treats it) can produce in a healthy organism in the most complete and similar way the totality of its symptoms, which at the same time are stronger than the illness" (ibid.).

To sum up, we can condense the classic formula of homeopathic similarity into three points:

- Every biologically active substance, whether it is a medicine or a toxin, a mineral or a plant extract, or even a bacterial product, produces some specific characteristic symptoms in the body of a person who takes it (*proving*) (Kent, 1991);

- Every sick person presents symptoms which are peculiar to the particular changes which have affected them (and it is on these symptoms that we base the diagnosis of a pathology), but also and more importantly, symptoms which are linked to the person's own individual reactivity and biological constitution and which are therefore personal symptoms;

- The recovery of a sick person may be induced or encouraged by administering a specific substance in the correct dilution (or with a high molecular dispersion of the active component). This substance can produce in a healthy person the same symptoms present in the pathology.

From an analysis of these three points, it is clear that the homeopathic *Principle* of *Similarity* is founded on a similarity of symptoms which is mainly subjective and therefore not acceptable to conventional medicine which generally tries to take account of objective data. In short, the choice of a medicine made on the basis of individual symptoms (even if they are specific) would seem to be contradictory to the guidelines dictated by modern scientific medicine, which looks for biochemical and molecular confirmation. In reality this contradiction is more apparent than real. We can in fact, regard every symptom as the clinical expression of a series of underlying physiopathological and biochemical changes. Craving, or the overwhelming yearning for sweet foods, especially in the evening, may depend on a reduction in serotonin levels. The desire for liquid, or thirst, can be

interpreted as a hypothalamic-pituitary response to liquid depletion (profuse sweating, diarrhea, blood loss etc.).

A high temperature is well known to be a response by the heat regulation centers in the hypothalamus to the release, activated by inflammation, of cytokines by specific cells.

In good medical practice, however, it is **always** the clinical symptom which determines a request for blood analyses or lab and other tests, **never** the contrary.

So if we analyze the problem from this perspective, homeopathic medical practice differs from the conventional mainly in the integration of all the information gathered from its own diagnostic procedures: the use of symptoms and signs on the basis of the procedure codified by Hahnemann could even offer different (but not conflicting) levels of comprehension of the pharmacological properties of biologically active compounds.

- Let's see why.

According to the principle of similarity, a substance capable of producing a series of disturbances in a healthy, sensitized body which manifest themselves as symptoms or as changes of a physiological type, could act on these same symptoms, or on changes which can be connected to them, when they are part of a pathological picture.

This hypothesis can be rationally acceptable if we consider that every substance, if it is capable of producing in a healthy organism symptoms similar to those produced by an illness, would in some way "touch" those same (or similar) homeodynamic regulating systems which are activated (and even altered) when the illness starts.

On the basis of the *Principle of the Inversion of Effects*, scientifically called **hormesis** (in Milani, 2008b), one would expect that the homeodynamic system altered by the illness would respond to the same substance in the opposite way (always in relation to the state of sensitization and responsiveness of the system and according to the doses used), encouraging the healing process in this way (Calabrese, 2001; Calabrese, 2005).

It is worth briefly mentioning this principle, which rules biological response.

Arndt and Shultz, when working on yeasts, observed that various types of toxic substances (iodine, bromide, mercuric chloride, arsenic acid, etc.) had a stimulating effect on metabolism if administered at low doses and, on the contrary, an inhibitory effect if administered at high doses.

This observation led to the formulation of the Principle of the Inversion of Effects which can be applied to all biological systems including that of humans. Weak stimuli provoke biological activity, strong stimuli suppress it.

In other words, the effect of a certain substance changes diametrically according to whether it is used in heavy or infinitesimal doses.

On this subject, before turning to some experiments relating to the above principle, it would seem opportune to look at the question of homeopathic dilution/potentisation ("potencies") which covers a wide range of concentrations in molecular terms. The widespread opinion that homeopathic remedies are always simply "plain water" because they contain no molecules of the original substance is not correct.

In reality, some of the homeopathic medicines contain molecular quantities of the active components, even if in low to extremely low concentrations.

The techniques for preparing the different types of remedies are codified in detail by the different Pharmacopeias, the most important of which are the French and German ones. To summarize: the raw materials are prepared by extracting the active components, which is done after dissolving in hydro-alcoholic mixtures or, if the substance is insoluble, after a process of pulverization and crushing in lactose followed by dissolving in water and alcohol.

The starting solutions for all dilutions of homeopathic remedies are known as Mother Tinctures and contain the maximum concentration of the active ingredients.

