Increasing Blood Oxygen Saturation following 6 minutes' Walk Test in Healthy Human Volunteers with *Coca erythroxylon* 6CH and *Vanadium metallicum* 6CH: A Double-blind, Randomized, Placebo-controlled Pilot Trial

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Abstract

Background: Oxygen saturation (SpO_2) is an essential component during patient care and management because a variety of acute negative consequences on specific organs and systems can result from hypoxemia. **Aim and Objective:** The effects of two homeopathic medicines, *Coca erythroxylon* 6CH and *Vanadium metallicum* 6CH, were explored against placebos on blood SpO_2 following a 6-min walk test (6MWT) in apparently healthy human volunteers after 3 days of intervention. **Subjects and Methods:** A 3-day, randomized (1:1:1), double-blind, placebo-controlled pilot trial was conducted on 60 healthy human volunteers. Participants were randomized to *Coca erythroxylon* ($n = 20$), *Vanadium metallicum* ($n = 20$), and identical-looking placebos ($n = 20$). Blood SpO_2% (primary), peak expiratory flow (PEF; mL), and breath holding timing (s) were measured at baseline once preintervention and postintervention and again before and after a 6MWT. Interventions were administered 4 times a day for 3 consecutive days. Group differences were estimated using a one-way analysis of variance. Significance levels were set at $P < 0.05$ two-tailed. **Results:** Statistically significant differences in pre- and postintervention mean changes were observed in blood SpO_2% in the *Coca erythroxylon* group in comparison with the others ($F_{2, 57} = 3.815$, $P = 0.028$); however, no such significant differences could be observed in PEF and breath holding time. No adverse events were reported. **Conclusion:** *Coca erythroxylon* significantly increased blood SpO_2% following a 6MWT in healthy human volunteers. It is necessary to conduct definitive trials to validate the findings.

Trial Registration: CTRI/2022/08/044810; UTN: U1111-1281-3263.

Keywords: Blood oxygen saturation, *Coca erythroxylon*, homeopathy, placebo, randomized controlled trial, *Vanadium metallicum*

Introduction

A hemoglobin molecule is considered saturated with oxygen when it has carried as many as four oxygen molecules. A molecule of hemoglobin is considered to have a 100% saturation if every blinding site on the molecule contains oxygen. Most of these process combines through the respiratory organs. While breathing air at sea level, a healthy person with normal lungs will have an arterial oxygen saturation (SpO_2) of 95%–100%.[1] A pulse oximetry can measure how much oxyhemoglobin in blood is carried. This is called SpO_2%. It is a painless test that uses a noninvasive sensor gadget placed over a person's fingertip or earlobe.[2] It provides a comfortable, noninvasive technique to measure blood SpO_2 continuously. When it comes to identifying hypoxia, pulse oximetry offers a 90% specificity and a 92% sensitivity at a threshold of 92%

Submitted: 21-Mar-2024 **Revised:** 27-Apr-2024
Accepted: 06-May-2024 **Published:** 29-Jun-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/dmms

DOI: 10.4103/jdmimsu.jdmimsu_173_24

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How to cite this article: Mandal D, Ansary S, Gunin A, Saha S, Midya A, Das S, *et al*. Increasing blood oxygen saturation following 6 minutes' walk test in healthy human volunteers with *Coca erythroxylon* 6CH and *Vanadium metallicum* 6CH: A double-blind, randomized, placebo-controlled pilot trial. J Datta Meghe Inst Med Sci Univ 2024;19:319-24.

SpO_2. As per the guidelines of the Indian Council of Medical Research, SpO_2 is 94% in room air. British Thoracic Society and the Thoracic Society of Australia and New Zealand issued guidelines for the acute use of oxygen in adults. They suggested an acceptable range of 94%–98% and 92%–96%, respectively.[3,4]

To evaluate a patient's ability to engage in functional activity after developing a chronic respiratory illness, the 6-min walk test (6MWT) is quite popular. It has shown to be dependable, affordable, secure, and simple to use.[5] The patient is instructed to walk as far as they can on a straight path that is between 400 and 700 m long as part of the test.[6] The test's main goal is to measure the overall distance walked, which is then interpreted in comparison with the reference standards. The distance walked and maximal oxygen intake have a gradual, incremental relationship.

