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A multi-centric double-blind randomized homoeopathic pathogenetic trial of *Gymnema sylvestre*

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ABSTRACT

Objective: To elicit the pathogenetic response of *Gymnema sylvestre* in homoeopathic potencies on apparently healthy human volunteers. **Methodology:** *Gymnema sylvestre* was proved by the Central Council for Research in Homoeopathy through double-blind placebo-controlled method. The study was carried out at four centers. The drug was proved in two potencies (6C and 30C) on 63 apparently healthy volunteers who were selected after conducting pre-trial medical examination by the medical specialists and routine laboratory investigations. In the first phase volunteers were given 56 doses (04 doses per day for 14 days) of placebo. In the next two phases 56 doses (04 doses per day for 14 days) of each potency or placebo were consumed. The symptoms generated during the trial period were noted by the volunteers and elaborated by the proving masters. The data obtained from all the four centers was compiled at proving-cum-data processing cell at CCRH headquarters after decoding. **Results:** Out of 37 provers who were on actual drug trial, 16 manifested symptoms. The drug was able to produce symptoms in each potency in most of the parts of the body. **Conclusion:** The pathogenetic responses elicited during the drug proving trial expand the scope of use of the drug *Gymnema sylvestre* and will benefit the research scholars and clinicians. The generated symptoms of the drug will carry more meaning when verified clinically.

Keywords: Drug proving, *Gymnema sylvestre*, Homoeopathic pathogenetic trial, Homoeopathy, Pathogenetic effect

INTRODUCTION

In recent years, ethnobotanical and traditional uses of the natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. They obviously deserve scrutiny on modern scientific lines such as physiochemical characterization, biological evaluation, toxicity studies, investigation of the molecular mechanism of action(s) of isolated phytoprinciple, and their clinical trials. These are necessary classical approaches in search of new lead molecule for management of various diseases. Many Indian herbs are being used in the traditional practices to control diabetes. *Gymnema sylvestre* has an important place among such antidiabetic medicinal plants and it can also be used in treating dyspepsia, constipation and jaundice, hemorrhoids, renal and vesicle calculi,

cardiopathy, asthma, bronchitis, amenorrhea, conjunctivitis, and leucoderma.[1]

Literature surveys reveal that *Gymnema sylvestre* is a popular plant used in treating various ailments and used as one of the important ingredient in several ayurvedic formulations, very little efforts have also been made to verify its efficacy through the scientific screening in animal models and clinical trials. As *Gymnema* possesses the virtue of abolishing the taste of sugar it has been appropriately called gur-mar thereby meaning sugar-killer, and the impression has become prevalent in some places that it might neutralize the abundance of sugar existing in the body in diabetes mellitus.[2]

Keeping in view the action of *G. sylvestre* available from various literatures this systematic study was conducted by Central Council for Research in Homoeopathy in homoeopathic potencies as per the approved protocol.

Description and Distribution

Taxonomy of *Gymnema sylvestre*[1]
Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae
Order: Gentianales
Family: Asclepiadaceae
Genus: *Gymnema*
Species: *Sylvestre*

G. sylvestre is a slow growing, perennial, woody climber, distributed throughout the India, in dry forests up to 600 m height. It is mainly present in the tropical forest of Central and Southern India. It is also found in Banda, Konkan, Western Ghats, Deccan extending to the parts of Western and Northern India.[1]

The plant is a large, more or less pubescent, climbing shrub. The leaves [Figure 1] are opposite, usually elliptic or ovate (1.25-2.0 inch × 0.5-1.25 inch). Flowers are small, yellow, in axillary and lateral umbel in cymes; Follicles are terete and lancelate up to 3 inches in length. The Calyx - 4.8 mm long, lobes are long, ovate, obtuse, and pubescent. Corolla - 4 mm across, pale yellow campanulate, valvate, corona single, and with five

Figure 1: Gymnema sylvestre: Leaves

fleshy scales. Scales adnate to throat of corolla tube between lobes, another connective produced into a membranous tip, pollinia two, erect, carpels two, unilocular, locules many ovuled. Seeds 12 mm long narrowly ovoid-oblong, flat and broadly marginated, and pale brown.[1,3]

Chemical Composition

Hooper (1887) made the 1st systematic examination of the leaves. He isolated two resins, the resin insoluble in alcohol forming the larger proportion. The resin soluble in alcohol was said to leave a tingling sensation in the throat. There was no tannin. He had also isolated an organic acid to be a glucoside and to possess anti-saccharine property. It was designated as gymnemic acid and the formula C82H55O12 was given to it. A new bitter principle, some tartaric acid and calcium oxalate were also isolated. Power and Tutin (1904) isolated hentriacontane C31H64 quercitol and gymnemic acid. Hopra, Bose and Chatterjee (1928) prepared different fractions from the leaves, isolated the gymnemic acid and prepared a sodium salt of the acid for both pharmacological and the clinical trials. They also isolated some enzymes and tested their sugar-hydrolyzing action.[2]

Mechanism of Action

G. sylvestre is a stomachic, diuretic, refrigerant, astringent, and tonic.[4] It has been found to increase urine output and reduce hyperglycemia in both animal and human studies. *Gymnema's* antidiabetic activity appears to be owing to a combination of mechanisms. Two animal studies on beryllium nitrate- and streptozotocin-diabetic rats found *Gymnema* extracts doubled the number of insulin-secreting

beta cells in the pancreas and returned blood sugars to almost normal.[5,6] *Gymnema* increases the activity of enzymes responsible for glucose uptake and utilization[7] and inhibits peripheral utilization of glucose by somatotrophin and corticotrophin.[8] Plant extracts have also been found to inhibit epinephrine-induced hyperglycemia.[9]

