

Use of Adverse Effects of Drugs in Modern Medicine for Developing Homeopathy Materia Medica with Some Insights for Modern Medicine: A Conceptual and Application Framework

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ABSTRACT

Homeopathy is now more than two centuries old science, using various substances for cures of human and animal health problems. Homeopathy's approach is to use serially diluted /potentized doses of substances for conditions that are otherwise recorded as side effects of these modern medicinal substances used in therapeutic doses. The double-blind randomized controlled trial is not a very suitable study design for generating evidence for the efficacy of homeopathy because of the process of individualized selection of a medicine. However, Evidence-Based-Medicine, combining case reports and case series of cures, along with physicians' experiences, and patients' opinions can to some extent help validate 'homeopathic' cures. The present article, assuming homeopathy works and cures, though not knowing how it may be working, presents a database of drugs and adverse effects (AE) developed by modern pharmacology tested in worldwide population of users and over a longer time frame, with a primary argument that the AE-data can be used for developing new medicines in homeopathy, added symptomatology and more cures in homeopathy using these modern medicines, with due approach of dilution and potentization and the proving of new remedies. The secondary argument here is about rethinking the dose-response relationship in modern pharmacology on the hormetic approach. The database is open to access for all practitioners to get drug-AE and AE-drug relationships.

Keywords: Adverse effects, Dose-response, Drugs, EBM, Homeopathy, Hormesis

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INTRODUCTION

Homeopathy has been in practice for more than two centuries. It has evolved because the mainstream medicines then had large and mixed doses and several toxic effects, whereas Hahnemann tried small, single, and potentised medicinal doses for the prevalent problems with reportedly astonishing results. The homeopathic system, although questioned on many grounds, has taken root in various countries, India included.^{1,2} It has a huge base in India with some 225 colleges.³ We have a National Institute of India for Homeopathy under the ministry of AYUSH.⁴ A report says, "Today there are over 1,50,000 institutionally qualified homeopaths, and over 2.5 lakh practitioners under certain legal rights and protection given to them. In addition, there are over ten lakh or more persons patronizing it as self-medicating Homeopathy knowing persons."⁵

Homeopathy literature is copious, mainly divided into Materia Medica (describing effects of various substances on healthy humans) and Repertories (some 2000 remedies listed under symptom groups). Both these are now available online.⁶ The current Homeopathic research is largely about case reports and case series. .

The Principal Author (referred to as PA in this article) is a lifelong student and follower of homeopathy (and also a science graduate) who has been studying the Adverse-effects (AE) of modern medicines and realized that the records of these read just like the Materia Medica books of homeopathy

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listing poisoning effects of the chemicals used as medicines. This implies that a book like the CIMS can be read alternatively as Materia Medica of Homeopathy. Thus, all those Modern medicines can become homeopathic medicines in one stroke. Hence the AE data is a goldmine for homeopathy and cannot be left without due consideration of this innovative prospect, though the transition is not easy. In this article, we examine the EBM context of homeopathy and then proceed to hypothesize on using AEs for homeopathy.

The problem of Homeopathy: 'Does it work?'

Despite such a large base of Homeopathy practitioners, remedies and literature, the established scientific system of

medicine, and science itself has several serious questions to ask of homeopathy. A critical review summarises the arguments against homeopathy as follows: Homeopathy lacks a plausible explanation of how it is likely to work, and its construct of evidence is unable to face scientific scrutiny. He further says that homeopathic remedies have proven ineffective in well-controlled trials.⁸

Homeopathy has two basic concepts about how it works: (a) "Let likes be cured by likes", which means a medicine that causes side effects/secondary effects in conventional therapeutic doses can be used to cure the same effects arising as a disease or a syndrome. (This is also akin to Hormesis) (b) For this remedial use, the said medicine has to be serially diluted and potentised (though homeopathy does not insist as a precondition of infinitesimally small dose). There are various theories about how the remedies bring about the effects, but without proofs from physics or chemistry. Since the serially diluted substance is hardly detectable by known scientific methods, how it works-if at all it does-is subject to further speculation. The large body of homeopathic research consists of case reports and case series, though some trials are available. Here are some recent examples from the Indian Journal of Research in Homeopathy.

