Effect of *Allium sativum* on Cardiovascular Consequence as Immunomodulator in Post Covid 19: A Review

Risla M.H.F.[1*] and Jamaldeen F.A.[2]

Abstract

The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is a novel coronavirus under the family Coronaviridae. COVID-19 has now spread globally with increasing amount of infected and death among all populations. COVID-19 disease develops after average incubation period of 4 days (2–7 days) following infection by SARS-CoV-2. Cardiac complications lean towards to occur 8–14 days after the viral infection. COVID-19 patients have commonly developed with coagulation disorder and fibrinolytic dysfunction even after the recovery. According to the Unani system of medicine, enhancing immunity with immune boosters is one of the main aims for preventing the disease and maintaining the health. Garlic (*Allium sativum*) is measured as a good plant source for maintaining the homeostasis of the immune system. From the ancient period, garlic is being used for treatment of cardiovascular diseases. The aim of this review was to provide modernized, wide-ranging and considered information on post COVID-19 cardiovascular consequences and the effects of garlic on cardiovascular consequences as an immunomodulator. Systematic literature searches were conducted on MEDLINE, PubMed, Science direct, Springer databases and popular search engines were included. The results gained garlic possesses hyperlipidemic, antithrombotic, anti-atherosclerotic properties. In addition to that it has a broad range of therapeutic effect from such as antibacterial to anti-cancer. Summary was formulated after a thorough reading of all reading materials. This review was concluded that garlic acts as an immunomodulator and minimize the consequences of cardiovascular ailments.

Keywords: COVID-19, Cardiovascular ailments, Immunomodulator, Fibrinolytic, *Allium sativum*

Introduction

Overview of COVID-19 and its effects on cardiovascular diseases

The Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus under the family Coronaviridae. It is the seventh human coronavirus and identified to be the responsible for the current epidemic. It was originated as acute atypical respiratory infections in Wuhan, China in early December 2019[1]. The disease caused by this virus, termed coronavirus disease 19 (COVID-19). It has rapidly spread throughout the world within a short period with increasing rates of morbidity and mortality. This has led to a pandemic emergency, and it has been declared by the WHO on March 11, 2020[2]. COVID-19 disease develops after average incubation period of 4 days (2–7 days)[3] following infection by SARS-CoV-2 virus. Cardiac complications lean towards to occur 8–14 days after the onset of the viral infection and predict poor prospects. Although the real implication of this is mysterious, as our understanding of the disease is improving, cardiac complications are being increasingly predictable[3].

[1]*Department of study in Unani, Institute of Indigenous Medicine, University of Colombo, Rajagiriya, Sri Lanka.*
[2]*Community Medical Officer, Central Ayurvedic Dispensary, Alayadivembu, Sri Lanka.*

**Correspondence: Risla M.H.F., Department of study in Unani, Institute of Indigenous Medicine, University of Colombo, Rajagiriya, Sri Lanka. Email: Rizla.zaki@gmail.com*

A study done on recently recovered patients from a German cohort revealed that cardiac involvement was present in 78% and ongoing myocardial inflammation in 60% of the patients[3].

COVID-19 patients commonly develop with coagulation disorder and fibrinolytic dysfunction even after recovery. Disseminated intravascular coagulation (DIC) is most commonly seen in COVID-19 infected persons. SARS-CoV-2 infection causes immune insufficiency, injuries in the endothelium, and activation of the platelet, and inflammatory mediators release (IL-6 and TNF-α), causing a procoagulant state. DIC can contribute to the injury of the myocardium causes microthrombus. The SARS-CoV-2 infection has allied to the harm of the endothelium, resulting in the huge spectrum of organ involvement (renal disease, thrombosis and pulmonary embolism, and cerebrovascular damages). The rates of thrombotic problems documented in the reviews were highly variable. Deep vein thrombosis, pulmonary embolism, and acute cor-pulmonale have been identified. Previous literatures recommended the use of pharmacological venous thromboembolism prophylaxis for hospitalized Covid-19 patients[3,4].

