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Probiotic Containing Foods in Military Dining: A Systematic Review

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ABSTRACT

Probiotics are known to impact positively on one's health, but this statement may have many concerns and challenges especially when it comes to military dining. The purpose of this review is to determine whether there is scientific research based justification to the recommend promotion of probiotic containing food(s) for service personal consumption. Several research findings have shown its beneficial effect on various conditions such as respiratory tract infections, gastro-intestinal diseases such as infectious diarrhoea, as well as for treating nosocomial infections when admitted to ICU. Peer reviewed literature was searched to identify original research related to the efficacy of pro/pre-biotic containing food(s) in prophylaxis or treatment of several service related ailments *viz.*, acute infectious diarrhoea, depression, service related GI and liver diseases, irritable bowel syndrome, respiratory tract infections, Allergic rhinitis, dental health issues and female urogenital conditions. Available scientific evidence can be wisely used by the practitioners for different conditions keeping in mind the probiotic strain, dose, and method of delivery as the effect is not always the same in every person.

Keywords: Probiotics; Infection; Gut microbiota; Multidrug resistance

1. INTRODUCTION

The human gut harbours around 40 trillion microbes, which is more than the number of cells in the human body, and is dominated by two broad phylogenetic groups namely Bacteroidetes and Firmicutes accounting to almost 90 per cent of the total microbiota in the gut[1]. These groups collectively encode over 100-fold more genes than the human genome. Over 316 million microbiome-encoded genes are known to be present when observed in the human microbiome[2]. These genes code for proteins that are involved in the biosynthesis of vitamins and isoprenoids through the 2-methyl-D-erythritol 4-phosphate pathway, metabolism of amino acids and glycans, metabolism of xenobiotics, etc.[3]. Further, it has been observed that the obese individuals have the gut microbiota composition that harvests more energy, leading to storage of the excess energy as more complex lipids in adipose tissue[4]. Hence, the alteration of the normal gut microbiota can bring about subtle changes in one's physiology. To investigate the presence and functioning of the microbes residing in the gut, the NIH project named Human microbiome Project (HMP) was initiated and conducted in two phases. The first phase was to identify and characterise human microbial flora[5], while the second phase was to elucidate the roles of microbes in health and diseases. It included microbiome dynamic changes studies and host under three circumstances: pregnancy and preterm birth; inflammatory bowel illnesses; and stressors that affect prediabetes individuals[6]. The key findings for phase two led people to rethink how the microbes present in the gut can be utilised to treat individuals with different illnesses using the microbes present in the healthy individuals. Since then various efforts have been made to treat people with certain diseases such as severe, refractory or recurrent *Clostridium difficile* (*C. difficile*) infection, Crohns's disease, autism, and other gastrointestinal problems using Fecal microbiota transplant (FMT) or what is commonly called as stool transplantation[7-9]. The gut bacteria present in the stool sample of a healthy donor is administered to the patients through nasogastric and nasoduodenal tubes, or through a colonoscope or as a retention enema. This has shown to be effective in 85-90 per cent of the patients who are suffering from antibiotic-resistant *C. difficile* infection and those who suffer from recurrent attacks of the same due to antibiotic usage[10]. Due to increased awareness about the gut health and the link between gut microbiome and the host, much research has been carried out in this field of science.

The story of probiotics started when Elie Metchnikoff, a Nobel laureate and a professor at the Pasteur Institute in Paris, found out that Bulgarians who drank fermented milk lived longer as compared to the people in France[11]. This inspired him to take up this work on probiotics further wherein he also said that animals would not be viable without their associated microbes[12]. Table 1 enlists the chronology of events in the evolution of probiotics. The term 'probiotic' was first used by the German scientist Werner Kollath in 1953 and defined as

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Table 1. History and origin of some fermented foods

Food origin	Approximate year of introduction	Region
Fermented milk	10,000 BC	Middle East
Fermented milk products	7000-5000 BC	Egypt, Greece, Italy
Mushrooms	4000 BC	China
Soy Sauce	3000 BC	China, Korea, Japan
Wine	3000 BC	North Africa, Europe, Middle East
Fermented rice	2000 BC	China, Asia
Fermented honey (mead)	2000 BC	North Africa, Middle East
Cheese	2000 BC	China, Middle East
Fermented malted cereals: Beer	2000 BC	China, Middle East, North Africa
Bread	1500 BC	Egypt, Europe
Fermented meats	1500 BC	Middle East
Sourdough bread	1000 BC	Europe
Fish Sauce	1000 BC	Southeast Asia, North Africa
Pickled vegetables	1000 BC	China, Europe
Garum (from fish gut)	400 BC	Greece, Italy (Rome)
Tea	200 BC	China

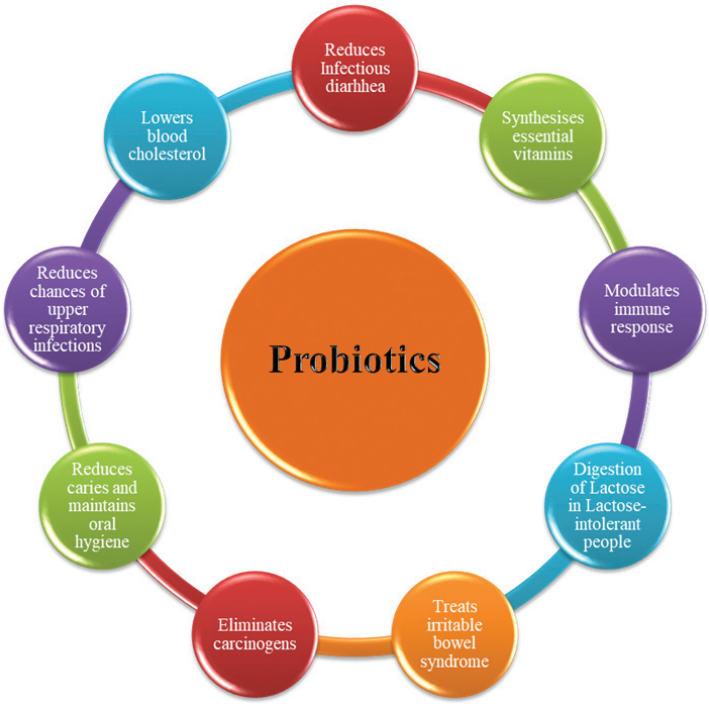

Figure 1: This figure shows some of the common health benefits conferred by probiotics.