In routine practice, homeopathic medicines, *Coca erythroxylon* and *Vanadium metallicum,* are used for the treatment of dyspnoea, anemia, and low saturation state. The homeopathic literature mentions the main function of *Vanadium* as that of an oxygen carrier and having a prominent action on anemia, especially when the patients are emaciated.[7] *Coca*, also known as the mountaineer's remedy, is claimed to be beneficial in a range of complaints related to climbing mountains, including dyspnea, anxiety, palpitation, and sleeplessness.[7] However, even after careful searches in different bibliometric and electronic databases, evidence in support of such claims remained minuscule.[8] No randomized trial substantiating the effect of *Coca erythroxylon* and *Vanadium metallicum* in improving SpO_2 of blood could be identified.

Subjects and Methods

Study design

This was a randomized (1:1:1), placebo-controlled, three parallel arms, double-blind pilot trial.

Study setting

This study was conducted at the outpatient department of the institution.

Trial registration and research ethics

The trial protocol (Memo. No. DHC/Eth-45/2018/440/8/2022; July 29, 2022) was authorized by the Institutional Ethics Committee (IEC) before commencement and was uploaded prospectively in the Clinical Trials Registry– India with reg. no. CTRI/2022/08/044810 [Supplementary File 1]. The essential elements of the protocol can be found online at https://ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid = 73141 and EncHid= and userName = effect%20of%20 homoeopathy%20on%20 bloo%20oxygen. The research was carried out in compliance with the ethical guidelines outlined in the World Medical Association Declaration of Helsinki.[9] Before enrolment, every participant received a participant details sheet in the local vernacular Bengali, which outlined the study's goals, methodology, potential benefits, and risks, as well as privacy issues. Subsequently, each participant was provided with informed consent to participate in the trial.

Participants

Inclusion criteria were the participants with no major diseases with apparently healthy status, no abnormality detected during clinical examination and laboratory examinations (complete hemogram, fasting blood sugar, lipid profile, liver enzymes, electrocardiogram, and chest X-ray), age from 18 to 65 years, of both gender or transgender, aware of the trial's requirements, and freely signed the written informed consent form the criteria for exclusion were the vulnerable population (e.g. unconscious, nonambulatory, too sick for consultation, differently abled, terminally or critically ill patients), recognized instances of various systemic illness or unstable mental health issues affecting the quality of life, any form of dependency or misuse of substances, currently receiving any therapy or treatment for any chronic condition for last 4 weeks, pregnant, puerperal and nursing mothers, immune-compromised conditions, and concurrent enrollment in any other clinical trial.

Intervention

In the verum group, either *Coca erythroxylon* 6CH or *Vanadium metallicum* 6CH was administered four times a day for 3 consecutive days. Each dosage comprised four no. 40 cane sugar globules moistened with the medicine, to be taken orally on a clean tongue and with an empty stomach. In the control group, the participants received placebos that were identical to the actual treatment. For consecutive 3 days, the placebo regimen was four cane sugar globules no. 40, moistened with rectified spirit, taken four times a day. The study subjects were instructed to abstain from smoking, drinking, and consuming any medicinal substances that might interfere with the intended medicinal action. The Hahnemann Publishing Company®, Kolkata, was the source of various commodities and homeopathic medications in bulk. The medicines and placebos were put back into identical glass bottles, given codes, names, and potencies on the labels, and served out following a confidential chart of random numbers.

Outcomes

1. Primary: Blood SpO_2% as measured by pulse oximeter before and after a 6MWT before and after intervention
2. Secondary: Breath-holding capacity (in seconds) measured by a stopwatch and peak flow rate measured by a peak flow meter before and after a 6MWT and after intervention.

