

CRITICAL EVALUATION OF *HEMAGARBHA POTTALI* IN COVID 19 PATIENTS WITH SPECIAL REFERENCE TO ITS IMMUNOMODULATORY ACTION

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ABSTRACT

The *Pottali rasayana* is a unique preparation in Ayurveda as it is very compact in structure and quick acting due to its high potency. *Hemgarbha pottali* rasa is a medicine which is known as emergency medicine of *Ras shastra*. COVID-19 (initially named 2019 novel coronavirus, or 2019-nCoV disease, after the first reported outbreak in 2019) has become the most widely spread global pandemic in the past century. It has affected 189 countries and regions with nearly 185 million confirmed cases and about four million reported deaths worldwide as of current statistics. The novel coronavirus responsible for this disease was named by the World Health Organization the Severe Acute Respiratory Syndrome Coronavirus-2(SARS-CoV-2) for

its genetic similarity to the coronavirus that caused the SARS outbreak in 2003 (SARS-CoV). In the current pandemic infection (COVID-19) it is clear that those with weak immune system are highly susceptible to this infection and its worst outcomes. In this regard, immunity enhancing *Ayurvedic* drugs may definitely be helpful for the body to fight COVID-19 infection. *Hemagarbha Pottali (Bhaishajya Ratnavali)* is one of the *Ayurvedic* preparations which is useful in the current pandemic situation for Acute Covid 19 Symptoms. **Aim & Objectives:** To critically evaluate the role of *Hemagarbha Pottali* in Covid 19 Patients w.s.r to Immunomodulatory Action. To & to study action of *Hemagarbha Pottali Kalpa* as an immunity modulator according to Ayurveda point of view. **Material and Methods:** An extensive literary search of different classical texts has been conducted to

collect classical references along with multiple databases (PubMed and Google Scholar) available online for the related published works. **Result and Conclusion:** The holistic approach of *Ayurveda* in the form of curative and preventive medication, *Rasayana Chikitsa* etc., will be helpful to manage immunity to avoid post covid symptoms. This article is going to dig out the treasure of *Ayurveda* in the form of holistic approach.

KEYWORDS: Covid 19, Immunity, Immunomodulatory Action, *Rasayan Chikitsa*, *Hemgarbha Pottali Rasa*.

INTRODUCTION

Covid19 is an infectious pandemic disease caused by the virus called as SARS-CoV-2. These pathogens primarily target the respiratory system of human beings. In January 2020, coronavirus SARS-CoV-2 was identified as the cause of an outbreak of severe pneumonia, now known to be a complication of the coronavirus disease 2019 (covid-19).^[1] Since then, the spread of covid-19 has increased exponentially, with the World Health Organization declaring a pandemic on 11 March.^[2] By 15 April, more than 1,900,000 cases and 1,23,000 deaths had been reported worldwide.^[3] Disease shows Acute symptoms like Fever, Cough, Tiredness, loss of taste or smell, Shortness of breath or difficulty in breathing, Muscle aches, Chills, Sore throat, Runny nose, Headache, Chest pain, Pink eye (conjunctivitis), Nausea, Vomiting, Diarrhoea and Rash. Also Systemic symptoms involve Gastrointestinal track in 2-40% of patients,^[5,6] and diarrhoea can be the initial manifestation of infection.^[7] Whether SARS-CoV-2 leads to such symptoms directly by infecting the gastrointestinal tract, indirectly by neurological involvement,^[8] or through production of cytokines remains unknown. Viral RNA has been detected in stool samples, sometimes at high levels.^[9] This raises the possibility of faecal-oral transmission,^[10] Taste or Olfactory disorders were noted in up to 53% of the cases in a small study from Italy,^[11] and now anosmia is being proposed as a criterion for testing, especially in young people with few other symptoms.¹² Ischaemic or Haemorrhagic stroke, Dizziness, Headache, Musculoskeletal disturbance, Altered mental state, Guillain-Barré syndrome, or Acute Necrotising Encephalopathy, without proof of direct viral invasion into the brain.^[13-14] patients with severe infections,^[15] Myocarditis^[16] and Myopericarditis with reduced systolic function,^[17-18] Cardiac Arrhythmias,^[19] Heart Failure, and Misdiagnosis as Acute Coronary Syndrome.

The concept of Immunity involves both specific and non-specific components. The non-specific components act either as barriers or as eliminators of wide range of pathogens

