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Application of probiotics in the xenobiotic detoxification therapy

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Abstract Many applications of probiotics have been described to date. In this paper, it is hypothesized that probiotic microorganisms can also be used to decrease the xenobiotics intake in humans. The use of probiotic bacteriae (e.g. strains of *Lactobacillus* sp. and *Bifidobacterium* sp.) and yeasts (*Saccharomyces* sp.) gives the opportunity for detoxification of various elements and compounds, considered as contaminants, directly in the lumen of human intestine. Some of these microorganisms are known to accumulate cesium, strontium and heavy metals to a great extent and also bind mycotoxins. Certainly, during the up-coming years, their native or genetically modified strains will be a part of treatment protocols in detoxification therapy. The utilization of probiotics, in the both therapy and nutrition of people living in the countries suffering from high food contamination, could result in the reduction of annual xenobiotic dose to be incorporated in their organisms.

Key words probiotics • detoxifiction therapy • radionuclides • heavy metals • mycotoxins

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The main ways of toxin incorporation to the human organism are: gastrointestinal and respiratory tracts, and skin. Thus, bioaccumulation of environmental contaminants in plants, mushrooms and animals, which constitute human foods, is a reason of exposure to many harmful species (heavy metals, radioisotopes and organic toxins). Farm animals and cultivated plants are also frequently exposed to a high level of pollutants [32]. Also, different plant species, occupying different habitats, accumulate heavy metals to an unequal extent [11]. Therefore, exposure to a contaminant also depends on climate and dietary customs and not only on its concentration in the soil. Local and temporary intoxication may also be due to a momentary contamination, as in case of ^{137}Cs fallout [9]. There are no good treatment procedures to avoid transfer and accumulation of the food contaminants in human organisms, and in many regions, contaminated food is still a major problem, which affects people's health [22].

It seems that apart of severe incidents, chronic intoxications have huge impact on human health and life quality [17]. A substance, which is incorporated to the organism via gastrointestinal tract, blocks important protein domains, eliminates bioelements from the organism and may also lock up active conformation of biomolecules. In case of radionuclides, ionizing radiation, emitted by them, may also cause somatic and genetic damage [37].

The growing interest in mammalian symbiotic microflora has resulted in many attempts to apply probiotic therapy in the treatment of numerous diseases. For years, microorganisms have been added to various foods, e.g. yoghurt, kefir or cheese, to improve technological processes or just because of their nutritional value. The beneficial role of probiotics has been a subject of several review papers [6, 19, 24, 25, 39]. Recently, it was also emphasized that genetically modified probiotics will play crucial role in the modern probiotic applications [1, 36]. Although, the primary application of probiotics was in the cure of diarrhoea [34, 35], the prospective application in the clinical treatment of many other diseases is very wide [1].

Brudnak [8] suggested the use of some probiotics in detoxification protocols during the treatment of patients suffering from mercury-derived autism. However, there is also a possibility to utilize probiotic organisms for detoxification of many other chemical species. Yeasts (*Saccharomyces cerevisiae*) seem to be the most promising species to achieve that goal. They are like to take up cesium [26, 31], strontium [3], cadmium [5] and lithium [29, 30]. Some other microorganisms are known to accumulate variety of xenobiotics, e.g. mycotoxins [4]. Both bacteriae and yeasts possess self-detoxification mechanisms, which enable them to survive environmental stress. They involve ionic efflux system [33], synthesis of chelating proteins [12, 38] and non-protein thiol compounds [27], and vacuolar upload [29, 31]. The last mentioned one can facilitate accumulation and improve the process of detoxification of human bowel.

Polyunsaturated fatty acids have been shown to enhance therapeutical values of probiotics [15]. They also make the yeasts more resistant for tributyltin [23] and stimulate accumulation of strontium [2] and cesium [20]. All these give a possibility to design the most efficient probiotic therapy to decrease the incorporation of chemical contamination of food into the human body. Apparently, genetical engineering may improve the accumulating properties of probiotics and also help to fulfill all the necessary criteria of a "biodrug", e.g. resistance to acid and bile, attachment to the epithelial cells, colonization of the intestine, etc. [18]. Huge effort must be done to validate such a therapy, to be applied finally in humans. Possibly some other species, already used in probiotic therapy, as *Saccharomyces boulardii* [14], will be suitable for detoxification therapy as well.

Saccharomyces cerevisiae is also known to take up inorganic selenium and incorporate it into proteins [16, 28]. In some bacterial strains, selenocysteine is encoded by UGA sequence, serving as a "stop" codon in the other species [13]. In yeasts, selenium is probably bound with cysteine during posttranslational modifications [16]. In yeast, inorganic selenium has antimutagenic properties, if applied in logarythmic or stationary growth phase [7]. Selenium speciation in Se-enriched yeasts is being intensively studied by now [10, 16], and hopefully it will also be possible to obtain modified strains metabolizing selenite in order to secrete a form of easily available organic selenium, which is beneficial for humans. This concept will lead to make the probiotic therapy more intelligent and applicable. Besides, transgenetic microorganisms are also supposed to produce physiologically active proteins of pharmaceutical interest [21], which can also act as heavy metal chelators.

Figure 1 shows the potential pathways of the xenobiotic species in respect to a probiotic cell when passing gastrointestional tract. Metal ions or solubilized compounds are taken up by the cell and transported into cytoplasm or adsorbed in the cell wall. They can be excreted by passive or active efflux or rinsed if adsorbed. But there is also a possibility of vacuolar or cytoplasmatic retention, in parallel with other detoxificatiom modes as complexation

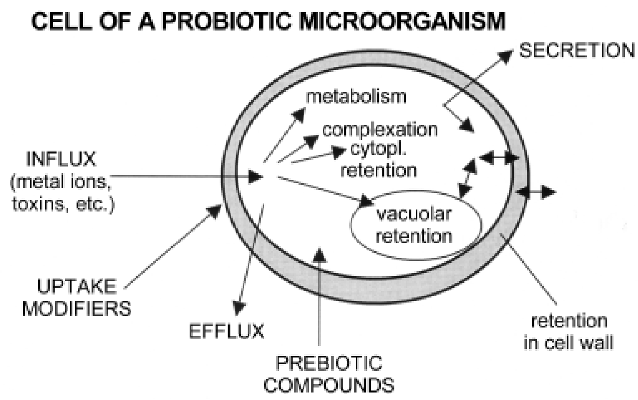

Fig. 1. Physiological functions of probiotics to be utilized in detoxification therapy.

by phytochelatines for instance, or specific inclusion in metabolites, e.g. selenoproteins [16]. That might be accompanied by secretion to the bowel lumen. Unfortunatelly, sometimes even more toxic compounds may be produced by microorganisms, for example organic mercury, which is said to be a negative side of detoxification therapy with application of probiotics [8]. The continuous growth, syntheses and mitotic divisions of the probiotic organism are conditioned by continuous supply of prebiotic substances, e.g. carbohydrates, macro and microelements. Moreover, the administration of probiotic may be concerted with the supply of some uptake modifiers (e.g. linoleate), which are capable of enhancing uptake of the xenobiotic. As well, it is worth pointing that "detoxification" term refers to two distinct processes in the above-cited literature, i.e. use of microorganisms as bowel cleaners and their adaptation to environmental stress.

Probiotics have enormous capacity for detoxification of human body from various contaminants, radionuclides, heavy metals and mycotoxins. Probably they will play an important role in therapeutical detoxification protocols but still much effort has to be done before such a therapy comes in life. Launching such a therapy has to be accompanied by many studies for safety assessment, especially in case of the genetically modified organisms.

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