Sample size

It was not possible to properly quantify the sample size at the outset of the investigation because there was not a single published study with a similar methodology. Since the study was exploratory, a target size of 60 (i.e., 20 × 3) was taken into consideration.

Randomization

A random sequence was constructed by an impartial third party

who was not allowed to have any influence over the trial using the permuted block randomization method (6 blocks of size 10). To dispense either coded medications or placebos, the blinded pharmacist was given access to this random number chart in coded form and under tight confidentiality; it was not, under any circumstances, divulged to the participants or investigators.

Blinding

The double-blind technique was used by masking the participants, investigators, outcome assessors, pharmacists, and data entry operators. The blinding process was carried out using identically coded containers (designated as "1," 2, and "3") that contained either of the two medications or a similar-looking placebo. The vials used to deliver the medication or the rectified spirit were also filled with globules no. 40. After the study was finished and the data set was frozen, the codes were broken.

Allocation concealment

The random number sequence was kept a secret from the trial recruiters to accomplish this.

Statistical methods

It adhered to the intention-to-treat plan as per the CONSORT guidelines:[10] however, no missing vales were reported. Within-group changes were evaluated using a paired *t*-test; between-group differences were examined using an unpaired *t*-test and one-way analysis of variance (ANOVA). Statistical significance was defined as $P < 0.05$. Statistical Package for the Social Sciences, version 23.0 (IBM Corp., IBM SPSS Statistics for Windows, Armonk, NY: USA) for Windows was used for all analyses.

Adverse event reporting

The physicians directed the participants to promptly report any adverse events during the trial. Patients were instructed to communicate such occurrences either directly during outpatient visits or through phone throughout the study.

Trial reporting

Reporting followed the RedHot guidelines and the CONSORT extension checklist for pilot and feasibility trials [Supplementary Files 2 and 3].[10,11]

Results

Participant flow

Sixty-six healthy human volunteers underwent eligibility screening; 6 were excluded of which 2 declined consent, and 4 were already undergoing homeopathic treatment. Sixty participants were randomized in a 1:1:1 ratio to *Coca* ($n = 20$), *Vanadium* ($n = 20$), and placebo ($n = 20$). There were no dropouts; the final analysis includes all 60 participants adhering to the trial protocol [Figure 1].

Recruitment

The screening process for all participants took place in the last week of August 2022. Following this, the intervention period was extended for 3 days, from August 24, 2022 to August 26, 2022. The final assessment was conducted on August 27, 2022.

Numbers analyzed

The final analysis included all 60 participants who took part in the *Coca* 20/20, *Vanadium* 20/20, and placebo 20/20.

Baseline confounders

At baseline, comparability between the two groups was established by the similar distribution of the probable confounders (sociodemographic variables) between groups without any significant differences (all $P > 0.05$) [Table 1].