There are some possible mechanisms by which the leaves extract of *Gymnema sylvester* or (Gymnemic acid) possess its hypoglycemic acid effects: (1) It promotes regeneration of islet cells, (2) It increases the secretion of insulin, (3) It causes inhibition of glucose absorption from intestine, (4) It increases utilization of glucose as it increases the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase.[1]

Uses

The root of the plant is considered by the Hindu physicians to be an excellent remedy for snake-bite. The root in a powdered form is externally used on the part bitten by the snake and a decoction is employed internally. It is an astringent, stomachic, tonic and refrigerant; given in fever and cough. The root powder mixed with castor oil is applied externally such as ipecac to snake and insect bites. The leaves are applied like varalians to enlarged liver or spleen; the leaves when chewed benumb for a time the taste for sweets and bitters such as sugar and quinine.[2]

Sushruta has found it useful in poisonous styes and headache due to catarrh and also in glycosuria. Bagbhata has recommended it in piles.[2]

Dr. Govinda Rama Sharma of Rawalpindi indicated this gurmar as almost specific for diabetes mellitus from the crude drug to the high potencies. He observed the action of gurmar on a patient that it diminishes the sugar in the urine in no time; the patient puts on flesh and weight and his appetite improves; the countenance assumes the healthy look; it improves him sexually, mentally, and physically; he is able to work hard and does not find himself exhausted after a little exertion as before; it prolongs diabetic patient's life.[2]

Numerous animal studies have confirmed the hypoglycemic effect of *G. sylvestre*.[10-12] Furthermore, in future study, the isolated principles from gurmar needs to be evaluated in scientific manner using a various innovative experimental models and the clinical trials to understand its mechanism of action, in search of other active constituents and hence that its other therapeutic uses can be widely explored.

Parts Used in Homoeopathy

Leaves.

Method of Preparation According to Homoeopathic Pharmacopoeia

a. Mother tincture Q drug strength 1/10
   - *G. sylvestre* in moderately coarse powder 100 g
   - Purified water 200 ml
   - Strong Alcohol in sufficient quantity to make 1 l of mother tincture.

b. Potencies: ×2 to contain one part of mother tincture, three parts strong alcohol.
   - ×3 and higher potencies are prepared with dispensing alcohol.[13]

OBJECTIVE

To elicit the pathogenetic response of the drug *G. sylvestre* on apparently healthy human volunteers in homoeopathic potencies.

MATERIAL AND METHODS

Study Design

The study was a randomized, double-blind, placebo controlled trial. The study was conducted according to the drug proving protocol designed by Central Council for Research in Homoeopathy.

Participants and Setting

The proving was conducted at four centers: Homoeopathic Drug Research Institute, Lucknow, (2009-10) Regional Research Institute (H), Gudivada (2010-11), Drug Proving Unit,

Bhubaneswar (2010-11) and Drug Proving Research Unit, Kolkata (2009-10). A total of 63 apparently healthy volunteers from above mentioned four centers between the age group 18-45 years were selected comprising 27 males and 36 females. Before commencing the study, all provers were screened strictly by the experts and apparently healthy provers between the age group of 18-45 years, both males and females were included in the drug proving trial. Pregnant and lactating mothers were excluded.

"Written informed consent" from each volunteer was obtained before starting the proving. Pre-trial medical

examination and terminal medical examination (TME) of the volunteers was carried out by General Physicians, Psychiatrists, Cardiologists, Ophthalmologists, ENT Specialists, Dermatologists, Gynecologists, Radiologists, and their routine laboratory investigations at the centers were carried out to ascertain their health status. After recommendation of experts, healthy volunteers were enrolled in the Homoeopathic Drug Proving Program. The study was conducted at four centers mentioned above. According to Central Council for Research in Homoeopathy (CCRH) drug proving protocol, the sample size included 30% volunteers under control group at each center. Hence, out of total 63 volunteers, 37 were kept on drug (verum) and 26 were on placebo (control) in all three phases. All the volunteers were assigned code numbers and the coded drugs of different potencies (including placebo) were supplied in separate glass phials bearing code numbers of the respective volunteers; keeping both provers and proving masters blind about what provers were consuming (drug or placebo).

Intervention

G. sylvestre was procured in 6C and 30C potencies. Globules (number 30) were medicated with these attenuations at the Council's headquarters office and sent to drug proving research units in coded phials (verum) along with placebo (control).

Placebo

Placebo was made up of plain globules (number 30) moistened with plain dispensing alcohol (unsuccussed) and was therefore indistinguishable from verum.

Methodology of Proving

The study consisted of 3 phases. Each phase consisted of 56 doses of coded drug or placebo.

Phase-1: Placebo phase. It is useful in generating prover's response to placebo and therefore symptoms generated by the prover in this stage act as control for subsequent phases

Phase-2: In 2nd phase, the proving was conducted with 6C potency

Phase-3: In 3rd phase, the proving was conducted with 30C potency.

The volunteers were instructed to take 4-6 globules of a particular potency of the coded drug, four times a day, dry on the tongue and also instructed to note down the details of their feelings/changes in mind and body, after taking the coded drug/placebo in 'prover's day book proforma' daily.

