A Review of Formulation and Evaluation Sustain Release Tablet for the Treatment of Microbial Disease

Arun Kumar Sahu[1], Divyanshu Sahu[1], Mauli Singh[1], Ms. Anjali sahu[2], Dr. Gyanesh Sahu[2], Dr. Chanchal Deep Kaur[1].

1. Rungta Institute of Pharamaceutical Sciences, Bhilai

2. Rungta Institute of Pharamaceutical Sciences & Research, Bhilai

Abstract:

Garlic (Allium sativum L., Family Liliaceae) is a strong antimicrobial, antioxidant and anti-inflammatory agent. Aged Garlic has more antioxidant and antimicrobial properties compared to fresh garlic. Garlic essential oil is one of the natural antimicrobial Agent which has broad spectrum of inhibition against microbes. Throughout human history, garlic has been widely used. Allin is enzymatically converted to allicin, the main active ingredient in recently damaged garlic. Allicin has also been suggested as a substitute for antibiotics and a way to prevent thrush. Allicin bioavailability is being thoroughly investigated because of its high instability. Garlic powder tablets have been shown to release allicin under simulated gastrointestinal condition, but their quick disintegration has resulted in low allicin levels and less than alliinase protection.

Key words: Allium Sativa, Garlic Extract, Antimicrobial activity, aged garlic extract, Black garlic.

1. Introduction:

Illnesses brought on by pathogenic microorganisms like bacteria, viruses, fungi, and parasites are known as microbial diseases. These microbes infiltrate the human body, proliferate, and disrupt regular bodily processes, resulting in illness and infection. Contaminated food and water, airborne droplets, direct contact with infected people, or vectors like flies and mosquitoes are some of the ways that microbial pathogens can spread.Once within the body, these microorganisms either produce toxins or cause detrimental immune reactions that harm organs and tissues. The type of pathogen, the host's immune system, and environmental factors all affect how serious microbial illnesses are. Common viral illnesses include COVID-19 and influenza, bacterial illnesses like cholera and tuberculosis, fungal illnesses like candidiasis, and parasitic illnesses like malaria. Microbial diseases continue to be a major global health concern, especially in developing nations where their spread is facilitated by inadequate sanitation, unclean drinking water, and a lack of medical facilities. Antibiotics, antiviral medications, vaccines, and enhanced diagnostic methods are examples of medical science advancements that have significantly aided in the management of numerous microbial infections. However, new pathogens and antimicrobial resistance continue to present significant obstacles. Therefore, effective prevention and management of microbial diseases depend on maintaining good hygiene, sanitation, vaccination, and early diagnosis.

1.1 Types of Microbial disease:

- Bacterial Disease
- Viral Disease
- Fungal Disease
- Protozoan Disease
- Helminthic (parasitic worm) Disease

1.1 Bacterial Disease:

Infections brought on by dangerous bacteria that enter the human body and interfere with regular bodily processes are known as bacterial diseases. Contaminated food and water, the air, direct contact with infected people, and wounds are all ways that these bacteria can spread. Once inside the body, bacteria grow quickly and release toxins that harm tissues

and lead to disease. Pneumonia, cholera, typhoid fever, and tuberculosis are common bacterial illnesses. Fever, inflammation, pain, and weakness are possible symptoms. Antibiotics, which help kill or stop the growth of bacteria, can be used to treat the majority of bacterial infections. Preventing bacterial diseases requires good hygiene, immunization, safe food and water, and prompt medical attention.

Common bacterial disease are - Cholera, Tuberculosis, typhoid fever

Fig: Bacterial infection

1.2 Viral Disease:

Viral diseases are infections brought on by viruses, which are incredibly tiny infectious agents that can only grow inside a host's living cells. In order to proliferate, viruses infiltrate the body and frequently cause harm or even death to the host cells. The air, contaminated food and water, direct contact with infected people, and vectors like mosquitoes can all spread viral infections.
Influenza, measles, dengue, hepatitis, and COVID-19 are common viral illnesses. Depending on the virus, fever, exhaustion, coughing, body aches, and inflammation are common signs of viral diseases. Antibiotics cannot be used to treat viral diseases, in contrast to bacterial infections. Rather, they are managed with supportive therapies, vaccines, and antiviral drugs. Preventive measures include immunization and good hygiene, and avoiding contact with infected individuals play an important role in controlling viral diseases.

