Original Article

Homoeopathic pathogenetic trial of *Cuprum aceticum*: A multicentric, double-blind, randomized, placebo controlled trial

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Abstract

Background: Although the symptomatology of *Cuprum metallicum* is quite vast, its other salts have fragmentary proving. Thus, homoeopathic pathogenetic trial for *Cuprum aceticum (Cu acet.)* was taken up. **Objective:** To elicit the pathogenetic response to *Cu acet.* in homoeopathic potencies on healthy human provers. **Materials and Methods:** A multi-center, double-blind randomized, placebo controlled, trial was conducted at three centers of Central Council for Research in Homoeopathy. Proving was conducted on 50 relatively healthy provers selected after conducting the Pretrial Medical Examination. All the provers were given placebo during the first phase of the trial. In the next two phases, *Cu acet.* was administered in 6 C and 30 C potencies, in the intervention group ($n = 34$); and placebo in the placebo group ($n = 16$), after randomization. The proving data so generated on *Cu acet.* were compiled and analyzed at the proving-cum-data processing cell. **Results:** Out of 34 provers who were on actual drug trial, only 12 provers manifested symptoms. Twenty-six and 20 symptoms were manifested in 6C and 30C potency, respectively. **Conclusion:** The pathogenetic response elicited during the proving trial expands the scope of use of the homoeopathic medicine *C. aceticum*. The symptoms generated in this trial will carry more value when verified clinically.

Keywords: *Cuprum aceticum*, Double blind, Drug proving, Homoeopathy, Pathogenetic effect, Placebo, Verdigris

Introduction

Cuprum aceticum (Cu acet.) is commonly known as acetate of copper. It is seen that cuprum and its salts are used for medical properties since ancient times. The book *De Materia Medica* by Dioscorides (first century A. D.) describes the use of verdigris (made by exposing metallic copper to vinegar steam to form copper acetate) in combination with copper sulfate as a remedy for bloodshot eyes, inflamed eyes, "fat in the eyes," and cataracts.[1] Copper was also employed in ancient India and Persia to treat lung diseases. The tenth century book, *Liber Fundamentorum Pharmacologiae* describes the use of copper compounds for medicinal purposes in ancient Persia. Powdered malachite was sprinkled on boils, copper acetate and copper oxide were used for diseases of the eye and for the elimination of "yellow bile." In 1885, the French physician, Luton, reported on using copper acetate in his practice to treat arthritis patients. For external application, he made a salve of hog's lard and 30% neutral copper acetate. For internal treatment, he used pills containing 10 mg of copper acetate.[2]

Quoting from the Allen's Encyclopedia of Pure Materia Medica, "Dr. Samuel Hahnemann, in his Fragmenta, 1805, gives symptoms under the heading of "*Cuprum vitriolatum"* and in 1824 contributed to Franz's collection in the Archiv. f. Hom., where *"Cu acet."* is directed to be used. Franz's collection also includes symptoms by Franz, Fr. H-n,

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Herrmann, and Ruckert, as well as various poisoning cases contributed by Dr. Hahnemann."[3]

Although the symptomatology of *Cuprum metallicum* is quite vast in homoeopathic materia medica, its other salts have fragmentary provings.

Homoeopathic drug proving is not only an integral part, but the first step to find out the pathogenetic effect of a drug substance. Hence, this proving was conducted to assess the therapeutic effect of *Cu acet.*

Description

Details and chemical properties of cuprum acetate are as follows:

Copper (II) acetate monohydrate (Cu [II] acetate) is odourless and efflorescent. It is soluble in alcohol and slightly soluble in ether and glycerol. Cu (II) acetate has many applications, as a fungicide, insecticide, catalyst for organic reactions, as well as applications in electrolysis and electroplating.[4]

Cu (II) acetate is used in the biochemical applications such as DNA extraction. Cu (II) complexes have been evaluated for anticancer, antibacterial, and antifungal activities. These are known to cleave DNA; however, increased efficiency is seen in the presence of an oxidizer (often hydrogen peroxide).[5]

Materials and Methods

Study design and study setting

A multicenter prospective, randomized, double blind, placebo controlled study with allocation ratio of verum: placebo as 70:30 was conducted at three institutes of the Central Council for Research in Homoeopathy (CCRH): Dr. D. P. Rastogi Central Research Institute of Homoeopathy, Noida, Regional Research Institute of Homoeopathy, Gudivada and Homoeopathic Drug Research Institute, Lucknow. Proving Master was Research Officer of the Council, having post graduate degree in Homoeopathy whereas, Honorary Consultants were the experts of various specialties of modern medicine engaged in the examination of volunteers/provers. Medical experts constituted both of them.

Participants

Selection of provers

Applications were invited from 15 to 20 volunteers (from each center) of both sexes and age 18 years and above through a notice placed on the notice board of the institutes and homoeopathic colleges. The volunteers of non-homoeopathic background were also considered for the study. Pretrial medical examination (PME) was then conducted for 76 volunteers after getting written informed consent from them, 05 of which were from the non-homoeopathic background. Detailed physical, pathological, and radiological examinations were conducted by the medical experts to ensure the health status of the volunteers before enrolment into the study. For the pathogenetic drug trial of *Cu acet,* a total of 50 volunteers were enrolled as provers.

Inclusion and exclusion criteria

Volunteers of both sexes with age more than 18 years, certified as healthy by the medical experts, found capable of carefully recording the facts, subjective, and objective symptoms generated by the drug during proving and those who had not taken any homoeopathic medicines in the last 2 months were included in the study.

Volunteers suffering from any acute or chronic disease, color blindness, anxiety or hysteria, having any addictions, undergoing any kind of medical treatment, undergone surgery in last 2 months, women during pregnancy, puerperium or lactating, and those who had participated in another clinical or proving trial during the last 6 months were excluded from the study.

Sample size

Sample size was determined as per the Drug Proving Protocol of the Council,[6] according to which there should be at least 15 provers at each center, 30% of whom shall act as control. Therefore, 50 provers were enrolled at three centers for this trial. 34 provers were under verum group and 16 were under placebo group.

Randomization and blinding

Provers were randomized in two groups using stratified randomization technique for each center, Group I: Homoeopathic medicine group and Group II: Placebo group. Random numbers were generated with the help of computer-based software available at www.randomizer.org,[7] and the random code for the provers along with the information about the group allocation was kept at CCRH headquarters. The decoding of the group was done after the compilation of the symptoms produced in both the groups.

Both homoeopathic drug and placebo were dispensed in identical form, visually indistinguishable from each other, from Nodal Office of Drug Proving Programme at Dr. D. P. Rastogi Central Research Institute (Homoeopathy), Noida. Provers, Proving Master and the Programme Officer were investigators and kept blinded to the group allocation and also to the identity of the drug. All the provers were assigned code numbers and coded drugs of different potencies were supplied in separate glass phials bearing code numbers of the respective prover.

Intervention

Homoeopathic group

Homoeopathic dilutions of *Cu acet.* in 6C and 30C potencies in 100 ml sealed bottles were procured from a Good Manufacturing Practices certified Homoeopathic Drug manufacturer, Hahnemann Publishing Company Private Ltd., Kolkata, India. Globules of number 30 were medicated with these dilutions at the proving-cum-data processing cell at Nodal office of Drug Proving.