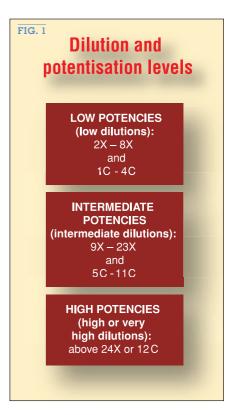
They cannot be considered homeopathic medicines.

The later dilutions, which constitute the true homeopathic remedies, are always submitted to succussion (vigorous agitation or potentisation). According to some authors, it is the succussion itself which causes the physical phenomena which give the homeopathic solution its particular properties (Elia et al., 2005). These researchers base their hypothesis on laboratory experiments conducted on water using tried and trusted technical methods. These experiments have shown that new chemical-physical properties arise in the water when it is used as a solvent in a homeopathic dilution (Elia and Niccoli, 1999) and subsequently vigorously agitated.

The new properties of the "homeopathic" water can be explained by hypothesizing the presence of dissipatory structures in it, which have formed spontaneously. Inside a dissipatory system, that is, one which can give out all of its internally produced energy (Prigogine, 1980), there is a network of "coherent dominions" or areas in which all the molecules move in set phases, setting in motion a chemical interaction channel which is much faster than the diffuse channels in which the molecules meet through chance movements (Del Giudice and Preparata, 1998).

Inside the water constituting the living matter, dominions of coherence can be observed and biological water possesses the property called coherence.

The experiments referred to allow us to hypothesize that the potentised water too possesses the same properties of coherence, suggesting a possible link between chemical and electromagnetic phenomena. But let's go back to the preparation of homeopathic medicine (French Pharmacopeia 10th edition; HAB 2000).



Homeopathic dilutions can be prepared in different strengths: Decimal scales (X) when one part of the concentrated tincture is diluted with 9 parts of solvent; hundredths scales (C) when one part of the concentrated solution is diluted with 99 parts of solvent.

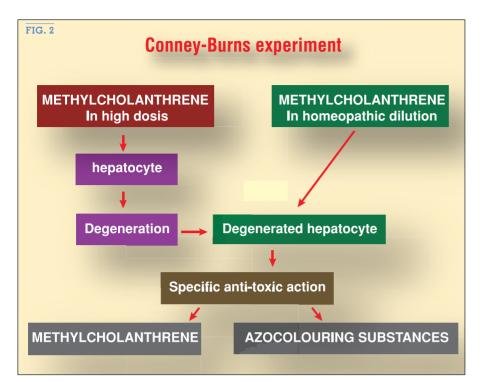
There are also other dilution scales whose preparation is particularly complex.

Homeopathic potencies can be identified according to the following dilution bands (see **FIG.** 1):

- Low potencies: prepared using the decimal scale between 2X and 8X or, on the hundredths scale, between 1C and 4C. It is calculated that this low level of dilution has molecular concentrations of potentially active agents between 10^{-5} e 10^{-12} (Linde *et al.*, 1997) depending also on the concentration of the original extract.

- Medium potencies (medium dilutions): prepared on the decimal scale between 9X and 23X or, on the hundredths scale between 5C and 11C. They are highly diluted preparations, but in theory, contain at least some molecules.

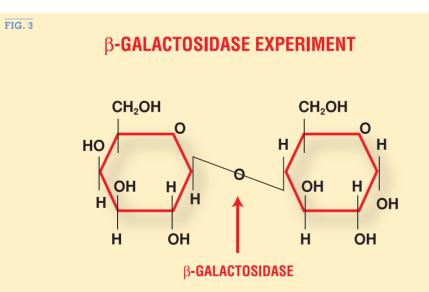
- High potencies (high or very high dilu-



tions): prepared on the decimal scale at over 24X or over 12C on the hundredths scale. They are preparations in which the dilution exceeds the Avogadro number and they do not contain any molecules of the original preparation.

As one of the main topics of argument in homeopathic theory is about the possibility that pharmacological properties may exist in the absence of molecules, the subject of high homeopathic dilutions is connected to the subjects of water biophysics and electromagnetism of which we have already spoken (Del Giudice *et al.*, 2007; Elia and Napoli, 2007). We could hypothesize that a highly diluted medicine (containing little or none of the original solution) possesses high information content capable, in the particular conditions where the system is sensitised, of forming a kind of orientation towards therapeutic reorganization (Bellavite, 1998).

This view of a medicine as a "catalyst"



The reaction speed increases as the reaction substrate is diluted (galactosyl-glycerol).

Induction: starting from 1:10.000, that is the homeopathic dilution 4X. INDUCTION: 10-20 MOLECULES = 22X-23X.

for reorganization means that we can look at the illness itself in a new way.