Fig: Viral infection

1.3 Fungal Disease:

Mycoviruses, another name for fungal viruses, are viruses that infect fungi. These viruses are frequently found in a variety of fungal species, and their genetic material is typically double-stranded RNA. The majority of fungal viruses do not exhibit overt symptoms in their host fungi, in contrast to many plant and animal viruses; however, some can inhibit fungal growth, virulence, and reproduction. Cell division, spore formation, or hyphal contact between fungi are the main ways that mycoviruses spread. They are crucial to the study of fungal biology and the management of disease.

Fungal viruses are sometimes employed as biological agents to lessen the pathogenicity of dangerous fungi that damage plants.

Fig: Fungal infection

1.4 Protozoan Disease:

Infections known as protozoan diseases are brought on by microscopic, single-celled organisms called protozoa. These organisms can be found in soil, water, or inside human and animal bodies. Insect bites, contaminated food or water, and direct contact with infected people are common ways that protozoan diseases are spread. Giardiasis, amoebiasis, and malaria are a few well-known protozoan illnesses. These infections can cause symptoms like fever, diarrhea, weakness, and abdominal pain by affecting various organs like the liver, blood, or intestines. In many developing nations, protozoan diseases pose a serious threat to public health, and managing and preventing them requires good sanitation, hygiene, and vector control.

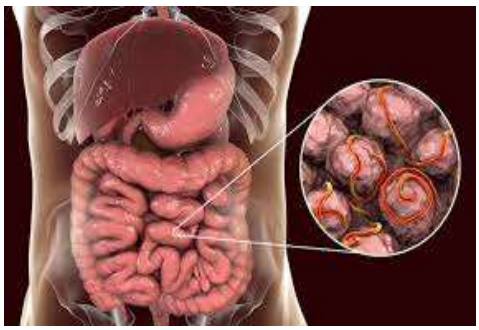

Fig: Protozoan infection

1.4 Helminthic Disease:

Helminthic diseases are infections caused by parasitic worms known as helminths. These worms live inside the human body, mainly in the intestines, and obtain nutrients from the host. Helminths are generally classified into three groups: nematodes (roundworms), cestodes (tapeworms), and trematodes (flukes). Infection usually occurs through contaminated food, water, soil, or poor hygiene practices. Common helminthic diseases include ascariasis, hookworm infection, and schistosomiasis. Symptoms may include abdominal pain, diarrhea, weakness, malnutrition, and anemia. Helminthic infections are more common in areas with poor sanitation and hygiene. Proper sanitation, safe food practices, and deworming medications help in prevention and treatment of these infections.

Fig: Helminthic infection

2. Mechanism of Action:

The main bioactive ingredient in garlic (Allium sativum), allicin, has broad-spectrum antibacterial activity against viruses, bacteria, fungi, and certain parasites. Its main mechanism is a chemical reaction with the thiol (-SH) groups found in proteins and enzymes in microorganisms. Because allicin is lipophilic, it is extremely reactive and can pass through microbial cell membranes. After entering the cell, it forms S-allylmercapto adducts by oxidizing cysteine residues in vital enzymes. Metabolic arrest results from this alteration's inactivation of important metabolic enzymes involved in DNA synthesis, energy production, and cell wall formation. Additionally, by changing the lipid composition and raising membrane permeability, allicin compromises the integrity of membranes, allowing essential intracellular components like proteins, ions, and ATP to seep out. It decreases virulence and biofilm formation in bacteria by blocking RNA synthesis and interfering with quorum sensing. Allicin produces reactive oxygen species (ROS) that harm proteins, lipids, and nucleic acids in fungi, impairing mitochondrial function and causing oxidative stress. Allicin targets several cellular pathways instead of just one, making it difficult for microbes to become resistant. In general, its antimicrobial action stems from oxidative damage, membrane disruption, enzyme inhibition, and interference with genetic processes, all of which ultimately result in the death of microbial cells.

3.Conclusion:

Pathogenic microorganisms, including bacteria, viruses, fungi, and parasites, are the cause of microbial diseases. Because of their rapid spread, mutation, and capacity to develop drug resistance, they continue to pose a serious threat to global health. Susceptibility is increased by inadequate hygiene, immunization, and compromised immunity. Although prevention and treatment have been greatly enhanced by developments in vaccines, antivirals, antibiotics, and diagnostic methods, public health is still at risk from newly emerging and re-emerging infections. Public awareness, rational drug use, early diagnosis, immunization, and hygiene are all necessary for effective control. In order to lower morbidity, mortality, and the socioeconomic burden globally, fighting microbial diseases necessitates concerted efforts in healthcare, research, and community involvement.