Placebo group

Placebo consisted of nonmedicated globules (number 30) moistened with nonmedicated dispensing alcohol (unsuccussed)

and was therefore indistinguishable from verum in appearance, taste, and color.

Duration of study

Proving period: 1 year (2014–2015).

Ethics and consent

The Council's 18th Ethical Committee approved the study protocol on June 19, 2014. Proving Masters with experience in drug proving were sensitized about the protocol. Written informed consent was received from all the volunteers prior to enrolment in the study, after providing the detailed information about the trial.

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013.[8]

Procedure

Study was conducted in three phases at each of the centers. In each phase, 12 doses of drug or placebo as per randomization were administered, divided in four doses/day for 3 days (if no symptom arises).

Phase-I: Placebo phase. All the provers were given Placebo in Phase I. It is useful in generating prover's response to placebo in both the groups, and therefore, symptoms generated by the prover in this stage act as control for subsequent phases.

Phase-II: In the 2nd phase, the verum group received the drug in 6C potency and Placebo group received optically identical placebo.

Phase-III: In the 3rd phase, the verum group received the drug in 30C potency and Placebo group received optically identical placebo.

At each study center, a Proving Master supervised the volunteers enrolled in the study. After receiving the informed consent, PME, the baseline characteristics equivalent to Homoeopathic interview and the findings with respect to all the systemic examination and laboratory investigations (Complete Blood Count, Blood Sugar Fasting, Lipid Profile, Liver Function Test, Kidney Function Test, Urine (routine and microscopy), Stool (routine and microscopy), electrocardiogram, Chest X-ray PA view and ultrasonography whole abdomen and pelvis) were filled in the pro forma. The volunteers were instructed to take four globules of the coded drug four times a day for a maximum period of 3 days. Orientation training programs were conducted for the staff, faculty and students of homoeopathic medical colleges to educate them about the process of drug proving and safety of proving substance before the initiation of the study. However, as it was a double-blind study, names of proving substance were not disclosed. The provers were asked to note down daily the details of their feelings/changes in mental and/or physical state, after taking the coded drug in "Prover's Day Book Proforma"©.

If sign(s)/symptoms(s) appeared

- The provers were asked to stop taking the drug/placebo as soon as they felt any change or any sign(s) and/or symptoms(s) developed during the trial
- The provers noted down the sequence of the appearance of new sign(s) and/or symptoms(s), their progress and the number of doses after which such sign(s) and/or symptoms(s) appeared, with date, time of onset and duration for which they persisted
- Any change in normal routine of the prover in respect of daily habits pertaining to diet, living conditions etc., any treatment taken was also noted in the Prover's Day Book Proforma.

After disappearance of sign(s) and/or symptom(s) produced by the drug, the volunteer had to wait for a further period of 30 days (wash out period) before starting the next phase following the same dose schedule as stated above.

The symptoms recorded in "Prover's Day Book Proforma" were verified by the Proving Master and completed through further interrogation with the provers in respect to their location(s), sensation(s), modalities and concomitants, extension of symptoms, causation, clinicopathological findings and other treatment taken, if any, in "Symptoms Elaboration Proforma."

During the course of proving, the provers were referred for specific laboratory investigation(s) to rule out any pathological cause of appearance of symptom(s). Since laboratory tests were performed to identify any correlation between the subjective and objective changes during the course of proving, the expert opinion of the honorary consultant(s) was obtained, wherever needed.

If no sign(s)/symptoms(s) appeared

The provers noted down "No Symptom" with date and time of intake of the respective dose of the drug/placebo in "Prover's Day Book Proforma."

Before commencing the administration of subsequent potencies (subsequent Phase) of the drug, the provers remained on a wash out period of 30 days and started taking next potency following the same procedure as mentioned above, till completion of all the doses/appearance of symptom. The same procedure was followed for the 3rd phase. After the completion of trial of all potencies, the provers underwent Terminal (Post Trial) Medical Examination (TME), following the same manner as done during PME.

On completion of all the phases of the drug proving, the compilation of data recorded in "Prover's Day Book Proforma," "Symptoms Elaboration Proforma," "Pathological Report Sheets" and "TME sheets," was done by the Drug Proving-cum-Data Processing Cell of the Council. After decoding, the sign(s) and/or symptom(s) generated by the provers kept on the drug were separated from those generated by the provers kept on placebo.

Management of adverse effects

A vial of medicated globules of *Camphora* 30C was sent with each quota to each center as "Antidote." As per

recommendation by a group of experts, *Camphora* 30C was used as an antidote. In case of prolonged or intensely disturbing symptoms, antidote was to be used by the Proving Master after consulting the medical expert.

Proving symptoms

The sign(s) and/or symptom(s) generated by verum (drug) or control (placebo) on each prover are noted down for each phase, number of doses after which each of the signs or symptoms appeared and the duration for which they persisted. The sign(s) and/or symptom(s) generated by verum group are separated from those generated by provers of control group. The sign(s) and/or symptom(s) which were produced by the placebo in control and verum group provers are not taken into consideration.

Statistical analysis

The consolidated standards of reporting trials[9] and Red Hot guidelines[10] were adhered to report the outcome of the trial. The compiled data of proving symptoms and the changes in the laboratory investigations were analysed using IBM Statistical Package for the Social Sciences (SPSS) version 20, USA for Windows was used for all the data analysis.

Comparisons between Homoeopathy and placebo groups were performed at baseline to assess randomization effect using independent "*t*-test" for the continuous variable and "Chi-square test" for the categorical variables. Further "descriptive analysis" was done for the data with respect to the pathogenetic effect (signs and/or symptoms) produced during trial.

To distinguish placebo effect and nocebo effect, intra and inter prover analysis was done in both the groups.

Pathogenetic effects

Pathogenetic effects (Proving symptoms) are defined as all changes in state of health and laboratory findings reported by the provers during the Homoeopathic Pathogenetic Trial and recorded in the final report. The incidence of pathogenetic effects per prover is defined as the total number of findings observed in verum group of the trial divided by the total number of provers.[11]

Pathogenetic effects were deduced from:

i. Comparison of symptoms developed in the placebo phase with symptoms during intervention phases (intra-prover comparison)
ii. Comparison of symptoms developed by provers on control (for all phases) with provers on actual drug trial (inter-prover comparison).

Results

From three drug proving centers where the study was conducted, a total of 76 volunteers were screened and 50 apparently healthy volunteers were enrolled as provers. Of 50 provers, 34 were on verum and 16 were on placebo. Figure 1 shows the flowchart of the number of volunteers who underwent screening, enrolled, randomized in two groups and number of provers who developed symptoms during the trial. The baseline information in both the groups was comparable ($P \geq 0.05$) and well matched as shown in Table 1.

Out of 50 enrolled provers, 42 provers underwent the TME. 06 provers dropped out from the verum group while 02 provers dropped out from placebo group. The descriptive data analysis was done for remaining 42 provers as per protocol.

