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A double-blind, placebo-controlled Homoeopathic Pathogenetic Trial of *Nanocurcumin* 6X

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ABSTRACT

Background: A double-blind, randomized, placebo-controlled Homoeopathic Pathogenetic Trial (HPT) of *Nanocurcumin* was conducted using the accepted guidelines, Ethical Committee approval, and scientific documentation. The standardized potentization method was adopted to enhance the quality of the pathogenetic trial. Various statistical calculations were used for evaluation of the symptoms.

Aim: The aim of the study was to conduct an HPT of *Nanocurcumin* 6X, a nano-substance in dilution.

Materials and Methods: The drug *Nanocurcumin* 6X was proved through double-blind, placebo-controlled method. The trial was done in 6X potency on 30 healthy provers who were screened by their pretrial medical examinations and routine laboratory investigations. Of 30 provers, 7 were on placebo and 23 were on drug. Medicine was prepared according to the principles of trituration given in Homoeopathic Pharmacopeia of India. The signs and symptoms generated during the trial period were noted by the provers and decoded and compiled afterwards.

Results: Of 23 provers who were on verum 17 provers manifested symptoms and out of 7 provers who were on placebo 2 manifested symptoms.

Conclusion: The drug pathogenesis evolved indicates its therapeutic use in sinusitis, migraine, dyspepsia, constipation, diarrhoea, dysmenorrhoea, pharyngitis, bronchitis, etc.

Keywords: Homoeopathic pathogenetic trial, *Nanocurcumin*, Pathogenetic effects, Proving

INTRODUCTION

For several millenia, *Curcumin* has been used as a medicinal substance. Turmeric has been grown in India since ancient times. It reached China by 700 AD, East Africa by 800 AD and West Africa by 1200. It was introduced to Jamaica in the 18th century. Today, turmeric is widely cultivated throughout the

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tropics. Turmeric was probably cultivated at first as a dye, and then became valued as a condiment as well as for cosmetic purposes. It is often used in cooking as a substitute for the more costly saffron. Sushruta Samhita dating back to 250 BC highly recommends turmeric for relieving food poisoning effect. Turmeric was introduced to China from India by 700 AD.[1]

Since, the time of Ayurveda (1900 BC) numerous therapeutic activities have been assigned to turmeric for a wide variety of diseases and conditions, including those of the skin, pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders.[2]

Curcumin, which gives the yellow color to turmeric, was first isolated almost two centuries ago, and its structure as diferuloylmethane ($C_{21}H_{20}O_6$) was determined in 1910.

Most currently available preparations of *curcumin* contain approximately 77% diferuloylmethane, 18% demethoxycurcumin, and 5% bisdemethoxycurcumin. Curcumin is hydrophobic in nature and frequently soluble in dimethylesulfoxide, acetone, ethanol, and oils. It has an absorption maximum around 420 nm. In a study, it was found that the aqueous dispersion of *Nanocurcumin* was much more effective than *curcumin* against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Penicillium notatum*, and *Aspergillus niger*. The results demonstrated that the water solubility and antimicrobial activity of *curcumin* markedly improved by particle size reduction up to the nano range. For the selected microorganisms, the activity of *Nanocurcumin* was more pronounced against Gram-positive bacteria than Gram-negative bacteria. Furthermore, its anti-bacterial activity was much better than anti-fungal activity.

There is large body of evidence showing that curcuminoids have wide-ranging biological and pharmacological activities including anti-oxident, anti-inflammatory, antibacterial, antifungal, anti-parasitical, anti-mutagen, anti-cancer, anti-detox, anti-hepatoma activity, anti-malarial activity, anti-tumor, anti-ischemic, and anti-amyloid properties.[3-7]

Nanoparticles-based materials have attracted much attention in recent years because of their characteristic size and geometry dependent chemical and physical properties. Nanoparticles are of great scientific interest as they are effectively a bridge between bulk materials and atomic or molecular structures. Literature survey suggests nanoparticle research is an area of intense scientific research, due to wide potential applications in human therapy. Nanoparticles are sized between 1 and 100 nm. Nanoparticles have a very high surface area to volume ratio. This makes the particles very reactive or catalytic. Nanoparticles are easier to pass through cell membranes in organisms and get interacted rapidly with biological systems. The nanotechnology helps in increasing the bioavailability and reduce perceived toxicity as they offer several other additional benefits such as improved cellular uptake, enhanced dissolution rates excellent biostability controlled release functions, and multifunctional design enhancement in its pharmacological activities (e.g., anti-oxidant and anti-hepatoma activities), etc.[8]

