Indian Journal of Traditional Knowledge
Vol 24(8), August 2025, pp 742-748
DOI: 10.56042/ijtk.v24i8.15558

Repurposing randomized, controlled, double-blinded homeopathic pathogenetic trial for determining the expiry of ultra-high diluted homeopathic drugs

Kurian Poruthukaren[a,b,*] & Vivek Sakthidharan[b,c]
[a]Department of Repertory, Yenepoya Homoeopathic Medical College, Yenepoya (Deemed to be University), AYUSH campus, Mangaluru 575 018
[b]Father Muller Homoeopathic Medical College, Deralakatte, Mangaluru 575 018
[c]Department of Homoeopathic Pharmacy, Government Homoeopathic Medical College, Iranimuttom, Thiruvananthapuram 695 009, India
[*]E-mail: drpjkurian@yenepoya.edu.in

Received 06 December 2024; revised 03 July 2025; accepted 30 July 2025

Unlike conventional pharmaceuticals, ultra-high diluted homeopathic drugs lack measurable molecular content, posing challenges for scientific expiry determination. Currently, global regulatory agencies apply arbitrary expiry durations, risking either premature disposal or prolonged use beyond efficacy. We aimed to propose and test a scientifically valid method for determining the expiry of ultra-high diluted homeopathic drugs by repurposing randomized, double-blind, placebo-controlled pathogenetic trials. We conducted the trial using *Allium cepa* 30C, a drug with a well-documented pathogenetic profile. We randomly assigned thirty-six healthy volunteers to: freshly prepared *Allium cepa* - New *Allium cepa*, 16-year-old *Allium cepa*, and the placebo. Participants recorded symptoms over seven days. We extracted and analyzed the symptom elements (location, sensation, modality). We used Jaccard similarity indices to estimate trial noise. Statistical analyses included the Kruskal-Wallis test and post-hoc comparisons. We calculated the effect size using epsilon squared. The New *Allium cepa* group showed the highest symptom production. The old *Allium cepa* group demonstrated a 59.61% reduction in pathogenetic ability compared to the New *Allium cepa*. While the difference was insignificant ($p = 0.108$), a large effect size ($\varepsilon^2 = 0.193$) indicated a potentially meaningful difference. Placebo had the fewest responses and symptom elements. We propose that the repurposed homeopathic pathogenetic trials provide a scientific, reproducible model to assess the expiry of ultra-high diluted homeopathic drugs. This novel approach may aid in developing global regulatory standards and enhance the reliability of homoeopathic practice.

Keywords: Drug evaluation, Drug stability, Homeopathic pathogenetic trials, Homeopathy

IPC Code: Int Cl.[25]: A61K 36/00, A61K 9/00

A drug's expiry date is a point in the time when its effectiveness, stability, and safety are within unacceptable limits. The regulatory guidelines of modern medicine define the expiry of a drug as the diminishment of its effectiveness to 90% of the stated label claim. These guidelines also insist on exhibiting the expiry dates on the product's label[1]. It is common knowledge that the expiry of the drugs should be determined scientifically. However, in homeopathy, the expiry is determined arbitrarily. For instance, the regulatory guidelines of India[2] suggest an arbitrary expiry of a maximum of five years for all homeopathic products, except homeopathic dilutions[3]. Contrastingly, the United States Food & Drugs Administration[4] regulatory guidelines exempt homeopathic manufacturers from exhibiting expiry dates for all homeopathic products, implying non-expiry of homeopathic products. In addition to arbitrarily determining the expiry, the practitioners of homeopathy often rely on the non-validated clinical experiences of other practitioners[5]. For instance, Hahnemann - the founder of Homeopathy - stated that the pills medicated by homeopathic dilutions retain their medicinal virtues for 18 to 20 years if they are protected from heat and sunlight[6]. Later, he modified his statement and stated that the medicated pills retain their medicinal virtues for many years if protected from heat and sunlight[7]. Thus, the expiry of homeopathic products is determined unscientifically.

