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DRUG PROVING

Carica papaya - a multicentric double blind homoeopathic pathogenetic trial

Rajpal[1,3*], Anil Khurana[1], V.A. Siddiqui[1], V.K. Singh[1], B.N. Dutta[2], Shakti Dey[2], R.D. Jayant[3]

[1] Central Council for Research in Homoeopathy, New Delhi, India
[2] Drug Proving Research Unit (H), Kolkata, West Bengal, India
[3] Homoeopathic Drug Research Institute, Lucknow, Uttar Pradesh, India

***Objective*: To elicit the pathogenetic response of the drug *Carica papaya* in homoeopathic potencies on healthy human volunteers.**

***Methodology:* Drug *Carica papaya* was proved by the Central Council for Research in Homoeopathy through double-blind placebo-controlled method. The study was conducted at 2 centers. The drug was proved in three potencies (6C, 30C and 200C) on 26 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 three 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, cross examined and elaborated by the Proving Masters. The data obtained from both the centers was compiled at proving-cum-data processing cell at CCRH headquarters after de-coding.**

***Observations:* Drug was able to produce symptoms in each potency more or less related to every part of the body.**

***Conclusion:* Pathogenetic responses (new and reproved) elicited during the proving trial expands the scope of use of the drug *Carica papaya* and will benefit the research scholars and clinicians. These symptoms will carry more value when verified clinically.**

***Keywords:* homoeopathy; pathogenetic response; homoeopathic drug proving; carica papaya**

Introduction

The green fruit is considered as an edible vegetable and largely used in making Indian curries; ripe one is sweet and delicious and both are used in liver complications and disorders of digestion as habitual constipation, dyspepsia and bleeding piles. Papain or papayotin, an albuminoid digestive or milk curdling ferment, is the principal constituent of its juice. Green fruit is laxative and diuretic; its juice is emmenagogue aiding the menstrual discharge. In large doses it acts as an ecbolic exciting uterine contraction. It induces abortion when locally applied to the mouth of the uterus. The milky juice and the seed also are considered best vermifuge especially for roundworms in children. For enlarged liver and spleen, dried and salted fruits are used with marvellous results.[1]

Milky juice of unripe fruits-used as a cosmetic to remove freckles and other blemishes from the skin; anthelmintic, particularly effective in the expulsion of lumbrici.[2]

Papayotin or Papain, a concentrated active principle, which is the proteolytic enzyme, is also found distributed in all parts of the tree. A good sample of Papayotin or papain, according to British Pharmacopeia Codex, resembles pepsin in its physiological properties and is capable of digesting 200-250 times its weight of fresh, pressed blood fibrin in 4-5 hours at the temperature of 45/50^{0}.[3]

** Address for Correspondence:*
Dr. Rajpal, Asstt. Director (H)
Central Council for Research in Homoeopathy
61-65, Institutional Area, Janakpuri, New Delhi- 110 058
Email: ccrhdp@yahoo.com

Carica papaya was first proved by Dr. D.N. Ray.[4] However, a systematic proving of Carica papaya in homoeopathic potencies was necessary to elicit its pathogenetic power, and therefore Central Council for Research in Homoeopathy (CCRH) undertook its systematic Homoeopathic Drug Proving as per the approved protocol.

Botanical name : *Carica papaya* Linn.[3]
Natural Order : Passifloreae[1,4]
Family : Caricaceae [4,5]

Common names[3]

English	:	Papaw or Papaya tree
Hindi	:	Popaiyah, Papita
Bengali	:	Penpe, Papeya
Punjabi	:	Aranda-kharpuza
Gujrati	:	Papai
Marhati	:	Popai
Oriya	:	Amruta bhanda
Telugu	:	Bappayi, Bobbasi
Tamil	:	Poppayi, Pappali
German	:	Melonenbaum
French	:	Papayer Commun.

Description

Small tree, 2 to 6 m high, tapering above to 12-13 cm in diameter, at top. Stem erect, soft and spongy wooded, hollow and bearing numerous leaf scars. Leaves large, palmately, 7-lobed, lobes divided into secondary lateral lobes, 60 cm across, long, hollow, petioled, arising horizontally from the stem. Flowers yellow, generally diocious, occasionally a few pistillate flowers on male plants; staminate, flowers in long drooping panicles and pistillate in sub-solitary or short clusters. Ovary 1-celled, stigma sessile, 5-lobed, lacerated. Fruit large, melon-like, 25 cm long, 7-12 cm broad, green or dingy greenish yellow, long stalked and arising below the crown of leaves. Seeds numerous, black, enclosed in sweet mucus pulp and covered with a loose hyaline skin of arillus; testa thick brittle.[4,5]

Distribution

This valuable tree is commonly cultivated in gardens throughout India; indigenous in America.[3]

Part Used

Green unripe fruit excluding seeds[5]

Objective

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

Materials and Methods

Location and duration of study

The proving was conducted at Drug Proving Research Unit (Homoeopathy), Kolkata and at Homoeopathic Drug Research Institute, Lucknow in January to December 1990.