irrespective of antigenic specificity. Other components of the immune system adapt themselves to each new disease encountered and are able to generate pathogen-specific immunity. Innate immunity or nonspecific immunity is the natural resistances with which a person is born. It provides resistances through several physical, chemical and cellular approaches.^[20] An immune modulatory Action can be defined as a substance, which can influence any constituent or function of the immune system in a specific or nonspecific manner including either innate or adaptive arms of the immune response.^[21] They are a diverse array of recombinant, synthetic and natural preparations, often cytokines. Concept of immunomodulation in Ayurveda is mentioned as - *Vyadhikshamatwa*.^[22] Acharya Chakrapanidatta has interpreted the term *Vyadhi-ksamatwa* as *Vyadhi bala Virodhitwa* i.e., antagonistic to the strength and virulence of the disease and *Vyadhyutpada Pratibandhakatwa* i.e., the capacity to inhibit and bind the causes and factors of the disease.^[23] In fact, one of the therapeutic strategies in *Ayurvedic* medicines is to enhance the body's overall natural resistance to the disease causing agent rather than directly neutralizing the agent itself. The use of herbs for improving the overall resistance of body against common infections and pathogens has been a guiding principle of *Ayurveda*.^[24] Such herbomineral preparation possessing immunomodulatory effects are referred to as *Rasayana* in *Ayurvedic* classics. They are supposed to have the ability of protecting the body against external factors that induce disease. This implied resistance against disease may represent the modern concept of immunity.^[25] The *Pottali rasayana* is a unique preparation in Ayurveda as it is very compact in structure and quick acting due to its high potency. Hemgarbha pottali rasa is a medicine which is known as emergency medicine of Ras shastra.^[26] So the disease needs the special attention according to *ayurveda*.

COVID-19 Samprapti (Pathology) as per Ayurveda-

If we look into the correlation between the concept of COVID-19 and *Ayurveda*, it shows similarity with *Sannipataja jwara*.^[27] The *samprapti* can be summarized as follows: the inhaled virus SARS-CoV-2 (agantuja nidana) likely binds to epithelial cells in the nasal cavity and starts replicating. Doshas aggravated by their causative factors reach *amashaya* and derange the function of Agni. Then, vitiated dosha mixes with rasa carrying ama and moves in upward direction obstructing the respiratory channels, *urdhwajatrugata pradesha* and then settles down at a *khavaigunya* region of *pranavaha Strotasa*.^[28] The seat of affliction of this disease is primarily Urah (chest region) with symptoms such as anosmia, anorexia, high-grade fever, body ache, headache, and dry cough. If oja is displaced due

to dhatupakavastha, the patient may suffer from severe respiratory distress with other symptoms and sometimes leading to death. COVID19 comes under the disease of *Abhyantara roga marga* as *jwara* (fever), *shwasa* (respiratory distress) and *kasa* (cough), the three major symptoms belong to this *roga marga*. *Abhyantara roga marga* is one among three *roga margas* (pathways of disease), as described by Acharya Vagbhata.^[29-30] The *rasayana chikitsa* is required for patients to maintain *bala* i.e Immunity. So all the ingredients of *Hemagarbha Pottali* were important to maintain the immunity.

AIM

To critically evaluate the role of *Hemagarbha Pottali* in Covid 19 Patients with special reference to Immunomodulatory Action.

OBJECTIVES

1. To study action of *Hemagarbha Pottali* as an immunity modulator according to *Ayurvedic* point of view.

MATERIALS AND METHODS

COVID-19, is an extremely infectious virus. It triggers immune responses, which makes the sickness period of this disease a prolonged illness. This in turn helps the virus to spread widely, thus leading to a global pandemic. A study published in the National Academy of Sciences” the team of scientists investigated how the virus unlocks the Semipermeable Tissues & cells of Human body using a surface spike protein as the "key." They made three important findings: the tip of the viral key binds strongly to human cells; the tip of the viral key is often hidden; and when new virus particles are made, the viral key is already pre-activated by a human enzyme. It targets surface cells all through the respiratory framework majorly affecting the lungs, heart and the other organs. The problem is, as the infective pathology props up, it will halt the entire immune system response & reaction with its multiple layers. This more viral action time may prompt an overreaction of the Immunity in our body, called a cytokine storm, which executes healthy cells, causing tissue harm and creates the weaker immunity.^[31]

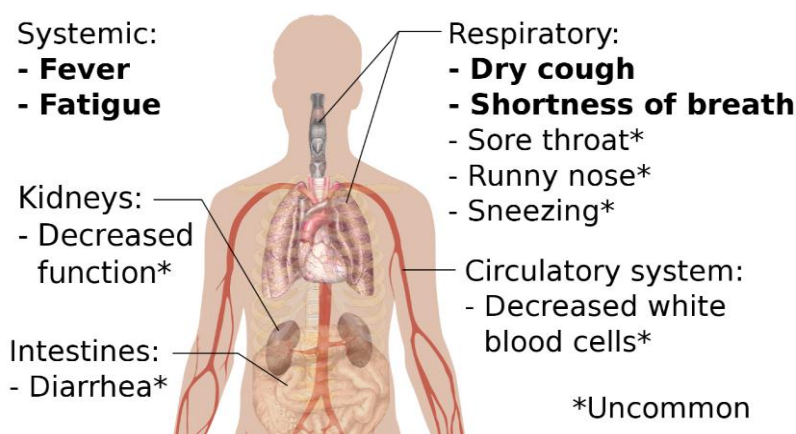
SIGNS AND SYMPTOMS

ACUTE SYMPTOMS

Fever, Cough, Tiredness, loss of taste or smell, Shortness of breath or difficulty in breathing, Muscle aches, Chills, Sore throat, Runny nose, Headache, Chest pain, Pink eye (conjunctivitis), Nausea, Vomiting, Diarrhoea, Rash.