"active ingredients are vital for a life's healthy development"[13] Later on, with too much research work on probiotics, its definition was modified and the final definition as given by WHO states "microorganisms give health benefit to the host when it administered in sufficient amounts."[14] The colonisation of microbes in the body starts right from the birth where the presence of Bifidobacterium in breast-fed infants is observed in stool samples[15]. The microbiota composition is dynamic and changes with changes in diet and lifestyle. This can be observed when a breastfed infant changes its diet from milk to solid food resulting in the lowering of bifidobacterium and an increase in the number of bacteroidetes and firmicutes[16]. This is a solid proof of how changes in diet can change the gut microbiota composition. And to mention, it's not just the commensal bacteria that reside in the gut, but also the potential pathogens that are present in small numbers in the gut[17]. These numbers are kept in check by the commensal microbes. Whenever the number of pathogens overtakes the number the commensals, it leads to a situation called 'dysbiosis'[18]. This dysbiosis is said to be the reason for many diseases of the gastrointestinal tract and other associated organs, including the brain. Consumption of unhygienic food and water may cause these kinds of diseases. Availability of clean drinking water in army deployments is mostly fulfilled in the ration, but during some emergency situations, where a continuous supply of water is not possible, servicemen often have to depend on local water bodies quenching the thirst. Stagnant water bodies are a source of potential pathogens which when ingested can cause serious infections of the gastrointestinal tract such as cholera, etc. Hence, there is a need to treat the servicemen from such kinds of situations in case they encounter some contagious diseases. Antibiotic therapy is the most abundant therapy used for treating such diseases[19]. But antibiotics come with certain limitations and side effects. They disturb the entire gut microbiota[20] eliminating most of the commensal microbes, and also antibiotic abuse can predispose a person to antibiotic resistance[21]. Antibiotics treatment on mice showed that it can render the mice susceptible to various infections such as *Salmonella typhimurium, Shigella flexneri* and *Vibrio cholera*[22-23]. This leads to the spreading-up of the contagious diseases to a major population and the episodes could be recurrent. There is a significant correlation between the host physiology gut microbiome (structure and diversity) with respect to physiological robustness and disease[24]. Hence we discuss here the benefits of probiotics (Fig. 1) in modulating host metabolism, physical endurance and treating various conditions mostly related to armed forces[25]. Food safety and standards authority of India (FSSAI) nodal regulatory agency meant for food business has recognised a list of strains indented to formulate probiotic foods (Table 2).

2. MAJOR HEALTH ISSUES IN MILITARY PERSONNEL

Septicaemia of the soldiers injured in various terrorist attacks led to multiple organ failure, severe head injury and pulmonary complications which led to higher reasons for mortality in soldiers. The rate of infection, closed mainly after debridement, was 8.97 per cent whereas the rate of infection treated by delayed primary suturing of war wounds was 6.89 per cent. Irreversible shock led to the death of 47 per cent of

Table 2. Food safety and standards authority of India (FSSAI) nodal regulatory agency meant for food business recognised list of strains indented to formulate probiotic foods

List of strains
Probiotics
Lactobacillus acidophilus
Lactobacillus plantarum
Lactobacillus reuterin
Lactobacillus rhamnosus
Lactobacillus salivarius
Lactobacillus casei
Lactobacillus brevis
Lactobacillus johnsonii
Lactobacillus delbrueckii sub-sp. bulgaricus
Lactobacillus gasseri
Lactobacillus fermentum
Lactobacillus caucasicus
Lactobacillus helveticus
Lactobacillus lactis
Lactobacillus amylovorus
Lactobacillus gallinarum
Lactobacillus delbrueckii
Lactobacillus paracasei
Bifidobacterium bifidum
Bifidobacterium lactis
Bifidobacterium breve
Bifidobacterium longum
Bifidobacterium animalis
Bifidobacterium infantis
Streptococcus thermophilus
Saccharomyces boulardii
Saccharomyces cerevisiae

soldiers, followed by septicaemia, 25 per cent, and severe head injury, 14 per cent. From 1990-1998, 44.37 per cent of people suffered from bullet injuries whereas 55.63 per cent of people suffered from injuries by fragments due to improvised explosive devices (IEDs), artillery shells and landmines[26]. As per the official report from Ministry of External Affairs, India, the casualty figure in Jammu & Kashmir from 1990 to 2001 stands at 9718 civilians and 3053 security forces[27]. From Jan 1999 to Dec 2006, terrorist rendered injuries in Kashmir valley accounted for 8.16 deaths per thousand troops deployed. While, enemy action from across the line of control accounted for 0.63 deaths per thousand troops. Stress induced due to military training changed the gut microbiota of the trainees in such a way that led to intestinal permeability by a whopping 62 per cent[28-29].

3. GASTROINTESTINAL DISORDERS FACED DURING DEPLOYMENT AT VARIOUS PLACES

U.S. defence personnel of 77 per cent (N=15,459) deployed in Iraq, and 54 per cent in Afghanistan experienced at least one episode of acute diarrhoea most of which is presumed to be infectious diarrhoea. A negative impact was observed for 2 days in 46 per cent of the survey respondents[30]. In another report with 1,599 personnel, it was found that the rate of infection in the case of U.S. military personnel deployed to Southwest Asia and the Middle East was 24-32 per cent[31]. The author also discusses the reporting bias as there was less hospitalisation at that area and the episodes were also shorter. The infections could be either traveler's diarrhoea or non-traveler's diarrhoea[32]. Meal, Ready-to-Eat ration diet alters fecal microbiota composition as compared to the usual *ad libitum* diet when observed over a 30 day period, with an increase in *Dorea* species. But, the positive income was that it lowered the bacteria *Desulfovibrio* that cause inflammation and also lowered the levels of potential pathogens such as *Haemophilus parainfluenzae* which is known to cause serious diseases such as pneumonia, abscesses, endocarditis and genital tract infections[33].