Sophisticated instruments like high-performance liquid chromatography, high-performance thin layer liquid chromatography, gas chromatography-mass spectrometry, etc[8] may be used for determining the expiry of mother tinctures and lower dilutions drugs –

[*]Corresponding author

homeopathic drugs lower than 12C – by estimating the appropriate chemical markers. However, these sophisticated instruments fail to detect the chemical markers in ultra-high dilutions: homeopathic drugs higher than 12C. Therefore, these instruments cannot determine the expiry of ultra-high dilutions by estimating the chemical markers. Many researchers tried to assess the biological activity of ultra-high dilutions by conducting biological assays[9]. However, these assays produced variable results[8]. Therefore, these assays are incapable of determining the expiry of ultra-high dilutions. In this scenario, we propose repurposing the double-blinded, randomized, controlled homeopathic pathogenetic trials to determine the ultra-high dilutions' expiry. Currently, researchers of homeopathy conduct these pathogenetic trials to ascertain the symptoms produced by the trial drug. These symptoms are known as symptom pictures or remedy pictures. Homeopathic practitioners use these pictures of symptoms to identify remedies for their patients.

We recommend these pathogenetic trials for determining the expiry of ultra-high dilutions because these trials are validated[10], generating reproducible symptom pictures that are recognizable[11,12] and specific[13,14] to the ultra-high dilution taken by the trial participant.

To determine the expiry, we suggest two steps. The first step is using the homeopathic pathogenetic trials to estimate the pathogenetic ability of ultra-high dilutions. Pathogenetic ability is the ability of the trial drug to produce symptoms in healthy humans, and it is estimated by counting the number of elements produced by the trial participants. The elements are distinct components of symptoms: locations, sensations, and modalities[15]. Counting the elements instead of symptoms provides the advantage of identifying and nullifying the noises in the homeopathic pathogenetic trial. Noises[16] are the elements (distinct components of symptoms) produced by the trial participants due to confounding factors such as spontaneous changes in daily life, myriad events, and life incidents. The second step is comparing the pathogenetic abilities of the old and the new ultra-high dilution using statistical tools.

We selected old pills of *Allium cepa* that were prepared 16 years ago (2003) to determine the expiry. These pills are cane sugar pills (sucrose). It became brown apparently due to the chemical reaction known as browning[17]: an amino–carbonyl reaction taking place during prolonged storage. This chemical reaction can alter the chemical composition of the pills[18]. Moreover, factors like temperature fluctuation and humidity affected the pills.

In the current study, we hypothesize that the old pills of *Allium cepa* expired due to the browning reaction, diminishing its pathogenetic ability compared to the recently manufactured *Allium cepa*. We selected *Allium cepa* because it has the least duration of pathogenetic action: one day[19].

Methods

The homeopathic pathogenetic trial was a randomized (1:1:1:1), double-blinded, placebo-controlled, parallel-group, cross-over design. During the trial, we removed the cross-over design because we failed to obtain 30 days of continuous symptom-free in the participants during the wash-out period. The effect modifiers (changes in food, weather, domestic situation) influenced the participants during the prolonged wash-out period.

After obtaining the participant's informed consent, we recruited them from the teaching faculty and the students of a homeopathic medical institute. The eligibility criteria for recruiting the participants to the trial are in Table 1. The principal author interviewed all the participants to obtain their present health status and history of any health issues that might be an effect modifier (hysterical tendencies, allergic tendencies). We established the baseline characteristics of each participant using day book entries 3 - 4 days before the trial. We followed the guidelines mentioned in the Homeopathic Pharmacopoeia Convention of the United States[20] for determining the sample size: a minimum of 10 participants in each arm.

Table 1 — Inclusion & Exclusion Criteria

Inclusion criteria	Exclusion criteria
1. Age: Above 18 years of age.	1. Hysterical or anxious individuals (such individuals display a high incidence of Placebo effects).
2. Sex: Both male and female individuals.	2. Individuals having a history of allergies and food hypersensitivity.
3. Individuals certified healthy as per pre-trial/post-trial medical report proforma.	3. Women during pregnancy, puerperium, and breastfeeding.
4. Individuals who were not on any medications for two months before the commencement of the trial.	4. Those who had taken birth control pills for six months before the commencement of the trial.
	5. Individuals having addictions - alcohol, narcotics, tobacco
	6. Individuals who have undergone surgery in the last two months.
	7. Individuals participated in other clinical/pathogenetic trials for six months before the commencement of the trial.

