

## ORIGINAL ARTICLE

# Hydroquinone: Homoeopathic Pathogenetic Trial

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### ABSTRACT

**Background:** A double-blind, randomized, placebo-controlled Homoeopathic Pathogenetic Trial (HPT/Drug Proving) of *Hydroquinone* was conducted, using the accepted guidelines, ethical approval and scientific documentation. The potentization method was standardized. Toward enhancing the quality of HPT, the investigator proposed and evaluated the data using the Quantitative Pathogenetic Index and Qualitative Pathogenetic Index. Usable symptoms were derived from the study. The medicine was suggested for the treatment of vitiligo, based on its known toxicological effects.

HPT of a new medicinal substance, using the established parameters, to evaluate symptoms in healthy volunteers was carried out using a controlled experiment.

**Aims:** The aim of the study was to conduct a HPT using the accepted and scientific guidelines to derive clinically usable symptoms.

**Material and Methods:** A double-blind, randomized, placebo-controlled homoeopathic pathogenetic trial was conducted in 22 volunteers (provers), out of whom 15 received *Hydroquinone* in 30C potency, thrice daily, for four weeks, while seven received the placebo. The volunteer's symptoms during the initial seven days of the run-in period were carefully noted, and these were used as a filter, by elimination of the same symptoms in that volunteer during the verum phase. Thorough documentation such as Informed Consent Form, approval by the Ethics Committee, laboratory investigations, and safety and ethical measures, were taken care of. The volunteers were trained to write data in the prescribed diaries which was analyzed at the end. The investigator introduced Quantitative and Qualitative Pathogenetic Indices as parameters in the evaluation of the data derived from the HPT.

**Results:** The HPT of *Hydroquinone* exhibited qualitatively distinct symptoms, which could be applied in clinical practice. Safe use was documented. An anecdotal study supported the proposed efficacy of *Hydroquinone* for the treatment of vitiligo and further exploration could be carried out.

**Conclusion:** The HPT of *Hydroquinone* brought in qualitative symptoms. It was noted that a potentized preparation could produce many functional symptoms, but could not produce degenerative pathological symptoms such as vitiligo. The preparation could be used by the profession for vitiligo on the basis of its toxicological effects, supported by the anecdotal study. The Quantitative and Qualitative Pathogenetic Indices could further be used in future HPTs as a tool.

**Keywords:** Double blind, Hydroquinone, Homoeopathic pathogenetic trial, Placebo control, Quantitative pathogenetic index, Qualitative pathogenetic index, Randomization, Vitiligo

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## INTRODUCTION


*Hydroquinone* is a phenol compound that is known to have melanocyte-specific cytotoxicity,<sup>[1]</sup> used in conventional medicine as a topical therapeutic agent to lighten pigmentation on skin, in conditions such as melasma.<sup>[2,3]</sup> Based on the Law of Similars, the investigator used potentized *Hydroquinone* in many patients having vitiligo or hypopigmentation in 1998, and later, with encouraging results. Subsequently, a double-blind, randomized, placebo-controlled homoeopathic pathogenetic trial was conducted to investigate this effects of the substance on healthy volunteers.

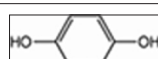
### General Information

*Hydroquinone* is a type of phenol, which is an aromatic organic compound.<sup>[2]</sup> It can be considered a simple polyphenol. It is a white granular solid substance. Substituted derivatives of this parent compound are also referred to as *hydroquinones*.<sup>[2]</sup>

### Specifications

*Hydroquinone's* chemical structure has two hydroxyl groups bonded to a benzene ring in a para position. Some specifications<sup>[4]</sup> of *hydroquinone* are as follows:

 Ball-and-stick model of the trans rotamer of *hydroquinone*<sup>[2,5]</sup>

 Structure of *hydroquinone*<sup>[2,6]</sup>

Other names	Quinol, Benzene-1,4-diol
Chemical formula	C <sub>6</sub> H <sub>4</sub> (OH) <sub>2</sub>
Molecular formula	C <sub>6</sub> H <sub>6</sub> O <sub>2</sub>
Relative molecular mass	110.11
Chemical and physical properties	Hexagonal prisms (Verschueren, 1996)
Boiling-point	287°C (Lide, 1997)
Melting-point	172.3°C (Lide, 1997)
Solubility	Soluble in water (5.9 g/100 mL (15°C), ethanol, and diethyl ether (Lewis, 1993)
Vapor pressure	532 Pa at 150°C; relative vapor density (air=1), 3.81 (Verschueren, 1996)
Flash-point	165°C, closed cup (American Conference of Governmental Industrial Hygienists, 1992)
Conversion factor	mg/m <sup>3</sup> =4.5×ppm
CAS Number	123-31-9

### *Hydroquinone*: Use in conventional medicine

*Hydroquinone* is an important industrial chemical. It is an ubiquitous chemical, readily available in cosmetic and nonprescription forms as a skin lighten agent.<sup>[7]</sup> It

is considered one of the most effective inhibitors of melanogenesis *in vitro* and *in vivo*. It causes reversible inhibition of cellular metabolism by affecting both the DNA and RNA syntheses<sup>[8]</sup> and can be considered a potent melanocyte cytotoxic agent with relatively high melanocyte-specific cytotoxicity.<sup>[1]</sup> In turn, it produces loss of pigment, which is comparable with vitiligo.

Two percent *Hydroquinone* is readily available over the counter in various cosmetic preparations in various countries. Evidence of improvement in the cases of hyperpigmentation with *Hydroquinone* (monotherapy) is usually observed in four-to-six weeks, with the improvement appearing to plateau at approximately four months. Concentrations as high as 10% can be compounded extemporaneously for refractory cases.<sup>[9]</sup>

### *Hydroquinone*: Known effects on humans and animals

In animals, the acute oral toxicity (LD50) is 320 mg/kg in rats. Acute dermal toxicity (LD50): 5970 mg/kg in mammals.<sup>[10]</sup> The toxicological effects of *hydroquinone* on humans and animals are known and may be summarized as under:

1. Hypopigmentation<sup>[1,2,4,7,11]</sup>
2. Skin irritation,<sup>[12,13]</sup> mild rash and burning,<sup>[12]</sup> and ulceration<sup>[11]</sup>
3. Exogenous ochronosis: <sup>[3,14]</sup> A condition where there is accumulation of homogentisic acid in the connective tissues
4. Long-term feeding of *Hydroquinone* to rats has led to aplastic anaemia, liver cord-cell atrophy, and ulceration of the gastric mucosa<sup>[4]</sup>
5. A single high dose was reported to induce renal tubule necrosis in rats<sup>[4]</sup>
6. Cancer: *Hydroquinone* has been suspected to be a carcinogen.<sup>[15]</sup> In skin painting studies in mice, *Hydroquinone* was inactive as an initiator of skin carcinogenesis. Oral ingestion of *Hydroquinone* did not produce cancer of the stomach or bladder in a study on mice.<sup>[4]</sup>
7. Eyes: Conjunctivitis, keratitis, and discolouration of the conjunctiva.<sup>[11,16]</sup> Causes eye irritation and possible burns. May cause redness, pain, blurring of vision and possible eye and cornea<sup>[13]</sup> damage.<sup>[11]</sup>
8. May cause dizziness, nausea, sense of suffocation, increased respiratory rate, vomiting, pallor, muscle twitching, cyanosis (bluish discolouration of skin due to deficient oxygenation of the blood), delirium, and collapse. May cause liver damage leading to jaundice. May cause harmful nervous system effects, including tremors and convulsions.<sup>[11]</sup>

9. May cause respiratory tract irritation. Inhalation may be fatal as a result of spasm, inflammation, oedema of the larynx and bronchi, chemical pneumonitis, and pulmonary oedema. Central nervous system effects may include confusion, ataxia (failure of muscular coordination), vertigo, tinnitus, weakness, disorientation, lethargy, drowsiness, and finally coma. May be harmful if inhaled. May cause burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea, and vomiting. Pure *hydroquinone* does not readily form a vapour at room temperature. The dust may cause irritation of the nose, throat, and upper respiratory tract.<sup>[11]</sup>
10. Tinnitus, nausea, dizziness, a sense of suffocation<sup>[11]</sup>
11. Dizziness, sense of suffocation, increased rate of respiration, vomiting, pallor, muscular twitching, headache, dyspnoea, cyanosis, and collapse.<sup>[17-19]</sup>

**Hydroquinone: A new medicine proposed in homoeopathy**  
*Hydroquinone* (Investigational Product – IP) as a new homoeopathic medicine is proposed as a single constituent formulation based on the simple logic that since it has a capacity to produce hypopigmentation (comparable with leucoderma or vitiligo), it could be applied homoeopathically as a remedy to treat hypopigmentation or vitiligo; and some other conditions presenting with hypopigmentation.

