

In Belgrade, March 17, 2023.

Imunolak Adults D3+Zn, Your reliable ally in both health protection and improvement

For more than 100 years, there has been knowledge about the use of probiotics in order to improve the general state of health. Élie Metchnikoff, a researcher who is considered by many as the "father of the term probiotics", noticed positive effects of lactic acid bacteria on the health of people who continuously used them in their diet; *The Prolongation of Life: Optimistic Studies* published in 1907. Since then, more than 20,000 studies have been published regarding probiotics and their positive effects on human health.

Scientific findings indicate that they play an important role in the process of food digesting, preventing various diseases and even in the synthesis of vitamins. Interest in their application continues to grow from year to year. The increase in the use of probiotics is a consequence of the scientific evidence derived from numerous clinical studies. The scientific community is increasingly realizing the importance of their application, not only for prevention of antibiotic associated diarrhea and/or fungal infections of the digestive tract during or after taking antibiotic therapy. Numerous studies have identified that probiotics, in addition to having a positive effect on the mucous membrane of our digestive tract, can also support immunity by modulating the body's immune response (which would have a beneficial effect in terms of preventing eczema, asthma, atopic dermatitis...), may help in reducing inflammation, may support prevention of malignant diseases (liver, colon, bladder...), have a beneficial effect on oral health (reducing gum inflammation, preventing tooth decay), calm the inflammatory process in the intestines, help in insulin resistance condition thus preventing the accumulation of fat body mass, etc. Practically, they help to maintain the balance in the body, thereby promoting a good general health condition of the body as a whole!

There are a large number of commercial probiotic preparations on the market and they are often used uncritically according to the principle: "any probiotic for everyone and for all indications". However, clinical practice indicates that it should not be a *cliché* and that the probiotic should be carefully selected and recommended exactly the one that can help a specific person in solving his specific health problem. It is necessary to keep in mind that not all probiotics are the same, neither in composition nor in the effects we want to achieve with them. I had experience with many probiotic strains, however my recent clinical experiences are most positive with the preparation called Imunolak Adults D3 + Zn. This preparation contains three probiotic strains in a total amount of 5 billion CFU of beneficial microorganisms.

One of the probiotic strains in this preparation is *Lactobacillus casei* BL2401. Similar probiotic strains are also found in fermented milk products. Studies have shown that it can improve the general condition of people suffering from arthritis, type 2 diabetes, while laboratory research on cell lines has shown that it has potentially anti-cancer properties ¹. Also,

it was discovered that it increases the antioxidant capacity of plasma, thus enhancing the body's defense against the harmful effects of free radicals ². This probiotic strain also improves liver function (study on animal model)³ and prevents the rise of cortisol, a hormone that rises in a situation of long-term stressful events ⁴. It has also been shown to accelerate the recovery of hemorrhoids in women after childbirth ⁵. In other studies, it has been established that it regulates bowel movement ⁶, reduces diarrhea caused by taking antibiotics ^{7,8}, and also reduces the value of oxidative stress parameters, protecting us from possible damage by free radicals ⁹.

Another probiotic strain in this preparation is *Lactobacillus salivarius* BL2201. It is present to a large extent in human saliva and is considered to have a beneficial effect on the immune system, to improve intestinal health and to have a beneficial effect on the general health of the body ¹⁰. Also, in clinical trials, it was found to have a positive effect on oral health by promoting the prevention of dental plaque formation ¹¹, reducing the risk of dental tooth decay¹², reducing bleeding from the gums, and eliminating bad breath ¹³⁻¹⁶. Some researches, although with limitations, indicated positive effects when it comes to obesity ¹⁷, reduction of fat as well as improving biochemical parameters of inflammation in the blood ¹⁸. The beneficial effect of this probiotic strain was also observed on the function of the immune system ¹⁹ by modulating both innate and acquired immunity ²⁰. It was also observed that it reduces the intensity of the clinical manifestations of dermatitis in children ^{21,22}, but also in adults with atopic dermatitis ²³. Also, it reduces the risk of mastitis in nursing mothers ²⁴.

The third probiotic strain in the Imunolak adults D3 + Zn formulation is *Bifidobacterium breve* BL3406. It is one of the most important probiotic strains that live in our body and forms the dominant flora in the colon of breastfed infants. This could also be the explanation why breastfed babies have a better immune system than babies who are fed with cow-milk formula for babies. This probiotic has several important functions in the human body, among which are the role in sugar fermentation, production of lactic and acetic acid, participation in food digestion, etc. The lack or insufficient amount of this probiotic strain in our body is linked to various health problems that we may have, such as diarrhea, allergies, excessive gas formation and flatulence, irritable bowel syndrome. In one pilot study, it was found that it has a beneficial effect on intestinal transit in children who have problems with constipation, but also reduces their stomach pain²⁵. It is believed that this probiotic strain inhibits the growth and reproduction of the *E. coli* bacteria, helps to establish a good immune response of our body, which improves the health of the respiratory system, skin, and the health of the genitourinary tract (in women notably). It reduces the frequency of infections and inflammatory processes, which is of particular importance for those people who suffer from irritable bowel syndrome type D²⁶. It was found that *Bifidobacterium breve* also helps to protect the mucous membrane of the gastrointestinal tract in people undergoing radiation and chemotherapy. In experimental models, its beneficial effect on asthma symptoms was also established thanks to its pronounced anti-inflammatory properties ²⁷.