Recently, targeted and triggered drug delivery systems accompanied by nanoparticle technology have emerged as prominent solutions to the bioavailability of therapeutic agents. Nanoparticle-based delivery systems will probably be suitable for highly hydrophobic agents like *curcumin* circumventing the pitfalls of poor aqueous solubility. However, very few studies have been published citing *Curcumin* nanoparticles. A recent study by Bisht *et al*. reported the synthesis, physicochemical characterization and cancer-related application of a polymer-based nanoparticle of *Curcumin* namely "nanoparticulate *Curcumin*" with <100 nm size. Nanoparticulate *Curcumin* is made up of the micellar aggregates of cross-linked and random copolymers of N-isopropylacrylamide, with N-vinyl-2-pyrrolidone and poly (ethylene glycol) monoacrylate. Nanoparticulate *Curcumin*, unlike free *Curcumin*, is readily dispersed in aqueous media. Nanoparticulate *Curcumin* was found to have similar *in vitro* activity as that of free *Curcumin* in pancreatic cell lines. Like free *Curcumin*, nanoparticulate *Curcumin* also inhibits activation of the transcription factor nuclear factor-kappa B, and reduces steady state levels of pro-inflammatory cytokines such as interleukins and tumor necrosis factor receptor.[8]

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structures. Literature survey suggests nanoparticle research is an area of intense scientific research, due to wide potential applications in human therapy. Nanoparticles are sized between 1 and 100 nm. Nanoparticles have a very high surface area to volume ratio. This makes the particles very reactive or catalytic. Nanoparticles are easier to pass through cell membranes in organisms and get interacted rapidly with biological systems. Recently, nanoparticle technology emerged as a potential area of targeted drug delivery systems and make biological availability of the therapeutic agent.

In a study, it was found that the aqueous dispersion of *Nanocurcumin* was much more effective than *curcumin* against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Penicillium notatum*, and *Aspergillus niger*. The results demonstrated that the water solubility and antimicrobial activity of *curcumin* markedly improved by particle size reduction up to the nano range. For the selected microorganisms, the activity of *Nanocurcumin* was more pronounced against Gram-positive bacteria than Gram-negative bacteria. Furthermore, its anti-bacterial activity was much better than anti-fungal activity. The mechanism of anti-bacterial action of *curcumin* nanoparticles was investigated by transmission electron micrograph (TEM) analysis, which revealed that these particles entered inside the bacterial cell by completely breaking the cell wall, leading to cell death.[10]

Pilot Phase I clinical trials have shown *curcumin* to be safe even when consumed at a daily dose of 12 g for 3 months. Other clinical trials suggested a potential therapeutic role for *curcumin* in diseases such as familial adenomatous polyposis, inflammatory bowel disease, ulcerative colitis, colon cancer, pancreatic cancer, hypercholesteremia, atherosclerosis, pancreatitis, psoriasis, chronic anterior uveitis, and arthritis.[11,12]

Multiple research show *curcumin* regulates various immune cells such as T lymphocytes (CD4), (CD8), B lymphocytes, natural killer cells, macrophages, dendritic cells, and other immune cells.[12]

Curcumin arrests the growth of cancer cells in the G2/S phases of cell cycle. Curcumin also aids in the control of tumor progression through its indirect actions and its ability to stimulate hosts' anti-cancer immune responses.[13]

A study was conducted to establish the inhibiting character of *curcumin* for proliferation of tumor cells. Pharmacologically safe compounds that can inhibit the proliferation of tumor cells have potential as anti-cancer agents. Curcumin, a diferuloylmethane, is a major active component of the food flavor turmeric (*Curcuma longa*) that has been shown to inhibit the proliferation of a wide variety of tumor cells.[14]

Study Rationale

Proving of *C. longa* 6X was done by Central Council for Research in Homoeopathy (CCRH) in 1973.[16] A clinical verification study of *C. longa* 6C, 30C and 200C was done by CCRH during 2005–2010.[17]

In parallel with the recent conventional medical researches, it is felt essential to carry out this type of evidence-based studies that is, application of nanoparticles in homoeopathic provings in homoeopathy. Keeping in view the results of the above studies, an effort has been made to prove the *Nanocurcumin* 6X on healthy individuals.

Objective

The objective of this study was to elicit the pathogenetic effects of the homoeopathic preparation of Nano *curcumin Nanocurcumin* on apparently healthy human provers in homoeopathic preparation.

MATERIALS AND METHODS

The material and methods were adopted from the protocol of Drug Proving Program CCRH (2010).[18]

Study Design

- Study type: Interventional study design
- Allocation: Randomized
- Control: Placebo control
- Masking: Double-blind.

Period of study

Between May 2013 and July 2013. The total proving period was of 6 weeks for all the provers starting from the administration of intervention up to the completion of the observation of disappearance of signs and symptoms.

Participants and setting

International Study and Research Centre on Homoeopathy, Bhubaneswar and Biju Pattnaik Homoeopathic Medical College and Hospital, Berhampur, Ganjam.

Selection of provers

The provers were selected from Biju Pattnaik Homoeopathic Medical College and Hospital, Berhampur, Ganjam and International Study and Research Centre on Homoeopathy, Bhubaneswar. There were 17 male and 13 female provers from the above two centers. From Biju Pattnaik Homoeopathic Medical College and Hospital, Berhampur, Ganjam there were 17 provers (7 males and 10 females) and from International Study and Research Centre on Homoeopathy, Bhubaneswar there were 13 provers (10 males and 3 females). The Provers were informed about the objectives and benefits of trial through 'Provers Information Sheet'. Selection of Provers was made according to the following inclusion and exclusion criteria.