Outcomes and estimation

1. SpO_2%: Preintervention significant changes after a 6MWT were observed in SpO_2% in the *Vanadium* and

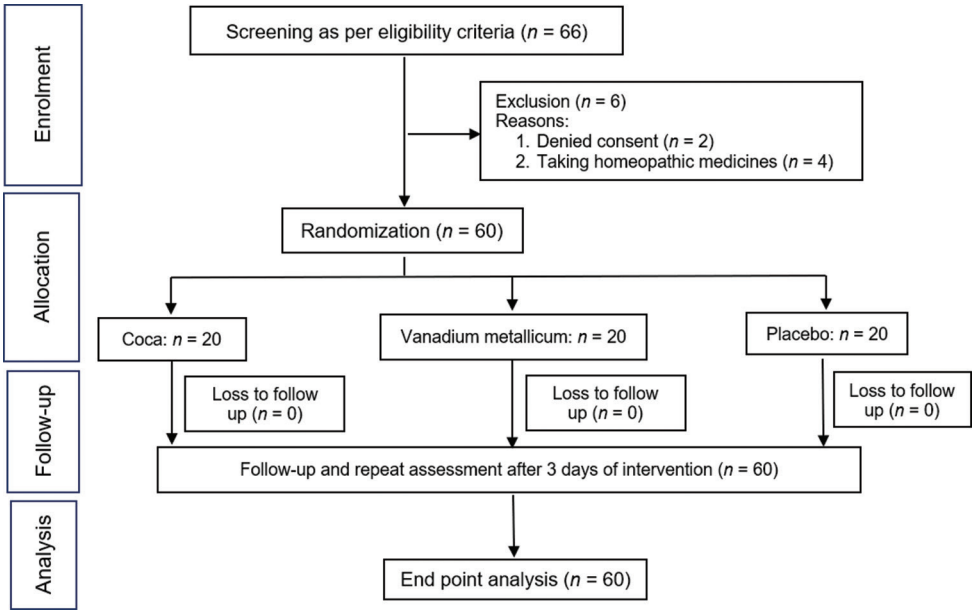

Figure 1: CONSORT study flow diagram

placebo groups, but not in *Coca*. Postintervention, significant changes observed in mean changes were statistically significant favoring *Coca* against *Vanadium* and placebo ($F_{2, 57} = 3.815$, $P = 0.028$, one-way ANOVA) [Table 2]

Table 1: Sociodemographic variables at baseline

Variables	*Coca*	*Vanadium*	Placebo	*P*
Age (years)[a]	27.5±7.6	27.0±5.7	29.5±7.0	0.479
Sex: Male/female[b]	18/2	16/4	17/3	0.675
Height[a]	168.4±9.5	163.3±8.9	167.2±9.3	0.199
Weight[a]	63.6±13.1	63.7±13.7	64.7±10.9	0.955
BMI[a]	22.3±3.9	23.8±4.1	23.1±3.3	0.498
Blood pressure (mm of Hg)[a]				
Systolic	122.9±7.0	124.3±9.9	124.8±8.5	0.780
Diastolic	71.6±7.8	72.7±5.3	72.1±6.4	0.870

[a]Continuous data presented as means ± standard deviations and and unpaired t-tests applied to detect mean differences; [b]Categorical data presented as absolute values (percentages) and Pearson's chi-squared or Fisher's exact tests applied to detect group differences. BMI: Body mass index

2. PEF: Preintervention significant within-group changes in PEF were observed in the *Coca* group only, but not in *Vanadium* and placebo. Postintervention, significant within-group changes occurred in both *Coca* and *Vanadium*, but not in placebo; however, the difference in mean changes could not achieve statistical significance ($F_{2, 57} = 20128$, $P = 0.128$, one-way ANOVA) [Table 3]
3. Breath holding time: Both pre- and postintervention changes in breath holding time (s) were significant in all three groups; however, the differences in mean changes were statistically nonsignificant ($F_{2, 57} = 0.927$, $P = 0.402$, one-way ANOVA) [Table 4].

Adverse events

None of the groups reported any significant adverse effects.

Discussion

This pilot study was intended to compare the effects of *Coca erythroxylon* 6CH and *Vanadium metallicum* 6CH against

Table 2: Comparison of oxygen saturation percentage

Groups	Pre-Rx			Post-Rx			Difference in mean changes±SE (95% CI)
	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	
Coca	97.2 (1.3)	97.5 (1.0)	0.3±1.1 (−0.8–0.2)	98.0 (0.8)	98.5 (0.7)	0.5±0.6 (−0.8–−0.2)**	−0.2±0.3 (−0.7–0.4)
Vanadium	97.1 (0.8)	97.6 (0.9)	0.5±0.9 (−0.9–−0.1)*	98.1 (0.7)	98.4 (0.7)	0.3±0.6 (−0.6–−0.1)*	0.2±0.2 (−0.3–0.6)
Placebo	97.5 (0.9)	98.1 (0.8)	0.6±0.9 (−1.0–−0.2)**	98.2 (0.7)	98.0 (0.8)	−0.2±0.9 (−0.2–0.6)	0.8±0.3 (0.2–1.4)
$F_{2,57}$	0.695	2.252	0.493	0.380	2.587	5.386	3.815
P	0.503	0.114	0.614	0.686	0.084	0.007**	0.028*