Systemic symptoms

The Respiratory (*Phupphus*), Cardiovascular (*Hrudaya*, *blood vessels*), Haematological (*Yakrut*, *Pliha*), Central Nervous (*Mastishka*), Gastrointestinal (*Amashaya Pakwashaya-Antra*), Renal (*Vrikka*)- all these systems and organs were involved in Covid 19 Infection.



COVID-19 is caused by a zoonotic type of RNA virus with crown-like spikes appearance under the microscope affecting primarily the smell and taste receptors and causing symptoms like fever, dry cough, shortness of breath and upper respiratory infections severe congestion, breathlessness and finally death. COVID-19 when compared with the symptoms and mode of spread, it can also be correlated with *Kapha-Vata jwaram* i.e. fever caused by unbalance in *Kapha* and *Vata doshas*, with *pitta* association, in the beginning and some clinical features are also similar to sannipata jwaram viz the vitiation in all three *doshas Vata, pitta*, and *Kapha*, as the condition progresses. Symptoms exhibited by *kapha-vataja jwara* are; *Sheeta*: Feeling of cold, *Gauravam*: Heaviness, *Tandra*: Drowsiness, *Kasa*: Cough, *Asweda*: Absence of sweating *Madhya-vega santapa*: Moderate rise in temperature, *Pratishyaya*: Running nose, *Shirograha*: rigidity of head and stiffness. Due to this the *Samprapti* shows the effect on weaker immune response to medicine that's why the patient needs emergency treatment which includes the Ayurvedic medicine like *Hemagarbha Pottali Rasa*. *Pottali* generally has *Parada*, *Gandhaka*, *Kajjali* (black sulfide of mercury) and the metals like *Swarna* (gold), etc.,

as ingredients. General preparation methods include mixing primary ingredients (mostly *Kajjali* mixed with other elements with small amounts of *Shudha Gandhaka*. The entire mixture is bandaged with a silk cloth in shape of a poultice. This poultice in Ayurveda terminology is known as *Pottali*. This *Pottali* is then transferred into an earthen vessel filled with melted *Gandhaka* and the entire setup is placed in a *Valuka Yantra* which is exposed to constant temperature for specific time and after cooling *Pottali* will be prepared.^[32]

Hemagarbhapottali rasa

रसभस्म त्रयो भागा भागैकं हेमभस्मकम् । मृत्तामस्य भागैकं भागैकं गन्धकस्य च ॥ मर्दयेच्चित्रक
द्रावैर्वियामान्ते समुद्धरेत् ।... (B. R. Rājyākṣmādhikāra 14 / 186-188)

Ingredients: *Rassindoora*, *Shuddha Swarna Bhasma*, *Shuddha Tamra Bhasma*, *Shuddha Gandhaka*^[33]

Bhavana Drava: *Chitraka moola kwatha*

Procedure

Rasasindoora + *Shuddha Gandhaka Mardan* + *Remaining Bhasma* -----> *Bhavana of Chitrak Moola Kwatha* -----> filled in *Varatika* after that *Varatika Samputa* with *Tankana* ---> *Gajaputa* -----> *Hemagarbha Pottali* Obtained.



OBSERVATIONS

Colour – Ash

Odour - Odourless

Taste- Kshariya

Dose –*Sharangadhara* has mentioned the dose as 1 Ratti for *Hemagarbha Pottali Rasa*. The normal dose is 30mg -125 mg. *Pottali* should be rubbed over a stone by applying ghee (*Ghrita*) or honey (*Madhu*) and the whole paste is administered orally.

Anupana – *Pippali churna*, *Madhu*, *Ardraka Swarasa* or According to *Vyadhi lakshana*

Indications

Rajyakshma, *VataKapha vikar*, *Sannipatak Jwara*, *Shwasa*, *Kasa*.

DISCUSSION

Ayurveda is a complete science of health supported by the empirical knowledge domain that covers all the aspects of life. Since the commencement of life, materials found on the world have been the foremost source of medication. These materials are one among the essential components that constitute the framework of Ayurvedic drugs. Covid 19 disease is a group of symptoms which can be co-related with involvement of all the *Strotas* (Systemic Involvement). The symptoms of Covid 19 like Fever (*Jwara*), Cough (*Kasa*), Shortness of Breath (*Shwasa*) and other symptoms associated with Acute Stage of disease. At this point the Acute Stage of disease needs the immediate relieve by treatment like *Atyayika Chikitsa* (Acute Management) for *Pranavaha Strotas Vyadhi* which is given by emergency drug like *Hemagarbha Pottali* which

1. Acts as Immunomodulator (*Rasayana Karma*),
2. Acts as Anti-inflammatory (*Shothahara*),
3. Acts as *Kaphaghna*, *Balya*, *Yogavahi*,
4. Acts as anti Bacterial – Antifungal and wound Healing.
5. Has *ushna-tikshna* properties which is helpful as *kaphahara*.

The *Anupana Dravya* has *Vata-kapha* hara effect on *pranavaha stotas*, so used as an Adjuvent. The fast absorption rate of drug depends on the Nanoparticle size of the *bhasma*. So the effect of drug distribution lasts up to the blood Stream and crosses the Blood Brain Barrier. So the *Hemagarbha Pottali* is important due to its ingredients which show quick relief and *Rasayan* effects on patient.