It has been understood that the application of the homoeopathic medicine is based on (1) Drug proving (2) Toxicological effects, and (3) Clinical use. There are a number of homoeopathic medicines, which are prescribed largely on the basis of their ability to produce certain symptoms or diseases; which may not have been proved in the pathogenetic trials. For example, the use of *Tuberculinum* in Tuberculosis, use of *Arsenic* in Cancer, use of *Phosphorus* and *Nitric acid* for vitiligo, and so on, where the said medicines have never produced the respective diseases in drug proving, but they are popularly used for those conditions based on their toxicology. Similarly, there are many remedies introduced on the basis of 'provings on the sick' (clinical provings), which have also served a useful purpose.<sup>[20]</sup> The proposed use of *Hydroquinone* is one such application of the homoeopathic principle, based on clinical proving, where the investigator has studied this preparation in a good number of cases of vitiligo. Of course, there will be indications besides vitiligo, based on the homoeopathic pathogenetic trial and other indications.

## HOMOEOPATHIC PATHOGENETIC TRIAL OBJECTIVE

This protocol is designed to conduct a homoeopathic pathogenetic trial for evaluating the effects of potentized *Hydroquinone* on healthy human volunteers.

## MATERIAL AND METHODS

The HPT of *Hydroquinone* was conducted by the author (Principal Investigator - PI), through a double-blind, randomized, placebo-controlled study, at the Life Force Research Center. The Life Force Research Center has a research staff of one principal investigator having 28 years of clinical practice (Hahnemannian style) and research experience; supported by five study members including four homoeopaths and one clinical trial expert, who had over 10 years of experience in research.

The IP was prepared as per the homoeopathic potentization method. The drug was proved in 30C potency on 22 volunteers with a randomization ratio of 2:1, wherein, 15 volunteers were given IP and seven volunteers were given a matching placebo, according to a pre-generated (through a software) random number table. The study involved 4 females and 18 males, out of 22 volunteers, three females were on the drug and one female was on placebo.

The dose and frequency of the investigational product was designed as 30C potency, six pills three times a day, for four weeks. The volunteers and investigator were blinded from the drug name and its allocation. The volunteers signed the Informed Consent Forms. The blind for randomization was maintained till the completion of the proving period. The proving volunteers were selected based on the inclusion and exclusion criteria, as per the protocol of the *Hydroquinone* study. The volunteers were in the age group of 18 to 45 years, mean age being 26.5 years, from different walks of life, from different locations, such as urban and various suburbs of Mumbai, having a different socioeconomic status, and having different occupations, including homoeopathic students and homoeopaths. The volunteers underwent pre-observation and post-observation investigations. Detailed present and past clinical histories of the volunteers were recorded in case record forms. Each volunteer had completed the intake of the doses as per the protocol schedule and the one-week doses

of placebo as a run-in period. Each volunteer visited the Life Force Center for screening and six weekly follow-up visits. At each visit, the volunteers were examined by the PI and study doctors. The symptoms generated during the trial period were noted (up to six weeks) by the volunteers in the diary provided to them and they were cross-examined and the symptoms were elaborated by the proving master. The proving master (investigator) had compiled the data after decoding (opening the blind).

### Source

*Hydroquinone* is available commercially in the pharmaceutical and research market, with a purity of about 99.5%. The inventor procured six grams of *Hydroquinone*.

### Vehicle Used for Dilution

Sterile water for injection was used to prepare up to 10C potency. Subsequently, higher potencies were prepared using dispensing alcohol (alcohol content 90% v/v), especially for storage and dispensing purpose.

Six grams of *Hydroquinone* was dissolved in 100 ml of water; 0.03 ml of solution was then mixed with 2.97 ml of water for injection (600 micrograms per ml) in a clean glass vial, using a micropipette, and labeled as HQM (*Hydroquinone* mother preparation).

### Potentization

HQM was potentized using an electromechanical potentiometer machine, with the following considerations:

- i. Machine standardization
  - Weight of arm: 7.5 kg
  - Arm length: 55 cm
  - Angle: 90 degrees
- ii. Force = Weight  $\times$  Gravitational acceleration  
 $= 7.5 \text{ kg} \times 9.8 = 73.5 \text{ Newton}$
- iii. Impact: Torque (Moment of Force)
- iv. Torque = (tau) =  $\tau = r \times F = 0.55 \times 73.5 = 40.43 \text{ Nm}$   
(Newton meter)  $\times 10 \text{ strokes} = 404.3 \text{ Nm}$
- v. Strokes: Number of strokes applied at each step of potentization was 10, which was counted with a digital device attached to the machine, avoiding human errors.

It may be noted that even if there is a change in the above parameters while preparing any new preparation or potency, it is scientifically indicated to have the documentation in place. Uniformity of the

impact is possible with the mechanical device, which can never be achieved with hand-made potencies.

### Centesimal and Decimal Scale Potency Preparation

HQM of 0.03 ml was mixed with 2.97 ml water for the injection (600 micrograms per ml) in a clean glass vial, using a micropipette, and labeled as *Hydroquinone*, for making *Hydroquinone* 1C potency. The proportion of 1: 99 was maintained; 0.03 mL of HQM 1C was then mixed with 2.97 mL water, and subjected to the above process of potentization to arrive at the *Hydroquinone* 2C potency. Likewise, *Hydroquinone* 10C, 17C, 20C, 30C, 50C, 100C, 200C, 500C, and 1000C potencies were prepared as per the Hahnemannian multi-vial dilution method and labeled accordingly. Similarly, the decimal potencies were prepared using a 1: 10 ratio. The potencies were prepared, labelled, and safely stored for use.

### Placebo

Identical (same size, shape, colour, taste) placebo pills provided were prescribed to the volunteers who were on placebo.

### Guidelines, Ethics, Compliance, and Approvals

The HPT was based on the guidelines advocated by Dr. Samuel Hahnemann, MD, in the Organon of Medicine, aphorisms 110-145,<sup>[21]</sup> the Central Council for Research in Homoeopathy (CCRH), Government of India,<sup>[22]</sup> and the European Committee for Homoeopathy (ECH) guidelines.<sup>[23]</sup> The project was reviewed and approved on 16 January, 2012, by the Institutional Ethics Committee, Homoeopathy India Pvt. Ltd., Mumbai, constituted as per the Indian Council of Medical Research (ICMR) guidelines.<sup>[24]</sup> The requirements regarding the obligations of investigators as per the 'Guidance on Good Clinical Practice' as per the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Independent Ethics Committee (ICH)<sup>[25]</sup> were met with. The drug proving project has been registered (Number: CTRI/2012/03/002506) with the Clinical Trials Registry-India (CTRI),<sup>[26]</sup> set up by the ICMR's National Institute of Medical Statistics (NIMS). When writing the manuscript, data reporting has been done in accordance with the Consolidated Standards of Reporting Trials (CONSORT) (RedHot) guidelines.<sup>[27]</sup>

## Investigations

Pre and Post drug administration investigations included complete blood count, erythrocyte sedimentation rate (ESR), blood biochemistry, urine routine analysis, pregnancy test, X-ray chest, and Electrocardiogram (ECG). Due care was taken to confirm that every female volunteer had a negative pregnancy test, before sending her for X-ray chest. Other investigations, if indicated, were done at the last visit.