- If no sign(s)/symptom(s) appeared
  - If no sign/symptom was observed, the volunteer noted down as 'no symptom' with date and time of intake of the respective dose of the drug/placebo.
- If sign(s)/symptom(s) appeared
  - The volunteers were asked to stop taking the drug/placebo as soon as he/she felt any change or any sign(s) and/or symptom(s) developed during the trial. The volunteer noted down the sequence of the appearance of new sign(s) and/or symptom(s), their progress and the number of doses after which each sign or symptom appeared with date, time of onset and duration for which it persisted. The intake of drug remained suspended till the sign(s) and/or symptom(s) totally disappeared. 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 the disappearance of sign(s) and/or symptom(s) developed by the drug, the volunteer had to wait for a further period of seven days before taking the remaining doses of that potency following the same dose schedule as stated above. In case of further appearance of new sign(s) and/or symptom(s), the same procedure as stated above was followed until the consumption of 56 doses of that potency by the volunteer. If the volunteer was experiencing the same symptom (s) what he/she had already shown, he/she was asked to stop the current quota and to switch over to the next quota after a washout period of 14 days.
  - Each prover was interrogated by the Proving Master about the appearance of new sign(s) and/or symptom(s) or progress of symptoms and noted down those in 'Symptoms Elaboration Proforma' with respect to appearance and disappearance of symptoms, their location, sensation/character, modalities, concomitants, extension of symptoms, causation, clinico-pathological findings and other treatment taken.

Before commencing the administration of subsequent potencies (subsequent phase) of the drug, the volunteers remained on a washout/rest period (a symptom free period between two phases of drug proving in which a volunteer does not take the

drug) for 14 days and started taking next potency following the same procedure as mentioned above, until completion of 56 doses. The same procedure was followed for the 3rd phase.

Each volunteer was interrogated by the Proving Master to verify the sign(s) and/or symptom(s) recorded by the volunteers. The symptoms recorded in 'prover's day book proforma' were verified by the proving master and completed through further interrogation with the volunteers in respect to their location/sensation/modalities/concomitants, if any, in 'Symptoms Elaboration Proforma.'

During the course of proving, the volunteers were referred for specific laboratory investigation(s) to rule out any pathological cause for appearance of new sign(s) and/or symptom(s). The laboratory tests were performed to identify any correlation between the subjective and objective changes during the course of proving. The opinion of the experts (honorary consultants) was also obtained, wherever needed.

After completion of trial of all potencies, the volunteers underwent TME. On completion of all the respective quotas of the proving program, the compilation of data recorded in "prover's day book proforma," "Symptoms Elaboration Proforma," "pathological report sheets" and "terminal medical examination sheets" were carried out at the Council's headquarters by the drug proving-cum-data processing cell. After decoding, the sign(s) and/or symptom(s) produced by the volunteers kept on the drug were separated from those produced by the volunteers kept on placebo. The sign(s) and/or symptom(s), which were common to both the groups that is placebo as well as drug groups were not taken into consideration while compiling the symptomatology of the proved drug.

Management of Adverse Effects

A vial of antidote was sent with each quota to each center. In this trial, homoeopathic potencies of *Camphora* were used as antidote as it is well known that *Camphora* can antidote nearly every vegetable medicine.[14] The proving master gives antidote to the volunteer if symptoms continue for a long time or intensity is much to cause discomfort. Proving master is also directed to take advice of honorary consultants and to get laboratory investigations carried out if required.

Pathogenetic Effects

Pathogenetic effects (proving symptoms) are defined as all changes in clinical events and laboratory findings reported by the volunteers during a homoeopathic pathogenetic trial and recorded in the final report. Total number of symptoms produced by 37 provers were 94. Among these, 45 symptoms were produced during 2nd quota i.e. by 6C [Table 1] and 49 symptoms were produced during 3rd quota i.e. by 30C [Table 2]. The incidence of pathogenetic effects per volunteer is defined as the total number of findings observed in the trial divided by the total number of provers.[15] Hence incidence in this proving was 2.54.

Pathogenetic effects were deduced

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

RESULTS

At Drug Proving Unit (H), Bhubaneswar out of 16 volunteers, 10 volunteers were on actual drug out of which only 03 volunteers reported symptoms. At Homoeopathic Drug Research Institute (H), Lucknow out of 15 volunteers, 10 volunteers were on actual drug out of which only 02 volunteers reported symptoms. At Regional Research Institute (H), Gudivada out of 16 volunteers, 11 volunteers were on actual drug and all the 11 volunteers reported symptoms. At Drug Proving Research Unit, Kolkata out of 16 volunteers, 06 volunteers were on actual drug but no symptoms/signs were reported by any one of them. There were 63 number of provers out of which 37 volunteers were on actual drug and out of these 37 provers 16 provers developed signs and symptoms. Hence, the % of responsive volunteers was 25.39. Claimed % of sensitive provers was 43.24.

