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Homoeopathic Medicine Arsenicum album, the prophylactic/immune booster in COVID-19 pandemic

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Background: Homoeopathic medicine *Arsenicum album* (*Ars. alb*) has been advised by the Ministry of AYUSH, Government of India based on the recommendations of Central Council for Research in Homoeopathy (CCRH) as a prophylactic/ immune booster for prevention of COVID-19 disease. This paper narrates available evidence from laboratory studies, clinical studies, toxicological studies for *Ars. alb.* as a prophylactic/ immune booster.

Methods: Published literature regarding immuno-modulatory, toxicological and therapeutic effects of the Homoeopathic Medicine *Ars. alb.* was reviewed.

Results: Homoeopathic literature records the use of *Ars. alb.* for fever, cough, shortness of breath, loss of smell, coryza, fatigue, diarrhea, nausea, etc. *Ars. alb.* in its crude form is toxic, acting over numerous systems of the human body. It acts over the macrophages and lymphocytes hindering normal immune response. The toxic effects of crude arsenic are neutralized by ultra-high dilution of arsenic trioxide thus stimulating an immune response, the memory of which retained by the organism helps to prevent the infection. Highly diluted *Ars. alb.* modulates reactive oxygen species (ROS), and cytokine secretion, decrease in interleukin-6 production in macrophages, which are central mediators of the immune system, wound healing, and body homeostasis. The molecular effects and clinical presentation of the COVID-19 and *Ars. alb.* are similar over the response to the immune system and clinically is similar to a great extent.

Conclusion: Primary evidence suggests possibility of homoeopathic medicine *Ars. alb.* as a prophylactic immune booster medicine, maintaining an optimal immune response in the human body. Further pre-clinical and clinical studies are warranted.

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Homoeopathic medicine *Arsenicum album*, the prophylactic/immune booster in COVID-19 pandemic

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Abstract

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Keywords: *Arsenicum album*, Homoeopathic medicine, Immune booster, India, Prophylaxis

INTRODUCTION

Coronavirus outbreaks are not new to humanity. In 2003, an outbreak of severe acute respiratory syndrome (SARS) took place in Hong Kong and in 2012 another outbreak of Middle East respiratory virus (MERS) took place in Middle East countries. However, such outbreaks were of a localized nature and did not take the form of a pandemic.^[1] Toward the end of the second decade of the 21st century, a novel virus belonging to the coronavirus family named: SARS-related coronavirus 2 (SARS-CoV2) emerged in Wuhan, China, has been declared as a global pandemic.^[2,3] Most of the coronavirus is zoonotically transferred to humans and in the case of SARS-CoV-2, the suspected disease reservoirs are as bats, snakes, and pangolins.^[1,3] With Sir Alexander Fleming's discovery of Penicillin in 1928, the antibiotic and antiviral era saw a decrease in the prevailing microbial infections and increased life expectancy in the world.^[4] Nonetheless, with such inventions the evils of antimicrobial resistance appeared which lead to mutation of

existing organisms [5,6]. As a result, novel infecting agents along with the further complication in the treatment strategies rise.

The homoeopathic medicine "*Arsenicum album*" (*Ars. alb*) was introduced into homoeopathic practice by Samuel Hahnemann,^[7] the discoverer of the homoeopathic system, and has been used successfully in practice since the very initial days. The medicine has been in use for various clinical conditions.^[8] With the emergence of COVID-19 disease and the issuance of Advisory^[9] by the Ministry of AYUSH, Government of India, the role of the medicine as an *immune booster* has invited

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criticism.^[10-14] Medical researchers throughout the globe are in search of curative and preventive therapies for this disease. The question arises whether this empirical use of homoeopathic medicine “*Arsenicum album*” is really warranted for effective treatment or prophylaxis of the COVID-19. The following discussion examines the prophylactic/immune booster role of *Ars. alb* in COVID-19.