Inclusion Criteria

- Both male and female above the age of 18 years
- No medication in last 2 months before the trial
- Recommendation of the examining physician in pretrial medical examination and in routine laboratory investigations of the provers
- Submitted "written informed consent."

Exclusion Criteria

- Provers suffering from any acute or chronic disease
- Provers under any kind of medical treatment
- Provers with any hysterical or anxious activities (such individuals display a high incidence of 'Placebo' effects)
- Provers having history of allergies, food hypersensitivity etc.
- Female provers during pregnancy, puerperium, or during breast-feeding
- Provers with color blindness
- Prover who has undergone surgery in last 2 months
- Previous homoeopathic treatment in last 2 months
- Participation in any clinical or proving trial during the last 6 months.

Sample Size

Thirty provers were enrolled for this proving program according to the above inclusion criteria.

Ethical Consideration

The drug proving protocol had been duly approved and cleared by the Ethical Committee of International Study and Research Centre on Homoeopathy, Bhubaneswar with the following observations/guidelines:

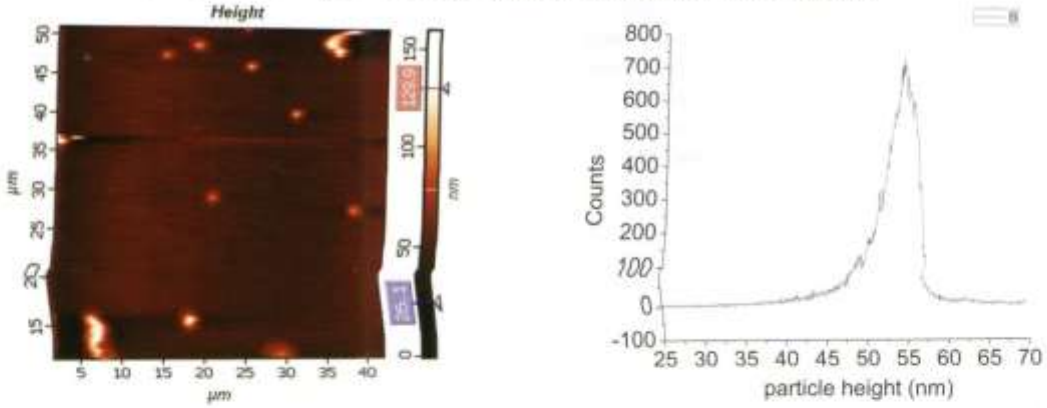
- Safety for the provers is an important prerequisite in drug proving
- The drug substance will be administered in 6X potency only, which is known to provoke transient 'proving symptoms,' but does not cause toxicological effects as it is in dilution form that is, potentized form
- The prover should be in such a mental, physical state as to be able to exercise fully his/her power of choice
- The nature and purpose of the drug proving must be explained to the provers
- The investigator or the investigating team should discontinue the proving if in his/her or their judgment, the proving, if continued, may be harmful (any serious adverse conditions due to the medicine) to the prover.

Study Medication

Nanocurcumin was procured in 6X trituration (powder form). Atomic force microscopy (AFM) study conducted on the raw material *Nanocurcumin* yielded large size particles of 50–60 nm, whereas, AFM study conducted on *Nanocurcumin* 6X showed nanoparticles of two different sizes, majority of small size of 3–8 nm and few of larger size of 15–20 nm. Characterization was carried out at Bhabha Atomic Research Centre Mumbai and *Nanocurcumin* was obtained from Konark Herbal Health Care Pvt. Ltd., Mumbai. The scanning electron microscope instrument used was from Seron Inc., make (Model AIS 2100) having standard tungsten filament. An accelerating voltage of 20 KV and magnification of 10 kx was used for recording the micrographs. The samples were spread over mirror polished single crystal of Si substrate prior to its mounting on the stub. Purity test of each substance that is, of *Nanocurcumin*, sugar of milk and alcohol were done before the preparation the drug. Preparation of dilution of *Nanocurcumin* 6X according to principles of trituration Homoeopathic Pharmacopoeia of India[19] was done at Dr. A. C. Homoeopathic Medical College and Hospital, mini pharmacy, Bhubaneswar with the prior permission of Principal-cum-Superintendent of that college. For placebo only sugar of milk was dispensed as doses in identical powder form to *Nanocurcumin* 6X trituration. Character analysis certificates of *Nanocurcumin*, sugar of milk, and alcohol are given in respectively. AFM study of *Nanocurcumin* is given in Table 1.