The Unani system of medicine explains to enhance immunity by using immune boosters is one of the main things for preventing disease and maintaining of health. Therefore, an approach to enhance immunity and provide a symptomatic cure in upper respiratory tract infection is advocated[2]. As per the saying "Prevention is better than cure", the Unani system of medicine has found more measures with diet and medicines. Garlic is measured as a good plant source for maintaining the homeostasis of the immune system. Thus, different reviews have established exciting advantageous effects of garlic on the immunity and immune cells[5]. Garlic has also been stated to protect from epidemic diseases. Plenty of studies exposed garlic to have antioxidant, anti-inflammatory, immune-modulating, antibiotic, bacteriostatic, antifungal, antiviral, anthelminthic, antithrombic, hypotensive, hypoglycemic, and hypocholesterolemia properties[6].

The purpose of this review is to provide modernized, comprehensive, and categorized information of post COVID-19 cardiovascular consequences and the effects of Allium sativum on cardiovascular consequences as an immunomodulator.

Materials and Methods

Systematic literature searches were conducted on Google scholar, MEDLINE, PubMed, Science Direct, Springer databases, and popular search engines were included to collect the necessary information. A huge number of recently published research papers were studied during the year 2020-2021 to collect the data about the effects and consequences of COVID-19 and garlic. In addition to those some medicinal plant hand books were reviewed to collect data about garlic. Data extraction was done by using the keywords as Allium sativum, garlic, allium, cardiovascular diseases, COVID-19 infection, antifibrinolytics, ant thrombolytics, immunomodulators.

Data arrangement

The results were construed and categorized on the basis of an application to the subtopics and, a summary of all effects was stated Each subtopic states a brief review of the plant and the information is supported by the results of various pharmacological studies conducted in that field. Finally, a conclusion was reached based on the reviewed information. The summary was done after a thorough reading of all reading materials.

Discussion

From the ancient period garlic is being used for the treatment of cardiovascular ailments. A systematic literature study shows in taking garlic has a significant effect on minimizing blood pressure, prevention of atherosclerosis, lowering of serum cholesterol and triglyceride, inhibition of platelet aggregation, and increasing fibrinolytic activity[7].

Allium sativum

Garlic, *Allium sativum* L. is a plant under the Liliaceae family, has been broadly recognized as a valued spice and a common remedy for various diseases and functional disorders[8]. Garlic, the name

may have initiated from the word 'all' meaning pungent. Sanskrit histories reveal its medicinal values dating back to 5000 years, and it has been used for a minimum of 3000 years in Chinese medicine. The Egyptians, Babylonians, Greeks, and Romans used garlic for healing diseases. In 1858, Pasteur pointed garlic's antibacterial property, and during World War I and World War II it was used as an antiseptic to stop gangrene[9]. Garlic currently used to prevent and cure cardiovascular disease by lowering blood pressure and cholesterol. It also prevents platelet aggregation, improves fibrinolytic activity, and reduces clots on injured endothelium. It also used as an antimicrobial agent, and as a preventive agent for cancer[9].

Classification of Allium sativum

Kingdom: Plantae, Subkingdom: Tracheobionta, Order: Asparagales, Family: Amaryllidaceae, Genus: Allium [10].

Vernacular Names

Sanskrit: *Lasuna*, *Rosona*, *Yovanesta*. English: Garlic, poorman's treacle Bangali: *Rosun*, Hindi: *Lashan*, *lahsun*. Arabic: *SaunTaum* German: *Knoblauch*, *Lauch*. Greek: *Allidion*, *Skorodon*. Italian: *Aglio*. Chinese: *Syuntauh*. Urdu: *Lehsun*. Malayalam: *Veluthull* [10].