Role of the immune system in COVID-19

The innate immune response forms the first line of defense against invading pathogens including white blood cells (neutrophils and macrophages).^[15] Pathogens that are not destroyed by this attack attract the attention of lymphocytes which embody the functions of adaptation and memory, allowing the immune system to make increasingly specific responses and include a “memory” that makes future responses against a specific antigen more efficient.^[15]

The SARS-CoV-2 virus’s spike protein binds to ACE 2 receptors of host’s epithelial cells of lungs, heart, kidneys, and other organs, like a key being inserted into a lock – before entry and infection of cells that cause COVID-19, downregulates the ACE 2 receptor, and reduces its expression on lung cells.^[16] The destruction of lung cells triggers a local immune response, releases cytokines, and prime adaptive T- and B-cell immune responses.^[16] In most cases, the body can resolve the infection with a strong and healthy immune system. However, in cases of a dysfunctional immune response, severe lung and systemic injury occurs.^[16] Virus-induced *pyroptosis* triggers a severe inflammatory response inducing a massive release of chemokines and cytokines called “cytokine storm.”^[16,17] This cytokine storm induces widespread lung injury and severe acute respiratory illness or acute respiratory distress syndrome.^[16] Therefore, a rapid and well-coordinated immune response is the key to the resolution of COVID-19.

APPROACH

In June 2020, the search was conducted to screen papers using keywords “*Arsenicum album*” “Arsenic trioxide,” “Immune modulation,” “Arsenic toxicology,” “Arsenic album clinical studies,” “Arsenic and leukocytes,” and “*Arsenicum album* Homoeopathy” at leading databases such as PubMed, HomBRex, ScienceDirect, Core-Hom, CamQuest, and Google Scholar. Abstracts were studied and relevant full-text articles were taken into consideration. Articles published in the English language were considered. References lists of the selected articles were searched for further reference. Fundamental research studies, literary reviews, perspectives, and some clinical research studies were included for consideration.

ARSENIC AS A CONVENTIONAL THERAPEUTIC AGENT

Arsenic trioxide, a common toxic heavy metal, has been used both as a “poison” and a “medicine.”^[18] Physicians use it to treat trypanosomiasis, syphilis, psoriasis, asthma, acute promyelocytic leukemia, and others.^[18]

Signs of arsenic poisoning include nausea, profuse watery diarrhea, colicky abdominal pain, and profuse salivation. Common hematological features include hemoglobinuria, intravascular coagulation, bone marrow depression, severe pancytopenia, and normocytic normochromic anemia and basophilic stippling, and other gross features include renal failure, respiratory failure, pulmonary edema, peripheral neuropathy, and encephalopathy.^[19] It is also a potential carcinogenic agent with an association of the substance for skin, lung, bladder, liver, and prostate cancers.^[20]

ARSENIC ALBUM AS A THERAPEUTIC AGENT IN HOMOEOPATHY

Conventionally, arsenic trioxide has been used by Styrian mountaineers in old times for strengthening muscles of extremities and respiration.^[8] *Ars. alb*, the homoeopathic medicine, is prepared from the same chemical, that is, white oxide of metallic arsenic (As_2O_3 or arsenic trioxide). Homoeopathic Pharmacopoeia of India mentions the preparation of homoeopathic medicine *Ars. alb* from arsenic trioxide by dilution and trituration process. The crude As_2O_3 is heated with glycerine and further mixed with diluted water and strong alcohol to produce the mother solution. Further potencies are obtained by serial dilution with dispensing alcohol and the succussion of the mother solution. Medicine is also prepared by triturating fine powder of As_2O_3 with sugar of milk.^[21] The medicine has been proved over healthy human beings (homoeopathic pathogenetic trials) by many authorities in homoeopathy including Samuel Hahnemann, Constantine Hering, T.F. Allen, Richard Hughes, J. P. Dake, and others.^[22] The medicine demonstrated action over different organs of the body during proving with predominant action over respiratory organs similar to symptoms of upper respiratory tract infection. Symptoms similar to febrile conditions are also demonstrated in the proving. Catarrhal changes in the nose, pharynx, larynx, and bronchial tubes have been observed in toxicological records as well as during homoeopathic drug proving.^[7,23,24] Homoeopathic remedies applied on the principle “*Similia similibus curentur*” act curatively over diseased individuals who present with symptoms similar to proving symptoms in healthy individuals. Hahnemann himself was cured of suffocative catarrh aggravated at night on lying down by *Ars. alb*.^[24] Clarke also mentioned “*When ‘colds’ appear in a family let all those who are unaffected take Ars. alb thrice daily.*”^[8] The other indications are fever, malaria, and food poisonings, especially in persons with low vitality.^[25] Homoeopathic literature contains details of this medicine from a clinical viewpoint. It is also the most researched medicine in basic research for homoeopathy.^[26] Central Council for Research in Homoeopathy (CCRH) under Ministry of AYUSH advised the use of *Ars. alb* as an immune booster for COVID-19 through reportorial analysis of available case reports of the outbreak in Wuhan, China, as well as previous research studies on influenza-like illness.^[27,28]

