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SCIENTIFIC ANALYSIS OF VAJRA KANDI CHENDURAM A SIDDHA FORMULATION TOWARDS ITS SAFETY, PHARMACOLOGICAL ACTION AND PROPOSED BENEFITS IN THE MANAGEMENT OF COVID-19

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ABSTRACT

Vajra kandi chenduram is a Siddha formulation has been widely used especially among traditional Siddha practioners towards the management of several acute and chronic ailments ranging from fever to chronic inflammatory disorders and immune mediated diseases. This literature review of Vajra kandi chenduram involves the scientific analysis of Lingam (Cinnabar), Veeram (Mercuric perchloride), Pooram (Hydragyrum subchloride), Rasa sinduram (Red sulphide of Mercury) that are ingredients as well as Annabedhi chenduram that can be used as an adjuvant. The search results confirm the antipyretic, anti-inflammatory, antioxidant activity of its ingredients. Based on this search and the clinical experiences of Siddha physiscians in the management of earlier epidemics, these results has derived a hypothetical claim that Vajra kandi chenduram through its antipyretic and anti-inflammatory properties can be effective in inhibiting the inflammatory mediators and cytokine storm of COVID-19 which is a major cause of serious lung complications. Therefore this formulation can be considered as a safe and effective supportive therapy in the absence of any specific target treatment measures.

KEYWORDS: Vajra kandi chenduram, COVID-19, Siddha, Antipyretic, Anti-inflammatory.

INTRODUCTION

In the past half century, the deadly disease outbreaks have been caused by Novel viruses of animal origin. They are Nipah virus in Malaysia, Hendra virus in Australia, Hanta virus in united states, Ebol; a virus in Africa along with HIV (Human immunodeficiency virus), several influenza subtypes, SARS (Sudden acute respiratory syndrome) and MERS (Middle east respiratory syndrome).[1] Corona virus is caused by rapidly dividing virus which works by injecting it's genome into other's gene and multiplies there hence it depends on other organisms for its growth and therefore makes it more difficult to vanish the disease-causing agent and it is becoming a great topic of research among the drug developers, researchers and scientists.[2]

At present, the outbreak of Covid-19 by a novel (new) coronavirus (named "2019-nCoV") first detected in Wuhan City, of China continues to extend worldwide despite every efforts.[1] With emerging scientific and technological advances around the globe, specific vaccination or a novel medication to combat this grave ailment is still at an early stage. In this scenario researches after the outbreak in China, Guangdong had reported a mortality of just 0.1% of infected people - compared with Wuhan's rate of 2.6% - and none of the confirmed patients in Zhejiang had died, the reason is that the patients in Guangdong and Zhejiang were given traditional medicines to relieve symptoms even before they were testing positive. The combination of modern and traditional therapy can notably reduce the intensity of symptoms, death rate and side effects as observed in China.[2] With these proven advantages of traditional medicines in China which had overcome this deadly disease, the present work has been initiated to highlight the therapeutic potential of Vajra kandi Chenduram a Siddha traditional formulation.

Traditional Systems of medicines are playing a key role in meeting the global health care needs. Siddha is the unique system of medicine which is originated from Tamil nadu and has its origins in Tamil language. Literally the word "Siddha" means "established truth"[3] Siddha system of medicine is claimed to alleviate the root cause of the diseases by maintaining the ratio of *Vatham, Pitham and Kapham*. The current review aims to explore about herbomineral formulation *Vajra kandi Chenduram* with special emphasis on purification, composition, traditional uses and toxicity and efficacy studies on the ingredients of *Vajra kandi Chenduram.*