Chemical constituents

Garlic contains 65% of water and it makes the highest contentand the remaining portion of the dry weight composed with fructose-containing carbohydrates, compounds of sulphur, proteins, fibers, several enzymes, and free amino acids. In addition, it contains high amount of potassium, zinc, sulphur, moderate amount of selenium, and low amount of calcium, magnesium, sodium, iron, and manganese. It also contains Vitamins A, C, and B-complex. Seventeen types of amino acids found in garlic; lysine, histidine, arginine, aspartic acid, threonine, swine, glutamine, proline, glycine, alanine, cysteine, valine, methionine, isoleucine, leucine, tryptophan, and phenylalanine. It contains at least 33 sulphur compounds such as alliin, allicin, ajoene, diallyltrisulfide (DATS), S-allyl cysteine, vinyl dithiines, allyl propyl disulfide, S-allylmercaptocystein. Garlic's characteristic pungent odor is produced from these Sulphur compounds. The most abundant compound of garlic is alliin it is relatively odorless. Garlic's characteristic pungent odor is present at 10 and 30 mg/g in fresh and dry garlic respectively. Phenolic compounds such as Caffeic acid & Ferulic acid are also contained in garlic in high numbers. During cutting or crushing an enzyme called alliinase comes in contact with alliin and produces allicin. The principal bioactive compound, Allicin (diallylthiosulfinate) is present in the aqueous extract of garlic or fresh garlic homogenate, which gives off off garlic's distinct characteristic fragrance. The compounds present in garlic are water-soluble [(97%) SAC(S-allylcystein), NAC(N-acetylcystein)] and small amounts of oil-soluble compounds [(0.15-0.7%) DATS (diallyl disulfide), DAS (diallyl sulfide)][7,11,12].

Pharmacological activities

Nature's one of the wonder plants is garlic and it has strong healing properties. It can stop the growth and kill micro-organisms. Also, it lowers blood pressure, blood cholesterol, blood sugar, and prevents blood clotting. Especially it contains anti-cancer properties. It can also enhance the immune system and protect health.

Compounds which are present in garlic which have the power to prevent the human body from a wide variety of diseases[12]. Such as hypertension, dyslipidemia, coronary heart disease, myocardial infarction, and atherosclerosis are being treated by garlic. Some types of cancers are also being treated and prevented with garlic and its compounds; colon cancer, rectal cancer, stomach cancer, breast cancer, prostate cancer, bladder cancer, and lung cancer. It is also used to cure enlarged prostate (benign prostatic hyperplasia - BPH). Diabetes mellitus, knee joint pain, allergic rhinitis, diarrhea, high blood pressure late in pregnancy (pre-eclampsia), common cold, and flu also could be treated with garlic. It is used to enhance the immune system, curing tick bites, and preventing and treating various types of infections [10]. Garlic is very useful to treat fever by reducing

temperature, productive coughs, chronic headache, stomach ache diseases, sinusitis, gouty arthritis, rheumatism, piles, asthma, chronic bronchitis, hypotension, hypo and hyperglycemia, and snakebites. It is also used to cure stress and fatigue, and maintaining healthy liver function. Further, garlic useful in the conditions of arthritis, sciatica, lower back pain, tuberculosis, malaria, several types of skin diseases including leprosy, vitiligo, discoloration of the skin, and itches. Garlic plays a great role in indigestion, colic pain, splenomegaly, fistula, bone fracture, kidney stone, anemia, jaundice, epilepsy, cataract, and night blindness. Garlic paly huge role in the area of pharmaceutical science [13].

Stimulant, antiseptic, anthelminthic, antihypertensive, carminative, diaphoretic, expectorant, diuretic, antiscorbutic, aphrodisiac, and anti-asthmatic properties have been recorded for garlic and its compounds. It is used for the relief of rheumatic pains. *Allium sativum* leaf lectin (ASAL) protein is a compound in garlic and that helps the blood to flow more freely and reduce the incidence of clots. A daily dose of 1 mL/kg body weight of garlic extract for six months can result in a substantial reduction in free radical stress in the blood of patients with atherosclerosis and cholesterol circulating in the bloodstream. Oxidation reactions are prevented by garlic may explain some of its advantageous effects in atherosclerotic cardiovascular diseases[14].

Hypolipidemic, antithrombotic, and anti-atherosclerotic properties of garlic were documented. In addition to that, a broad range of therapeutic effects such as antibacterial, immunomodulatory and anticancer effects also have been included[15].