4. RESPIRATORY DISEASES IN MILITARY PERSONNEL

Furthermore, in the U.S. Army basic training Soldiers, the incidence of the acute respiratory disease varies from 0 to 1.2 cases per 100 trainees per week, depending on the location and time of the year[34]. Respiratory infections happen to be the most commonly diagnosed medical condition in the U.S. Military trainee groups, assessed to be liable for ~36,000 to 1,00,000 clinical encounters that influences an estimated 25,000 to 80,000 recruits every year. It has also been found that the respiratory diseases in defence personnel are 3 to 4 fold more than an adult civilian, leading to loss of days in military training and the number of beds occupied because of Acute Respiratory Diseases (ARD)[35]. Disclosure to novel respiratory pathogens may happen during deployments in areas of endemic diseases. In the entire history of the U.S. military, the number of non-battle injuries and illnesses have outpaced the battle wounds numbers. Respiratory diseases accounted for the third highest reason for hospitalisation due to illness after diarrhoea and non-combat injuries in U.S. military deployments in Iraq and Afghanistan in the year 2003 to 2004. In a case study from 2008-2012, as many as 7,000 to 25,000 cases of influenza was reported per week in Military Health System (MHS), of which 3,000 to 16,000 (40 % to 65 %) involved military personnel[36].

5. MULTIDRUG RESISTANT ENTERIC PATHOGENS IN INDIA

Infectious diseases affect most of the people in the world by spreading from person to person, either directly through physical contact or through various indirect ways such as cough droplets that cause tuberculosis, pneumonia- of which Coronavirus is in highlight recently, and various other

diseases[37]. Even though it looks like viruses are the major ones that spread infections, it somehow is not true. Bacteria are known to cause 54 per cent of global infectious diseases[38]. Antimicrobials are the major tools that can fight against bacteria, viruses, parasites and fungi and are used for different infections. Antimicrobials hinder the normal physiology of the microbes by impeding essential cellular processes such as DNA, RNA and protein synthesis, cell wall biosynthesis, etc.[39] Due to the ability of the bacteria to adapt to adverse conditions, there has been an increased incidence of antibiotic resistance that prevails all across the globe. This resistance is acquired due to antibiotic abuse in most cases. The microbes that survive the antibiotic treatment alter the environment where they reside so as to make it suitable for the resistant ones to grow and susceptible ones to eliminate[40]. This trait of resistance is acquired either by spontaneous mutations or by horizontal gene transfer. Mutations alter the target sequence where the antibiotics bind and exhibit their effect. Another way of resistance through mutation is the overexpression of efflux pumps that expel out the antibiotics that enter the cell. Other ways of resistance include hydrolysis or chemical modification of the antimicrobials[41].

Adaptation of various bacteria to harsh conditions has led to the emergence of anti-microbial resistant Gram-negative bacterial strains that have created a serious worldwide health emergency and challenges the effectiveness of the mostly available over-the-counter antibiotics used to treat bacterial infections. Out of 654 enteric pathogens investigated, which in aggregate encode resistance against 22 antibiotics, ~97% of the total isolates are resistant against ≥2 antibiotics whereas ~24% of isolates are resistant against ≥10 antibiotic and ~3% isolates are resistant against ≥15 antibiotics. The Sequences whole genome show the presence of mobile genetic elements physically linked with resistance traits and these elements play a major role in disseminating drug resistance among the pathogenic bacteria through horizontal gene transfer.The emergence of antimicrobial-resistant pathogens *viz, Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Pseudomonas aeruginosa, Providencia stuartii* and several strains of *Shigella* are resistant to most of the class of antibiotics used for the treatment of several diseases[42].

6. EFFECTS OF PROBIOTICS IN ALLEVIATING RESPIRATORY DISEASES

Daily administration of probiotics has shown a positive influence on markers of systemic and mucosal immunity[43], as well as a reduced incidence of the colonisation of potentially pathogenic bacteria in the nasal cavity, suggesting that probiotic administration can reduce the incidence, severity and duration of the disease[44]. When *Lactobacillus* and *Bifidobacterium* species, such as *L. fermentum, B. longum* and *B. bifidum*, were given to patients containing 10^9 cfu/mL, the duration of common cold infection reduced to 21.5 per cent as compared to the control group and also the number of days of respiratory symptoms were lower (30 days) in the probiotic group as compared to more number of days (72 days) in the case of placebo group. Another report on Finnish military personnel says that even though probiotics reduced the time period required to heal from picornavirus infection, it did not reduce the occurrence of the disease. This may be because of the restriction of using only two strains of probiotics (*Lactobacillus rhamnosus GG* and *Bifidobacterium animalis ssp. lactis BB-12*) which may not colonise in the gut or the respiratory tract for a longer period of time[45].

Looking at all of these data we can conclude that probiotics cannot completely protect a person from respiratory infections,