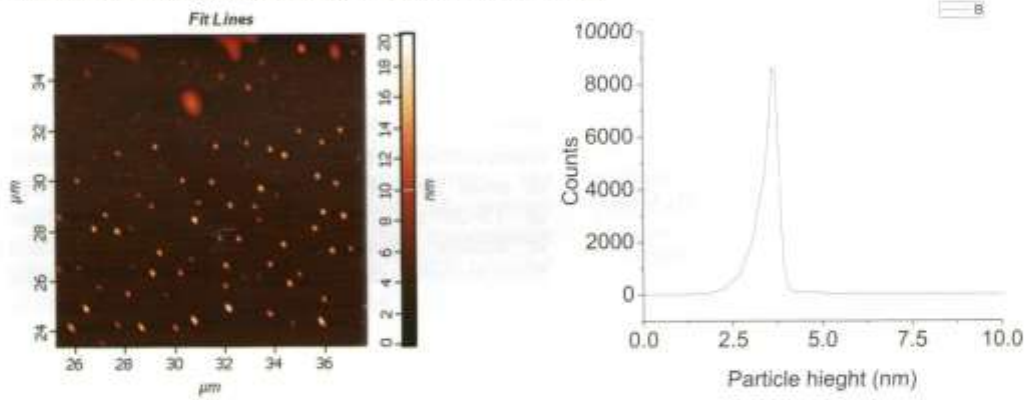
Table 1: AFM study of *Nanocurcumin*

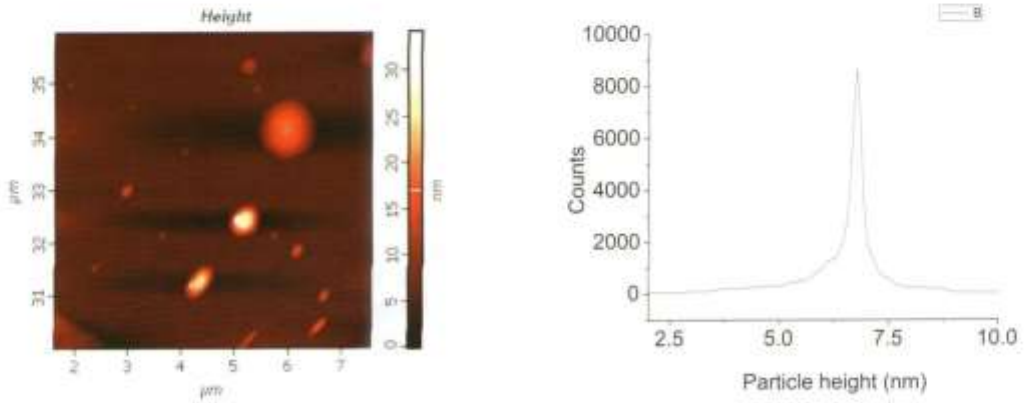
Raw material (orange color) AFM pictures are presented below obtains from BARC Mumbai



Good quality AFM pictures could not be obtained for this sample as sample strongly interacts with AFM tip. Particle heights are in the range of 50-60 nm

AFM picture of Nanocurcumin 6X obtained from BARC Mumbai





Majorities are very small particles and particle heights are in the range of 3-8 nm. Few particles having height in the range of 15-20 nm are also present

AFM: Atomic Force Microscopy; BARC: Bhabha Atomic Research Centre

Preparation of Nanocurcumin 6X

As the drug is in powdered (dry) form the method of preparation of dry substances laid down in Homoeopathic Pharmacopoeia of India was adopted. The preparation of *Nanocurcumin* 6X was done by trituration process under decimal scale.

Principle of trituration process under decimal scale: 1 part by weight of medicinal substance is mixed with 9 parts by weight of sugar of milk.

Trituration

At first, in decimal scale the drug substance was prepared up to 6X as follows:

The 9 parts by weight of sugar of milk was divided in the proportion 1:3:5 parts. First, 1 part by weight of crude drug that is, *Nanocurcumin* was taken in a sterilized mortar and 1 part by weight of sugar of milk was added in the crude substance. The mixture was grinded or rubbed thoroughly for 6 minutes by a sterilized pestle. After 6 minutes of rubbing, the mixture was scraped and stirred by a sterilized spatula for 4 minutes. Then again the mixture was rubbed with pestle for 6 minutes and scraped for 4 minutes. Then 3 parts by weight of sugar of milk was added to the mixture and the same procedure of 6 minutes of rubbing and 4 minutes of scrapping was repeated twice. Then 5 parts by weight of sugar of milk was added to the mixture and the same procedure was repeated for the same time duration as stated before. Likewise, 1 hour time duration was completed and now the strength of drug material was 1X potency. The next higher potencies that is, 2X, 3X...up to 6X were prepared by employing the same process.

Methodology of Proving

All the provers were screened according to the above mentioned inclusion criteria. Pretrial medical examinations were done by experts/specialists and case taking of all the provers was done by the investigators.

Randomization, Coding and Blinding

Pregenerated randomized numbers obtained from the website www.randomization.org were used in the study. Each prover was allotted a code number which bears the drug code. The same code number was also labeled on the phial containing the trial product (drug/placebo). The coding of the drug/placebo was done by the principal investigator. The investigators as well as the provers were kept blind about the trial substance that is, to whom drug was given and to whom the placebo was given.

Qualitative Indices

For verum group:

Qualitative pathogenetic index = Total number of symptoms of a particular intensity divided by the total number of provers contributed to that particular symptom.

Percentage of symptoms of severe intensity = Number of symptoms of severe intensity divided by total number of symptoms of the trial.

