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Prevention of urogenital infections by oral administration of probiotic lactobacilli

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Summary

In general, lactobacilli are nonpathogenic part of the normal urogenital microflora and have been recognized as a barrier against colonization of unwanted (pathogen) microflora. The results of many *in vitro* studies suggest following mechanisms of probiotic lactobacilli action in urogenital tract: adhesion to urogenital cells, competition with pathogens for adhesive sites, production of biosurfactants, co-aggregation with pathogens, production of antimicrobial substances (organic acids, hydrogen peroxide and bacteriocins) and stimulation of immune system. From 80 different lactobacilli species isolated from human or animal intestinal and urogenital tract, only few lactobacilli strains possess optimal properties to be effective as probiotic therapeutics against infections in the urogenital tract. Combination of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 was proposed as the best one for epithelial vaginal cells colonization and inhibition of uropathogens adhesion. The results of a number of clinical studies confirmed beneficial role of oral lactobacilli. However, the most of commercially available *Lactobacillus* strains, which are ordinary used in fermented dairy products, are seriously limited in protection of urogenital tract when they are ingested orally.

Key words: probiotic lactobacilli, urogenital infections, oral ingestion, protective effect

Introduction

Lactobacilli are part of the normal oral, intestinal and vaginal microflora (Reid, 2001). Lactobacilli have long been subject of interest of the food, especially of the dairy industry (Klaenhammer, 1982; Tamime et al., 2003). Consumption of lactobacilli has been connected to the positive effects of human health for a long time. In general, lactobacilli have not been associated with disease and have been regarded as nonpathogenic members of the intestinal and urogenital flora (Merk et al., 2005). Moreover, many of them have been recognized as probiotics. Probiotics have been defined as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (FAO/WHO, 2001; Hoesl and Altwein, 2005). Many positive actions of probiotics in human gastrointestinal tract have been well known and investigated (Reid et al., 2003; Saarela et al., 2000; Samaržija et al., 2009). The rationale for the use of probiotics is based on the gastrointestinal regulatory role played by autochthonous micro flora and the need for restoration of this ecosystem after disruption (Barrons and Tassone, 2008). Except in gastrointestinal disorders, role of probiotics in a number of health damages have been intensively investigated (Reid, 2004; Anuradha and Rajeshwari, 2005). Between many of scientifically confirmed health-beneficial effects, the use of probiotic lactobacilli in prevention of urinary tract infections (UTI) has been emphasized as an alternative way of treatment (Hoesl and Altwein, 2005). Although the use of probiotics (lactobacilli) as protection agents against UTI still has been strongly controversial, in many countries

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their pharmaceutical application for the treatment of urogenital infections (UGI) in women already exists (Kaur et al., 2002; Nomoto, 2005).

Reid et al. (2001a,b) reported that oral probiotics can resolve UTI, as well as can prevent recurrence of UGI in women (Reid et al., 1995). Many fermented food products with probiotics today exist on global world market. According to the results of some studies (Neri et al., 1993; Reid et al., 1995; Reid et al 2001a; Kontiokari et al., 2001; Reid et al., 2003b; Forsum et al., 2005; Anukam et al., 2006) ingestion of probiotics with fermented food could potentially influence prevention of UTI or UGI. Reid et al. (2001b) reported that probiotics go beyond the intestinal tract and are capable to colonize urogenital cells. Although clinical evidence of the tangible benefits of probiotics from food is mounting, this does not yet reflect the commercial front (Reid, 2003a). Unfortunately, many so-called probiotic products on the world market have not been properly identified, documented, manufactured or proven clinically (Reid and Bruce, 2006; Reid, 2010). In such situation, consumers and caregivers are not sure that they are using reliable products, and have been confided only to pharmaceutical preparations.

Because the urogenital infections represent a great medical problem in the world, every effort to find some alternative way for their prevention and treatment is worth while. In this paper, rationale for using probiotic lactobacilli to prevent urogenital infection will be reported.