Table 1: Pathogenetic effects of 6C (2nd quota drug) in chronological order (according to doses taken)

Location	Symptoms	No. of dose after which symptom developed
Head	Severe headache and vomiting. Next day, same symptom with drowsiness and nausea. On 3rd day, drowsiness with dry cough and cold.	7
Throat	Burning sensation in throat, cold. On 3rd day pain extending to the left ear	9
Stomach	Stomach pain, *amel*. by lying on the abdomen	9
Head	Slight frontal headache, *agg*. eating. It is accompanied with nausea.	10
Head	Frontal headache. Next day, same symptom with abdominal distension.	11
Nose	Coryza with obstruction of the left nostril and throbbing pain in the left parietal region of head, *amel*. open air	11
Cough	Dry cough, irritation in throat, expectoration scanty, yellowish, tinged with black spot, *agg*. cold drink, morning at 6:15 am; *amel*. hot drink	12
Throat	Throat pain, sensation as if something is present in the throat, *agg*. during swallowing, night, early morning, drinking cold water; *amel*. by drinking hot milk	14
Stool	Stool semi-solid, offensive, urgent, painless, *agg*. evening, night	15
Head	Throbbing headache, sweating on forehead, *agg*. thinking; *amel*. sleep	16
Abdomen	Pain in umbilical region of the abdomen with gradual onset, *amel*. rubbing. It is accompanied with nausea.	18
Vertigo	Vertigo, reeling sensation, *agg*. evening; *amel*. rest	19
Head	Headache, heaviness of head, *agg*. morning	19
Cough	Dry cough with coryza, sneezing and frontal headache. It was later followed by reeling sensation and pain in the abdomen.	19
Throat	Throat pain with burning and itching sensation, pain while swallowing liquid or solid	20
Skin	Red rashes all over the body, mainly covered part, burning and itching, *agg*. warmth; *amel*. open air	23
Generalities	Profuse sweating with insomnia, tiredness and fatigue. Next day, same symptoms with no inclination to do any work. Then prover felt abdominal distension with increased appetite and mild headache, *amel*. after dinner. No sleep during night with nightmares. On 3rd day, no free passage of faeces with marked distension of abdomen.	23
Cough	Dry cough, scanty, white expectoration tinged with black spot, *agg*. cold drink, morning.	24
Rectum	Diarrhea with nausea	25
Back	Low backache, *agg*. standing, evening, bending forward; *amel*. lying on a hard surface	25
Head	Severe headache	27
Cough	Dry cough with pain in the chest region, *agg*. evening; *amel*. cold water intake. It is accompanied with feeling of chest oppression.	29
Fever	Slight rise of temperature which raised to 103°F, *agg*. early morning. Next day, fever was associated with body pain and chill. Fever was also associated with severe headache, cold and dry cough.	30
Skin	Itching of the whole body, *agg*. after a bathing. Scratching gives no relief.	31
Head	Frontal headache with burning of eyes and exhausted feeling. Fatigue after walking a small distance. Tired feeling and sleepy all the time with marked drowsiness. Next day, same symptoms with marked appetite. No interest in doing work. Headache with insomnia.	33
Extremities	Burning of hands and feet, *agg*. evening; *amel*. morning, cold application	34
Generalities	Severe body pains	36
Rectum	Watery diarrhea with pain in the abdomen	37
Rectum	Severe headache, *agg*. talking	39
Rectum	Diarrhea, *agg*. after eating. Urge for stool soon after eating.	39
Abdomen	Cramping pain in left hypochondrium, *amel*. hard pressure, lying on abdomen, knee elbow position. Cutting pain in the umbilicus with mucous stool. It is accompanied with nausea. (Took antidote three times for 2 days)	40
Sleep	Disturbed sleep, sleeplessness	40
Generalities	Hot flushing	40
Head	Drawing pain in the frontal region, *agg*. pressure; *amel*. rest, tight bandage	43

(contd....)

Table 1: Contd...

Mind	Irritability, purposeless shouting on others, *agg*. evening, dysmenorrhoea. The irritability decreased with relief in dysmenorrhoea.	43
Female genetalia	Delayed menses with dysmenorrhoea; flow profuse, offensive, dark red in color	43
Rectum	Diarrhea with semi-liquid, sour smelling, light yellow stool, *agg*. morning; *amel*. evening	44
Head	Slight headache with nightmares, sleeplessness, sweating. Next day, very drowsy with abdominal distension, *amel*. a passing stool. Frontal headache with burning eyes, *amel*. evening, taking rest	45
Rectum	Diarrhea after eating. It is accompanied with vomiting and headache.	49
Teeth	Toothache	51
Extremities	Sweating on palms with tiredness and exhausted feeling, no strength to walk with muscle fatigue. It is accompanied with drowsiness, abdominal distension, headache and sleeplessness.	52
Mouth	Stomatitis over inner-side of the lower lip with a burning sensation, *agg*. touch, spicy food	54
Nose	Cold, always running nose with whitish nasal discharge, *agg*. morning. It is accompanied with flushes of face, heaviness of head and headache, *agg*. stooping	56
Teeth	Toothache in the right side, *agg*. cold, hot, sour, sweet. It is accompanied with headache.	56
Back	Low backache, *agg*. standing, evening, bending forward, morning; *amel*. lying on a hard surface, afternoon	56

Table 2: Pathogenetic effects of 30C (3rd quota drug) in chronological order (according to doses taken)