ARSENIC – As IMMUNOMODULATOR

Modulation of the immune system plays a critical role in the management of health and disease processes within humans. The importance of the immune system stems from the need to eliminate and modulate both pathogenic and non-pathogenic microorganisms that could hinder the body's ability to maintain homeostasis.^[29] Exposure to arsenic alters normal biological functions, resulting in the direct initiation of disease or, at least, predisposition for disease. Studying the impact of arsenic on the ability to fight viral and bacterial infections through specific immune responses is particularly important for a full understanding of its overall effects on health.^[30] The multiple effects of arsenic on the immune system tend to decrease the immune surveillance system and increase the rate of infection, autoimmune disease, cancer, and other immune-mediated problems, as exposed individuals show induction of oxidative stress, inflammation, and impaired lymphocyte activation.^[31] On the other hand, it had been observed that based on the hypothesis of paradoxical pharmacology,^[32] homoeopathic medicine *Ars. alb* has the potential to repair the damages in the cells caused by arsenic trioxide molecules even at molecular levels in protein and nucleic acids.^[33]

Action on macrophages

The macrophage is an important element of the innate immune system which functions to engulf and digest microbes, cellular debris, and cancer cells by phagocytosis.^[34] The differentiation of primary monocytes to macrophages is impaired due to arsenic and differentiated macrophages show defective cell adhesion properties, F actin expression, nitric oxide production, and phagocytic activity.^[34,35] Arsenic trioxide also induces apoptosis in the monocytes during the process of differentiation to macrophages by suppression of p65 nuclear factor-kappa B through decreased DNA binding.^[36] Metalloid-exposed macrophages display increased secretion of the pro-inflammatory chemokines CXCL2 and CCL18 and a decreased expression of several macrophage markers, including metalloproteinase 7, 9, and 12.^[34,37] Chronic exposure to arsenic is also correlated with high CD14 expression and elevated levels of pro-inflammatory cytokines.^[34] Changes in microglia and dendritic cells have also been observed due to the effect of arsenic.^[34]

Action on lymphocytes

T- and B-lymphocytes are the essential components of cellular and humoral immunity which are also affected by arsenic. The activation of leucocytes leads to the differentiation of CD4 + T helper cells and CD8 + T cytotoxic cells.^[34] A decreased percentage of CD4+ cells and altered CD4/CD8 ratio has been observed from chronic arsenic exposure.^[38-40] Upregulation of pro-inflammatory cytokines, growth factors, and chemokines is also induced by arsenic.^[41] In the case of B-lymphocytes, the effect on B cells is not so significant but arsenic reduces significant pre-B-cell development from hemopoietic stem cells.^[34]

Activation of reactive oxygen species (ROS)

The arsenic trioxide produces ROS in human monocyte-derived macrophages by directly activating NADPH oxidase at the plasma membrane.^[34,36] To stimulate this superoxide-generating enzymatic complex, the metalloid induces the phosphorylation and subsequent membrane translocation of the p47^{phox} NADPH oxidase partner through a Rho-kinase/p38-kinase signaling pathway.^[34] At a higher concentration (5 µM), arsenic significantly decreases the mitochondrial transmembrane potential, increases ROS levels, and triggers caspase-dependent apoptosis in human CD4+ and CD8+ T cells.^[34,42]