Urogenital infections (UGI): pathology and status in the health care system

Non-sexually transmitted urogenital infections affecting urethra, periurethra, bladder, kidney, vagina and cervix are highly common with an estimation of one billion patients per year worldwide (Asano et al., 1986; Aso et al., 1995; Campieri et al., 2001; Hoesl and Altwein, 2005). Urogenital infections (UGI) include urinary tract infections (UTI), bacterial vaginosis (BV) and yeast vaginitis (Reid et al., 2001a). Scientific data indicates that the vast majority of UTI in non-hospitalized community is caused by *Escherichia coli* (70 %), followed by other uropathogens such as *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, group B streptococci, *Providencia stuartii*, and *Staphylococcus epidermis* (Reid and Seidenfeld, 1997; Reid and Bruce, 2001). BV is an infection of female genital tract characterized by an overgrowth of aerobic, anaerobic and micro-aerophilic species such as *Gardnerella vaginalis*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Peptostreptococcus* spp., *Prevotella* spp. and *Mobilnicus* spp. (Rosenstein et al., 1996). BV has been associated with a higher risk of preterm labor and acquisition of sexually transmitted diseases (Martin et al., 1999). On the other hand, recurrent UTI have been shown to have a negative impact on the quality of patient's life, as well as on the total health condition of patients (Ellis and Verma, 2000). Effectiveness of antibiotic therapy of BV and UTI has been closely related to uropathogen resistance (Marelli et al., 2004). A great problem in treatment of patients with BV and UTI is the increase of pathogen drug resistance in many countries (Reid and Seidenfeld, 1997; Gupta et al., 1999; Felmingham, 2000). In Croatia, similar like in other European countries, UGI are considered to be the most frequent human infections (Marijan et al., 2007). Jovanović et al. (2006) reported that four family medicine offices found an incidence of urinary infections greater than 5 % in a sample of 7679 patients in a four-month research period. Report of PLIVA (2007) show that from 3188 investigated UTIs' 25 % was in male and 75% was in female. 77 % of these cases were caused by *E. coli*, what is in close correlation with the clinical results from other European countries (Felmingham, 2000). Furthermore, Andrašević and Tambić Andrašević (2006) reported that many of in Croatian medicine centers isolated uropathogens (especially *E. coli*) have been resistant on wide range of antibiotics.

Probiotic lactobacilli and urogenital infectios: scientific base and mode of action

Lactobacilli are gram-positive rods, facultative or strict anaerobes which prefer an acidic environment and help create one by producing lactic and other acids (Marelli et al., 2004; Saarela, 2000). Many examples can be found in which lactobacilli have been used to treat or prevent infection of intestinal and urogenital tracts with different degrees of success (Saarela et al., 2000; Reid, 2001; Reid and Bruce, 2006; Anuradha and Rajeshwari,

2005). The use of probitics for the health of female urogenital tract goes back to the early part of 20th century (Newman, 1915), but real scientific information on the most suitable probiotic strains, their efficacy and optimal treatment has become available only recently.

A main concept and scientific basis of urogenital infections prevention by probiotic treatment was recommended by the research group of Reid (Hoesl and Altwein, 2005). This concept has been based on pre-clinical as well as clinical studies, for identification, selection and test the most effective strains. Why the lactobacilli were recognized as an important protective factor in urinary tract? The largest part of vaginal flora consists of lactobacilli, which possess antimicrobial properties that regulate other urogenital microbiota (Forsum et al., 2005). Urogenital infections in women are often characterized by an alteration of the local flora from a predominance of "good" lactobacilli to "bad" coliform uropathogens as results of mental stress, hormone deficiency, sexual activity and contraceptive measures (Sweet, 2000). There are more than 80 known species of lactobacilli in the intestines and vagina (Barrons and Tassone, 2008). Individual species may differ in their ability to restore normal flora and regulate the overgrowth of uropathogens (Morelli et al., 2004; Falagas et al., 2008).