Location	Symptoms	No. of dose after which symptom developed
Head	Severe headache with nausea in the evening	5
Generalities	Body pain	5
Head	Aching pain in the frontal region of head, *agg*. evening; *amel*. closing eyes. The symptom is accompanied with constipation.	6
Female genetalia	Profuse menstrual flow and severe pain during menses	6
Head	Slight headache and vertigo	7
Nose	Coryza and dry cough	7
Teeth	Toothache	9
Back	Burning and itching of the posterior surface of body (esp. back), *agg*. during night; *amel*. cold water bath	9
Fever	Fever and body pains. Later fever blister on the upper lip. Fever disappeared with sweating on 5th day.	9
Head	Headache with cold	10
Throat	Burning sensation in the throat	10
Nose	Obstruction of the left nostril, watery discharge from both nostrils, *agg*. sitting; *amel*. lying down	13
Cough	Dry cough with tickling in larynx, *agg*. lying down; *amel*. sitting	14
Head	Headache and heaviness of head, *agg*. bending forward; *amel*. applying pressure	15
Mouth	Bleeding gums and pain in teeth	15
Fever	Fever with temporal headache, abdominal distension and constipation. It is accompanied with burning in eyes, *amel*. rest	15
Vertigo	Reeling sensation, *agg*. rest; *amel*. evening	16
Throat	Throat pain	16
Extremities	Pain in lower limbs, extends from knee joints to ankle joints, *agg*. by walking; *amel*. sitting	16
Fever	Fever with chills	16
Head	Slight headache in the frontal region	19
Head	Headache, nausea after any intake of the food	19
Abdomen	Pain in the abdomen with bodyache	20
Abdomen	Severe abdomen pain during menses	21
Extremities	Rashes on skin esp. hands	24

(contd...)

Table 2: Contd...

Abdomen	Severe abdomen pain during menses	21
Extremities	Rashes on skin esp. hands	24
Head	Mild temporal headache, *amel*. rest	25
Back	Low backache on the right side, *agg*. bending forward; *amel*. lying down	25
Fever	Fever with hot flushes, sweating, desire for cool things, *agg*. midnight; *amel*. rest, morning. It is accompanied with body pains.	25
Head	Hair falling	26
Extremities	Exfoliation of skin of feet, peeling off of hard skin at the heel and sides of foot	26
Head	Slight headache	28
Stomach	Slight epigastric pain appeared after intake of food, *agg*. eating	28
Head	Severe headache	29
Throat	Sore throat, pain during swallowing, sensation as if something is obstructing. Pain extending to the right ear, *agg*. Swallowing, early morning.	32
Abdomen	Pain in the abdomen below the umbilicus	34
Teeth	Toothache, all the teeth are painful, *agg*. cold things, sweets, chewing	38
Generalities	Itching sensation in all over the body, *agg*. night	38
Nose	Sneezing with coryza and irritation of throat, *amel*. rest	39
Stomach	Epigastric pain with nausea, slight headache, pain in lower limbs and restlessness	39
Female genetalia	Delayed menses with dysmenorrhoea, flow clotted, dark chocolaty in color. Pain extends to back and thighs, *amel*. warm application.	42
Throat	Throat pain with tickling sensation with whitish expectoration associated with temporal headache on both sides	43
Stomach	Vomiting sensation with vertigo and body pains	45
Mind	Irritable	51
Head	Temporal headache, body pains, *amel*. rest	51
Rectum	Constipation	51
Extremites	Cramps in limbs	51
Stomach	Burning pain in the stomach	52
Extremities	Drawing type of pain in inter-phalangeal joints, toes of left foot, *agg*. continuous walk; *amel*. slow walking. Pain extending to left leg, thigh and hip joint.	52

Information regarding parentheses:

- In the 1st parenthesis, the 1st number given after every symptom denotes the number of volunteers who produced that particular symptom and 2nd number denotes potency used
- In 2nd parenthesis, the 1st number denotes of number of doses after which the drug produced that particular symptom and 2nd number denotes the duration (in days) for which the symptom lasted.

The following symptoms were observed during the drug proving:

Mind

- Irritability; *agg.* evening. (1, 6C) (43, 5)
- Irritability; *agg*. dysmenorrhea and *amel*. with relief in dysmenorrhea. (1, 6C) (43, 5)
- Irritable. (1, 30C) (51, 1).

Vertigo

- Vertigo, reeling sensation; *agg.* evening; *amel.* rest. (1, 6C) (19, 2)
- Vertigo, reeling sensation; *amel*, evening; *agg.* rest. (1, 30C) (16, 1).

Head

- Severe headache. (1, 6C) (27, 1) (1, 30C) (29, 1)
- Drawing pain in the frontal region, *agg.* pressure; *amel.* rest, tight bandage. (1, 6C) (43, 3)
- Slight frontal headache, *agg.* eating. It is accompanied with nausea. (1, 6C) (10, 5)
- Severe headache, *agg.* talking. (1, 6C) (39, 4)
- Headache, heaviness of head, *agg.* morning. (1, 6C) (19, 6)
- Frontal headache. Next day, same symptom with abdominal distension. (1, 6C) (11, 2)
- Frontal headache with burning of eyes and exhausted feeling. Fatigue after walking a small distance. Tired feeling and sleepy all the time with marked drowsiness. Next day, same symptoms with marked appetite. No interest in doing work. Headache with insomnia. (1, 6C) (33, 2)

- Slight headache with nightmares, sleeplessness, sweating. Next day, very drowsy with abdominal distension, *amel.* passing stool. Frontal headache with burning eyes, *amel.* by evening taking rest. (1, 6C) (45, 2)
- Severe headache and vomiting. Next day, same symptom with drowsiness and nausea. On 3rd day, drowsiness with dry cough and cold. (1, 6C) (7, 3)
- Throbbing headache, sweating on forehead, *agg.* thinking; *amel.* sleep. (1, 6C) (16, 3)
- Slight headache and vertigo. (1, 6C) (7, 3)
- Slight headache in the frontal region. (1, 30C) (19, 3)
- Headache and heaviness of head, *agg.* bending forward; *amel.* an applying pressure. (1, 30C) (15, 3)
- Severe headache with nausea in the evening. (1, 30C) (5, 3)
- Headache, nausea after any intake of food. (1, 30C) (19, 2)
- Slight headache. (1, 30C) (28, 2)
- Mild temporal headache, *amel.* rest. (1, 30C) (25, 1)
- Temporal headache, body pains, *amel.* rest. (1, 30C) (51, 1)
- Headache with cold. (1, 30C) (10, 2)
- Aching pain in the frontal region of head, *agg.* evening; *amel.* closing eyes. The symptom is accompanied with constipation. (1, 30C) (6, 2)
- Hair falling. (1, 30C) (26, 3)

