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ORIGINAL PAPER

New homeopathic medicines: use of modern drugs according to the principle of similitude

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Background: **The homeopathic method is based on the application of the principle of therapeutic similitude (similia similibus curentur), using medicines that cause effects similar to the symptoms of disease in order to stimulate the reaction of the organism against disturbances. Such vital, homeostatic or paradoxical reaction of the organism can be scientifically explained on the basis of the rebound effect of modern drugs.**
Aims: **This article presents the conclusion of a study aiming at a method to use modern drugs with homeopathic criteria.**
Methods: **Adverse effects as catalogued in United States Pharmacopoeia Dispensing Information Drug monographs were collected.**
Results: **A homeopathic materia medica and repertory comprising 1251 modern drugs to be employed according to the principle of therapeutic similitude was developed.**
Conclusion: **Besides supplying a basis for homeopathy as a medical rationale related to scientific pharmacology, this study makes available a method that may broaden the scope of intervention of homeopathy in present day diseases.** *Homeopathy* (2011) **100**, 244–252.

Keywords: Homeopathy; Similitude; New homeopathic medicines; Secondary effect; Rebound effect; Paradoxical reaction; Withdrawal syndrome

Introduction

While questioning the efficacy of the palliative or enantiopathic method of treatment (Organon of Medicine,[1] paragraphs 23, 52–62, 69), Samuel Hahnemann advocated the homeopathic method of treatment as the most effective manner to employ medicines, by prescribing to ill individuals a remedy able to elicit an artificial morbid state similar to the totality of symptoms of the individual case of disease to be healed (Organon, paragraphs 24–27).

In studying the effects of the medical drugs common in his time,[2] he observed a secondary action (indirect effect or reaction) of the organism following the primary action (direct effect). Hahnemann enunciated a principle to explain the effects of any medicine on the state of health of human beings:

> "*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 endeavors 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, paragraph 63)

He exemplified this phenomenon with the description of the primary action of several medicines that, by causing alterations in the physiology provoke a secondary action of the organism (vital reaction or conservation force), manifesting as effects opposite to the initial ones, tending to neutralizing the primary alterations elicited by the drugs and restore the organism to the state of equilibrium previous to the pharmacological intervention (Organon, paragraphs 59, 65).

Emphasizing that the secondary reaction of the organism (opposite to the primary action of drugs) appears 'in every

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case without any exception' after the use of either 'excessively large' or infinitesimal doses by individuals both healthy and ill, Hahnemann raised the principle of similitude to the level of a 'natural law' (Organon, paragraphs 58, 61, 110−112).

By prescribing to ill individuals remedies provoke similar symptoms appear (similia similibus curentur), the principle of therapeutic similitude seeks to stimulate a healing homeostatic reaction that leads the organism to react against its own disturbances. The terms secondary action, vital reaction and homeostatic reaction denote the same phenomenon: the tendency or ability of living beings to maintain the constancy of the internal environment through automatic self-adjustments of physiological processes.

In the terms of scientific rationality and modern pharmacology, Hahnemann's primary action corresponds to the therapeutic, adverse and side effects of conventional drugs, whereas the secondary action (vital reaction) corresponds to the rebound effect of modern drugs (paradoxical reaction of the organism) appearing after the discontinuation or alteration of dosage (withdrawal syndrome) of all classes of drugs that act contrarily to the symptoms of diseases.[3−9]

As evidenced by clinical and experimental pharmacology,[8,9] the properties of the paradoxical reaction (rebound effect) of the organism are the same as those of the vital reaction (secondary action) described by Hahnemann (Organon, paragraphs 59, 64, 69): (1) it appears only in susceptible individuals, who present in their constitution symptoms similar to the pathogenetic effects of the drug; (2) it does not depend on the drug, repetition of doses or type of symptoms (disease); (3) it appears after the primary action of the drug (discontinuation), as an automatic manifestation of the organism; (4) it induces an organic state (symptoms) opposite and greater in intensity and/or duration than the primary action of the drug; (5) the magnitude of its effect is proportional to the intensity of the primary action (dose) of the drug.

Analogous to the traditional secondary action of homeopathic medicines,[3−9] the rebound effect of modern drugs can be used for therapeutic purposes,[10,11] to stimulate homeostatic healing reactions provided they are prescribed according to the principle of similitude of symptoms.

This article reports a research project aimed at developing a method to use modern drugs according to the principle of therapeutic similitude.[10,11] The first part discusses the possibility of assimilating the adverse events of conventional drugs to pathogenetic effects or new symptoms of these drugs when used in substantial doses on ill individuals. The second part describes the development of a homeopathic materia medica and repertory based on the adverse events (primary effects) of modern drugs, illustrating and systematizing their therapeutic application in present day diseases.

Homeopathic pathogenetic experimentation

In order to learn the healing properties of the medicines to be prescribed according to the principle of therapeutic similitude, homeopathy employs pathogenetic experimentation, also known as homeopathic pathogenetic trials (HPTs), as its model of clinical pharmacological research (similar to the modern 'phase I studies' of modern pharmacological clinical research). HPTs take into account all kinds of primary actions or pathogenetic manifestations (mental, general and local symptoms) elicited by drugs on the state of health of human beings, which are known in modern pharmacology as therapeutic, adverse or side effects of drugs.

Hahnemann stipulated strict conditions for pathogenetic trials (Organon, paragraphs 105−145). Nevertheless, the actual homeopathic materia medica is a compilation of the signs and symptoms observed after the experimentation of thousands of substances on both healthy and ill individuals with substantial (substances in crude state) or infinitesimal (potentised medicines) doses, resulting in artificial morbid states that allow for the application of the homeopathic method of treatment.

Ideally, Hahnemann indicated that pathogenetic trials ought to be carried out with 'moderate doses' of drugs on 'healthy individuals' to avoid confounding the true effects of drugs and the symptoms of disease (Organon, paragraphs 106−109). Nevertheless, he himself tested medicines in substantial doses and/or on ill individuals as it can be seen in Fragmenta de viribus medicamentorum positivis, Materia Medica Pura and Chronic Diseases.