## Inclusion, Exclusion and Withdrawal Criteria

Preferably homoeopathic doctors or students, who had knowledge of drug proving, were included in the study. However, non-medico participants were also included, after giving adequate training with regard to the proving and symptom recording method.

### Inclusion Criteria

1. Healthy volunteers of both sexes in the age group of 18-45 years without significant psychic or physical symptoms, confirmed by history and physical examination. A careful record of the volunteer's present health status, symptoms and reports was maintained in case record.
2. The persons who were trustworthy, able and ready to express and describe their experiences during the study.
3. Volunteers with no plans for important life changes like relocating, change of job, marriage, medical or surgical treatment. The usual habits and conduct of life continued.
4. Volunteers were in such a mental and legal that they were able to exercise fully their choice and written consent.
5. Their ECG and X-ray reports were within normal limits.

### Exclusion Criteria

1. Current medical treatments or Homoeopathy drugs in the preliminary observation period or during the study.
2. Consumption of prescribed drugs (including Homoeopathy) in the past four weeks (to be judged by the PI).
3. Contraceptive pills in the past three months.
4. Surgical treatment within the past two months.
5. Pregnancy, breastfeeding.
6. Persons suffering from allergic manifestations particularly pertaining to the respiratory system and skin should not be included in proving (to be judged by the PI).

7. Volunteers with a history of diabetes, hypertension, and hypothyroidism should not be included in proving.
8. Volunteers who are drug addicts should not be included in proving.

### Withdrawal Criteria (i.e. terminating drug proving)

1. If a volunteer has to be withdrawn because of a severe adverse event like accident or hospitalization, the data recorded until the event occurrence for such volunteers will be considered for analysis, depending on the investigators discretion, and the volunteers will be marked as 'withdrawal'
2. No replacement of withdrawn volunteers
3. Volunteer lost to follow up
4. Volunteer withdraws consent to continue in the drug proving study by himself/herself
5. If a volunteer experiences Serious Adverse Events or serious symptoms due to the drug proving.

### Co-interventions

Volunteers were advised to continue the routine lifestyle and avoid any Complementary and Alternative Medicine (CAM) or mainstream interventions. However, volunteers requiring any interventional treatment were documented. None of the volunteers required an antidote during the study period.

### Training

Volunteers were trained to note down the symptoms in the diaries provided to them, as soon as possible. The proving coordinator was trained to study cases, review symptoms, and coordinate with the volunteers.

### Data Handling and Record Keeping

Records have been maintained in the original handwritten diaries filled in by the volunteers. Data is organized in excel sheets and word documents, subsequently.

### Run-In Period, dose, and Repetition

Every volunteer was given doses of placebo, six pills, three times a day, for one week, and observed for the symptoms. The first week was a run-in period. The symptoms experienced during the run-in period were documented carefully. Two volunteers produced the same symptoms during the run-in period as well as after the intake of the medicine; these symptoms were not incorporated in the final analysis. The dose of six pills (30c potency), three times a day, was administered to every volunteer, for four subsequent weeks; unless there were severe symptoms or Serious Adverse Events (SAE).

### Adverse Event and Withdrawal of Volunteers

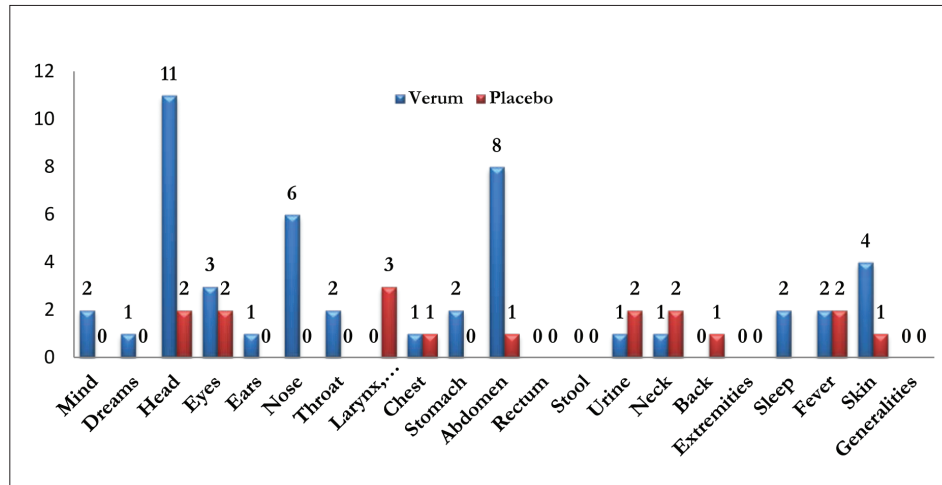
An adverse event is defined as any untoward medical occurrence in a volunteer administered a proving substance, which does not necessarily have a causal relationship with the action of the substance. None of the volunteers developed adverse events during the course of the trial.

### Serious Adverse Events

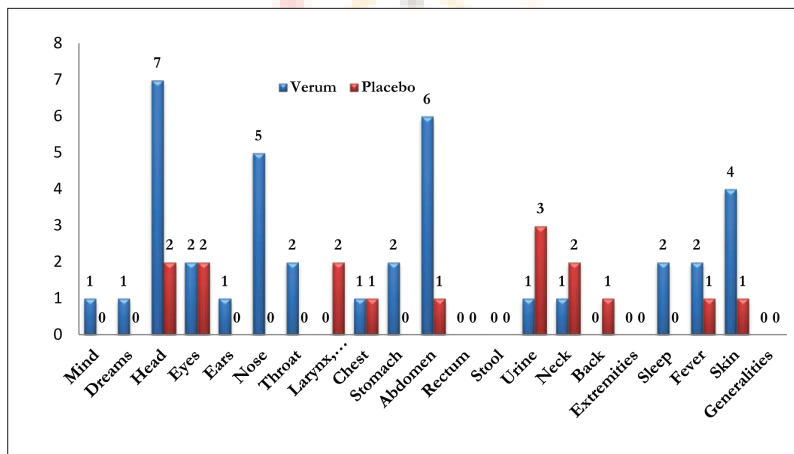
No volunteer reported Serious Adverse Event or Serious Adverse Drug Reaction during the course of drug proving.

### The Pathogenetic Effect<sup>[28]</sup>

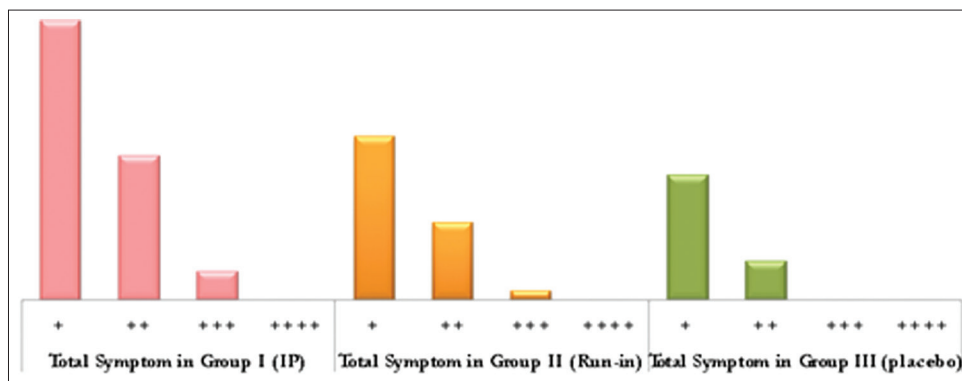
The Pathogenetic effect is defined as any change in



Graph 1: Number of symptoms (Verum vs. Placebo)



Graph 2: Number of provers (Verum vs. Placebo)



Graph 3: Qualitative analysis (intensity-wise, in IP, run-in, and placebo groups)

clinical events and laboratory findings reported by volunteers during a homoeopathic pathogenetic trial and recorded in the final report.<sup>[28]</sup>

The overall incidence of pathogenetic effects<sup>[28]</sup> and the incidence of pathogenetic effects per volunteer were calculated as under

The overall incidence of pathogenetic effects<sup>[28]</sup>

= Number of volunteers who had at least one reported pathogenetic effect/Total number of volunteers taking the medicine and who contributed to the symptoms or signs.

