Review Article

Homoeopathic drug proving researches (1996–2018): A scoping review

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Abstract

Background: A systematic review on homoeopathic pathogenetic trials (HPTs) from 1945 to 1995 was published in 2007, and the basic question whether the effect produced by homoeopathic drugs in healthy human volunteers is equivalent to placebo or otherwise remained unanswered. There is a need to take up another review of HPTs conducted in the last two decades, to assess the changes in the methodologies adapted and to assess whether the effects produced in apparently healthy volunteers is due to homoeopathic medicines in high dilutions or not. **Objective:** To seek, collect, review and describe HPTs published during 1996–2018. **Materials and Methods:** A comprehensive literature search, both electronic and manual, was done using search terms 'homoeopathic drug proving' and 'homoeopathic pathogenetic trial' with time constraint of 1996–2018 in English language. As per the inclusion and exclusion criteria, the papers were selected for extraction of data in the predefined extraction form. **Results:** One hundred and forty-seven eligible records (74 peer-reviewed [PR] and 73 non-peer-reviewed [NPR]) of HPTs of 214 drugs were identified and subjected to the extraction of data. Majority of the drug proving records were contributed by the Central Council for Research in Homoeopathy which included 86 records (24 PR and 62 NPR) with the data of 24 and 63 drugs, respectively, and by Riley, one book (NPR) with data of 68 drugs. Heterogeneity was encountered in all aspects – design, conduct, participants and outcome reporting. **Conclusion:** This preliminary study is the basis for data recovery and for the forthcoming program of systematic review and meta-analysis, which may include the HPTs published in other languages.

Keywords: Homoeopathic drug proving, Homoeopathic pathogenetic trial, Scoping review

Introduction

Homoeopathic drug proving (HDP), also known as homoeopathic pathogenetic trial (HPT), is a clinical trial aimed at systematic observation and recording of symptoms occurring after the defined administration of a proving substance in a serially agitated non-toxic dilution, prepared according to a homoeopathic pharmacopeia to 'apparently healthy' volunteers ('provers') for the purpose of using it as a homoeopathic remedy according to the principle of similarity in a sick person.[1,2] These provings are considered to play a pivotal role in Homoeopathy since its inception. Results of these trials have been disseminated and applied in clinical practice by physicians, worldwide. Hence, to standardise them and then subjecting these towards vigorous systematic review is the dire need today. The proving substance produces reversible symptoms at physical and psychic levels, which are systematically observed and recorded by the provers and the investigator(s) as well. In quasi-experimental studies (one-group pretest–posttest design), Hahnemann tested such 99 substances.[3] To minimise bias, he recommended the selection of trustworthy and conscientious healthy human volunteers, use of only one medicine in its purest form and in moderate dose, close supervision of the subjects and some rules for controlling confounders as diet, life style, ingestion of medicines and consumption of alcohol and coffee.[4] Naturally, overestimations of pathogenetic effects derived

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Received: 04.05.2019; **Accepted:** 18.02.2020; **Published:** 09.04.2020.

Access this article online

Quick Response Code:

Website: www.ijrh.org

DOI: 10.4103/ijrh.ijrh_32_19

How to cite this article: Manchanda RK, Khurana A, Fisher P, Arya BS, Mehra P, Saha S, *et al*. Homoeopathic drug proving researches (1996–2018): A scoping review. Indian J Res Homoeopathy 2020;14:24-49.

from such studies were predicted[5] along with the existence of substantial methodological shortcomings and heterogeneity.[6] To overcome such problems, HPTs with defined methodologies began to evolve since 1835.[7,8]

A systematic review of HPTs from 1945 to 1995 has been published,[2] in which it has been reported that the HPTs were found suffering from design flaws, heterogeneity and low methodological quality, and above all, whether homoeopathic medicines in high dilutions can provoke effects in healthy volunteers remained inconclusive. Since then, many more HPTs have been published across the globe. There is a need to evaluate the collective outcome of these studies in terms of their methodology and the quality of information generated and to make further recommendations for undertaking similar studies. Hence, another systematic review and meta-analysis of these studies have been planned. Two institutions, namely Central Council for Research in Homoeopathy (CCRH), under the Ministry of AYUSH, Government of India, in association with Royal London Hospital of Integrated Medicine, are collaborating to take up the systematic review and meta-analysis of the HPTs published in these two decades, i.e., from 1996 to 2018; however, keeping in mind the possibilities of heterogeneity, initially, a scoping review has been performed.[9] This is a preliminary paper wherein an up-to-date and comprehensive systematic categorisation of the international HDP literature published in English language in the last two decades has been covered. An 'eligible' record for full data extraction is defined as any substantive report of HDP in healthy humans published in books, research journals or bulletins. In a series of papers planned to follow, eligible HPTs will be short-listed and will ultimately be appraised for internal validity (risk of bias) against pre-defined criteria (not yet determined) and included in appropriate meta-analysis models if data permit. Majority of the proving elicits qualitative data; hence, meta-analysis might seem to be inappropriate; still, a considerable number of experiments dichotomizes the outcome reporting in terms of incidence rates (i.e., producers of proving symptoms) in the verum and control groups those can be pooled successfully in meta-analysis models. Thus, if the data allow, meta-analysis of proving may prove to be successful venture to test whether homoeopathic potentised medicines can produce symptoms beyond mere placebo.

The objective of this self-audit is to seek, collect, review and describe HPTs published during 1996–2018 to identify the caveats and improve the adopted methodologies.

Materials and Methods

Search strategy

Trials were sought by manual search of books, research bulletins and journals and electronic search into eight major bibliographic bio-medical databases (PubMed, ScienceDirect, Cochrane, Virtual Health Library, LILACS, BioMed Central, Wiley Online Library and ChiroACCESS), three major trial registries (ClinicalTrials.gov, ISRCTN and CTRI) and one specialised homoeopathic database – CORE-Hom [Table 1]. Search terms used were "homoeopathic pathogenetic trial" and "homoeopathic drug proving" in English language with year restriction used as 1996–2018. The inclusion and exclusion criteria considered were as follows:

Inclusion criteria

- Written information of HPTs in English language from 1996 to 2018 in the public domain
- Prospective, double-blind, randomised, placebo-controlled studies using diluted and potentised homoeopathic medicines
- Studies in which a non-randomised method of sequence generation and/or a single-blinded approach is used
- Trials having a cross-over design, only data from the first randomisation period have been considered due to concerns over carryover effects.

Exclusion criteria

- Studies in which mother preparations (tincture, solution, powder) are used
- Studies where Homoeopathy is combined with another intervention
- 'Dream provings' and 'meditation provings'
- Studies in which no data are provided or data are otherwise not extractable
- Self-experiments, repeat or redundant publications and translations and papers dealing with theoretical/methodological aspects of HPTs and papers not reporting any experimental results
- Publications before 1996 and after 2018 were excluded
- Proceedings, posters or reports of homoeopathic meetings – congresses, seminars, symposiums, workshops, etc., and private reports of HPTs by homoeopathic companies and data claimed by non-peer-reviewed (NPR) websites
- Repeat publications, translations and papers dealing only with theoretical or methodological aspects of HPTs and not reporting any experimental data.

Materials

A data extraction form was developed to collect relevant information on the intervention, dosage, study design and schedule, volunteers and overall results as reflected in the HDP reports. Methodological analysis remains to be appraised in future publications. For each medicine, the name, dilution(s), dose, repetition and duration were extracted. The study design was assessed in terms of randomisation, sequence generation of subjects, allocation concealment, masking (blindness), use of placebo, comparative group and parallel or cross-over. Study schedule was checked for pre-trial observation ('run-in') period with or without placebo and washout period (post-treatment observation). For study population, data were sought for the total number of verum and control group volunteers, sex and age. For the presentation of results, we extracted information on reported incidence of symptom(s) per group and enlisting of observed pathogenetic effects (proving symptoms). Proving symptoms were defined as any change in normal objective and/or subjective state of mind or body as experienced by the

Table 1: Preliminary search results

Electronic databases	Search term: 'Homoeopathic pathogenetic trial'		Search term: 'Homoeopathic drug proving'	
	Category: All	Restriction: 1996-2018	Category: All	Restriction: 1996-2018
Bibliographic				
PubMed/MEDLINE	23	23	30	30
Science direct	183	160	3902	1784
Cochrane	12	12	18	18
Virtual health library	32	31	24	20
LILACS	7	7	2	2
BioMed central	6	6	7	7
Wiley online library	88	83	1056	1056
ChiroACCESS	7	7	7	7
Trial registers				
ClinicalTrials.gov	1	1	4	4
ISRCTN	0	0	1	1
CTRI	3	3	3	3
Specialised:				
CORE-Hom	2	2	-	-
Total	364	335	5054	2932
Manual search in CCRH Library				
Drug proving books	-	-	82	82
Drug proving monographs	-	-	28	17
CCRH Quarterly Bulletin	-	-	53	24
Total	-	-	163	123

LILACS: Latin American and Caribbean Health Sciences Literature, ISRCTN: The International Standard Randomised Controlled Trial Number, CTRI: Clinical Trials Registry - India, CORE-Hom: Clinical Outcome Research in Homoeopathy

prover, or as observed by proving investigator and/or others occurring during proving period, which are possibly related to the proving substance.[10,11] Reporting adhered to the PRISMA extension guidelines for scoping reviews.[12]

Results

Selection and characteristics of sources of evidence

After screening for entries in different databases and books, a total of 5054 records of drug proving were identified. After applying year restriction (1996–2018), the number was reduced to 2932. The details of the search results from electronic databases and manual search are given in Table 1. Then, 394 reports on HDPs were retrieved excluding the redundant entries and irrelevant ones. Again, 256 papers were excluded dealing with theoretical and methodological aspects of HDPs, editorials and commentaries, reviews, conference reports, guidelines, protocols, reprint articles, private reports, proving done in mother tincture form and websites. Finally, 147 eligible papers were subjected for extraction of data [Tables 2 and 3]. Among these, 82 were published research papers and rest were published in the form of books presenting homoeopathic proving reports of total 207 drugs.

Under the NPR publications:

- CCRH published proving data of 74 drugs in the form of research papers published in NPR CCRH Quarterly Bulletin, six volumes of Drug Provings and New Drugs Proved by CCRH books
- Riley's book contained HPTs of 68 drugs
- Koster published one article but names of 15 drugs proved are not clearly mentioned
- One research paper was published by Maishi containing proving data of one drug.

Cardiospermum halicacabum has been proved by CCRH and Reily; thus, names of 214 drugs are enlisted in Table 4.

