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World Health Organisation's
Randomized Clinical Trial Registry #ISRCTN13311119
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TN G.O.(Ms). No.201
Dated 23 April 2020



EXTRA MURAL RESEARCH Reviewed & Approved by Committee



Official Siddha Drug Partners - Global



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Siddha cure drugs combination for COVID-19 Scientific RCT results and Lab Evidences

START (Siddha Treatment Accelerating Recovery from SARS-CoV-2 Test)

Prospective, Multicenter, Randomized, Open-Label, Proof-of-Concept (PoC) Study to Evaluate the Efficacy and Safety of Siddha Treatment in Patients with Novel Coronavirus Infectious Disease

Principal Investigator	Dr. A. Vinoth Kumar, M.D
Co – Investigator	Dr. P. Selva Shunmugam, M.D(Siddha)., Ph.D., Dr. J Jeya Venkatesh M.D(Siddha)
Our Siddha team along with CMC Hospital Staff	Dr. P Senthil Kumar, Dr. B Manikandan, Dr. M Vasanth Kumar, Dr. K Thiru Gnanam, Dr. K Karpagavalli, Dr. M Tamizhinian, Dr. S Guptaj, Dr. M Naveen Kumar, Dr. S Abdul Sadiq, Dr. G Narmada Devi, Dr. V G Divya Deepa, Dr. N Siva Manikandan, Dr. Jeeva Gladys, Dr. Aarthi (CCRS), Mr Lokesh JR, Mr Partheeban
Bio Chemist and Clinical Lab	Dr. Ezhilarasan Kailasam, Ph.D, Dr. M Naga Jothi, Dr. Tamilarasan
Clinical Data Analysis & Bio-stats	Mr. M.Subramaniyan, Mr. Rajesh
Advisory, Support & Guidance	M. Vijaya Kumar, IAS, ELCOT, Govt. of Tamil Nadu Prof. Dr. Jeyaprakash Narayanan, Ex-Chairman CCRS Prof. Dr. Banumathi, Ex-Director NIS Dr. Kannan, IMPCOPS Dr. Pitchiah Kumar, Siddha Drug Control Authority
Sponsor for India	Eminentlabs Business Solutions Pvt Ltd, Chennai, India
Sponsor for all countries out of India	Eminentlabs GmbH, Dusseldorf, Germany

Program Overview – Key Dates

6 March 2020	AYUSH Ministry, Government of India released an Advisory for Siddha Medication . Our core team was formed with ONE motto "Save as many lives as possible, faster and at lowest cost".
19 March 2020	Government of India opened up DBT-BIRAC funds for research . We submitted proposal to AYUSH Ministry with all scientific evidences for efficacy of Siddha drugs.
20 March 2020	Our team designed the Siddha Drug Regimen for COVID-19: Stage 1 – Fever, Stage 2 - Respiratory Illness and Stage 3 - Viral Pneumonia, with all the supporting references & scientific documents
27 March 2020	Our team presented the proposal to CM Office, Tamil Nadu - a state with 82 Million population, capacities to manufacture 7500 Tonnes of Siddha drugs and a task force to implement it at the lowest budget. Our proposal also includes, a tracker mobile app for Govt. officials to track the effectiveness of the program, a Doctors App for Siddha doctors and a Public App for family health care, along with Toll-Free phone numbers.
1 April 2020	CM Office, Tamil Nadu CMO asked us for the scientific evidences through clinical trail results for our proposal, designed to be conducted at multiple sites.
6 April 2020	Navitas Life Sciences, Germany has been selected as our partner. We have designed the global trial with multi-site RCT for our drugs. This trial is being conducted in accordance with the Declaration of Helsinki and Good Clinical Practice. Due to lockdown situation and shipment issues of drugs to Germany, the first site was decided as India - Tamil Nadu in the program design
15 April 2020	Extra Mural Research (EMR) application was prepared and submitted on 20 April to AYUSH
21 April 2020	Government of India published a Gazette Notification on approvals of all RCT for Siddha medicines at fast track
23 April 2020	Based on the above Gazette notification, Tamilnadu Govt released a Government Order (dated 23 April 2020) supporting the fast track of all the RCTs for Siddha. Kabasura Kudineer(An immunity booster Siddha medicine) has been distributed to more than 30 Million out of the 82 Million public. The public who have taken this medication, even after being infected with COVID-19, get cured within short duration, is a derived proof from the field.
14 May 2020	Principal Investigator Dr. Vinod Kumar submitted to CMC, Chengalpattu, the protocol for Approval at institutional Ethics Committee and same was approved, afterdue diligence.
30 May 2020	EMR was approved by AYUSH for Eminentlabs GmbH . Director General Dr. Anil Khurana is our guide and support to carry out the trial in Germany and other countries. AYUSH has updated the official website with Bramanandha Bairavam(One of the key Drugs for curing COVID-19) . Director of Indian Medicine has placed a huge order with our Drug partner IMPCOPS, to support the public through Primary Health Centres.