During the pathogenetic trial, out of 34 provers who were in verum group, only 12 (35%) provers reported symptoms consequent upon the administration of the drug. In the placebo group, five (31%) provers produced the symptoms. The symptoms developed after the administration of both the potencies, i.e., 6C and 30C. Out of 46 symptoms which were produced by the provers of verum group in the 2nd and 3rd phases, 26 symptoms were produced in 6C potency [Table 2] while 20 symptoms were produced in 30C potency [Table 3]. In 6C potency, majority of symptoms developed after the administration of 10–12 doses while in 30C potency symptoms developed after administration of 4–5 doses only.

The following proving symptoms appeared in both 6C and 30C potency:

1. Loquacity (talking about irrelevant things), did not want to be interrupted, if interrupted feels like hitting
2. Bursting pain in the frontal region of the head
3. Stitching pain in right lower molar
4. Gripping, colicky pain in the abdomen
5. Dry cough
6. Stitching pain in lower extremities especially calf muscles
7. Fever.

Loquacity, stitching pain in right lower molar, stitching pain in lower extremities especially calf muscles and fever symptoms are reported by the same prover in both 6C and 30C potency. They were reported singularly by different provers in the verum group only. They were not observed in the placebo group or the placebo phase of the verum group.

Analysis was also done considering the physical built, physical generals and mental generals of the provers in the verum group who have produced symptoms but no significant similarities were found in these provers, which could have been considered the constitutional symptoms. Further, inter-group analysis considering the above parameters were done in the provers who have produced symptoms in the

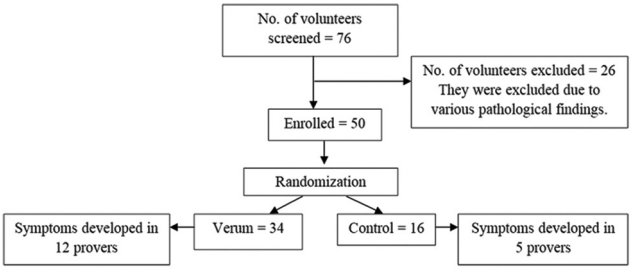

Figure 1: Flow chart of study participants

Table 1: Baseline information

Variable	Homoeopathy (*n*=34)	Placebo (*n*=16)	*P*
Age (years)	23.8±4.1	23.6±3.7	0.794§
Gender, *n* (%)			
Male	16 (47.1)	7 (43.8)	0.827¥
Female	18 (52.9)	9 (56.2)	
BMI	21.5±3.01	22.28±4.54	0.473§
HB (g/dl)	12.98±1.58	13.03±1.58	0.895§
TLC	7465.3±896.1	7319.3±1371.7	0.654§
ESR (mm after 1 h)	11.44±8.63	11.31±6.48	0.958§
Fasting BS (mg/dl)	79.86±9.79	81.28±8.43	0.619§
Total cholesterol (mg/dl)	154.1±25.76	141.53±29.84	0.133§
SGOT (U/L)	16.55±6.85	16.94±5.18	0.843§
SGPT (U/L)	22.51±11.93	20.82±7.81	0.609§
Alkaline phosphatase	144.63±21.76	138.36±21.58	0.345§

Values are expressed in (%), mean±SD, §Independent t-test, ¥Chi-square test. BMI: Body mass index, SD: Standard deviation, HB: Hemoglobin, TLC: Total Leucocyte Count, ESR: Erythrocyte Sedimentation Rate, SGPT: Serum glutamic-pyruvic transaminase, SGOT: Serum glutamic-oxaloacetic transaminase, BS: Blood Sugar

Table 2: Symptoms produced with 6C potency of *Cu acet*.

Location	Symptoms observed	Doses	Symptom duration in days
Mind	Loquacity (talking about irrelevant things), didn't want to be interrupted, if interrupted feels like hitting	12	3 days
Vertigo	Vertigo; aggravation afternoon, amelioration evening	12	10 days
Head	Bursting pain in frontal region of head; aggravation night	12	7 days
	Pain in head as if head would burst (10 am to12 noon); aggravation stooping	12	2 h
	Dull, aching pain in the frontal region of the head with coryza; aggravation Walking, bending forward, afternoon till night, amelioration pressure, after sleep	2	1 day
Eyes	Swelling of both lower eyelids, aggravation morning	12	4 days
Nose	Sneezing with watery nasal discharge; aggravation morning	12	4 days
Mouth	Aphthae on lower lip, white in color, with red margins, and burning pain; aggravation eating, talking	12	3 days
	Aphthae in mouth with burning pain, whitish in color, red in margin with dry tongue	12	6 days
	Dryness of mouth with excessive thirst and desire for cold water	3	3 days
Teeth	Stitching pain in right lower molar; aggravation eating	12	5 days
Throat	Sore throat A/F exposure to dust; aggravation noon to evening, cold water, amelioration taking tea, gargling by hot water	2	4 h
Stomach	Nausea with weakness; aggravation 9 am	12	10 days
Abdomen	Cutting pain in abdomen; aggravation eating	12	5 days
	Aching pain in abdomen at 6 pm (umbilical region). Next day pain increased in intensity with loose watery stool (3-4 times/day); aggravation eating	11	2 days
	Gripping pain in abdomen with loose stool (3 times/day), associated with great thirst, loss of appetite, and bitter taste	12	7 days
Rectum	Stool mixed with blood, burning sensation in rectum; amelioration cold application	2	5 days
Cough	Dry cough, aggravation night	12	1 day
Back	Aching pain in the nape of the neck from 2 pm to 7 pm; aggravation looking upwards. Next day the intensity of symptom increased from the morning till the evening and continued for 2 more days	10	4 days
	Dull aching pain with stiffness in lumbar region; aggravation afternoon till night, walking, lying down, amelioration massaging	2	1 day
Extremities	Stitching pain in lower extremities especially calf muscles; aggravation night	12	6 days
	Itching in the right leg, scratching leads to burning	10	1 day
Sleep	Sleeplessness	12	5 days
Fever	Fever with chills and body ache in the evening; aggravation cold weather	12	1 day
Skin	Small red macules on the left side of the neck and shoulder without itching for 8 days. Then only on the neck since the 9th day and disappeared after 5 days	12	14 days
	Small, red papular eruptions on the right arm and front of the neck, associated with itching and burning; aggravation touch, night, amelioration rubbing	12	6 days

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Table 3: Symptoms developed by 30C potency of *Cu acet.*