Regarding experimentation on the sick, Hahnemann considered valid the pathogenetic manifestations arising from a 'simple medicine employed for a curative purpose', provided one can select "*the symptoms which, during the whole course of the disease, might have been observed only a long time previously, or never before, consequently new ones, belonging to the medicine*" (Organon, paragraph 142).

Although in the same place Hahnemann highlights the difficulty of distinguishing between the effects of a remedy and the symptoms of disease ["*(it) is a subject appertaining to the higher art of judgment, and must be left exclusively to masters in observation*"], according to the strict protocols of modern clinical research of new drugs (phases I−IV studies) and the resulting classification of the adverse events observed, the predictability, frequency and causality of such effects are sufficient grounds to assimilate them to 'new symptoms' of tested drugs as follows.

To substantiate the validity of pathogenetic trials with substantial doses and/or on ill individuals, Hahnemann observed that the effects of experiments described by previous authors carried out with 'large doses of medicinal substances' on healthy (poisonings) and ill (therapeutic overdoses) individuals were similar to his observations while testing the very same substances on himself and other healthy individuals (Organon, paragraphs 110−112).

Analogous to the classification of the frequency of adverse events of modern drugs, Hahnemann writes that "*some symptoms are produced by the medicines more frequently − that is to say, in many individuals, others more rarely or in few persons, some only in very few healthy bodies*" (Organon, paragraph 116). Thus, "*all the symptoms peculiar to a medicine do not appear in one person, nor*

all at once, nor in the same experiment", and for this reason it is needed 'numerous observations on suitable persons' in order to find out the full picture of the medicinal disease (Organon, paragraphs 134−136).

According to their power to cause alterations in the state of health of human beings (pathogenicity), Hahnemann classified drugs in 'strong' (heroic), 'moderate' and 'weak', and recommended to employ them in doses inversely proportional to their pathogenetic power (Organon, paragraph 121).

Regarding the pharmacotechnical preparation of the tested drugs, Hahnemann noticed that substances in 'crude state' (substantial doses) "*do not exhibit nearly the full amount of the powers that lie hidden in them, which they do when they are taken for the same object in high dilutions potentized by proper trituration and succussion*". For this reason, he suggested to carry out pathogenetic trials with daily doses of 4−6 globules of the 30th centesimal potency and to increase progressively the number of globules according to individual susceptibility (Organon, paragraphs 128−129). Furthermore, after the initial intake of a 'sufficiently strong dose', the experimental subject can perceive "*the order of succession of the symptoms*" and "*the duration of the action of a drug*" (Organon, paragraph 130), whereas with the use of increasing and successive doses, he or she can learn "*the various morbid states that this medicine is capable of producing in a general manner, but he cannot ascertain their order of succession or duration of the action*" (Organon, paragraphs 131, 132).

Pathogenetic trials with substantial doses on healthy or ill individuals

Ideally HPTs ought to be carried out on healthy individuals, but the homeopathic materia medica includes many signs and symptoms derived from the use of medicines in substantial doses and/or on ill individuals. Analogously, homeopathic treatment has also used substantial doses on the grounds of the pathogenetic manifestations observed after the intake of substantial doses by healthy (poisonings) and ill (therapeutic overdoses) individuals.

In order to have a clearer notion of these singular features of homeopathic practice, the following summary of the historical reviews by Dudgeon[12] and Hughes[13] might be useful.

In the early years of homeopathy, Hahnemann applied the principle of therapeutic similitude with drugs in substantial doses on the grounds of the pathogenetic symptoms awakened by such substances on healthy and ill individuals. This allowed him to heal a series of chronic, acute and epidemic diseases, as described in Essay on a new curative principle,[2] published in 1796. By keeping the same procedure, he was also able to heal a large number of patients suffering from continual and remittent fevers.[14]

In 1799, during an epidemic of scarlet fever,[15] Hahnemann used for the first time diluted and agitated doses in order to decrease the pathogenetic power of doses and thus avoid aggravation.[16] In 1814, during the treatment of typhus or hospital fever,[17] Hahnemann outlined the method of potentiation (serial dilutions with strong agitation). The *theory of potentisation* strictly speaking only appeared in 1827,[18] when Hahnemann incorporated the processes of trituration and succussion in order to develop and exalt the 'dynamic medicinal powers of natural substances'.

In 1805, Hahnemann stipulated the conditions for pathogenetic trials with minimal doses and on healthy individuals in The medicine of experience,[19] as the outcome of his previous testing of medicines on himself, friends and relatives. The same year he published the pathogenetic studies of 27 remedies in a book entitled Fragmenta de viribus medicamentorum positivis, sive in sano corpore humano observatis,[20] which thus represents the first homeopathic materia medica that Hahnemann used in his clinical practice. The sources of the pathogenetic symptoms listed were his own observations (of poisonings, therapeutic overdoses, self-experimentation and tests on other healthy individuals) as well as the ones 'by others' and reported in the literature. Although he gave no information about the doses and mode of administration of the drugs, it is believed that he began with single strong doses (in solution), to repeat them whenever he thought it was needed, after the end of the action of the previous dose, thus complying with the premises he had stated earlier.[19]

Six years later, in 1811, Hahnemann published the first volume of Reine Arzneimittellehre (Materia Medica Pura),[21,22] which included 6 new and 6 older (already published in Fragmenta) pathogenetic studies, with significant additions of symptoms. In 1816, the second volume was published containing the pathogenetic effects of 8 remedies and 3 trials with magnet; in 1817, the third volume, with 8 remedies; in 1818, the fourth volume, with 12 remedies; in 1819, the fifth volume, with 11 remedies; and finally in 1812, the sixth volume, with 10 remedies. Therefore, the complete work comprised 61 medicines (besides magnet), 39 of which were new, while the remaining 22 were extended studies of medicines already published in Fragmenta. For this project, Hahnemann had the assistance of 37 experimental subjects/disciples (3 of whom manifested symptoms of their own diseases in all the remedies they tested), with very few data on the doses and mode of administration of the drugs.[13]