Rasoushadhies (*herbometallic* drugs) - These are mainly prepared from metals, *herbometallic* drugs, which play a vital role in asymptomatic as well as symptomatic conditions of COVID-19 and require a minimal dosage, easy for administration, act as a *Rasayana* with

high potency, and their properties make them more popular, superior over the other medicines.^[33] The *herbometallic* formulations like *Hemagarbha Pottali* containing gold *Bhasma* plays a key role in overall efficacy, Research works had been proved that the *herbometallic* formulations containing gold *bhasma* help to regulate antigen-specific immune response as nanoparticles of gold possess immunomodulatory, free radical scavenging, antistress, analgesic and antioxidant properties.^[34] Mercurial preparation with arsenic along with medicinal herbs makes it less toxic and converts its inorganic nature to organic nature, so it acts as a carrier of herbs in very less dosage.^[35] One of the widely used metal oxide based is *Tamra Bhasma*. *Tamra Bhasma* is derived from metallic copper and is recommended for different ailments of liver and spleen, abdominal pain, heart disease, tumors, anemia, loss of appetite, tuberculosis, as well as eye problems.^[36] *Tamra Bhasma* is quoted for its following actions—*Kasa Shwas viyadhi shamaka* (decreases the intensity of cough and respiratory distress), *Jwarharam* (provides relief from fever), *Gadaharam* (pacifies the effect of accumulated poisons), *Aayushyam* (increases lifespan), effective in *Peenasa* (chronic rhinitis/sinusitis). *Tamra Bhasma* is also quoted in diseases related to gastrointestinal tract. *Tamra bhasma* increases the defensive mucopolysaccharides including sialomucin and fucose (glycoprotein) and decreases DNA in gastric juice suggesting decrease in cell shedding and increase in life span of mucosal cells, with no change in mucosal DNA and incorporation of [3H]-thymidine uptake in mucosal tissues, indicating an absence of activity on cell proliferation. This can be helpful to break *sampapti* of COVID-19.^[37] Immunity is influenced by race/ geography/ age/ season and other individual factors.^[38] According to *Acharya Charaka*, people are not equally capable of resisting disease and also have no equal ability to resist the onset of the disease.^[39] *Rasayan dravyas* work as Immunomodulators and have antioxidant activity as well. In relation to nonspecific immunity these drugs increase activation of poly morpho neutrophils (PMN) for phagocytosis and enhance their chemo-attractant capacity. In relation to specific immunity, they lead to proliferation of lymphocytes leading to production and also cytotoxic induction of T-helper and Natural Killer (NK) cells and activation of complement pathways. Also they significantly increase immunoglobulin levels. Immunostimulants offer promise in enhancing antigen specific i.e (vaccine) and (*Rasayan Chikitsa*) immune response against infections.^[40] *Rasayana* mentioned as a class of important drugs in the *Ayurvedic* system of medicine is reputed to promote physical as well as mental health, improve defense mechanism and enhance longevity by maintaining the good immune response. Each ingredient in *Hemagarbha Pottali* shows the immunomodulatory action as follows- *Swarna bhasma* plays an important role as an

immunity modulator or enhancer and oxygen scavenging activity. The stress, unhealthy nutrition and continuous exposure to several toxins in the present era lead to compromised immune system. Therefore, immunomodulation should be of central importance in medical field to combat several infective, chronic, autoimmune & inflammatory diseases. The crossing of the Blood Brain Barrier can be seen due to its nano sizing which is helpful for acute management of Covid 19. Recent research has revealed that gold nanoparticles exhibit size-dependent absorption through rat skin and intestine, with smaller particles (~15 nm) absorbed more than larger particles (>100 nm).^[41] Nanoparticles can also be absorbed through sublingual route directly into the blood stream.^[42] Therefore, it can be presumed that some *Swarna bhasma* particles may get absorbed through the sublingual route directly into the blood stream. Acute oral administration (continuous for 8 weeks on albino mice; 10 mg/20g b.w./day) of *Swarna bhasma* had not reported any toxic effects as assessed by liver function tests and histological investigations.^[43] In modern aspect, gold nanoparticles find significant applications in drug delivery as they are capable of encapsulating active drugs and targeting. Colloidal gold nanoparticles represent a completely novel technology in the field of particle-based targeted drug delivery.^[44] *Tamra Bhasma* is used for the management of liver disorder, arthritis, old age disorders, leukoderma, etc. It shows the pharmacological activity like hepatoprotective effect on cumene hydro-peroxide-induced per-oxidation ; significant reduction in the level of lipid per-oxidation, *Tamra Bhasma* is a strong antioxidant drug and could be used in the management of lipid peroxidation, it showed no acute detectable adverse effects; levels of SOD were also enhanced by *Tamra Bhasma*.^[45] The effect of *Kajjali* may be multi-dimensional, free radicals scavenging, antioxidant, antimicrobial, catalytic, proenzymatic, immunomodulator. *Kajjali* complex Like *Rasasindoor* is also more effective because of its longer stay and timed and sustained release; it shows gastrointestinal adsorption / stimulant and neuro-chemical irritability. It also suppresses auto immune reaction, adverse drug reactions and deranged hepatic metabolism. Black sulphide of mercury (*kajjali*) holistically and synergistically acts along with the herbal ingredients to bring multi systemic target organ effect in its complete sense. *Kajjali kalpas* also possess *rasayan* property.^[46] So the *Rasasindoor* is proven for *Rasayana* effect by maintaining optimum alkalinity for optimum health, provide protection to the kidneys, intestines and liver, maintain stronger bones, alleviate insomnia and depression, keeps rhythmic heart beating and arrhythmias and minerals balance, helps metabolize iron in body, Aid nervous system, Neutralize harmful acids that lead to illness, Achieve a healthy alkaline level by neutralizing acid, Protect body from free radical damage.^[47] *Rasayana* drugs are capable of impelling the