Location	Symptoms observed	Doses	Symptom duration in days
Mind	Anger with irritability when contradicted; amelioration being alone. This is associated with thoughts of committing suicide	5	4 days
	Loquacity (talking about irrelevant things), did not want to be interrupted, if interrupted feels like hitting	5	4 days
Head	Bursting pain in head; aggravation night, amelioration pressure	4	5 day
	Pain in head with feeling as if head would burst in small pieces associated with sleepiness; aggravation bending forward	5	6 day
	Bursting pain in frontal region of head; aggravation walking, noise, amelioration tight bandaging	5	1 day
Eyes	Heaviness in both eyes followed by retro-orbital pain with burning in eyes, aggravation after studying. Next day lachrymation in both eyes with itching and puffiness around the eyes; aggravation after studying	4	5 days
Nose	Coryza with watery nasal discharge; aggravation morning, night	4	3 days
Teeth	Stitching pain in first right lower molar radiating to right ear; aggravation cold drink, amelioration warm water	4	2 days
Abdomen	Heaviness and stinging pain in whole abdomen; aggravation eating, amelioration pressure	4	3 day
	Heaviness in the epigastric region	5	1 day
	Colicky pain in abdomen; aggravation eating, drinking, amelioration pressure, bending forward	5	1 day
Rectum	Hard, unsatisfactory stool	5	4 days
Cough	Dry cough with scanty, white expectoration associated with throbbing pain in head on coughing, heaviness in head throughout the day and fever (99.6°F). However, cough symptoms continued for the next 2 days and fever again on the third day (99°F)	10	4 days
Back	Cutting pain in lumbar region; aggravation lying down, walking, amelioration sitting, warmth	4	3 days
Extremities	Stitching pain in claves; aggravation walking, amelioration pressure	4	4 days
	Stitching pain in both legs; aggravation night, amelioration pressure	4	3 h
Sleep	Sleepiness	4	1 days
Fever	Fever (102°F) associated with vomiting (once of undigested food particles), vertigo, restlessness, weakness, reduced appetite, and disturbed sleep during day and night	5	3 days
Generalities	Weakness of whole body associated with vertigo	4	5 days
	Burning sensation in the whole body	5	2 days

verum group and control group but no distinct similarities or dissimilarities were found.

A comprehensive qualitative symptom profile of intervention group, control group, and former homoeopathic proving symptoms found in the literature [Table 4] reflect that:

- Symptoms were generated in intervention group and were placed in regional spheres (following the Schema Repertory of the Homoeopathic Materia Medica by J. T. Kent[12]) of Mind, Vertigo, Head, Eyes, Nose, Mouth, Throat, Abdomen, Rectum, Cough, Back, Extremities, Sleep and Skin in the present study and were found to have striking similarities to the symptoms present in the homoeopathic literature[3,13,14]
- In addition to the above, symptoms were also generated in intervention group in regional spheres of teeth, stomach, fever, and generalities.

A brief summarization of the main symptoms observed which are also mentioned in the homoeopathic literature is as follows:

1. Anger and attacks of rage
2. Violent pain in the frontal region of the head
3. Eyelids swollen
4. Dryness of mouth with thirst for cold water
5. Sore throat
6. Colicky, gripping pain in the abdomen and diarrhea
7. Dry cough with tearing/throbbing pain in the head
8. Pain in nape of neck, aggravation (*agg.)* looking upward or bending head backward
9. Pain and cramp in the extremities especially calf muscles
10. Complete sleeplessness in 6C and sleepiness in 30C potency.

The incidence of pathogenetic effects in this study has been found to be 1.35.

Placebo symptoms developed during the trial are placed in Table 5.

Discussion

In the present study, when the symptoms generated in the verum group, placebo group and the earlier proving symptoms available in the homoeopathic literature were compared, it was found that marked mental symptoms were elicited in this proving and many symptoms were similar to those mentioned in the literature. Characteristic symptoms were produced related to head, eye, mouth, abdomen, rectum, cough, back and extremities, sleep and fever with marked modalities, and associated symptoms. Well-defined skin symptoms with finer details were observed in comparison with a few vague symptoms mentioned in the homeopathic literature.

Table 4: Qualitative symptom profiles of intervention group, control group, and former Homoeopathic drug proving symptoms

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Mind		Loquacity (talking about irrelevant things), didn't want to be interrupted, if interrupted feels like hitting	Anger with irritability when contradicted, amelioration being alone. This is associated with thoughts of committing suicide Loquacity (talking about irrelevant things), did not want to be interrupted, if interrupted feels like hitting		Extreme anguish[13] Attacks of rage[3] Talks all the time[3] Disconnected, delirious talking[3]
Vertigo	Vertigo with heaviness of head Vertigo with malaise and low BP-110/60 mm Hg; aggravation evening, lying down and next day BP-110/50 mm Hg; aggravation evening Vertigo with dizziness and drowsiness; amelioration lying down	Vertigo, aggravation afternoon, amelioration evening		Vertigo	Vertigo[3] Vertigo, marked and persistent, with stupefaction[14]
Head	Heaviness in head; aggravation evening, amelioration rest Dull aching pain in frontal region of head with drowsiness and vertigo; aggravation 3 pm to 5 pm, amelioration placing hand on forehead. Next day same symptom persisted for whole day Aching pain in frontal and supra-orbital region of head; aggravation motion, amelioration pressure Bursting pain at vertex extending to frontal region; aggravation night. Next day onwards associated with sleepiness Heaviness in occipital region of head (10 am to 6 pm). Next day aching pain in head. Heaviness in the occipital region of the head reappeared after 4 days and continued for 3 days Heaviness of the head Aching pain in the frontal region of the head extending to vertex; aggravation after waking. This was associated with vomiting (two episodes) on the 2nd day	Bursting pain in frontal region of head; aggravation night Pain in head as if head would burst (10 am to 12 noon); aggravation stooping Dull, aching pain in frontal region of head with coryza; aggravation walking, bending forward, afternoon till night, amelioration pressure, after sleep	Bursting pain in head; aggravation night, amelioration pressure Pain in head with feeling as if head would burst in small pieces associated with sleepiness; aggravation bending forward Bursting pain in frontal region of head; aggravation walking, noise, amelioration tight bandaging	Dull aching pain in frontal region of head	Headache in nearly all cases. Very violent, especially in the forehead and vertex, becoming less after 1 or 2 days, sometimes however returning[3] Sensation of pressure and heaviness in the head[3] Throbbing pain in whole head. Beating headache. Violent headache[3] Violent pain in the frontal region. Violent pains in the forehead[3]

Contd...

Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
	Aching pain in whole head with vertigo, sleeplessness and nausea (9 am to 12 noon); amelioration by pressing Aching pain in left side of head associated with heaviness of whole head and over eyebrows (12 noon to 4 pm); amelioration by pressing, after sleep Aching pain in occipital region of head; aggravation moving head in lying position, amelioration drinking tea Bursting pain in occipital region radiating to eyeballs; aggravation pressure, night Pain in bi-temporal region with sensation of heaviness; aggravation opening eyes, talking, amelioration closing eyes Left sided headache at 2: 30 pm for 2-3 min				
Eye	Swelling of both lower eye lids for 2 days. After a gap of 1 day felt heaviness in eyes as if swollen which persisted for 4 days	Swelling of both lower eyelids; aggravation morning	Heaviness in both eyes followed by retro-orbital pain with burning in eyes; aggravation after studying. Next day lachrymation in both eyes with itching and puffiness around the eyes; aggravation after studying	Swelling of both lower eyelids	Eyelids very red and swollen, so that they could hardly be opened[3]
Nose	Sneezing (5-6 bouts) with watery nasal discharge and lachrymation associated with retro-orbital pain Watery nasal discharge with sneezing Coryza with watery nasal discharge and sneezing; aggravation morning, cold air, amelioration afternoon, evening Watery nasal discharge with right-sided frontal headache at 5 pm for 5 min	Sneezing with watery nasal discharge; aggravation morning	Coryza with watery nasal discharge; aggravation morning, night	Sneezing with watery nasal discharge	Very violent fluent coryza, with lachrymation and smarting in the eyes[3]
Face	Red-colored papule on right cheek with throbbing pain				