Percentage of symptoms of moderate intensity = Number of symptoms of moderate intensity divided by total number of symptoms of the trial.

Percentage of symptoms of mild intensity = Number of symptoms of mild intensity divided by total number of symptoms of the trial.

For placebo group:

Incidence of pathogenetic effects of the trial = Number of provers who had produced symptoms divided by total number of provers taking medicine.

Methodology of Proving

Phase-I

Before commencing the administration of the intervention every prover was observed for a symptom-free period of 1-week Phase-II. Then every prover was given four doses of intervention (drug/placebo) every day up to 3 days that is, a maximum of twelve doses of intervention were given to all provers. Each prover was advised to note down daily the details of his/her feelings/changes in mind and body after taking the drug. The total proving period was of 6 weeks for all the provers starting from the administration of intervention up to the completion of the observation of disappearance of signs and symptoms. Provers were instructed to follow the dietary guidelines laid down by Hahnemann in his Organon of Medicine and this was given in prover's information sheet.

Recording of Sign(s) and/or Symptom(s)

Some provers did not develop any sign/symptom after taking the scheduled twelve doses of intervention and also during the scheduled post intervention period. It was marked as 'No Symptom.' When the provers developed signs and/or symptoms then they were instructed to stop taking further doses of intervention.

The provers were instructed to note down the sequence of the appearance of new sign(s) and/or symptoms(s), their progress and the number of doses after which each sign and/or symptom appeared with date, time of onset, and duration for which it persisted.

Each prover was asked to write down the everyday changes in mind and body in a day book proforma and then each prover was interrogated by the investigators to verify those sign(s) and/or symptom(s) recorded by him/her in that proforma. Then the verified symptoms were recorded in complete details in respect of their location, sensation, modalities, and concomitants by the principal investigator.

After completion of proving period, the provers were examined by the specialists again for post trial medical examinations along with the laboratory investigations.

Adverse Effects

During proving, no serious adverse events occurred.

Compilation

The proved drug was decoded by the principal investigator after completion of proving period. The sign(s) and/or symptom(s) produced by each prover of both verum (drug) and placebo (control) group were noted down with prover code, 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) produced by verum group were separated from those generated by provers of control group. The sign(s) and/or symptom(s) which were commonly produced by the placebo as well as the drug in provers were not taken into consideration. The sign(s) and/or symptom(s) generated by the provers kept on drug were compiled as per the schema of the Kent's Repertory that is, mind, vertigo, head, eye, ear…generalities.

RESULTS

The pathogenetic effects of verum group and placebo group are given in Tables 2 and 3 respectively. The graphical presentation regarding the number of symptoms of verum group versus placebo group, number of provers of verum group versus placebo group producing the symptoms in various systems of the body, comparison between the intensities of the symptoms of verum group versus placebo group, qualitative pathogenetic indices of various intensities of both verum and placebo group and overall assessment of quantitative pathogenetic indices of both verum and placebo group are given in Figures 1-5, respectively.

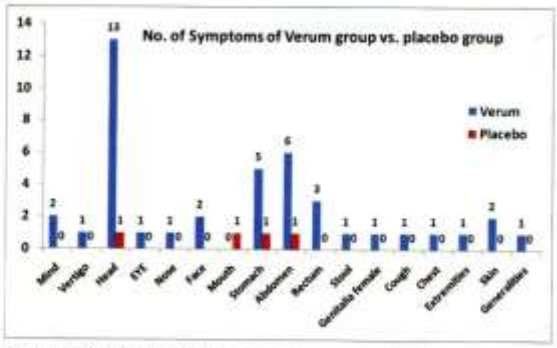


Figure 1: Pathogenetic effects verum group versus placebo group

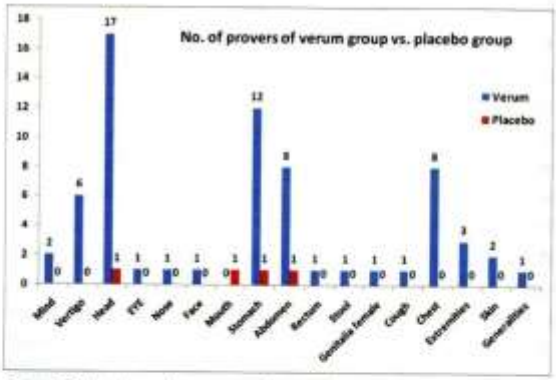


Figure 2: Number of provers producing the symptoms in verum group versus placebo group

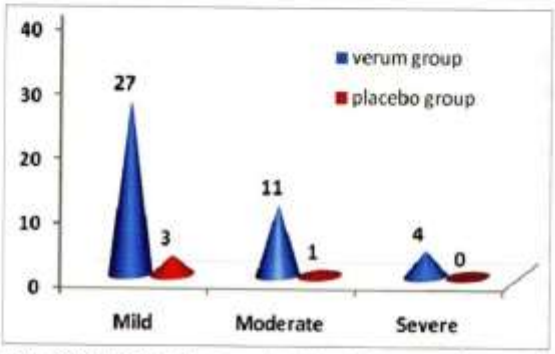


Figure 3: Comparison in various intensities of symptoms of verum and placebo group