"Ichthyosis vulgaris successfully treated with individualized homeopathic medicine (Dulcamara 200C).⁹ Polycystic ovarian syndrome and homeopathic management: A case series.¹⁰ Cholelithiasis improved with Lycopodium."¹¹

Clinical trials are not the forte of homeopathy. However, there are attempts to try homeopathy for some health problems diagnosed in the modern medical system. For example, the Indian Journal of Research in Homeopathy reported some recent trials in India.

Vitiligo patches reduced in size in an open-label trial.¹² A Single arm study showed "individualized homeopathic medicines are useful in improving social interaction in the cases of childhood autism" and "Median scores of ISAA and VSMS at baseline were 132 and 39 which were improved to 35.5 and 56, respectively, at the end of the study."¹³ Homeopathic medicines improved lower urinary tract symptoms in benign prostatic hyperplasia: A multi-centric prospective observational study.¹⁴ Further, the Cochrane database lists eight reviews/Meta-analysis reports of homeopathic trials on the following conditions: Asthma, Dementia, Irritable bowel syndrome, induction of labour, attention deficit, acute respiratory tract infections in children, influenza, bleeding due to placental retention after birth, cancer treatment adverse effects.¹⁵⁻²³ All these reviews except on calendula use in dermatitis after cancer radiotherapy conclude as 'not-enough-evidence'. However, A Cochrane review of reported critiques of homeopathy concludes with the following "Contrary to our hypothesis, the critical discussion on the basic concepts of homeopathy does not seem to be very intense at the academic level. Therefore, we conclude that a scientific discussion about the basic concepts

of homeopathy has not taken place in the academic literature, contrary to the perception circulated in the mainstream public media."²⁴

Clinical trials of homeopathic remedies are of two types: (a) A single remedy is used for the given illness-symptom-complex in all selected subjects. This kind of trial is un-homeopathic because homeopathy works on individualized selection of a remedy and homeopathy does not recognise a 'disease' entity as in the modern medicine. (b) Homeopathic remedy is individualized from a shortlist of remedies, which is more in line of homeopathy. The Cochrane review lists 13 reviews of several trials each.²⁴ However, most of the reviews suggest risk of bias and the OR (odds ratio) being not robust.

Given the equivocal nature of effectiveness and efficacy of homeopathy from the point of view of modern medicine; homeopathy is still a vibrant idea considering the fact of acceptance of hormesis, the occurrence of paradoxical reaction phenomenon and the idea of vaccination and Isopathy (like cures the like principle). On this background, our AE data is a valuable database from the Homeopathic viewpoint.

In this perspective article, the main argument is that the rich and verified AE data of some 629 modern medicines can be used for further systematic development of homeopathic Materia Medica, and the 'Repertoire of homeopathy'. Further, in this study of AEs, it appeared that many symptoms are not recorded in the current literature of homeopathy. To search for this, one can go through the list of symptoms given the database. There are many 'PQRS' (Peculiar, Queer, Rare, Strange) symptoms here. The AEs of Modern Medicine include signs or the 'objective' symptoms (like for example 'wart' which is perceived by both the patient and the physician). AEs also include pathological data like raised blood urea or reduced platelet count. Both these aspects raise an important academic question for homeopathy regarding whether this data could be included in its Repertoires and added to the 'totality of symptom picture of the remedy?' In the earlier days of homeopathy symptoms like high BP and body temperature could not be measured and therefore, the data about the signs or the 'objective symptoms' do not appear in the literature of homeopathy. Now, it has become easy to add that data. On this background, the first argument of this article is that the very same medicines that show AE in modern medicine can be used by homeopathy for treating the AE-syndromes after serial dilutions and potentization. A secondary argument here is that modern medicine may find it helpful to use the established medicines in ways of Hormesis (much smaller dose) for exploring newer ways of therapeutics and hitherto unsolved problems like parkinsonism.