For the purpose of more effective immunomodulation, vitamin D3 in a dose of 2700 I.U. was added, which additionally contributes to the health of the bone and joint system, as well

as 12mg of zinc in a Hypro-ri^R form for better bioavailability. Zinc promotes normal immune system function, improves cell protection against oxidative stress, and contributes to normal fertility and reproductive health in synergism with other compounds.

In my clinical practice so far, Imunolak Adults D3 + Zn has proven to be an effective and safe probiotic formulation that I recommend to adults (best in the morning before breakfast) who:

- have symptoms and signs of weakened immunity (e.g., frequent infections of the upper respiratory tract, frequent occurrence of herpes, tendency to develop pneumonia, urinary tract infections, appearance of herpes zoster...),
- have constipation or loose stools,
- have identified deficit and/or they have an increased need for vitamin D and zinc,
- show tendency towards seasonal allergies (e.g., red eyes accompanied by itching, sneezing, stuffy nose), as well as skin manifestations of allergic reactions (eczema, atopic dermatitis),
- with and after antibiotic therapy (at least two hours apart from antibiotic taken orally), and then ten days after the cessation of antibiotic therapy.

It should also be noted that the best results of treatment with probiotic preparations, even with Imunolak Adults D3+Zn, are achieved with the simultaneous additional correction of unfavorable lifestyle habits that have a harmful effect on health and continuously reduce the functionality of the immune system. Habits that have adverse effects on the general health of the organism and immune system are well known and include inadequate nutrition, insufficient water intake, not enough sleep, lack of physical activity, etc.

In cases with deteriorated health conditions, but also for maintaining and improving general state of health, my warm recommendation to health care professionals and to those interested in being healthy is Imunolak Adults D3 + Zn.

Professor Dušan Vešović, MD

Literature:

