IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Review

Probiotics as Promising Immunomodulatory Agents to Prevent COVID-19 Infection: A Narrative Review

Muhammad Luthfi Adnan,[1] Miranti Dewi Pramaningtyas.[2]

Abstract

After the outbreak in December 2019, Coronavirus Disease (COVID-19) has become a global health problem because of its rapid spread throughout the world. To date, there are no effective therapies to treat or prevent COVID-19 infection. Probiotic bacteria are widely used to prevent gastrointestinal infections by modulating intestinal microbiota. Therefore, this literature review focuses on the potential possessed by probiotic bacteria for the prevention of future COVID-19 infections. Information was extracted from PubMed and Google Scholar using the keywords: "COVID-19", "immunomodulator", "inflammation", and "probiotic" and synthesized into this narrative review. The results showed that probiotic bacteria have immunomodulatory activity that can increase immunity against pathogens by regulating the immune system through modulation of intestinal microbiota and interactions with the lymphatic system in the digestive tract. The ability of the immune system regulation by probiotic bacteria has the effect of increasing the body's defense mechanisms against pathogens that infect the respiratory tract. However, further evidence is still needed regarding the effect of probiotic immunomodulators in combating future COVID-19 infections.

Key Words: COVID-19; Immune system; Inflammation; Probiotics (Source: MeSH-NLM).

Introduction

Since its appearance in December 2019 in Wuhan, China, Coronavirus Disease (COVID-19) has become a worldwide pandemic by infecting more than 43,000 people in 28 countries as of February 11, 2020 and becoming a health problem in many countries. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes COVID-19 and can be transmitted through patient droplets or direct contact with COVID-19 patients.[1] The SARS-CoV-2 virus is a type of virus of the genus β-coronavirus that is enveloped in a non-segmented positive-sense RNA virus.[2] The SARS-CoV-2 virus has the same genus as SARS-CoV, known for the SARS outbreak in 2003, and the Middle East respiratory syndrome coronavirus (MERS-CoV) which can cause deadly respiratory infections.[2]

Symptoms of COVID-19 patients include symptoms similar to influenza infections such as fever, coughing, muscle aches and dyspnea.[3] Treatment for COVID-19 patients is still limited to giving symptomatic therapy to patients. Providing care to patients is done to prevent complications that arise. Some of the treatments that are often used include the use of invasive mechanical ventilation, systemic corticosteroids and antiviral therapy. The most common complications that arise are acute respiratory distress syndrome (ARDS), anemia, acute heart injury and secondary infection.[3] However, some of the uses of the treatment are still unclear as to their effectiveness and there are currently no effective drugs for treating COVID-19.[3]

Treatment through immune system modulation has attracted much attention because it initiates the body's immune response to fight bacterial and viral infections.[4] The use of many immunomodulating agents was developed to initiate the body's immune system against infection and reduce the risk of damage to the host due to the activity of the immune response from proinflammatory cytokines. With research on vaccines to prevent COVID-19 still in development stages, the use of immunomodulators in modulating the immune system may be useful for pathology related to viral infections.[4]

Recent studies have shown the immunomodulatory effects of probiotic bacteria.[5] Probiotics are defined as being "living microorganisms which, when consumed in sufficient quantities, provide health benefits to the host".[5] Probiotics are widely used in the fermented food processing industry such as cheese, yoghurt or as supplements. Many studies show the health benefits of probiotics, one of which is to modulate the immune system to prevent viral infections through modulation of probiotic bacteria with the immune system in the intestinal mucosa.[5]

The purpose of this literature review is to discuss the immunomodulatory effects and the potential of probiotics to prevent COVID-19 infection.

Methods

Literature Search Strategy

A comprehensive electronic literature search was carried out using search tools from Medline (PubMed) and Google Scholar to identify relevant publications regarding COVID-19, immunomodulators, and probiotics. Database parameters performed using keywords include "COVID-19", "immunomodulator", "inflammation", and "probiotic". The literature used is full-text written in English and published within the last 10 years. The literature used consists of keywords that include "COVID-19", "immunomodulator", "inflammation", and "probiotic".