Between 1822 and 1827, Hahnemann published the second and extended edition of Materia Medica Pura, also in 6 volumes comprising the same pathogenetic studies as the first edition and 3 new ones that were included in the last volume. According to Hughes' analysis,[13] there is a significant increase in the number of symptoms listed in the first volume, arising from trials on healthy individuals (whereas the first edition only listed 'observations by others'). Moreover, repeat provings are more frequent for the drugs described in the first 4 volumes, since beginning 1821, after the move to Köthen and having Hahnemann reached his eighth decade of life, he was physically distant from the experimental subjects/disciples and also too old to continue his self-experiments. In this context, it is worth to remind that 'observations by others' (namely, reports of poisonings in healthy individuals and therapeutic overdoses in the ill)

represent a large fraction of most pathogenetic studies in Materia Medica Pura; as a fact, only 13 remedies lack such data.[13]

While still in Köthen, Hahnemann published between 1828 and 1830 the 4 volumes of the first edition of Chronic Diseases,[23] which introduced 17 new and 5 extended pathogenetic studies of remedies already published in Materia Medica Pura. With the only exception of *Kalium carbonicum* and *Natrum muriaticum* − which were tested in potentised doses (30cH) and in (2 and 3, respectively) healthy individuals − the remainder of medicines were tested in diversified potencies (e.g. 'small portions of a grain'; 2nd and 3rd trituration; 6th and 30th potency) and on individuals suffering from chronic diseases.[13]

The second edition of Chronic Diseases, published between 1830 and 1835, added 25 pathogenetic studies (13 new and 12 already published in Materia Medica Pura and extended) to the 22 listed in the first edition. In both editions, the pathogenetic manifestations listed are adverse and side effects of drugs prescribed to patients suffering from chronic diseases, as Hughes stated:

> "*[…] Hahnemann's own additions to the second issue of his work must be of the same character as his contributions to the first, i.e., they must be collateral effects of the drugs observed on the patients to whom he gave them*".[13]

Just as there are countless pathogenetic manifestations derived from the testing of drugs in substantial doses and/or on ill individuals in the works on materia medica written by Hahnemann, later authors (Jahr, Allen, etc.) also published new studies or additions to previous pathogenetic trials following the same procedure.[12,13]

Material and methods

In developing a homeopathic materia medica and repertory based on the adverse events of modern drugs, The United States Pharmacopeia Dispensing Information (2004) was used with databases, grouping all pathogenetic effects or primary actions (intended therapeutic, and unintended adverse and side effects) in accordance to the traditional structure (chapters) of the homeopathic materia medica and repertory. A score was given to the frequency of incidence of the pathogenetic effects of modern drugs, represented in the text by different styles of fonts, and were distributed along 'rubrics', 'sub-rubrics', etc. in the homeopathic repertory. All the modern drugs were represented in the homeopathic repertory using abbreviations.

Adverse events as pathogenetic manifestations of modern drugs

Adverse events or reactions to drugs are defined by the World Health Organization (WHO) as "*a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function*".[24] According to the Guideline of Good Clinical Practice,[25] any research involving human beings must comply with definite scientific and ethical rulings,[26] in order to ensure the safety, protection and well-being of the participants. Surveillance, classification and notification of adverse effects, thus, are a mandatory requirement in protocols of research of new drugs.[27]

During the study of a new drug (phases I−IV studies),[28] besides the expected therapeutic effect, also adverse effects appear (adverse/side effects), which can be classified according to criteria such as predictability, frequency, intensity, causality and severity.[29] For the purposes of the present study, namely to assimilate the adverse/side effects of modern drugs to pathogenetic effects (new symptoms) of such drugs on the state of health of human beings, the criteria that make evident this relationship are predictability, frequency and causality (Table 1).

'Predictable' adverse effects are those that are already described in the literature (in the product's description, in the investigator's manual, or in the study protocol); conversely, the 'unpredictable' ones have not yet been reported.[29] In the present study, I used the adverse effects described in drug monographs (The United States Pharmacopeia Dispensing Information, USP DI),[30] therefore all are predictable and are likely to reappear in future trials.

In turn, 'predictable' adverse effect are further classified according to their frequency or incidence of expression by the Council for International Organizations of Medical Sciences (CIOMS)[31] as: (1) 'very common': frequency ≥10.0%; (2) 'common': ≥1.0−10.0%; (3) 'not common': ≥0.1−1.0%; (4) 'rare': ≥0.01−0.1%; and (5) 'very rare': <0.01%.

The drug monographs used in the present study (USP DI)[30] classify the adverse/side effects of drugs according to their frequency in 3 groups, which are closely related to CIOMS categories: (1) 'more frequent': ≥4.0%; (2) 'less frequent': ≥1.0−4.0%; and (3) 'rare': <1.0%. Both CIOMS and USP DI classifications can be correlated (Table 2).

It is worth remembering here that before any new drug can be approved and marketed it must undergo phase I−III studies, where adverse events are observed in thousands of individuals. Phase IV studies refer to the surveillance and pharmaco vigilance of a drug after it entered the market, which widens the scope of observation to tens of thousands of individuals and also on the long run. The results are incorporated then into the drug monographs, which are periodically updated (USP DI).