Among the 74 peer-reviewed (PR) research papers, the proving data of 74 drugs has been published between 1996 and 2018 [Figure 1], CCRH published 24 HPTs, Shah published four HPTs, and the rest were from different countries. Proving of *Galphimia glauca*, *Okoubaka aubrevillei*, *Ozone*, *Sulphur*, *Bryonia alba* and *Calendula officinalis* has been published by two different authors, and proving of *Belladonna* has been published by three different authors. The names of 74 drugs published in PR journals are added in Table 4. The list of references of the studies included, excluded papers and unrecovered literature are mentioned in Appendices 1-3 (available in online version of this article), respectively.

Results of individual sources of evidence

Among the searched literature, the trials were found to have methodological differences –

- observational (pre–post or repeated measure), observational and self-experimental (pre–post),
- randomised/nonrandomised,
- single/double blind,
- placebo controlled or single arm, parallel arm (two or more) or crossover (inter- or intra- group),

Table 2: Non-peer-reviewed clinical studies of homoeopathic drug proving; 1996-2018

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[1]	CCRH	2005	*Acalypha indica* 6C, 30C, 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 29, verum 19, placebo 10; mean age 25.2 (SD 5.2); male - 19, female - 10	Proving symptoms enlisted	Incidence rate per group not reported
[2]	CCRH	2005	*Acid butyricum* 6C and 30C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 15, verum 10, placebo 05; mean age 25.2 (SD 5.2); male - 7, female - 8	Proving symptoms enlisted	Incidence rate per group not reported
[3]	CCRH	2005	*Alfalfa* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 25; allocation unclear; age 18-33, male - 22, female - 3	Proving symptoms enlisted	Incidence rate per group not reported
[4]	CCRH	2005	*Aranea diadema* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 16; allocation unclear; age 19-51, male - 12, female - 3	Proving symptoms enlisted	Incidence rate per group not reported
[5]	CCRH	2005	*Theridion* 30C and 200C; (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (only 'double-blind' mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 28, verum 18, placebo 10; mean age 24.3 (SD 6.3); male - 21, Female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[6]	CCRH	1996	Spider remedies (*n*=7)*; potency used and dosage details not reported	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	Not detailed	Not reported	Proving symptoms enlisted	Incidence rate per group not reported
[7]	CCRH	2005	*Magnesium sulphuricum* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30, allocation unclear; mean age 22.8 (SD 6.7); male - 19, female - 11	Proving symptoms enlisted	Incidence rate per group not reported
[8]	CCRH	2005	*Glycyrrhiza glabra* 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 27, allocation unclear; mean age 27.0 (SD 5.8); male - 20, female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[9]	CCRH	2005	*Mangifera indica* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 17, allocation unclear; mean age 34.7 (SD 8.2); male - 14, female - 3	Proving symptoms enlisted	Incidence rate per group not reported
[10]	CCRH	2005	*Mygale lasidora* 6C, 30C and 200C; (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 22, allocation unclear; mean age 34.7 (SD 8.2); male - 18, female - 4	Proving symptoms enlisted	Incidence rate per group not reported

Contd...

Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[11]	CCRH	1997	*Phyllanthus niruri* 30C, 6C and Q (descending order), dosage details not reported	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	Not detailed	Total 29, allocation unclear; mean age 28.5 (SD 6.8); male - 20, female - 9	Proving symptoms enlisted	Incidence rate per group not reported
[12]	CCRH	2005	*Terminalia chebula* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30, allocation unclear; mean age 26.3 (SD 5.4); male - 21, female - 9	Proving symptoms enlisted	Incidence rate per group not reported
[13]	CCRH	2005	*Nyctanthes arbor-tristis* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 27, allocation unclear; mean age 24.8 (SD 6.8); male - 14, female - 13	Proving symptoms enlisted	Incidence rate per group not reported
[14]	CCRH	2005	*Aranea diadema* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30; male - 18, female - 12	Proving symptoms enlisted	Incidence rate per group not reported
[15]	CCRH	2005	*Baryta iodata* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30; male - 18, female - 12	Proving symptoms enlisted	Incidence rate per group not reported
[16]	CCRH	2005	*Arsenicum bromatum* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 wk after completion of each potency	Total 28; allocation unclear; mean age 22.9 (SD 6.0); male - 17, female - 11	Proving symptoms enlisted	Incidence rate per group not reported
[17]	CCRH	2002	*Chromium kali sulphuratum* 30C; dosage details not reported	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	Not detailed	Total 24; allocation unclear; mean age 23.6 (SD 5.0); male - 16, female - 8	Proving symptoms enlisted	Incidence rate per group not reported
[18]	CCRH	2005	*Euphorbia lathyris* 200C and 30C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 12	Proving symptoms enlisted	Incidence rate per group not reported
[19]	CCRH	2005	*Ocimum canum* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 25; allocation unclear; mean age 26.4 (SD 4.8); male - 18, female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[20]	CCRH	2005	*Oxytropis lamberti* 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 24; verum 18, placebo 6; mean age 24.8 (SD 7.1); male - 13, female - 11	Proving symptoms enlisted	Incidence rate per group not reported

Contd...

Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[21]	CCRH	2005	*Rauwolfia serpentina* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 28; verum 19, placebo 9; mean age 25.0 (SD 7.8); male - 20, female - 8	Proving symptoms enlisted	Incidence rate per group not reported
[22]	CCRH	2005	*Ricinus communis* 200C, 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 22; allocation unclear; mean age 23.0 (SD 6.5); male - 10, female - 12	Proving symptoms enlisted	Incidence rate per group not reported
[23]	CCRH	2002	*Staphylococcinum* 200C and 30C (descending order); dosage details not reported	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 23; verum 17 placebo 6; mean age 24.0 (SD 4.3); male - 18, female - 5	Proving symptoms enlisted	Incidence rate per group not reported
[24]	CCRH	2005	*Tarentula cubensis* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 21; verum 17 placebo 6; mean age 24.0 (SD 4.3); male - 17, female - 4	Proving symptoms enlisted	Incidence rate per group not reported
[25]	CCRH	2005	*Bellis perennis* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 21; allocation unclear; age 18-41; male - 13, female - 8	Proving symptoms enlisted	Incidence rate per group not reported
[26]	CCRH	2005	*Calotropis gigantea* 200C and 6C (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 15; allocation unclear; age 21-28; male - 9, female - 6	Proving symptoms enlisted	Incidence rate per group not reported
[27]	CCRH	2005	*Ichthyolum* 200C, 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 28; allocation unclear; age 18-26; male - 21, female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[28]	CCRH	2005	*Pyrus americana* 30C and 6C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 21; allocation unclear; age 18-56; male - 17, female - 4	Proving symptoms enlisted	Incidence rate per group not reported
[29]	CCRH	2005	*Tribulus terrestris* mother tincture and 30C (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 15; allocation unclear; age 18-56; male - 10, female -5	Proving symptoms enlisted	Incidence rate per group not reported
[30]	CCRH	2005	*Boerhaavia diffusa* 6C, 30C and 200C (descending order); 56 doses (4 Arica doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 29; allocation unclear; age 18-56; male - 19, female - 10	Proving symptoms enlisted	Incidence rate per group not reported

Contd...

Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[31]	CCRH	2005	*Cuprum oxydatum nigrum* 6C and 200C (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 33; allocation unclear; age 18-56; male - 26, female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[32]	CCRH	2005	*Curcuma longa* 6X; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	Single stage (verum or placebo) of 2 weeks with one potency and wash-out for 1 week after completion of the potency	Total 11; allocation unclear; age 18-56; male - 8, female - 3	Proving symptoms enlisted	Incidence rate per group not reported
[33]	CCRH	2005	*Embelia ribes mother tincture*, 6C, 30C and 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 45; allocation unclear; age 18-56; male - 34, female - 11	Proving symptoms enlisted	Incidence rate per group not reported
[34]	CCRH	2005	*Formic acid* 6C and 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 14; allocation unclear; age 18-56; male - 9, female - 5	Proving symptoms enlisted	Incidence rate per group not reported
[35]	CCRH	2005	*Holarhenna antidysentrica* 6C, 30C and 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 27; allocation unclear; age 18-56; male - 20, female - 7	Proving symptoms enlisted	Incidence rate per group not reported
[36]	CCRH	2005	*Hydrocotyle asiatica mother tincture*, 6C and 200C (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 1 week after completion of each potency	Total 29; allocation unclear; age 18-56; male - 20, female - 9	Proving symptoms enlisted	Incidence rate per group not reported
[37]	CCRH	2005	*Lapis alba* 3X; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	single stage (verum or placebo) of 2 weeks with single potency and wash-out for 1 week after completion of each potency	Total 14; allocation unclear; age 18-56; male - 13, female - 1	Proving symptoms enlisted	Incidence rate per group not reported
[38]	CCRH	2005	*Thea chinensis* 3X, 6C, 30C and 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30; allocation unclear; age 18-56; male - 21, female - 9	Proving symptoms enlisted	Incidence rate per group not reported
[39]	CCRH	2005	*Thymol* 3X, 6C and 200C (descending order); 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 30; allocation unclear; age 18-56; male - 18, female - 12	Proving symptoms enlisted	Incidence rate per group not reported
[40]	CCRH	2005	*Tylophora* 6C, 30C and 200C (descending order); 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 22; allocation unclear; age 18-56; male -16, female - 6	Proving symptoms enlisted	Incidence rate per group not reported

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Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[41]	CCRH	2008	*Cassia fistula mother tincture*, 6C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 28; allocation unclear; age - 17-50; male - 22, female 6	Proving symptoms enlisted	Incidence rate per group not reported
[42]	CCRH	2008	*Cassia sophera mother tincture*, 30C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms (not mentioned)	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 1 week after completion of each potency	Total 89; allocation unclear; age 17-50; male - 59, female - 30	Proving symptoms enlisted	Incidence rate per group not reported
[43]	CCRH	2009	*Chelone glabra* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 26; verum 17 placebo 9; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[44]	CCRH	2009	*Cornus circinata* 6C, 30 C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 26; verum 16 placebo 10; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[45]	CCRH	2009	*Juglans regia* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 34; verum 21 placebo 13; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[46]	CCRH	2009	*Liatris spicata* 6C, 30C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 22; verum 16 placebo 6; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[47]	CCRH	2009	*Ocimum sanctum* 6C, 30C and 200C; 56 doses (4 doses/ day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 28; verum 18 placebo 10; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[48]	CCRH	2009	*Senega* 6C, 30C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 30; verum 20 placebo 10; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[49]	CCRH	2009	*Thyroidinum* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 21; verum 15 placebo 6; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[50]	CCRH	2009	*Tinospora cordifolia* 6C, 30C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	3 stages (verum or placebo), each stage of 2 weeks with 3 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 28; verum 19 placebo 9; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported

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Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[51]	CCRH	2011	*Cardiospermum halicacabum* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 63; verum 40 placebo 23; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[52]	CCRH	2011	*Coleus aromaticus* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 47; verum 32 placebo 15; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[53]	CCRH	2011	*Clerodendron infortunatum* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 32; verum 22 placebo 10; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[54]	CCRH	2011	*Cynara scolymus* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 66; verum 44 placebo 22; age 18-50	Proving symptoms enlisted	Incidence rate per group not reported
[55]	CCRH	2013	*Avena sativa* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 33; verum 21 placebo 12; age 18 years and above; male - 5, female - 28	Proving symptoms enlisted	Incidence rate per group not reported
[56]	CCRH	2013	*Azathioprine* 30C and 200C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 54; verum 36 placebo 18; age 18-50; male - 21, female - 33	Proving symptoms enlisted	Incidence rate per group not reported
[57]	CCRH	2013	*Foeniculum* 6C and 30C; 56 doses (4 doses/day for 14 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 2 weeks with 2 potencies one after another and wash-out for 2 weeks after completion of each potency	Total 65; verum 41 placebo 24; age 18-50; male - 28, female - 37	Proving symptoms enlisted	Incidence rate per group not reported
[58]	CCRH	2013	*Magnolia grandiflora* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 48; verum 32 placebo 16; age 18 years and above; male - 14, female - 34	Proving symptoms enlisted	Incidence rate per group not reported
[59]	CCRH	2013	*Persea americana* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 48; verum 31 placebo 17; age 18 years and above; male - 20, female - 28	Proving symptoms enlisted	Incidence rate per group not reported
[60]	CCRH	2013	*Psoralea corylifolia* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 48; verum 30 placebo 18; age 18 years and above; male - 24, female - 24	Proving symptoms enlisted	Incidence rate per group not reported

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Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[61]	CCRH	2018	*Acorus calamus* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 65; verum 44, placebo 21; age 19-32 years; male - 35, female - 30	Proving symptoms enlisted	Incidence rate in verum 18/44, but in placebo group not reported
[62]	CCRH	2018	*Apium graveolens* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 41; verum 27, placebo 14; age 17-56 years; male - 18, female - 23	Proving symptoms enlisted	Incidence rate in verum 9/27, but in placebo group not reported
[63]	CCRH	2018	*Brassica oleracea* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 48; verum 32, placebo 16; age 18-30 years; male - 25, female - 23	Proving symptoms enlisted	Incidence rate in verum 16/32, but in placebo group not reported
[64]	CCRH	2018	*Cochlearia armoracia* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 46; verum 31, placebo 15; age 18-49 years; male - 22, female - 24	Proving symptoms enlisted	Incidence rate in verum 7/31, but in placebo group not reported
[65]	CCRH	2018	*Datura arborea* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 67; verum 44, placebo 23; age 19-52 years; male - 31, female - 36	Proving symptoms enlisted	Incidence rate in verum 12/44, but in placebo group not reported
[66]	CCRH	2018	*Datura metel* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 63; verum 40, placebo 23; age 20-56 years; male - 24, female - 39	Proving symptoms enlisted	Incidence rate in verum 11/40, but in placebo group not reported
[67]	CCRH	2018	*Ephedra vulgaris* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 49; verum 34, placebo 15; age 18-29 years; male - 17, female - 32	Proving symptoms enlisted	Incidence rate in verum 8/34, but in placebo group not reported
[68]	CCRH	2018	*Jalapa* 6C and 30C; 12 doses (4 doses/day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 32; verum 22, placebo 10; age 19-29 years; male - 14, female - 18	Proving symptoms enlisted	Incidence rate in verum 7/22, but in placebo group not reported
[69]	CCRH	2018	*Leucas aspera* Q, 6C, 30C and 200C; 12 doses (4 doses/ day for 3 days)	Double-blind, randomised, placebo-controlled, two parallel arms	2 stages (verum or placebo), each stage of 3 days with 2 potencies one after another and wash-out for 30 days after completion of each potency	Total 64; verum 42, placebo 22; age 17-56 years; male - 26, female - 38	Proving symptoms enlisted	Incidence rate in verum 14/42, but in placebo group not reported
[70]	Nagpaul VM CCRH	2005	*Tarantula hispanica* 200C, 30C and 6C; 4 doses a day for 14 days	Double-blind, randomised, placebo-controlled, four parallel arms	Run-in observation 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 28; verum 20, placebo 8; age 22-36, male - 22, female - 6	Proving symptoms enlisted	Incidence rate per group not reported

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Table 2: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results	Comments
[71]	Koster D	1998	Fifteen 'inadequately known' homoeopathic medicines in D6/C30; 5 granules twice a day, 6 doses or three days at the most	Double-blind, randomised, placebo-controlled, cross-over	Run-in 1 week, baseline observation 1 week; cross-over after 4 weeks	Total 13 out of 24; no further details	Most optimistic scenario guessing was statistically significant (P=0.035); most subjects were able to guess correctly which treatment was active and which placebo; 110 verum and 60 placebo symptoms; not proportionally more mind and general symptoms in the verum phase; more dreams in the placebo phase	Results disputable (non-estimation and no supervisor in one subject each); Incidence rate per group not reported; symptoms not enlisted
[72]	Maishi AI	1998	*Parthenium hysterophorus* 2X, 1-3 ml doses daily in water	Double-blind, randomised, placebo-controlled, two parallel arms	Not detailed	Total 70; age range 18-50 years, male - 56, female - 14	Proving symptoms enlisted	Incidence rate per group not reported
[73]	Riley DS	2012	New and old homoeopathic medicines (n=68)**; 12C, 3 doses (mostly globules) daily until symptoms appeared, 6-9 weeks	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo, followed by verum or placebo (details not reported)	Age range 18-75 years, both sexes (details not reported)	Proving symptoms enlisted	Incidence rate per group not reported

**Tarentula hispanica, Tarentula cubensis, Aranea diadema, Mygale lasiodora, Theridion, Tela aranea* and *Aranea scinencia* are published in CCRH Quarterly Bulletin but except for *Tela aranea* and *Aranea scinencia*, the data of rest of the five drugs has been published in Drug Proving Volumes. Thus, to avoid repetition these two drugs are considered here. ***Acidum cis aconiticum, Acidum citricum, Acidum ketoglutaricum, Acidum oroticum, Acidum succinicum*, AMP, ATP, *Agnus castus, Anthrachinon, Arteria suis, Ascophyllum nodosum, Bacterium coli, Barium oxalsuccinicum, Bryonia alba, Bryonia dioica, Calendula officinalis, Cardiospermum halicacabum, Cartilago suis, Caulophyllum thalictroides, Citrullus colocynthis, Coenzyme A, Cuprum formicium, Embryo suis, Fucus vesiculosus, Fumaria officinalis, Funiculus umbilicalis, Galphimia glauca, Geranium robertianum, Glandula suprarenalis, Glyoxal, Hepar suis, Human growth hormone, Hydrochinon, Insulin-like growth factor-1, Kalium tetraiodobismutate, L-Cysteine, Luffa operculata, Mahonia aquifolium, Medulla ossis suis, Methylglyoxal, Mucosa nasalis, Myosotis arvensis, Naphthochinon, Natrium oxalaceticum, Natrium pyruvicum, Nicotinamide,* NAD, *Okoubaka aubrevillei, Oleander, Oleum pini, Oxalis acetosella, Pancreas suis, Placenta suis, Potentilla erecta, Pyridoxinum hydrochloricum, Riboflavinum, Sinusitisinum, Staphylococcus nosode, Streptococcus nosode, Symphytum officinalis, Terebinthina laricina, Thiamini hydrochloricum, Thioctic acid, Trichinoyl, Urtica urens, Veronica officinalis, Zincum aceticum and Zinc gluconate. ATM: Adenosine triphosphate, NAD: Nicotinamide adenine dinucleotide, AMP: Adenosine monohydrogen phosphate 3'5'*, CCRH: Central Council for Research in Homoeopathy, PL: Placebo

- using different dilutions of the same medicine or one medicine in a single dilution,
- different study schedules – pretrial observation ('runin') period with or without placebo and washout period (posttreatment observation) with inconsistent duration, and
- different dilutions were used – 3X, 6X, 4C, 6C, 12C, 30C, 90C, 200C, and 200K in variable dosage, order, frequency and duration.

This has been reflected in Tables 2 and 3.

Synthesis of results

Thus, the study reporting was heterogeneous. The proving symptoms' incidence rates per group were also searched in each of these trials, and it was found that none of the NPR studies and only six PR studies reported this outcome completely. PR papers were subject to selective reporting, preferably for the verum group only in most occasions. Continuous outcomes were also reported in terms of number of symptoms produced and mean difference between groups. Pathogenetic effects are enlisted in most of the studies [Tables 2 and 3]. However, the question that whether the results of provings are due to the placebo effect is yet to be answered subsequent to the upcoming programme of meta-analysis.

Discussion

Our search findings and initial data extraction have provided an expanded and refined view of the HDP literature. Like any event, this literature search cannot be regarded as completely successful, especially in the context that a significant part of proving literature is in the German language that was not assessed in this study. Full texts of 30 articles could not be recovered. The efforts will be made to do so and, if possible,