MATERIAL AND METHODS

The major exercise in this work was to organise AEs of the various modern medicines from literature. The PA has used various sources for pooling AE data under each given

medicine, say for instance carbamazepine used in epilepsy causes sedation, vertigo etc. Notable sources are CIMS (PA has used edition, 2010), and Pharmacology textbook.²⁵ The example of Carbimazole-an anti-thyroid medication- in the box explains how homeopathy can harness modern drugs and the AEs to homeopathic use.

Carbimazole and Homeopathy in Covid-19 Epidemic

In the epidemic of Covid-19 we had no specific medicine for the disease, except immunization at a later stage. The medical treatment for fever was the only 'symptomatic' treatment. However, Homeopathic treatment is always symptomatic in its peculiar ways. One has to find one substance, one compound which is capable of producing as many similar symptoms as possible to the set of symptoms presented by the patient. In the present case it was Covid-19. It was an ideal condition of what is called in homeopathy as 'genus epidemicus' where a large number of people are suffering from a similar 'set of symptoms' (or 'disease'). This indication for a medicine is all the stronger if the symptom is in some way peculiar, queer, rare, strange etc.

Many people afflicted with Covid-19 reported fairly consistently an altered sense of taste or loss of taste with fever. While searching for a potential homeopathic medicine for Covid-19 from our database and using filters for the symptoms 'loss of taste' and then with 'rising fever', the PA arrived at Carbimazole, an anti-thyroid drug. From the drug-AE database, the symptom picture of this drug shown as 'side effects' especially regarding fever and its development over time was remarkably close to the epidemic of Covid-19. (see table- 3)

The PA zeroed on Carbimazole and potentized (trichurition, and serial dilution) it to the 4 X level (i.e. on a decimal scale. Therefore, the homeopathic drug finally had the concentration of 1/10000 of the original quantity of the drug that is 20 mg. It is a well-known fact that Carbimazole is capable of producing agranulocytosis as a side-effect and causes both throat pain as well as loss of taste.

The PA tried using this medicine without any fees for friends who came for help in the epidemic. Seven persons reported quick relief, while no other results were available. Hence this remedy needs further systematic documentation and exploration. This process of finding the medicine is typical of homeopathy and suggests a method of using the drug-AE database.

The PA has earlier taken help of software engineers to prepare the database and app in Visual basic on drugs-wise AEs and conversely AE-causing drug agents. Using this if we select 'carbamazepine', an anti-epileptic drug, all the AEs will appear in the AEs window. Conversely if an AE selected,

Table1: Alphabetical list of Adverse Effects of Carbamazepine from our database.

AE S.No.	Adverse Effect
13	Abdominal Pain
611	Abnormalities of Liver & Kidney Function
245	Agranulocytosis
1	Anorexia
618	Aplastic Anaemia
293	Arrhythmias
267	Ataxia
343	Cholestatic Jaundice
619	CV Effects (e.g. CHF)
5	Diarrhoea
17	Dizziness
46	Drowsiness
226	Dry mouth
614	Dystonia & Dyskinesias w/ asterixis
160	Eosinophilia
613	Galactorrhoea
165	Gynaecomastia
2	Headache
19	Hepatitis
617	HLA-B* 1502 & HLA-A* 3101 Allele
224	Hyponatraemia
227	Impotence
606	Leucocytosis
615	Local Irritation w/ rectal use
158	Lymphadenopathy
612	Male Infertility
604	Mild Skin Reactions
3	Nausea
69	Oedema
72	Paraesthesia
610	Pneumonitis
607	Purpura
616	Serious Dermatologic Reactions (e.g. Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis)
609	Splenomegaly
248	Thrombocytopenia
605	Transient Leucopenia
4	Vomiting

like sedation for example, a list of drugs will appear in the next column. This will help modern medicine physicians to know more about the drugs and AEs, and homeopaths to try these potentised drugs for treating the AEs, aided with peculiar symptoms. This database of drugs and AEs compiled from standard sources of pharmacology and CIMS is made available on Google-link for open access.