Significance of herbomineral preparations in siddha system of medicine

In Siddha system of medicine the commonly used formulations in combination with minerals are *Parpam* (mineral/metallic oxides), *Chendooram* (mineral/metallic sulphides), *Chunnam* (caustic or major oxides) and *Pathangam* (sublimation). Among them *Chendooram* has a long shelf life for 75 years.[4] *Rasa vatham* is an ancient Indian practice in which herbs are deliberately combined with metals (e.g., mercury, lead, iron, zinc), minerals (e.g., mica) and gems (e.g., pearl) According to the tradition, these processes would eliminate the harmful effects of metals. Metallic herbal preparations offer advantages over plant-based drugs by virtue of their stability over a longer period, lower dosage, easy storability and sustained availability.[5]

Preparation of vajra kandi chenduram

The raw drugs were properly collected from country drug merchant shop, Tanjore and the above drugs will be certified by geochemists as genuine one according to the physical and chemical nature of the compound.[6]

The following are the ingredients of Vajra kandi Chenduram according to Siddha literature.

Table 1: Ingredients of Vajra kandi Chenduram.

S. no	Ingredients	Quantity
1.	Purified *Lingam* (Cinnabar)	400gms
2	Purified *Veeram* (Mercuric perchloride	25 gms
3	Purified *Pooram* (Hydragyrum subchloride) (Calomel)	50 gms
4	Purified *Rasa senduram* (Red sulphide of Mercury)	100gms

Purification of ingredients[7]

Purification of Lingam (Cinnabar)

Before the actual preparation process, as per the procedure, Cinnabar is supposed to be processed with certain juices to detoxify (purify). Cinnabar was purified by immersion into mother's milk or cow milk each for 3 days from 6 am. The milk is to be changed each day at every 24 hours and then soaked with lime juice for one day.

Purification of veeram (Mercuric perchloride)

Camphor is mixed with tender coconut water and placed in a mud pot. Veeram is tied in a cloth and soaked in the pot without touching the water and the pot is burnt out for 3 Hours then Veeram is taken out and washed.

Purification of Pooram (Hydragyrum subchloride) (Calomel)

The poultice made of betel leaf(Piper betel) and pepper(Piper nigrum) each 8.75gm was taken and dissolved in 1.3 litre of water, calomel 35gm was tied with a cloth and immersed in the liquid from the cross bar (*Thulayanthram* process) and heated. After the water reduced to ¾ of its volume, the calomel was taken out, washed with water and dried to get it in purified form.

Purification of rasa senduram (Red sulphide of Mercury)

Rasa senduram (Red sulphide of Mercury) was immersed 3 days in lime juice. The lime juice is to be changed every 24 hours.

Process of preparation

The above ingredients are to be grinded with ginger extract for about 48 hours and then with lime juice for one hour and the medicine is allowed to dry and stored in an ceramic or glass container.

Dosage

The dosage has been fixed based on previous clinical experience of the Siddha practitioner and based on the uniform measurement for chenduram as indicated in Siddha literature.

Adults - 50mg

5-12 yrs - 25mg

Adjuvant- 30-50mg of *Vajra Kandi* + *Chenduram* Annabedhi chenduram (100mg).

Indications- Relief of all fevers within 3 days, It is also indicated for inflammatory conditions such as arthritis.

Duration of treatment: Thrice a day after food for three days. If needed, can be repeated after 5 days depending on patient's condition.

Adverse events: Not observed in clinical practice if occurs, very minimal. For which a decoction made of Pepper, Cumin and Betel leaves can be administered.

Dietary instructions

Patients are advised to take easily digested food like rice porridge, Idly, Idiyappam, milk rice etc. Tamarind, sour diet, alcohol, tobacco, bitter gourd should be avoided.

Non-vegetarian foods should be avoided 24 hours before treatment till 15 days.