Table 3: Peer-reviewed clinical studies of homoeopathic drug proving; 1996-2018

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[1]	Khanna VK	2007	*Agave americana*; potency and dosage not detailed	Not detailed; double-blind, randomised, placebo-controlled, two parallel arms probably	Not detailed	Total 28; age range 18-49 years, male - 22, female - 6	Proving symptoms enlisted, incidence rate per group not reported
[2]	Dey NR	2008	*Argemone mexicana* 200C, 30C and 6C (descending order); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	No run-in phase; verum (200C) or placebo for 2 weeks (stage 1) - to wait for disappearance of symptoms and resume 2nd and 3rd stages with 30C and 6C respectively for 2 weeks each; followed by wash-out for 1 week after each stage	Total 38; verum 25, placebo 13; age 18-45 years, male - 29, female - 9	Proving symptom enlisted and incidence rate in verum group 18/25 and in placebo group -/13
[3]	Dey NR	2008	*Cephalandra indica* 6C, 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	No run-in phase; 3 stages verum or placebo, each stage of 2 weeks with 3 potencies followed by wash-out for 1 week after each stage	Total 27; verum 17, placebo 7; age 18-45, male - 18, female - 9	Proving symptom enlisted and incidence rate in verum group: 10/17 and in placebo group -/10
[4]	Dey NR	2008	*Ficus religiosa* 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week; 2 stages verum or placebo, each stage of 2 weeks with wash-out for 1 week	Total 24; verum 17, placebo 7; age 18-50 years, male - 19, female - 5	Proving symptom enlisted and incidence rate in verum group: 11/17 and in placebo group -/7
[5]	Dey NR	2008	*Paraffin* 6C, 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	No run-in; 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 43; verum 30, placebo 13; age 18-50 years, male - 28, female - 15	Proving symptom enlisted and incidence rate in verum group: 13/30 and in placebo group -/13
[6]	Shaw R	2009	*Pothos foetidus* 6C, 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	No run-in; 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 25; verum 18, placebo 7; age 18-50 years, male - 20, female - 5	Proving symptom enlisted and incidence rate in verum group: 11/18 and in placebo group -/7
[7]	Nayak C	2009	*Saraca indica* 6C, 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 42; verum 29, placebo 13; age 18-50 years, male - 31, female - 11	Proving symptom enlisted and incidence rate in verum group: 8/29 and in placebo group -/13
[8]	Shaw R	2009	*Cuscuta reflexa* 200C, 30C, 6C (descending order); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 13; verum 9, placebo 4; age 18-50 years, male - 7, female - 6	Proving symptom enlisted and incidence rate in verum group: 8/9 and in placebo group -/4
[9]	Nayak C	2009	*Mimosa humilis* 6C, 30C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 16; verum 10, placebo 6; age 18-50 years, male - 9, female - 7	Proving symptom enlisted and incidence rate in verum group: 5/10 and in placebo group -/6
[10]	Khurana A	2010	*Skookum chuck* 6C, 30C, 200C (order not specified); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 30; verum 20, placebo 10; age 18-50 years, male - 18, female - 12	Proving symptom enlisted and incidence rate in verum group: 14/20 and in placebo group -/10

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[11]	Rajpal	2010	*Carica papaya* 200C, 30C, 6C (descending order); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 26; verum 17, placebo 9; age 18-50 years, male/female not mentioned	Proving symptom enlisted and incidence rate in verum group: -/17 and in placebo group -/10
[12]	Rajpal	2010	*Azadirachta indica* 200C, 30C, 6C (descending order); 56 doses schedule, 4-6 globules no. 30, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 27; verum 18, placebo 9; age 18-50 years, male - 18, female - 9	Proving symptom enlisted and incidence rate in verum group: -/18 and in placebo group -/9
[13]	Rajpal	2011	*Amoora rohituka* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 53; verum 35, placebo 18; age 18-50 years, male - 14, female - 39	Proving symptom enlisted and overall incidence rate 29/53
[14]	Rajpal	2011	*Andrographis paniculata* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 39; verum 23, placebo 16; age 18-50 years, male - 26, female - 13	Proving symptom enlisted and incidence rate in verum group: 6/23 and in placebo group -/16
[15]	Rajpal	2011	*Asclepias curassavica* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 67; verum 44, placebo 23; age 18-50 years, male - 38, female - 29	Proving symptom enlisted and incidence rate in verum group: 21/44 and in placebo group -/23
[16]	Rajpal	2011	*Bacopa monnieri* 6C, 30C, 200C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 3 stages verum or placebo, each stage of 2 weeks with 3 potencies and wash-out for 1 week	Total 32; verum 20, placebo 12; age 18-50 years, male - 29, female - 3	Proving symptom enlisted and incidence rate in verum group: 7/20 and in placebo group -/12
[17]	Rajpal	2012	*Buxus sempervirens* 6C and 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 57; verum 40, placebo 17; male - 17, female - 40	Proving symptom enlisted and incidence rate in verum group: 23/40 and in placebo group -/17
[18]	Rajpal	2012	*Caesalpinia bonducella* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 50; verum 34, placebo 16; age 18-50 years, male/female not mentioned	Proving symptom enlisted and incidence rate in verum group: 12/34 and in placebo group -/16
[19]	Rakshit G	2013	*Gymnema sylvestre* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 63; verum 37, placebo 26; age 18-45 years, male - 27, female - 36	Proving symptom enlisted and incidence rate in verum group: 16/37 and in placebo group -/26
[20]	Rakshit G	2013	*Cyclosporin* 6C, 30C (ascending order); 56 doses schedule, 4 doses/day for 14 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 50; verum 33, placebo 17; age 19-29 years, male - 12, female - 38	Proving symptom enlisted and incidence rate in verum group: 11/33 and in placebo group -/17

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Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[21]	Rakshit G	2014	*Hygrophila spinosa* 6C, 30C (ascending order); 56 dose/12 dose schedule, 4-6 globules 4 times a day	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week	Total 48; verum 32, placebo 16; age 18-32 years, male - 15, female - 33	Proving symptom enlisted and incidence rate in verum group: 14/32 and in placebo group -/16
[22]	Mohanty N	2015	*Nanocurcumin* 6X trituration; 12 doses/day; 4 doses daily for 3 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week - verum/placebo -symptoms noted up to 6 weeks	Total 30; verum 23, placebo 7; age above 18 years; male - 17, female - 13	Proving symptom enlisted and incidence rate in verum group: 17/23 and in placebo group 2/7
[23]	Manchanda RK	2016	*Allium sativum*; 12 doses; 4 doses daily for 3 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week up to 6 weeks	Total 33; verum 21, placebo 12; mean age 22.1 years (verum) and 22.0 years (placebo), male - 9, female - 24	Proving symptom enlisted; incidence rate in verum group: 9/21 and in placebo group 8/12
[24]	Mehra P	2017	*Withania somnifera*; 12 doses; 4 doses daily for 3 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - 2 stages verum or placebo, each stage of 2 weeks with 2 potencies and wash-out for 1 week up to 6 weeks	Total 63; verum 43, placebo 20; mean age 24.1 years (verum) and 25.4 years (placebo), male - 31, female - 32	Proving symptom enlisted; incidence rate in verum group: 15/43 and in placebo group 4/20
[25]	Shah R	2015	*HIV nosode* 30C; 6 globules of size 30; 4 such doses; once a week for 4 weeks	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week - verum/placebo for 4 weeks - symptoms noted up to 6 weeks	Total 22; verum 15, placebo 7; mean age 26.6 years; male - 19, female - 3	Verum: 130 symptoms; placebo: 60 symptoms; significant difference between groups (P=0.002); no serious adverse events; proving symptoms enlisted.
[26]	Shah R	2014	*Capsicin*, *Dihydrocapsicin* 30C; 6 pills, 3 times a day for 4 subsequent weeks	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week - trial (verum) 4 weeks [symptoms noted up to 6 weeks]	Total 22; verum 15, placebo 7; age 18-45 years, male - 18, female - 4	Incidence rate 14/15 and -/7; qualitatively and quantitatively ('pathogenetic indices') distinct symptoms identified; proving symptoms enlisted; safety profile discussed
[27]	Shah R	2013	*Hepatitis C Nosode* 30C; single dose, once a week for 4 weeks	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week - trial (verum) once a week for 4 weeks (symptoms noted up to 6 weeks)	Total 22; verum 15, placebo 7; mean age 26.14 years, male - 15, female - 7	Incidence rate: 15/15 and -/7; qualitatively and quantitatively distinct symptoms identified; proving symptoms enlisted; safety profile discussed
[28]	Shah R	2013	*Hydroquinone* 30C; 6 pills thrice daily for 4 weeks	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in (placebo) 1 week - trial (verum) 4 weeks (symptoms noted up to 6 weeks)	Total 22; verum 15, placebo 7; mean age 26.5 years, male - 18, female - 4	Incidence rate per group not reported; 'qualitative and quantitative pathogenetic indices' showed distinct symptoms different from placebo; proving symptoms enlisted; safety profile discussed

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[29]	Goodyear K	1998	*Belladonna* 30C; twice a day for two weeks	Double-blind, randomised, placebo-controlled, two parallel arms	No run-in, verum for 2 weeks	Total 47 out of 60 (per protocol); verum 20, placebo 27; age 21-23 years, male - 24, female - 23	Incidence rate: 5/20 and 1/27 (P=0.07); intention-to-treat population0; number of 'true' and 'false' symptoms elicited could not be distinguished between groups; proving symptoms not enlisted
[30]	Walach H	2001	*Belladonna* 30C; globules no. 3 in 5 g containers; 8-week trial	Double-blind, randomised, placebo-controlled, single-arm, with intra-group cross-over	Baseline observation 2 weeks - run-in (placebo) 1 week - verum or placebo 1 week -observation 1 week - wash-out 1 week - cross-over and placebo or verum 1 week - observation 1 week	Total 87 out of 118 (per protocol); age and gender distribution not clear	Insignificant tendency for subjects to report more Number of symptoms with *Belladonna* [mean 27.37; SD 24) as compared to observation (mean 24.26, SD 22.15) or placebo (mean 24.17, SD 23.74); no indication of subjects reacting differently to Homoeopathy than to placebo; proving symptoms not enlisted
[31]	Fisher P	2001	*Acidum malicum* 12C; *Acidum ascorbicum* 12C; two granules no. 6 for 3 times a day	Double-blind, randomised, placebo-controlled, balanced cross-over	Volunteers randomly assigned to one of two sequences - 1 week for each phase, wash-out (1-3 weeks): (1) Run-in - verum - placebo - placebo -verum; or (2) Run-in - placebo - verum - verum - placebo	20 for each medicine; age 21-30 years: 13, 31-40 years: 14, 41-50 years: 9, above 50 years: 4; male - 15, female - 25	*Acidum malicum*: 79 symptoms identified, 57 analysed finally, 22 in verum periods *Acidum ascorbicum*: 55 symptoms identified, 39 analysed, 16 in verum periods. Proving symptoms enlisted
[32]	Vickers AJ	2001	*Bryonia alba* 12C; 1 pill 3 times a day for 1 week	Double-blind, randomised, placebo-controlled, single-arm, with intra-group cross-over	Verum 1 week - wash-out 2 weeks - verum 1 week	Total 50 out of 70 (per protocol); age 18 years or above, male - 31, female - 19	60% correctly identified the bottle containing *Bryonia* (n=40; 95% CI 43% to 75%; P=0.27). Proving symptoms not enlisted.
[33]	Vickers AJ	2001	*Mercurius* 12C, five pellets, three times a day for a week; 3 week trial	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - verum or placebo 1 week - run-out placebo 1 week	Total 104 out of 118 (per protocol); verum 52, placebo 52; median age 30 years (IQR 27-39), exact gender distribution not clear	1/52 and 5/52; mean difference score 20.125 (SD 3.47) for *Mercurius* and 20.221 (SD 3.010 for placebo (P>0.2). No significant differences between groups. Proving symptoms enlisted
[34]	Brien S	2003	*Belladonna* 30C, twice daily for two weeks; 4 week trial	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in placebo 1 week - verum or placebo 2 weeks - run-out placebo 1 week	Total 206 out of 253; verum 101, placebo 105; age verum 22.5±3.8, placebo 22±2.2; male - 42, female - 164	14/101; 15/105; mean difference (−0.4)%, 95% CI 9.3, 10.1; safety profile discussed; proving symptoms not enlisted