Nose

- Cold, always running nose with whitish nasal discharge, *agg.* morning. It is accompanied with flushes of face, heaviness of head and headache, *agg.* stooping. (1, 6C) (56, 7)
- Coryza with obstruction of the left nostril and throbbing pain in the left parietal region of head, *amel.* open air. (1, 6C) (11, 2)
- Sneezing with coryza and irritation of throat, *amel.* rest. (1, 30C) (39, 1)
- Coryza and dry cough. (1, 30C) (7, 1)
- Obstruction of the left nostril, watery discharge from both nostrils, *agg.* sitting; *amel.* lying down. (1, 30C) (13, 3).

Teeth

- Toothache (1, 6C) (51, 2) (1, 30C) (9, 1)
- Toothache in the right side, *agg.* cold, hot, sour, and sweet. It is accompanied with headache. (1, 6C) (56, 3)
- Bleeding gums and pain in teeth. (1, 30C) (15, 2)
- Toothache, all the teeth are painful, *agg.* cold things, sweets, chewing. (1, 30C) (38, 2).

Mouth

- Stomatitis over inner-side of the lower lip with a burning sensation, *agg.* touch, spicy food. (1, 6C) (54, 1).

Throat

- Throat pain with burning and itching sensation, pain although swallowing liquid or solid. (1, 6C) (20, 2)
- Burning sensation in throat, cold. On 3rd day, pain extending to the left ear. (1, 6C) (9, 5)
- Throat pain, sensation as if something is present in the throat, *agg.* during swallowing, night, early morning, drinking cold water; *amel.* by drinking hot milk. (1, 6C) (14, 7)
- Throat pain with tickling sensation with whitish expectoration associated with temporal headache on both sides. (1, 30C) (43, 2)
- Throat pain. (1, 30C) (16, 3)
- Sore throat, pain during swallowing, sensation as if something is obstructing. Pain extending to the right ear, *agg.* swallowing, early morning. (1, 30C) (32, 4)
- Burning sensation in the throat. (1, 30C) (10, 2).

Stomach

- Pain in stomach, *amel.* by lying on abdomen. (1, 6C) (9, 3)
- Nausea with vertigo and body pains. (1, 30C) (45, 4)
- Slight epigastric pain appeared after intake of food, *agg.* eating. (1, 30C) (28, 2)
- Epigastric pain with nausea, slight headache, pain in lower limbs and restlessness. (1, 30C) (39, 3)
- Burning pain in the stomach. (1, 30C) (52, 1).

Abdomen

- Cramping pain in left hypochondrium, *amel.* hard pressure, lying on abdomen, knee elbow position. Cutting pain in the umbilicus with mucous stool. It is accompanied with nausea. (Took antidote 3 times for 2 days). (1, 6C) (40, 3)
- Pain in umbilical region of the abdomen with gradual onset, *amel.* rubbing. It is accompanied with nausea. (1, 6C) (18, 3)
- Pain in the lower abdomen with bearing down sensation, *agg.* evening. (1, 30C) (25, 2)
- Pain in the abdomen with bodyache. (1, 30C) (20, 1)
- Pain in the abdomen below the umbilicus. (1, 30C) (34, 3).

Rectum

- Stool semi-solid, offensive, urgent, painless, *agg.* evening, night. (1, 6C) (15, 3)
- Diarrhea with semi-liquid, sour smelling, light yellow

stool, *agg.* morning; *amel.* evening. (1, 6C) (44, 3)
- Diarrhea with nausea. (1, 6C) (25, 4)
- Diarrhea, *agg.* after eating. Urge for stool soon after eating. (1, 6C) (39, 4)
- Diarrhea after eating. It is accompanied with vomiting and headache. (1, 6C) (49, 3)
- Watery diarrhea with pain in the abdomen. (1, 6C) (37, 3)
- Constipation. (1, 30C) (51, 1).

Female Genitalia

- Delayed menses with dysmenorrhea; flow profuse, offensive, dark red in color. (1, 6C) (43, 5)
- Severe abdomen pain during menses. (1, 30C) (21, 3)
- Profuse menstrual flow and severe pain during menses. (1, 30C) (6, 3)
- Delayed menses with dysmenorrhea, flow clotted, dark chocolaty in color. Pain extends to back and thighs, *amel.* warm application. (1, 30C) (42, 2).

Cough

- Dry cough, irritation in throat, expectoration scanty, yellowish, tinged with black spot, *agg.* cold drink, morning at 6:15 am; *amel.* hot drink. (1, 6C) (12, 19)
- Dry cough, scanty, white expectoration tinged with black spot, *agg.* cold drink, morning. (1, 6C) (24, 4)
- Dry cough with coryza, sneezing and frontal headache. It was later followed by reeling sensation and pain in the abdomen. (1, 6C) (19, 5)
- Dry cough with tickling in larynx, *agg.* lying down; *amel.* sitting. (1, 30C) (14, 2).

