

## F O R E W O R D

## The nutraceuticals: a new therapeutic strategy in the management of digestive and respiratory disorders

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**Summary.** Nutraceuticals represents an intriguing challenge in clinical practice. They are currently used worldwide in all fields of Medicine. The present Supplement reports two Italian surveys concerning a probiotic mixture employed in patients with chronic intestinal disorders and a Medical Device used in patients with upper respiratory diseases. These surveys were conducted on a group of Italian gastroenterologists and on a group of Italian otolaryngologists respectively. Both surveys demonstrated that these compounds may represent a useful therapeutic option in clinical practice. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** nutraceuticals, probiotics, gastroenterologist, otolaryngologist, survey

The term ‘nutraceutical’ has been coined by Stephen L. Defelice in 1989 (1). The use of this term, evaluated from frequencies in papers indexed in PubMed, has progressively increased since 2000. However, there is no internationally recognized definition of a nutraceutical, and various confusing and contradictory definitions have appeared. In this regard, the European Nutraceutical Association defines nutraceuticals as “nutritional products which have effects that are relevant to health, which are not synthetic substances or chemical compounds formulated for specific indications, containing nutrients partly in concentrated form” (2). Nutraceuticals are neither nutritious nor pharmaceutical (3). However, nutraceuticals represent an interesting and exciting challenge in clinical practice. Actually, many doctors and patients look at complementary medicine as they scare the pharmacological compounds because of their adverse effects. At present, nutraceuticals are used in every field of Medicine.

On the basis of this background, this Supplement reports two surveys concerning the therapeutic effectiveness and safety of two nutraceuticals, the first tested in patients with chronic intestinal disorders and the

second used in patients with upper respiratory diseases), in clinical practice. These surveys have been conducted on a group of Italian gastroenterologists and on a group of Italian otolaryngologists respectively.

The first innovative product is an oral nutraceutical containing a probiotic mixture with *Lactobacillus plantarum* LP01 (1 billion of living cells), *Lactobacillus lactis subspecies cremoris* LLC02 (800 millions of living cells), and *Lactobacillus delbrueckii* LDD01 (200 millions of living cells). The survey about this probiotic mixture included patients with chronic intestinal disorders, patients undergoing bowel preparation, or patients undergoing abdominal surgery.

Probiotics are living microorganisms that confer a health benefit to the host when administered in adequate amounts; when ingested, probiotics produce microbial transformation in the intestinal microbiota and exert several health-promoting properties, including maintenance of the gut barrier function and modulation of the host immune system (4). Moreover, the effects of probiotic mixtures may be complementary (also referred to additive) or synergistic (5). In general, probiotic strains produce growth factors that strengthen

the gut epithelium and antimicrobial-anti-inflammatory mediators (e.g., short chain fatty acids, bacteriocins, hydroperoxides, bile acids, and lactic acids) killing harmful microorganisms (6). As a consequence, their cellular components are released in the gut environment, activating immune responses by modulating the pro-inflammatory cytokines production and immunoglobulin synthesis, besides of improving macrophage and lymphocytes activity (7). In addition, non-immunological benefits associated to probiotics include the digestion and absorption processes, competition with potential pathogens for nutrients and intestinal adhesion sites, pH alterations, agglutination of pathogenic microorganisms, and sequestration of metabolic toxins (8). Animal models and *in vitro* assays describe that probiotics also decrease the apoptosis, increase the mucus synthesis, tissue repair, redistribution and production of tight junctions in gut epithelial cells, thus reducing the intestinal permeability and enhancing the barrier protection and function (9). However, it has to underline that the underlying mechanisms of probiotics are dependent on the specific microbial strain and the effectiveness is also disease-specific. Thus, the probiotic choice should be carefully oriented to a specific strain in a specific disease.

The second product is a Medical Device class II CE formulated as solution for aerosol. This innovative compound contains salso-bromo-iodine thermal water (spring of Medesano, PR, Italy), hyaluronic acid (HA), and grapefruit seed extracts. The salso-bromo-iodine thermal waters are very well known and appreciated for their positive effects in the treatment of upper respiratory tract infections, indeed it has been demonstrated that enhance mucociliary clearance, as well as improve the cough due to post-nasal drip (10). HA is a fundamental component of the connective tissue. HA is able to modulate inflammatory response, cellular proliferation, and remodelling of extracellular matrix (11). Grapefruit seed extract exerts an antimicrobial activity (12). Therefore, the reported survey was conducted on patients suffering from acute, chronic or flare-up upper respiratory tract infections.