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[35]	Möllinger H	2004	*Calendula officinalis* 30C; *Ferrum muriaticum* 30C; dose not specified, taken until symptoms occurred, but maximally 5 days, an after inquiry, stopped when discernible symptoms showed	Double-blind, randomised, placebo-controlled, three parallel arms	Observation 1 week - verum max 5 days	Total 21; allocation unclear; age distribution not clear; male - 13, female - 8	Incidence rate per group not reported; number of mean symptoms for *Calendula* 12.86 (SD 5.8); *Ferrum muriaticum* 14 (SD 8.3); and placebo: 3.14 (SD 4.2). Proving symptoms not enlisted
[36]	Walach H	2004	*Cantharis* 30C; max 6 doses over 2 days and to stop intake as soon as symptoms appeared	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - verum or placebo 2 weeks	Total 11, allocation unclear; age and gender distribution not mentioned	Incidence rate per group not reported; group differences not significant; effect sizes for the difference between the proving and control group for typical and atypical symptoms d=0.4 and 0.6 respectively. Proving symptoms not enlisted
[37]	Escola Paulista de Homoeopatia	2004	*Lapis lazuli* 90CK; one daily dose for 30 days	Single-arm, interventional, pre-post, no control	Pre-trial auto-observation run-in for 30 days	Total 8, no further details	Proving symptoms enlisted; no further details
[38]	Riley D	2005	RNA 2X; 10 drops once daily for 3 weeks; trial duration 6 weeks	Double-blind, randomised, placebo controlled, two parallel arms	Run-in observation 1 week - verum or placebo 3 weeks - run-out 2 weeks	Total 25; allocation unclear, age group 16-72 years, male - 7, female - 18	Incidence rate per group not reported; proving symptoms enlisted
[39]	Signorini A	2005	*Plumbum metallicum* 30C; *Piper methysticum* 30C; 5 drops 4 times daily, until the onset of unbearable symptoms, or at most for 1 week	Double-blind, randomised, placebo-controlled, three parallel arms	Observation 1 week - verum or placebo 1 week - observation 1 week	Total 31; Piper methysticum 13, Plumbum metallicum 7, placebo 11; mean age 41.7 years (SD 6.3); male - 17, female - 14	Incidence rate 10/13, 7/7, and 7/11. Proving symptoms enlisted.
[40]	Grimes MJ	2005	*Enallagma carunculatum* (Tule Bullet Dragonfly) 30C; no further details	Single arm, pre-post, interventional, no control	Not detailed	Total 25; no further details	Proving symptoms enlisted; no further details
[41]	Spada MF	2005	*Titanium metallicum* 30C, 200K; dosage not detailed	Double-blind, placebo-controlled, three parallel arms		Total 24; verum 30C - 8, verum 200K - 8, placebo - 8	Proving symptoms enlisted; 145 symptoms in verum and 20 in placebo (cumulative); no further details
[42]	Sevar R	2005	*Leycesteria formosa* (Himalayan Honeysuckle) 30C	Single-arm, pre-post, interventional, single-blind	Not detailed	Total 7/9; male - 3, female - 6; no further details	Proving symptoms enlisted; no further details

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[43]	Dominici G	2006	*Etna lava* 30C; *Hydrogenium peroxidatum* 30C; 10 drops three times daily	Double-blind, randomised, placebo-controlled, parallel arms	Observation 2 weeks - verum or placebo for no>days	*Etna lava*: 11 (verum 8, placebo 3); *Hydrogenium peroxidatum*: 10 (verum 7, placebo 3); *Etna lava*: mean age 41 years (30-54), *Hydrogenium peroxidatum*: mean age 37 years (26-48), PL: mean age 38 years (30-45); gender distribution male/female *Etna lava*: 3/5, *Hydrogenium peroxidatum*: 3/4, PL: 2/4	Incidence rate per group not reported; new symptoms proportions (symptoms/total) EL 0.46, HP 0.44, Pl 0.34; exceptional symptoms proportions EL 0.13, HP 0.15, Pl 0.01; mean symptoms/prover EL 47.12 (SE 5.85), HP 27 (SE 1.05), Pl 18 [SE 3.76]; total symptoms EL 377, HP 189, Pl 108. Proving symptoms not enlisted.
[44]	Pitt R	2006	*Petroleum*; no further details	Single-blind controlled trial	Not mentioned	Total 15; no further details	Proving symptoms enlisted; no further details
[45]	Haukaa K	2006	*Rosa canina*; no details available	Not mentioned	Not mentioned	Not mentioned	Proving symptoms enlisted; no further details
[46]	Creveld M	2007	*Pinus longaeva* 200K orally for three consecutive nights, smelt, and 'put under pillow'; no further details available	Single-blind 'dream' provings, single-arm, pre-post, interventional, no control	Not mentioned	Total 28; male - 9, female - 19, no further details	23/28 incidence (=occurrence of dreams), proving symptoms enlisted; no further details
[47]	Shukla C	2007	PC-Cancer and PC-AIDS; dosage and further details not mentioned	Single-blind, pre-post, single-arm, interventional, no control	Not mentioned	PC-Cancer: Total 7, male - 5, female - 2; PC-AIDS: Total 6, male - 2, female - 4; no further details	Proving symptoms enlisted; no further details
[48]	Walach H	2008	Study 1: *Ozone* 30C Study 2: *Ozone* 30C, *Iridium* 30C; 5 globules several times a day until symptom (s) experienced	Study 1: Double-blind, randomised, placebo-controlled, two parallel arms Study 2: Double-blind, randomised, placebo-controlled, three parallel arms	Observation 1 week - verum or placebo 3 days - observation 2 weeks	Study 1: total 17, *Ozone* 10, placebo 7 Study 2: total 36, *Ozone* 11, Iridium 12, placebo 13 Study 1: Mean age 28.4 years (sd 8.5, range 21-58), female - 17; Study 2: mean age 43.9 years (sd 6.2, range 34-56), male - 16, female - 20	Pooled results of the two studies showed that homoeopathic remedies produce significantly more symptoms (P=0.011) typical for a remedy than non-typical symptoms with indication of probable entanglement in homoeopathic systems. Proving symptoms enlisted.

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[49]	Teut M	2008	*Galphimia glauca* 12C; 5 globules 5 times a day for 5 days	Double-blind, randomised, placebo-controlled, two parallel arms	Baseline 1 week, verum or placebo for 4 weeks, follow-up for 2 weeks	Total 15 of 18; verum 11, placebo 4; age 18 years and above, both sexes (details not reported)	Incidence rate per group not reported; proving symptoms enlisted. The number of proving Symptoms per prover was greater for placebo (mean±SD 72.3±37.3) than for *Galphimia* (35±24.2), but the group difference was not significant (*P*=0.097)
[50]	Shah P	2009	*Columba livia* 30C single dose; no further details	Single-blind, single arm, pre-post, interventional, no control	Not detailed	Total 8; male - 3, female - 8; no further details	Proving symptoms enlisted; no further details
[51]	Möllinger H	2009	*Natrum muriaticum* 30C; *Arsenicum album* 30C; 5 globules on the 1st day, 2×5 globules on the 2nd, or until symptoms appeared	Double-blind, randomised, placebo-controlled, three parallel arms	No run-in, verum or placebo for 2 or more days	Total 25; *Natrum muriaticum* 10, *Arsenicum album* 8, placebo 7; mean age 42.3 years (SD 6.58); male - 6, female - 19	Incidence rate per group not reported; symptoms typical for the respective remedy groups more frequent; non-specific symptoms more frequent in the placebo group; differences were significant overall (*P*=0.0002) and significantly different from placebo (*P*=0.001). Proving symptoms enlisted
[52]	Piltan D	2009	*Aconitum napellus* 30C; 5 globules 3 times daily for 3 days	Double-blind, randomised, placebo-controlled, cross-over, two parallel arms	3 phases - followed by 14 days follow-up: run-in for 1 week (phase 1) - verum or placebo for 3 days and wash-out for 4 days (phase 2) - switched over to 2nd treatment (phase 3) to complete the 2×7-day crossover	Total 27 of 33; group 1 (*n*=16), group 2 (*n*=17); mean age 41 years (sd 8.9); male - 9, female - 18	Correct identification: 9/14 and 9/13 (1st phase treatment); 9/13 and 11/14 (2nd phase treatment) (per protocol population); crossover differences yielded statistical significance between the classified reactions towards Aconite and to placebo (*P*=0.004). Proving symptoms not enlisted
[53]	Wichmann J	2009	*Betula alba* 30C; dosage not detailed	Single-blind, single-arm, pre-post, interventional, no control	Not detailed	Total 19; male - 2, female - 8, Supervisors - 9	Proving symptoms enlisted; no further details

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[54]	Teixeira MZ	2009	Three 'Polycrests' (*Arsenicum album, Lachesis muta, Sulphur*) in 30C; one dose per week for 4 weeks	Double-blind, randomised, placebo-controlled, cross-over	2 phases - No run-in; verum for 4 weeks - cross-over - placebo for 4 weeks	Total 33 students; *Arsenicum album* (*n*=11; male - 5, female - 6, mean age 21.4 years); *Lachesis muta* (*n*=9; male - 3, female - 6, mean age 21.3 years); *Sulphur* (*n*=13; male - 7, female - 6; mean age 21 years)	Symptom incidence rate per group not reported and compared with source books; proving symptoms enlisted
[55]	Creveld M	2009	*Welwitschia mirabilis* (Tweeblaarkanniedood); no further details	Single-blind 'dream' provings, single-arm, pre-post, interventional, no control	Not mentioned	Total 31; male - 10, female - 21; age 30-71 years, no further details	Proving symptoms enlisted; no further details
[56]	de Azevedo APE	2010	*Serotonin sulphate* 30C; details not found	Single-arm, pre-post, interventional, no control	Details not found	Total 18; details not found	Total 370 symptoms recorded; details not found
[57]	Botha I	2010	*Vibhuti* 1C to 4C Trit; no further details	Single-blind provings, single-arm, pre-post, interventional, no control [the male prover was not blind]	Not mentioned	Total 6; male - 1, female - 6	Proving symptoms enlisted; no further details
[58]	Botha I	2010	*Protea cynaroides* 4C and 30C	Double-blind, randomised, placebo-controlled, two parallel arms; also single-blind 'dream' provings, single arm, pre-post, interventional, no control	Not mentioned	Total 70; verum 60, placebo 10	Proving symptoms enlisted; no further details
[59]	Bell IR	2011	*Sulphur* 6C, 12C, 30C; *Pulsatilla* 6C, 12C, 30C; series of 3 once weekly double-blind sessions of sniffing the remedy for 2 sec (8 sniffs of each of 4 different succession) in randomly assigned order	Double-blind, repeated measure study at the same time of day, once per week for 3 weeks	One dilution per week in randomised and ascending order at all the four different succession levels	*Sulphur* 51; *Pulsatilla* 45; *Sulphur*: mean age 19.2 (SD 2.0), male - 35, female - 16; *Pulsatilla*: mean age 19 years (SD 0.98), male - 8, female - 37	Significant main effects ($P<0.001$) for remedy type (*Sulphur>Pulsatilla*) in both EEG alpha bands averaged over 19 electrode sites
[60]	Renoux H	2011	*Morpho menelaus occidentalis,* no further details	Double-blind, probably placebo-controlled, not detailed	Not mentioned	Total 30; no further details	Proving symptoms enlisted; no further details
[61]	Naudé DF	2011	*Loxodonta africana* 30C in lactose powder, 3 times a day for 2 days	Double-blind, randomised, placebo-controlled, two parallel arms	Not mentioned	Total 26; verum 20, placebo 6; no further details	Proving symptoms enlisted; no further details
[62]	Jordan L	2011	*Melatonin* 6X 3 times/ day for 5 days or until symptoms appeared	Double-blind, randomised, placebo-controlled, two parallel arms	Pre-trial placebo run-in; further details not mentioned	Total 8; male - 1, female - 7	Proving symptoms enlisted; no further details