Immunomodulatory effects of garlic

Garlic produces immunomodulatory properties with its contents. Antiviral activity of the garlic extract against influenza B, herpes simplex, and coxsackieviruses were documented. In this review, the highest virucidal activity was observed in ajoene followed by allicin, allyl-methyl thiosulphinate, and lastly methyl-allylthiosulphinate. Its action against cytomegalovirus and Avian infectious bronchitis virus are also identified later. It has also been detected to stimulate macrophages and encourage immunoglobulins to enhance immunity. Specific to the respiratory system, garlic was methodically considered to improve lung function in heavy smokers. Its consequence in the common cold was found evidently by some researchers as reducing the quality and quantity of the exudates. Efficacy of garlic extract in asthma-like condition of lungs as examined and verified that it has immunomodulatory properties[6].

Sulfur-containing amino acids and other compounds are contained in garlic that appears to increase the activity of the immune system. It is one of the remarkable conductors of the body's immune system; which arouses immune function by making macrophages or killer cells more energetic. People are regularly affected by insufficient nutrition, smoking habit, physical damage, psychological impact, and chemical pollution.

Its content of germanium alone provides admirable immune stimulation. In addition to germanium, garlic contains thiamine, sulfur, niacin, phosphorous, and selenium[8].

In order to fight with the infectious diseases, additional nutrients like garlic are obviously needed to boost our immune system.

Superior immunomodulatory effects are shown in aged garlic extract (AGE) than raw garlic; these effects are ascribed to the converted organosulfur compounds. Recent reviews have shown that the extract of aged garlic also contains some immunomodulatory proteins (SAC(S-allylcystein), SAMC (S-allylmercaptocysteine) such as immunoglobulin which have been identified as the major garlic proteins or agglutinins. Further, the results suggest that immunomodulatory proteins and fructans contribute to the therapeutic potential of extract of aged garlic, in addition to the crucial transformed organosulfur compounds[14].

Garlic acts as an immunity booster. It can be used in respiratory tract infections such as common cold, allergic rhinitis, asthma, and acute and chronic bronchitis. Studies have proven the binding modes of its chemical constituents for natural remedies of garlic against COVID-19[24].

Cardio protective activity of garlic

Garlic is a popular supplement considered a healthy choice for people who are looking to increase cardiovascular wellness. Approximately 4% of all cardiovascular disease patients and 30% of cardiovascular patients who use herbal supplements to treat cardiovascular ailments used to take garlic in their remedies. Indeed, as early as the 1920s and 1930s, numerous studies do bear beneficial cardiovascular effects of garlic. Garlic reduces cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutaryl-CoA. It has also been shown to inhibit LDL oxidation, platelet aggregation, arterial plaque formation, decrease homocysteine, lowers blood pressure, and increase microcirculation, which can helps in prevent diabetes, heart disease and dementia[10].

Both experimental and clinical studies on garlic and its different preparations demonstrate significant effects on cardiovascular diseases (CVDs) that includes lowering blood pressure, prevention of atherosclerosis, reduction of serum cholesterol and triglyceride, inhibition of platelet, aggregation, and increasing fibrinolytic activity. These favorable cardiovascular effects of garlic decrease the risk of peripheral arterial occlusive diseases, plasma viscosity, and unstable angina and increase the elasticity of blood vessels and capillary perfusion. Daily in taking of cloves of raw garlic bulb for 6 months shows an 80% reduction of serum thromboxane B2 in middle-aged men. In situ study in a rat model, showed that an overall antithrombotic effect of garlic due to modulation of fibrinolytic activity through increased plasminogen activation and thrombin inhibition[7,12,17,18]. Garlic and its preparations have been widely known for its preventive and treatment purposes of many cardiovascular diseases (CVDs) that include atherosclerosis (narrowing of the blood vessels), hyperlipidemia, thrombosis, and hypertension[12].

The positive effect of garlic on the circulatory system is extremely well documented and it has been proved to; lower blood pressure decreases platelet aggregation and lower serum triglycerides and LDL-cholesterol levels increase serum HDL-cholesterol and the process through which the body breaks up blood clots. And also, it stimulates the production of nitric oxide in the inside layer of blood vessel walls, a substance that helps them to relax. As a result of these beneficial actions, garlic helps to prevent arteriosclerosis and thereby reduces the risk of heart attack or stroke. Two or three cloves a day have cut the risk of subsequent heart attacks in half of the heart patients. Garlic's ability to reduce the number of free radicals in the bloodstream may be the reason for these beneficial effects of garlic[8].