Scientific validation of Ingredients of vajra kandi chenduram

1. Cinnabar (*Lingam)*

Siddha literature consider *Lingam* (*Cinnabar* or Mercury sulfide) as the safest among mercurial drugs.[8] Siddhars have converted potentially toxic heavy metals and its salts such as elemental mercury and its compounds, arsenic, copper sulphate, etc., into good medicines by removing their toxicity by a special process of *Suddhi* (purification). A study by N.R. Pillai conducted the anti-pyretic, hypothermic and analgesic activity of *Linga chendooram* which has *Lingam* as chief ingredient at different dose levels. *Linga chendooram* (LC) at 100 mg/kg showed significant anti-pyretic activity against Brever's Yeast induced pyrexia when compared with the standard drugs acetyl salicylic acid and paracetamol in albino rats. LC also showed analgesic activity against hot plate induced algesia at 100 mg/kg b.w.[9] Toxicity study evaluated of LC in mice by Punitha et al. In acute toxicity study, the animals treated with LC at a dose of 1000mg/kg showed negligible toxic signs. In sub acute toxicity study, the animals treated with 50,100,200 mg/kg of LC were shown significant changes in body weight, haematological parameters and in biochemical parameters during the dosing period of 28 days.[10] There was no renal impairment even at high dose (20mg/kg). at high dose produced toxicity in blood parameters, liver functions and lipid profile, and showed mild histological changes. Also the drug *Linga pathangam* was considered to be safe up to 10mg/kg in rats, which corresponds to human dose of 112mg/70kg in man.[8]

2. Rasa Sinduram (Red sulphide of mercury)

Red sulfide of mercury which is known in ancient Indian literature as *Rasa sinduram* (*rasasindura, rasasindoor, rasasinduram, sindur, or sindoor*) and is used extensively in various ailments and diseases. From various physico-chemical characterizations it is concluded that *rasasindur* is chemically pure α-HgS with Hg:S ratio as 1:1. Analysis of rasa sindur vide Transmission Electron Microscopy (TEM) showed that the particles are in nanoscale. It also act as a potential protease inhibitor which may prevent the unwanted cell damage and act as a drug against the disease caused by excessive proteolysis. Binding capacity of serum albumins has a great impact on the pharmaco kinetic properties of therapeutic drugs Since Rasasindur is a traditional drug is attempted to study its interaction with bovine serum albumin (BSA). BSA is highly homologous to human serum albumin (HSA) and is often chosen as a model protein to study small molecule albumin interactions

The interaction of rasasindur with BSA was studied by monitoring the quenching of tryptophan fluorescence. The intrinsic tryptophan fluorescence of BSA decreased gradually on increasing rasasindur concentration These results clearly revealed that, rasasindur inhibited the proteolytic cleavage of BSA by trypsin.[11]

Oral acute toxicity study of *Rasa sindura* was carried at the limit dose of 2000 mg/kg orally in rats. For chronic toxicity, *Rasa sindura* with adjuvant was administered at therapeutic equivalent dose (45 mg/kg, orally), therapeutic equivalent dose×5 (225 mg/kg, orally), therapeutic equivalent dose×10 (450 mg/kg, orally) for 90 days and an additional recovery group of therapeutic equivalent dose×10 for 30-day observation after the treatment period. Acute toxicity result showed that drug did not produce any signs and symptoms of toxicity or mortality up to an oral dose of 2000 mg/kg in rats. Although the drug produced mild to moderate adverse changes (in kidney, liver, intestine, and stomach) at therapeutic equivalent dose×10 dose level, equivalent of which are unlikely to be ever employed in a clinical trial.

The observed changes were not seen at the lower dose levels as well as in the recovery study.

Hence, it is suggested that the *Rasa sindura*, along with the adjuvant prepared as per the customary method, is safe for consumption at the therapeutic dose level. Further, drug did not affect the cytoarchitecture of major organs like heart, kidney, liver, uterus, and ovary which suggest that LD50 value may be higher than 2000 mg/kg by oral route. As per UN classification, any substance, which has oral LD50 of more than 2000 mg/kg is considered as low hazard potential and categorized as UN 6.1 PG III.[12] Antioxidant activity was carried out using DPPH scavenging activity with *Rasa sindur* in a range of concentration from 10 to 1000 µg/ml. It was observed that the free radical scavenging activity or percent (%) inhibition of the *Rasa sindur* increased in a concentration dependent manner which saturated at 800 µg/ml highest antioxidant property obtained for Ras sindur at 800µg/ml was 24%.