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[63]	Mehta A	2011	*Riccia gangetica* 30C; no further details	Single-blind provings, single-arm, pre-post, interventional, no control	Not mentioned	Total 10, of different ages and both sexes; no further details	Proving symptoms enlisted; no further details
[64]	Teut M	2013	*Okoubaka aubrevillei* 12C; five globules taken five times per day over a maximum period of 5 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in for 1 week - verum or placebo for 5 days - observation for 16 days	Total 29 of 31; verum 19, placebo 12; verum: Mean age 33.9 years (SD 8.5), male - 7, female - 11; PL: mean age 41.1 years (SD 8.9), male - 3, female - 8	Symptom incidence rate per group not reported; number of characteristic symptoms: *Okoubaka* 5.4 (SD 6.0) and placebo 4.9 (SD 5.6), OR=1.11, 95% CI 0.4-3.05, *P*=0.843; number of proving symptoms: *Okoubaka* 8.8 (SD 9.6) and placebo 9.6 (SD 10.6), OR=1.04, 95% CI 0.33-3.29, *P*=0.951; no significant difference in either occasion. Proving symptoms enlisted
[65]	Shukla C	2013	*Ayahuasca* 200CK; dosage not detailed	Single-arm, pre-post, interventional, no control	Not detailed	Total 5 provers; not detailed	Proving symptoms enlisted; no further details
[66]	Gupta VK	2013	*Catharanthus roseus;* 3X, 6X and 30C in ascending order, 4-5 pills 4 times a day for max. 10 days, or mother tincture 10 drops four times a day for max. 10 days	Double-blind for potencies (Gr. A) and single-blind for mother tincture (Gr. B); parallel arms	No pre-trial placebo run-in; 10 and 20 days wash-out in between repetition of the same quota dose and switch over to higher quota potencies respectively	Total 20; age 19-25 years; Gr. A -*n*=13, verum 9, placebo 4; Gr. B -*n*=7, verum 5, placebo 2; male - 9, female - 11	Proving symptoms enlisted along with symptoms relieved during proving; no further details
[67]	Sherr J	2014	*Ozone* 30C; dosage details not specified	Single (volunteers - homoeopaths) blind single arm medicine identification study on a set of symptoms generated during an unpublished HPT of the trial medicine	Not detailed	Total 7; age distribution not mentioned; male - 1, female - 6	Two homoeopaths succeeded in determining the correct medicine out of 2372 possible medicines; *P*<0.0001; demonstrating that HPTs generate specific and recognisable sets of symptoms
[68]	Jansen JP	2014	*Potentilla anserine* 30C, 200C; max 6 doses over 2 days	Double-blind, randomised, placebo-controlled, two parallel arms	Run-in observation 1 week - verum or placebo for 2 days - observation for 12 days	Total 10, verum 6 (30C: 4, 200C: 2), placebo 4, age range 30-55 years, male - 3, female - 7	Incidence rate per group not reported; feasibility issues addressed; proving symptoms list to be published elsewhere
[69]	Lalor L	2014	*Desmodium elegans* 30C, 200C; single dose, to repeat every 3 days	Single-arm, pre-post, interventional, two groups for two potencies	Not mentioned	Proving 1: Total 21, placebo 7, 200C - 7, 30C - 7; proving 2: placebo 3, 200C - 4, 30C - 6	Incidence rate per group not reported; proving symptoms enlisted

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Table 3: Contd...

Reference	First author	Year	Medicine, dosage	Study design	Study schedule	Volunteers	Results
[70]	Shukla C	2014	*Natural Silver*; potency or dosage not specified	Single-blind, pre-post, interventional, no control	Not mentioned	Total 22, no details	Proving symptoms enlisted; no further details
[71]	Scholten J	2015	*Paraponera clavata* (Bullet ant); direct bite of ants on arm	Self-proving	-	Single prover; male	Sequential record of 'proving' (bite) symptoms; no further details
[72]	Hatherly P	2015	*Lac macropi gigantei* (Kangaroo milk), *Uluru* (Ayer's Rock; dream/ contact proving), and *Brachychiton* rupestris (Queensland bottle tree; trituration); no further details.	Not mentioned	Not mentioned	Not mentioned	Proving symptoms enlisted; no further details
[73]	Salvi PS	2015	*Melopsittacus undulates* 30C; single dose; two provers repeated the dose after 2nd week	Double-blind; no further details	Not mentioned	Total 7; age range 25-40 years; male - 3, female - 4	Proving symptoms enlisted; no further details
[74]	van Helmond W	2015	*Melanerpes formicivorus* (Acorn Woodpecker); trituration C4	Single-blind (probably); no further details	Not mentioned	Total 6; no further details	Proving symptoms enlisted; no further details

OR: Odds ratio, SD: Standard deviation, CI: Confidence interval, CCRH: Central Council for Research in Homoeopathy, HPT: Homoeopathic pathogenetic trials, EEG: Electroencephalography

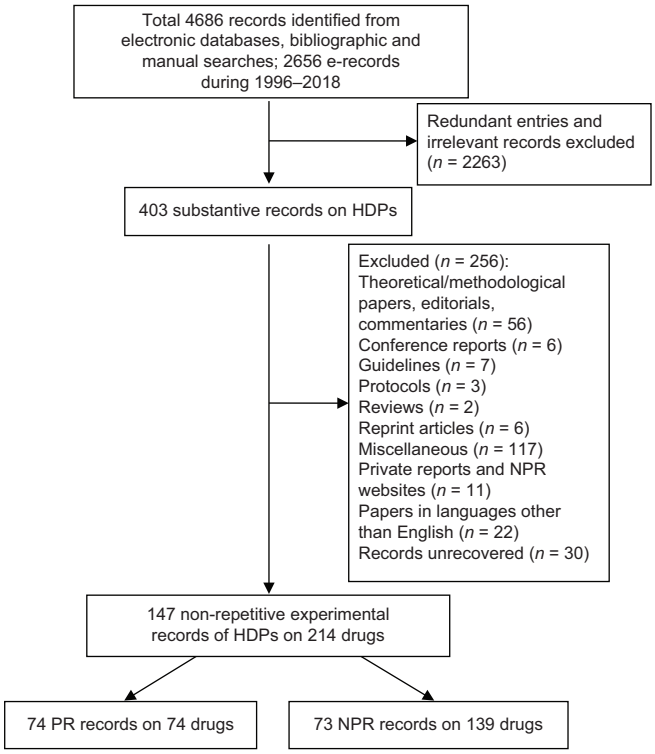

Figure 1: PRISMA flowchart: Inclusion and exclusion of records reporting HDPs and HPTs in Homoeopathy. PR: Peer-reviewed; NPR: Non-peer reviewed; HDPs: Homoeopathic drug provings; HPTs: Homoeopathic pathogenetic trials

to present all the recovered data in a standardised database. Owing to the narrative nature of this review, any conclusion regarding whether the results of provings are due to the placebo effect cannot be arrived at and is possible subsequent to the upcoming programme of meta-analysis, if feasible at all. There is a need to undertake similar exercise in publications in other languages, e.g., Spanish, German, Dutch, French, Portuguese and Russian, to the extent possible. Like the earlier systematic review,[2] groundwork scrutiny has again discovered substantial heterogeneity in the HDPs, especially in terms of study design or methodology, study population, intervention used, and outcome reporting. Most of the trials were randomised, double-blind, placebo-controlled, parallel arm design (HPTs); still, other study designs were also adopted. There were lacunae in the studies undertaken by CCRH, especially under-reporting, that is, the incidence rate of proving symptoms (=symptom producers) were not reported till 2007 papers. After that, selective reporting was identified in the verum group only, but inconsistently, till 2014. Since 2015, the incidence has been reported in both groups. Even though there were variations in reporting, the HPTs done by CCRH seem to be relatively homogenous.