Eligibility Criteria

Excluded articles did not have a full-text publication or were not written in English. Inclusion criteria parameters include full-text in English,

1 Medical Student, Universitas Islam Indonesia, Sleman, Indonesia.
2 Master of Science, Department of Physiology, Universitas Islam Indonesia, Sleman, Indonesia

About the Author: *Muhammad Luthfi Adnan is currently a 4th year medical student of Faculty of Medicine, The Universitas Islam Indonesia of a 6-years medical program. His several research studies have been published at the 7th International Congress on Lipid Metabolism & Atherosclerosis (ICoLA 2018) in Seoul, South Korea, the Indonesia International (Bio)Medical Students' Congress (INAMSC) 2019 in Jakarta, Indonesia and the 30th European Student Conference (ESC) 2019 in Berlin, Germany.*

Correspondence:
Muhammad Luthfi Adnan
Address: Kaliurang St No.Km. 14,5, Krawitan, Umbulmartani, Ngemplak, Sleman Regency, Indonesia.
Email: 16711133@students.uii.ac.id

Editor: Francisco Javier Bonilla-Escobar & Mihnea-Alexandru Găman
Student Editors: Andrew Stanton Kucey
Submission: Apr 7, 2020
Revisions required: Apr 7, 2020; Apr 27, 2020; May 5, 2020
Received in revised form: Apr 14, 2020; Apr 29, 2020; May 6, 2020
Acceptance: May 6, 2020
Publication: May 8, 2020
Process: Peer-reviewed

published less than 10 years ago, articles have the keywords "COVID-19", "immunomodulator", "inflammation", and "probiotic", articles studying COVID-19, probiotics, probiotic activity as an immunomodulator, and probiotic immunomodulatory activity in the respiratory tract.

Results & Discussion

Pathogenesis of COVID-19

The SARS-CoV-2 virus, is closely related to the SARS-CoV-1 virus that targets angiotensin-converting enzyme 2 (ACE2) cells as receptor cells in host targeting.[6] The virus has an incubation period of 2-14 days during which the host is infectious.[6] The greatest burden of the virus is contained in the lung organs, causing symptoms similar to pneumonia with characteristic changes in lung opacity on CT imaging. Other symptoms of COVID-19 that are similar to that of pneumonia include fever, cough, shortness of breath and sore throat.[6] Some other symptoms of COVID-19 include gastrointestinal symptoms such as diarrhea, nausea and vomiting. This may be due to ACE2 receptors also found in intestinal epithelial cells. The finding of SARS-CoV-2 nucleic acid in a patient stool reveals a potential route for viral infection through feces.[7]

COVID-19 also impacts the body's immune system during the infection stage. For example, an increase in the ratio of neutrophils to lymphocytes (NLR) and T lymphopenia and a decrease in CD4 + T cells are found in patients with COVID-19. These findings indicate the presence of immune system dysregulation induced by viral activity targeting T lymphocytes. NLR, which is a systemic infection marker, was also found as part of a proinflammatory cytokine storm (TNF-α, IL-1, IL-6) and chemokine (IL-8) which correlated with the severity of COVID-19 patients.[8] The cytopathic effect of proinflammatory cytokine activity results in systemic inflammation which has the potential to cause death.[8]

The emergence of cytokine storms is in this case an overzealous immune response against viral infections. Cytokine storms are a form of immune homeostasis disorder and self-tolerance through interference with regulatory T cells that play a role in the control of systemic and tissue-specific autoimmunity. The high level of proinflammatory signals in cytokine storms results in collateral host tissue damage.[8] Uncontrolled cytokine storm activity in the immune system's reaction to a viral infection affects the process of remodeling airway tissue which risks increasing the severity of infection and damage to important organs causing a risk of death.[9,10]

Potential Health Effects of Probiotics

Probiotics are types of bacteria that can provide health benefits to the host. Some characteristics possessed by probiotic bacteria are (1) having the ability of probiotic bacteria to survive and reproduce in the intestine; (2) having benefits for the host through growth in the host body; (3) being non-pathogenic or toxic; (4) protect against pathogens (*i.e.*, bacteria, viruses or fungi); and (5) are resistant to transfer of antibiotic resistance. Probiotic bacteria of different strains can provide different benefits to the health of the host.[11]

Bacteria from the genus *Lactobacillus* and *Bifidobacterium* are widely used probiotics known as probiotic lactic acid bacteria (LAB). Probiotics work in part by binding to the intestinal mucosa and producing antimicrobial compounds, increasing the defense function of the intestinal barrier, and modulating immunity against intestinal pathogen infections.[12] Probiotics have an important role to play in fighting diarrhea, antibiotic-related diarrhea, prevention of colorectal cancer, and treatment agents for gastroenteric infections caused by various pathogens such as *Escherichia coli*, *Bacillus, Salmonella, Shigella*, *Vibrio cholera, Klebsiella* and *Pseudomonas*.[12]