Participants

Total 26 apparently healthy volunteers from above mentioned two centers, between the age group of 18 to 50 years, comprising of 18 males and 8 females, were enrolled in this study. Pre-trial Medical Examination (PME) and Terminal Medical Examination (TME) of the volunteers were carried out by General Physicians, Psychiatrists, Cardiologists, Ophthalmologists, ENT Specialists, Dermatologists, Gynaecologists, Radiologists and their routine laboratory investigations at both the centers were done to ascertain their health status. After recommendation of experts, healthy volunteers were enrolled in the Homoeopathic drug proving programme.

Drug

Carica papaya was procured in 6C, 30C and 200C potencies from M/s. Hahnemann Publishing Co. Pvt. Ltd., Kolkata, West Bengal, India, which have been prepared from back potencies in 30 ml. sealed phials of each dilution. Globules (number 30) were medicated with these attenuations at the headquarters office and sent to both the centers 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.

Study Design

The study was a randomized double blind placebo controlled trial.

Methods

Before commencing the study, all provers were screened strictly by the experts and apparantly healthy provers between the age group of 18-50 years, both male and female 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 (PME) was conducted to confirm health status of the volunteers. Volunteers declared healthy, were enrolled in the study. The study was conducted at two centers. According to CCRH Drug

proving protocol, the sample size included 30% volunteers under control group at each center. So, out of 26 volunteers, 17 were kept on drug (verum) and 9 were on placebo (control) in all four 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).

The study consisted of four phases. Each Phase consisted of 56 doses of drug or placebo.

Phase-I : It was a placebo phase. Its usefulness is that we get the prover's response to placebo and therefore acts as control for subsequent phases.

Phase-II : In 2nd phase, the proving was done with 200C potency.

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

Phase-IV : In 4th phase, the proving was done with 6C potency.

Procedure of Proving

The volunteers were asked to take 4-6 globules of a particular potency of the coded drug, four times a day, dry on tongue.

The volunteers were 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 sign(s)/symptoms(s) appeared*

The volunteers were asked to stop taking the drug/placebo as soon as they felt any change or any sign(s) and/or symptoms(s) developed during the trial.

The volunteer noted down the sequence of the appeared new sign(s) and/or symptoms(s), their progress and the number of doses after which such sign(s) and/or symptoms(s) appeared with date, time of onset and duration for which they persisted. Intake of drug remained suspended till the sign(s) and/or symptoms(s) totally disappeared. Any change in normal routine of the prover in respect to daily habits pertaining to diet, living conditions etc./any treatment taken was also noted in the Prover's Day Book Proforma.

After disappearance of sign(s) and/or symptom(s) produced by the drug, the volunteer had to wait for a further period of 07 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 till the consumption of 56 doses of that potency by the volunteer.

If the prover 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 everyday by Proving Master about the appearance of new symptom(s) or progress of symptoms and noted those in 'Symptom 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.

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

If no symptom was observed, the volunteers noted down as 'No Symptom' with date and time of intake of the respective dose of the drug/placebo.

Before commencing the administration of subsequent potencies (subsequent Phase) of the drug, the volunteers remained on a washout/rest period (it should be a symptom free period between two phases of drug proving in which a volunteer does not take any drug) for 14 days and started taking next potency in the same procedure as mentioned above, till completion of 56 doses.

The same procedure was followed for the 3rd and 4th phases.

Each volunteer was interrogated by the Proving Master to verify the sign(s) and/or symptom(s) recorded by the volunteer. The symptoms recorded in 'Prover's Day Book Proforma' were verified by the Proving Master and completed through further interrogation with the provers in respect to their location/ sensations/ modalities and 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 of appearance of symptom(s). Since laboratory tests were performed to identify any correlation between the subjective and objective changes during the course of proving, the expert opinion of the honorary consultant(s) was obtained, wherever needed.

After completion of trial of all potencies, the volunteers had undergone the 'Terminal Medical Examination' (TME).

On completion of all the respective Phases of the proving, the compilation of data recorded in 'Prover's Day Book Proforma', 'Symptoms Elaboration

Proforma', 'Pathological Report Sheets' and 'Terminal Medical Examination sheets', was done at the Council's headquarters by the Drug Proving-cum-Data Processing Cell. After decoding, the sign(s) and/or symptom(s) generated by the volunteers kept on the drug were separated from those generated by the volunteers kept on placebo. The sign(s) and/or symptom(s) which were common to both the groups i.e. placebo as well as drug groups were not taken into consideration while compiling the symptomatology of the drug.