Findings

Table-1 offers a drug say, Carbamazepine to AE matrix. This shows all the known and listed pharmacological AEs of the drug. Table-2 shows an AE, sedation, is caused by many possible drugs in the modern pharmacopoeia. The drug-AE package therefore gives alphabetical listing of both drugs and AEs and the prompts can be used to search in both directions.

The 640 drugs listed here in our database show some 2733 AEs that are officially reported during drug development and post market surveillance. The same database can give us a group of drugs that can elicit a given AE, like say, sedation.

Table 3 shows adverse effects of carbimazole, including loss of taste.

Table 2: Alphabetical list of Drugs that cause an SE 'Sedation' in the database.

Drug S.No.	Name Of Drug
149	Clozapine
135	Clemastine
350	Loratadine
420	Nitrazepam
114	Chlorphenamine
48	Baclofen
460	Pheniramine
480	Pregabalin
316	Ketotifen
181	Diphenhydramine
456	Pentazocine
21	Alprazolam
221	Etizolam
351	Lorazepam
111	Chlordiazepoxide
145	Clonidine
599	Trifluoperazine
242	Fluphenazine
230	Fentanyl
144	Clonazepam
429	Olanzapine
158	Cyproheptadine
172	Diazepam

Table3: Carbimazole related AE symptoms and signs.

Symptom No.	Symptom_name	Disorder_no	Disorder_name
2	Headache	83	Carbimazole
3	Nausea	83	Carbimazole
7	Fever	83	Carbimazole
11	Malaise	83	Carbimazole
62	Neutropenia	83	Carbimazole
71	Arthralgia	83	Carbimazole
164	Alopecia	83	Carbimazole
245	Agranulocytosis	83	Carbimazole
435	Mouth Ulcer	83	Carbimazole
473	Bruising	83	Carbimazole
546	Sore Throat	83	Carbimazole
618	Aplastic Anaemia	83	Carbimazole
627	Mild Leucopaenia	83	Carbimazole
628	Rarely Cholestatic Jaundice	83	Carbimazole
629	Nephrotic Syndrome	83	Carbimazole
630	Loss of Taste	83	Carbimazole
631	Hypoprothrombinaemia	83	Carbimazole
632	Hypothyroidism & Goitre	83	Carbimazole

DISCUSSION

The authors are well aware about the EBM challenges in the context of homeopathy. While case reports abound and many hits and misses go unreported, hard evidence of successes of homeopathy, and how it works, is a grey area for modern scientific methods. However, the numerous case reports and experiences of formal and informal practitioners have created a niche for homeopathy in many countries. India also has a huge base of homeopathy infrastructure, human resources, and drug manufacturing. The trust in homeopathy by committed practitioners and patients seeking cures for chronic conditions and unsolved health problems by homeopathic remedies does hold ground. This is one good reason to keep exploring the EBM aspects of homeopathy.

EBM mainly banks on double-blind randomised clinical trials, conducted rigorously, for evaluating a drug against a defined condition, say an antiviral agent for a new viral infection. Homeopathy does not satisfy both these necessary preconditions of a 'specific' remedy and a 'well-defined' health problem called diagnosis. Homeopathy is about selecting a remedy from nearly 2000+ proven remedies in the Materia Medica, based on its logic of subjective symptoms and objective clues in some defined sequence. Thus 'typhoid' means little to the homeopath, since each subject may have a different set of symptoms around the reported type of fever. Hence, the remedy also is variable. Hence, clinical trial that requires a specific substance agent for treating a specific well defined biomedical problem in some framework of

intervention and outcomes is a misfit in homeopathy. If there is a trial, against a broad condition like vitiligo for example, the trial scientist has to offer a possible list of remedies to choose from. A single remedy trial is inherently of limited value in homeopathy. Hence, rigorous epidemiological or clinical trials of homeopathic remedies are beset with rigour issues to begin with. What then is feasible is individual case reports and case series.