*P<0.05, **P<0.01. SD: Standard deviation, CI: Confidence interval, 6MWT: 6-min walk test, SE: Standard error

Table 3: Comparison of peak expiratory flow (mL)

Groups	Pre-Rx			Post-Rx			Difference in mean changes±SE (95% CI)
	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	
Coca	638.5 (70.4)	650 (67.0)	11.5±10.9 (−16.6–−6.4)***	648.5 (64.6)	656.5 (64.1)	8.0±10.0 (−12.7–−3.3)**	3.5±3.3 (−3.2–10.2)
Vanadium	610. (68.4)	611.5 (69)	1.5±8.1 (−5.3–2.3)	618 (70.4)	623 (69.8)	5.0±7.6 (−8.6–−1.4)**	−3.5±2.5 (−8.5–1.5)
Placebo	614 (81.3)	616.5 (78.4)	2.5±7.4 (−5.8–0.8)	630 (82.5)	631 (82.2)	1.0±7.2 (−4.4–2.4)	1.5±2.3 (−3.1–6.1)
$F_{2,57}$	0.880	1.706	7.710	0.889	1.167	3.515	2.128
P	0.420	0.191	0.001**	0.417	0.319	0.036*	0.128

*P<0.05, **P<0.01, ***P<0.001. SD: Standard deviation, CI: Confidence interval, 6MWT: 6-min walk test, SE: Standard error

Table 4: Comparison of breath-holding time (s)

Groups	Pre-Rx			Post-Rx			Diff in mean changes±SE (95% CI)
	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	Before 6MWT	After 6MWT	Mean difference±SD (95% CI)	
Coca	39.4 (9.5)	34.1 (9.4)	−5.3±6.4 (2.3–8.3)**	43.1 (9.7)	37.3 (9.0)	−5.8±4.6 (3.7–8.0)***	0.5±1.7 (−3.0–4.1)
Vanadium	37.9 (9.5)	34.3 (9.0)	−3.5±3.7 (1.8–5.3)***	41.8 (9.6)	35.9 (8.7)	−5.9±4.4 (3.8–8.0)***	2.4±1.3 (−0.3–5.0)
Placebo	39.5 (14.0)	34.3 (11.9)	−5.2±6.6 (2.1–8.3)**	40.9 (13.0)	35.9 (11.9)	−5.0±3.4 (3.4–6.6)***	−0.2±1.7 (−3.6–3.2)
$F_{2,57}$	0.132	0.002	0.583	0.207	0.126	0.293	0.927
P	0.877	0.998	0.561	0.813	0.882	0.747	0.402