Program Overview – Approvals and Participants

Tamil Nadu Government	Ethics Committee Approval	Clinical Trial Registry @ W.H.O
Health Ministry ✓	Indian Government Virology Labs ✓	http://www.isrctn.com/ISRCTN13311119 ✓
Pharmacopia ✓	CTRI ✓	CTRI/2020/06/025625 ✓
Tampcol ✓	CDSCO ✓	
PHCs ✓	DCGI ✓	
Universities ✓	AYUSH ✓	
Tanjore Library ✓	CCRS ✓	
	NIS ✓	
	IMPCOPS ✓	
	NRPHC ✓	

Eminentlabs Clinical Trial Site Overview @ CMC , Chengalpattu

- Counselling of Subjects with check on Inclusion and Exclusion Criteria
- Screening for eligibility to the Randomized Clinical Trial
- Randomization
- Assigning Subjects to Clinical Trial – Trial Medicines admitted as per IEC Approved protocol
- Siddha therapies provided to patients daily for first 3 days as per protocol designed at CMC, Chengalpattu:

Morning	Afternoon	Evening
<ul style="list-style-type: none">▪ 6:00 AM: Vazhalai Vaanguthal with Karisalai Nei▪ 6:15 AM: Naadi examination and record the result▪ 6:30 AM: Vedhu Pidithal (Herbal Steam Inhalation) with Fresh Nochi leaves in hot water▪ 7:00 AM: Ottaradam (Herbal Fermentation) with the same hot Nochi leaves▪ 7:15 AM: Neer kuri and Nei kuri Urine tests and record the result▪ 7:30 AM: Kabasura Kudineer given for Siddha trial subjects▪ 7:45 AM: Manikadai Nool test and record the result▪ 8:00 AM: BreakFast▪ 8:30 AM: Adathodai Manapagu + Hot Water & Brammanda Bairavam + Honey	<ul style="list-style-type: none">▪ 1:30 PM: Lunch as per Siddha diet regime <p>Note: Breakfast, Soup, Lunch, Soup and Dinner is siddha food without chemical preservatives. Strictly No smoking, No Alcohol, No Tea, No Coffee, No Cooldrinks, No ICE Creams</p>	<ul style="list-style-type: none">▪ 5:00 PM: Prepare Kabasura Kudineer▪ 6:00 PM: Kabasura Kudineer given for Siddha trial subjects▪ 7:00 PM: Naadi examination and record the result▪ 7:15 PM: Manikadai Nool test and record the result▪ 7:30 PM: Dinner▪ 8:00 PM: Night Dose of Adathodai Manapagu + Hot Water & Brammanda Bairavam + Honey

- PCR test for COVID-19 on 3rd Day of drug Regime
- COVID-19 Negative patients are discharged and others are continued with the treatment until PCR test for COVID-19 becomes negative

Eminentlabs COVID-19 Solution: Siddha Drug Design, RCT results with Lab Evidences