Quantitative Indices

For verum group:

Incidence of pathogenetic effects of the trial = Number of provers who had produced

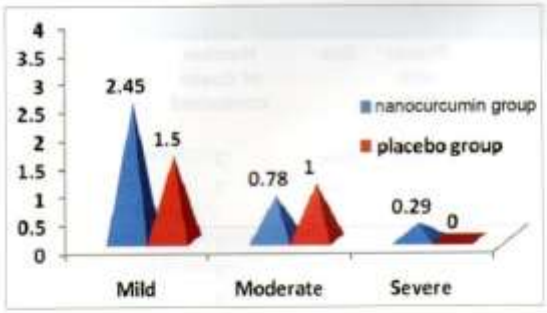


Figure 4: Qualitative pathogenetic indices of various intensities of both verum and placebo group

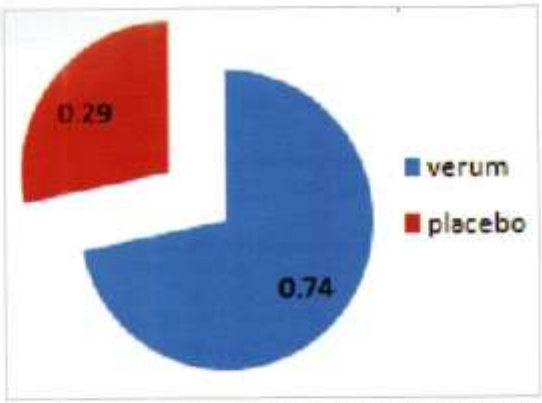


Figure 5: Overall assessment of quantitative indices of verum versus placebo group

symptoms divided by total number of provers taking medicine = 17/23 = 0.74 × 100 = 74%.

Incidence of pathogenetic effects per prover = Total number of symptoms produced during the trial divided by total number of provers taking medicine and included in final compilation = 42/17 = 2.47.

For placebo group

Incidence of pathogenetic effects of the trial = Number of provers who had produced symptoms divided by total number of provers taking medicine = 2/7 = 0.29 × 100 = 29%.

DISCUSSION

The pathogenetic trial of *Nanocurcumin* of 6X was done on 30 healthy human provers. Among the 30 provers 23 were kept on actual drug and 7 were kept on placebo. Provers from 23 of verum group 17 produced signs and symptoms and from 7 provers of placebo group 2 produced signs and symptoms.

Total number of signs and symptoms of the trial was 42. Of these 42 symptoms 4 symptoms were of severe intensity, 11 symptoms were of moderate intensity, and 27 symptoms were of mild intensity. These 4 symptoms of severe intensity were produced by 14 provers, 11 symptoms of moderate intensity were produced by 14 provers and 27 symptoms of mild intensity were produced by 11 provers [Figure 3].

Symptoms pertaining to the Mind have not been found to be so prominent. Symptoms related to male sexual organs have not been produced. The symptom 'Vertigo with nauseating tendency started in evening and night' appeared in 6 provers; 'Heaviness of head in frontal region along with both eyes in morning' appeared in 10 provers; 'Canine hunger' appeared in 9 provers and, Severe pain in chest as if ribs were broken worse between 6 p.m. and 10 p.m.' appeared in 8 provers. The drug developed different types of headache with heaviness. More symptoms were produced pertaining to the gastro-intestinal system. Mental symptoms were scarce in the trial. The symptoms which were produced in more provers were of more intensity.

Withdrawal percentage was zero that is, no prover withdrew from the proving program during the trial and there were no adverse effects in the trial. There were no discernible changes in the laboratory investigation reports.

CONCLUSION

Foundation of research is based on following factors such as sample size, randomization as sampling method, control and blinding. Out of 23 provers of verum group 17 provers manifested symptoms and as evident the incidence of pathogenetic effect of the trial is 74% and the incidence of pathogenetic effect per prover is 2.47. There were only 4 symptoms as severe out of 42 symptoms produced while 11 were moderate and 27 were mild symptoms.

This particular drug is having various therapeutic properties known before our study such as anti-inflammatory, anti-oxidant, anti-bacterial, anti-fungal, anti-parasitical, anti-cancer, anti-detox, anti-mutagenic, anti-hepatoma activity, anti-malarial activity, anti-ischemic, anti-myeloid properties, and anti-tumor properties, but from our study it is not evident clearly about the above qualities of

Table 2: Pathogenetic effects of *Nanocurcumin* 6X (symptoms produced in verum group)