We conducted the trial at a homeopathy institute in South India from November 2019 to February 2020. We completed the trial within that period to avoid the influence of an effect modifier: change of weather.

We prepared three categories of number 20-sized sucrose pills for the trial: pills medicated with recently (February 2019) manufactured *Allium cepa* 30C – the new *Allium cepa* - manufactured by Father Muller Homeopathic Pharmaceutical division; pills medicated 16 years ago with *Allium cepa* – the old *Allium cepa* - manufactured by Dr. Willmar Schwabe (September 2003, Batch number 2372186); and pills moistened with 95% v/v ethyl alcohol - the placebo. Both manufacturers followed the guidelines of Homeopathic Pharmacopoeia of India for manufacturing the *Allium cepa* 30C. The old *Allium cepa* pills were stored in an amber-colored glass bottle, kept in a cool, dark place (inside a carton box), and protected from direct heat and sunlight. The bottle was opened multiple times between 2003 and 2019 for dispensing. During this period, the pills were exposed to fluctuations in temperature and humidity typical of a tropical monsoon climate. We did not perform any periodic quality control checks on the pills.

The participants were randomly allocated to four arms: A, B, C, and D, using the systematic random sampling technique, and used the random.org[21] website to generate the random sequence. The participants of Group A received the new *Allium cepa*; the participants of Group B received the old *Allium cepa*; the participants of Groups C and D received the placebo. The participants and the investigators were blinded; the drugs were coded; and the codes were secured in a sealed envelope.

Four pills were adminstered four times a day for up to one week to the participants. The pills were crushed in lactose powder (3 g - 4 g) before administering them to the participants. Crushing these pills in the lactose ensured similarity in appearance and uniformity in dosage. We considered the symptoms produced within one week after the intervention as the primary endpoint. We advised the participants to stop the medication when they develop symptoms, to report to us when they develop symptoms, and to note down their symptoms in the day book provided to them. The principal author went through the day books of all the participants, confirmed their symptoms in the day book by interviewing them, and clarified some of the symptoms regarding their location, sensation, and modalities.

The primary outcome was the number of elements of symptoms produced by each group. We confirmed the hypothesis by conducting the Kruskal-Wallis test, followed by post-hoc and effect size analyses; all performed using Jamovi software (version 2.3.15.0, available at https://www.jamovi.org/) on Ubuntu 24.04.2 (available at https://ubuntu.com/desktop). We computed the magnitude of the noises in the pathogenetic trial by estimating the Jaccard similarity index[22] and deducted these noises while estimating the pathogenetic ability of the drugs. We performed the index computation in the LibreOffice Calc software (version 6.4.7.2, available at https://www.libreoffice.org/) installed in Ubuntu 20.04.4.

The Institutional Ethics Committee approved the research proposal on 26/11/18. The reference number is FMIEC/CCM/06/2018. We registered the trial in the Clinical Trial Registry of India. The registration number is CTRI/2019/01/016859.

Results

Figure 1 shows the participant's flow. We observed the pathogenetic ability of the old *Allium cepa*