biological systems in a multidimensional manner and it is equally worthwhile to examine them for other effects such as anti-stress adaptogenic and antiviral activities. The *Rasayana* category contains a plethora as constituents with similar, synergistic or antagonistic properties.^[48]

CONCLUSION

During ancient era, the physicians have to carry the medicine with them and there were every chances of breakage and destruction of medicine during transportation, so because of these factors the *Pottali Kalpana* came into existence,^[49] as it was safe to carry, easy to administer, and no chances of destruction due to its hard and solid form. It is administered by rubbing it on a hard surface or stone applied with 1-2 drop of *Ghrita* or honey and then taken orally. The medicinal properties of *Pottali* were enhanced by the process of formation and it was an additional achievement. It was a medicine which gives quick response in emergency situations.⁵⁰ If *Pottali rasayan* is researched keeping in mind its antimicrobial and antiviral effects, could be proved a milestone in the history of Ayurvedic antibiotics. Among the description of *Pottali* in Ayurvedic texts, the most described *Pottali* is *Hemgarbh pottali Rasa* because of its efficacy. Lots of references are available in *Rasashstra* for its preparation.^[51,52,53,54,55,56]

The Acute Symptoms of Covid 19 are similar as *Pranavaha StrotasVyadhi*, so the drug *Hemagarbha Pottali* used in *Atyayika Chikitsa* (Acute Management) due to its *Vyavayi - Vikasi- Yogavahi Karma and Rasayana, Balya, Vata-Kapha hara, Deepana- Pachana* effects of ingredients, also the Study shows the *bhasma* are believed to be nanomedicine^[57] and are more efficacious than any other healing system. This is because the nanosized particles can get absorbed and enter into the blood stream and, are more biocompatible as compared to any chemically produced entity due to its size/volume ratio. The size of nanoparticles^[58] lies between 1 and 100 nm at least in one dimension.^[59] So the drug having nanoparticles in it, which is proven for its quick absorption and Anti-viral, Anti-Inflammatory effects. So it can be said that *Ayurvedic Metal Nanoparticles* in the *bhasma* form used in *Hemagarbha Pottali* play a major role against Covid 19 Disease by showing its Anti-viral, Anti-inflammatory and immunomodulatory effect. In this situation, the holistic approach of *Ayurveda* in the form of curative and preventive medication, Immunomodulatory action with *Rasayana Chikitsa* will be helpful to manage this disease. On the basis of this review, we can conclude that the use of Ayurvedic drug *Hemagarbha Pottali* and formulations in the nanocarriers will increase its

potential to treat COVID 19 disease. They will effectively increase the bioavailability and stability and will also reduce the dose of this potent drug.

RESULT

Efficacy of *Hemagarbha Pottali Rasa* in the management of coronavirus shows result in the treasure of spectacular and miraculous pharmaceutical dosage forms with the principles apply to analyzing the strategies of not only preventing the disease but also showing Immunomodulatory action effectively. Quoting a reference of *Vagbhata* from *Rasa ratna samuccaya.*, “*Alpamaatropayogitwaat Aruce Aprasangataha, Kshipram Aarogyadaayitwat Aushadhyebhyo Adhiko Rasaha; na doshanam na roginam samyageva pareekshanam, na deshasysa kalasya kriyam rasa cikitsite*” Ayurvedic herbo-mineral drugs and formulations have maximum potency with a minimum, dosage with three characteristic attributes: Instant effectiveness, The requirement of very small doses and easy to administration. In addition, a large number of new molecules are directly obtained either from natural products or from their derivatives.^[60-61] *Ayurveda* is the Indian traditional healthcare system which has been used for centuries to deal with various ailments.^[62] It is considered as a complete self-sustainable system of medicine.^[63] Various Ayurveda formulations like *Hemagarbha Pottali Rasa* are in practice to limit the fevers of any origin^[63-65] as immunomodulator, emergency medicine for prevention and curation. Several of these Drugs have been extensively studied for their immune-enhancing, modulating and antiviral effects.^[66-67] All the collected data and relevant research works show the effect of *Hemagarbha Pottali Rasa* in COVID19 patients as Emergency medicine with a definite Immunomodulatory Action.