Symptoms	Prover with code	Sex	Number of doses consumed	Duration of persistence of the symptoms
Mind				
Forgetfulness in morning and evening (+)	1105	Male	3	2 days
Forgetfulness in evening (+)	1112	Male	3	2 days
Vertigo				
Vertigo with nauseous tendency started in evening and night (+++)	1105	Male	3	3 days
	1107	Female	3	2 days
	1108	Male	5	3 hours
	1111	Female	4	6 days
	1114	Male	4	2 days
	1119	Male	3	5 days
Head				
Heaviness of head in frontal region along with both eyes in morning (+++)	1101	Male	4	9 days
	1102	Female	3	1 day
	1103	Male	3	6 days
	1106	Male	3	1 day
	1107	Female	3	1 day
	1108	Male	5	1 day
	1111	Female	4	6 days
	1114	Male	4	2 days
	1117	Male	4	2 days
	1119	Male	3	5 days
Heaviness of head in frontal region with headache in morning (+)	1112	Male	3	5 days
Bursting type of headache in frontal region > by pressure started in night (++)	1114	Male	4	2 days
Heaviness in head in noon (+)	1105	Male	3	1 day
Pulsating pain Frontal and temporal region of head with heaviness in evening (+)	1120	Male	5	2 days
Frontal headache with feeling of drowsiness in afternoon (++)	1125	Female	5	3 days
Left sided headache starting from occiput to frontal region in noon (++)	1126	Female	4	2 days
Dull headache in left frontal and temporal region extending to occiput (+)	1126	Female	4	2 days
Left sided dull frontal headache with sensation of heat in vertex (+)	1126	Female	4	2 days
Right sided frontal headache in night (+)	1127	Female	3	4 hours
Heaviness of head with sneezing and nasal obstruction in night (+)	1127	Female	3	6 hours
Frontal dull headache with heaviness in early morning (++)	1127	Female	3	1 day
Mild frontal headache with heaviness of head in morning (++)	1128	Male	7	5 days
Eyes				
Swelling of eyes in morning (+)	1126	Female	4	1 day
Nose				
Sneezing with coryza in morning (+)	1120	Male	3	2 days
Face				
Swelling of face in morning (+)	1126	Female	4	1 day
Swelling of face with chillness in morning (+)	1126	Female	4	1 day
Stomach				
Canine hunger (+++)	1101	Male	4	9 days
	1102	Female	3	4 days
	1103	Male	3	6 days
	1106	Male	3	2 days
	1108	Male	5	1 day
	1112	Male	3	5 days
	1119	Male	3	5 days
	1125	Female	5	3 days

Contd...

Table 2: Contd...

Symptoms	Prover with code	Sex	Number of doses consumed	Duration of persistence of the symptoms
	1128	Male	7	2 days
Indigestion in afternoon (+)	1106	Male	3	3 hours
	1111	Female	4	5 days
Indigestion in evening (+)	1117	Male	4	2 days
Indigestion after eating in night (+)	1119	Male	3	4 days
Nauseous feeling in morning (+)	1126	Female	4	1 day
Abdomen				
Feeling of softness of abdomen with hunger in morning (++)	1103	Male	3	1 day
Feeling of softness of abdomen with hunger in evening (++)	1102	Female	3	1 day
	1111	Female	4	6 days
	1117	Male	4	2 days
Feeling of softness of abdomen with hunger in night (++)	1101	Male	4	2 days
	1105	Male	3	3 days
Flatulence in abdomen in evening (++)	1120	Male	5	2 days
Distension of abdomen in afternoon (+)	1126	Female	4	1 day
Distension of abdomen with unsatisfactory stool (+)	1126	Female	4	1 day
Rectum				
Constipation with no stool (+)	1114	Male	4	1 day
Loose stool in morning (+)	1114	Male	4	1 day
Alternate constipation and diarrhea (+)	1114	Male	4	2 days
Stool				
Stool offensive, frothy (+)	1126	Female	4	2 days
Genetalia - female				
Menses on time but painful (++)	1126	Female	4	3 days
Cough				
Dry cough without expectoration in evening (+)	1102	Female	3	3 days
Chest				
Severe pain in chest as if ribs were broken < between 6 pm and 10 pm (+++)	1101	Male	4	2 hours
	1102	Female	3	3 days
	1103	Male	3	1 hours
	1106	Male	3	2 days
	1107	Female	3	2 days
	1112	Male	3	5 days
	1114	Male	4	2 days
	1119	Male	3	5 days
Extremities				
Undefined pain in both knees started in evening (++)	1107	Female	3	2 days
	1108	Male	5	5 days
	1111	Female	4	6 days
Skin				
Old symptoms of skin eruptions reappeared (+)	1117	Male	4	8 days
Prickly heat like eruptions on face and neck without itching appeared in morning (+)	1126	Female	4	3 days
Generalities				
Feeling of weakness in evening (+)	1120	Male	5	2 days

+: Mild intensity; ++: Moderate intensity; +++: Severe intensity

Nanocurcumin. For this more number of provers and various sophisticated laboratorial procedures are required. Apart from that, it can be used in sinusitis, migraine, dyspepsia, constipation, diarrhea, dysmenorrhea, pharyngitis, etc., as evident from the pathogenetic effects obtained in the study.