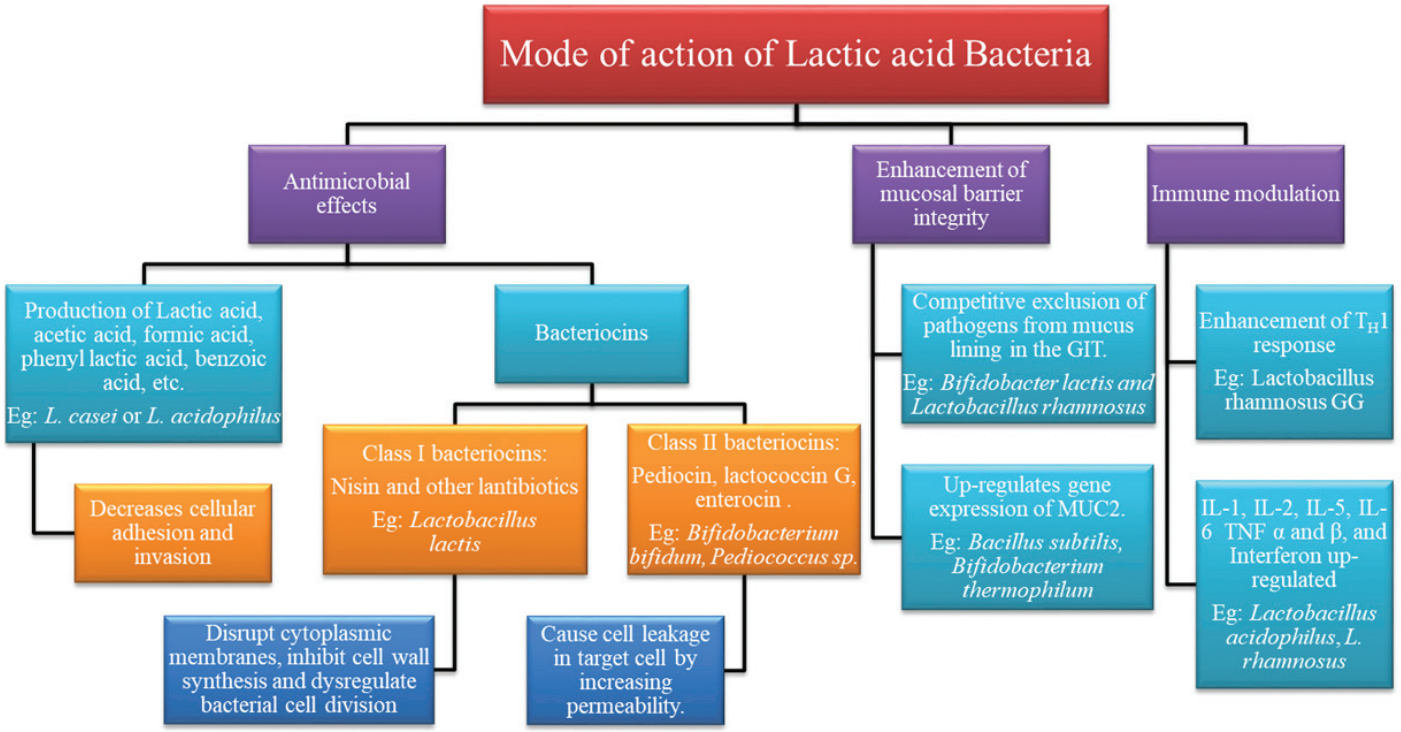

Figure 2. Flow diagram indicating health benefit mechanism of action conferred by probiotic foods/strains.

but can reduce the time and the severity of the infection by competitively inhibiting the potentially pathogenic organism and making the environment less likely for the pathogen to survive and reproduce.

7. PROBIOTICS FOR DENTAL HEALTH

Even though the amount of lactobacilli residing in the oral cavity is less than 1 per cent of the total cultivable microbiota, the role that it plays in maintaining oral health is important[46]. As per the report of WHO, an adult will be affected by dental caries at least once in his lifetime[47]. Mutants Streptococci are the major organisms involved in dental caries. About 17 per cent of all military personnel have lost a permanent tooth since joining the military, with over 50 per cent of tooth loss due to cavities[48]. a higher number of L. *gasseri* and *L. Ultunensis* were found in carious dentine than other *Lactobacillus* species[49-50]. *Lactobacillus rhamnosus GG* and *Lactobacillus casei* showed protective nature against *S. mutans*[51] thereby decreasing their count in the oral cavity and reducing caries. *L. salivarius* has shown the highest antibiofilm and peroxide dependent antimicrobial activity among the other bacteria in the normal oral microflora. Probiotics have shown the ability to modulate local and systemic immunity by reducing the markers of inflammation[52].

8. SAFETY ASPECT OF PROBIOTICS

Probiotics have been considered to be safe since it has a long history of safe usage in humans as it was used to preserve food by fermenting it, and the history of fermentation dates back to as long as 6000 B.C[53]. Fermentation lowers the pH and allows mostly Lactic Acid Bacteria (LAB) to grow in it. *S. boulardii* was shown to be effective against *Clostridium difficile* infection that causes severe diarrhoea[54]. But this also is shown to be more effective on children rather than adults. Probiotics play an important role in modulating the expression of immune-related genes, inflammatory pathway activity and immune marker levels[55-56]. Flow diagram indicating health benefit mechanism of action conferred by probiotic foods/ strains (Fig. 2).

But, recent studies in ICU patients have shown the invasion of the probiotic bacteria into the blood stream causing bacteraemia and in certain people, it has also ended up into sepsis. In one patient, non-synonymous SNP conferring antibiotic resistance was detected in the lactobacillus isolate taken from blood sample[57]. Multi-drug resistance in a large population of people is recognised by the World Health Organisation as a public