This Supplement contains also 3 clinical studies concerning: i) the use of visual analogue scale (VAS) in assessing the perception of antihistamines took by patients with allergic rhinitis, ii) the impact of to-

bacco smoke in allergic rhinitis, and iii) the relevance of sleep-disordered breathing (SDB) on oral health in children. The first study pertained the use of VAS as a parameter widely measured in the second survey, reinforcing its validity in clinical practice. The second study confirmed the negative impact of tobacco smoke on airways in patients suffering from allergic disorders. The last study demonstrated that SDB significantly affect oral wellbeing in childhood. Notably, as these conditions are chronic and frequently associated with inflammatory/infectious comorbidity, it may be fruitful to combine pharmacological treatments with complementary medicine, including thermal water, hyaluronic acid, and food supplements, such as bromelain and grapefruit seed. Actually, complementary medicine usually is associated with very few side effects and may be consequently assumed safely for long periods.

In conclusions, the current outcomes have a clinical relevance as they were obtained in real-world settings. There are also some implications considering the close link between upper and lower airways, so improvement of upper airways disorders may also ameliorate lower airways comorbidity (13,14). Therefore, nutraceuticals, including probiotics and plant-derived components, may represent a reliable therapeutic option in clinical practice.

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## References

1. The Foundation for Innovation in Medicine. Available at: <http://www.fimdefelice.org>.
2. European Nutraceutical Association. Health, wellness and fitness. Available at: <https://www.linkedin.com/company/europeannutraceutical-association>.
3. Aronson JK. Defining 'nutraceuticals': neither nutritious nor pharmaceutical. *Br J Clin Pharmacol* 2017; 83: 8-19.
4. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol* 2014; 11: 506-514.
5. Ruiz FO, Gerbaldo G, Asurmendi P, Pascual LM, Giordano W, Barberis, IL. Antimicrobial activity, inhibition of urogenital pathogens, and synergistic interactions between lactobacillus strains. *Curr Microbiol* 2009; 59: 497-501.

6. Konieczna P, Akdis CA, Quigley EM, Shanahan F, O'Mahony L. Portrait of an immunoregulatory Bifidobacterium. *Gut Microbes* 2012; 3: 261-6.
7. Markowiak P, Slizewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients* 2017; 9: E1021.
8. Gagliardi A, Totino V, Cacciotti F, Iebba V, Neroni B, Bonfiglio G, et al. Rebuilding the gut microbiota ecosystem. *Int J Environ Res Public Health* 2018; 15: E1679.
9. Caballero-Franco C, Keller K, De Simone C, Chadee K. The VSL#3 probiotic formula induces mucin gene expression and secretion in colonic epithelial cells. *Am J Physiol Gastrointest Liver Physiol* 2007; 292: G315-G322.
10. Keller S, König V, Mösges R. Thermal water applications in the treatment of upper respiratory tract diseases: a systematic review and meta-analysis. *J Allergy* 2014; 2014: 943824.
11. Gelardi M, Taliente S, Fiorella ML, Quaranta N, Ciancio G, Russo C, et al. Ancillary therapy of intranasal T-LysYal for patients with allergic, non-allergic, and mixed rhinitis. *J Biol Reg Homeost Ag* 2016; 30: 99-106.
12. Shankar S, Rhim JW. Preparation of antibacterial poly(lactide)/poly(butylene adipate-co-terephthalate) composite films incorporated with grapefruit seed extract. *Int J Biol Macromol* 2018; 120(Pt A): 846-52.
13. Ciprandi G, Cirillo I. The lower airway pathology of Rhinitis. *Update Review J Allergy Clin Immunol* 2006; 118: 1105-1109.
14. Ciprandi G, Caimmi D, Miraglia del Giudice M, La Rosa M, Salpietro C, Marseglia GL. Recent developments in united airways disease. *Allergy Asthma Immunol Res* 2012; 4: 171-7.

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