Lactobacillus and *Bifidobacterium* bacteria have the structure of lipoteichoic acid (LTA), surface layer associated proteins (SLAPs) and mucin binding proteins (Mubs) that bind to glycocalyx in the intestinal epithelial layer.[13] Glycocalyx contains glycolipids and glycoproteins that interact with the structure layers of LTA, SLAPs and Mubs from probiotic bacteria. The composition between the structure of probiotic bacteria and intestinal mucosa has hydrophobic and adhesion properties that can synthesize the extracellular matrix components of fibronectin, collagen, and laminin.[13,14] Through the mechanism of adhesion on the surface of the intestinal epithelium, probiotic bacteria exert an increased effect on the integrity of the intestinal barrier and result in maintenance of immune tolerance, decreases the translocation of pathogenic bacteria across the intestinal mucosa, and prevent phenotypic changes due to diseases such as gastrointestinal infections, irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).[15] The immune tolerance response from the interaction between the intestinal mucosa and the probiotic bacteria induces a balance in the microflora in the intestinal environment.[16]

In probiotic bacteria, antitoxins can produce a serine protease and phosphatase that degrades toxins from *E. coli* and *Clostridioides difficile,* as well as displaying the ability to destroy intersections between pathogenic bacteria with epithelium and viruses with enterocytes.[17] Probiotic bacteria also can interact with other microbiota in the intestinal environment and can rehabilitate intestinal microbiota balance in diarrheal infection conditions.[17]

Beyond the microbiome homeostasis effects of probiotics, their ability to fermentation non-digestible polysaccharides is an important attribute which is thought to affect host metabolism in a meaningful manner. Disorders caused by intestinal microbiota dysbiosis correlate with the onset of hypertension, obesity, and metabolic syndrome.[18] With this interaction activity between intestinal microbiota and host metabolism, probiotic bacteria may have potential as antihypertensive and hypocholesterolemic interventions in metabolic syndrome.[18,19]

Probiotic Immunomodulatory Activity

Some probiotic bacteria display an immunomodulatory function, regulating the production of two types of cytokines namely anti-inflammatory cytokines such as interleukin-10 (IL-10) and proinflammatory cytokines such as interleukin-6 (IL-6). In addition, the immunomodulatory activity of probiotics also works by balancing the T-helper (T_h)1 / T_h2 immune response through interactions on antigen-presenting cells (APC) in lymphocyte-dense Peyer's patches on part of the intestinal epithelium.[20,21] The ability to initiate immune system modulation from probiotics may minimize epithelial injury resulting from the inflammatory response. [22]

The immunobiotic ability of *Lactobacillus* and *Bifidobacterium* bacteria through the production of lactic acid can modulate the immune response in the intestinal mucosa by interacting with Toll-like Receptor 2 (TLR2).[21] Probiotic interactions in the intestinal environment induce a T_h1 immune response that results in the production of interferon cytokines (IFN)-β and activate the bactericidal activity of macrophages.[23] The host of intestinal probiotic interactions triggers lymphatic maturation, epithelial repair through endotoxin signaling and promotes intestinal microbial mucosal tolerance.[24]

The ability of probiotic bacteria to modulate the host immune system through activation of natural killer cells, dendritic cells, intraepithelial lymphocyte cells and macrophages that have an important role in the innate immune system. Probiotic bacteria work by binding to aryl hydrocarbon receptors and activating macrophages and dendritic cells so that there is a stimulus to release TNF-α proinflammatory cytokines from epithelial cells and enhance the immune system. Research conducted by Villena *et al.* (2014) showed the defense mechanism of intestinal cells through the administration of probiotic bacteria through immunoregulators with the production of proinflammatory cytokines such as IL-6 and TNF-α in response to pathogens and the production of anti-inflammatory cytokines IL-10.[21]