Management of adverse effects – A vial of antidote is sent with each quota to each center. In this trial homoeopathic potencies of *Camphor* were used as antidote as it is believed that *Camphor* can antidote nearly every vegetable medicine.[6] 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 done, if required.

Pathogenetic effects

Pathogenetic effects were deduced

(i) from comparison of symptoms developed in placebo phase with symptoms during intervention phases (Intraprover comparison)

(ii) from comparison of symptoms developed by provers on control (for all four phases) with provers on actual drug trial (Interprover comparison)

Results

The following symptoms were observed during the drug proving-

- In parenthesis, 1st number denotes number of volunteers eliciting the particular symptom and 2nd number denotes potency used.
- *agg.*: aggravation, *amel.*: amelioration

Head

- Heaviness in head with feverish feeling, *agg.* sitting; *amel.* pressure, lying down (1,6C)
- Heaviness in head with throbbing sensation in ears and dry cough (1,30C)
- Headache with heaviness and pain around eyes, burning in eyes and nostrils, *amel.* bathing. (1,30C)
- Dull, aching pain in head, *agg.* reading; *amel.* lying down, rest (1,30C)
- Bursting pain in head with feeling of tightness and laziness, *agg.* movement, sitting; *amel.* lying down (1,6C)
- Bursting pain with throbbing sensation in frontal region from sunrise to sunset, *amel.* pressure (1,6C)
- Stitching pain in forehead, *agg.* standing; *amel.* closing eyes, lying down (1,200C)
- Sudden stitching pain in forehead, *agg.* mental exertion, afternoon, reading, writing; *amel.* moving freely (1,200C)
- Throbbing pain in frontal region, *agg.* taking food, journey, thinking about examination; *amel.* rest. (1,6C)
- Aching pain in occipital region after rising in morning with constipation, *amel.* pressure (1,30C)
- Bursting pain in occipital region, *agg.* stooping, motion, hot application; *amel.* rest, pressure, lying down (1,30C)

Eyes

- Redness of right eye with itching and swelling in upper eyelid. Pressing pain in both eyes, *agg.* night, pressure, closing the eyes; *amel.* hot fomentation. (1,6C)
- Watery discharge from both eyes, *agg.* sunlight. (1,200C)

Nose

- Dry coryza with nasal obstruction and heaviness of head, *agg.* open air; *amel.* inside room. (1,200C)
- Thin bland discharge from nose with cough and scanty expectoration. (1,30C)
- Epistaxis, *amel.* applying cold water. (1,200C)

Mouth

- Dryness of mouth, *amel.* drinking water in large quantity. (1,30C)
- Dryness of mouth with thirst, frequent desire for large quantity of cold water. (1,200C)
- Painful aphthae on tongue with stinging pain and increased salivation, *agg.* touch of teeth. (1,200C)

Throat

- Stitching pain in throat, *agg.* swallowing, drinking cold water, morning; *amel.* warm drinks, hot water gargles. (1,30C)

- Pain in throat with rough sensation, mucus comes out easily on coughing, left nostril blocked with mucus. (1,30C)
- Pain in throat on deglutition with red and enlarged tonsils, frequent loose cough and sneezing. (1,30C)

Stomach

- Heartburn, sour eructation with loss of appetite. (1,30C)
- Acidity with loss of appetite, *agg.* after drinking cold water in large quantity. (1,6C)

Abdomen

- Fullness of abdomen as if it would burst due to flatulence, uneasy feeling in abdomen (1,200C)
- Abdomen distended after taking meals with burning sensation in throat, sour eructation, *amel.* after eructations, drinking cold water. (1,6C)
- Spasmodic pain in abdomen with loose, watery, yellowish stool with general weakness, *amel.* passing flatus, after stool. (1,200C)
- Spasmodic pain in abdomen with heaviness, loose stool; ineffectual urge and lassitude, *amel.* passing flatus, stool. (1,30C)
- Spasmodic pain in abdomen with ineffectual desire to pass stool, *amel.* passing flatus, movement. (1,6C)
- Dull aching pain in hypochondrium with laziness and dryness of mouth, *amel.* rest, passing flatus, after stool. (1,200C)
- Griping pain around umbilicus; gradually increased, *agg.* while sitting; *amel.* pressure. (1,200C)
- Stitching pain around umbilicus with dryness of lips at night; *amel.* pressure. (1,30C)