#	Siddha Drug	Randomized Clinical Trial Results - Mode of Action	Lab Evidences
1	Karisalai Nei (Eclipta prostata and Eclipta alba)	<ul style="list-style-type: none"> Extracts of Eclipta alba are proven to have strong Mucolytic activity, Improves mucociliary clearance, Antiviral, Anti-inflammatory, Strengthens nasal associated lymphoid tissues that fight against any foreign invaders Methods include using suction to remove fluids and placing the patient in a position that allows secretions to drain by gravity Vazhalai vaanguthal is a set of methods used to clear mucus and secretions from the airways. the mucociliary clearance system and the ability to cough. Impaired mucociliary clearance is linked to poor lung function in a broad range of diseases and disabilities Pulmonary hygiene prevents atelectasis (the collapse of the alveoli of the lungs) and rids the respiratory system of secretions, which could cause respiratory infections. It can also decrease pulmonary shunting, increase the functional reserve capacity of the lungs, and prevent respiratory infection after chest trauma 	<ul style="list-style-type: none"> The reduction in inflammatory markers Ferritin, LDH, CRP and ESR shows the Anti-inflammatory of Karisalai nei
2	Kabasura Kudineer	<ul style="list-style-type: none"> Has the lead molecule that inhibits COVID-19's target of main protease of COVID 19 and SARSCoV-2 dependent RNA polymerase6. These lead molecules target ACE2 receptor and their potential of impeding host-viral interface. The phytochemicals Zingiberene, Vasicine, Andrographolide, Apigenin, Carvacol, Costunolide, Eugenol, Pyrethrin, Cucurbitacin B, Cardiofolioside A & B, Cardiofoliate B showed promising activity against the viral spike glycoprotein. More effective phyto compounds in Kabasura Kudineer prevents the spike proteins to bind with host cell receptor. The spikes of RdRp protein of the Virus is locked and movement is restricted. 	<ul style="list-style-type: none"> Based on the microbiologist report found that 3.21×10^4 RNA copies/ml (Range is 2.21×10^2 to 4.71×10^5 RNA copies/ml) there is a significant reduction in viral load – based on CT value
3	Brammananda Bhairavam	<ul style="list-style-type: none"> It has been used for the treatment of pyretic phase of many pandemic diseases 	<ul style="list-style-type: none"> Covid Positive become negative after 3 days. Inflammatory markers like IL-6 and ESR is significantly decreased
4	Adathodai Manapagu	<ul style="list-style-type: none"> Prevents chemotaxis and release of cytokines and chemokines. Alkaloids vasicine and vasicinone in combination shows bronchodilator activity. Leaf has anti-inflammatory action. It also triggers new platelet formation, thus prevents blood clotting related complications. The soothing action helps irritation in the throat and the expectorant helps loosen phlegm deposits in the airway which makes adathodai a good remedy for sore throat. This herb exhibits antispasmodic, expectorant and blood purifying qualities. 	<ul style="list-style-type: none"> The reduction of Interleukin-6(IL-6) in blood shows adathodai manapagu prevents the release of cytokines and its anti-inflammatory effect. The increase of Platelets in blood is a proof for the triggering effect of adathodai manapagu in new platelet formation.
5	Nochi Leaves Steam Inhalation (Leaves of Vitex negundo)	<ul style="list-style-type: none"> The leaves of Vitex negundo contains alkaloids such as nishindine, hydrocotylene, glyofavinoids, orientin, isoorientin. These are potent in the treatment of fever, cough, headache. The vapour inhalation of leaves of Vitex negundo relieves nausea, cold, cough, fever, headache. Steam inhalation definitely improves nasal mucocilliary clearance. Has Mucolytic activity, Improves mucociliary clearance, Removes mucus secretions, Maintains respiratory tract sterilization. Helps to de-congest nose to become normal and hence in Siddha we check the olfaction (the sense of smell) as a parameter. Nasal vowels and nasal consonants are produced in the process of nasalisation (function of speech) hence this is also a siddha parameter to examine. 	<p>Creatine Kinase is an iso-enzyme found in body (Cardiac, Brain & Muscle). CK level increase during cough & chest congestion.</p> <ul style="list-style-type: none"> Lab results show reduction of CK level in blood. The reduction of CK level after treatment indicates that the response is due to physiological effect of Nochi Leaves fomentation.
6	Nochi Leaves fomentation	<ul style="list-style-type: none"> The alcoholic extract of this leaf is having bronchodilating activity and decreases bronchial hyperactivity. This activity is due to the presence of flavinoids, phenolic compounds and terpens. A fomentation consists of a local application of moist heat to the body surface. A fomentation is usually made of blanket material: 50% wool to retain heat and 50% cotton to retain moisture and be more durable. 	