REFERENCES

1. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, 2020; 579: 270-3. 10.1038/s41586-020-2012-7 32015507
2. World Health Organization. WHO director-general's opening remarks at the media briefing on covid-19. 11 March 2020. <https://www.who.int/dg/speeches/detail/who-director-generals-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>
3. World Health Organization. Coronavirus disease 2019 (covid-19). Situation report 85. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200415-sitrep86-covid-19.pdf?sfvrsn=c615ea20_2

4. Li R, Pei S, Chen B, *etal.* Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). *Science*, 2020; eabb3221. 10.1126/science.abb3221 32179701
5. Guan WJ, Ni ZY, Hu Y, *etal.* China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.*, 2020. 10.1056/NEJMoa2002032 32109013.
6. Zhang JJ, Dong X, Cao YY, *etal.* Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan. *Allergy*, 2020; 10.1111/all.14238.
7. Song Y, Liu P, Shi XL, *etal.* SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. *Gut*, 2020; gutjnl-2020-320891. 10.1136/gutjnl-2020-320891 32139552
8. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*, 2020. 10.1002/jmv.25824 32104915
9. Wölfel R, Corman VM, Guggemos W, *etal.* Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020.
10. 1038/s41586-020-2196-x 32235945 10 Hui DSC, Zumla A. Severe acute respiratory syndrome: historical, epidemiologic, and clinical features. *Infect Dis Clin North Am.*, 2019; 33: 869-89. 10.1016/j.idc.2019.07.001 31668196
11. Giacomelli A, Pezzati L, Conti F, *etal.* Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. *Clin Infect Dis.*, 2020; ciaa330. 10.1093/cid/ciaa330 32215618
12. Temmel AF, Quint C, Schickinger-Fischer B, Klimek L, Stoller E, Hummel T. Characteristics of olfactory disorders in relation to major causes of olfactory loss. *Arch Otolaryngol Head Neck Surg*, 2002; 128: 635-41. 10.1001/archotol.128.6.635 12049556.
13. Mao L, Wang M, Chen S, *et al.* Neurological manifestations of hospitalized patients with covid-19 in Wuhan, China: a retrospective case series study. SSRN 3544840 [Preprint]. 2020.
14. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. Covid-19-associated acute hemorrhagic necrotizing encephalopathy: CT and MRI features. *Radiology*, 2020; 201187. 10.1148/radiol.2020201187 32228363
15. Li Y, Wang M, Zhou Y, *etal.* Acute cerebrovascular disease following covid-19: a single center, retrospective, observational study. SSRN (Preprint). 10.2139/ssrn.3550025.
16. Yang X, Yu Y, Xu J, *etal.* Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective,

- observational study. *Lancet Respir Med.*, 2020; S2213-2600(20): 30079-5. 10.1016/S2213-2600(20)30079-5 32105632
17. Bonow RO, Fonarow GC, O’Gara PT, Yancy CW. Association of coronavirus disease 2019 (covid-19) with myocardial injury and mortality. *JAMA Cardiol* 2020. 10.1001/jamacardio.2020.1105 32219362 20 Inciardi RM, Lupi L, Zacccone G, etal. Cardiac involvement in a patient with coronavirus disease 2019 (covid-19). *JAMA Cardiol* 2020. 10.1001/jamacardio.2020.1096 32219357
18. Driggin E, Madhavan MV, Bikdeli B, etal. Cardiovascular considerations for patients, health care workers, and health systems during the coronavirus disease 2019 (covid-19) pandemic. *J Am Coll Cardiol*, 2020; S0735-1097(20): 34637-4. 10.1016/j.jacc.2020.03.031 32201335
19. Wang D, Hu B, Hu C, etal. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan. *JAMA*2020; 10.1001/jama.2020.1585.
20. Immunity (medical) [Internet]. 2013 [updated 2013 Nov 4; cited 2013 Nov 5]. Available from: http://en.wikipedia.org/wiki/Immunity_%28medical%29
21. Gulati K, Ray A, Debnath PK and Bhattacharya SK: Immunomodulatory Indian medicinal plants. *Journal of Natural Remedies*, 2002; 2(2): 121-131.
22. Masihi KN: —Fighting infection using immunomodulatory agents. *Expert Opin Biol Ther.*, Jul, 2001; 1(4): 641–53.
23. Rajagopala S, Ashok BK and Ravishankar B: Immunomodulatory activity of Vachadhatryadi Avaleha in albino rats. *Ayu.*, Apr-Jun, 2011; 32(2): 275–278.
24. Tripathi JS, Singh RH: The Concept and Practice of Immunomodulation in Ayurveda and the Role of Rasayanas as Immunomodulators. *Ancient Science of Life*, Jul, Aug, Sep, Oct, 1999; 19(1&2): 59-63.
25. Patwardhan B, Warude D, Pushpangadan P and Bhatt N: Ayurveda and traditional Chinese medicine: A comparative overview. *Evid Based Complement Alternat Med.*, 2005; 2: 465–73.
26. Singh RH, Udupa KN. Bhattacharyaa SK and Muruganandam AV: Clinical and experimental studies on Rasayana drugs and Rasayana therapy. Adaptogenic activity of *Withania somnifera* - an experimental study using a rat model of chronic stress. *Pharmacol Biochem Behav*, 2003; 75: 547–55.
27. Charaka Samhita, Chikitsasthana, Jwarachikitsaadhyaya 3/103-108. Available on: Available from: <http://niimh.nic.in/ebooks/echarak>. [Last accessed on 2020 Oct 05].