Table 3: Symptoms produced in placebo group

Symptoms	Prover with code	Sex	Number of doses consumed and the day developed the symptom	Duration of persistence of the symptoms
Head				
Mild aching pain in forehead with coryza and sneezing in morning (+)	1122	Female	On day 8	2 days
Mouth				
Mouth ulcer (++)	1122	Female	On day 11	3 days
Stomach				
Nausea with vertigo in evening (+)	1110	Male	After taking 2 doses on day 1 and after that again on day 5	1-day
Abdomen				
Feeling of discomfort in abdomen with nausea in evening (+)	1122	Female	On day 2 after taking 4 doses	1-day

+: Mild intensity; ++: Moderate intensity; +++: Severe intensity

Data Sharing

Final compiled proved data (drug pathogenesis) of the drug would also be made available to college authorities for academic interest and for conducting clinical verification in patients.

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Conflicts of Interest

There are no conflicts of interest.

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सार

पृष्ठभूमि: स्वीकृत दिशानिर्देशों का उपयोग करते हुए नैनो–करक्यूमिन 6एक्स का एक डबल ब्लाईड, यादृच्छिकृत, प्लासिबो नियंत्रित होम्योपैथिक रोगजनक परीक्षण (एचपीटी) संचालित किया गया, नैतिकता समिति का अनुमोदन एवं उसके संकेतों व लक्षणों का वैज्ञानिक प्रलेखन भी किया गया। रोगजनक परीक्षण की गुणवत्ता को बढ़ाने के लिए मानकीकृत शक्तिवर्धन विधि को अंगीकार किया गया। लक्षणों के मूल्यांकन हेतु विभिन्न सांख्यिकीय गणनाओं का प्रयोग किया गया।

लक्ष्य: अध्ययन का लक्ष्य नैनो–करक्यूमिन 6एक्स नामक एक नैनो पदार्थ का तनुता में एचपीटी संचालित करना था।

सामग्रियां एवं विधियां: औषधि नैनो–करक्यूमिन 6एक्स को डबल ब्लाईड, प्लासिबो नियंत्रित विधि के माध्यम से प्रमाणित किया गया था। परीक्षण 6एक्स शक्ति में 30 स्वस्थ प्रमाणकों (प्रमाणक) पर किया गया जिनकी स्क्रीनिंग (आरंभिक छंटाई) उनकी परीक्षण–पूर्व चिकित्सीय जांचों एवं नेमी प्रयोगशाला जांचों द्वारा की गई थी। 30 प्रमाणकों में से 7 प्लासिबो पर और 23 औषधि पर थे। भारतीय होम्योपैथिक भेषजकोश में दिए गए सिद्धांतों के अनुसार औषधि तैयार की गई थी। परीक्षण अवधि के दौरान उत्पन्न संकेतों व लक्षणों को प्रमाणकों द्वारा लिखा गया एवं बाद में उनका कूटवाचन एवं संकलन किया गया।

परिणाम: जो 23 प्रमाणकों वीरम पर थे उनमें से 17 प्रमाणकों ने लक्षण प्रदर्शित किए एवं जो 7 प्रमाणक प्लासिबो पर थे उनमें से 2 ने लक्षण प्रदर्शित किए।

निष्कर्ष: विकसित हुए औषधि रोगजनन से नासाविदरशोथ, अर्धकपारी, अग्निमांद्य, मलबंध, अतिसार, कष्टार्तव, ग्रसनीशोथ, श्वसनीशोथ आदि में इसके उपचारार्थ उपयोग का संकेत मिलता है।

Patogenesia homeopática a doble ciego y controlada con placebo de la nano-curcumina 6X

RESUMEN

Fundamentos: Se realizó un ensayo patogenésico homeopático (EPH) a doble ciego y controlado con placebo de la nano-curcumina utilizando las directrices aceptadas. Para el ensayo se obtuvo la aprobación del Comité de Ética y se registró la documentación científica de sus signos y síntomas. Se adoptó un método de potenciación estandarizado para mejorar la calidad de la patogenesia. Para la evaluación de los síntomas se aplicaron diferentes cálculos estadísticos.

Objetivo: El objetivo del estudio fue realizar un EPH de la nano-curcumina 6X, una nanosustancia en dilución.

Materiales y métodos: El medicamento nano-curcumina 6X fue ensayado aplicando un método a doble ciego y controlado con placebo. En el ensayo, realizado con el medicamento a la 6X, se incluyeron 30 voluntarios sanos (voluntarios) que fueron seleccionados según los exámenes médicos preensayo y los análisis de laboratorio rutinarios. Siete de los 30 voluntarios recibieron placebo, mientras que 23, el medicamento de estudio. El medicamento fue preparado conforme a los principios establecidos en la Farmacopea Homeopática de la India. Los signos y síntomas manifiestos durante el periodo del ensayo fueron registrados por los voluntarios y se decodificaron y compilaron posteriormente.

Resultados: Diecisiete de los 23 voluntarios con el medicamento de estudio manifestaron síntomas, mientras que solo pudieron observarse síntomas en 2 de los 7 voluntarios con placebo.

Conclusiones: La patogenesia realizada indica que el uso terapéutico del medicamento se centra en sinusitis, migraña, dispepsia estreñimiento, diarrea, dismenorrea, faringitis, bronquitis, etc.