Besides their immunomodulator role in the immune system, probiotics have anti-inflammatory potential through bioactive peptide compounds.[25] The compounds produced from these probiotic bacteria can restore intestinal permeabilities. Also, the probiotic activity suppresses the activity of T_h2 cells to produce IgE, interleukin-4 (IL-4) and IL-13 preventing asthma and allergic reactions.[25,26] Anti-inflammatory activity in the lungs plays a role in decreasing lung inflammation such as decreasing the levels of proinflammatory cytokines and C-reactive protein (CRP).[27]

Probiotic bacteria produce metabolites in the form of short-chain fatty acids (SCFA) consisting of acetate, propionate, and butyrate which are widely present in the colon epithelium. Parts of the butyrate are used as energy by the colonocytes while the rest of the other SCFA are absorbed into the portal circulation through the intestine.[28] The SCFA metabolite binds specifically to the G-protein-coupled receptor 43 / free fatty acid receptor 2 (GPR43 / FFAR2), GPR41 / FFAR3 and GPR109A. Interactions on these receptors result in the development of macrophages and increase the differentiation of dendritic cell precursors that can migrate to the lungs and change the regulator T cells with T_h2 cells.[29]

Interaction between the intestinal relationship with the lungs is mediated by the lymphatic system through the TLR4 dependency mechanism and produces IgA associated with gut-associated lymphoid tissue (GALT).[30] These probiotic bacteria will induce regulatory T cells and initiate T helper 17 (T_h17) production and T_h1 immune memory response.[30] The circulation of the lymphatic system from the gut-lung axis enables T_h17 cells to be transferred from the intestinal mucosa to the bronchial epithelial mucosa in lymph nodes in the airways. Besides suppressing the activity of pathogens that attack the respiratory system, the activity of probiotic interactions in the intestine with the airways prevents damage to the airway tissue by controlling the defense of the host immune system in the lungs.[30]

Immunomodulatory Effect from Probiotic Against Covid-19

COVID-19 infection attacks the lung tissue and activates inflammation in the airways.[31] The results from serum sampling of COVID-19 patients has shown an increase in the number of proinflammatory cytokines such as IL-1B, IL-6, IL-15, IL-15, IL-17 IFN-γ and TNF-α.[31] This leads to the emergence of cytokine storms and correlates with the severity of the disease.[31] The emergence of cytokine storms can lead to pulmonary fibrosis and damage to respiratory organs.[32] This inflammatory stimulus-response may be due to the activation of the T_h1 cell response.[33]

The potential effect of probiotics in influencing the activity of cytokine storms due to COVID-19 infection may be through interactions in the gut microbiota with the immune system.[34] Disruption to the intestinal microbiota environment results in an imbalance of T_h1 / T_h2 cells, which results in the production of proinflammatory cytokine storms in the lungs.[34] Through modulation of intestinal microbiota, there is a shift in the balance between T_h1 / T_h2 cells which could theoretically reduce the inflammatory response in the respiratory tract, thereby reducing the severity of disease.[34]

The activity of modulating intestinal microbiota through administration of probiotic bacteria has an impact on controlling the lung immune system response to viral infections. Probiotic bacteria can reduce the excessive inflammatory response in the face of viral infections by influencing T cells to produce IFN-γ.[35] The activity of probiotic bacteria in regulating the immune system is carried out through interactions with regulatory T cells in Peyer's patches on the intestinal surface thereby preventing excessive cytokine storm activity in fighting viral infections.[36]

In addition to stimulating the regulation of T_h1 / T_h2 cell balance, the activity of probiotic bacteria can initiate a defense system in the airway mucosa.[37] As a result of the response of proinflammatory cytokines in the airway mucosal epithelium, airway remodeling activity causes narrowing of the airways. Airway remodeling arising from pro-inflammatory cytokines can lead to breathing difficulties and a worsening of patient condition.[38] Prevention of airway remodeling due to viral infection creates therapeutic targets for probiotic bacteria to potentially prevent worsening the condition of patients in COVID-19.[39,40]

Conclusion

With the development of therapies and vaccines for the prevention of COVID-19 infection still ongoing, the immunomodulatory effects of probiotic bacteria may have the potential to help with COVID-19 infection. The ability of probiotic bacteria to regulate the gut microbiota may in turn modulate immune system in a manner which could be useful in COVID-19. The findings from previous studies still need further research on broader subject matter to ensure the safety of therapy, so that the immunomodulatory potential of the probiotic bacteria can be maximized in the fight against COVID-19 infection in the future.