1. Kim SN, Lee WM, Park KS, Kim JB, Han DJ, Bae J. The effect of *Lactobacillus casei* extract on cervical cancer cell lines. *Contemp Oncol (Pozn)*. 2015;19(4):306-12. doi: 10.5114/wo.2014.45292. Epub 2015 Aug 13. PMID: 26557779; PMCID: PMC4631296.
2. Kleniewska P, Hoffmann A, Pniewska E, Pawliczak R. The Influence of Probiotic *Lactobacillus casei* in Combination with Prebiotic Inulin on the Antioxidant Capacity of Human Plasma. *Oxid Med Cell Longev*. 2016;2016:1340903. doi: 10.1155/2016/1340903. Epub 2016 Mar 14. PMID: 27066188; PMCID: PMC4808675.
3. Hathout AS, Mohamed SR, El-Nekeety AA, Hassan NS, Aly SE, Abdel-Wahhab MA. Ability of *Lactobacillus casei* and *Lactobacillus reuteri* to protect against oxidative stress in rats fed aflatoxins-contaminated diet. *Toxicon*. 2011 Aug;58(2):179-86. doi: 10.1016/j.toxicon.2011.05.015. Epub 2011 May 31. PMID: 21658402.
4. Kato-Kataoka A, Nishida K, Takada M, Kawai M, Kikuchi-Hayakawa H, Suda K, Ishikawa H, Gondo Y, Shimizu K, Matsuki T, Kushiro A, Hoshi R, Watanabe O, Igarashi T, Miyazaki K, Kuwano Y, Rokutan K. Fermented Milk Containing *Lactobacillus casei* Strain Shirota Preserves the Diversity of the Gut Microbiota and Relieves Abdominal Dysfunction in Healthy Medical Students Exposed to Academic Stress. *Appl Environ Microbiol*. 2016 May 31;82(12):3649-58. doi: 10.1128/AEM.04134-15. PMID: 27208120; PMCID: PMC4959178.
5. Sakai T, Kubota H, Gawad A, Gheyle L, Ramael S, Oishi K. Effect of fermented milk containing *Lactobacillus casei* strain Shirota on constipation-related symptoms and haemorrhoids in women during puerperium. *Benef Microbes*. 2015;6(3):253-62. doi: 10.3920/BM2014.0076. PMID: 25380801.
6. Aoki T, Asahara T, Matsumoto K, Takada T, Chonan O, Nakamori K, Nonaka C, Yamaji I, Hisamoto T, Sato M, Matsuda T, Nomoto K. Effects of the continuous intake of a milk drink containing *Lactobacillus casei* strain Shirota on abdominal symptoms, fecal microbiota, and metabolites in gastrectomized subjects. *Scand J Gastroenterol*. 2014 May;49(5):552-63. doi: 10.3109/00365521.2013.848469. Epub 2014 Mar 13. PMID: 24621348.
7. Wong S, Jamous A, O'Driscoll J, Sekhar R, Weldon M, Yau CY, Hirani SP, 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 Feb;111(4):672-8. doi: 10.1017/S0007114513002973. Epub 2013 Sep 18. PMID: 24044687.
8. Dietrich CG, Kottmann T, Alavi M. Commercially available probiotic drinks containing *Lactobacillus casei* DN-114001 reduce antibiotic-associated diarrhea. *World J Gastroenterol*. 2014 Nov 14;20(42):15837-44. doi: 10.3748/wjg.v20.i42.15837. PMID: 25400470; PMCID: PMC4229551.
9. Mei LH, Zheng WX, Zhao ZT, Meng N, Zhang QR, Zhu WJ, Li RD, Liang XL, Li QY. A Pilot Study of the Effect of *Lactobacillus casei* Obtained from Long-Lived Elderly on Blood Biochemical, Oxidative, and Inflammatory Markers, and on Gut Microbiota in Young Volunteers. *Nutrients*. 2021 Oct 29;13(11):3891. doi: 10.3390/nu13113891. PMID: 34836153; PMCID: PMC8622130
10. Neville BA, O'Toole PW. Probiotic properties of *Lactobacillus salivarius* and closely related *Lactobacillus* species. *Future Microbiol*. 2010 May;5(5):759-74. doi: 10.2217/fmb.10.35. PMID: 20441548.
11. Mayanagi G, Kimura M, Nakaya S, Hirata H, Sakamoto M, Benno Y, Shimauchi H. Probiotic effects of orally administered *Lactobacillus salivarius* WB21-containing tablets on periodontopathic bacteria: a double-blinded, placebo-controlled, randomized clinical trial. *J Clin Periodontol*. 2009 Jun;36(6):506-13. doi: 10.1111/j.1600-051X.2009.01392.x. Epub 2009 Apr 22. PMID: 19453574.
12. Nishihara T, Suzuki N, Yoneda M, Hirofuji T. Effects of *Lactobacillus salivarius*-containing tablets on caries risk factors: a randomized open-label clinical trial. *BMC Oral Health*. 2014 Sep 2;14:110. doi: 10.1186/1472-6831-14-110. PMID: 25178882; PMCID: PMC4236677.
13. Iwamoto T, Suzuki N, Tanabe K, Takeshita T, Hirofuji T. Effects of probiotic *Lactobacillus salivarius* WB21 on halitosis and oral health: an open-label pilot trial. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010 Aug;110(2):201-8. doi: 10.1016/j.tripleo.2010.03.032. PMID: 20659698.
14. Suzuki N, Yoneda M, Tanabe K, Fujimoto A, Iha K, Seno K, Yamada K, Iwamoto T, Masuo Y, Hirofuji T. *Lactobacillus salivarius* WB21--containing tablets for the treatment of oral malodor: a double-blind, randomized, placebo-controlled crossover trial. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2014 Apr;117(4):462-70. doi: 10.1016/j.oooo.2013.12.400. Epub 2013 Dec 20. PMID: 24556493.
15. Chen LJ, Tsai HT, Chen WJ, Hsieh CY, Wang PC, Chen CS, Wang L, Yang CC. In vitro antagonistic growth effects of *Lactobacillus fermentum* and *Lactobacillus salivarius* and their fermentative broth on periodontal pathogens. *Braz J Microbiol*. 2012 Oct;43(4):1376-84. doi: 10.1590/S1517-838220120004000019. Epub 2012 Jun 1. PMID: 24031966; PMCID: PMC3769017.
16. Suzuki N, Tanabe K, Takeshita T, Yoneda M, Iwamoto T, Oshiro S, Yamashita Y, Hirofuji T. Effects of oil drops containing *Lactobacillus salivarius* WB21 on periodontal health and oral microbiota producing volatile sulfur compounds. *J Breath Res*. 2012 Mar;6(1):017106. doi: 10.1088/1752-7155/6/1/017106. Epub 2012 Feb 27. PMID: 22368259.
17. Sáez-Lara MJ, Robles-Sanchez C, Ruiz-Ojeda FJ, Plaza-Diaz J, Gil A. Effects of Probiotics and Synbiotics on Obesity, Insulin Resistance Syndrome, Type 2 Diabetes and Non-Alcoholic Fatty Liver Disease: A Review of Human Clinical Trials. *Int J Mol Sci*. 2016 Jun 13;17(6):928. doi: 10.3390/ijms17060928. PMID: 27304953; PMCID: PMC4926461.
18. Rajkumar H, Kumar M, Das N, Kumar SN, Challa HR, Nagpal R. Effect of Probiotic *Lactobacillus salivarius* UBL S22 and Prebiotic Fructo-oligosaccharide on Serum Lipids, Inflammatory Markers, Insulin Sensitivity, and Gut Bacteria in Healthy Young Volunteers: A