28. Charaka Samhita, Vimanasthanam, Strotovimanaadhyaya 5/7-8. Available from: <http://niimh.nic.in/ebooks/echarak>. [Last accessed on 2020 Oct 05].
29. Murthy KR. Ashtanga Hridaya, Sutrasthana. Ch. 12/46. Varanasi: Chaukhamba Krishnadas Academy, 2018; 175.
30. Sushrut Smahita, Nidansthana, Kusthanidanaadhyaya 5/32-33. Available from: <http://niimh.nic.in/ebooks/esushruta/index.php>. [Last accessed on 2020 Oct 05].
31. Pedersen A, Zachariae R, Bovbjerg DB. Influence of psychological stress on upper respiratory infection – A metaanalysis of prospective studies. *Psychosom Med.*, 2010; 72: 823-32.
32. Sharma Ved Bhushan, Sharma Parul, Saxena G.K., Sharma Usha. Pharmaceutical Study of Hemgarbha Pottali Rasa. *International Journal of Ayurveda and Pharma Research*, 2015; 3(3)
33. Shastri Ambikadatta. Bhaishajya Ratnavali of Shri Govind Das with Vidyotini Hindi commentary. ED/18th. Varanasi: Chaukhamba Prakashan, 2007; 426.
34. Ashok Satpute, Rasendra Sar Sangraha ¼, Chaukhamba Krishnadas Academy, Varanasi, 2018; 4. 26. Shingadiya RK, Chaudhary S, Joshi K, Bedarkar P, Patgiri BJ, Prajapati PK. Evidence-based safety and efficacy of Ayurvedic herbo-metallic preparations containing gold, iron, and mercury with special reference to paediatrics, *Medical Journal of DY Patil Univ*, 2017; 10: 222-8.
35. Pandit Kashinath Shastri, Rasatarangini, 6/112-128, Motilal Banarasidas publication, 2014; 126-8. 28. Goel RK, Sairam K. Anti-ulcer drugs from indigenous sources with emphasis on *musa sapientum*, *tamrabhasma*, *asparagus racemosus* and *Zingiber officinale*, *Indian. J Pharmacol*, 2002; 34: 100-10.
36. Sharma Mishra G, Choukhambha Bharti Academi. Varanashi, 2007; vol. 3:343. Google Scholar
37. Bhattacharya SK, Sen AP, Ghosal S. Effects of Shilajit on biogenic free radicals. *Phytother Res*, 1995; 9: 56-9.
38. Ch. Su. 11/36 Charaksamhita of Agnivesa Edited by „Vaidyamanorama“ Hindi commentary by Acharya Vidyadhar Shukla and Prof. Ravi Dutta Tripathi Published by Chaukhamba Sanskrit Pratishthan Delhi, Sutrasthan, 11/36; 171: 11/36.
39. Charaksamhita of Agnivesa Edited by „ Vaidyamanorama“ Hindi commentary by Acharya Vidyadhar Shukla and Prof. Ravi Dutta Tripathi Published by Chaukhamba Sanskrit Pratishthan Delhi, Sutrasthan Ch. Su., 28/6: 429: 28/6.

40. Ullagaddi, S.S., Screening of Free Radical Scavenging activity and immunomodulatory effect of Vanga Bhasma, Dissertation submitted Rajiv Gandhi University of Health Sciences, Bangalore.)
41. Sonavanea G, Tomoda K, Sano A, Ohshima H, Terada H, Makino K. In vitro permeation of gold nanoparticles through rat skin and rat intestine: Effect of particle size. *Colloids and Surfaces B: Biointerfaces*, 2008; 65: 1–10. [PubMed] [Google Scholar] [Ref list]
42. Batheja P, Thakur R, Michniak B. Basic biopharmaceutics of buccal and sublingual absorption. In: Touitou E, Barry BW, editors. *In Enhancement in Drug Delivery*. New York: CRC Press, 2007. [Google Scholar] [Ref list]
43. Mitra A, Chakraborty S, Auddy B, Tripathi T, Sen S, Saha AV, et al. Evaluation of chemical constituents and free-radical scavenging activity of Swarnabhasma (gold ash), an Ayurvedic drug. *J Ethnopharmacol*, 2002; 80: 147–53. [PubMed] [Google Scholar] [Ref list]
44. Ghosh P, Han G, De M, Kim CK, Rotello VM. Gold nanoparticles in delivery applications. *Adv Drug Deliv Rev.*, 2008; 60: 1307–15. [PubMed] [Google Scholar] [Ref list]
45. Pattanaik N, Singh AV, Pandey RS, Singh BS, Kumar M, Dixit SK, et al. Toxicology and free radicals scavenging property of Tamra bhasma. *Indian J Clin Biochem*, 2003; 18: 181–9. [PMC free article] [PubMed] [Google Scholar] [Ref list]
46. <http://drshriraj.blogspot.com//2009/01/pharmacology of kajjali kalpas>.
47. Sharm DC. India raises standards for traditional drugs. *Lancet*, 2000; 356: 231. [PubMed] [Google Scholar]
48. Devsagayam TP, Sainis KP. Immune system and antioxidants especially those derived from Indian medicinal plants. *Indian J Experiment Biol.*, 2002; 40: 639-55.
49. Pt. Hariprapannaji Sharma, Rasayoga Sagar, Vol. I, 2nd edition, 1983, Krishnadas Academy, Varanasi, 705.
50. Yadavji Trikamji, translated by Dr. D. Joshi, Rasamritam, 1st edition, 1998, Chaukhambha Sanskrit Bhavan, Varanasi, 315.
51. Pt. Hariprapannaji Sharma, Rasayoga Sagar, edition, Krishnadas Academy, Varanasi, 1998; II: 577.
52. Yadavji Trikamji, translated by Dr. D. Joshi, Rasamritam, 2nd edition, 2003, Chaukhambha Sanskrit Bhavan, Varanasi, 250.
53. Indradeva Tripathi, Rasendra Sara sangraha with Rasa Vidyotini commentary, 2nd edition, Chaukhambha Orientalia, Varanasi, 1998; 209.