**P<0.01, ***P<0.001. SD: Standard deviation, CI: Confidence interval, 6MWT: 6-min walk test, SE: Standard error

placebos on SpO_2% following a 6MWT in healthy human volunteers. According to the study, there were significant differences in blood SpO_2% between the *Coca* group and the other groups. However, PEF and breath-holding time did not reveal any significant difference between the groups. The findings suggest a potential positive effect of *Coca erythroxylon* 6CH on blood SpO_2 in healthy individuals after physical exertion. This result aligns with the known physiological effects of *Coca*, which has been traditionally used for its stimulant properties and is believed to enhance physical endurance and reduce fatigue. The increase in blood SpO_2% observed in the *Coca* group indicates a potential improvement in oxygen uptake and utilization, which can have significant implications for overall health and performance. Interestingly, no significant differences were observed in PEF and breath-holding time among the groups. These parameters are commonly used as indicators of respiratory function and efficiency. The lack of significant changes in PEF and breath-holding time suggests that the observed effect of *Coca* on blood SpO_2% may not be primarily mediated through improvements in lung function or breath-holding capacity. This indicates that *Coca* might influence oxygenation at the systemic level, possibly through mechanisms related to vascular and oxygen transport processes. The absence of adverse events reported during the trial is an important finding, suggesting that the interventions (*Coca*, *Vanadium*, and placebo) were well-tolerated by the participants. This is particularly relevant when considering potential therapeutic applications of *Coca erythroxylon* 6CH, as safety is a crucial aspect of any treatment. The absence of adverse events supports the feasibility and safety of conducting larger definitive trials to further investigate the effects of *Coca* on blood SpO_2. It is important to take into account certain limitations when interpreting the pilot trial's findings. First, the study included a relatively small sample size, which may limit the generalizability of the findings. Conducting larger definitive trials with a larger number of participants will provide more robust evidence. Second, the study focused on healthy human volunteers, and the results may not necessarily apply to individuals with specific health conditions or compromised oxygenation. More research is needed to investigate the effects of *Coca* in different demographics, including patients with respiratory or cardiovascular disorders. The trial utilized the "gold standard" randomized clinical trial design, which helped minimize biases and increase the reliability of the findings. The allocation of participants to different groups in a 1:1:1 ratio further enhances the study's internal validity. However, it is important to note that the placebo effect cannot be completely ruled out, as participants and researchers were unaware of the treatment assignments. Further studies could consider including an additional control group receiving no intervention to better evaluate the specific effects of *Coca* and *Vanadium*. In conclusion, this pilot trial provides preliminary evidence suggesting that *Coca erythroxylon* 6CH may have a positive effect on blood SpO_2 following a 6MWT in healthy human volunteers. The observed increase in blood SpO_2% supports the traditional use of *Coca* for its potential beneficial effects on physical endurance and fatigue reduction. However, larger definitive trials with diverse populations are required to confirm these results and establish the underlying mechanisms of action.

The safety profile observed in this study encourages further research into the potential therapeutic applications of *Coca erythroxylon* 6CH in improving oxygenation and overall well-being.

Conclusion

In this trial, *Coca erythroxylon* in comparison with *Vanadium metallicum* and placebos significantly increased blood SpO_2% following a 6MWT in healthy human volunteers. Further definitive and robust trials are warranted with independent replications to arrive at any confirmatory conclusion.

Data availability statement

This article contains all the data that was collected or examined during the investigation. The appropriate author can be contacted with any further inquiries.

Ethical statement

Complying with the World Medical Association Declaration of Helsinki, the research was conducted in accordance with ethical principles. The Institutional Ethics Committee gave its approval to the protocol. A patient information leaflet explaining the goals, procedures, risks and rewards of participating, as well as confidentiality concerns, was given to each participant in the local vernacular of Bengali. Written informed consent was obtained from each participant before enrollment.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary file 1

Clinical Trial Details (PDF Generation Date :- Wed, 20 Mar 2024 03:27:19 GMT)

CTRI Number	CTRI/2022/08/044810 [Registered on: 22/08/2022] - **Trial Registered Prospectively**
Last Modified On	20/03/2024
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Homeopathy
Study Design	Randomized, Parallel Group, Placebo Controlled Trial
Public Title of Study	Effects of homeopathic medicines on blood oxygen
Scientific Title of Study	Effects of Coca erythoxylon 6CH and Vanadium metallicum 6CH on blood oxygen saturation following 6 minutes' walk test on healthy human volunteers: Double-blind, randomized, placebo-controlled pilot trial

Secondary IDs if Any

Secondary ID	Identifier
U1111-1281-3263	UTN

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Source of Monetary or Material Support

Source of Monetary or Material Support
> D N De Homoeopathic Medical College and Hospital, Govt. of West Bengal, 12, Gobinda Khatick Road, Tangra, Kolkata 700046, West Bengal