The earlier systematic review concluded that the HPTs were of low methodological quality and were suffering from substantial heterogeneity.[2] Although we are in the process of developing psychometrically valid tool/criteria aimed at evaluating methodological qualities of HPTs consistently, overall heterogeneity of the studies still emerges. In contrast with the earlier systematic review by Dantas *et al*., this scoping review limits itself to systematic data extraction and charting only. We restrained from doing methodological quality scoring of the identified trials, because the scoring system – i.e., Methodological Quality Index (MQI) proposed by Dantas *et al*. has not been validated formally. Further,

Table 4: Alphabetical list of the 214 homoeopathic drugs proved during 1996-2018

Acalypha indica	*Cassia fistula*	Magnesium sulphuricum	*Pinus longaeva*
Acid butyricum	*Cassia sophera*	*Iridium*	*Piper methysticum*
Acidum ascorbicum	*Coleus aromaticus*	*Jalapa*	*Placenta suis*
Acidum cis aconiticum	*Cornus circinata*	*Juglans regia*	*Plumbum metallicum*
Acidum citricum	*Catharanthus roseus*	*Kalium tetraiodobismutate*	*Potentilla anserine*
Acidum ketoglutaricum	*Caulophyllum thalictroides*	*Lac macropi gigantei (Kangaroo milk)*	*Potentilla erecta*
Acidum malicum	*Cephalandra indica*	*Lachesis*	*Pothos foetidus*
Acidum oroticum	*Chelone*	*Lapis alba*	*Protea cynaroides*
Acidum succinicum	*Chromium kali sulphuratum*	*Lapis lazuli*	*Psoralea corylifolia*
Aconitum napellus	*Citrullus colocynthis*	*L-Cysteine*	*Pulsatilla*
Acorus calamus	*Clerodendron infortunatum*	*Leucas aspera*	*Pyridoxinum hydrochloricum*
Adenosine monophosphate	*Cochlearia armoracia*	*Leycesteria formosa*	*Pyrus americana*
ATP	*Coenzyme A*	*Liatris spicata*	*Rauwolfia serpentine*
Asclepias curassavica	*Columba livia*	*Loxodonta africana*	*Riboflavinum*
Agave americana	*Cuprum formicium*	*Luffa operculata*	*Riccia gangetica*
Agnus castus	*Cuprum oxydatum nigrum*	*Magnesium sulphuricum*	*Ricinus communis*
Apium graveolens	*Curcuma longa*	*Melatonin*	*Ribonucleic acid*
Argemone mexicana	*Cuscuta reflexa*	*Mahonia aquifolium*	*Rosa canina*
Arsenicum album	*Cyclosporin*	*Mangifera indica*	*Saraca indica*
Arsenicum bromatum	*Cynara scolymus*	*Magnolia grandiflora*	*Senega*
Alfalfa	*Datura arborea*	*Medulla ossis suis*	*Serotonin sulphate*
Allium sativum	*Datura metel*	*Melanerpes formicivorus*	*Silver* (Natural)
Amoora rohituka	*Desmodium elegans*	*Melopsittacus undulatus*	*Sinusitisinum*
Andrographis paniculata	*Embelia ribes*	*Mercurius*	Skookum chuck
Anthrachinon	*Embryo suis*	*Methylglyoxal*	*Staphylococcinum*
Aranea diadema	*Enallagma carunculatum*	*Mimosa humilis*	*Streptococcus nosode*
Aranea scinencia	*Ephedra vulgaris*	*Morpho menelaus occidentalis*	*Staphylococcus nosode*
Arteria suis	*Etna lava*	*Mucosa nasalis*	*Sulphur*
Ascophyllum nodosum	*Euphorbia lathyris*	*Mygale lasiodora*	*Symphytum officinale*
Avena sativa	*Ferrum muriaticum*	*Myosotis arvensis*	*Tarentula cubensis*
Ayahuasca	*Ficus religiosa*	*Nanocurcumin*	*Tarentula hispanica*
Azadirachta indica	*Foeniculum vulgare*	*Naphthochinon*	*Tela aranea*
Azathioprine	*Formic acid*	*Natrium oxaloaceticum*	*Terebinthina laricina*
Bacopa monnieri	*Fucus vesiculosus*	*Natrium pyruvicum*	*Terminalia chebula*
Bacterium coli	*Fumaria officinalis*	*Natrum muriaticum*	*Thea chinensis*
Glyoxal	*Funiculus umbilicalis*	*Nicotinamide*	*Theridion*
Baryta iodide	*Galphimia glauca*	*Nicotinamide adenine dinucleotide*	*Thiamini hydrochloricum*
Belladonna	*Geranium robertianum*	*Nyctanthes arbor-tristis*	*Thioctic acid*
Bellis perennis	*Glandula suprarenalis*	*Ocimum canum*	*Thymol*
Betula alba	*Glycyrrhiza glabra*	*Ocimum sanctum*	*Thyroidinum*
Boerhaavia diffusa	*Glyoxal*	*Okoubaka aubrevillei*	*Tinospora cordifolia*
Brachychiton rupestris	*Gymnema sylvestre*	*Oleander*	*Titanium metallicum*
Brassica oleracea	*Paraponera clavata (Bullet ant)*	*Oleum pini*	*Tribulus terrestris*
Bryonia alba	*Hepatitis C Nosode*	*Oxalis acetosella*	*Tylophora indica*
Bryonia dioica	*HIV Nosode*	*Oxytropis lamberti*	*Trichinoyl*
Buxus sempervirens	*Holarhenna antidysentrica*	*Ozone*	*Uluru (Ayers Rock)*
Caesalpinia bonducella	*Human growth hormone*	*Pancreas suis*	*Urtica urens*
Calendula officinalis	*Hydrochinon*	*Paraffin*	*Veronica officinalis*
Calotropis gigantea	*Hydrocotyle asiatica*	*Paraponera clavata (Bullet ant)*	*Vibhuti*
Cantharis	*Hydrogenium peroxidatum*	*Parthenium hysterophorus*	*Welwitschia mirabilis*
Capsicin and Dihydrocapsicin	*Hydroquinone*	*Glyoxal*	*Withania somnifera*
Cardiospermum halicacabum	*Hygrophila spinosa*	*Persea americana*	*Zinc gluconate*
Carica papaya	*Ichthyolum*	*Petroleum*	*Zincum aceticum*
Cartilago suis	*Insulin-like growth factor-1*	*Phyllanthus niruri*	

ATP: *Adenosine triphosphate*

our review was confined to the drug proving research trials published in English only, whereas Dantas *et al*. covered studies published in German, Dutch, French, Spanish and Portuguese also. In both the reviews, the authors of both the papers abstained from conducting meta-analysis due to substantial heterogeneity of data. One of the major problems in today's proving is that different countries are following different protocols for drug proving. Different schools have evolved with different lines of thought. This lack of uniformity generates substantial amount of heterogeneous data and poses a considerable threat to the reliability of the study findings. Previous systemic review of HPTs of 50 years published in six different languages covers 156 HPTs on 143 medicines, whereas in this scoping review of HPTs of 20 years, systemic review published in English language only includes 147 HPTs on 214 drugs. Thus, there has been a paradigm-shift in the last two decades towards conducting more HPTs than earlier. As we are in the process of developing tools for transparent assessment of internal validity of the trials, formal quality assessment of the HPTs will be done in the upcoming systematic review in the near future. The problem of heterogeneity can be resolved to a great extent by paying attention to the basic framework of protocol development and reporting following harmonised guidelines having enough scientific rigors. In comparison with the 'polychrest' ones, much importance has been given to rare or indigenous drugs. The authors believe that the research priority should not change from fragmentarily proved drugs or indigenous drugs, but the focus on the methodology adopted and transparency in reporting the results should increase. Further, focus should be to validate the signs/symptoms/syndromes developed during proving or claimed to be effect of proving substance.

Since publication of the earlier systematic review,[2] two different drug proving schools emerged and focused on different areas of interest. One of these schools preferred to keep HDPs for collecting new symptoms epistemologically separated from those designed to quantitatively test hypotheses about the generation of new symptoms. They continued carrying out HDPs in single arm, pre–post, interventional design without placebo control.[13] This study design is criticised for its inherent limitations, e.g., the placebo effect, the therapeutic relationship with the clinician (empathy, compassion, social desirability, etc.), the regression effect towards the mean and the effects of undisclosed interventions, if any. The other school considered HDPs as phase 1 clinical trials[13] and continued performing studies in double-blind, randomised, placebo- controlled, parallel arms design. This school generated heterogeneous data – either due to the absence of any standardised generic protocol for HPTs or due to under-reporting to a considerable extent. Both the schools, especially the former, adopting their own ideologies, generated an enormous display of symptoms – both generals and particulars. To some extent, the HPTs and phase 1 clinical trials are similar but overall clearly distinct from each other. Differences exist in terms of trial objectives, eligibility criteria, dosage of investigational medicinal product (IMP), endpoints and analysis of efficacy and safety. Similarity exists in terms of study designs – both single-arm trials as proof of concept and randomised, double-blind, parallel group or cross-over designs are adopted. Conventional phase 1 trials are actually non-therapeutic exploratory trials in usually healthy human subjects who can generally expect no therapeutic benefit from the IMP. These trials are performed to obtain pharmacokinetic, pharmacodynamic, toxicokinetic, safety, and tolerability data using dose escalation or repeat dose method following definite GCP/ICH guidelines with no obvious placebo control.[14]

The standardisation of a proving process and the quality of proving studies have been major considerations for research over the years.[15] HPT guidelines and protocols are being developed and continuously being updated,[16-21] and very recently, the latest harmonised guideline has been outlined by CCRH.[11] Checklist for quality assessment of HDPs needs to be developed further and adopted in adherence with the proposed one.[10] Still, some issues remain unaddressed, e.g., pre-defining dosage of the IMP in HPTs, which may contribute to the low prior probabilities to such an extent that it may make no sense.[22] Although a low theoretical prior probability is a questionable argument for rejecting further trials, because prior chance combined with Bayes' theorem demonstrates that extremely low priors are consecutively increased by new evidence that is positive.[23] However, the (prior) chances of producing symptoms with inert substances and toxic/poisonous substances in same dosage may influence the outcomes. Other potential sources of bias (e.g., age, sex, demographics, ethnicity, socio-economic status, food, religion and cultural practices) can be evaluated by undertaking intercontinental studies. The investigators should try to stick to the adopted strategies to minimise heterogeneity and generate reliable drug pictures in the future.

Conclusion

This scoping review helped in the identification of the HPTs/HDPs conducted between 1996 and 2018 and organised illustration of the trials in terms of study design, interventions, volunteers and overall results. Despite a clear trend of gradually improving quality in terms of adopted study designs, much heterogeneity still existed in study planning, execution and reporting. The 147 accepted records are the first for data recovery and assessing and analysing the possibility of conducting a systematic review and meta-analysis, which may include the HPTs published in other languages and is aimed at evaluating methodological qualities of the HPTs using valid criteria and statistical pooling of the trial results if the data permit.

Acknowledgement

We deeply acknowledge Dr Chaturbhuja Nayak, Former Director General, CCRH, Dr Alok Kumar, Former Director General In-Charge, CCRH, Dr Vikram Singh, Deputy Director, CCRH, Dr V A Siddiqui, Former Assistant Director (H), CCRH, and Dr Rajpal, Scientist-4, CCRH for their contribution towards the monitoring of Drug Proving Research Programme

of the Council. As this article has maximum research papers from the Council, the authors are grateful to the Drug Proving Masters for data collection for these trials. We gratefully acknowledge the active co-operation and participation made towards the study by the provers and the supporting staffs.

Financial support and sponsorship

The project was funded by Central Council for Research in Homoeopathy, under the Ministry of AYUSH.

Conflicts of interest

None declared.