Chest

- Dry cough with pain in the chest region, *agg.* evening; *amel.* cold water intake. It is accompanied with feeling oppression. (1, 6C) (29, 3).

Back

- Low backache, *agg.* standing, evening, bending forward; *amel.* lying on a hard surface. (2, 6C) (25, 2) (56, 2)
- Low backache, *agg.* morning; *amel.* afternoon. (1, 6C) (56, 2)
- Low backache on the right side, *agg.* bending forward; *amel.* lying down. (1, 30C) (25, 2)
- Burning and itching of the posterior surface of body (esp. back), *agg.* during night; *amel.* cold water bath. (1, 30C) (9, 3).

Extremities

- Burning of hands and feet, *agg.* evening; *amel.* morning, cold application. (1, 6C) (34, 3)
- Cramps in limbs. (1, 30C) (51, 1)
- Drawing type of pain in inter-phalangeal joints toes of left foot, *agg.* continuous walk; *amel.* slow walking. Pain extending to left leg, thigh and hip joint. (1, 30C) (52, 4)
- Pain in lower limbs, extends from knee joints to ankle joints, *agg.* by walking; *amel.* sitting. (1, 30C) (16, 3)
- Rashes on hands. (1, 30C) (24, 2)
- Sweating on palms with tiredness and exhausted feeling. (1, 6C) (52, 2).

Sleep

- Disturbed sleep. (1, 6C) (40, 2)
- Sleeplessness. (1, 6C) (40, 2).

Fever

- Slight rise of temperature, which raised to 103°F, *agg.* early morning. Next day, fever was associated with body pain and chill. Fever was also associated with severe headache, cold and dry cough. (1, 6C) (30, 7)
- Fever and body pains. Later fever blister on the upper lip. Fever disappeared with sweating on 5th day. (1, 30C) (9, 7)
- Fever with chills. (1, 30C) (16, 4)
- Fever with temporal headache, abdominal distension and constipation. It is accompanied with burning in eyes, *amel.* rest. (1, 30C) (15, 2)
- Fever with hot flushes, sweating, desire for cool things, *agg.* midnight; *amel.* rest, morning. It is accompanied with body pains. (1, 30C) (25, 2).

Skin

- Red rashes all over the body, mainly covered part, burning and itching, *agg.* warmth; *amel.* open air. (1, 6C) (23, 2)
- Itching of the whole body, *agg.* after bathing; Scratching gives no relief. (1, 6C) (31, 2)
- Itching sensation in all over the body, *agg.* night. (1, 30C) (38, 2)
- Exfoliation of skin of feet, peeling off of hard skin at the heel and sides of the foot. (1, 30C) (26, 5).

Generalities

- Hot flushing. (1, 6C) (40, 2)
- Severe body pains. (1, 6C) (36, 4) (1, 30C) (5, 2)
- Profuse sweating with insomnia, tiredness and fatigue. Next day, same symptoms with no inclination to do any work; then felt abdominal distension with increased appetite and mild headache, *amel.* after a dinner. No sleep during the

night with nightmares. On 3rd day, no free passage of stool with marked distension of abdomen. (1, 6C) (23, 3)
- Tiredness and exhausted feeling, no strength to walk with muscle fatigue; accompanied with drowsiness, abdominal distension, headache and sleeplessness. (1, 6C) (52, 2).

DISCUSSION

There is a dearth of symptoms in the available literature, but in the present study the drug was able to produce symptoms in 6C and 30C. About 94 symptoms were produced in different organs and systems of the body. Maximum symptoms were produced in head. Most of the organs developed symptoms. Out of 37 volunteers of verum group, 08 volunteers produced maximum symptoms. 09 volunteers developed repeated frontal headache.

The symptoms, which were earliest to appear in 30C in a weeks time were:
- Severe body pains (appeared after taking five doses)
- Severe headache and nausea in the evening (appeared after taking five doses)
- Profuse menstrual flow and severe pain during menses (appeared after taking six doses)
- Aching pain in the frontal region of head, agg. evening; *amel*. closing eyes. The symptom is accompanied with constipation. (appeared after taking six doses)
- Coryza and dry cough (appeared after taking seven doses)
- Headache and vertigo (appeared after taking seven doses).

The symptoms which were earliest to appear in 6C in a weeks time were:
- Severe headache and vomiting. Next day, same symptom with drowsiness and nausea; On 3rd day, drowsiness with dry cough and cold (appeared after taking seven doses).

The symptom, which lasted for maximum days was:
- Dry cough, irritation in throat, expectoration scanty, yellowish, tinged with black spot, *agg.* cold drink, morning at 6:15 am; *amel.* hot drink. This symptom was produced by 6C and lasted for 19 days.