Analgesic and Anti inflammatory efficacy of RC at the doses of 50 mg/kg and 100 mg/kg of body weight in experimental animals. Analgesic activity was evaluated by Chemical induction method and Anti inflammatory activity was evaluated by Carrageenan induced paw edema in rats. Diclofenac sodium 50 mg/kg of body weight was employed as standard drug for both studies. Animals were randomized into 4 group (n=6).Control group receives vehicle only. RC treated with low and high dose which produced significant inhibition of edema and

pain. This study confirms RC possesses significant Analgesic and Anti inflammatory efficacy.[13]

3. Pooram (Hydragyrum subchloride/Calomel)

Pooram is also called as Mercurous chloride or Mercury (I) chloride is odourless solid and dense white or yellowish-white in colour. It is the principal example of a Mercury (I) compound. It is composed of Mercury and Chlorine (Mercury 84.98% Chlorine 15.02%). It is also referred to as the mineral horn quicksilver or horn Mercury. Historically, Calomel was used to treat yellow fever during its outbreak in Philadelphia in 1793 and also used in the treatment of syphilis, until the early 20th century. It was used as a laxative and disinfectant.

In the 18th and 19th centuries, the majority of British doctors working in India still believed in humoral medicine and they used Calomel for inflammations of the liver and bilious fevers in a tropical environment.[14] Calomel is regarded as one of the major ingredient to cure various types of pain and rheumatism. The Siddha traditional preparation *Chandamarutha chenduram* in which calomel is a major ingredient is found to be very effective in treating post Chikungunya arthritis. Management of Chikungunya through Ayurveda and Siddha- a technical report.[15]

Acute and long term toxicity studies were carried out in swiss albino mice and wistar albino rats in Poora parpam, a calcined preparation of calomel following WHO guidelines mentioned for traditional herbal medicines. In acute toxicity study 10 times more than the therapeutic dose of drug prescribed was given as single oral dose to the test animals and no sign of mortality was observed. Long term toxicity studies were carried out in different groups in which test drug was administered orally to rats at dose levels of 0.1296 mg/ animal, 0.648 mg/ animal and 1.296 mg/ animal respectively. Detailed hematological, biochemical, morphological and histopathological evaluation of organs was performed for all animals at the end of the study. Haematogical and biochemical analysis revealed no abnormalities. Histopathological analysis of brain, heart, kidney, liver, lungs of treated groups does not show any signs of toxicity. Thus *Poora parpam* was well tolerated by the treated groups and showed the therapeutic dose mentioned in the literature was safe for human consumption.[16]

Cancer medicines which contain rasa karpooram as chief ingredient: Also various Siddha medicinal formulation such as *Karpoora Chindhamani Mathirai*, *Namachivaya Chendooram*, *Rasa karpoora kuligai* contains *Pooram*. All these preparations were tested through