health threat of global concern. The pace at which a pathogen acquires antibiotic resistance is faster than the discovery of new antibiotics. Hence this lag is of major concern causing more than 2.8 million antibiotic-resistant infections and 35,000 deaths each year in the U.S. alone[59]. Hence an effort to substitute antibiotics with probiotics has been attempted in several health conditions such as spinal cord injury (SCI), hospital acquired pneumonia (HAP), sepsis, acute pancreatitis, urinary tract infection (UTI) etc. [60-61] The results are not the same in every condition. In SCI, there is a high risk of multi-resistant organism (MRO) colonisation or infection resulting from prolonged hospitalisation making 43 per cent of the total inpatients to carry one or more MROs[62]. The use of probiotics *Lactobacillus rhamnosus* GG + Bifidobacterium lactis BB-12 (LGG-BB12) and Lactobacillus reuteri RC-14 + Lactobacillus rhamnosus GR-1 (RC14-GR1) in treating SCI patients with MRO proved ineffective but, RC14-GR1 is effective at preventing new colonisation with multi-resistant gram-negative organisms (MRGNs)[63]. Patients admitted in ICU, who acquired ventilator-acquired pneumonia (VAP) were given *Lactobacillus plantaris* (300 m CFU), *Lactobacillus casei* (300 m CFU), *Lactobacillus bulgaricus* (300 m CFU), *Bifidobacterium infantis* (300 m CFU), *Bifidobacterium breve* (300 m CFU), *Streptococcus thermophiles* (300 m CFU), *Bifidobacterium longum (*400 m CFU), *Lactobacillus rhamnosus* (400 m CFU) and *Lactobacillus acidophilus* (700 million CFU). Mortality rate decreased from 48.6 per cent to 17.1 per cent after the administration of probiotics twice daily for 7 days or until discharge, whichever was earlier[64]. Patients with acute pancreatitis suffered a huge losses as the death rate among the patients increased after the consumption of probiotics (16 % as compared to 6 % in the placebo group). But, the increased number of deaths was because the patients were already suffering from organ failure who did not respond to the treatment, while those who did not have organ failure responded well to the probiotic therapy. The exact mechanism that causes death due to bowel ischemia in case of organ-failure patients is not clearly known[65]. Even in case of sepsis, a severe systemic infection, probiotics proved to be useful reducing the risk of post-operative sepsis by 38 per cent when administered with *Bifidobacterium longus, Lactobacillus acidophillus, L. bulgaricus, L. casei, L. plantarum, L. paracasei, L. paracasei, Bifidobacterium breve, Bifidobacterium lactis, Leuconostoc mesenteroides, Streptococcus thermophiles* and *Pediacoccus pentosaceus* along with prebiotics[66].