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Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Mouth	Burning sensation in the mouth with red discoloration of buccal mucosa and ulcer on edge and tip of tongue	Aphthae on lower lip, white in colour, with red margins, and burning pain; aggravation eating, talking Aphthae in mouth with burning pain, whitish in colour, red in margin with dry tongue Dryness of mouth with excessive thirst and desire for cold water			Dryness of the mouth[3] Great thirst for cold water[3]
Teeth		Stitching pain in right lower molar; aggravation eating	Stitching pain in first right lower molar radiating to right ear; aggravation cold drink, amelioration warm water		
Throat	Rawness in throat Pain in throat (soreness with hoarseness) with general weakness, tiredness and heat in palms and body; aggravation on swallowing Soreness in throat with dryness and difficulty in eating food Soreness of throat with tingling sensation Soreness in throat with excessive salivation and difficulty in swallowing Soreness in throat associated with dryness of mouth and malaise; aggravation swallowing solid food	Sore throat A/F exposure to dust; aggravation noon to evening, cold water, amelioration taking tea, gargling by hot water		Sore throat	Inflammation of the throat, preventing swallowing[3]
Stomach	Vomiting of mucus in morning followed by nausea Nausea for 2 days. Reappeared after 7 days for 2 days Heaviness in epigastric region with nausea and bloating of abdomen; aggravation evening till mid night Burning pain in epigastric region, associated with nausea and belching; aggravation lying down, amelioration after vomiting (thrice) of undigested food Nausea with sensation of obstruction in throat; aggravation after dinner Vomiting of food eaten (twice at 6:30 am and 6 pm) with bleeding from left nostril; aggravation after breakfast	Nausea with weakness; aggravation 9 am		Nausea	

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Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Abdomen	Aching pain in abdomen with heaviness; aggravation morning Aching pain in epigastric region with drowsiness; aggravation before and after eating Cutting pain in epigastric region aggravation 12 noon to 2 pm. Next day aching pain in abdomen for same timings. After a gap of 1 day aching pain in abdomen reappeared and continued for 4 days Aching pain in right hypochondrium with dark colored stool in morning; amelioration pressure. Symptom continued whole day but intensity of pain much reduced when woke up next day and subsided after stool Macular eruption with itching on abdomen turned into boils next day Aching pain in right hypochondrium; aggravation 9 am to 1 pm Cutting pain in abdomen associated with diminished appetite and increased thirst for cold water; aggravation 2 pm Aching pain in lower abdomen; aggravation lying on back, amelioration lying on abdomen Aching pain in both hypochondrium (6 pm to 9 pm)	Cutting pain in abdomen; aggravation eating Aching pain in abdomen at 6 pm (umbilical region). Next day pain increased in intensity with loose watery stool (3-4 times/day); aggravation eating Gripping pain in abdomen with loose stool (3 times/day), associated with great thirst, loss of appetite, and bitter taste	Heaviness and stinging pain in whole abdomen; aggravation eating, amelioration pressure Heaviness in epigastric region Colicky pain in abdomen; aggravation eating, drinking, amelioration pressure, bending forward	Aching pain in abdomen Cutting pain in abdomen	Tearing-cutting pain in the abdomen[3] Occasional griping pains in abdomen[3] Profuse diarrhoea; the stools continues for a long time with tenesmus and prostration, only relieved after 8 days[3] Pain in region of stomach[3] Violent colic in stomach and bowels[3]
Rectum	Bleeding per rectum while passing soft stool Fruity smell in stool (one episode)	Stool mixed with blood, burning sensation in rectum; amelioration cold application	Hard, unsatisfactory stool	Bleeding per rectum	Smarting at the anus after stoo[3]
Urine	Profuse urination (without reason)				

Contd...

Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Cough	Dry cough associated with running nose and fever (100°F); amelioration warm drinks. No fever for next 2 days but heat of body present (URTI) Cough with mucoid expectoration associated with coryza and heaviness in chest; aggravation morning, while sleeping, amelioration warm drinks, warm room Dry cough with pain in throat, nasal obstruction and yellowish nasal discharge; aggravation morning, daytime, after eating, cold things	Dry cough; aggravation night	Dry cough with scanty, white expectoration associated with throbbing pain in head on coughing, heaviness in head throughout the day and fever (99.6°F). But cough symptoms continued for next 2 days and fever again on the third day (99°F)	Dry cough	Frequent, violent, dry cough, with tearing pain in the head; the cough was followed by violent pulsation of the heart, lasting several min; at this time the anxiety and pressure in the chest returned, especially while sitting; cough came on at night between 11 and 1[3]
Chest	Itching on sub-mammary region, scratching leads to burning; amelioration undressing				
Back	Stitching pain in lumbar region with restlessness, extending towards right side; amelioration massaging (temporary relief)	Aching pain in nape of neck from 2 pm to 7 pm; aggravation looking upwards. Next day the intensity of symptom increased from morning till evening and continued for 2 more days Dull aching pain with stiffness in lumbar region; aggravation afternoon till night, walking, lying down, amelioration massaging	Cutting pain in lumbar region; aggravation lying down, walking, amelioration sitting, warmth	Pain in lumbar region	Lancinating pain at the nape of neck, on bending head backwards[3] Pain in the loins[3]
Extremities	Aching pain in lower extremities; aggravation night Stitching pain with stiffness and difficulty in movement of right shoulder (4 pm to 8 pm) Tearing, bony pain in left forearm with inability to hold anything (8 am to 11 am) Aching pain in right leg over shin; aggravation walking for 10 days. This was associated with numbness in both lower extremities; aggravation sitting for 5-10 min with folded legs which lasted for 1 more day	Stitching pain in lower extremities especially calf muscles; aggravation night Itching in right leg, scratching leads to burning	Stitching pain in calves; aggravation walking, amelioration pressure Stitching pain in both legs; aggravation night, amelioration pressure	Pain in lower extremities	Pain and cramp in the extremities[3] Violent cramping, paroxysmal, in the calves[3] Violent drawing and tension in limbs[14]

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Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Sleep		Sleeplessness lasting 5 days	Sleepiness		Complete sleeplessness, frequently lasting three or 4 days[3] Great sleepiness[3]
Fever	Fever (101°F) with chills associated with sore throat and watery discharge from nose; amelioration warm application, warm drinks, gargles. On 3rd day only watery nasal discharge Fever (99.8°F) with body ache and malaise Fever with bodyache, nausea and dizziness started in evening and persisted till morning	Fever with chills and body ache in the evening; aggravation cold weather	Fever (102°F) associated with vomiting (once of undigested food particles), vertigo, restlessness, weakness, reduced appetite and disturbed sleep during day and night	Fever with chills and fever with bodyache	
Skin	Itching followed by redness and eruptions (wheal formation) on whole body associated with sleepiness on and off whole night; aggravation after taking bath. Itching reappeared around 1 pm with small red eruptions on the hands. Same symptoms reappeared at 10 pm with sleepiness and continued till 2 days Eruptions with itching on lateral side of both elbows; aggravation 4 pm and 8 pm, amelioration morning Itching whole body Itching on lateral sides of both arms just below shoulders aggravation 9 to 9:30 pm for 3 days. On 4th day eruptions also appeared at the same site with itching which are hard to touch. On the 11th day, skin become hyperpigmented on the spot of eruption while itching continued, then turned into wheal with occasional bleeding on scratching Itching all over body with macular eruptions which are red in colour Itching with macular eruptions on lateral side of left arm just below the shoulder. Next day wheal formation; aggravation after undressing (9 pm to 1 am). On 4th day only itching remained	Small red macules on the left side of the neck and shoulder without itching for 8 days. Then only on neck since the 9th day and disappeared after 5 days Small, red papular eruptions on the right arm and front of the neck, associated with itching and burning; aggravation touch, night, amelioration rubbing		Eruptions with itching	Eruptions on the skin[3]

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Table 4: Contd...

