Similitude and Rebound Effect of Drugs

Scientific Evidence and Therapeutic Application

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In Ancient Greece, *Hippocrates* classically taught that there were two approaches to the treatment of disease, namely the principle of contraries and the principle of similars. Treatment according to the principle of contraries employs drugs that act contrary to or by palliating ("anti-") the symptoms of the disease (e.g., anti-inflammatories, antacids, antidepressants, etc.). This is the main approach to treatment applied by conventional medicine, also known as "allopathy". Treatment according to the principle of similars is used by homeopathy, and it employs medicines that cause symptoms similars ("homeo") to the symptoms of the disease (e.g., coffee causes insomnia, and is homeopathically used to treat insomnia; chamomile causes colic, and is homeopathically used to treat colic; belladonna causes fever, and is homeopathically used to treat fever, etc.).

Upon founding homeopathy in 1796, *Samuel Hahnemann* grounded this homeopathic therapeutic principle on the careful observation of the drugs used in his time on the human body, and postulated a universal "mechanism of action of drugs":

"Every agent that acts upon the vitality, every medicine, deranges more or less the vital force, and causes a certain alteration in the health of the individual for a longer or a shorter period. This is termed **primary action**. […]. To its action our vital force endeavours to oppose its own energy. This resistant action is a property, is indeed an automatic action of our life-preserving power, which goes by the name of **secondary action** or **counteraction**".

(Organon of Medicine, paragraph 63)

To illustrate this *natural phenomenon,* Hahnemann listed the *primary actions of the medicines* employed in his time that promoted alterations in the different systems of the human body, and the following *secondary action of the organism (vital reaction or conservation force).* The latter acts by neutralising the primary disorders caused by drugs, in an attempt to maintain the balance of the internal milieu or homeostasis:

"[…] Excessive vivacity follows the use of strong coffee (primary action), but sluggishness and drowsiness remain for a long time afterwards (reaction, secondary action), if this be not always again removed for a short time by imbibing fresh supplies of coffee (palliative). After the profound stupefied sleep caused by opium (primary action), the following night will be all the more sleepless (reaction, secondary action). After the constipation produced by opium (primary action), diarrhoea ensues (secondary action); and after purgation with medicines that irritate the bowels, constipation of several days' duration ensues (secondary action). And in like manner it always happens, after the primary action of a medicine that produces in large doses a great change in the health of a healthy person, that its exact opposite, when, as has been observed, there is actually such a thing, is produced in the secondary action by our vital force".

(Organon of Medicine, paragraph 65)

Based on this postulate or "natural law", **homeopathy makes use of the secondary action of the organism as a therapeutic reaction,** and prescribes to ill individuals medicines that cause symptoms similar to the disorders they themselves cause (principle of therapeutic similitude), thus stimulating the organism to react against its own disease.

Although little was divulged by modern pharmacology, since it opposes conventional treatment, this same **secondary action** or **homeostatic reaction of the organism** has been observed with the use of several types of modern palliative (antipathic or enantiopathic) drugs as a **rebound effect** or **paradoxical reaction of the organism**. We have been systematically studying for the last fifteen years the rebound effect of modern drugs, and thus we were able to confirm by means of scientific evidence both Hahnemann's postulate (a drug *primary action* is followed by the *secondary and opposite reaction* of the organism) and the homeopathic principle of healing [1 – 11].

To illustrate: drugs classically used in the treatment of *angina pectoris* (*β*-blockers, calcium channel blockers, nitrates, etc.) with beneficial effects in their primary effect (anti-angina), might awaken a paradoxical increase of the frequency and intensity of chest pain after discontinuation or irregular use of doses, which sometimes does not respond to any therapeutic means.