preclinical research studies and were found to have significant Analgesic, Anti Inflammatory, Antipyretic Effects. Moreover in acute toxicity testing of *Karpoora Chindhamani Mathirai* in experimental animals at the dose of 2000 mg/kg/po did not exhibit any mortality in rats. The Human papilloma virus (HPV) HPV 16 and HPV 18 are responsible for 93% of Cancer cervix. Analysis of pharmacological activity of *Namachivaya Chendooram* through HeLa and SIHA cell lines validation explained about its anticancer activity. It can be observed by the result of MTT assay that the IC dose of Namachivaya Chendooram is 50µg/ml. As the dose increases the HeLa cell viability decreases.[17] In acute toxicity test the *Namachivaya chendooram* was found to be non toxic at the dose level of 200mg/ kg body weight. The sub acute toxicity study at 20mg, 40mg/kg of *Namachivaya chendooram* also showed that all the animals were free of intoxicating signs throughout the dosing period of 28 days.[18] Similar anticancer effects against HeLa cell lines on cervical cancer caused by HPV and non-toxic effects were also observed in *Rasa karpoora kuligai* through previous preclinical research studies. Further the Antioxidant activity of the drug *Rasakarpoora Kuligai* (RKK) tested by DPPH assay showed that there was a concentration dependent Antioxidant activity of crude extract of *Rasakarpoora Kuligai* (RKK). At the concentration increased from 10 to 100µg/ml, percentage of inhibition increased from 50% to 78%. At a concentration of 100µg/ml there was an increased percentage of inhibition (78%) in scavenging the free radicals (DPPH). The IC50 value was obtained at 12.70µg/ml. It showed that *Rasakarpoora Kuligai* (RKK) is having significant anti oxidant activity .Most of the particles present in the sample is nano size and near nano size, average particle size is 4.64µm - 7.51µm which increase the efficacy and bio availability of the test drug. So, very minimal quantity of the medicine is enough to treat the disease.[19]

4. Veeram (Mercuric perchloride)

Perchloride of Mercury was first used as a therapeutic agent for venereal diseases during the middle of the eighteenth century in western countries. But for many centuries the Perchloride of Mercury has been used in India for the treatment of various disorders. *Dalachikna* also known as *Shavirum* in Siddha system of medicine .Elemental Analysis Report revealed that *Dalachikna* contains Mercury 74.00%, Chlorine 45.36 ppm, Lead 0.08 ppm, Arsenic 0.03 ppm, Chromium 0.06 ppm and Cadmium 0.08 ppm. These proportions indicate that dalachikna is compound mixture of mercury and chloride.[20]

Toxicity studies suggest that the *Veera Chenduram* is practically toxic or lethal after an acute exposure at the dose level of 1g/kg. and affects the vital organs at the maximum dose range of 200mg/kg. But normal human dose is very minimal to compare the study group doses. If given the test drug as per literature it does not produce toxicity. Hence, to avoid the major adverse reactions the duration of treatment is minimized. Because of an ideal man of 70 k.g. body weight requires 4mg of the drug two times daily. But body weight of rats are approximately 100 – 120gms and so they have been given 50mg /kg, 100mg/kg, 200mg/kg daily which is doses are more than human dose. Hence we can conclude that the drug in normal dose it might not produce any pathological changes.[21] Another herbomineral formulation *Panchamuga Chenduram* (PMC) which contains veeram was investigated for acute and repeated 28 days oral toxicity studies. The results showed that it did not produce any toxicity signs in Wistar albino rats. Daily administration of PMC at different doses 10mg/kg, 20mg/kg for 28 days were tolerated by the rats without any mortality and morbidity, indicates the drug tolerance. Toxicity signs such as piloerection, salivation, tremors, signs of convulsion, lacrimation were not observed. Mice treated with PMC at high dose 20mg showed minimal increase in Cholesterol, Triglyceride, Total Bilirubin, SGPT .The histology assessment in the spleen and liver did not reveal any vascular changes. Analysis of kidney tissue revealed normal histopathology in all treatment groups.[22]

Veera mezhugu is a polyherbometallic preparation consisting of 13-drugs also contains veeram is found to. possess both antioxidant and anticancer potentials.[23] Another preclinical research work mechanism of action of the *Divya Amvatari Ras* (DAR) a traditional Indian herbo-mineral medicine was studied, on the modulation of IL-1β, IL-6, and TNF-α cytokines in LPS stimulated human monocytic (THP-1) cells. Treatment of the LPS-stimulated cells with the DAR between the concentration of 0.1 and 10 mg/ml significantly reduced the levels of IL-1β cytokine in a dose-dependent manner. Both the IL-6 and TNF-α cytokines were found to be significantly reduced in the DAR (0.1–10 mg/ml) treated LPS stimulated THP-1 cells. The highest reduction of TNF-α cytokine release in the LPS stimulated THP-1 cells was detected at the DAR dose of 10 mg/ml ($p < 0.01$). The mechanism of modulation is through the inhibition of the production of free radicals, and expression of pro-inflammatory cytokines such as IL-6, TNF-α, LOX-1, COX-2, and NFκB in monocytes (THP-1) and macrophages (RAW 264.7) under *in vitro* conditions, and in CA-stimulated animals.