Section	Placebo (C)	*Cuprum aceticum* 6C	*Cuprum aceticum* 30C	Common symptoms of verum and placebo groups	Profile of *cuprum aceticum* by previous homoeopathic provings
Generalities	Weakness and does not want to talk to anyone. After 2 days interval weakness of whole body reappeared with sensation of fatigue, malaise, wants to lie down and does not want to talk to anyone General weakness and tiredness of whole body; aggravation evening Weakness Weakness with fatigue and malaise with low BP (110/50 mm Hg). Next day BP=90/60 mm Hg	Weakness of whole body associated with vertigo Burning sensation in whole body		Weakness of whole body	

URTI: Upper respiratory tract infection, BP: Blood pressure

Table 5: Placebo symptoms developed during the trial

Each one of these symptoms mentioned below were developed and reported by single prover

Location	Symptoms observed	Doses	Symptom duration in days
Vertigo	Vertigo with heaviness of head	6	3 days
	Vertigo with malaise and low BP-110/60 mm Hg; aggravation evening, lying down and next day BP-110/50 mm Hg; aggravation evening	8	2 days
	Vertigo with dizziness and drowsiness, amelioration lying down	4	6 days
Head	Heaviness in head; aggravation evening, amelioration rest	12	3 h
	Dull aching pain in frontal region of head with drowsiness and vertigo; aggravation 3 pm to 5 pm, amelioration placing hand on forehead. Next day same symptom persisted for whole day	6	2 days
	Aching pain in frontal and supra-orbital region of head; aggravation motion, amelioration pressure	12	3 days
	Bursting pain at vertex extending to frontal region; aggravation night. Next day onwards associated with sleepiness	8	10 days
	Heaviness in occipital region of head (10 am to 6 pm). Next day aching pain in head. Heaviness in occipital region of head reappeared after 4 days and continued for 3 days	5	5 days
	Heaviness of head	4	1 day
	Aching pain in frontal region of head extending to vertex; aggravation after waking. This was associated with vomiting (two episodes) on 2nd day	4	2 days
	Aching pain in whole head with vertigo, sleeplessness and nausea (9 am to 12 noon); amelioration by pressing	12	3 h
	Aching pain in left side of head associated with heaviness of whole head and over eyebrows (12 noon to 4 pm); amelioration by pressing, after sleep	12	4 h
	Aching pain in occipital region of head; aggravation moving head in lying position, amelioration drinking tea	3	2 days
	Bursting pain in occipital region radiating to eyeballs; aggravation pressure, night	7	5 h
	Pain in bi-temporal region with sensation of heaviness; aggravation opening eyes, talking, amelioration closing eyes	8	4 days
	Left sided headache at 2:30 pm for 2-3 min	6	2-3 min
Eye	Swelling of both lower eye lids for 2 days. After a gap of 1 day felt heaviness in eyes as if swollen for 4 days	8	6 days
Nose	Sneezing (5-6 bouts) with watery nasal discharge and lachrymation associated with retro-orbital pain	8	9 days
	Watery nasal discharge with sneezing	8	3 days
	Coryza with watery nasal discharge and sneezing; aggravation morning, cold air, amelioration afternoon, evening	8	3 days
	Watery nasal discharge with right sided frontal headache at 5 pm for 5 min	8	5 min

Contd...

Table 5: Contd...

Each one of these symptoms mentioned below were developed and reported by single prover			
Location	**Symptoms observed**	**Doses**	**Symptom duration in days**
Mouth	Burning sensation in the mouth with red discoloration of buccal mucosa and ulcer on edge and tip of tongue. Dryness of mouth	11	4 days
Face	Red coloured papule on right cheek with throbbing pain	8	15 days
Throat	Rawness in throat	6	6 days
	Pain in throat (soreness with hoarseness) with general weakness, tiredness and heat in palms and body; aggravation on swallowing	6	4 days
	Soreness in throat with dryness and difficulty in eating food	6	1 day
	Soreness of throat with tingling sensation	4	5 days
	Soreness in throat with excessive salivation and difficulty in swallowing	11	4 days
	Soreness in throat associated with dryness of mouth and malaise; aggravation swallowing solid food	7	3 days
Stomach	Vomiting of mucus in morning followed by nausea	8	2 days
	Nausea for 2 days. Reappeared after 7 days for 2 days	8	4 days
	Heaviness in epigastric region with nausea and bloating of abdomen; aggravation evening till mid night	4	1 day
	Burning pain in epigastric region, associated with nausea and belching; aggravation lying down, amelioration after vomiting (thrice) of undigested food	12	1 day
	Nausea with sensation of obstruction in throat; aggravation after dinner	4	2 days
	Vomiting of food eaten (twice at 6:30 am and 6 pm) with bleeding from left nostril; aggravation after breakfast	4	1 day
Abdomen	Aching pain in abdomen with heaviness; aggravation morning	12	3 h
	Aching pain in epigastric region with drowsiness; aggravation before and after eating	6	2 days
	Cutting pain in epigastric region aggravation 12 noon to 2 pm. Next day aching pain in abdomen for same timings. After a gap of 1 day aching pain in abdomen reappeared and continued for 4 days	8	6 days
	Aching pain in right hypochondrium with dark colored stool in morning; amelioration pressure. Symptom continued whole day but intensity of pain much reduced after waking up next day and subsided after stool	12	2 days
	Macular eruption with itching on abdomen turned into boils next day	5	2 days
	Aching pain in right hypochondrium; aggravation 9 am to 1 pm	5	4 h
	Cutting pain in abdomen associated with diminished appetite and increased thirst for cold water; aggravation 2 pm	8	3 days
	Aching pain in lower abdomen; aggravation lying on back, amelioration lying on abdomen	4	3 days
	Aching pain in both hypochondrium (6 pm to 9 pm)	7	3 h
Rectum	Bleeding per rectum while passing soft stool	4	2 days
Stool	Fruity smell in stool (one episode)	5	1 day
Urine	Profuse urination (without reason)	4	30 days
Cough	Dry cough associated with running nose and fever (100°F); amelioration warm drinks. No fever for next 2 days but heat of body present (URTI)	12	3 days
	Cough with mucoid expectoration associated with coryza and heaviness in chest; aggravation morning, while sleeping, amelioration warm drinks, warm room	4	3 days
	Dry cough with pain in throat, nasal obstruction and yellowish nasal discharge; aggravation morning, daytime, after eating, cold things	3	5 days
Chest	Itching on sub-mammary region, scratching leads to burning; amelioration undressing	4	6 days
Back	Stitching pain in the lumbar region with restlessness, extending toward right side; amelioration massaging (temporary relief)	8	4 days
Extremities	Aching pain in lower extremities; aggravation night	8	4 days
	Stitching pain with stiffness and difficulty in the movement of the right shoulder (4 pm to 8 pm)	6	4 h
	Tearing, bony pain in the left forearm with inability to hold anything. (8 am to 11 am)	3	3 h
	Aching pain in the right leg over shin; aggravation walking for 10 days. This was associated with numbness in both lower extremities; aggravation sitting for 5-10 min with folded legs which lasted for 1 more day	8	11 days

Contd...