Table 1 Classification of adverse events

Adverse events		
Predictability	*Frequency*	*Causality*
Predictable	Very rare (<0.01%)	Defined
Already reported in other studies	Rare (≥0.01% and <0.1%)	Probable
	Not common (≥0.1% and <1%)	Possible
Unpredictable	Common (≥1% and <10%)	Unlikely or unrelated
Unknown (uncertainty)	Very common (≥10%)	
	Not quantified (chance)	

Table 2 Frequency of adverse events – comparison between classifications

Frequency of adverse events	
Classification in *USP DI*[30]	Classification in *CIOMS*[31]
Incidence more frequent (≥4%)	Very common (≥10%) Common (≥1% and <10%)
Incidence less frequent (≥1% and <4%)	Common (≥1% and <10%)
Incidence rare (<1%)	Not common (≥0.1% and <1%) Rare (≥0.01% and <0.1%) Very rare (<0.01%)

In this way, the adverse events used in the present study as pathogenetic manifestations of drugs (new symptoms) were observed in the lowest frequencies (about 1.0%) in hundreds of individuals, a fact that strengthens the validity of the present proposal.

Regarding the aspect of causality, according to the WHO,[29,32] an adverse event is related to a drug according to the following categories: 'defined', 'probable', 'possible', 'improbable', 'conditional' and 'unclassifiable', depending on the degree of certainty of the corresponding interaction. By definition, adverse events whose causality is rated as 'defined' or 'probable' exhibit temporal sequence (i.e., there is a temporal connection between the administration of the drug and the appearance of the adverse event); typical reaction; they disappear when the drug is discontinued; and cannot be explained out of the underlying disease or other therapeutic means.

The causal link between a drug and an adverse event (risk evaluation) is retrospectively established as of cause-effect. 'Predictable' and 'quantified' (i.e., determined frequency) have 'probable causality'.[29] For this reason, the adverse/side effects used in the present study (USP DI) have evident causal relation to the corresponding drugs (predicted risk) and thus "*are new symptoms that belong to the drug*" (Organon, paragraph 142).

Use of modern drugs according to therapeutic similitude

Following the pattern of traditional homeopathy, this study proposes to employ modern drugs according to the principle of therapeutic similitude, stimulating the healing rebound effect (vital reaction) of the organism through the administration of substances (in substantial or infinitesimal doses) that caused similar symptoms in healthy human.

To operationalise this proposal a Homeopathic Materia Medica of Modern Drugs (HMMMD) was elaborated, where the therapeutic, adverse and side effects of drugs (USP DI) were grouped following the structure of the traditional homeopathic materia medica, while giving particular value to the frequency of the symptoms observed during the phases of study of the drugs.

In order to facilitate the selection of the individualized remedy (i.e., similar to the totality of symptoms of the patient), and thus the clinical application of the present proposal, at a later stage it was also elaborated a Homeopathic Repertory of Modern Drugs (HRMD), where symptoms and medicines are arranged as in the traditional homeopathic repertories.

Homeopathic Materia Medica of Modern Drugs

In principle, to elaborate a HMMMD, any pharmacological compendium containing the results of the clinical studies of conventional drugs (drug monographs) can be used as a source, provided it is reliable and does not exhibit conflict of interest with the pharmaceutical industry. Following these requirements, for the present study it was initially chosen USP DI, 2004,[30] although at a later stage it might be complemented with other reference works.[33–36]

The first stage of analysis of the drug monographs focused on the following items: (1) name of the drug; (2) commercial name; (3) category (drug classes); (4) conventional indications; and (5) adverse/side effects (more frequent, less frequent and rare; overdose).

Then, the resulting data were systematized according to the traditional structure of the homeopathic materia medica. The pathogenetic symptoms or primary effects (i.e., therapeutic, adverse and side effects) of each drug were distributed among the following chapters: Mind; Vertigo; Head; Eye; Vision; Ear; Hearing; Nose; Face; Mouth; Teeth; Throat; External Throat; Stomach; Abdomen; Rectum; Stool; Bladder; Kidneys; Prostate Gland; Urethra; Urine; Genitalia Male; Genitalia Female; Larynx and Trachea; Language, Conversation and Voice; Respiration; Cough; Expectoration; Chest; Back; Extremities; Nails; Sleep; Dreams; Chill; Fever; Perspiration; Skin; Generalities. A new chapter was added to these traditional ones, comprising the alterations caused in diagnostic tests ('Diagnostic Tests').

Also keeping in with the homeopathic tradition, as well as complying with the classification of adverse events mentioned above, a score was given to the frequency of incidence of the pathogenetic effects of drugs (therapeutic, adverse and side effects), represented in the HMMMD by different styles of fonts. In this regard, it must be mentioned that the therapeutic effects of drugs (conventional indications) received the highest scores since they are virtually observed in all patients (Table 3).

When arranging the pathogenetic effects in the HMMMD, syndromes (i.e., modern clinical diagnoses) were kept as such, but their component symptoms were separated and included in the corresponding chapter of the HRMD. The first version of HMMMD comprises 1251 modern drugs, whose symptoms were systematized according to the homeopathic model allowing for their

Table 3 Description of symptoms (adverse events) in the text

Description of symptoms in the text		
Frequency of incidence	*Score*	*Font style*
Very common (therapeutic effects)	5 Points	***Bold italic***
More frequent (≥4%)[30]	4 Points	**Bold**
Less frequent (≥1% and <4%)[30]	3 Points	*Italic underline*
Rare (<1%)[30]	2 Points	*Italic*
Overdose	1 Point	Normal