The incidence of pathogenetic effects per volunteer<sup>[28]</sup> = total number of findings claimed in the trial/total number of subjects using the medicine and included in its final pathogenetic description.

**Table 1: Quantitative symptom analysis [Graph 1 and 2]**

Organ	IP group (n=15) (Duration=5 weeks)					Run-in period (n=15) (Duration=1 week)					Placebo group (n=7) (Duration=6 weeks)				
	Main symptoms	Sub symptoms	Total number of symptoms	Volunteers	Volunteers with intensity	Main symptoms	Sub symptoms	Total number of symptoms	Volunteers	Volunteers with intensity	Main symptoms	Sub symptoms	Total number of symptoms	Volunteers	Volunteers with intensity
Mind	2	0	2	1	1 <sup>++</sup>	0	0	0	0	0	0	0	0	0	0
Dreams	1	0	1	1	18 <sup>+</sup>	2	2	2	2	9 <sup>++</sup> , 22 <sup>+</sup>	1	0	0	0	0
Head	3	10	11	7	4 <sup>+</sup> , 7 <sup>+++</sup> , 13 <sup>++</sup> , 16 <sup>++</sup> , 18 <sup>++</sup> , 19 <sup>+</sup> , 22 <sup>++</sup>	3	6	7	6	6 <sup>+</sup> , 9 <sup>++</sup> , 10 <sup>++</sup> , 13 <sup>++</sup> , 16 <sup>+</sup> , 19 <sup>+</sup>	1	2	2	2	14 <sup>++</sup> , 23 <sup>++</sup>
Eyes	2	2	3	2	4 <sup>++</sup> , 13 <sup>++</sup>	1	0	1	1	13 <sup>++</sup>	2	0	2	2	14 <sup>+</sup> , 17 <sup>+</sup>
Ears	1	0	1	1	4 <sup>++</sup>	0	0	0	0	0	0	0	0	0	0
Nose	2	5	6	5	4 <sup>+++</sup> , 9 <sup>++</sup> , 16 <sup>+</sup> , 18 <sup>+</sup> , 22 <sup>+</sup>	1	0	1	1	22 <sup>+</sup>	0	0	0	0	0
Throat	2	0	2	2	18 <sup>+</sup> , 19 <sup>+</sup>	0	0	0	0	0	0	0	0	0	0
Larynx, cough, expectoration	0	0	0	0	0	1	0	1	1	16 <sup>+</sup>	2	2	3	2	11 <sup>++</sup> , 21 <sup>+</sup>
Chest	1	0	1	1	16 <sup>+</sup>	1	0	1	1	22 <sup>+</sup>	1	0	1	1	11 <sup>+</sup>
Stomach	2	0	2	2	5 <sup>+</sup> , 19 <sup>+</sup>	1	0	1	1	10 <sup>+</sup>	0	0	0	0	0
Abdomen	1	8	8	6	8 <sup>+</sup> , 10 <sup>++</sup> , 16 <sup>+</sup> , 19 <sup>+</sup> , 20 <sup>++</sup> , 22 <sup>+</sup>	1	2	2	2	8 <sup>+</sup> , 20 <sup>+</sup>	1	0	1	1	11 <sup>++</sup>
Rectum	0	0	0	0	0	1	0	1	1	6 <sup>+</sup>	0	0	0	0	0
Stool	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Urine	1	0	1	1	13 <sup>+</sup>	1	3	1	3	10 <sup>++</sup> , 16 <sup>+</sup> , 20 <sup>+</sup>	2	1	2	3	12 <sup>+</sup> , 14 <sup>+</sup> , 15 <sup>+</sup>
Neck	1	0	1	1	20 <sup>+</sup>	1	0	1	1	10 <sup>++</sup>	1	2	2	2	11 <sup>+</sup> , 12 <sup>+</sup>
Back	0	0	0	0	0	1	0	1	1	19 <sup>+</sup>	1	0	1	1	12 <sup>+</sup>
Extremities	0	0	0	0	0	2	0	2	2	7 <sup>+</sup> , 19 <sup>+</sup>	0	0	0	0	0
Sleep	2	0	2	2	18 <sup>+</sup> , 24 <sup>+++</sup>	1	0	1	1	18 <sup>+</sup>	0	0	0	0	0
Fever	1	2	2	2	10 <sup>+</sup> , 22 <sup>+</sup>	0	0	0	0	0	1	2	2	1	17 <sup>+</sup>
Skin	2	3	4	4	9 <sup>+</sup> , 13 <sup>++</sup> , 16 <sup>+</sup> , 22 <sup>+</sup>	2	1	2	1	13 <sup>++</sup> , 22 <sup>+</sup>	1	0	1	1	17 <sup>+</sup>
Generalities	0	0	0	0	0	1	0	1	1	19 <sup>+++</sup>	0	0	0	0	0
Total symptoms	24	30	47			21	12	26			14	9	17		
Incidence of Pathogenetic effect (IPE) per volunteer			3.357					1.857					2.429		
Incidence of Pathogenetic effect (IPE) volunteer per day			0.096					0.265					0.067		

**Table 2: Qualitative symptom Intensity wise**

Location	Group I (IP)					Group II (RUN-IN)					Group III (Placebo)				
	+	++	+++	++++	Total	+	++	+++	++++	Total	+	++	+++	++++	Total
Mind	1	1	0	0	2	0	0	0	0	0	0	0	0	0	0
Dreams	1	0	0	0	1	1	1	0	0	2	0	0	0	0	0
Head	4	6	1	0	11	3	4	0	0	7	0	2	0	0	2
Eyes	1	2	0	0	3	0	1	0	0	1	2	0	0	0	2
Ears	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
Nose	4	1	1	0	6	1	0	0	0	1	0	0	0	0	0
Throat	2	0	0	0	2	0	0	0	0	0	0	0	0	0	0
Stomach	2	0	0	0	2	1	0	0	0	1	0	0	0	0	0
Abdomen	5	3	0	0	8	2	0	0	0	2	0	1	0	0	1
Rectum, stool	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0
Urinary organ	1	0	0	0	1	1	0	0	0	1	3	0	0	0	3
Neck	1	0	0	0	1	0	1	0	0	1	2	0	0	0	2
Back	0	0	0	0	0	1	0	0	0	1	0	1	0	0	1
Extremities	0	0	0	0	0	2	0	0	0	2	0	0	0	0	0
Sleep	1	0	1	0	2	1	0	0	0	1	0	0	0	0	0
Fever	2	0	0	0	2	0	0	0	0	0	2	0	0	0	2
Skin	3	1	0	0	4	1	1	0	0	2	1	0	0	0	1
Generalities	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
Larynx, cough, expectoration	0	0	0	0	0	1	0	0	0	1	2	1	0	0	3
Chest	1	0	0	0	1	1	0	0	0	1	1	0	0	0	1
Total	29	15	3	0	47	17	8	1	0	26	13	4	0	0	17
No. of volunteers	13	9	3	0	3.357	9	3	1	0	1.857	6	5	0	0	2.429
Qualitative pathogenetic Index	0.063	0.047	0.028	0	0.035	0.285	0.142	0.016	0	0.111	0.052	0.019	0	0	0.018

**Table 3: Qualitative analysis (Intensity wise)**

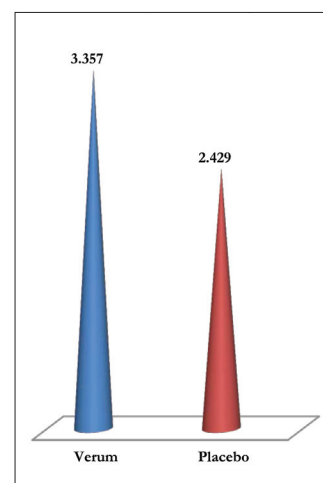
Total symptom in group I (IP)				Total symptom in group II (Run-in)				Total symptom in group III (placebo)			
+	++	+++	++++	+	++	+++	++++	+	++	+++	++++
29	15	3	0	17	8	1	0	13	4	0	0

**Quantitative and Qualitative Pathogenetic Indices**

The incidence of the pathogenetic effect<sup>[28]</sup> is a useful index for a systematic review. However, the author proposes two more indices for enhanced evaluation of the data by accounting (a) the number of days and (b) strength of each symptom. The author has used these indices in the evaluation of three more HPTs (data not yet published).