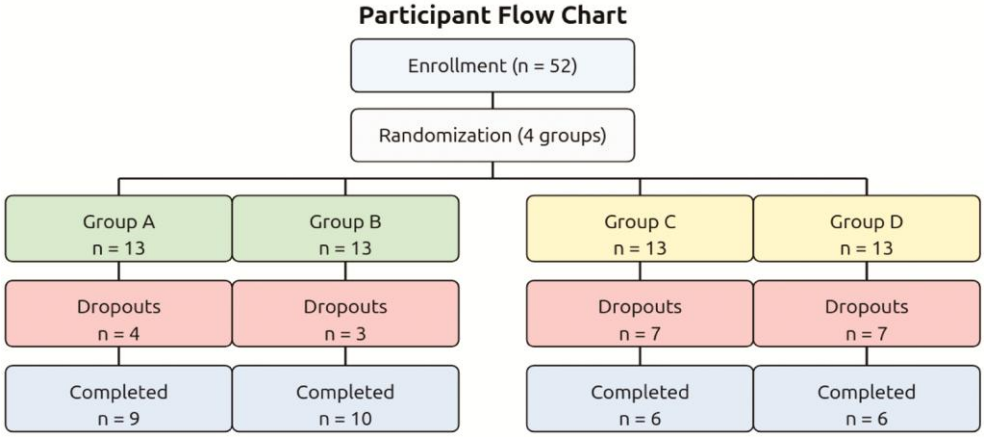

Fig. 1 — Participants flow chart. Group A: New *Allium cepa;* Group B*:* Old *Allium cepa;* Group C & D*:* Placebo

59.61% less than the new *Allium cepa* - $\frac{52-21}{52}x100$. Table 2 shows the pathogenetic ability of the *Allium cepa* and the noises. Additionally, the old *Allium cepa* exhibited 49% lesser response than the new *Allium cepa:* 4 out of 10 participants responded to the old *Allium cepa;* 8 out of 9 participants responded to the new *Allium cepa.* Table 3 shows these responses.

Furthermore, the mean value of elements per participant for the old *Allium cepa* was 53.7% lower than the new *Allium cepa* - Old *Allium cepa:* 5.43(SD 6.37); New *Allium cepa:* 10.10 (SD 6.37). In Figure 2, the Box and the whisker diagram show the declining trend of the elements per participant. The new *Allium cepa* has the maximum elements, and the placebo has the least. The figure also hints that 50% of the participants in the placebo group had no symptoms. We obtained close-by values for the Jaccard similarity indices for the new and old *Allium cepa* (Table 2). These close-by values depict a similar magnitude of noises in both groups.

Although there is an apparent difference between the pathogenetic ability of the new and the old *Allium cepa*, the Kruskal-Wallis test depicted that difference as non-significant. Table 4 shows the p-value as 0.108 at a 95% confidence interval. Furthermore, the post-hoc analysis also depicted a non-significant difference among the pairs. Table 5 shows the p-value of the analysis. We derived information from the data of 24 participants. We merged the participants of groups C and D (placebo) to state the result. Table 6 displays the symptoms and the elements of each group.

The participants did not report any serious adverse events, severe aggravation or unintended effects during the trial.

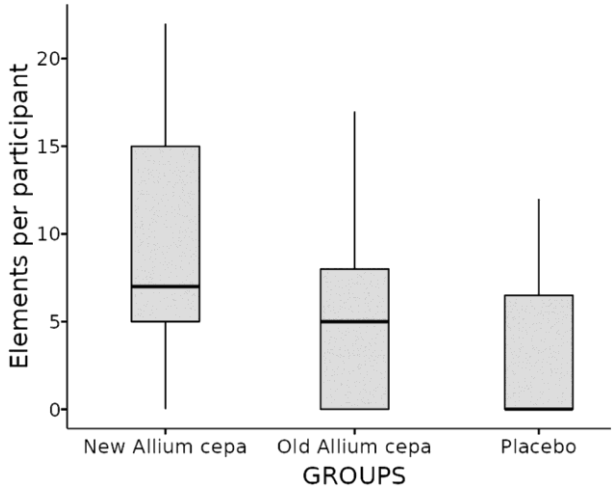

Fig. 2 — Elements per participant from each group. The elements are distinct components of symptoms

Table 2 — Estimation of the pathogenetic ability, and the noises in the new & the old *Allium cepa* groups.