9. CONCLUSION

Probiotics have emerged as a novel functional food that has the ability to modulate one's health in a positive way with very few side effects such as bloating, nausea, and increased flatulence. Adverse effects have been observed mostly in immune-compromised people and living alone as solider, the meal only along with probiotics dietary food pattern is strongly affected by many lifestyle factors, weight control, anemic condition, weakness and shorter sleep. The weightage of the beneficial effect as compared to the adverse effects observed from the studies are higher paving the way for probiotics to be used for treating certain conditions.

The biggest question now, when it comes to defence personnel is that whether or not probiotics should be considered for the treatment of military-relevant health conditions. We can even suggest providing probiotic drinks to be procured and promoted in military dining facilities if the cost of doing so is negligible. But intense care has to be taken to what should be included in the list before it is being even provided. Probiotics can be provided to a service person who is supposed to be a part of an operation where the conditions are harsh or the immunological behavior is going to be really challenged. A suitable-strain-containing probiotics relevant against the challenging biological situation will protect him from the

consequences of the upcoming health issues as it is rightly said that "prevention is better than cure". The inclusion of probiotics in the Indian Armed Forces is a debatable question and many higher authorities have declined the use of probiotics in military dining menus. But it won't be long before probiotics will be a part of the menu in military dining as general usage, probiotic foods with high viability standards are superior to supplements.

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REFERENCES

1. Sender, R.; Fuchs, S. & Milo, R. Revised estimates for the number of human and bacteria cells in the body. *PLoS Biol.,* 2016, **14**(8), e1002533-e1002533. doi: 10.1371/journal.pbio.1002533.
2. Thomas, A.M. & Segata, N. Multiple levels of the unknown in microbiome research. *BMC Biol.*, 2019, **17**(1), 48. doi: 10.1186/s12915-019-0667-z.
3. Gill, S.R.; Pop, M.; DeBoy R.T.; Eckburg, P.B.; Turnbaugh, P.J.; Samuel, B.S.; Gordon, J.I.; Relman, D.A.; Fraser-Liggett, C.M. & Nelson, K.E. Metagenomic analysis of the human distal gut microbiome. *Science*, 2006, **312**(5778), 1355-1359. doi: 10.1126/science.1124234.
4. Turnbaugh, P.J.; Ley, R.E.; Mahowald, M.J.; Magrini, V.; Mardis, E.R. & Gordon, J.I. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature,* 2006, **444**(7122), 1027-1031. doi: 10.1038/nature05414.
5. Turnbaugh, P.J.; Ley, R.E.; Hamady, M.; Fraser-Liggett, C.M.; Knight, R. & Gordon, J.I. The human microbiome project. *Nature*, 2007, **449**(7164), 804-810. doi: 10.1038/nature06244.
6. Proctor, L.M.; Creasy, H.H.; Fettweis, J.M..; Lloyd-Price, J.; Mahurkar, A.; Zhou, W.; Buck, G.A.; Snyder, M.P.; Strauss, J.F.; Weinstock, G.M.; White, O. & Huttenhower, C. The integrative human microbiome project. *Nature,* 2019, **569**(7758), 641-648. doi: 10.1038/s41586-019-1238-8.
7. Millan, B.; Park, H.; Hotte, N.; Mathieu, O.; Burguiere, P.; Tompkins, T.A.; Kao, D.; Madsen, K.L. Fecal microbial transplants reduce antibiotic-resistant genes in patients with recurrent Clostridium difficile infection. *Clin. Infect. Dis*., 2016, **62**(12), 1479-1486. doi: 10.1093/cid/ciw185.
8. Suskind, D.L.; Brittnacher, M.J.; Wahbeh, G.; Shaffer, M.L.; Hayden, H.S.; Qin, X.; Singh, N.; Damman, C.J.; Hager, K.R.; Nielson, H. & Mille, S.I. Fecal microbial transplant effect on clinical outcomes and fecal microbiome in active Crohn's disease. *Inflamm. Bowel. Dis.,* 2015, **21**(3), 556-563. doi: 10.1097/MIB.0000000000000307.
9. Kang, D-W.; Adams, J.B.; Coleman, D.M.; Pollard, D.L.; Maldonado, J.; McDonough-Means, S.; Caporaso, J.G. & Krajmalnik-Brown, R. Long-term benefit of microbiota transfer therapy on autism symptoms and gut microbiota. *Sci. Rep*., 2019, **9**(1), 5821. doi: 10.1038/s41598-019-42183-0.
10. Zuo, T.; Wong, S.H.; Cheung, C.P.; Lam, K.; Lui, R.; Cheung, K.; Zhang, F.; Tang, W.; Ching, J.Y.L.; Wu, J.C.Y.; Chan, P.K.S.; Sung, J.Y.Y.; Yu, J.; Chan, F.K.L. & Ng, S.C. Gut fungal dysbiosis correlates with reduced efficacy of fecal microbiota transplantation in Clostridium difficile infection. *Nat. Commun.,* 2018, **9**(1), 1-11. doi: 10.1038/s41467-018-06103-6.
11. Metchnikoff, I.I. The prolongation of life: Optimistic studies. 2004: Springer Publishing Company. Medical – pp 264
12. Gordon, H.A. & L.J.B.r. Pesti, The gnotobiotic animal as a tool in the study of host microbial relationships. *Bacteriol. Rev.,* 1971, **35**(4), 390. doi:10.1128/br.35.4.390-429.1971
13. Kollath, W. The increase of the diseases of civilisation and their prevention. *Munch*. *Med. Wochenschr*., 1953, **95**(47), 1260-1262. PMID: 13132859
14. Butel, M.J.; Waligora-Dupriet, A.J. & Wydau-Dematteis, S. The developing gut microbiota and its consequences for health. Journal of developmental origins of health and disease. *J. Dev. Orig. Health Dis.,* 2018, **9**(6), 590-597. doi: 10.1017/s2040174418000119.
15. Roger, L.C.; Costabile, A.; Holland, D.T.; Hoyles, L. & McCartney, A.L. Examination of faecal Bifidobacterium populations in breast-and formula-fed infants during the first 18 months of life. *Microbiol.,* 2010, **156**(11), 3329-3341. doi: 10.1099/mic.0.043224-0.
16. Yoshioka, H.; Iseki, K-I. & Fujita, K.J.P. Development and differences of intestinal flora in the neonatal period in breast-fed and bottle-fed infants. *Pediatrics,* 1983, **72**(3), 317-321. PMID: 6412205
17. Stecher, B.; Maier, L. & Hardt, W.D. 'Blooming' in the gut: how dysbiosis might contribute to pathogen evolution. *Nat. Rev. Microbiol.,* 2013, **11**(4), 277-284. doi: 10.1038/nrmicro2989.
18. Carding, S.; Verbeke, K.; Vipond, D.T.; Corfe, B.M. & Owen, L.J. Dysbiosis of the gut microbiota in disease. *Microb. Ecol. Health Dis.,* 2015, **26**(1), 26191. doi: 10.3402/mehd.v26.26191.
19. Oldfield, E.C. & M.R.J.G.C. Wallace, The role of antibiotics in the treatment of infectious diarrhea. *Gastroenterol. Clin. North Am*., 2001. **30**(3), 817-835. doi: 10.1016/s0889-8553(05)70212-0.
20. Maruvada, P.; Leone, V.; Kaplan, L.M. & Chang, E.B. The human microbiome and obesity: Moving beyond associations. *Cell Host Microbe.*, 2017. **22**(5), 589-599. doi: 10.1016/j.chom.2017.10.005.
21. Davies, J. & Davies, D. Origins and evolution of antibiotic resistance. *Microbiol. Mol. Biol. Rev.,* 2010, **74**(3), 417-433. doi: 10.1128/MMBR.00016-10.
22. Bohnhoff, M.; Drake, B.L. & Miller, C.P. Effect of streptomycin on susceptibility of intestinal tract to