5. Adjuvant- annabedhi chenduram

*Annabeth*i is a common hydrochemical drug, which is popularly known as green vitriol (chemical name is ferric sulphate). Naturally Annabethi is collected in hills and also synthesized, which is green in colour with crystal form, nauseous astringent taste and has solubility in water. It is commercially prepared by mixing iron wire with sulphuric acid and evaporating the solution to crystallization. *Chenthuram*' is a category of medicine with reddish colour and powder form and it retain potency for 75 y.[24] Formulary of Siddha medicine shows the usage of *Annabethi chenthuram* for treating fever, dysentery, amenorrhea and jaundice. The common procedure of *Annabethi chenthuram* preparation involves detoxification, incineration, trituration and verification. For detoxification, *Annabethi* (1 kg) was dissolved in water and filtered through muslin cloth in order to remove the dust and other impurities. Use of any one of herbal ingredients (lime juice, sour rice water, *Mollugo lotoides* plant juice) is recommended for the preparation of *Annabethi chenthuram* as per Siddha literature.[25] and in this study we have used Mollugo root juice. This mixture was kept under shaded condition for 12 h and kept under sunlight till it fully dried. After drying, *chenthuram* was incinerated with 50 cow dung cakes for one time by traditional method (*Pandri putam*,).

Annabethi chenthuram preparation method prescribed in Siddha system involves scientific and systematic detoxification processes with enhanced therapeutic potential.[26] The conversion of non haem iron is required due to the better absorption nature of haem iron compared to non haem iron. The usage of ferrous salt is attributed to the better absorption nature of ferrous iron in the duodenum and proximal jejunum compared to all other forms of iron. Absorption of non-haem iron is enhanced by factors such as ascorbic acid (vitamin c), citric acid, sugars and hydrochloric acid. The drying and incineration is carried out to modify the oxidation number of iron from +2 to +3 through the formation of mixed oxide of iron (Fe2O3) from the raw material ferrous sulphate. The FTIR spectra clearly confirm the presence of organic moieties along with the formation of iron complexes. BET surface area analysis, SEM and PXRD analysis once again confirms the reduction in particle size of the drug compared to the raw material used for the preparation of iron based traditional drug *Annabethi chendooram*.[27]

In Acute toxicity study, there were no abnormal signs reported at the dose level of 250 mg/kg/b.wt within 24hours in Wistar Albino Rats. No mortality and No gross pathological

changes have been seen in the internal organs of both control and treated groups in the 14 days of study period. Long-term Toxicity Study was conducted for about 90 days as per WHO guideline in 3 doses low dose (25mg/kg b.wt), mid dose (125mg/kg b.wt), high dose (250mg/kg b.wt). The histopathological study on the organs such as brain, heart, lung, kidney, spleen, liver, stomach, uterus, ovary and testes was normal in high dose groups when compared to control. Based on these results it can be concluded that the safer dose of Annabethi chendooram is 65 to 130 mg (BD/day)) for human consumption.[28] Pharmacological analysis shows that the drug has got significant Anti – ulcer activity.[29]

DISCUSSION

Hypothetical target of *Vajra kandi chenduram* against COVID-19

Targeting key molecules within the inflammatory cytokine network such as interleukin-6 (IL-6) is a novel strategy for COVID-19 induced cytokine released syndrome (CRS).