It would be (at least in the initial stages) like a disturbance in a series of electromagnetic communications between molecules making up tissues, nerve centers and organs. These, in the final analysis, are biological structures made up of elements oscillating at coherent and specific frequencies and therefore capable of resonance. Up to now the working hypotheses of researchers in the different branches of scientific knowledge (chemistry, physics, biology) have been based on looking for an explanation for the growing number of observed "facts".

These facts are the good clinical results obtained by doctors who are expert in Homeopathy, even though not always in randomized studies.

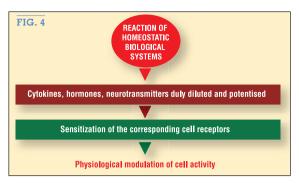
These facts are also all the laboratory experiments carried out to validate the hypothesis of a possible biological effect of homeopathic preparations. One among many is the experiment of Conney and Burns (Conney and Burns, 1963) (FIG. 2). The two English scientists carried out particularly interesting experiments on rats. The laboratory animals were given intraperitoneal injections of massive doses of *methylcholanthrene*, an azulene dye with strong hepatocarcinogenic properties (similar experiments can be conducted using CCl4).

The rats rapidly developed degenerative pathology of the liver. At a second stage the same animals were given decreasing doses of *methylcholanthrene* until they reached a homeopathic concentration of 3X-4X ($10^{-3}-10^{-4}$).

At this point the degeneration was seen to regress.

The hypothesis, based on the Arndt-Shultz law of inverse effect, is that the infinitesimal doses of methylcholanthrene could have stimulated the synthesis of a specific anti-toxin enzyme (N-dimethylamino-oxidase) in the hepatocytes capable of neutralizing the *methylcholanthrene* molecules.

The scientists observed also that the antitoxin-specific enzymes were not only active against the *methylcholanthrene* which had induced them but also towards all the azodyes, that is, towards the "poisons" similar to *methylcholanthrene* capable of inducing degenerative damage to the hepatocytes (criterion of similarity).



Another significant experiment is that on *beta-galactosidase* (Wallenfels and Weil, 1972) (**FIG. 3**).

Beta-galactosidase is a hydrolytic enzyme which is a catalyst for hydrolysis of terminal residues of β - D - galactose in well-known polysaccharides like β -galactosidase, through breaking the β -glycosidase terminal links.

Beta-galactosidase plays a further important role in the story of molecular biology in that the *E. coli* bacteria gene which codifies for this enzyme, called LacZ, was the first example studied in detail of the regulation of genetic expression of which it constitutes a classic model (Kuby and Lardy, 1953). In fact this gene is part of a body of genes regulated in a coordinated way (*operone lac*), whose expression depends on the presence or absence of lactose and on other sources of energy involved in growth.

Beta-galactosidase synthesis is therefore induced by the substratum of the reaction, i.e. the lactose.

It is known that lactose is a dimer formed by one molecule of galactose and one of glucose joined together by a β -glycoside link.

The lactose dimer as such, cannot be used by the organism.

The β -galactosidase is indispensable for hydrolyzing the β -glycoside link and liberating the glucose and galactose so that the organism can make use of the valuable glucose.

Wallenfels and Weil's experiment showed that if galactose-glycerin (a molecule quite similar to lactose although formed of galactose and glycerin instead of glucose) and not lactose itself was used in the experimental system (*E. coli* culture), a strange phenomenon was noted: the speed of the reaction increases because of greater induction of the β *galactosidase* (Principle of Similarity) and it increases more when the galactoseglycerin is diluted more (Principle of Inverse Effect). An enzyme induction effect is seen starting from a concentration of 1:10.000, that is... the homeopathic 4X dilution. It is surprising to note that the same induction effects are observed in concentration Ms of 10-20 molecules of galactose-glycerin for every incu-

bating *E. coli* cell, that is dilutions of about 22X-23X.

- In the light of the above, it was possible to develop a therapeutic system founded on the use of substances with a biological action, such as cytokines, hormones and neurotransmitters in a homeopathic form.

We know that these substances, which are produced in our body, can be considered the indispensable "phonemes" for structuring intercellular language, that is, they are capable of transmitting information between groups of cells belonging to different tissues working in synergy. Cytokines, hormones and neurotransmitters, correctly diluted and potentised, become active, probably through a mechanism of sensitization, on the corresponding cellular receptors, not with steric type properties, but rather using an "information" system.

The result of the action of these medicines is a physiological modulation of the cell's activity, when this is inhibited or disturbed by endogenous or exogenous stressors which are too aggressive, and restoration of the capacities for cellular self-regulation which are indispensable for maintaining homeostasis.