Primary Sponsor

Primary Sponsor Details	
Name	D N De Homoeopathic Medical College Hospital
Address	12, Gobinda Khatick Road, Tangra, Kolkata 700046, West Bengal
Type of Sponsor	Government medical college

Details of Secondary Sponsor

Name	Address
Nil	NA

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
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Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Institutional Ethical Committee of D. N. De Homoeopathic Medical College and Hospital	Approved	29/07/2022	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Healthy Human Volunteers	No major diseases with apparently healthy status, no abnormality detected during clinical and laboratory examinations

Intervention / Comparator Agent

Type	Name	Details
Intervention	Coca erythroxylon 6CH	Coca erythroxylon 6CH, four times a day for 3 consecutive days. Each dose consists of 4 cane sugar globules no. 40 moistened with the medicine, to be taken orally on clean tongue with empty stomach. All medicines and sundry items will be procured from a Good Manufacturing Practice (GMP)-certified firm. Route of administration: per oral. Duration of therapy: 3 days
Intervention	Vanadium metallicum 6CH	Vanadium metallicum 6CH, four times a day for 3 consecutive days. Each dose consists of 4

		cane sugar globules no. 40 moistened with the medicine, to be taken orally on clean tongue with empty stomach. All medicines and sundry items will be procured from a Good Manufacturing Practice (GMP)-certified firm. Route of administration: per oral. Duration of therapy: 3 days
Comparator Agent	Placebo	This group will receive placebos, identical in appearance with the verum, four times a day for 3 consecutive days. Each dose consists of 4 cane sugar globules no. 40 moistened with non-medicinal rectified spirit, to be taken orally on clean tongue with empty stomach. Route of administration: per oral. Duration of therapy: 3 days.

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	65.00 Year(s)
Gender	Both
Details	a) No major diseases with apparently healthy status b) No abnormality detected during clinical examination and laboratory examinations (complete hemogram, fasting blood sugar, lipid profile, liver enzymes, electrocardiogram and chest x-ray) c) Age 18-65 years d) Participants of either sex e) Participants providing with written informed consent

Exclusion Criteria

Exclusion Criteria	
Details	a) Vulnerable population – unconscious, ambulatory, too sick for consultation, differently abled, terminally or critically ill patients b) Diagnosed cases of unstable psychiatric complaints or other systemic diseases affecting quality of life c) Any kind of substance abuse and/or dependence d) Currently receiving standard any therapy or homoeopathic treatment for any chronic condition within last 4 weeks. e) Pregnant and puerperal women, lactating mothers f) Self-reported immune-compromised conditions

Method of Generating Random Sequence	Permuted block randomization, variable
Method of Concealment	Pre-numbered or coded identical Containers
Blinding/Masking	Participant, Investigator, Outcome Assessor and Date-entry Operator Blinded

Primary Outcome

Outcome	Timepoints
Blood SpO2% as measured by pulse oximeter	Before and after a 6 minutes walk test before and after intervention

Secondary Outcome

Outcome	Timepoints
Breath holding capacity (in seconds) measured by a stop watch	Before and after a 6 minutes walk test before and after intervention
Peak flow rate measured by a peak flow meter	Before and after a 6 minutes walk test before and after intervention