Reference:

1. Bjarnsholt, T.; Ciofu, O.; Molin, S.; Givskov, M.; Hoiby, N. Applying insights from biofilm biology to drug development—Can a new approach be developed? *Nat. Rev. Drug Discov.* 2013, 12, 791–808. DOI: https://doi.org/10.1038/nrd4000

2. Irie, Y.; Borlee, B.R.; O'Connor, J.R.; Hill, P.J.; Harwood, C.S.; Wozniak, D.J.; Parsek, M.R. Self-produced exopolysaccharide is a signal that stimulates biofilm formation in *Pseudomonas aeruginosa*. *Proc. Natl. Acad. Sci. USA* 2012, 109, 20632–20636. DOI: https://doi.org/10.1073/pnas.1217993109

3. Gupta, P.; Sarkar, S.; Das, B.; Bhattacharjee, S.; Tribedi, P. Biofilm, pathogenesis and prevention—A journey to break the wall: A review. *Arch. Microbiol.* 2016, 198, 1–15. DOI: https://doi.org/10.1007/s00203-015-1148-6

4. Costerton, J.W.; Geesey, G.G.; Cheng, K.J. How bacteria stick. *Sci. Am.* 1978, 238, 86–95. DOI: https://doi.org/10.1038/scientificamerican0178-86

5. Costerton, J.W.; Stewart, P.S.; Greenberg, E.P. Bacterial biofilms: A common cause of persistent infections. *Science* 1999, 284, 1318–1322. DOI: https://doi.org/10.1126/science.284.5418.1318

6. Donlan, R.M. Biofilms: Microbial life on surfaces. *Emerg. Infect. Dis.* 2002, 8, 881–890. DOI: https://doi.org/10.3201/eid0809.020063

7. Sutherland, I. Biofilm exopolysaccharides: A strong and sticky framework. *Microbiology* 2001, 147, 3–9. DOI: https://doi.org/10.1099/00221287-147-1-3

8. Singh, S.; Datta, S.; Narayanan, K.B.; Rajnish, K.N. Bacterial exopolysaccharides in biofilms: Role in antimicrobial resistance and treatments. *J. Genet. Eng. Biotechnol.* 2021, 19, 140. DOI: https://doi.org/10.1186/s43141-021-00242-y

9. Limoli, D.H.; Jones, C.J.; Wozniak, D.J. Bacterial extracellular polysaccharides in biofilm formation and function. *Microbiol. Spectr.* 2015, 3. DOI: https://doi.org/10.1128/microbiolspec.MB-0011-2014

10. Vandana; Das, S. Structural and mechanical characterization of biofilm-associated bacterial polymer in the emulsification of petroleum hydrocarbon. *3 Biotech* 2021, 11, 239. DOI: https://doi.org/10.1007/s13205-021-02792-7

11. Chen, M.Y.; Lee, D.J.; Tay, J.H.; Show, K.Y. Staining of extracellular polymeric substances and cells in bioaggregates. *Appl. Microbiol. Biotechnol.* 2007, 75, 467–474. DOI: https://doi.org/10.1007/s00253-006-0824-8

12. Hussain, M.; Wilcox, M.H.; White, P.J. The slime of coagulase-negative staphylococci: Biochemistry and relation to adherence. *FEMS Microbiol. Rev.* 1993, 10, 191–207. DOI: https://doi.org/10.1111/j.1574-6976.1993.tb00015.x

13. Costerton, J.W.; Lewandowski, Z.; Caldwell, D.E.; Korber, D.R.; Lappin-Scott, H.M. Microbial biofilms. *Annu. Rev. Microbiol.* 1995, 49, 711–745. DOI: https://doi.org/10.1146/annurev.mi.49.100195.003431

14. Stoodley, P.; Lewandowski, Z.; Boyle, J.D.; Lappin-Scott, H.M. Oscillation characteristics of biofilm streamers in turbulent flowing water as related to drag and pressure drop. *Biotechnol. Bioeng.* 1998, 57, 536–544. DOI: https://doi.org/10.1002/(SICI)1097-0290(19980305)57:5<536::AID-BIT7>3.0.CO;2-P

15. Chen, M.; Yu, Q.; Sun, H. Novel strategies for the prevention and treatment of biofilm related infections. *Int. J. Mol. Sci.* 2013, 14, 18488–18501. DOI: https://doi.org/10.3390/ijms140918488