experimental *Salmonella* infection. *Proc. Soci. Experi. Biol. Medi.*, 1954, **86**(1), 132-137.
doi: 10.3181/00379727-86-21030.

23. Smith, T.J.; Margolis, L.M. & Young, A.J. Should military dining facilities offer and promote consumption of probiotic-containing foods? *Mil. Med.*, 2010, **175**(10), 770-783.
doi: 10.7205/MILMED-D-10-00024
24. Agans, R.T.; Giles, G.E.; Goodson, M.S.; Karl, J.P.; Leyh, S.; Mumy, K.L.; Racicot, K. & Soares, J.W. Evaluation of probiotics for warfighter health and performance. *Front. Nutr.,* 2020, **7**(70), 1-23.
doi: 10.3389/fnut.2020.00070
25. Sotelo-Díaz, I. & Blanco-Lizarazo, C.M. A systematic review of the nutritional implications of military rations. *Nutr. Health*, 2019, **25**(2), 153-161.
doi: 10.1177/0260106018820980
26. Rai, K.M.; Kale, R.; Mohanty, S.K.; Chakrabarty, A.; Waghray, M.R.; Kumar, R.; Prasad, D. & Lahiri, A.K. Treatment of casualties in a forward hospital of Indian army: Nine year experience. *Med. J. Armed Forces India*, 2004, **60**(1), 20-24.
doi: 10.1016/S0377-1237(04)80151-5.
27. *Fact Sheet on Jammu & Kashmir*, G.o.I. Ministry of External Affairs, 2002: India. Report: The Accession of Jammu and Kashmir to India-1947.
28. Karl, J.P.; Armstrong, N.J.; McClung, H.L.; Player, R.A.; Rood, J.C.; Racicot, K.; Soares, J.W. & Montain, S.J. A diet of U.S. military food rations alters gut microbiota composition and does notincrease intestinal permeability. *J. Nutr. Biochem.,*, 2017, **72**,108217.
doi: 10.1016/j.jnutbio.2019.108217.
29. Karl, J.P.; Margolis, L.M.; Madslien, E.H.; Murphy, N.E.; Castellani, J.W.; Gundersen, Y.; Hoke, A.V; Levangie, M.W.; Kumar, R.; Chakraborty, N.; Gautam, A.; Hammamieh, R.; Martini, S.; Montain, S.J. & Pasiakos, S.M. Changes in intestinal microbiota composition and metabolism coincide with increased intestinal permeability in young adults under prolonged physiological stress. *Am. J. Physiol-Gastro Liv. Physiol.*, 2017, **312**(6), G559-G571.
doi: 10.1152/ajpgi.00066.2017.
30. Sanders, J.W.; Putnam, S.D.; Frankart, C.; Frenck, R.W.; Monteville, M.R.; Riddle, M.S.; Rockabrand, D.M.; Sharp, T.W. & Tribble, D.R. Impact of illness and non-combat injury during Operations Iraqi Freedom and Enduring Freedom (Afghanistan). *Am. J. Trop. Med. Hyg*., 2005, **73**(4), 713-719.
doi: 10.4269/ajtmh.2005.73.713.
31. Smith, T.J.; Margolis, L.M. & Young, A.J. Should military dining facilities offer and promote consumption of probiotic-containing foods? *Mil. Med.,* 2010, **175**(10), 770-783.
doi: 10.7205/milmed-d-10-00024.
32. Smith, T.J.; Walker, L.; Cummins, D.; Crombie, A.; Funderburk, L.; Young, A.J. & Touger-Decker, R. Case study: Efficacy of Orlistat 60 mg treatment for Weight Loss. *Top. Clin. Nutr.*, 2012. **27**(4). 339–347.
doi: 10.1097/TIN.0b013e31826f8e02
33. PhilipKarl, P.J.; Armstrong, N.J.; McClung, H. L.; Player, R.A.; Racicot, K.; Soares, J.W. & Montain, S.J. A diet of U.S. military food rations alters gut microbiota composition and does not increase intestinal permeability. *J. Nutri. Biochem.*, 2019, **72**, 108217.
doi: 10.1016/j.jnutbio.2019.108217.
34. Sanchez, J.L.; Cooper, M.J.; Myers, C.A.; Cummings, J.F.; Vest, K.G.; Russell, K.L.; Sanchez, J.L.;. Hiser, M.J & Charlotte, A. Gaydos respiratory infections in the U.S. military: Recent experience and control. *Clin.. Microbiol. Rev.,* 2015, **28**(3), 743-800.
doi: 10.1128/cmr.00039-14.
35. Gray, G.C.; Callahan, J.D.; Hawksworth, A.W.; Fisher, C.A. & Gaydos, J.C. Respiratory diseases among U.S. military personnel: Countering emerging threats. *Emerg. Infect. Dis.*, 1999, **5**(3), 379-385.
doi: 10.3201/eid0503.990308.
36. Sanchez, J.L. & Cooper, M.J. Influenza in the US military: An overview. *J. Infec. Dis .Treat.,* 2016, **2**, 1.
doi: 10.21767/2472-1093.100010.
37. Wright, B.A. & Jeffrey, P.H. Lipoid pneumonia. *Semin. Respir. Infect.*, 1990, **5**(4), 314-321.
38. Jones, K.E.; Patel, N.P.; Levy, M.A.; Storeygard, A.; Balk, D.; Gittleman, J.L. & Daszak, P. Global trends in emerging infectious diseases. *Nature*, 2008, **451**(7181), 990-993.
doi: 10.1038/nature06536.
39. Andersson, D.I. & Hughes, D. Microbiological effects of sublethal levels of antibiotics. *Nat. Rev. Microbiol*., 2014, **12**(7), 465-478.
doi: 10.1038/nrmicro3270.
40. Roberts, M.C. Acquired tetracycline and/or macrolide–lincosamides–streptogramin resistance in anaerobes. *Anaerobe*, 2003, **9**(2), 63-69.
doi: 10.1016/s1075-9964(03)00058-1.
41. Holmes, A.H.; Moore, L.S.P.; Sundsfjord, A.; Steinbakk, M.; Regmi, S.; Karkey, A.; Guerin, P.J. & Piddock, L.J.V. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet.,* 2016, **387**(10014), 176-187.
doi: 10.1016/s0140-6736(15)00473-0.
42. Kumar, P.; Bag, S.; Ghosh, T.S.; Dey, P.; Dayal, M.; Saha, B.; Verma, J.; Pant, A.; Saxena, S.; Desigamani, A.; Rana, P.; Kumar, D.; Sharma, N.C.; Hanpude, P.; Maiti, T.K.; Mukhopadhyay, A.K.; Bhadra, R.K.; Nair, G.B.; Ramamurthy, T. & Das, B. Molecular insights into antimicrobial resistance traits of multidrug resistant enteric pathogens isolated from India. *Sci. Rep.*, 2017, **7**(1), 1-12.
doi: 10.1038/s41598-017-14791-1.
43. de Vrese, M.; Winkler, P.; Rautenberg, P.; Harder, T.; Noah, C.; Laue, C.; Ott, S.; Hampe, J.; Schreiber, S.; Heller, K. & Schrezenmeir, J. Probiotic bacteria reduced duration and severity but not the incidence of common cold episodes in a double blind, randomized, controlled trial. *Vaccine.*, 2006, **24**(44-46), 6670-6674.
doi: 10.1016/j.vaccine.2006.05.048.