Target Sample Size	**Total Sample Size=**60 **Sample Size from India=**60 **Final Enrollment numbers achieved (Total)=**60 **Final Enrollment numbers achieved (India)=**60
Phase of Trial	Phase 2
Date of First Enrollment (India)	24/08/2022
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**0 **Months=**0 **Days=**15
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Completed
Publication Details	None yet; to be published later on
Brief Summary	Oxygen saturation (SpO_2) is an essential component during patient care and management because hypoxemia can lead to many acute adverse effects on individual organs and systems. The effects of two homeopathic medicines *Coca erythroxylon* 6CH and *Vanadium metallicum* 6CH explored against placebos on blood SpO_2 following a 6-minute walk test (6MWT) in healthy human volunteers after three days of intervention. A 3-day, randomized (1:1:1), double-blind, placebo-controlled, pilot trial was conducted on 60 healthy human volunteers. Participants were randomized to *Coca erythroxylon* ($n = 20$), *Vanadium metallicum* ($n = 20$), and identical-looking placebos ($n = 20$). Blood SpO_2% (primary), peak expiratory flow (PEF; ml), and breath holding timing (sec) were measured at baseline once pre-intervention and post-intervention, and again before and after a 6MWT. Interventions were administered 4 times a day for 3 consecutive days. Group differences were estimated using a one-way analysis of variance. *P* values were set at 0.05 two-tailed as statistically significant. Statistically significant differences in pre- and post-intervention mean changes were observed in blood SpO_2% in the *Coca erythroxylon* group in comparison with the others ($F_{2, 57} = 3.815$, $P = 0.028$); however, no such significant differences could be observed in PEF and breath holding time. No adverse events were reported. *Coca erythroxylon* significantly increased blood SpO_2% following a 6MWT in healthy human volunteers. Definitive trials are warranted to confirm the findings.

Supplementary file 2: CONSORT 2016 checklist of information to include when reporting a randomised pilot trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	3-4
	2b	Specific objectives or research questions for pilot trial	3-4
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	5-6
	4b	Settings and locations where the data were collected	5
	4c	How participants were identified and consented	5-6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	6
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	NA
	6c	If applicable, pre-specified criteria used to judge whether, or how, to proceed with future definitive trial	-
Sample size	7a	Rationale for numbers in the pilot trial	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	7
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	7
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	7

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	7
	11b	If relevant, description of the similarity of interventions	6
Statistical methods	12a	Methods used to address each pilot trial objective whether qualitative or quantitative	7
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the pilot trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	9
Outcomes and estimation	17a	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	9-10
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	9-10
	19a	If relevant, other important unintended consequences	-
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	11-12
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	11-12
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	11-12
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	5
Protocol	24	Where the pilot trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	14
	26	Ethical approval or approval by research review committee, confirmed with reference number	5

Supplementary file 3: RedHot checklist of information to include when reporting randomized trials of homeopathy

Item	Treatment (CONSORT item number)	Description	Reported on page No
1	Rationale (2)	*Type of homeopathy*	
		Individualized/Specific	3-4
		Formula	-
		Isopathy	-
		Evidence base	
		Sources, references	3-4
2	Participants (3)	Knowledge condition	5-6
		Baseline health definition in proving	NA
3	Medications (4)	*Manufacture*	
		• Manufacturer, Pharmacopoeia (or process), references	6
		• Potency and scale	6
		• Dilution method	6
		Nomenclature	
		• Individualized: list or frequency table	NA
		• Formula: constituents, trade name	NA
		Dosage	
		• Dose, timing, form	6
4	Consultations (4)	Setting	
		Clinical history detail	6
		Duration, frequency	6
		Number needed to agree prescription	-
		Group process or expert consultation	-
		Confidence in prescriptions	-
5	Practitioners (4)	Number in study	-
		Experience, accreditation, qualifications	-

		Current schools or styles of homeopathy	5-6
6	Co-interventions (4)	*Included*	
		Rationale, intended effect, references	NA
		Duration, frequency	NA
		Excluded	
		Stopping of mainstream interventions	NA
		Antidotes	NA
7	Control interventions (4)	*Active*	NA
		Rationale, references	NA
		Placebo	5-6
		Manufacturing process	5-6
8	Adverse events (8)	Aggravations	7-8, 10

Statement, to be included with checklist:
These guidelines are intended as a supplement to, not a substitute for, the CONSORT Statement, to improve the reporting of homeopathic treatments. We strongly recommend that reports of clinical trials of homeopathy follow the CONSORT guidelines, particularly the flowchart.

The points above are specific to homeopathy. All points refer to controlled clinical trials, all but item 7 to uncontrolled outcome studies.

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