SUMMARY

Samuel Hahnemann **systematised the homeopathic model and the effects of drugs on the state of human health, describing a primary action of the drugs followed by a secondary and opposite action of the organism. In modern pharmacology, this secondary action is known as the rebound effect or paradoxical reaction of the organism, being described after the discontinuation of several classes of palliative (enantiopathic) drugs, i.e., those that act according to the principle of contrary *(contraria contrariis curentur)*. Besides being able to cause severe and fatal iatrogenic events when appearing after the palliative use of modern drugs, the rebound effect might awaken a healing reaction if the very same drugs involved were employed according to the principle of similitude *(similia similibus curentur)*.**

KEYWORDS Homeopathy, Pharmacology, Adverse effect, Secondary effect, Rebound effect, Paradoxical reaction, Law of similarity

Drugs used for the control of *arterial hypertension* (α-2 agonists, β-blockers, ACE inhibitors, MAO inhibitors, nitrates, sodium nitroprusside, hydralazine, etc.) might produce rebound arterial hypertension as a paradoxical reaction of the organism to the primary stimulus; *antiarrhythmic* drugs (adenosine, amiodarone, β-blockers, calcium channel blockers, disopyramide, flecainide, lidocaine, mexiletine, moricizine, procainamide, quinidine, digital, etc.) may awaken rebound exacerbation of basal ventricular arrhythmias when treatment is interrupted. *Anticoagulant* drugs (argatroban, bezafibrate, heparin, salicylates, warfarin, clopidogrel, etc.), employed due to their primary effect in the prophylaxis of thrombosis, can promote thrombotic complications as paradoxical reaction of the organism. Drugs that have a vasculoprotector (pleiotropic) primary effect (statins, for example) can wake up stroke paradoxically.

In the use of psychiatric drugs such as *anxiolytics* (barbiturates, benzodiazepines, carbamates, etc.), *sedative-hypnotics* (barbiturates, benzodiazepines, morphine, promethazine, zopiclone, etc.), *stimulants of the central nervous system* (amphetamines, caffeine, cocaine, mazindol, methylfenidate, etc.), antidepressants (tricyclic, MAO inhibitors, serotonin reuptake inhibitors, etc.) or antipsychotic (clozapine, phenothiazines, haloperidol, pimozide, etc.), a paradoxical reaction of the organism may be observed in the attempt of keeping organic homeostasis, thus promoting the appearance of symptoms contrary to the ones expected from their primary therapeutic use, and consequently worsening the initial clinical picture.

Drugs with *anti-inflammatory* primary action (corticoids, ibuprofen, indomethacin, paracetamol, salicylates, etc.) might trigger paradoxical reactions of the organism that increase inflammation together with its mediator's serum concentration. Drugs with *analgesic* primary action (caffeine, calcium channels blockers, clonidine, ergotamine, methysergide, opiates, salicylates, etc.) may exhibit significant hyperalgesia as a rebound effect. *Diuretics* (furosemide, torasemide, triamterene, etc.), enantiopathically used to diminish the volume of plasma (oedema, arterial hypertension, congestive heart failure, etc.), may cause rebound retention of sodium and potassium, thus increasing the basal volume of plasma. Drugs primarily used as *anti-dyspeptic* (antacids, H_2 antagonists, misoprostol, sucralfate, proton pump inhibitors, etc.) in the treatment of gastritis and gastroduodenal ulcers might promote, after the primary decrease of acidity, a rebound increase of the production of hydrochloric acid by the stomach, eventually causing perforation of chronic gastroduodenal ulcers. *Bronchodilators* (adrenergic drugs, sodium chromoglycate, epinephrine, ipratropium, nedocromil, salmeterol, formoterol, etc.) used in the treatment of bronchial asthma may worsen bronchial constriction as a paradoxical response of the organism to the interruption or discontinuation of treatment. Drugs indicated for the treatment of osteoporosis (bisphosphonates, denosumab, odanacatib, among others) can cause paradoxical atypical fractures after the biological effect (half-life) as a result of an increased rebound of the osteoclastic activity. Immunomodulatory drugs (natalizumab, fingolimod, among others), used in the treatment of multiple sclerosis, can cause paradoxical worsening of the disease when treatment is interrupted. And others [1–11].