Table 4 Example of systematization of symptoms (adverse events) in *HMMMD*

Dihydroergotamine *(Antimigraine agent)*	
Chapters	*Primary actions or pathogenetic symptoms*
Mind	*Anxiety*; *confusion*; *depression*; *euphoria* (unusual feeling of well being); *nervousness*; delirium
Vertigo	**Dizziness**
Eye	*Conjunctivitis* (red or irritated eyes); *pain*; *watering, increased*
Vision	*Blurred vision*
Hearing	*Tinnitus* (ringing or buzzing in the ears)
Nose	**Irritation in the nose** (burning or tingling sensation, dryness, soreness or pain in the nose; runny and/or stuffy nose; unexplained nosebleeds); **sinusitis** (runny or stuffy nose; headache)
Face	*Edema* (swelling of face)
Mouth	**Dryness**; **taste perversion** (change in sense of taste); *salivation, increased* (increased watering of the mouth)
Throat	**Pharyngitis** (sore throat); *dysphagia* (difficulty swallowing)
Stomach	**Nausea**; **vomiting**; *anorexia* (decreased appetite); *dyspepsia* (heartburn); *pain*
Rectum	**Diarrhea**
Respiration	*Bronchitis* (congestion in chest; cough; difficult and/or painful breathing); *dyspnea* (shortness of breath); *infection, upper respiratory tract* (cough, fever, sneezing, or sore throat); depression, respiratory (shortness of breath)
Chest	*Angina pectoris*; *arrythmias* (irregular heartbeat); *bronchitis* (congestion in chest; cough; difficult and/or painful breathing); *infarction or ischemia, myocardial* (feeling of heaviness in chest; pain in back, chest, or left arm; shortness of breath or troubled breathing); *palpitations* (pounding heartbeat); *vasospasm, coronary, induced* (chest pain)
Extremities	**Stiffness, muscle**; *edema* (swelling of fingers, feet or lower legs); *ischemia, peripheral* (itching of skin; numbness and tingling of face, fingers, or toes; pain in arms legs, or lower back, especially pain in calves and/or heels upon exertion; pale, bluish-colored, or cold hands or feet; weak or absent pulses in legs); *tremors* (trembling or shaking of hands or feet); *weakness, muscle*; numbness in the legs or arms; pain in the legs or arms; tingling in the legs or arms
Sleep	**Somnolence** (sleepiness); *insomnia* (trouble in sleeping); *yawning, increased*
Fever	*Fever*
Perspiration	**Sweating, increased**
Skin	*Cold, clammy skin*; *petechia* (pinpoint red spots on skin); *pruritus* (itching of the skin); *skin rash*
Generalities	**Asthenia** (unusual tiredness or weakness); **fatigue** (unusual feeling of tiredness); **hot flashes** (sudden sweatings and feelings of warmth); **paresthesia** (sensation of burning, warmth, heat, numbness, tightness, or tingling); **sinusitis** (runny or stuffy nose; headache); **stiffness, muscle**; *arrythmias* (irregular heartbeat); *infection, upper respiratory tract* (cough, fever, sneezing, or sore throat); *hypotension* (dizziness or lightheadedness when getting up from a lying or sitting position; sudden fainting); *palpitations* (pounding heartbeat); *tremors* (trembling or shaking of hands or feet); *weakness, muscle*; convulsions; hypertension (dizziness; headaches, severe or continuing; increase in blood pressure).

Table 5 Example of description of symptoms in *HRMD* (Chapter Mind)

Schizophrenia (See Psychotic reactions; Confusion of mind, identity)

- Catatonic-like state or reaction, catatonia (decreased awareness or responsiveness; mimicry of speech or movements; mutism; negativism; peculiar postures or movements, mannerisms or grimacing; severe sleepiness): *AnthisP-syst.*, *BetBA-syst.*, *BetBAT-syst.*, *Valp-syst.*, *Ven-syst.*
- Depersonalization: Aman-syst., **Amph-syst.**, *Andro-syst.*, *Atorv-syst.*, *Carbam-syst.*, *Cital-syst.*, *ConjE-syst.*, *Dipy-syst.*, *Efav-syst.*, *Eton-vag.*, *Fent-trsyst.*, *Fent-trsyst.*, *Flum-syst.*, *Fluorq-syst.*, *Leve-syst.*, **MedE-syst.**, *Mir-syst.*, *Nef-syst.*, *Riba-syst.*, **Sir-syst.**, *Testos-syst.*, *Tiz-syst.*, *TramA-syst.*, **Valp-syst.**, *Ven-syst.*, *Zale-syst.*, *Zic-syst.*, *Zop-syst.*
  - ☐ Feeling of unreality; sense of detachment from self or body: *Clar-syst.*, *Fluorq-syst.*, *Paro-syst.*
  - ☐ Feelings of: *AntinfN-syst.*, *Bupre-syst.*, *Opi-syst.*
  - ☐ Loss of sense of reality: *Benzod-syst.*, *Efav-syst.*, *Gadov-syst.*
- Derealization (alteration in the perception or experience of the external world) (See Confusion of mind, depersonalization; Derealization): *Nef-syst.*

  Personality changes/disorder: *AppSupS-syst.*, BronA-syst. [Ephedrine]
  - ☐ In pediatric patients:

    3–12 Years of age: **Gab-syst.**

    With juvenile rheumatoid arthritis: *Etan-syst.*
- Schizophrenic-type thought disorder: *BronA-syst. [Epinephrine]*
- Schizophrenic or schizophreniform, behavior (agitation; delusions; hallucinations): *Zon-syst.*