1. Quantitative Pathogenetic Index
2. Qualitative Pathogenetic Index

Qualitative Pathogenetic Index is an index where in every symptom is given a qualitative grade, namely, mild (+), moderate (++), severe (+++), and very severe (++++), for all organ locations. The Qualitative Pathogenetic Index [Graph 3] =



**Graph 4: Quantitative pathogenetic index**

Total number of symptoms for a particular intensity/ Number of volunteers contributing the symptoms/ Number of days. As it can be seen in Table 1, the indices in the verum group are found to be higher than in the placebo group.

A = Quantitative Pathogenetic Index, [Graph 4]



B = Total number of findings claimed in the trial,  
 C = Total number of subjects using the medicine  
 and included in its final pathogenetic description,  
 and D = Number of days.

Quantitative Pathogenetic Index (A) = (B/C)/D

a = Qualitative Pathogenetic Index, [Graph 6 and Tables 2,3]  
 b = Total number of symptoms for a particular  
 intensity, c = Number of volunteers who contributed  
 the above symptoms, d = Number of days.

Qualitative Pathogenetic Index (a) = (b/c)/d

The incidence of pathogenetic effects of verum per  
 volunteer = Total number of findings claimed in the  
 trial, 47/Total number of subjects using the medicine  
 and included in its final pathogenetic description  
 (14) = 47/14 = 3.357

Similarly, the incidence of pathogenetic effects of  
 placebo per volunteers is calculated as 17 symptoms/  
 number of volunteers (7\*) = 17/7 = 2.429.

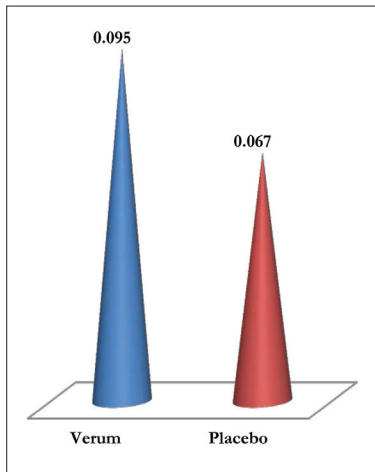
The author proposes to compute the pathogenetic  
 effect of the verum and placebo per volunteer, per  
 day, [Graph 5] by dividing the Pathogenetic effect  
 per volunteer by the number of day doses taken:

Verum group: 3.357/35 = 0.095

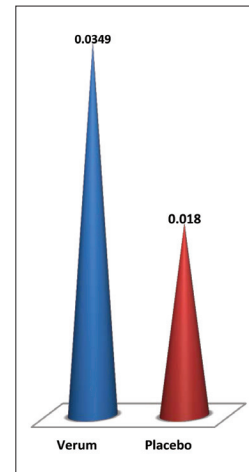
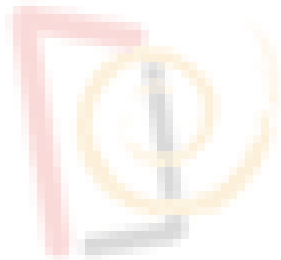
Placebo group: 2.429/42 = 0.067

### Methodological Quality Index

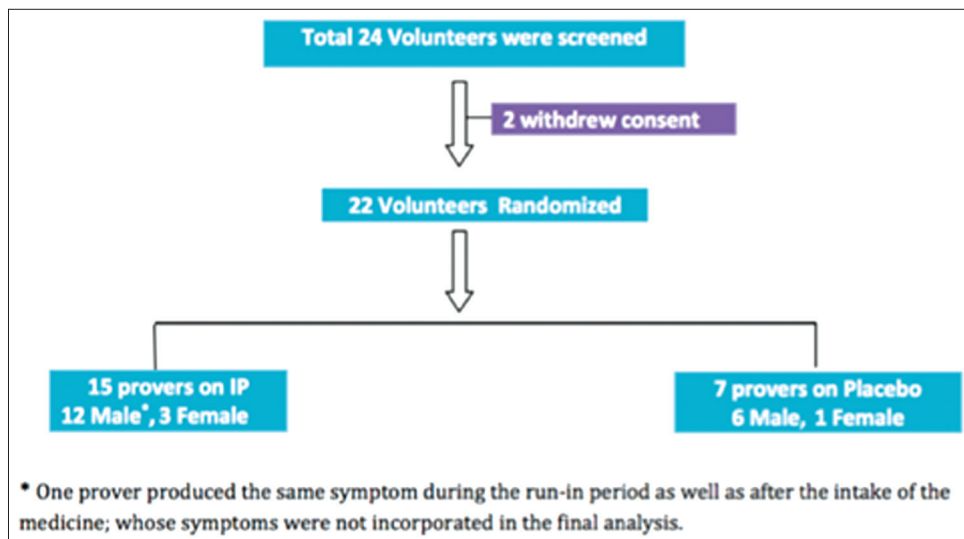
It is based on the key components of methodological  
 quality, including internal and external validity  
 items. The Methodological Quality Index (MQI)<sup>[28]</sup>  
 includes aspects such as randomization, inclusion and  
 exclusion criteria, blinding, and criteria for selection  
 of pathogenetic effects, with values ranging from 1



**Graph 5:** Pathogenetic effect of the verum and placebo per volunteer per day



**Graph 6:** Qualitative pathogenetic index



**Flow chart:** Volunteers' screening, recruitment, randomization, and study completion

to 4 for each component, giving a range from 4 to 16. The scores were divided into four methodological classes, where class I is the worst and class IV is the best, with arbitrary cut off points. ( $\leq 6$  for Class I; 7-10 for Class II; 11-13 for Class III;  $> 14$  for Class IV).

- I. Randomization: Pre-generated (computerized program) Random number table was used to allocate the randomization kits to the volunteers as per the recruitment sequence. (Score: 4)
- II. Blinding: Double-blind, the participant and investigator were blinded. The blind for randomization was maintained till the completion of the proving period. The blind was opened post trial and verified by the volunteers for drug and placebo. (Score: 4)
- III. Inclusion and exclusion criteria: Inclusion and exclusion criteria were clearly defined in the protocol. (Score: 4)
- IV. Criteria for selection of effects: Six criteria were defined:
  1. All the symptoms produced during the run-in period and if repeated by the same volunteer in subsequent weeks (first week, with placebo) were excluded.
  2. Symptoms produced, if any, by the volunteers who were dropped out from study due to adverse events, symptoms of such volunteers were excluded.
  3. Symptoms produced by placebo group, for five weeks and symptoms produced by volunteer on the drug were analyzed quantitatively as well as qualitatively. If the placebo and drug groups experienced the same symptom, they were evaluated on the basis of intensity and duration. For example, if the symptom of headache in the placebo group was reported to be of mild (+) intensity, while of severe (+++) intensity in the drug group, it was not eliminated.
  4. All symptoms were reported quantitatively, day wise, with duration and frequency, for example, dull headache with heaviness of head all over  $< 1-4$  pm associated with sleepiness. (Number of volunteer: 1) [9<sup>+</sup> (day 22 for 2-3 hours)]
  5. Every symptom described by the volunteers has been graded as + (mild), ++ (moderate), +++ (severe) and ++++ (very severe). This method allowed qualification grading.
  6. Volunteers who had exhibited some symptoms prior to the HPT, (as per the history), were eliminated, if the volunteer also exhibited same or similar symptoms as an effect of the medicine.