Rectum & Stool

- Constipation, painful hard stool. (1,6C)
- Constipation; hard, slimy stool with pain and bleeding from anus. (1,200C)
- Constipated hard stool, no urge; or loose, mucoid, muddy, adherent stool with flatulence. (1,30C)
- Black, hard stool with bleeding from anus; itching, burning in anus after scratching. (1,6C)
- Stool hard, painful, ineffectual urge; unfinished sensation with tenesmus in umbilical region and lower abdomen (1,200C)
- Loose, offensive, yellowish stool with pain in lower abdomen, weakness and sweat on forehead after stool. (1,6C)
- Loose stool with mucus, blood and pain in abdomen or hard stools with no urging and no pain in abdomen. (1,6C)
- Loose stool with constant mild pain in umbilical region and foul eructations. (1,6C)
- Mucoid or blackish yellow stools with offensive odor; copious with flatulence, acidity and weakness after stool. (1,200C)
- Frequent, offensive, yellow stool with spasmodic pain in abdomen and weakness in calf muscles, *amel.* passing stool. (1,30C)
- Profuse, sour smelling, loose, mucoid stool with weakness and increased appetite. (1, 200C)
- Scanty, yellow, semisolid stool with mild pain in abdomen and general weakness before stool. (1,200C)
- Painful boil near anus, burning pain during stool, *agg.* touch; *amel.* pressure, lying down in supine position, cold application. (1,6C)

Respiration/Cough

- Dry cough with sneezing, *agg.* morning. (1,6C)

Chest

- Pain in the chest with cough, scanty, thick, yellow expectoration. (1,30C)
- Burning pain, redness and soreness in left axilla, *agg.* from sweating, moving the arm. (1,6C)

Neck/Back

- Stiffness of neck with intolerable pain on left side, *agg.* turning head on either side, least motion, 10 a.m. to 4 p.m.; *amel.* lying down with support of pillow. (1,30C)

Extremities

- Acute cramping pain, coming suddenly disappearing gradually; extending from hip to ankle, *agg.* standing; *amel.* sitting. (1,200C)
- Cramping pain in calf muscles with feverish and chilly feeling, *agg.* movement; *amel.* rest, lying down. (1, 6C)
- Dragging pain in both extremities, *agg.* movement; *amel.* lying down, rest. (1, 30C)
- Dry, reddish eruptions, on right elbow with itching, *agg.* night, warmth; *amel.* cold application. (1,6C)

- Aching pain in triceps, *agg.* pressure, motion. (1,6C)

Sleep

- Sleeplessness due to flatulence. (1, 30C)

Fever

- Flushes of heat with dryness of mouth, *amel.* evening, after sweating. (1,200C)
- High fever with chill and drowsiness with temporal headache, dry tongue, thirst for large quantity of water at long interval, *agg.* cold application; *amel.* covering, warmth. (1,200C)
- High fever with chill without thirst and general weakness, *agg.* after sweating. (1,6C)

Generalities

- Weakness with aversion to work, *amel.* rest, specially by lying down. (1,200C)
- Severe bodyache with weakness, feverish, chilly, restless with loss of appetite. (1,200C)

Discussion

The drug was able to produce symptoms in 6C, 30C and 200C potencies. Sixty symptoms appeared in the volunteers through three potencies. Headache, epistaxis and tonsillitis are included in the pathogenesis of *Carica papaya*. A lot of symptoms related to gastro-intestinal tract viz. heartburn, distension of abdomen, spasmodic, stitching and gripping type of pain in abdomen appeared during the trial. In the literature the drug has been recommended for use in dyspepsia and indigestion.[1] This proving trial has confirmed its role in the management of dyspepsia, where symptoms like heartburn, sour eructations, flatulence have appeared in many provers. This can be compared with *Nux vomica* in constipation for ineffectual desire to pass stool. This drug will be of usage in acute dysentery where there is spasmodic pain, mucoid stool with blood, weakness in calf muscles. It can also be used for haemorrhoids, when associated with constipation. Symptom of pain in forehead from sunrise to sunset indicates its usage for acute frontal sinusitis. Character of pains appeared during the proving are bursting, stitching, throbbing and cramping types. Though produced in only one prover, stiffness of neck with intolerable pain on left side, indicates that this drug can be used for cervical spondylosis with particular time modality.

The symptom generated during the proving shows that the drug has wide clinical application which should be put to use in the treatment of patients so as to confirm the pathogenetic process of this drug.

Related remedies in the literature

Nux vom. (constipation with frequent unsatisfatory urge, passing small quatities, sensation as if not finished); *Merc. sol.* (Dysentery, stool slimy, bloody); *Merc. cor.* (stool, scanty, bloody, slimy, offensive); *Kalmia lat.* (headache begins at sunrise, < at noon and leaves at sunset); *Iris ver.* (profuse flow of saliva, deficient appetite); *Paris quadrifolia* (sense of weight and weariness in nape of neck, neuralgia beginning in left intercostal region).

Conclusion

The symptoms appeared during the trial will add to the available literature on this medicine and benefit the research scholars and clinicians. These proved symptoms need further verification through clinical applications in different settings.

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