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होम्योपैथिक दवा साबित करने वाले शोध (1996–2018): एक विस्तृत समीक्षा

पृष्ठभूमि : 1945–1995 से होम्योपैथिक रोगजनक परीक्षण (एचपीटी) पर एक व्यवस्थित समीक्षा 2007 में प्रकाशित हुई थी और यह बुनियादी सवाल था कि क्या स्वस्थ मानव स्वयंसेवकों में होम्योपैथिक दवाओं द्वारा उत्पादित प्रभाव के बराबर है या नहीं अनुत्तरित रहा हैं। पिछले दो दशकों में आयोजित एचपीटी की एक ऐसी समीक्षा करने की आवश्यकता है, जो कि अंगीकृत तरीकों में बदलावों का आकलन करे व इस बात का स्पष्ट रूप से निर्धारण करें कि स्वस्थ स्वयंसेवकों में उत्पन्न होने वाले प्रभाव उच्च घोल में होम्योपैथिक दवाओं के कारण है या नहीं।

उद्देश्य: 1996–2018 के दौरान प्रकाशित होम्योपैथिक पैथोजेनेटिक परीक्षणों की खोज, संग्रह, समीक्षा और वर्णन करना।

विधि: 1996 –2018 के बीच अंग्रेजी भाषा में प्रकाशित होम्योपैथिक साहित्य में एक व्यापक इलेक्ट्रॉनिक और मैनुअल साहित्य खोज ष्ब्द ष्होम्योपैथिक ड्रग प्रूविंग ष और ष्होम्योपैथिक रोगजनन परीक्षणष का उपयोग करके की गई। समावेशन और बहिष्करण मानदंडों के अनुसार, पूर्वनिर्धारित निष्कर्षण के रूप में आंकड़ों के निष्कर्षण के लिए दस्तावेजों का चयन किया गया था।

परिणाम: एक सौ सैंतालीस योग्यअभिलेख (74 पीयर रिव्यूड (पीआर) और 73 नॉन पीयर रिव्यूड (एनपीआर) की पहचान की गई और डेटा के निष्कर्षण के अधीन किया गया। केन्द्रीय होम्योपैथी अनुसंधान परिषद द्वारा 86 (24 पीआर और 62 एनपीआर) और 24 और 63 दवाओं के आंकड़े और एक पुस्तक रिले डीएस (एनपीआर) द्वारा 68 दवाओं के आंकड़ों द्वारा औषधि प्रमाणित साबित करने वाले अभिलेखों का योगदान दिया गया। सभी पहलुओं – रचना, आचरण, प्रतिभागियों, और परिणाम की सूचना में विषमता का सामना किया गया था।

निष्कर्ष: यह प्रारंभिक अध्ययन आंकड़ों की पुनःप्राप्ति के लिए और व्यवस्थित समीक्षा और मेटा–विश्लेशण के आगामी कार्यक्रम के लिए आधार है, जिसमें अन्य भाषाओं में प्रकाशित एचपीटी शामिल हो सकते हैं।

Recherches prouvant les médicaments homéopathiques (1996-2018): un examen de la portée

Contexte: Une revue systématique des essais homéopathiques pathogènes (ESPs) de 1945 à 1995 a été publiée en 2007 et la question fondamentale de savoir si l'effet produit par les médicaments homéopathiques chez des volontaires humains sains est équivalent à un placebo ou reste sans réponse. Il est nécessaire de reprendre un autre examen des ESPs effectués au cours des deux dernières décennies, pour évaluer les changements dans les méthodologies adaptées et si les effets produits chez des volontaires apparemment en bonne santé sont dus ou non à des médicaments homéopathiques à haute dilution.

Objectif: Rechercher, réunir, réviser et décrire les essais homéopathiques pathogénétiques publiés au cours de la période 1996-2018.

Méthodes: Une recherche documentaire complète, électronique et manuelle a été effectuée en utilisant les termes de recherche «homoeopathic drug proving» et «homoeopathic pathogenetic trial» avec une contrainte de temps de 1996-2018 en langue anglaise. Conformément aux critères d'inclusion et d'exclusion, les articles ont été sélectionnés pour l'extraction des données sous la forme d'extraction prédéfinie.

Résultats: Cent quarante-sept enregistrements éligibles (74 évalués par les pairs (PR) et 73 non évalués par les pairs (NPR)) de ESPs sur 214 médicaments ont été identifiés et soumis à l'extraction des données. La majorité des dossiers prouvant les médicaments ont été fournis par le Conseil central pour la recherche en homéopathie 86 (24 PR et 62 NPR) avec des données de 24 et 63 médicaments respectivement et par Riley DS, un livre (NPR) avec des données de 68 médicaments. Une hétérogénéité a été rencontrée dans tous les aspects - conception, conduite, participants et compte rendu des résultats.

Conclusion: Cette étude préliminaire est la base de la récupération des données et du prochain programme d'examen systématique et de méta-analyse qui peut inclure les ESPs publiés dans d'autres langues.

Investigaciones de patogenesias de medicamentos homeopáticos (1996-2018): Revisión sistemática (scoping)

Fundamentos: En 2007, se publicó una revisión sistemática de los Ensayos de Patogenesias Homeopáticas (EPH) de 1945 a 1995, quedando si respuesta la pregunta básica de su el efecto de los medicamentos homeopáticos en voluntarios sanos es equivalente o no al placebo. Se han de realizar otras revisiones de los EPH realizados en las últimas dos décadas para evaluar los cambios en las metodologías adaptadas y si los efectos generados en voluntarios sanos se deben o no a los medicamentos homeopáticos en altas diluciones.

Objetivos: Buscar, recopilar, revisar y describir los ensayos de patogenesias homeopáticas publicados de 1996 a 2018.

Métodos: Se efectuó una búsqueda bibliográfica integral, electrónica y manual, aplicando los términos de búsqueda *homoeopathicdrugproving* (patogenesia homeopática) y *homoeopathicpathogenetic trial* (ensayo de patogenesia homeopática) restringidos a la época de 1996 a 2018 en habla inglesa. Para la transferencia de datos al formulario de extracción predefinido, se seleccionaron los artículos que cumplían los criterios de inclusión y exclusión.

Resultados: Se identificaron 147 registros elegibles (74 revisados por pares [RP] y 73 no revisados por pares [NRP]) de los EPH de 214 medicamentos, los cuales se sometieron a extracción de datos. La mayoría de losregistros de prueba de drogas fueron aportados pordel CCRH (*Central Council forResearch in Homoeopathy*), (86; 24 RP y 62 NRP de 24 y 63 medicamentos, respectivamente) así como de Riley DS, un libro (NRP) con datos de 68 medicamento. Se observó heterogeneidad en todos los aspectos: diseño, realización, participantes e informes de los resultados.

Conclusiones: Este estudio preliminar constituye la base para la recuperación de datos ypara el programa futuro de la revisión sistemática y metaanálisis que pueden incluir los EPA publicados en otros idiomas.

Homöopathische Drogenprüfung forscht(1996-2018): UmfangÜberprüfung (1996-2018): EinÜberblicküber den Anwendungsbereich

Hintergrund: EinesystematischeÜbersichtüberhomöopathischepathogenetischeStudien (HPTs) von 1945-1995 wurde 2007 veröffentlicht, und die grundlegendeFrage, ob die WirkunghomöopathischerArzneimittelbeigesundenmenschlichenProbandenmit Placebo gleichwertigistoderanderweitigunbeantwortetbleibt, wurdenichtbeantwortet. Esbesteht die Notwendigkeit, einweitereÜberprüfung der HPTs der letztenzweiJahrzehnteaufzugreifen, um die Veränderungen in den angepasstenMethodenzubewerten und um zubeurteilen, ob die beischeinbargesundenFreiwilligenerzeugtenEffekte auf homöopathischeMedikamente in hoherVerdünnungzurückzuführensindodernicht.

Ziel: Suche, Sammlung, Überprüfung und Beschreibung von homöopathischenpathogenetischenStudien, die zwischen 1996-2018 veröffentlichtwurden.

Methoden: EineumfassendeLiteraturrecherche, elektronisch und manuell, wurdemit den Suchbegriffen 'homöopathischeArzneimittelprüfung' und 'homöopathisch-pathogenetischeStudie' mitZeitbeschränkung von 1996-2018 in englischerSprachedurchgeführt. Entsprechend den Ein- und Ausschlusskriterienwurden die Papierefür die Extraktion von Daten in der vordefiniertenExtraktionsformausgewählt.

Ergebnisse: Einhundertvierzigsieben in FragekommendeDatensätze (74 Peer-Review- (PR) und 73 nicht Peer-Review- (NPR)) von HPTs zu 214 Medikamentenwurdenidentifiziert und einerDatenextraktionunterzogen. Die Mehrheit der UnterlagenzumNachweis von ArzneimittelnwurdevomZentralratfürForschung in der Homöopathie 86 (24 PR und 62 NPR) mitDaten von 24 bzw. 63 Arzneimitteln und von Riley DS, einemBuch (NPR) mitDaten von 68 Arzneimitteln, beigesteuert.Heterogenitätwurde in allenAspekten - Design, Durchführung, Teilnehmer und Ergebnisberichterstattung - festgestellt.

Schlussfolgerung: DiesevorläufigeStudieist die Grundlagefür die Datenwiederherstellung und für das bevorstehendeProgramm der systematischenÜberprüfung und Meta-Analyse, das auch die in anderenSprachenveröffentlichten HPTs umfassenkann.

順勢療法藥物驗證研究（1996-2018）：範圍綜述

背景：對1945-1995年的順勢療法致病性測試（Homoeopathic Pathogenetic Trials，HPTs）進行的系統回顧在2007年發表，究竟順勢療法藥物在健康志願者身上產生的作用是否等同於安慰劑這個基本問題仍然未有答案。對過去20年中進行的HPTs進行另一次回顧是有需要的，以評估所採用方法的變化，以及明顯健康的志願者所產生的影響是否由於高稀釋度的順勢療法藥物所致。

目的：尋找、收集、回顧和描述1996-2018年間發表的順勢療法致病性測試。

方法：採用英文檢索詞「homoeopathic drug proving」（順勢療法藥物驗證）和「homoeopathic pathogenetic trial」（順勢療法致病性測試）及1996-2018年的時間限制進行文獻檢索、電子檢索和手工檢索。根據納入和排除準則，論文選擇以預先定義的抽取形式抽取數據。

結果：共識別出147個HPTs的合格記錄（74份同行評審（peer-reviewed，PR）和73份非同行評審（non peer-reviewed，NPR））包括214種藥物，並進行了數據提取。絕大多數的藥物驗證記錄都是由順勢療法研究中央委員會提供的，86個記錄（24 PR和62 NPR）分別包括24種和63種藥物；以及由Riley DS提供，有一本書（NPR）包括68種藥物。異質性存在於各個方面——設計、實驗方法、參與者和結果報告。

結論：此初步研究爲數據恢復和下一步的系統回顧和薈萃分析提供基礎，這可能將包括以其他語言發表的HPTs。