Based on the above criteria, the MQI = 4 + 4 + 4 + 4 = 16.

## RESULTS

The flow chart of volunteers' screening, recruitment, randomization, and study completion is shown here.

### Hydroquinone HPT Symptoms (Verum Group)

#### Mind

Mind: (Number of volunteers: 1) [1<sup>++</sup>]

1. Mind, mood swings, getting angry without reasons [1<sup>+</sup> (day 12, 13 for a day)]
2. Mind, sometimes without any reason feeling upset does not like to do anything, feeling sleepy [1<sup>++</sup> (day 16 for a day)]<sup>[2]</sup>

#### Dreams

Dreams: (Number of volunteers: 1) [18<sup>+</sup>]

3. Dreams, going to his native place [18<sup>+</sup> (day 9)]<sup>[3]</sup>

#### Head

Head: (Number of volunteers: 7) [4<sup>+</sup>, 7<sup>+++</sup>, 13<sup>++</sup>, 16<sup>++</sup>, 18<sup>++</sup>, 19<sup>+</sup>, 22<sup>++</sup>]

4. Head: Aching pain (Number of volunteers: 2) [4<sup>+</sup>, 7<sup>+++</sup>]
  - a. Aching pain in the right temporal region, in afternoon [4<sup>+</sup> (day 9 for 1-2 hours)]
  - b. Aching pain in forehead from 5 pm to 7 pm, < evening [7<sup>+++</sup> (day 33 for 2 hours)]
5. Head, throbbing pain, > pressure [16<sup>++</sup> (day 24 for a day)]
6. Headache (Number of volunteers: 5) [13<sup>++</sup>, 16<sup>+</sup>, 18<sup>++</sup>, 19<sup>+</sup>, 22<sup>++</sup>]
  - a. Headache, from 10 am to 10.30 am, > after sleep [13<sup>++</sup> (day 15, 16 for half-an-hour)]
  - b. Headache, for 1 hour (10 am to 11 am), < sunlight [18<sup>++</sup> (day 11 for one hour)]
  - c. Headache, from 3 pm to 3.30 pm, > after sleep [13<sup>++</sup> (day 20, 21 for half-an-hour)]
  - d. Headache, for 10-15 minutes, < afternoon [16<sup>+</sup> (day 15 for 10-15 minutes)]
  - e. Headache, for half-an-hour at night [18<sup>++</sup> (day 17, 26 for half-an-hour)]
  - f. Headache, in afternoon at 12 noon, > rest [22<sup>+</sup> (day 11 for 1-2 hours)]
  - g. Headache [22<sup>++</sup> (day 18, 33 for half-an-hour)]
  - h. Headache, for a day [19<sup>+</sup> (day 25, for a day)]<sup>[14]</sup>

#### Eyes

Eyes (Number of volunteers: 2) [4<sup>++</sup>, 13<sup>++</sup>]

7. Eyes, itching, wants to rub eye, lachrymation, < cold [4<sup>+</sup> (day 8, 9, 10 for a day)].

8. Eye, pain (Number of volunteers: 2) [4<sup>++</sup>, 13<sup>++</sup>]  
a. Eye, pain since morning to night for 8-10 hours < cold [4<sup>++</sup> (day 21 for 8-10 hours)].  
b. Eye, pain [13<sup>++</sup> (day 13 for a day)]<sup>[17]</sup>

#### Ears

Ears (Number of volunteers: 1) [4<sup>++</sup>]

9. Ear, pain in both ears, 2-3 hours at night [4<sup>++</sup> (day 21 for 2-3 hours)]<sup>[18]</sup>

#### Nose

Nose (Number of volunteers: 5) [4<sup>+++</sup>, 9<sup>++</sup>, 16<sup>+</sup>, 18<sup>+</sup>, 22<sup>+</sup>]

10. Nose, running nose (Number of volunteers: 5) [4<sup>+++</sup>, 9<sup>++</sup>, 16<sup>+</sup>, 18<sup>+</sup>, 22<sup>+</sup>]  
a. Running nose, watery secretions with redness, < cold, < dust [4<sup>+++</sup> (day 8, 9, 10, 21 for a day)]  
b. Running nose, watery secretion, from afternoon till evening, < cold drinks, < ice cream [9<sup>++</sup> (day 16, 24 for two days)]  
c. Running nose [16<sup>+</sup> (day 15 for a day)]  
d. Running nose, watery secretions with sneezing, < cold water [18<sup>+</sup> (day 13, for 2-3 hours in evening)]  
e. Running nose < cold food < ice cream [22<sup>+</sup> (day 20 for a day)]  
11. Nose, sneezing three to four times [18<sup>+</sup> (day 20 for 1-2 hours)]<sup>[24]</sup>

#### Throat

Throat, (Number of volunteers: 2) [18<sup>+</sup>, 19<sup>+</sup>]

12. Dryness in throat, with thirst, had to drink water every 10 to 15 minutes, > drinking water [18<sup>+</sup> (day 29, for a day)]  
13. Dryness of throat with irritation [19<sup>+</sup> (day 24 for a day)]<sup>[26]</sup>

#### Chest

Chest (Number of volunteers: 1) [16<sup>+</sup>]

14. Chest pain, aching pain, both sides of the chest for 5-10 minutes, < morning, > cold water, > pressure [16<sup>+</sup> (day 16 for 5-10 minutes, day 23 for a day)]<sup>[27]</sup>

#### Stomach

Stomach (Number of volunteers: 2) [5<sup>+</sup>, 19<sup>+</sup>]

15. Burning sensation in stomach with gases and acidic taste in mouth in the morning [(5<sup>+</sup> (day 9 for a day)]  
16. Vomiting four to five times a day, pain in abdomen, after eating outside food, < drinking water, < sight of food [19<sup>+</sup> (day 33 for a day)]<sup>[29]</sup>

#### Abdomen

Abdomen (Number of volunteers: 6) [8<sup>+</sup>, 10<sup>++</sup>, 16<sup>+</sup>, 19<sup>+</sup>, 20<sup>++</sup>, 22<sup>+</sup>]

17. Abdomen, pain (Number of volunteers: 6) [8<sup>+</sup>, 10<sup>++</sup>, 16<sup>+</sup>, 19<sup>+</sup>, 20<sup>++</sup>, 22<sup>+</sup>]

- a. Pain in abdomen in the right iliac fossa, pain radiates toward back, sudden pain, needle prick sensation, < coughing, < sitting for long, < standing up suddenly [8<sup>+</sup> (day 8, 9, 10, 11, 12, 13, 14 for entire day)]  
b. Pain in abdomen in the afternoon < after food [10<sup>++</sup> (day 9, 16 for entire day)]  
c. Pain in abdomen with discomfort for 2-3 hours [10<sup>++</sup> (31 for 2-3 hours)]  
d. Pain, discomfort, feeling of fullness of abdomen, in the evening, urge for stool even after defaecation [16<sup>+</sup> (day 22 for a day)]  
e. Pain, at 12 noon [20<sup>++</sup> (day 11 for one- to one-and-a-half-hours)]  
f. Pain in the right iliac fossa, > diverting mind to work [20<sup>+</sup> (day 12 for 1 hour)]  
g. Pain, in the epigastric region, > passing flatus [19<sup>+</sup> (day 34 for a day)]  
h. Pain, < fasting, > after meal [22<sup>+</sup> (day 20 for a day)].<sup>[37]</sup>

#### Urine

Urine (Number of volunteers: 1) [13<sup>+</sup>]

18. Urine burning, more at night (may be due to less intake of water as he moved out in the sun on the previous day) [13<sup>+</sup> (day 11, 14 for a day)]<sup>[38]</sup>