Arsenic as an antiviral

Arsenic trioxide in crude forms also demonstrated antiviral properties over viral strain bacteriophage.^[43] The antiviral activity of metal oxides, arsenic (As₂O₃) at 10 and 12 ppm completely inhibited the viral multiplication in the host strain is an indication of the virucidal nature of metal oxides. Therefore, there is positive evidence that *Ars. alb* can act as a potential antiviral agent.

Role of *Ars. alb* in immune modulation

A study conducted by Ive et al.^[44] showed that *Ars. alb* in 6C, 30C, and 200C increased and restored the viability of MT4 cell lines which had been intoxicated with the arsenic trioxide. The destructive function of the arsenic trioxide on leukocytes and stimulation of pro-inflammatory cytokines, chemokines are rather neutralized by ultra-high dilutions of *Ars. alb*. This provides evidence that ultra-high dilutions of *Ars. alb* maintain an optimal function of the human leukocytes. Both succeeded and unsucceeded *Ars. alb* were used in increasing potencies from 6CH to 200CH although succession did not make any difference to the results. As mentioned earlier, an optimal regulation of human leukocytes and macrophages is vital in recovery from COVID-19.

Studies also demonstrate the capability of homoeopathically prepared *Ars. alb* helps in reducing the DNA and RNA damage and restoring them in arsenic-induced cytotoxicity in mice models.^[33] The study has also shown the reduction of intracellular ROS generation in arsenic-treated *Escherichia coli*.^[45]

Ars. alb is shown to decrease IL-6 production in laboratory models, which is an important inflammatory marker and responsible for the inflammatory process and inducing cytokine storm. Decreased production prevents the damage of the human body from such severe inflammatory responses. Dalboni et al.^[46] conducted the experiment on macrophages cell lines using high dilutions of *Ars. alb* 200C potencies showed a decrease in interleukin-6 production in macrophages. *Ars. alb* 30C administration reduced lipid peroxidation, protein carbonylation, DNA damage, ROS formation, and Msn 2 and Yca 1 expressions in arsenate-treated *Saccharomyces cerevisiae* yeast. Das et al.^[47] in their study demonstrated *Ars. alb* 30C increasing cell viability, GSH, G6PDH, CAT, and SOD significantly.

ARS. ALB SYMPTOMS SIMILAR TO COVID-19

Homoeopathy never treats a disease according to diagnosis or the causative organisms of the disease, rather it treats the person based on the symptomatology of the disease. The action of the remedies is noted from their effects on healthy human beings and recorded in the homoeopathic Materia Medica. These symptoms are matched with the diseased individuals and the remedy containing the most similar symptoms to the disease is prescribed. The symptoms present in homoeopathic Materia Medica^[7,23] under *Ars. alb* were similar to the observed symptomatology of COVID-19. CCRH conducted a reportorial analysis of the symptoms of COVID-19 for releasing such an advisory which is used conventionally as a tool for matching the symptoms of Materia Medica and the disease. The symptoms of the medicine demonstrated a significant similarity with the disease picture of COVID-19 available from reports of the disease in Wuhan, China.^[1,48] Most of the presenting symptoms of the disease are well covered by *Ars. Alb*, especially fever, cough, shortness of breath, loss of smell, coryza, fatigue, diarrhea, nausea, and others. The medicine is frequently used by homoeopathic physicians in the treatment of conditions similar to COVID-19, especially in influenza-like illnesses.^[49]