Note: Arthritis drug Tocilizumab seeing increased use, but cost, limited stock, deterrents. One vial of 400 mg costs Rs 40,000

Tocilizumab is an immunosuppressive drug, mainly for the treatment of rheumatoid arthritis (RA) and systemic juvenile idiopathic arthritis, a severe form of arthritis in children. It is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R). Interleukin 6 (IL-6) is a cytokine that plays an important role in immune response and is implicated in the pathogenesis of many diseases, such as autoimmune diseases, multiple myeloma and prostate cancer.

Eminentlabs COVID-19 Solution: Effects of Siddha Treatment

Day	COVID PCR Test	Platelet Cells/ mm ³	IL-6 ng/ml	CRP mg/L	Ferritin ng/ml	CK U/L	LDH U/L	ESR mm	D-Dimer mg/L
Day 1	Positive (Ct 29.63)	209000	9.5	2.7	38.6	53.5	353	30	0.2
Day 2	Siddha treatment								
Day 3	Siddha treatment	249000	3.84	3.5	31.2	43.3	269	7	0.2
Day 5	Negative								

- ✓ COVID-19 Positive becomes negative after 3 days of siddha treatment in moderate cases
- ✓ Platelet is significantly increased within two days of treatment
- ✓ Inflammatory markers like IL-6 and ESR is significantly decreased within two days of treatment.
- ✓ Acute phase reactant like ferritin also significantly decreased within two days of treatment
- ✓ LDH an iso-enzyme which usually elevated during pulmonary endothelial cell damage is decreased here in siddha treatment which shows the effect of adathoda manapagu
- ✓ Overall the decrease in inflammatory markers is due to anti-inflammatory of Karisalai Nei, reduction in the viral load, decrease in IL-6, inflammatory markers and increase in platelet is due to Siddha treatment.

Eminentlabs COVID-19 Solution: Psychological Observation

Day	Psychological Condition of Randomized Clinical Trial Subjects
Day -1	<p>(Screening Day) Subjects were bit anxious about the whole treatment procedure which includes siddha treatment also because the subjects never experienced any siddha treatment before</p> <p>Note: screening process which includes laboratory testing like (RT-PCR, Blood sample, ECG etc) has been explained to remove fear of the procedures.</p>
Day 0	<p>(Randomization Day) Subjects were cognitively affected & depressed about her health conditions and also, about staying away from family.</p>
Day 1	<p>(Siddha Dosing Starts) Subjects were selected under siddha arm treatment and procedures were done. After treatment procedure subject's feedback were documented in their individual case summary. All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>
Day 2	<p>Subjects were persuaded and really happy about drastic changes happened in body condition. All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>
Day 3	<p>Subjects were physically and also mentally became active. All were really happy about how they became better day by day. All started talking about their positive effects of siddha with her known circles. All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>
Day 4	<p>Subject's self-esteem were so high and confident and everyone felt so relieved. All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>
Day 14	<p>All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>
Day 28	<p>All the detailed feedback of Anandamaykosam, Vignanamayakosam, Manomayakosam, Pranamayakosam and Annamayakosam were collected and documented for the day.</p>

Eminentlabs COVID-19 Solution: Siddha Drug Designed in this Randomised Clinical Trial

#	MEDICINES	DOSAGE	ADJUVANT	#DAYS / TIME	INDICATIONS
2	Bramanandha Bairavam ✓	100mg	Honey or Ginger Juice	2 times per day (30 minutes after food)	Kaba suram (Fever with cough dyspnea)
3	Kabasura Kudineer ✓	30 - 60 ml	Hot water	3 days / 6 times (2 bd)	Kaba suram (fever with cough, dyspnea)
4	Karisolai nei ✓	5 mg	Cow's Ghee	1 time per day	*Vazhalai vaanguthal to eliminate viral growth in throat
5	Adathoodai Manapagu ✓	5-10 ml	Hot water	3 times per day	All 64 types of fever, cough, dyspnea
9	Notchi (Vitex negundo) ✓ (for external use - steam)	Fresh leaves	500 ml water	2 times per day	Steam will immediately release the nasal block, sinusitis, dyspnoea.