#### Neck

Neck (Number of volunteers: 1) [20<sup>+</sup>]

19. Neck Pain, mild stiffness, < morning [20<sup>+</sup> (day 33 for one- to one-and-a-half-hours)]<sup>[39]</sup>

#### Sleep

Sleep (Number of volunteers: 2) [18<sup>+</sup>, 24<sup>+++</sup>]

20. Disturbed sleep, could sleep around 12 midnight [18<sup>+</sup> (day 15 for a night)]  
21. Feeling sleepy in the morning [24<sup>+++</sup> (day 22 for one hour)]<sup>[41]</sup>

#### Fever

Fever (Number of volunteers: 2) [10<sup>+</sup>, 22<sup>+</sup>]

22. Fever (Number of volunteers: 2) [10<sup>+</sup>, 22<sup>+</sup>]  
a. Fever, mild at night 10.30 pm [10<sup>+</sup> (day 12 for a night)]  
b. Fever, mild at night 12 midnight [22<sup>+</sup> (day 16 for a day)]<sup>[43]</sup>

#### Skin

Skin (Number of volunteers: 4) [9<sup>+</sup>, 13<sup>++</sup>, 16<sup>+</sup>, 22<sup>+</sup>]

23. Skin, pimples (Number of volunteers: 3) [9<sup>+</sup>, 16<sup>+</sup>, 22<sup>+</sup>]  
a. Face, pimples, slightly painful on cheeks [16<sup>+</sup> (day 32 for a day)]  
b. Pimples on right cheek, painful [22<sup>+</sup> (day 33, 35 for a day)]<sup>[46]</sup>  
c. Chest, red eruptions, 2-3 spots on chest with mild burning, < sunlight [9<sup>+</sup> (day 25 for a day)]  
24. Face, itching on cheeks with mild rash < after shave [13<sup>++</sup> (day 12, 28, 32 for a day)]<sup>[47]</sup>

Note:

Analysis strategies: A systematic review of the symptoms was done and the symptoms exhibited by the volunteers were reported organ-wise from head to toe, including the general symptoms, under different headings (as per the Kent Analysis Method and based on the above criteria for selection of effects mentioned in the MQI). The symptoms were numbered as the main symptom, based on distinction within the particular organ/location, for example, Mind (heading) (1) Mind, irritability, (2) Mind, depressed (Main symptoms).

The main symptoms were followed by sub-symptoms, described in detail, (e.g. Mind (heading) (1) Mind, irritability (a) irritable by noise (b) irritable, when asked something (sub-symptoms), and so on.

The total number of symptoms was counted by eliminating the recurrence of the symptom as the main symptom. That is, in the cases where sub-symptoms were observed, the counting of the main symptom was eliminated, and thus, the cumulative total number of symptoms (represented at the end of each heading in a square bracket, in bold) was considered for the calculation of different indices.

### Prominent and Clinically Applicable Symptoms

Chief symptoms from the HPT may be shortlisted here:

1. Mind: [1<sup>++</sup>] Mood swing, anger, feels upset. No desire to do anything feeling sleepy
2. Head [4<sup>++</sup>, 7<sup>+++</sup>, 13<sup>++</sup>, 16<sup>++</sup>, 18<sup>++</sup>, 19<sup>+</sup>, 22<sup>++</sup>] Headache. [13<sup>++</sup>, 16<sup>+</sup>, 18<sup>++</sup>, 19<sup>+</sup>, 22<sup>++</sup>] <10 am to 11 am
3. Eyes [4<sup>++</sup>, 13<sup>++</sup>] Pain in eyes. Itching, rubbing, lachrymation
4. Ears [4<sup>++</sup>] Earache, at night
5. Nose [4<sup>+++</sup>, 9<sup>++</sup>, 16<sup>+</sup>, 18<sup>+</sup>, 22<sup>+</sup>] Coryza, Running nose. <Cold food, ice cream. Watery discharge, sneezing
6. Throat, Larynx [18<sup>+</sup>, 19<sup>+</sup>] Dryness of throat (with irritation), >drinking water.
7. Chest (Number of volunteers: 1) [16<sup>+</sup>] Pain
8. Stomach [5<sup>+</sup>, 19<sup>+</sup>] Burning with acidic taste in mouth, in the morning. Thirst, drinks often with dryness in throat. Vomiting.
9. Abdomen [8<sup>+</sup>, 10<sup>++</sup>, 16<sup>+</sup>, 19<sup>+</sup>, 20<sup>+</sup>, 22<sup>+</sup>] Pain in abdomen. Pain in the right iliac fossa. Fullness. <Afternoon
10. Urine [13<sup>+</sup>] Burning
11. Neck [20<sup>+</sup>] Pain, mild stiffness, <morning
12. Sleep [18<sup>+</sup>, 24<sup>+++</sup>] Disturbed sleep. Feeling sleepy in the morning
13. Fever [10<sup>+</sup>, 22<sup>+</sup>] Fever, mild, before midnight

14. Skin [9<sup>+</sup>, 13<sup>++</sup>, 16<sup>+</sup>, 22<sup>+</sup>] Face, acne, and red eruptions on cheeks. Itching.

### Deviations in Laboratory Reports

One volunteer was found to have an increase in Serum Glutamic Pyruvic Transaminase (SGPT) (normal range: 30-65 U/l) from 88 to 116, while another volunteer had a reduction in SGPT from 157 to 117. Both were clinically asymptomatic before as well as after the trial. There were no clinically significant changes after the HPT, with respect to complete blood count, liver function tests, renal function tests, urine analysis and ECG. All pre and post-investigation reports were documented.

### Safety Report

Safety of volunteers was evaluated based on pre-investigation at screening and post-drug administration investigations. There were no adverse events reported during the proving period.

### DISCUSSION

*Hydroquinone*, a homoeopathic potentized preparation was made with the substance being sourced with precise information of the chemical properties, using well-defined potentization parameters, inclusive of standardized force parameters applied in potentization; which would allow the making of standardized and reproducible homoeopathic medicine, now and in the future. A double-blind, randomized, placebo-controlled HPT of *Hydroquinone* exhibited distinct symptoms, which could be applied in clinical practice. *Hydroquinone* (in potency) intake proved to be safe for the volunteers.

Fourteen volunteers from the IP group (n = 15) produced 47 symptoms (numbers super scripted at end of last symptom under each system/anatomical part) in five weeks; the placebo group (n = 7) produced 17 symptoms in six weeks, while the run-in period (n = 15) produced 26 symptoms in one week. It must be noted that symptoms with description of location, sensation, modality, and concomitants, along with the duration, days, and intensity, have been listed as sub-symptoms. The volunteers (with prior training), coordinator, and principal investigator carefully noted and verified the intensity of each symptom, with every detail. The outcome was 47 symptoms produced by verum, which was quantitatively more than the symptoms produced in comparative groups, which could be

appreciated by examining the higher intensity of symptoms in the verum group.

*Hydroquinone* was selected for exploring its homoeopathic use based on the pre-knowledge that it has a capacity to induce hypopigmentation, and should, in turn, have a capability to treat the same. Also, the investigator used the potentized preparation of *Hydroquinone* in a series of patients having hypopigmentation (vitiligo), with encouraging and verifying results, calling for a larger clinical application.

Careful appraisal of symptoms produced during the verum phase, placebo, and run-in period was carried out observing the following filters in determining the prominence of symptoms.

- a. Those observed in more than one volunteer
- b. Those that lasted for a significant period
- c. Those, which were very intense, without the volunteer having experienced similar symptoms in the past one year; and without any apparent (causal) reason
- d. The symptoms should finally be compared with the symptoms based on the known effects of the source substance, which was adequately established.