Intervention groups	Cumulative number of elements* in the intervention group (I)	Cumulative number of elements in the placebo group (P)	Cumulative number of elements of intervention group common to the placebo group. $I \cap P$	Aggregate of the elements of intervention and placebo groups $I \cup P$	Jaccard similarity index $\frac{I \cap P}{I \cup P}$	Pathogenetic ability**
New *Allium cepa* (prepared in 2019)	61	23	9	61+23- 9 = 75	9/75 = 0.120 (12.00%)	61-9 = 52 elements
Old *Allium cepa* (prepared in 2003)	27	23	6	27+23- 6 = 44	6/44 = 0.136 (13.6%)	27-6 = 21 elements

*Elements are units of symptoms: Location, Sensation, and Modalities. 'I' is the intervention group (*Allium cepa*), and 'P' is the placebo group.
**The noises are reduced from the elements' aggregate to estimate each drug's pathogenetic ability.

Table 3 — Distribution of participants into various groups, their mean age with standard deviation, and gender frequency

Intervention	Age – Mean with Standard deviation	The number of participants who produced symptoms and included for data analysis.	The number of participants who did not produce any symptoms and included for data analysis.	The number of participants whose symptoms were excluded due to doubtful origin.*	The total number of participants with the frequency of gender in brackets.
Group A -New *Allium cepa* (prepared in 2019)	20.66 (SD 2.59)	8	1	0	9 (6 females, and 3 males)
Group B - Old *Allium cepa* (prepared in 2003)	22.10 (SD 4.90)	4	3	3	10 (9 females, and 1 male)
Group C & D - Placebo	22.58 (SD 5.82)	3	5	4	12 (6 females, and 6 males)
Total		15	9	7	31 (21 females, and 10 males)

*Various reasons for doubtful origin are: the excitement of emotions; injury to gums, hence emergency treatment; expected symptoms during that season; "got infected from room-mates"; consumed certain drugs unwittingly during the trial.

Discussion

This study suggests that the old *Allium cepa* pills may have retained some pathogenetic activity. We observed a non-significant difference in pathogenetic effects between the old and new *Allium cepa* preparations (p = 0.182). Our results align with Adler *et al.*[23], who demonstrated pathogenetic activity in 25-year-old ultra-high dilutions of *Opium* and *Erythroxylum coca*.

Table 4 — Kruskal-Wallis test to determine significant differences in the pathogenetic ability of the new *Allium cepa*, the old *Allium cepa* and the placebo group

Groups	χ^2	Degrees of freedom	P value (95% confidence interval)	Effect size ε^2
New *Allium cepa*				
Old *Allium cepa*		2	0.108	0.193
Placebo	4.44			

Table 5 — Post hoc analysis by Dwass-Steel-Critchlow-Fligner test for pairwise comparisons

Pair	Standardized test statistic value	P value (95% confidence interval)
New *Allium cepa* - Old *Allium cepa*	-1.88	0.376
New *Allium cepa* - Placebo	-2.853	0.108
Old *Allium cepa* - Placebo	-0.889	0.805

Table 6 — The list of symptoms of *Allium cepa* as observed in the trial participants belonging to different groups