Aman-syst.: Amantadine (Systemic); Amph-syst.: Amphetamines (Systemic); Andro-syst.: Androgens (Systemic); AnthisP-syst.: Antihistamines, Phenothiazine-derivative (Systemic); AntinfN-syst.: Anti-inflammatory Drugs, Nonsteroidal (Systemic); AppSupS-syst.: Appetite Suppressants, Sympathomimetic (Systemic); Atorv-syst.: Atorvastatin (Systemic); Benzod-syst.: Benzodiazepines (Systemic); BetBA-syst.: Beta-adrenergic Blocking Agents (Systemic); BronA-syst. [Ephedrine]: Bronchodilators, Adrenergic (Systemic) [Ephedrine]; Bupre-syst.: Buprenorphine (Systemic); Carbam-syst.: Carbamazepine (Systemic); Cital-syst.: Citalopram (Systemic); Clar-syst.: Clarithromycin (Systemic); ConjE-syst.: Conjugated Estrogens and Medroxyprogesterone For Ovarian Hormone Therapy (OHT) (Systemic); Dipy-syst.: Dipyridamole (Systemic); Efav-syst.: Efavirenz (Systemic); Etan-syst.: Etanercept (Systemic); Eton-vag.: Etonogestrel and Ethinyl Estradiol (Vaginal); Fent-trsyst.: Fentanyl (Transdermal-Systemic); Flum-syst.: Flumazenil (Systemic); Fluorq-syst.: Fluoroquinolones (Systemic); Gab-syst.: Gabapentin (Systemic); Gadov-syst.: Gadoversetamide (Systemic); Leve-syst.: Levetiracetam (Systemic); MedE-syst.: Medroxyprogesterone and Estradiol (Systemic); Mir-syst.: Mirtazapine (Systemic); Nef-syst.: Nefazodone (Systemic); Opi-syst.: Opioid (Narcotic) Analgesics (Systemic); Paro-syst.: Paroxetine (Systemic); Riba-syst.: Ribavirin (Systemic); Sir-syst.: Sirolimus (Systemic); Testos-syst.: Testosterone (Systemic); Tiz-syst.: Tizanidine (Systemic); TramA-syst.: Tramadol and Acetaminophen (Systemic); Valp-syst.: Valproic Acid (Systemic); Ven-syst.: Venlafaxine (Systemic); Zale-syst.: Zaleplon (Systemic); Zic-syst.: Ziconotide (Systemic); Zop-syst.: Zopiclone (Systemic).

Table 6 Examples of application of therapeutic similitude with modern drugs

Chapters	*Application of therapeutic similitude (main rubrics)*
Mind	Agitation, amnesia, anxiety, coma, delirium, delusions, dementia, depression, disorientation, forgetfulness, hyperactivity, irritability, lethargy, mania, nervousness, panic, schizophrenia, suicidal disposition, etc.
Vertigo	Dizziness, faintness, gait disorders, lightheadedness, orthostatic hypotension, syncope, unsteadiness, vertigo, etc.
Head	Aneurysm, cerebral (arteritis; edema; hemorrhage), encephalitis, headache, intracranial hypertension, meningitis, migraine, seborrhea, stroke, etc.
Eye	Astigmatism, atrophy, bleeding, cataract, chemosis, cornea disorders, dryness, glaucoma, inflammations, keratopathy, necrosis, neuritis, nystagmus, papilledema, paralysis, pupils disorders, retina disorders, etc.
Vision	Amblyopia, blindness, blurred, decreased, diplopia, hypermetropia, myopia, presbyopia, scotoma, etc.
Hearing	Buzzing, deafness, hyperacusis, hypoacusis, ringing, tinnitus, etc.
Nose	Congestion, coryza, dryness, epistaxis, rhinitis, sinusitis, sneezing, etc.
Face	Gestures, heat flushes, hirsutism, neuritis, paralysis, swelling, trismus, etc.
Mouth	Bleeding, discoloration, dryness, gengivitis, glossitis, mucositis, sialorrhea, speech disorders, stomatitis, taste disorders, ulcers, etc.
Throat	Angioedema, dryness, dysphagia, esophagitis, pharyngitis, ulcers, etc.
External throat	Goitre, heat flushes, hyperthyroidism, hypothyroidism, lymphadenopathy, parotiditis, parotitis, torticollis, etc.
Stomach	Anorexia, cramps, dyspepsia, eructations, gastritis, gastroenteritis, hemorrhage, hiccough, nausea, polydipsia, reflux, ulcers, vomiting, etc.
Abdomen	Ascites, appendicitis, cholelithiasis, cholestasis, cirrhosis, colitis, gastroenteritis, hemorrhage, hepatic (insufficiency; necrosis; steatosis), hepatitis, hepatomegaly, paralyticus ileus, inflammatory bowel disease, intestinal (obstruction; perforation), malabsorption syndrome, pancreatitis, peritonitis, splenomegaly, tumors, etc.
Rectum	Constipation, diarrhea, hemorrhage, hemorrhoids, mucositis, tenesmus, etc.
Bladder	Hemorrhage, infection urinary tract, urinary disorders, etc.
Kidneys	Calculi, edema, inflammation (interstitial; glomerulonephritis; pyelonephritis), renal insufficiency, tubular disorders, urinary disorders, etc.
Urine	Acetonuria, albuminuria, colors, glycosuria, hematuria, oliguria, polyuria, proteinuria, pyuria, sediment, etc.
Genitalia male	Atrophy testes, desire sexual disorders, edema, function sexual disorders (ejaculation; erection; fertility; orgasm), inflammation, etc.
Genitalia female	Abortion, cancer, contraception, desire sexual disorders, function sexual disorders, hemorrhage, hormonal dysfunctions, inflammation, lactation disorders, menses disorders, ovaries disorders, uterus disorders, tumors, etc.
Larynx and Trachea	Inflammation, laryngismus, edema (glottis, larynxs), etc.
Respiration	Accelerated, arrested, asthma, breathing, bronchitis, difficult, distress, dyspnea, insufficiency, impeded, infection, irregular, slow, sounds, wheezing, etc.
Chest	Acute myocardial infarction, angina pectoris, arrhythmias (atrial fibrillation, heart block, ventricular tachycardia), heart failure, effusion (pericardial, pleural), inflammation (alveolitis, endocarditis, pneumonitis, pericarditis, pleuritis), pulmonary (edema, embolism, fibrosis), etc.
Extremities	Arthrosis, ataxia, edema, exostosis, fractures, gout, incoordination, inflammation (arthritis, myositis, neuritis, flebitis, tendinitis), myopathy, neuropathy, osteoporosis, paralysis, stiffness, weakness, etc.
Generalities	Adult respiratory distress syndrome, anaphylaxis, anemia, anesthesia, convulsions, demyelinating disorders, diabetes, edema, encephalopathy, fatigue, hypertension, hyperthermia, hypotension, hypothermia, influenza, lymphadenopathy, neuropathy, Stevens–Johnson syndrome, thromboembolism, weight (gain, loss), etc.

therapeutic application as prescribed by the principle of similitude. An example is given in Table 4.