16. Chen, M.; Yu, Q.; Sun, H. Novel strategies for the prevention and treatment of biofilm related infections. *Int. J. Mol. Sci.* 2013, 14, 18488–18501. DOI: https://doi.org/10.3390/ijms140918488

17. Paharik, A.E.; Horswill, A.R. The Staphylococcal Biofilm: Adhesins, Regulation, and Host Response. *Microbiol. Spectr.* 2016, 4. DOI: https://doi.org/10.1128/microbiolspec.VMBF-0022-2015

18. Zaborowska, M.; Tillander, J.; Branemark, R.; Hagberg, L.; Thomsen, P.; Trobos, M. Biofilm formation and antimicrobial susceptibility of staphylococci and enterococci from osteomyelitis associated with percutaneous orthopaedic implants. *J. Biomed. Mater. Res. B Appl. Biomater.* 2017, 105, 2630–2640. DOI: https://doi.org/10.1002/jbm.b.33764

19. Khan, M.S.; ur Rehman, S.; Ali, M.A.; Sultan, B.; Sultan, S. Infection in orthopedic implant surgery, its risk factors and outcome. *J. Ayub Med. Coll. Abbottabad* 2008, 20, 23–25. DOI: Not available

20. Cerca, N.; Pier, G.B.; Vilanova, M.; Oliveira, R.; Azeredo, J. Quantitative analysis of adhesion and biofilm formation on hydrophilic and hydrophobic surfaces of clinical isolates of *Staphylococcus epidermidis*. *Res. Microbiol.* 2005, 156, 506–514. DOI: https://doi.org/10.1016/j.resmic.2005.01.007

21. Rahim, M.I.; Rohde, M.; Rais, B.; Seitz, J.M.; Mueller, P.P. Susceptibility of metallic magnesium implants to bacterial biofilm infections. *J. Biomed. Mater. Res. A* 2016, 104, 1489–1499. DOI: https://doi.org/10.1002/jbm.a.35686

22. Koseki, H.; Yonekura, A.; Shida, T.; Yoda, I.; Horiuchi, H.; Morinaga, Y.; Yanagihara, K.; Sakoda, H.; Osaki, M.; Tomita, M. Early staphylococcal biofilm formation on solid orthopaedic implant materials: In vitro study. *PLoS ONE* 2014, 9, e107588. DOI: https://doi.org/10.1371/journal.pone.0107588

23. Glage, S.; Paret, S.; Winkel, A.; Stiesch, M.; Bleich, A.; Krauss, J.K.; Schwabe, K. A new model for biofilm formation and inflammatory tissue reaction: Intraoperative infection of a cranial implant with *Staphylococcus aureus* in rats. *Acta Neurochir.* 2017, 159, 1747–1756. DOI: https://doi.org/10.1007/s00701-017-3264-0

24. Oliveira, W.F.; Silva, P.M.S.; Silva, R.C.S.; Silva, G.M.M.; Machado, G.; Coelho, L.; Correia, M.T.S. *Staphylococcus aureus* and *Staphylococcus epidermidis* infections on implants. *J. Hosp. Infect.* 2018, 98, 111–117. DOI: https://doi.org/10.1016/j.jhin.2017.11.008

25. Zheng, Y.; He, L.; Asiamah, T.K.; Otto, M. Colonization of medical devices by staphylococci. *Environ. Microbiol.* 2018, 20, 3141–3153. DOI: https://doi.org/10.1111/1462-2920.14129

26. Bowen, A. C., Mahé, A., Hay, R. J., et al.
The Global Epidemiology of Impetigo: A Systematic Review of the Population Prevalence of Impetigo and Pyoderma.

27. Gershon, A. A., Takahashi, M., Seward, J. F.*Varicella vaccine.*The Lancet, 2014; 383(9927):1535–1543.

28. Griffiths, C. E. M., & Barker, J. N. W. N.*Pathogenesis and clinical features of psoriasis.*
The Lancet, 2007; 370(9583):263–271.

29. Bethony, J., Brooker, S., Albonico, M., et al. *Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm.*The Lancet, 2006; 367(9521):1521–1532.

30. Michael, E., Bundy, D. A. P., & Grenfell, B. T. *Re-assessing the global prevalence and distribution of lymphatic filariasis.* Parasitology, 1996;113(4):409–428.