Group	Symptoms collated from the participants	Elements* of the symptoms
New *Allium cepa* – Group A	Fever: heat in the head; burning eyes$_2$; hot breath; throat pain; mucous discharge from the nose; headache, predominantly forehead; sneezing$_3$** aggravated in the morning$_2$ and afternoon; mucous discharge from the nose$_2$; heat all over the body; aggravated during menses; itching of eyes with frontal headache; pain in umbilicus ameliorated by pressure; increased thirst; waking frequently from sleep; mouth ulcer inside lower lip; heaviness of head$_2$, and tight feeling of head aggravated by: physical exertion, light, eye strain, closing of eyes, cold exposure, and movement of head; ameliorated by lying down, and pressure$_3$; posterior nasal discharge; dryness of eyes; unrefreshing sleep; nose block; nausea; vertigo; tremors in hand; loss of power in hand; loss of appetite for lunch; mouth ulcers; did not feel urge to pass stool; bad breath; bursting pain$_2$ in left forehead, aggravated by sun, eye strain; ameliorated by stooping; pulling pain around eyes; unsatisfied stool, aggravated at night; weakness after stool; tightness of abdomen ameliorated by passing stool; constricting pain in the right side of the occiput; aggravated in the evening.	{Head, heat in head, eyes, burning in eyes, hot breath, throat, throat pain, nose, mucous discharge from the nose, headache, forehead, sneezing, aggravated in the morning, aggravated in the afternoon, heat all over the body, aggravated during the menses, itching of the eyes, frontal headache, umbilicus, pain in umbilicus, ameliorated by pressure, thirst increased, waking frequency from sleep, mouth, mouth ulcer, heaviness of head, tight feeling of head, aggravated by physical exertion, aggravated by light, aggravated by eye strain, aggravated by closing eyes, aggravated by cold exposure, aggravated by movement of head, ameliorated by lying down, posterior nasal discharge, lower extremities, dryness of eyes, un-refreshing sleep, nose block, nausea, vertigo, hand, tremors in hand, loss of appetite for lunch, loss of power in hand, did not feel the urge to pass stool, bad breath, bursting pain in the forehead, aggravated by the sun, bursting pain in the head, ameliorated by stooping, pulling pain around the eyes, unsatisfied stool, aggravated at night, weakness after stool, abdomen, tightness of abdomen, ameliorated by passing stool, occiput, constricting pain in the occiput, aggravated in the evening}
Old *Allium cepa* – Group B	Nose block$_3$ with drowsiness, followed by throat pain; throat pain aggravated by swallowing; heat all over the body; itching in the throat; pulsating pain from occiput to frontal, aggravated by stooping; heaviness of head; mucous discharge$_2$ from the nose, aggravated at night; appetite increased in the morning; sleep unrefreshing; ear pain, more on right side, pain extending to the throat, aggravated by swallowing, and talking; irritation in the throat, aggravated in the morning$_2$; sneezing in the evening; sensation of dryness of eyes with lachrymation.	{Nose, nose block, drowsiness, throat, throat pain, aggravated by swallowing, heat all over the body, itching in the throat, pulsating pain in the head, head (occiput to frontal), heaviness in the head, aggravated by stooping, mucous discharge from the nose, aggravated at night, appetite increased, aggravated in the morning, sleep unrefreshing, ear, ear pain, pain extending from the ear to throat, aggravated by talking, irritation in the throat, sneezing, aggravated in the evening, eyes, dryness of eyes, lachrymation}
Placebo – Group C & D	Awakened from sleep – around 3 am - due to pain in abdomen; discomfort in epigastrium with nausea; empty eructation and passing offensive flatus; Mucus secretion from nose$_2$ with partial heat on face; sneezing$_2$ due to irritation in nose; appetite increased; heaviness of head; itching of skin without eruption; aggravation by cold temperature. Burning in eyes; appetite diminished.	{Abdomen, pain in abdomen, waking from sleep due to pain, 3 am aggravation, discomfort in epigastrium***, nausea, empty eructation, offensive flatus, nose, mucus discharge from nose, face, heat in face, sneezing, irritation in nose, appetite increased, head, heaviness of head, skin, itching without eruption, aggravated by cold temperature, eyes, burning in eyes, appetite diminished}

*Elements are distinct components of symptoms – Location, sensation, and modalities.**The subscript numbers denote the frequency of the symptoms.***The element 'abdomen' includes the epigastrium, hence not included as a separate element.

However, we are cautious while interpreting the results. Although the Kruskal-Wallis test did not reach statistical significance, the large effect size (ε^2 = 0.193) indicates a potentially meaningful difference between groups. We observed a trend in the number of symptoms reported: new *Allium cepa* induced the most symptoms, followed by old *Allium cepa*, with placebo inducing the least. This pattern of diminishing pathogenetic ability is noteworthy and may represent a gradual loss of efficacy with aging.

The Dwass-Steel-Critchlow-Fligner pair wise comparisons also failed to reach significance. However, the largest difference was found between the new *Allium cepa* and placebo, while the smallest difference occurred between the old *Allium cepa* and placebo. This suggests that the old preparation's pathogenetic ability may resemble placebo more closely than the new preparation. The overall effect size might largely stem from the contrast between the new preparation and placebo.