+ Siddha diet regimen for all the patients

#	MEDICINES	DOSAGE	ADJUVANT	#DAYS / TIME	INDICATIONS
1	Nellikaai Legium ✓✓	5-10 gm	Milk	2 times per day	Immuno booster For bronchitis, fever in the bones
2	Kabasura Kudineer ✓✓	30 - 60 ml	Hot water	3 days / 6 times (2 bd)	Kaba suram (fever with cough, dyspnea)

✓ Siddha Drug Regimen used in the Clinical Trial

✓✓ Siddha Drug Regimen for Doctors and paramedical staffs protection in the Clinical Trial

Eminentlabs COVID-19 Solution: Siddha Drugs Details

#	MEDICINES	PREPARATION AND DIRECTION OF USE		
1	Bramanandha Bairavam	<ul style="list-style-type: none"> Supplied as a tablet The tablet is crushed with motor and pestle The crushed contents are mixed with honey or ginger juice and provided to the patients twice daily 30 minutes after food 		
2	Kabasura Kudineer	<ul style="list-style-type: none"> Supplied as a powder Five grams of powder is required to be mixed with 240 ml of water and boil until it reduces to 60 ml The decoction to be consumed within 3 hours of preparation. If not consumed immediately the decoction needs to be stored in a thermal flask A test dose of 5 mL may be given prior to use to check if the patient has any allergic reactions to the study medication Patients will be asked to drink 60 mL of the decoction at lukewarm temperature twice a day 30 to 90 minutes before food 		
3	Karisalai nei	Procedure for Vazhalai vaanguthal: 1 to 2 gms to be applied on the thumb or index finger, to be inserted, smeared and rotated on upper soft palate gently touching the uvula until the phlegm expels out		
4	Adathoodai Manapagu	<ul style="list-style-type: none"> Supplied as a syrup 15 mL to be mixed with 60 mL of lukewarm water 		
5	Notchi (Vitex negundo) – for external use only	<table border="1"> <tr> <td> <p>Procedure for Inhalation:</p> <ul style="list-style-type: none"> Boil 2 litre of water with 100 grams of leaves Transfer the contents into another bowl Patient to close their eyes and slowly lower the head toward the hot water in the bowl. The patient's head should be kept 12 inches away from the upper level of liquid Drape the clean towel over the back of the head and neck Inhale slowly and deeply through the nose for at least two to five minutes for a cycle. Repeat the inhalation cycles 2 to 3 times with an interval of 1 to 2 minutes The total duration of the inhalation will be no longer than 12 to 15 minutes </td> <td> <p>Procedure for fomentation:</p> <p>Fried & hot Notchi leaves are packed in a cloth bundle</p> <p>Patient is positioned in supine position and sliding using back rest in a cot so that the head and chest are elevated</p> <p>The bundle is applied repeatedly on the chest with a short interval</p> <p>The application should be upwards (from diaphragm to clavicle)</p> <p>Turn on a timer not longer than 10 minutes</p> </td> </tr> </table>	<p>Procedure for Inhalation:</p> <ul style="list-style-type: none"> Boil 2 litre of water with 100 grams of leaves Transfer the contents into another bowl Patient to close their eyes and slowly lower the head toward the hot water in the bowl. The patient's head should be kept 12 inches away from the upper level of liquid Drape the clean towel over the back of the head and neck Inhale slowly and deeply through the nose for at least two to five minutes for a cycle. Repeat the inhalation cycles 2 to 3 times with an interval of 1 to 2 minutes The total duration of the inhalation will be no longer than 12 to 15 minutes 	<p>Procedure for fomentation:</p> <p>Fried & hot Notchi leaves are packed in a cloth bundle</p> <p>Patient is positioned in supine position and sliding using back rest in a cot so that the head and chest are elevated</p> <p>The bundle is applied repeatedly on the chest with a short interval</p> <p>The application should be upwards (from diaphragm to clavicle)</p> <p>Turn on a timer not longer than 10 minutes</p>
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Thank you

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