References

1. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents. 2020 Mar;55(3):105924.
2. Guo Y-R, Cao Q-D, Hong Z-S, et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. Mil Med Res. 2020 Mar;7(1):1-10.
3. Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. J Med Virol. 2020 Feb:0-1.
4. Malemud CJ. Immunomodulators in Autoimmunity and Viral Infections. J Clin Cell Immunol. 2018 Jan;09(01).
5. Kanauchi O, Andoh A, AbuBakar S, Yamamoto N. Probiotics and Paraprobiotics in Viral Infection: Clinical Application and Effects on the Innate and Acquired Immune Systems. Curr Pharm Des. 2018;24:710-717.
6. Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. Asian Pacific J allergy Immunol. 2020 Mar;38(1):1-9.
7. Jin X, Lian JS, Hu JH, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut. 2020:1-8.
8. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clin Infect Dis. 2020 Mar.
9. Mahallawi WH, Khabour OF, Zhang Q, Makhdoum HM, Suliman BA. MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile. Cytokine. 2018 Jan;104:8-13.
10. Raoult D, Zumla A, Locatelli F, Ippolito G, Kroemer G. Coronavirus infections: Epidemiological, clinical and immunological features and hypotheses. Cell Stress. 2020 Mar;4(4):66-75.
11. Lehtoranta L, Pitkäranta A, Korpela R. Probiotics in respiratory virus infections. Eur J Clin Microbiol Infect Dis. 2014 Aug;33(8):1289-1302.
12. Mohanty D, Ray P. Evaluation of probiotic and antimicrobial properties of lactobacillus strains isolated from dairy products. Int J Pharm Sci. 2016 Oct;8(11):230-234.
13. Monteagudo-Mera A, Rastall RA, Gibson GR, Charalampopoulos D, Chatzifragkou A. Adhesion mechanisms mediated by probiotics and prebiotics and their potential impact on human health. Appl Microbiol Biotechnol. 2019 Aug;103(16):6463-6472.
14. Garcia-Gonzalez N, Prete R, Battista N, Corsetti A. Adhesion properties of food-associated lactobacillus plantarum strains on human intestinal. Front Microbiol. 2018 Oct;9:1-11.
15. Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: Mechanisms of intestinal immunomodulation and neuromodulation. Therap Adv Gastroenterol. 2013 Jan;6(1):39-51.
16. Zhang C xing, Wang H yu, Chen T xin. Interactions between Intestinal Microflora/Probiotics and the Immune System. Biomed Res Int. 2019 Nov;2019.
17. McFarland L V. Systematic review and meta-analysis of saccharomyces boulardii in adult patients. World J Gastroenterol. 2010 May;16(18):2202-2222.
18. Arora T, Singh S, Sharma RK. Probiotics: Interaction with gut microbiome and antiobesity potential. Nutrition. 2013 Apr;29(4):591-596.
19. Bellikci-Koyu E, Sarer-Yurekli BP, Akyon Y, et al. Effects of regular kefir consumption on gut microbiota in patients with metabolic syndrome: A parallel-group, randomized, controlled study. Nutrients. 2019 Sep;11(9):1-23.
20. Lazarenko LM, Babenko LP, Bubnov R V, Demchenko OM, Zotsenko VM, Boyko N V. Imunobiotics are the novel biotech drugs with antibacterial and immunomodulatory properties. Mikrobiol Zh. 2017;7(1):66-75.
21. Villena J, Chiba E, Vizoso-Pinto MG, et al. Immunobiotic Lactobacillus rhamnosus strains differentially modulate antiviral immune response in porcine intestinal epithelial and antigen presenting cells. BMC Microbiol. 2014 May;14(1):1-14.
22. Tada A, Zelaya H, Clua P, et al. Immunobiotic Lactobacillus strains reduce small intestinal injury induced by intraepithelial lymphocytes after Toll-like receptor 3 activation. Inflamm Res. 2016 Oct;65(10):771-783.
23. Zhang H, Yeh C, Jin Z, et al. Prospective study of probiotic supplementation results in immune stimulation and improvement of upper respiratory infection rate. Synth Syst Biotechnol. 2018 Jun;3(2):113-120.