A key limitation of this trial is the small sample size, which may have resulted in insufficient power to detect significant differences. Although this reduces the external validity of the findings, the large effect size suggests that replication with a larger sample may support the hypothesis that old *Allium cepa* pills have diminished efficacy due to aging. Another limitation involves the indirect nature of the expiry assessment. While the study was randomized, placebo-controlled, double-blinded, and included noise estimation, it remains susceptible to confounders. Notably, whether the aging affected the sucrose pills, the 30C dilution, or both is unclear. Moreover, the *Allium cepa* used in the old and new preparations came from different botanical sources, limiting direct comparability. Therefore, homeopathic pathogenetic trials may more accurately determine the expiry of ultra-high dilutions of mineral origin stored in ethanol (which may minimize pill-related variability).

Despite these limitations, the observed 59.61% reduction in pathogenetic ability in the old preparation may hold clinical relevance. Importantly, this trial presents a scientific method for assessing the expiry of homeopathic products based on their pathogenetic effect- a novel and practical approach.

Conclusion

We propose a scientific, reproducible method for determining the expiry of homeopathic ultra-high dilutions through structured trials. To our knowledge, this is the first method of its kind.

This approach can potentially evaluate the effects of various factors- such as storage materials, ultraviolet and infrared radiation, temperature, and X-ray exposure- on ultra-high dilutions. If validated in multi-centric studies, this method may contribute to developing globally harmonized expiry standards for homeopathic drugs. Currently, regulations vary from country to country. A standardized scientific approach, as proposed here, could bridge such regulatory gaps and offer a foundation for evidence-based policy across countries.

Although this method is time-intensive, it represents a step forward in the scientific validation of homeopathic preparations. In the future, it may complement laboratory-based techniques and pave the way toward simpler, reliable tools for determining the shelf life of ultra-high dilutions.

Acknowledgments

Authors acknowledge Ms Sushma N Bhat, Department of Bio-Medical Engineering, MGM College of Engineering and Technology, Navi Mumbai, Maharashtra, India, for providing input during data analysis.

Authors thank Father Muller Homoeopathic Medical College, Mangaluru, India, for providing logistic support.

Funding

The Rajiv Gandhi University of Health Sciences, Bangalore, Karnataka, India, funded the trial. [Grant number RGU: RGU/ADV.RES/BR/018/2018-19]

Conflict of Interest

Authors declare that there is no competing or conflict of interest.

Author Contributions

KP contributed to the conceptualization, formal analysis, funding acquisition, supervision, writing - original draft, review, and editing. VS contributed to the conceptualization, formal analysis, funding acquisition, supervision, writing - review, and editing.

Ethics Approval

The Institutional Ethics Committee approved the research proposal on 26/11/18. The reference number is FMIEC/CCM/06/2018. We followed the required procedure of securing ‘informed consent’ from each participant.

Data Availability

The manuscript contains all the data required to justify the conclusions. However, the corresponding author will share the data upon reasonable request.

References

1 Dawson M, Expiry dates, *Aust Prescr*, 17 (1994) 46-48. https://doi.org/10.18773/austprescr.1994.051

2 Ministry of health and family welfare, Government of India, *Drugs and Cosmetics (5th Amendment) Rules, 2006*, The Gazette of India; PART II- Section 3- Sub-section (i); 2006.

3 Ministry of health and family welfare, Government of India, *Drugs and Cosmetics (11 Th Amendment) Rules, 2017*, The Gazette of India; PART II- Section 3- Sub-section (i); 2017.

4 Homeopathic Pharmacopœia of the United States, *HPUS Homeopathic Drug Stability Guidelines*, (April) (2014) 3-5. https://www.hpus.com/homeopathic-drug-stability-guidelines-4-14.pdf

5 Valavan R & Cesar A, Current status of expiry of homeopathic medicines in Brazil, Germany, India and the United States: A critical review, *Homeopathy*, 108 (4) (2019) 232-239. https://doi.org/10.1055/s-0039-1692208

6 Hahnemann S, *Organon of medicine* - Fifth edition, translated by R E Dudgeon, (Indian Books & Periodicals Publishers, New Delhi), Footnote to aphorism, 288 (2012).