Garlic and its derivatives have proven inhibition of platelet aggregation in vitro and in animals and reduction of platelet-dependent thrombus formation. Anti-platelet activity may be attributable to garlic constituents including adenosine, allicin, and paraffinic polysulfides19. Fibrinolytic activity has found that garlic increased fibrinolytic activity in healthy individuals as well as in acute myocardial infarction patients[20].

Platelet aggregation is a leading cause of thrombosis and myocardial infarction. The prostaglandin and prostacyclin produced by endothelial cells lining the blood vessels prevent adherence to the blood vessels. Therefore, disc-shaped blood platelets come into contact with foreign surfaces, collagen in the injured vessels wall, and form plaques that inhibit the flow of blood. This process is platelet activation. The stimulated platelets alternate their shape, put out pseudopodia, release their granules, and stick to other platelets, beginning the process of platelet aggregation. Studies have shown that fresh garlic, garlic powder, and garlic oil have great potential in inhibiting platelet aggregation. Several garlic compounds contribute to the anti-thrombotic effect. These effects appear to be important contributors to garlic's beneficial effects in atherosclerotic conditions[21,22].

Allicin is the main bioactive compound found in garlic which has beneficial effects on the cardiovascular system. From the pharmacokinetic reviews, allicin is known to be aquaphobic and can be willingly absorbed through the cell membrane without encouraging harm to the phospholipid bilayer and then rapidly absorbed to exert pharmacological

properties that are important to the cardiovascular system. It was found to provide cardio-protective effects by inducing vasorelaxation and alleviating various pathological conditions of the cardiovascular system, including cardiac hypertrophy, angiogenesis, platelet aggregation, hyperlipidemia, and hyperglycemia[23].

Conclusion

Since ancient period, garlic (Allium sativum. L) has been described to various pathological conditions. Biological active constituents of garlic contribute an energetic role in various disease conditions including COVID-19 infection. Furthermore, the study revealed the potential pharmacological activities against cardiovascular diseases and its consequences after COVID-19 infection. Garlic produces immunomodulatory properties with its contents and acts as an immunity booster. This review was concluded as Allium sativum acts as an immunomodulator and to minimize the consequences of cardiovascular ailments.

Reference

1. Marco C., Massimo C., Alessandro T., Wen-Can J., Cheng-Bin W and Sergio B., (2020). The COVID-19 pandemic. *Critical reviews in clinical laboratory sciences*;57(6): 365–388.
2. Amreen Z., Abdul M., Mursaleen N., Maryam Z., Yasra F. and Kehkashan., (2021). Implications of Unani medicine in the management of Covid-19: An overview. *International Journal of Unani and Integrative Medicine*; 5(1): 20-23.
3. Keri, Vishakh C. H., Amit K., Parul R. L., Brunda J., Pankaj W. and Naveet., (2020). Intricate interplay between Covid-19 and cardiovascular diseases, *Reviews in Medical Virology*, Rev Med Virol,Volume - 31, Issue – 4.
4. Giacomo R., Alessandro M., Valentina G., Marco B., Filippo L., Massimiliano M., Enzo G., Iside C., Matteo P., Laura G., Nicola U., Claudio R., Oscar M. E. and Cristina G. (2021). Covid and Cardiovascular Diseases: Direct and Indirect Damages and Future Perspective. High Blood Pressure and Cardiovascular Prevention https://doi.org/10.1007/s40292-021-00464-8
5. Mouna M., Norddine H. and Abdallah B., (2018). In Vitro and In Vivo Immunomodulator Activities of Allium sativum L. Evidence-Based, *Complementary and Alternative Medicine*, Volume 2018, Article ID 4984659,10 pages https://doi.org/10.1155/2018/4984659
6. Shabir A. B., Shameem A. R, Arsheed I., Haider A. and Naquibul I., (2020). Immunomodulators for Curtailing COVID-19: a Positive Approach. *Journal of drug delivery and therapeutics*; 10(3-s): 286-294.
7. Bhushan R. G., Minakshee G. N., Wrushali A. P., Ashish B. W., Jagdish V. M. and Ravindra L. B., (2021). *Allium sativum*, a potential phytopharmacological source of natural medicine for better health. *GSC Advanced research and reviews*; 06(03): 220–232.
8. Singh P., Singh J., Singh S. and Singh B. R., (2014). Medicinal values of Garlic (Allium sativum L.) in Human Life: An Overview. *Greener journal of agricultural sciences*; 4 (6): 265-280.
9. Londhe V. P., Gavasane A. T., Nipate S. S., Bandawane D. D. and N. Chaudhari P. D., (2011). Role of garlic (*Allium sativum*) in various diseases: an overview. *Journal of Pharmaceutical research and opinion*; 4 (2011): 129 – 134.
10. Dr. MdKhorshed A., Dr. MdObydul H. and Dr. MdShahab U., (2016). Medicinal plant Allium sativum = A Review. *Journal of Medicinal Plants Studies*; 4(6): 72-79.