44. Winkler, P.; de Vrese, M.; Laue, C. & Schrezenmeir, J. Effect of a dietary supplement containing probiotic bacteria plus vitamins and minerals on common cold infections and cellular immune parameters. *Int. J. Clin. Pharmacol. Ther.*, 2005, **43**(7), 318-326. doi:10.5414/cpp43318
45. Lehtoranta, L.; Kalima, K.; He, L.; Lappalainen, M.; Roivainen, M.; Närkiö, M.; Mäkelä, M.; Siitonen, S.; Korpela, R. & Pitkäranta, A.Specific probiotics and virological findings in symptomatic conscripts attending military service in Finland. *J. Clin. Virol*., 2014, **60**(3), 276-281. doi: 10.1016/j.jcv.2014.03.021.
46. Ahrné, S.; Nobaek, S.; Jeppsson, B.; Adlerberth, I.; Wold, A.E. & Molin, G.The normal Lactobacillus flora of healthy human rectal and oral mucosa. *J. Appl. Microbiol*., 1998, **85**(1), 88-94. doi: 10.1046/j.1365-2672.1998.00480.x.
47. WHO. Oral health. 2012 April 2012; https://web.archive.org/web/20141208132427/http://www.who.int/mediacentre/factsheets/fs318/en/# (Accessed on 12-09-2020).
48. Bray, R.M.; Pemberton, M.R.; Hourani, L.L.; Witt, M.; Olmsted, K.L.R.; Brown, J.M.; Weimer, B.; Lane, M.E.; Marsden, M.E.; Scheffler, S.; Vandermaas-Peeler, R.; Aspinwall, K.R.; Anderson, E.; Spagnola, K.; Close, K.; Gratton, J.L.; Calvin, S. & Bradshaw, M. DoD Survey of Health Related Behaviors Among Active Duty Military Personnel.pdf>. 2008
49. Caufield, P.W.; Schön, C.N.; Saraithong, P.; Li, Y. & Argimón, S. Oral Lactobacilli and dental caries: A model for niche adaptation in humans. *J. Dent. Res*., 2015, **94**(9 Suppl), 110S-8S. doi: 10.1177/0022034515576052
50. Badet, C. & Thebaud, N.B. Ecology of lactobacilli in the oral cavity: A review of literature. *Open Microbiol. J.,* 2008, **2**, 38. doi: 10.2174/1874285800802010038
51. Wu, C-C.; Lin, C-T.; Wu, C-Y.; Peng, W-S.; Lee, M-J.; & Tsai, Y-C. Inhibitory effect of Lactobacillus salivarius on Streptococcus mutans biofilm formation. *Mol. Oral Microbiol.,* 2015, **30**(1),16-26. doi: 10.1111/omi.12063
52. Featherstone, J.D.B. Dental caries: A dynamic disease process. *Aust. Dent. J.,* 2008, **53**(3), 286-291. doi: 10.1111/j.1834-7819.2008.00064.x
53. Fuller, R. History and development of probiotics, in Probiotics. 1992, Springer. p. 1-8. doi: 10.1007/978-94-011-2364-8_1.
54. Castagliuolo, I.; LaMont, J.T.; Nikulasson, S.T. & Pothoulakis, C. Saccharomyces boulardii protease inhibits *Clostridium difficile* toxin A effects in the rat ileum. *Infect. Immun.,* 1996, **64**(12), 5225-5232. doi: 10.1128/iai.64.12.5225-5232.
55. Picchietti, S.; Fausto, A.M.; Randelli, E.; Carnevali, O.; Taddei, A.R.; Buonocore, F.; Scapigliati, G. & Abelli, L. Early treatment with *Lactobacillus delbrueckii* strain induces an increase in intestinal T-cells and granulocytes and modulates immune-related genes of larval *Dicentrarchus labrax* (L.). *Fish Shellfish Immunol.,* 2009, **26**(3), 368-376. doi: 10.1016/j.fsi.2008.10.008.
56. Meybodi, N.M. & Mortazavian, A.M. Probiotic Supplements and Food Products: A Comparative Approach. *Biochem. Pharmacol.,* 2017, **6** (2), 227-234 doi: 10.4172/2167-0501.1000227.
57. Yelin, I.; Flett, K.B.; Merakou, C.; Mehrotra, P.; Stam, J.; Snesrud, E.; Hinkle, M.; Lesho, E.; McGann, P.; McAdam, A.J.; Sandora, T.J.; Kishony, R.; & Priebe, G.P. Genomic and epidemiological evidence of bacterial transmission from probiotic capsule to blood in ICU patients. *Nat. Med.*, 2019, **25**(11), 1728-1732. doi: 10.1038/s41591-019-0626-9
58. Centers for disease control and prevention (CDC). 2009. More people in the United States dying from antibiotic-resistant infections than previously estimated. United States, 2019 AR threats report: https://www.cdc.gov/DrugResistance/biggest-threats.html. doi: 10.15620/cdc:82532.
59. Wong, S.; Jamous, A.; O'Driscoll, J.; Sekhar, R.; Weldon, M.; Yau, C.Y.; Hirani, S.P.; Grimble, G. & Forbes, A. A *Lactobacillus casei* Shirota probiotic drink reduces antibiotic-associated diarrhoea in patients with spinal cord injuries: A randomised controlled trial. *Br. J. Nutr.,* 2014, **111**(4), 672-678. doi: 10.1017/S0007114513002973.
60. Morrow, L.E.; Kollef, M.H. & Casale, T.B. Probiotic prophylaxis of ventilator-associated pneumonia: A blinded, randomised, controlled trial. *Am. J. Respir. Crit. Care Med.,* 2010, **182**(8), 1058-1064. doi: 10.1164/rccm.200912-1853OC.
61. Besselink, M.G.; van Santvoort, H.C.; Buskens, E.; Boermeester, M.A.; van Goor, H.; Timmerman, H.M.; Nieuwenhuijs, V.B.; Bollen, T.L.; van Ramshorst, B.; Witteman, B.J.; Rosman, C.; Ploeg, R.J.; Brink, M.A.; Schaapherder, A.F.; Dejong, C.H.; Wahab, P.J.; van Laarhoven, C.J.; van der Harst, E.; van Eijck, C.H.; Cuesta, M.A.; Akkermans, L.M. & Gooszen, H.G. Dutch acute pancreatitis study group. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. *Lancet.*, 2008, **371**(9613), 651-659. doi: 10.1016/S0140-6736(08)60207-X.
62. Toh, S.L.; Lee, B.B.; Simpson, J.M.; Rice, S.A.; Kotsiou, G.; Marial, O. & Ryan, S. Effect of probiotics on multi-resistant organism colonisation in persons with spinal cord injury: secondary outcome of ProSCIUTTU, a randomised placebo-controlled trial. *Spinal. Cord.*, 2020, **58**(7), 755-767. doi: 10.1038/s41393-020-0420
63. Banupriya, B.; Biswal, N.; Srinivasaraghavan, R.; Narayanan, P. & Mandal, J. Probiotic prophylaxis to prevent ventilator associated pneumonia (VAP) in children on mechanical ventilation: an open-label randomised controlled trial. *Intensive Care Med.* 2015, **41**(4), 677-685.

doi: 10.1007/s00134-015-3694-4.
64. Bongaerts, G.P.A. & Severijnen, R.S.V.M. A reassessment of the PROPATRIA study and its implications for probiotic therapy. *Nat. Biotechnol.,* 2016, **34**(1), 55. doi: 10.1038/nbt.3436
65. Arumugam, S.; Lau, C.S.M.; & Chamberlain, R.S. Probiotics and synbiotics decrease postoperative sepsis in elective Ggastrointestinal surgical patients: A meta-analysis. *J. Gastrointest. Surg.,* 2016, **20**(6), 1123-1131. doi: 10.1007/s11605-016-3142-y.
66. Sirisinha, S. The potential impact of gut microbiota on your health: Current status and future challenges. *Asian Pac. J. Allergy Immunol*., 2016, **34**, 249-264. doi: 10.12932/AP0803.

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