- In conclusion, it is possible to consider Homeopathy as the basis of a real Physiological Regulating Medicine, in that a purely biological therapeutic system is founded on the homeopathic principles of similarity and dilution/potentisation.

This therapeutic system supports and assists the self-regulation typical of living matter, acting on the modulation of the delicate mechanisms which control the neuro- endocrino-immunology network (FIG. 4).

References

- Bellavite P., Signorini A. Homeopathy: a Frontier in Medical Science. Experimental Studies and Theoretical Foundations. North Atlantic Books, Berkeley; 1995.
- Bellavite P., Signorini A. Biologische Wirkungen electromagnetischer Fielden. In: Homöopathie und Bioresonanztherapie. Physiologische und Physikalische Voraussetzungen Grundlagenforschung (P.C. Endler und J.Schulte, Hrsg.). Medizinverlag Maudrich, Wien; 1996. 65-76.
- Bellavite P. Biodinamica: basi fisiopatologiche e tracce di metodo per una Medicina Integrata. Tecniche Nuove, Milano; 1998.
- Calabrese E.J. The future of hormesis: where do we go from here? Crit.Rev. Toxicol; 2001. Jul.31 (4-5): 637-48.
- Calabrese E.J. Toxicological awakenings: the rebirth of hormesis as a central pillar of toxicology. Toxicol. Appl. Pharmacol; 2005. 204 (1): 1-8 review.
- Conney A.H., Burns J.J.-In Advanc. Enzyme Regul., Vol. 1, Oxford: Pergamon Press, 1963.
- Del Giudice E., Preparata G. A new QED picture of water: understanding a few fascinating phenomena. Sassaroli et Al. Editors, Macroscopic Quantum Coherence, World Scientific; 1998. 49-64.
 Del Giudice E. et Al. - II ruolo dell'acqua nella ma-
- teria vivente. La Med. Biol., **2007**/4; 37-39.
- Elia V., Niccoli M. Thermodynamics of Extremely Diluted Aqueous Solutions. Annals of the New York Academy of Sciences; 1999. 879,241.
- Elia V., Niccoli M. New physico-chemical properties of extremely diluted aqueous solutions. Journal of Thermal Analysis and Calorimetry; 2004. 75: 815-836.
- Elia V., Marchese M., Montanino M. et Al. Hydrohysteric phenomena of "extremely diluted solutions" induced by mechanical treatments. A calorimetric and conductometric study at 25° C. Journal of Solution Chemistry; 2005. 34(8): 947-960.
- Elia V., Napoli, E. Strutture dissipative nelle soluzioni estremamente diluite della medicina omeopatica. La Med. Biol., 2007/4; 13-22.
- Hahnemann C.F.S. Essay on a new principle for ascertaining the curative power of drugs, and some examinations of the previous principles. Hufeland's Journal; **1796**. 2: 391-439.
- Hahnemann C.F.S. Organon of medicine. Edited from the 5th and 6th edition (1842) by Joseph Reves. Homeopress Ltd, Haifa; 1994.
- Kent J.T. Lezioni di filosofia omeopatica. Red, Como; 1991.
- Kuby S.A., Lardy H.A. Purification and kinetics of β-galactosidase from Escherichia Coli, strain K-12. J.Am. Chem. Soc. 75 (1953) 890-6.
- Lazzarato L. et Al. Modelli vegetali per la ricerca di base in omeopatia. La Med. Biol., 2007/2; 15-17.
- Linde et Al. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. Lancet, **1997**; 350:834-843.
- Milani L. (Advisory Committee Coordinator) Homeopathy; the scientific proofs of efficacy. Guna Ed., Milano; 2002.
- Milani L. (Coordinatore dell'International Advisory Committee) - Omeopatia-Omotossicologia. Gli studi scientifici che ne provano l'efficacia. Guna Ed., Milano; 2008; 4º edition (a).
- Milani L. Da un dogma infranto al futuro delle scienze bio-mediche *low dose*. L'ormesi e il principio omeopatico di similitudine. La Med. Biol., 2008/2; 21-31 (b).
- Pennec J. P., Aubin M. Effect of Aconitum and Veratrum on the isolated perfused heart of the common eel. Comp. Biochem. Physiol., 1984,776:367o
- Prigogine I. From being to becoming. Time and Complexity in the Physical Sciences. Freeman Ed., San Francisco; 1980.
- 24. Wellenfels K., Weil R. Enzyme, 1972, 7, 617.

Author's address

Dr. Lucilla Ricottini, MD - Specilist in Paediatrics Via Eutropio, 33 I - 00136 Roma