11. Bhandari P.R., (2012) Garlic (Allium sativum L.): A review of potential therapeutic applications. *Int J Green Pharm*; 6: 118-29.
12. Shubha R. S. and Supriya S., (2017). Medicinal uses of garlic (allium sativum l.) In human health. The Journal of University Grants Commission; 6(1): 160-168.
13. Shakeel A. K., Mehwish J., Sadia K. and Sammia S., (2017). Medicinal Importance of Allium Species: A current review. *International Journal of Pharmaceutical Science and Research*; 2(3): 29-39.
14. Anushree R. and Ashwani K., (2014). Allium sativum - A Global Natural Herb with Medical Properties. *Journal Academica*; 4(1): 33-37.
15. Verma S. K., Rajeevan V., Jain P. and Bordia A., (2003). Effect of garlic (*Allium sativum*) oil on exercise tolerance in patients with coronary artery disease. *Indian Journal of Physiology and Pharmacology*; 49(1): 115-118.
16. Ana H. M., (2016). A Review of Medicinal Plants Used in Therapy of Cardiovascular Diseases. *International Journal of Pharmacognosy and Phytochemical Research*; 8(4): 572-591.
17. Singh R. N., Navneet K. and Pradeep K., (2019). Garlic (Allium sativum): Mankind's Health Superstar. *Interdisciplinary Journal of Contemporary Research*; 6(6): 93-98.
18. Bathaei F. S. and Akhondzadeh S., (2008) Cardiovascular Effects of Allium Sativum (Garlic): An Evidence-Based Review. J Tehran Heart Cent. 1; 3(1): 5-10.
19. Azene T. and Work M., (2015). Traditional Uses, Phytochemistry and Pharmacological Properties of Garlic (*Allium Sativum*) and its Biological Active Compounds; (1)5: 142-148.
20. Abdul N., Gazala F., Naziya N. and Aftab A. M., (2020). Pharmacological and therapeutic attributes of garlic (*Allium sativum* Linn.) with special reference to Unani medicine-A review. *Journal of medicinal plants studies*; 8(3): 06-09.
21. Manoranjan A. and Jaime A. T. D. S., (2010). Garlic (*Allium sativum*) and its beneficial effect on cardiovascular diseases – a review. *International journal of biomedical and pharmaceutical sciences*; 4(1): 1-20.
22. Sanjay K. B. and Subir K. M., (2002). Effect of garlic on cardiovascular disorders: a review. *Nutrition Journal*; 1(4): 1-14.
23. Suweesha A. and Dulan J., (2017). A review on garlic (*Allium sativum* L.) as a functional food. Journal of pharmacognosy and phytochemistry; 6(6): 1777-1780.
24. Deepti C., Bharti B. and Shridhar D., (2021). Beneficial role of Indian medicinal plants in COVID-19. *MGM Journal of Medical Sciences*; 8 (2): 166-170.