Homeopathic Repertory of Modern Drugs

The pathogenetic symptoms described in the HMMMD were systematized following the traditional pattern of the homeopathic repertories. Thus, all drugs that awakened a same symptom were grouped together and mentioned by its corresponding 'abbreviation'. The code of fonts used to write the abbreviated name of each remedy corresponds to the score and code used in the HMMMD (Table 3).

As it was mentioned above, in the case of the HRMD the symptoms composing syndromes (clinical diagnoses) were separated and listed in the corresponding chapter in order to facilitate a more accurate individualization of each case.

The HRMD also keeps the traditional hierarchical structure of the homeopathic repertories regarding the description of symptoms and their modalities. This is to say, the pathogenetic manifestations were distributed along 'rubrics', 'sub-rubrics', etc. Also seeking to facilitate the search of the most accurate symptom, all chapters include 'cross-references' between similar pathogenetic manifestations. Table 5 presents an example of the model here proposed, in this case of 'schizophrenia', listed in chapter 'Mind' of HRMD.

Discussion

Following the Aristotelian deductive logic on which Hahnemann based homeopathic treatment, I have worked for the last 12 years to ground the principle of therapeutic similitude on the rebound effect of modern drugs through studies of clinical and experimental pharmacology. Since it exhibits properties similar to the vital reaction adduced by the homeopathic model, this paradoxical reaction (rebound effect) of the organism can be used for healing purposes provided it is administered to patients drugs that caused similar symptoms in other (healthy or ill) individuals.

Although ideally, pathogenetic trials ought to be carried out with potentised medicines on healthy individuals to avoid confounding the true pathogenetic effects of drugs and the symptoms of disease, the traditional homeopathic materia medica comprises symptoms and signs observed after testing of drugs on healthy and ill individuals with either substantial or infinitesimal doses. In this way, it

contains the picture of the artificial morbid states that allow for the application of therapeutic similitude.

The features predictability, frequency and causality of adverse events considered in clinical research on new drugs (phases I–IV studies) and described in the drug monographs show that they are true pathogenetic manifestations (new symptoms) of these drugs. This fact gives further support to their use according to the principle of therapeutic similitude.

In order to broaden the scope of application of therapeutic similitude to include thousands of new drugs, each of which has been tested in thousands of individuals following strictly designed protocols, it was elaborated a HMMMD and a HRMD on the traditional model of this genre of homeopathic literature. In the HMMMD, the symptoms of each drug were distributed in chapters representing an anatomical-functional dynamics and were scored according to their frequency of manifestation in the population of experimental subjects. The HRMD in turn groups together all the drugs that awakened a same symptom in the experimental subjects together with their corresponding scores.

Since the notification of the adverse events of modern drugs through the standard forms provided by pharmacovigilance schemes does not require a thorough description of their modalities,[37] the peculiarities of symptoms (idiosyncrasy) usual in the homeopathic traditional pathogenetic descriptions are lacking, i.e., the singular features required to individualize homeopathic remedies (Organon, paragraphs 133, 139, 140). The fact that conventional drugs are tested in their 'crude state' (non-potentised doses) also conspires to limit the full expression of 'their wealth of hidden powers'.

On the other hand, these drugs showed high pathogenetic power when administered in therapeutic doses, making their effects appear in hundreds or thousands of individuals. This fact warrants the validity of their homeopathic use in infinitesimal doses provided they are selected according to the totality of symptoms of the patient, minimizing the deficiency of idiosyncratic symptoms.

This proposal makes it possible to use other drugs to relieve clinical complaints ordinarily treated by homeopathy, as well as it opens the path for new applications of therapeutic similitude to encompass modern signs, symptoms and complex syndromes (Table 6).

Conclusion

The main goal of this study was to develop a method to use modern drugs according to the principle of therapeutic similitude. It was possible to add 1251 drugs to the homeopathic materia medica. On the other hand, by identifying the operation of the principle of similitude also in conventional experimental pharmacology, this study also broadens the evidence supporting some aspects of the medical rationality of homeopathy in the light of modern scientific research.

Due to the lack of descriptions of idiosyncratic aspects (characteristic symptoms) in most pathogenetic manifestations of modern drugs, which hinders their immediate use for the selection of an individualized remedy, it is suggested an initial clinical approach (selection of pathognomonic signs and symptoms, pathological or syndromic diagnosis, etc.) encompassing the full set of manifestations of the individual disease (totality of symptoms), despite their poor modalization, in order to choose the specific means of cure.

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 6cH (10^{-12} M) and adjust 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.

However, the validation of the method here proposed requires the collaboration of homeopathic professionals at different levels: physicians to prescribe the medicines and then report the results (clinical cases), pharmacists to prepare the potentised medicines, and researchers to design experimental protocols. If such collaborative enterprise could be accomplished, the initial project would be discussed and reviewed, extended and then translated into different languages.

Entitled "New homeopathic medicines: use of modern drugs according to the principle of similitude",[38] the initial project is divided into 3 parts: (1) Scientific Basis of the Principle of Similitude in Modern Pharmacology; (2) HMMMD; and (3) HRMD. In order to make it available to the homeopathic community with the purpose of applying and discussing it, to contribute with criticism, suggestions and revisions, it will be posted soon online in English and Portuguese at www.newhomeopathicmedicines.com.[38]

Future studies on this subject will also be posted online with the hope of contributing to the scientific grounding of homeopathy and the homeopathic treatment of modern diseases.