24. Dickson RP, Erb-Downward JR, Huffnagle GB. The role of the bacterial microbiome in lung disease. Expert Rev Respir Med. 2013 Jun;7(3):245-257.
25. Rosa DD, Dias MMS, Grześkowiak ŁM, Reis SA, Conceição LL, Peluzio MDCG. Milk kefir: Nutritional, microbiological and health benefits. Nutr Res Rev. 2017 Jun;30(1):82-96.
26. Oeser K, Maxeiner J, Symowski C, Stassen M, Voehringer D. T cells are the critical source of IL-4/IL-13 in a mouse model of allergic asthma. Allergy Eur J Allergy Clin Immunol. 2015 Nov;70(11):1440-1449.
27. Li B, Zheng J, Zhang X, Hong S. Probiotic Lactobacillus casei Shirota improves efficacy of amoxicillin-sulbactam against childhood fast breathing pneumonia in a randomized placebo-controlled double blind clinical study. J Clin Biochem Nutr. 2018 Nov;63(3):233-237.
28. Natarajan N, Pluznick JL. From microbe to man: The role of microbial short chain fatty acid metabolites in host cell biology. Am J Physiol - Cell Physiol. 2014 Dec;307(11):C979-C985.
29. Shukla SD, Budden KF, Neal R, Hansbro PM. Microbiome effects on immunity, health and disease in the lung. Clin Transl Immunol. 2017 Mar;6(3):e133-12.
30. He Y, Wen Q, Yao F, Xu D, Huang Y, Wang J. Gut–lung axis: The microbial contributions and clinical implications. Crit Rev Microbiol. 2017 Feb;43(1):81-95.
31. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Jan;395(10223):497-506.
32. Tisoncik JR, Korth MJ, Simmons CP, Farrar J, Martin TR, Katze MG. Into the Eye of the Cytokine Storm. Microbiol Mol Biol Rev. 2012 Mar;76(1):16-32.
33. Raphael I, Nalawade S, Eagar TN, Forsthuber TG. T cell subsets and their signature cytokines in autoimmune and inflammatory diseases. Cytokine. 2015 Jul;74(1):5-17.
34. Qian LJ, Kang SM, Xie JL, et al. Early-life gut microbial colonization shapes Th1/Th2 balance in asthma model in BALB/c mice. BMC Microbiol. 2017 Jun;17(1):1-8.
35. Grayson MH, Camarda LE, Hussain SRA, et al. Intestinal microbiota disruption reduces regulatory T cells and increases respiratory viral infection mortality through increased IFN γ production. Front Immunol. 2018 Jul;9(JUL):7-9.
36. Mortaz E, Adcock IM, Folkerts G, Barnes PJ, Paul Vos A, Garssen J. Probiotics in the management of lung diseases. Mediators Inflamm. 2013 May;2013.
37. Vareille-Delarbre M, Miquel S, Garcin S, et al. Immunomodulatory effects of lactobacillus plantarum on inflammatory response induced by klebsiella pneumoniae. Infect Immun. 2019 Oct;87(11).
38. Wu CT, Chen PJ, Lee YT, Ko JL, Lue KH. Effects of immunomodulatory supplementation with Lactobacillus rhamnosus on airway inflammation in a mouse asthma model. J Microbiol Immunol Infect. 2016 Oct;49(5):625-635.
39. Kuo C, Lim S, King NJC, et al. Rhinovirus infection induces expression of airway remodelling factors in vitro and in vivo. Respirology. 2011 Feb;16(2):367-377.
40. Azad MAK, Sarker M, Wan D. Immunomodulatory Effects of Probiotics on Cytokine Profiles. Biomed Res Int. 2018 Oct;2018.

Acknowledgments

None.

Conflict of Interest Statement & Funding

The Authors have no funding, financial relationships or conflicts of interest to disclose.

Author Contributions

Conceptualization: MLA. Methodology: MLA. Software: MLA. Validation: MLA. Formal Analysis: MLA. Data Curation: MLA. Investigation: MLA. Resources: MLA. Writing – Original Draft: MLA. Writing – Review & Editing: MLA. Visualization: MLA. Supervision: MDP. Project Administration: MLA. Funding Acquisition: MLA.

Cite as:

Adnan ML, Pramaningtyas MD. Probiotics as Promising Immunomodulatory Agents to Prevent COVID-19 Infection: A Narrative Review. Int J Med Students. 2020 May-Aug;8(2):121-5.

ISSN 2076-6327

This journal is published by the University Library System, University of Pittsburgh as part of the Digital Publishing Program and is co-sponsored by the University of Pittsburgh Press.

ULS