Table 5: Contd...

Each one of these symptoms mentioned below were developed and reported by single prover			
Location	**Symptoms observed**	**Doses**	**Symptom duration in days**
Fever	Fever (101◦ F) with chills associated with sore throat and watery discharge from nose; amelioration warm application, warm drinks, gargles. On the 3rd day, only watery nasal discharge	12	3 days
	Fever (99.8°F) with body ache and malaise	10	4 days
	Fever with body ache, nausea, and dizziness started in the evening and persisted till the morning.	11	1 day
Skin	Itching followed by redness and eruptions (wheal formation) on whole body associated with sleepiness on and off whole night; aggravation after taking bath. Itching reappeared around 1 pm with small red eruptions on the hands. Same symptoms reappeared at 10 pm with sleepiness and continued till 2 days	12	4 days
	Eruptions with itching on lateral side of both elbows; aggravation 4 pm and 8 pm, amelioration morning	12	5 days
	Itching whole body	5	6 days
	Itching on the lateral sides of both arms just below shoulders aggravation 9 to 9:30 pm for 3 days. On the 4th day, eruptions also appeared at the same site with itching which are hard to touch. On the 11th day, skin become hyperpigmented on the spot of eruption while itching continued, then turned into wheal with occasional bleeding on scratching	12	15 days
	Itching all over the body with macular eruption which are red in color	7	12 days
	Itching with macular eruption on the lateral side of the left arm just below the shoulder. Next day wheal formation; aggravation after undressing (9 pm to 1 am). On the 4th day, only itching remained	12	4 days
Generalities	Weakness and does not want to talk to anyone. After 2 days interval weakness of whole body reappeared with sensation of fatigue, malaise, wants to lie down, and does not want to talk to anyone	8	3 days
	General weakness and tiredness of whole body; aggravation evening	3	4 h
	Weakness	8	1 day
	Weakness with fatigue and malaise with low BP (110/50 mm Hg). Next day BP=90/60 mm Hg	8	4 days

URTI: Upper respiratory tract infection, BP: Blood pressure

Certain symptoms developed during the proving trial were quite similar to those found in previous literature. Thus, it can be considered as a characteristic for this drug. However, there have been additional findings as well in a few of these symptoms which need to be clinically verified. A few symptoms which are overlapping in both the groups could be due to the nocebo effect or due to confounding factors such as alteration in weather, food or regimen. Although adequate efforts were made to rule out such effects by proper record keeping, these can't be ruled out completely. The pathogenetic findings of this drug need further verification by using it for therapeutic purposes in the patients reporting with similar symptoms.

In one of the articles, Dr. Teut[15] has mentioned that 'placebo proving occasionally seem to produce similar symptoms to the proving symptoms, thus casting further doubt on the use of this medium in proving' and has attributed it to nocebo effect. A nocebo response is explained as subject's own negative expectations and/or negative suggestions from therapists/clinical staff in the absence of any treatment. Nocebo phenomena are generally explained by Pavlovian conditioning and expectations induced by verbal information and suggestions. In this trial also nocebo phenomenon can be considered and apart from the individual's own perception, this can be attributed to the discussion which usually takes place among the students of homoeopathic colleges who are the participants in the study. This poses a limitation as it is difficult to keep a check on them for not discussing or sharing the experiences. The massive number of symptoms developed in the control group could be considered because of such discussions among the students.

There are certain other limitations in the study apart from the nocebo effect; like no defined parameters for the classification of characteristic symptoms and less number of provers which may be addressed in future studies.

Conclusion

The pathogenesis of the *Cu acet.* found in this study has produced symptoms which were already noted in the homoeopathic literature and there are many symptoms which are new. These signs and symptoms need to be subjected to clinical verification study for confirming their therapeutic utility. This will further enhance the scope and utility of this drug by the profession.

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Conflicts of interest

None declared.

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क्यूप्रम एसेटिकम का होम्योपैथिक रोगजनक पैथोजेनेटिक परीक्षणः एक बहुकेन्द्रिक, डबल . – ब्लाइंड यादृच्छिक, प्लासिबो नियंत्रित परीक्षण

पृष्ठभूमिः यद्यपि क्यूप्रम मेटेलिकम का लक्षण विज्ञान बेहद विस्तृत है, इसके अन्य क्षार अपूर्ण रूप से सिद्ध हैं। अतः, क्यूप्रम एसेटिकम के लिए होम्योपैथिक रोगजनक पैथोजेनेटिक परीक्षण किया गया था। **उद्देश्यः स्**वस्थ मनुश्य प्रूवर्स पर होम्योपैथिक प्रभावों में क्यूप्रम एसेटिकम के प्रति पैथेजेनेटिक प्रतिक्रिया का सार निकालना। **सामग्रियाँ एवं पद्धतियाँः** केन्द्रीय होम्योपैथिक अनुसंधान संस्थान (सीसीआरएच) के तीन केन्द्रों पर एक बहु–केन्द्रिक डबल– ब्लाइंड यादृच्छिक, प्लासिबो नियंत्रित,परीक्षण संचालित किया गया था। पूर्व–परीक्षण चिकित्सीय जाँच को संचालित करने के पष्चात् चुने गए 50 संबंधित स्वस्थ प्रूवर्स पर प्रूविंग अध्ययन संचालित किया गया। सभी प्रूवर्स को परीक्षण के प्रथम चरण के दौरान प्लासिबो दी गई थी। अगले दो चरणों में, यादृच्छिकीकरण के पष्चात्, क्यूप्रम एसेटिकम को हस्तक्षेपीय समूह में (एन = 34), तथा प्लासिबो समूह में (एन = 16) 60 सी एवं 30 सी प्रभावों में व्यवस्थित किया गया था। क्यूप्रम एसेटिकम से उपार्जित प्रभावित आंकड़ों को अध्ययन –सह–आँकड़ा प्रक्रमण प्रकोष्ठ में संकलित एवं मूल्यांकित किया गया था। **परिणामः** 34 प्रूवर्स में से जो वास्तविक दवा परीक्षण पर थे, केवल 12 प्रूवर्स ने ही लक्षणों को व्यक्त किया था। 30 सी एवं 200सी प्रभावशीलता में क्रमशः 26 एवं 20 लक्षण व्यक्त किए गए थे। **निष्कर्षः** अध्ययन परीक्षण के दौरान प्राप्त हुई पैथोजेनेटिक प्रतिक्रिया ने क्यूप्रम एसेटिकम होम्योपैथिक दवा के इस्तेमाल की संभावना को बढ़ा दिया है। इस परीक्षण में उपार्जित लक्षणों की बहुमूल्यता नैदानिक सत्यापन करने पर और ज्यादा बढ़ेगी।