The emergence of Evidence-Based Medicine (EBM) combines clinical trial outcomes with individual practitioner's experiences/opinions and also integrate experience of patients. Homeopathy may find a closer ally in EBM, which combines the trio of clinical evidence, physician experience and patient opinion.²⁷ We quote from a recent article on EBM as follows. "This evidence-based approach worked well for most of the patients; however, this one-size-fits-all approach does not consider the differences between each patient. Each human is different and is a complex form of various biological systems. There may be a significant sub-group of patients who have not responded to or benefited from the said processes and are subject to a bias of statistical insignificance. A substantial number of 'human beings' may be outliers and suffer from inferior medical treatment as they may fall away from the median or mean of the bell curve. This led many researchers to question the validity of research evidence. This review is an attempt to bring to light the research question: How viable and applicable is the practice of Evidence-Based Medicine for each patient at the personal level?"²⁷ Hence for EBM in the context of homeopathy we need to work out a track B as we suggest here. In the absence of RCT evidence due to study design problems, we have to bank on (a) case reports and case series as evidence for homeopathy, while (b) physician experience and (c) patient opinions need to be recorded systematically.

Assuming homeopathic remedies work in some hitherto unknown ways, we have some ground to develop it further. The AE data of modern medicines, developed for many years and from many subjects and users can be a useful resource for developing the homeopathy Materia Medica further. In addition, there are some clues or insights for modern medicines to reflect on the dose-response issues based on homeopathic ways. This article examines these points and presents some views on how this can be done.

Thus, the present work primarily lists drug-wise AEs and AE-wise drugs. Apparently, this is now quite easy in the days of AI. Official sites such WebMD <https://www.webmd.com/drugs/2/drug-1493-5/carbamazepine-oral/carbamazepine-oral/details> can give this information on each drug.²⁷ There are also sites offering drug-lists linked to an AE like sedation (<https://www.medindia.net/drugs/side-effects/sedation.htm>).²⁸ However, the AEs to their causative drugs is a less developed area while our work gives both information in the same matrix, using different filters.

AEs in modern medicine have been classified into five categories under ABCDE. An automatic or mechanical, meaning that the use of the drug is commonly or always

accompanied by the AE due to its very pharmacologic properties, like gastric irritation by aspirin when given in anti-inflammatory dose. B is bizarre or unexpected AEs, like allergies or idiosyncrasies, the example being anaphylaxis due to penicillin. C is AEs due to chronic use like gum hypertrophy due to phenytoin. D is delayed AEs, like tardive dyskinesia due to antipsychotics. E is the end of use AEs, like worsening of Angina due to stoppage of beta blockers.²⁹ Although we have not listed the AEs in these categorical ways, developing homeopathic remedies from these drugs for these AEs needs to factor in the categorical ABCDE nature of AEs. Also, we have to bear in mind that in homeopathy, the remedies are selected by a logical general to specific symptomatic flowchart and the homeopath has to bank upon many specific features while interpreting symptoms, like the concomitant mental symptoms.

The more important point in our work is to look at the AEs, for potential cures with dosage modifications, going by the list of drugs/ medicines. Primarily homeopathy as an 'alternative' system of medical treatment can bank on this time-tested scientific drug-AE information rather than doing individual experiments. The drug to AEs database documented over far more users/ subjects and over many years systematically is more reliable than homeopathy has been doing in some ways historically. The present database constructed by the PA is available for users on the Google-link (https://docs.google.com/spreadsheets/d/1SLr7OhOTUvHrPxtaEwPtavzmlGWFERDSeBDkkVh6c8g/edit?usp=drive_link). Continuous updating is necessary in this work. The same drugs can be used in homeopathic doses and ways to cure the symptoms they are otherwise known to cause.