Although a **rebound effect** or **paradoxical reaction of the organism** usually occurs in a small number of individuals as a function of idiosyncrasy, its effects can be dramatic (both in intensity and duration), thus strengthening the rationale for their use in homeopathy.

Admitting that the main premise of homeopathic treatment is the **use of medicines that cause symptoms similar to the disease to be treated**, it may apply to any kind of medicine, either natural or synthetic, in ponderable or infinitesimal doses provided that the principle of similitude is observed. Consequently, "allopathic" drugs may also be employed according to the principle of therapeutic similarity *when their primary action (therapeutic, adverse and side) effects are similar to the symptoms of the patient*. By acting in this manner, we make profit of the rebound effect of modern drugs for the sake of healing.

To illustrate this possible "off-label" use of countless classes of modern drugs according to the homeopathic principle, tens of drugs causing blood pressure to increase as a primary effect (adalimumab, cyclosporine, dopamine, anti-inflammatory agents, etc.) might be homeopathically used to treat arterial hypertension, **since the drug's other pathogenetic effects show similarity with the patient's individuality.** Drugs increasing blood sugar (amprenavir, corticotropin, diazoxide, œstrogens, etc.) might be homeopathically employed to treat hyperglycaemia/diabetes. Drugs that cause immunosuppression (cyclosporine, corticoids, immunosuppressants, etc.) might be used to stimulate the immune system in immunosuppressed patients. Drugs causing attention/concentration disorders (amantadine, interferons, topiramate, etc.) might be used to improve attention disorder in children, and so forth.

Grounded in Hahnemann's premise, since 2003 we systematically propose to employ modern drugs according to the homeopathic healing principle [12–16]. To allow for actual application of this proposal, a **"Homeopathic Materia Medica of Modern Drugs"** was compiled including all the primary (therapeutic, adverse and side) effects of 1250 "allopathic" drugs as described in *The United States Pharmacopeia Dispensing Information* (*USP DI,* 2004), following the chapter structure of the traditional works on homeopathic materia medica.

To facilitate the **selection of an individualised homeopathic medicine** (**similar to the totality of symptoms of the patient**), which is the essential requirement for safety and therapeutic success of homeopathic treatment, the next step was to elaborate a **"Homeopathic Repertory of Modern Drugs"**, where symptoms and their corresponding medicines are displayed analogously to classic homeopathic repertories.

Due to the high pathogenetic power of modern drugs it is expected that infinitesimal doses will be sufficient to trigger the healing vital reaction of the organism. For this reason, it is suggested to start treatment with potency 6C and adjust the potencies and the repetition of doses to the individual pattern of susceptibility of each patient. In this way it will be possible to evaluate the therapeutic results of these medicines in intermediate concentrations and to relate them to the pathogenetic effects of the substantial doses while avoiding aggravation and intense adverse events [14–16].

Entitled **"New Homeopathic Medicines: Use of Modern Drugs According to the Principle of Similitude"**, this project comprises three parts: (1) **"Scientific Basis of the Principle of Similitude in Modern Pharmacology";** (2) **"Homeopathic Materia Medica of Modern Drugs"**; and (3) **"Homeopathic Repertory of Modern Drugs"**.

To facilitate global access to this project, all three works extending along thousands of pages are available at a bilingual (English

and Portuguese) website. Access is simple and free, registration of e-mail address, name and occupation are the only data required to obtain a password. In this way, the clinical protocol might be analysed and used by homeopaths worldwide: www.newhomeopathicmedicines.com

For this method to be included in homeopathic standard practice, **homeopaths need to unite around this project: physicians** to apply it in clinical practice and describe results (case reports), **pharmacists** to prepare the corresponding homeopathic medicines, and **investigators** to design research protocols.

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Vita

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