Comparison with Previous Provings and Therapeutic Uses

It was first proved by Lt. Col. R. N. Chopra. The drug was tried in a number of cases of diabetes mellitus in order to see if it produced any reduction in the amount of sugar present in the blood or urine. All the patients were uncomplicated cases of diabetes and were kept in hospital under strict observation. They were all kept on a fixed diet, which was strictly under control. The total quantity of urine passed in 24 h was carefully collected, measured and a portion of it was examined every day for the quantity of sugar present. The sugar content of blood was estimated from time to time, the fasting level of blood sugar being always recorded. The patients were regularly weighed during the course of treatment. Of the six cases treated, four were given finely powdered leaves of *G. sylvestre* in doses of one drachm of the powdered leaves, three times a day. The total intake per day was 12 g or 180 grains of the powdered leaves. The drug produced no appreciable effect in reducing either the blood sugar or the total daily output of the urinary sugar.[2]

According to the findings of the workers of the school of tropical medicine the leaves of *G. sylvestre* contain a substance which has hydrolytic action on cane sugar. There is also an oxidase-like substance which produces glycolysis in a solution containing glucose. The extracts made from the leaves as well as gymnemic acid and its sodium salts have no effect on the blood sugar when given by subcutaneous injection to rabbits. Powdered leaves and alcoholic extracts prepared from the leaves of *G. sylvestre* have no effect on the blood or urine sugar of patients suffering from diabetes. According to Mhaskar and Caius, the drug appears to be useful in checking glycosuria, when administered in 2-4 g. dosage.[2]

The leaves when chewed benumb for a time the taste for sweets and bitters such as sugar and quinine.[2] Everything else could be tasted, as the ginger, in gingerbread, but not the sweet. Quinine tasted like chalk.[16]

Symptoms given by Dr. Govind Ram Sharma as mentioned in the book entitled ' Drugs of Hindoosthan'[2]

Mind:	Despondent
Muscles:	Relaxation of muscles, but the patient is hopeful of his recovery even on the death-bed.
Urine:	Urine is loaded with sugar; after

passing urine, the patient exclaims, "this passing of urine in large quantities has made me very weak." The color of the urine is white, its quantity is copious, passes several times in a day and night; specific gravity is high, large amount of sugar is found in urine.

Skin: There is burning all over body; boils and carbuncles burn; diabetic carbuncle may appear anywhere on the body.

Thirst: Drinks water often in copious quantities.

Weakness: The patient feels his growing weakness.

Aggravation: Sexual intercourse increases flow of urine and sugar.

Sexual power: Almost gone or lost.

Recorded Symptoms in Lotus Materia Medica by Robin Murphy

G. sylvestre will abolish the taste of bitter things, sense of taste altered, powdered root for snake bite. Sore throat, dark livid of fauces and erysipelatous swelling of the face are most marked. Headache, throbbing in the forehead and temples, and over eyes with the bluish-white coating of tongue and burning in eyes. Desire for heat and quiet.[17]

In the present proving symptoms, when compared with the previous literatures it was found that there was no urinary symptoms as history says its therapeutic action on urine is marked and all the other symptoms do not correspond to the previous recorded symptoms in different Materia Medica books.

CONCLUSION

This drug seems to be useful in clinical conditions such as headache, vertigo, common cold, cough, diarrhea, etc. Further, work is necessary to find out the real value of the drug in diabetes. The symptoms appeared during the trial will add more information on this medicine and benefit research scholars and clinicians. These proved symptoms need further verification through Clinical application in different clinical settings.

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उद्देश्यः इस अध्ययन का उद्देश्य स्वस्थ मानव प्रतिभागियों पर गुरमार बूटी का होम्योपैथी पोटेंसी में विकारी प्रतिक्रिया पर प्रकाश डालना है ।

सामग्री और तरीकेः गुरमार औषधि को केन्द्रीय होम्योपैथी अनुसंधान परिषद् द्वारा यादृच्छिक डबल ब्लाईंड नियंत्रित प्लेसबो विधि के माध्यम से सिद्ध किया गया । चार केन्द्रों में इस अध्ययन को जांचा गया । पूर्व परीक्षण चिकित्सा परीक्षा और नियमित प्रयोगशाला जांच आयोजित करने के बाद चुने गए 63 स्वस्थ प्रतिभागियों पर दवा चिकित्सा विशेषज्ञों द्वारा दो पोटेंसियों (6C और 30C) में औषधि का सिद्धिकरण किया गया । पहले चरण में, प्रतिभागियों को प्लेसिबो की 56 खुराक (14 दिनों के लिए प्रति दिन 04 खुराक दी गयी । अगले 2 चरणों में, प्रत्येक पोटेंसी या प्लेसबो की 56 खुराक (14 दिनों के लिए प्रति दिन 04 खुराक दी गयी । परीक्षण अवधि के दौरान उत्पन्न लक्षणों को स्वयंसेवकों द्वारा नोट किया गया और सिद्ध कर्त्ता द्वारा विस्तृत किया गया । डिकोडिंग के बाद, सभी तीन केन्द्रों से प्राप्त आंकड़ों को केन्द्रीय होम्योपैथी अनुसन्धान परिषद्, नई दिल्ली (सीसीआरएच) मुख्यालय में संकलित किया गया ।

टिप्पणीः 37 स्वयंसेवकों (Provers) में से, जो वास्तविक तौर पर दवा परीक्षण में थे, उनके 16 प्रकट लक्षणों को स्पष्ट किया गया । यह औषधि शरीर के अधिकांश भागों में प्रत्येक पोटेंसी में लक्षण उत्पन्न करने में सक्षम था ।

निष्कर्षः सिद्ध औषधि परीक्षण के दौरान गुरमार के रोगजनक विकारी प्रतिक्रिया की जानकारी मिलती है, जिससे गुरमार के उपयोग के दायरे का विस्तार होता है और इससे अनुसंधान विद्वानों और चिकित्सकों को फायदा होगा । औषधि से उत्पन्न लक्षण को जब चिकित्सकीय सत्यापित किया जायेगा, तब इससे और लाभ मिलेगा ।

खोजशब्दः सिद्ध औषधि, गुरमार, होम्योपैथी, होम्योपैथी विकारी परीक्षण, विकारी प्रभाव ।