7 Hahnemann S, *Organon of medicine* – 6th edition, Kunzili J, Naude A, Pendleton P, (Eds), (JP Tarcher, J P Tarcher Inc, Los Angeles), Footnote to aphorism, 272 (1982).

8 Kardile M V, Patil C, Haidar A, Mahajan U B & Goyal S, Homeopathic drug standardization through biological evaluations: An untrodden avenue, *Int J High Dilution Res*, 14 (4) (2015) 16-37. https://doi.org/10.51910/ijhdr.v14i4.768

9 Witt C M, Bluth M, Albrecht H, Weißhuhn T E R, Baumgartner S, *et al*., The *in vitro* evidence for an effect of high homeopathic potencies – A systematic review of the literature, *Complement Ther Med*, 15 (2) (2007) 128-138. https://doi.org/10.1016/j.ctim.2007.01.011

10 Sherr J, Quirk T & Tournier A L, Do homeopathic pathogenetic trials generate recognisable and reproducible symptom pictures? Results from a pilot pathogenetic trial of Ozone 30c, *Homeopathy*, 103 (2) (2014) 108-112. https://doi.org/10.1016/j.homp.2013.12.001

11 Vickers A, McCarney R, Fisher P & van Haselen R, Can homeopaths detect homeopathic medicines? A pilot study for a randomised, double-blind, placebo controlled investigation of the proving hypothesis, *Br Homeopath J*, 90 (3) (2001) 126-130. https://doi.org/10.1054/homp.1999.0475

12 Piltan D, Rist L, Simões-Wüst P & Saller R, Test of a Homeopathic Dilution of Aconitum napellus, *Complement Med Res*, 16 (3) (2009) 168-173. https://doi.org/10.1159/000219316

13 Walach H, Möllinger H, Sherr J & Schneider R, Homeopathic pathogenetic trials produce more specific than non-specific symptoms: results from two double-blind placebo controlled trials, *J Psychopharmacol*, 22 (5) (2008) 543-552. https://doi.org/10.1177/0269881108091259

14 Möllinger H, Schneider R & Walach H, Homeopathic pathogenetic trials produce specific symptoms different from placebo, *Complement Med Res*, 16 (2) (2009) 105-110. https://doi.org/10.1159/000209386

15 Boenninghausen C V, *Boenninghausen's Therapeutic Pocket Book*, translated by Allen T F, (B Jain Publishers Private Limited, New Delhi, India), (2003) p. 19.

16 Dantas F, Fisher P, Rastogi D P, Teixeira H, Eizayaga J, *et al*., Authors' response: we must distinguish symptoms caused by the medicine from other symptoms, *Homeopathy*, 96 (4) (2007) 275-276. https://doi.org/10.1016/j.homp.2007.08.004

17 Friedman M, Food browning and its prevention: An overview, *J Agric Food Chem*, 44 (3) (1996) 631-653. https://doi.org/10.1021/jf950394r

18 Kaanane A & Labuza T P, The Maillard reaction in foods, *Prog Clin Biol Res*, 304 (1989) 301-327.

19 Miller R G, *Relationship of Remedies: With Approximate Duration of Action*, (Homoeopathic Pub. Co, London), (1910) p.01.

20 Homeopathic Pharmacopœia Convention of the United States, *HPCUS Proving Guidelines*, Published online 2015. https://www.hpus.com/HPCUS-Proving-Guidelines-2015.pdf

21 RANDOM.ORG - Sequence Generator, Avaialbe online: https://www.random.org/sequences/ (Accessed on 17 December 2021)

22 Poruthukaren K, An attempt to estimate the noises in homeopathic pathogenetic trials by employing the Jaccard Similarity Index and Noise Index, *Homeopathy*, 111 (3) (2022) 176-183. https://doi.org/10.1055/s-0041-1735983

23 Adler U C, Acorinte A C, Calzavara F O, da Silva A A, de Toledo Cesar A, *et al*., Double-blind evaluation of homeopathy on cocaine craving: a randomized controlled pilot study, *J Integr Med*, 16 (3) (2018) 178-184. https://doi.org/10.1016/j.joim.2018.03.004