There are other sources of databases on the toxic effects of chemical substances like the (MSDS or Material Safety Data Sheets) and this can also be used to develop remedies for many unsolved problems (i.e. the so-called incurable diseases) and yet there are many other databases of AEs like from agricultural sites on insecticides, weedicides and antifungal agents. We suggest that all these AE data can be beneficially used with the logic of homeopathy.

Modern Pharmacology re-deploying AE Data

Apart from homeopathy gaining from the drug-wise AEs to develop new remedies, modern medicine, and pharmacology can think anew from the differential dose-response angle.

Biphasic dose-response or hormesis is a contested concept and phenomenon in pharmacology.³⁰ An article by Calabrese EJ concludes: "The hormesis concept helps researchers better address the issue of low dose responses, including areas such as enhancing adaptive capacities, slowing down the onset of chronic degenerative diseases, and improving biological performance in many other ways."

To understand paradoxical response of a drug, the biphasic response, also known as J-shaped or U-shaped response, may be explained by hormesis. For example, alcohol has a J-shaped response; beneficial in low doses and adverse in higher doses.³¹

The vaccination approach in modern medicine uses a low dose of the same disease-causing substance (germs or toxins) to generate an immune response to fight the disease. The immune pathway here is well known and herein homeopathy looks close to pharmacology. However, the role of immunization is preventive. Homeopathy does deploy some preventive measures. Homeopathic remedies can be used as prophylactics. This is all the more applicable in the case of 'nosodes' (meaning noxious or damaging exudates from diseased tissues).

In summary we argue here, that (a) homeopathy can harness the huge and reliable drug-AE database of modern medicine, and (b) Modern medicine may get new insights in drug use with hormetic approach and even new cures with same medicines.

CONCLUSION

Homeopathy, based on principle of 'let likes be cured by likes', uses adverse effects of substances on human subjects, and then employs the same substances in serially diluted dose or potentization to cure the conditions characterised with these effects. The system of homeopathy has been questioned on several grounds like the near absence of the drug molecule in thus prepared homeopathic remedies, absence of disease diagnosis and lack of evidence in the form of randomised double-blind trials. The highly individualized approach of homeopathy, based on primary and specific symptoms and thus syndromes, is an obstacle for clinical trials of 'a substance' or the drug. However, Evidence based medicine, using case reports and case series approach may be helpful in validating homeopathy. In this perspective paper, we propose that the vast data on adverse effects recorded in pharmacology can be used to harness over 600 modern medicines to further add to the homeopathic Materia Medica. The author 1 has prepared and uploaded a usable 600 drug-AE matrix on a web-link that practitioners of modern medicine and homeopathy can use for their own work. The drug-wise dose-response relation, especially the biphasic response or hormesis is also something to take note of. The most important point of this suggested study is perhaps the 'use' of the huge pile of data classed as the Adverse Effect data which finds a great curative application from the view point of homeopathy. This data of Adverse Effects presently considered a mere pile of 'waste'.

Limitations

The authors are aware of problems of homeopathy in the EBM context. Further we have banked on various sources of literature mainly from year 2010 and, which needs updating. The AEs have been listed without assigning category like ABCDE. The visual basic app used for this program needs to be updated and made available for public use.

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Roles of authors and Conflict of Interests

Most of the conceptual and practical work of this paper is done by author 1 referred to as PA, and he has no financial interest in publishing this article or the weblink, which is done in public interest. Author 1, now close to 77-years, has spent a lifetime in studying homeopathy without a formal degree, as so happened in homeopathy in the older generation, and has kept records of remedies and their action since at least 1980s. Author 2, a teacher and researcher in community medicine has helped rewrite the article as a research consultant for version for this journal and has no financial gains from the publication of this work or the web-link, but has been supported for this work by GP trust for Health. Author 3, has been a practicing homeopath and has edited this article, and also has no financial interests in this publication or the web-link.

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