PATHOPHYSIOLOGIC RELATION OF ARS. ALB AND SYMPTOM SIMILARITY WITH COVID-19

The physiological antagonism between large and small doses is an illustration of the homoeopathic law of posology as mentioned by Stuart Close.^[50] The principle of hormesis is applicable in the case of homoeopathic medicine *Ars. alb* where low doses of the substance seem to act in a beneficial manner which is toxic in higher doses.^[51] In crude form, arsenic induces changes in the immune system which mimics the pathophysiology of COVID-19. As mentioned earlier, the induction of apoptosis in macrophages by arsenic molecules^[36] in toxic doses is similar to SARS-CoV-2 viral-induced *pyroptosis*.^[16,17] The pathology of the induction of *cytokine storm* in SARS-CoV-2 infection is similar to the increased pro-inflammatory cytokine secretion by metalloids arsenic. The virus also inhibits the innate immune system, especially macrophages through inhibition of NF- κ B^[16] similar to that of arsenic. Laboratory and clinical studies have demonstrated that homoeopathic medicine *Ars. alb* inhibits and corrects the pathological changes in the immune system as caused by metalloids arsenic.

Arsenic molecules are generally absorbed in the body through *aquaglyceroporin* channels, the same channel is used for the transfer of glycerol and water.^[52] When such medicines are ingested by healthy individuals, being highly diluted in nature, they are only sufficient to develop an immune response that subsides subsequently due to the very low dose of the medicine. Similar to the theory of vaccination, the human body retains the memory of the immune response and prevents the disease similar in manifestations until the memory lasts. The symptoms

of *Ars. alb*, as recorded in different Materia Medica, are similar to manifestations of COVID-19 (also confirmed by reportorial analysis), therefore, the medicine can have some preventive action on COVID-19.

Homoeopathy and immunology have a strong analogy as a principle of homoeopathy deals with healing with the help of intrinsic responses of the living organism.^[53] Bell *et al.*^[54] mentioned that the concept of “*Similia Similibus Curentur*” in homoeopathy has a relation with modern immunological evidence of non-linear or even opposite responses to antigens, cytokines, and other immunoregulatory agents.^[54] Homoeopathic medicine selected based on similitum and in minimum dose elicits immune regulatory responses in the human body. *Ars. alb* elicits similarity not only to the disease picture of COVID-19 but also to the molecular changes which are observed in the disease pathogenesis. Such pieces of evidence provide a certain hint of the positive action of *Ars. alb* over COVID-19 when used from a therapeutic aspect.

Organon of Medicine written by Samuel Hahnemann under aphorisms 100–102^[55] mentions the instructions for homoeopathic practitioners for investigations of an epidemic and sporadic diseases and selection of homoeopathic specific remedy for the same. Although the homoeopathic treatment focuses on the individualization of a patient, in the case of epidemics as the disease is originating from a common source of infection, the collective picture of the disease is the guide for the selection of homoeopathic medicine.^[55] This specific medicine will act both as prophylactic and may also act as curative medicine. The term “*Genus epidemicus*” was coined by H.C. Allen for this homoeopathic specific remedy for epidemics.^[56]

Aaron *et al.*^[57] mentioned a case of COVID-19 presenting with diarrhea and vomiting, who were symptom free within 3 days after the administration of *Ars. alb* 30C. The patient was improved by almost 50% within 12 h of administration of the remedy.

Homoeopathic medicine *Ars. alb* has previously shown positive results over laboratory studies over the harmful effects of arsenic trioxide over human cell lines and animal models. Clinical trials have also been conducted to demonstrate the encouraging effects of *Ars. alb* over arsenic toxicity.^[58] Homoeopathic medicines are vital to maintaining homeostasis as mentioned in homoeopathic philosophies, where ultra-diluted medicine acts in a process of restoring the normal optimal functioning of the body. Therefore, by prescribing medicine to healthy persons as well as diseased individuals; the medicine maintains a healthy immune response and even acts curatively based on the principle of *Similia*.

CONCLUSION

Homoeopathic medicine *Ars. alb* is an apt choice as a prophylactic intervention for COVID-19 as per the above

discussion and has the potential for immune modulation. It needs to be further researched as a prophylactic immune booster for COVID-19, along with its clinical benefits.

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None declared.

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