Conflict of interest

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References

1 Hahnemann S. *Organon of medicine* [Boericke W, Trans.]. 6th edn. New Delhi: B. Jain Publishers, 1991.
2 Hahnemann S. Essay on a new principle for ascertaining the curative power of drugs, with a few glances at those hitherto employed. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
3 Teixeira MZ. *Semelhante cura semelhante: o princípio de cura homeopático fundamentado pela racionalidade médica e científica*. [Similar cures similar: the homeopathic cure principle based by the medical and scientific rationality]. São Paulo: Editorial Petrus, 1998.
4 Teixeira MZ. Similitude in modern pharmacology. *Homeopathy* 1999; **88**(3): 112–120.

5 Teixeira MZ. Evidence of the principle of similitude in modern fatal iatrogenic events. *Homeopathy* 2006; **95**(4): 229−236.
6 Teixeira MZ. NSAIDs, myocardial infarction, rebound effect and similitude. *Homeopathy* 2007; **96**(1): 67−68.
7 Teixeira MZ. Bronchodilators, fatal asthma, rebound effect and similitude. *Homeopathy* 2007; **96**(2): 135−137.
8 Teixeira MZ. Antidepressants, suicidality and rebound effect: evidence of similitude? *Homeopathy* 2009; **98**(1): 114−121.
9 Teixeira MZ. Statins withdrawal, vascular complications, rebound effect and similitude. *Homeopathy* 2010; **99**(4): 255−262.
10 Teixeira MZ. Homeopathic use of modern medicines: utilisation of the curative rebound effect. *Med Hypotheses* 2003; **60**(2): 276−283.
11 Teixeira MZ. 'Paradoxical strategy for treating chronic diseases': a therapeutic model used in homeopathy for more than two centuries. *Homeopathy* 2005; **94**(4): 265−266.
12 Dudgeon RE. *Lectures on the theory and practice of homoeopathy.* New Delhi: B. Jain Publishers, 1982 [Reprint edition]. Lectures VII e XII.
13 Hughes R. *A manual of pharmacodynamics*. 6th edn. New Delhi: B. Jain Publishers, 1980 [Second reprint edition]. Lecture II.
14 Hahnemann S. Some kinds of continued and remittent fevers. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
15 Hahnemann S. Cure and prevention of scarlet-fever. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
16 Hahnemann S. On the power of small doses of medicine in general, and of Belladonna in particular. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
17 Hahnemann S. Treatment of the typhus or hospital fever at present prevailing. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
18 Hahnemann S. How can small doses of such very attenuated medicines as homoeopathy employs have any action on the sick? In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
19 Hahnemann S. The medicine of experience. In: Dudgeon RE (ed). *The Lesser Writings of Samuel Hahnemann*. New Delhi: B. Jain Publishers, 1995 [Reprint edition].
20 Wettemann M. Hahnemann's use of 'Fragmenta de viribus medicamentorum' in his early medical practice: analysis based on a patient file. *Med Ges Ghesch* 2001; **20**: 221−230.
21 Hahnemann S. *Reine Arzneimittellehre* [German Edition]. Ann Arbor: Scholarly Publishing Office, University of Michigan Library, 1830, p. 472.
22 Hahnemann S. *Materia Medica Pura*. New Delhi: B. Jain Publishers, 1994 [Reprint edition]. 2v.
23 Hahnemann S. *Chronic diseases* [Dudgeon RE, Trans.]. New Delhi: B. Jain Publishers, 1983. 2v.
24 World Health Organization (WHO), The Uppsala Monitoring Centre. *The importance of pharmacovigilance. Safety monitoring of medicinal products*. Available from: http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf; 2002.
25 European Medicines Agency. *Guideline for good clinical practice*. Available from: http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf; 2002. London.
26 World Health Organization (WHO), Council for International Organizations of Medical Sciences. *International ethical guidelines for biomedical research involving human subjects*. Available from: http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm; 2002. Geneva.
27 World Health Organization (WHO). *Guidelines for good clinical practice (GCP) for trials on pharmaceutical products*. Technical report series, No. 850, annex 3. Available from: WHO http://apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf; 1995.
28 United States. *Code of Federal Regulations. 21 CFR. Food and drugs. 312 Investigational new drug application*. Available from: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=312; 2003. Washington.
29 Marodin G, Goldim JR. Confusions and ambiguities in the classification of adverse events in the clinical research. *Rev Esc Enferm USP*(3): 690−696, Available from: http://www.scielo.br/pdf/reeusp/v43n3/en_a27v43n3.pdf, 2009;**43**.
30 The United States Pharmacopeial Convention. *The United States pharmacopeia dispensing information*. Easton: Mack Printing Co., 2004.
31 World Health Organization (WHO), Council for International Organizations of Medical Sciences. *Guidelines for preparing core clinical safety information on drug from CIOMS working group III*. Available from: https://apps.who.int/dsa/cat98/zcioms8.htm; 1995. Geneva.
32 World Health Organization (WHO), The Uppsala Monitoring Centre. *Safety monitoring of medicinal products. Guidelines for setting up and running a Pharmacovigilance Centre*. Available from: http://apps.who.int/medicinedocs/en/d/Jh2934e/; 2000.
33 *American Hospital Formulary Service drug information*. Bethesda: American Society of Hospital Pharmacists, 2010.
34 British Pharmacopoeia Commission. *The British pharmacopoeia*. Belfast: The Stationery Office, 2010.
35 European Pharmacopoeia Commission. *European pharmacopoeia*. 6th edn. Belfast: The Stationery Office, 2009.
36 Sweetman SC. *Martindale: the complete drug reference*. 36th edn. London: The Pharmaceutical Press, 2009.
37 United States, Food and Drug Administration. *MedWatch: the FDA safety information and adverse event reporting program*. Form FDA 3500A − mandatory reporting. Available from: http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082728.pdf; 2009. Washington.
38 Teixeira MZ. *New homeopathic medicines: use of modern drugs according to principle of similitude*. Available from: São Paulo: Marcus Zulian Teixeira www.newhomeopathicmedicines.com; 2010. 3v.