Crude *Hydroquinone's* effects on humans and animals is known; it produces skin irritation, rash, burning, gastritis, and ulceration, ochronosis, aplastic anaemia, and of course, vitiligo. It is exciting to document that the effects of an ultra small dose of potentized *Hydroquinone* in 30C potency, in a controlled trial, were comparable with that of its crude effects, such as skin rash, burning in epigastrium, vomiting, and ear-nose-throat irritation.

Symptoms pertaining to the mind and dreams have not been found to be prominent. Similarly, symptoms of generalities have not been produced. The substance has produced a limited number of symptoms, as its effects on humans have also been found to be limited to certain symptoms. Its effects on blood related to aplastic anaemia and on the kidney, producing tubular necrosis, were obviously not reflected in the symptomatology; as the potentized dose would not produce pathological symptoms to that extent.

It must be noted that *Hydroquinone* did not produce any hypopigmentation or vitiligo in the HPT. The investigator did not expect vitiligo as a symptom or sign as potentized dose is not expected to produce such pathological symptoms. It may be recalled that none of commonly used medicines for vitiligo, namely, *Phosphorus*,<sup>[29]</sup> *Arsenic-sulphuricum flavum*,<sup>[30]</sup>

*Nitricum acidicum*,<sup>[29]</sup> *Kali carbonicum*,<sup>[31]</sup> and *Sepia*<sup>[32]</sup> ever produced vitiligo in drug proving. This common observation should also stimulate another discussion on, how important is it to conduct a homoeopathic pathogenetic trial for new substances having well-established pathogenesis or scope of action. The process of new homoeopathic drug discovery may be boosted by allowing the introduction of new medicines on the basis of known toxicological effects and clinical evidence, and not only on the basis of the homoeopathic pathogenetic trial.

Clinically, based on the sphere of action of *hydroquinone*, its use may be explored in the cases of vitiligo, gastritis, peptic ulcer, upper respiratory tract affections, headache, aplastic anaemia, renal necrosis, and ochronosis.

The Quantitative Pathogenetic Index and Qualitative Pathogenetic Index indices proposed and used here by the investigator, add a new dimension toward developing the method of qualitative and quantitative research in systematic reviews, aimed at minimizing the bias, and are not to be considered as mandatory in terms of application for the study of a HPT.

## CONCLUSION

*Hydroquinone* was identified for exploring its effects on human volunteers in a homoeopathic, potentized dose. The potentization was carried out with documented force parameters. A double-blind, randomized, placebo-controlled HPT, as per the accepted guidelines, with 15 volunteers and seven controls, with an initial seven days of run-in period, led to 47 symptoms, quantitatively and qualitatively higher than the placebo groups; comparable with the toxicological symptoms, and with documented safety in the healthy volunteers, and thus, clinically usable data was generated.

The Quantitative Pathogenetic Index and Qualitative Pathogenetic Index proposed by the investigator are important parameters, which may help in deciding the quality of data produced by the HPT.

The HPT has produced clear symptomatology, which can easily be applied in clinical practice for a set of symptoms. As potentized preparations are known for not producing significant pathological symptoms such as vitiligo, it is seen that *hydroquinone* has not produced any hypopigmentation; which is not to be considered as a limitation of the trial.

Further research on similar lines may help in

homoeopathic drug discovery. Further clinical trials and evaluation can enhance the strength of the current experiment and its outcome.

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**सारांश:** स्वीकृत दिशा-निर्देशों, नैतिक अनुमोदन और वैज्ञानिक प्रलेखीकरण का इस्तेमाल करके डबल ब्लाइंड, यादृच्छिककृत, प्लासिबो नियंत्रित होम्योपैथिक रोगमूलक परीक्षण (औषध प्रमाणन) किया गया। पोर्टेसीकरण की पद्धति को मानकीकृत किया गया था। एच पी टी की गुणवत्ता में वृद्धि करने के प्रति, अनुसंधाता ने, मात्रात्मक रोगमूलक सूचकांक और गुणवत्तात्मक रोगमूलक सूचकांक का इस्तेमाल करके आंकड़ों का प्रस्ताव और मूल्यांकन किया। अध्ययन से इस्तेमाल करने योग्य संलक्षण लिये गए थे। इसके ज्ञात विष-विज्ञान संबंधी प्रभावों के आधार पर श्वेत कुष्ठ रोग के उपचार के लिए इस औषधि का सुझाव दिया गया।

**संदर्भ:** स्वस्थ वालंटियरों में संलक्षणों का मूल्यांकन करने के लिए सुस्थापित मापदंडों का इस्तेमाल करते हुए, एक नियंत्रित प्रयोग का इस्तेमाल करके एक नए औषधीय सार का होम्योपैथिक रोगमूलक परीक्षण, किया गया।

**उद्देश्य:** इस अध्ययन का उद्देश्य, नैदानिक रूप से इस्तेमाल करने योग्य संलक्षण निकालने के लिए स्वीकार किए गए और वैज्ञानिक दिशानिर्देशों का इस्तेमाल करके एक होम्योपैथिक रोगमूलक परीक्षण करना था।

**सामग्री और पद्धतियाँ:** एक डबल ब्लाइंड, यादृच्छिककृत, प्लासिबो नियंत्रित होम्योपैथिक रोगमूलक परीक्षण 22 प्रमाणकर्ताओं में किया गया, जिनमें से 15 को 30 सी पोर्टेसी में चार सप्ताह तक प्रतिदिन 3 बार हाइड्रोक्वोनोन दी गई, जबकि सात को प्लासिबो दी गई। औषधि दी जाने की अवधि के आरंभिक सात दिनों के दौरान प्रमाणकर्ताओं के संलक्षणों को सावधानीपूर्वक नोट किया गया और वेरम चरण के दौरान उस प्रमाणकर्ताओं में उन्हीं संलक्षणों का विलोपन करके इन्हें एक फिल्टर के रूप में इस्तेमाल किया गया। सघन प्रलेखन जैसे संसूचित सहमति फार्म, नैतिकता समिति द्वारा अनुमोदन, प्रयोगशाला जांच-पड़तालें और सुरक्षा तथा नैतिकता उपायों का ख्याल रखा गया। वालंटियरों को विनिर्धारित डायरियां लिखने के लिए प्रशिक्षित किया गया और आंकड़ों का विश्लेषण किया गया। होम्योपैथिक रोगमूलक परीक्षण से लिए गए आंकड़ों के मूल्यांकन में अनुसंधाता ने मात्रात्मक और गुणवत्तात्मक रोगमूलक संकेतकों को मापदंडों के रूप में आरंभ किया।

**परिणाम:** हाइड्रोक्वोनोन होम्योपैथिक रोगमूलक परीक्षण ने गुणवत्तात्मक रूप में भिन्न संलक्षण दर्शाए, जिनका अनुप्रयोग नैदानिक अभ्यासों में किया जा सकता था। सुरक्षित इस्तेमाल का प्रलेखन किया गया था। एक अध्ययन ने, श्वेत कुष्ठ रोग के उपचार के लिए हाइड्रोक्वोनोन की प्रस्तावित प्रभावोत्पादकता का समर्थन किया जिस पर आगे अनुसंधान किया जा सकता है।

**निष्कर्ष:** हाइड्रोक्वोनोन के होम्योपैथिक रोगमूलक परीक्षण से गुणवत्तात्मक संलक्षण प्राप्त हुए। यह नोट किया गया था कि एक पोर्टेसीयुक्त सम्पाक अनेक कार्यात्मक संलक्षण उत्पन्न कर सकता है परंतु श्वेत कुष्ठ रोग जैसे अपकर्षक रोगात्मक संलक्षण उत्पन्न नहीं कर सकता। इसके विष-विज्ञान संबंधी प्रभावों के आधार पर, इस सम्पाक का इस्तेमाल, व्यवसाय द्वारा श्वेत कुष्ठ रोग के लिए किया जा सकता है। मात्रात्मक और गुणवत्तात्मक रोगमूलक संकेतकों का इस्तेमाल भावी होम्योपैथिक रोगमूलक परीक्षणों में एक साधन के रूप में किया जा सकता है।