Essai homéopathique pathogénétique de Cuprum aceticum: essai multicentrique, en double-aveugle, randomisé et contrôlé par placebo

Contexte: Bien que la symptomatologie de Cuprum metallicum soit assez vaste, ses autres sels ont des preuves fragmentaires. Ainsi, un essai pathogénique homéopathique pour Cuprum aceticum a été entrepris. **Objectif:** Provoquer la réponse pathogénique à Cuprum aceticum en puissances homéopathiques sur des prouveurs humains en bonne santé. **Matériels et méthodes:** Un essai multicentrique randomisé en double-aveugle, contrôlé par placebo, a été mené dans trois centres du Conseil central pour la recherche en homéopathie (CCRH). L'épreuve a été menée sur 50 prouveurs relativement en bonne santé sélectionnés après avoir effectué l'examen médical préalable au procès. Tous les prouveurs ont été donnés un placebo au cours de la première phase de l'essai. Au cours des deux phases suivantes, Cuprum aceticum a été administré à des concentrations de 6C et 30C, dans le groupe d'intervention (n=34); et placebo dans le groupe placebo (n=16), après randomisation. Les données probantes ainsi générées sur Cuprum aceticum ont été compilées et analysées dans la cellule d'épreuve-cum-traitement des données. **Résultat:** Sur les 34 prouveurs ayant participé à un essai de médicament, seuls 12 témoins ont manifesté des symptômes. 26 et 20 symptômes ont été manifestés respectivement à puissance 30C et 200C**. Conclusion:** La réponse pathogénique suscitée au cours de l'essai d'épreuve élargit le champ d'utilisation du médicament homéopathique Cuprum aceticum. Les symptômes générés dans cet essai auront plus de valeur lorsqu'ils seront vérifiés cliniquement.

Ensayo patogenético homeopático de Cuprum aceticum: Ensayo multicéntrico, doble ciego, aleatorizado, controlado con placebo

Fundamento: Aunque la sintomatología de *Cuprum metallicum* es bastante extensa, sus otras sales tienen pruebas fragmentarias. Así, se realizó un ensayo patogenético homoeopático para Cuprum aceticum. **Objetivo:** Para obtener la respuesta patogénica a *Cuprum aceticum* en potencias homeopáticas en demostradores humanos sanos. **Materiales y métodos:** Se llevó a cabo un ensayo multicéntrico doble ciego aleatorizado, controlado con placebo, en tres centros del Consejo Central para la Investigación en Homeopatía (CCRH). Se realizaron pruebas en 50 probadores relativamente sanos seleccionados después de realizar el examen médico previo al ensayo. Todos los probadores recibieron placebo durante la primera fase del ensayo. En las dos fases siguientes, *Cuprum* aceticum se administró en potencias 6C y 30C, en el grupo intervención (n=34); y placebo en el grupo placebo (n=16), después de la aleatorización. Los datos de prueba así generados en Cuprum aceticum fueron compilados y analizados en la celda de procesamiento de pruebas y datos. **Resultado:** De 34 probadores que estaban en *ensayo real de la droga, solamente 12 probadores manifestaron síntomas. 26 y 20 síntomas* fueron manifestados en potencia 30C y 200C respectivamente. **Conclusión:** La respuesta patogenética que se produjo durante el ensayo clínico de prueba amplía el alcance del uso de la medicina homeopática Cuprum aceticum. Los síntomas generados en este ensayo tendrán más valor cuando se verifiquen clínicamente.

Homöopathische pathogenetische Studie an Cuprum aceticum: Eine multizentrische, doppelblinde, randomisierte, placebokontrollierte Studie

Hintergrund: Obwohl die Symptomatik von Cuprum metallicum ziemlich groß ist, haben seine anderen Salze fragmentarische Beweise. Daher So wurde die homöopathische pathogenetische Studie für Cuprum aceticum aufgenommen. **Ziel:** Die pathogenetische Reaktion auf Cuprum aceticum in homöopathischen Potenzen auf gesunde menschliche Provers hervorzurufen. Um die pathogenetische Reaktion auf Cuprum aceticum in homöopathischen Potenzen bei gesunden menschlichen Prüfern auszulösen**. Materialien und Methoden:** Eine multizentrische, randomisierte, placebokontrollierte Doppelblindstudie mit mehreren Zentren wurde an drei Zentren des Central Council for Research in Homöopathy (CCRH) durchgeführt. Der Nachweis wurde an 50 relativ gesunden Testern durchgeführt, die nach Durchführung der medizinischen Voruntersuchung ausgewählt wurden. Alle Prüfer Prover erhielten in der ersten Phase der Studie ein Placebo. In den nächsten zwei Phasen, Cuprum aceticum wurde in den Potenzen 6C-und 30C-Potenzen in der Intervention verabreicht gruppe (n=34); und Placebo in der Placebogruppe (n=16) nach Randomisierung. Die auf Cuprum aceticum so erzeugten Nachweisdaten wurden in der Proving-cum-data processing cell zusammengestellt und analysiert. **Ergebnisse Ergebnis:** Von 34 Probanden, die an einer Arzneimittelprüfung Wirkstoffstudie teilnahmen, zeigten nur 12 Probanden Symptome. 26 und 20 Symptome zeigten sich in 30C bzw. 200C Potenz. **Schlussfolgerung:** Die pathogenetische Reaktion, die während der Proving-Studie hervorgerufen wurde, erweitert den Anwendungsbereich des homöopathischen Arzneimittels Cuprum aceticum. Die in dieser Studie erzeugten Symptome haben einen höheren Wert, wenn sie klinisch verifiziert werden.

醋酸铜的顺势病理实验：多中心、双盲、随机、安慰剂对照试验

背景：虽然铜金属的症状是相当庞大的，它的其他盐有零碎的证明。 因此，采取了铜针的顺势疗法的致病性试验。目的：探讨顺势疗法对健康人的病理反应。 材料和方法：在顺势疗法研究委员会（CCRH）的三个中心进行了一项多中心双盲随机安慰剂对照试验。 在进行审前体检后选择的50名相对健康的证明者上进行了证明。 在试验的第一阶段，所有证明者都给予安慰剂。 在接下来的两个阶段,在干预组(n=34)分别以6C和30C的剂量给药；和安慰剂组(n=16)。在验证实验数据处理单元上，对由此产生的丙酮铜的验证数据进行编辑和分析。结果：34名实际药物试验者中，只有12人出现症状。30C和200C的药力分别表现出26和20种症状。结论：在验证试验中引发的病理反应扩大了同种顺势疗法药物醋酸铜的应用范围。临床验证时，此试验产生的症状将更有价值。