54. Prof. Dattatreya Anant Kulkarni, Ras Ratna Samuccaya, edition, Meharchand lachhmandas publications, Delhi, chapter 14, rajyakshama prakaran, 2006; verse no.23-26, 18.
55. Acharya Siddhinandan Mishra, Rasa Prakash Sudhakara, 2nd edition, Chaukhambha Orientalia, Varanasi, 277.
56. Chudamani Mishra, Santosh Sharma, Rasa Kamdhenu, IVth chikitsa pad, Chaukhambha Orientalia, Varanasi, 2nd edition, 2003; 46.
57. Chudamani Mishra, Santosh Sharma, Rasa Kamdhenu, IVth chikitsa pad, Chaukhambha Orientalia, Varanasi, 2nd edition, 2003, pp -46. **Translational biotechnology: A transition from basic biology to evidence-based research**, Translational Biotechnology, 2021.
58. Department of Fundamental Medicine, School of Biomedicine, Far Eastern Federal University, Vladivostok, Russia, Personalized therapy and stem cell transplantation for pro-inflammatory modulation of cancer stem cells microenvironment in glioblastoma: Review International Review of Neurobiology, 2020.
59. Y.W. Jun, Y.M. Huh, J.S. Choi, J.H. Lee, H.T. Song, Yoon S. Sungium, *et al.* Nanoscale size effect of magnetic nanocrystals and their utilization for cancer diagnosis via magnetic resonance imaging **J Am Chem Soc**, **2005**; **127**: 5732-5733. [10.1021/ja0422155](https://doi.org/10.1021/ja0422155)
60. Diallo D, Hveem B, Mahmoud MA, Berge G, Paulsen BS, Maiga A. An ethnobotanical survey of herbal drugs of Gourma District, Mali. *Pharm Biol.*, 1999; 37: 80–91. doi: 10.1076/phbi.37.1.80.6313. [CrossRef] [Google Scholar] [Ref list]
61. Tewari D, Sah AN, Bawari S, Bussmann RW. Ethnobotanical investigations on plants used in folk medicine by native people of Kumaun Himalayan Region of India. *Ethnobot Res Appl*, 2020; 20: 1–35. [Google Scholar]
62. Tewari D, Rawat P, Singh PK. Adverse drug reactions of anticancer drugs derived from natural sources. *Food Chem Toxicol*, 2019; 123: 522–535. doi: 10.1016/j.fct.2018.11.041. [PubMed] [CrossRef] [Google Scholar] [Ref list]
63. Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *J Nat Prod.*, 2020; 83: 770–803. doi: 10.1021/acs.jnatprod.9b01285. [PubMed] [CrossRef] [Google Scholar]
64. Mukherjee PK, Harwansh RK, Bahadur S, Banerjee S, Kar A, Chanda J, Biswas S, Ahmmmed SM, Katiyar CK. Development of Ayurveda - tradition to trend. *J Ethnopharmacol*, 2017; 197: 10–24. doi: 10.1016/j.jep.2016.09.024. [PubMed] [CrossRef] [Google Scholar]

65. Katoch D, Sharma JS, Banerjee S, Biswas R, Das B, Goswami D, Harwansh RK, Katiyar CK, Mukherjee PK. Government policies and initiatives for development of Ayurveda. *J Ethnopharmacol*, 2017; 197: 25–31. doi: 10.1016/j.jep.2016.08.018. [PubMed] [CrossRef] [Google Scholar]
66. Kaushik S, Jangra G, Kundu V, Yadav JP, Kaushik S. Anti-viral activity of Zingiber officinale (Ginger) ingredients against the Chikungunya virus. *Virusdisease*, 2020; 31: 1–7. doi: 10.1007/s13337-020-00584-0Dhawan BN. Anti-viral activity of Indian plants. *Proc Natl Acad Sci India Sect B.*, 2012; 82: 209–224. doi: 10.1007/s40011-011-0016-7. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
67. Jadhav P, Kapoor N, Thomas B, Lal H, Kshirsagar N. Antiviral potential of selected Indian medicinal (ayurvedic) plants against herpes simplex virus 1 and 2. *N Am J Med Sci.*, 2012; 4: 641–647. doi: 10.4103/1947-2714.104316. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]