Interleukin-6 (IL-6) inhibitors may ameliorate severe damage to lung tissue caused by cytokine release in patients with serious COVID-19 infections. Several damage to lung tissue caused by cytokine release in patients with serious COVID-19 infections. Several studies have indicated a “cytokine storm” with release of IL-6, IL-1, IL-2 and IL-8 along with tumour necrosis factor alpha (THFalpha) and other inflammatory mediators.[30]

However, the efficacy of corticosteroids, commonly utilized anti-inflammatory agents, to treat COVID-19-induced CRS is controversial. There is an urgent need for novel therapies to treat COVID-19-induced CRS. The British Pharmacological Society has responded to concerns that the use of non-steroidal anti-inflammatory drugs (NSAIDs), could exacerbate symptoms of the novel coronavirus infection, COVID-19.The World Health Organization on March 18, 2020 released a statement, that it "is aware of concerns on the use of ibuprofen for the treatment of fever for people with COVID-19.[31] Hence at this juncture, the use of Siddha anti-inflammatory , antipyretic and immune modulatory agents can provide immense support towards the management of CRS.

Besides this, the host cell proteases also makes a tempting target. An identified protease is found to be essential for coronavirus spike protein’s activation. The spike protein has to be primed by an enzyme called a protease in order for the virus to complete entry into the cell. The study showed that similar to SARS-CoV, SARS-CoV-2 uses a protease called TMPRSS2

to complete this process. An inhibitor of protease has been found to block corona virus infections in cultured cells. Hence this may be another promising avenue of drug targets.[11]

Protease Inhibitors have received great interest for various applications in biomedicine and biotechnology in addition to its application in protein–protein interaction studies, focused mainly in therapeutics. Potentiality and therapeutic efficiency of serine protease inhibitors have been exemplified in treating immune, inflammatory, respiratory diseases, AIDS, cardiovascular, and neurodegenerative disorders (as Alzheimer disease). Therefore, protease inhibitors could be useful in drug design to prevent organisms' propagation that provokes dangerous diseases, such as AIDS, cancer, and malaria.[32] The Siddha formulation *Vajra kandi chenduram* has not been explored to have antiviral activity against SARS -COV-2 and we are not claiming it to have a target action on Corona virus. Instead, the anti inflammatory, antipyretic activity of all the ingredients of the drug in addition to the protease inhibiting action of *Rasa sinduram* and inhibition of the production of free radicals, and expression of pro-inflammatory cytokines such as IL-6, TNF-α, LOX-1, COX-2 of the anti-inflammatory ingredients of the formulation may provide an add on effect in reducing the cytokine inflammatory network causing cytokine storm which is the most important target in reducing mortality. Thereby it can aid in the prevention of stage-I Corona virus into the next stages and can prevent the morbidity and mortality of COVID-19 patients. Hence the drug is safe to be administered at prescribed doses under medical supervision of Siddha physician. Moreover all the ingredients have been tested toxicologically and has been found to be safe in humans. Therefore the above said Siddha formulation may be considered to be of public use during this global pandemic. The claim for the use of *Vajra kandi Chendooram* for COVID-19 is based on the practitioners clinical experiences during viral fevers and other epidemics and also based on the exploration of published research works on its ingredients. Further preclinical studies on its anti-inflammatory, antipyretic, antiviral actions of the Siddha formulation *Vajra kandi Chendooram* may be warranted to confirm our hypothesis scientifically and has been planned to be performed shortly.

CONCLUSION

Through this review work, all the ingredients of *Vajra kandi Chendooram* have been explored scientifically for its pharmacological actions, toxicity evaluation and has been found to be safe in humans. Hence the above said Siddha formulation may be considered to be of public use during this global pandemic. Further preclinical studies on its anti-inflammatory,

antipyretic, antiviral actions of the Siddha formulation *Vajra kandi Chendooram* may be warranted to confirm our hypothesis scientifically and has been planned to be performed shortly.

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