- Randomized Controlled Single-Blind Pilot Study. *J Cardiovasc Pharmacol Ther.* 2015 May;20(3):289-98. doi: 10.1177/1074248414555004. Epub 2014 Oct 20. PMID: 25331262.
19. Sierra S, Lara-Villoslada F, Sempere L, Olivares M, Boza J, Xaus J. Intestinal and immunological effects of daily oral administration of *Lactobacillus salivarius* CECT5713 to healthy adults. *Anaerobe.* 2010 Jun;16(3):195-200. doi: 10.1016/j.anaerobe.2010.02.001. Epub 2010 Feb 14. PMID: 20159049.
 20. Pérez-Cano FJ, Dong H, Yaqoob P. In vitro immunomodulatory activity of *Lactobacillus fermentum* CECT5716 and *Lactobacillus salivarius* CECT5713: two probiotic strains isolated from human breast milk. *Immunobiology.* 2010 Dec;215(12):996-1004. doi: 10.1016/j.imbio.2010.01.004. Epub 2010 Feb 6. PMID: 20219262.
 21. Niccoli AA, Artesi AL, Candio F, Ceccarelli S, Cozzali R, Ferraro L, Fiumana D, Mencacci M, Morlupo M, Pazzelli P, Rossi L, Toscano M, Drago L. Preliminary results on clinical effects of probiotic *Lactobacillus salivarius* LS01 in children affected by atopic dermatitis. *J Clin Gastroenterol.* 2014 Nov-Dec;48 Suppl 1:S34-6. doi: 10.1097/MCG.0000000000000233. PMID: 25291124.
 22. Wu KG, Li TH, Peng HJ. *Lactobacillus salivarius* plus fructo-oligosaccharide is superior to fructo-oligosaccharide alone for treating children with moderate to severe atopic dermatitis: a double-blind, randomized, clinical trial of efficacy and safety. *Br J Dermatol.* 2012 Jan;166(1):129-36. doi: 10.1111/j.1365-2133.2011.10596.x. Epub 2011 Dec 6. PMID: 21895621.
 23. Drago L, Iemoli E, Rodighiero V, Nicola L, De Vecchi E, Piconi S. Effects of *Lactobacillus salivarius* LS01 (DSM 22775) treatment on adult atopic dermatitis: a randomized placebo-controlled study. *Int J Immunopathol Pharmacol.* 2011 Oct-Dec;24(4):1037-48. doi: 10.1177/039463201102400421. PMID: 22230409.
 24. Fernández L, Cárdenas N, Arroyo R, Manzano S, Jiménez E, Martín V, Rodríguez JM. Prevention of Infectious Mastitis by Oral Administration of *Lactobacillus salivarius* PS2 During Late Pregnancy. *Clin Infect Dis.* 2016 Mar 1;62(5):568-573. doi: 10.1093/cid/civ974. Epub 2015 Nov 26. PMID: 26611780.
 25. Tabbers MM, de Milliano I, Roseboom MG, Benninga MA. Is *Bifidobacterium breve* effective in the treatment of childhood constipation? Results from a pilot study. *Nutr J.* 2011 Feb 23;10:19. doi: 10.1186/1475-2891-10-19. PMID: 21345213; PMCID: PMC3048518.
 26. Natividad JM, Hayes CL, Motta JP, Jury J, Galipeau HJ, Philip V, Garcia-Rodenas CL, Kiyama H, Bercik P, Verdu EF. Differential induction of antimicrobial REGIII by the intestinal microbiota and *Bifidobacterium breve* NCC2950. *Appl Environ Microbiol.* 2013 Dec;79(24):7745-54. doi: 10.1128/AEM.02470-13. Epub 2013 Oct 4. PMID: 24096422; PMCID: PMC3837813.
 27. Sagar S, Morgan ME, Chen S, Vos AP, Garssen J, van Bergenhenegouwen J, Boon L, Georgiou NA, Kraneveld AD, Folkerts G. *Bifidobacterium breve* and *Lactobacillus rhamnosus* treatment is as effective as budesonide at reducing inflammation in a murine model for chronic asthma. *Respir Res.* 2014 Apr 16;15(1):46. doi: 10.1186/1465-9921-15-46. PMID: 24735374; PMCID: PMC4029990.