There is another basic question: what properties do these lactobacilli strains have that make them effective probiotic agents in urogenital tract? According to general theory, two main criteria for the selection of probiotic strains exist: 1) ability to colonize the host without any adverse side effects, and 2) ability to inhibit urogenital pathogens (Reid et al., 1995). The mode of probiotic action on urogenital infections has not been proven *in vivo*, and is believed to be multifactorial and complex (Reid et al., 2001b). Based on a number of *in vitro* data the involvement of following potential mechanisms was proposed:

1. ability of adhesion to vaginal epithelial cells (McLean and Rosenstein, 2000; Ehström et al., 2010),
2. production of biosurfactants and collagen-binding proteins as antiadhesive molecules for pathogen adhesion (Velraeds et al., 1998; Heinemann et al., 2000),
3. production of antimicrobial substances such as organic acids and hydrogen peroxide (Salminen et al., 1998; Reid et al., 2001b) and bacteriocin-like compounds (Aroutcheva et al., 2001; Rodriguez et al., 2003; Leboš Pavunc et al., 2009).

The results of various *in vitro* and animal studies led to the conclusion that three lactobacillus strains, namely *L. rhamnosus* GR-1, *L. fermentum* RC 14 and *L. crispatus* CTV-05 possess optimal properties to be effective as probiotic therapeutics against infections in the urogenital tract (Reid and Bruce, 2001; Osset et al., 2001; Gardiner et al., 2002). Accessible scientific data show that many other lactobacilli have some properties to be effective in urogenital tract, such as commercially available intestinal probiotic *L. rhamnosus* GG (Gardiner et al., 2002), *Lactobacillus casei* strain Shirota (Asahara et al., 2001) and *Lactobacillus acidophilus* NCFM (Reid, 2000), but not in full. All of these three strains possess antimicrobial capacity against uropathogens, but also have some of defective properties in urogenital environment. For example, *L. acidophilus* NCFM might be feasible if applied directly to the vagina, it would be not optimal choice of strain for oral delivery (Reid, 2000). A given strain of *Lactobacillus* can express several, but not necessarily all of the known key factors and be able to compete in the urogenital environment. Bacterial adherence is considered to be an important first step in the colonization of urogenital tissue (McLean and Rosenstein, 2000). *Lactobacilli* can use many mechanisms to adhere surfaces in urogenital tract, such as electrostatic, hydrophobic, hydrophilic, capsular and fimbrial mechanisms (Andreu et al., 1995). *L. rhamnosus* GR-1 colonizes the surfaces of urogenital tract by hydrophilic mechanics, while the *L. fermentum* B-54 colonizes the surface of urogenital tract by hydrophobic mechanism (Reid, 2001). Boris et al. (1998) also showed that several ways of adherence exist: *L. acidophilus* and *L. gasseri* proteins and carbohydrates participate in the adherence, whereas *L. jensenii* seems to depend on carbohydrates alone. Chan et al. (1985) suggested that lipoteichoic acid participates in the adherence of lactobacilli. Reid et al. (1996) identified two adhesins, an extracellular, probably proteinaceous, and a trypsin intensive cell-wall adhesion. Furthermore, some strains can bind better to intestinal cells and inhibit pathogen adhesion (Reid et al., 1993; Hudault et al., 1994), but

they may not be able to effectively inhibit growth of uropathogens (Reid et al., 1987; Osset et al., 2001). Studies on vaginal colonization by lactobacilli in humans have focused largely on oral or intravaginal therapy with the combination of *L. rhamnosus* Gr-1 and *L. fermentum* RC-14 (Reid et al., 2001c; Reid et al., 2003b; Barrons and Tassone, 2008). Combination of these two probiotic lactobacilli was proposed as the best one for use to colonize epithelial vaginal cells and to inhibit adhesion of uropathogens.

In addition, lactobacilli may offer protection against urogenital infections through production of biosurfactants. Biosurfactants obstruct the growth of uropathogens by inhibiting adhesion of microorganisms along uroepithelial cells. The fifteen strains of lactobacilli were found to produce biosurfactant (Valraeds et al., 1995). These lactobacilli produced varying amounts of biosurfactants that provided up to 82 % inhibition of *Enterococcus faecalis* adhesion to glass surface of vagina. The antiadhesive molecule produced by certain lactobacilli hold promise for application to many human sites where pathogen attach, colonize and confer disease (Marelli et al., 2004). Biosurfactants produced by lactobacilli are most frequently glycolipids but also lipopeptides, protein-like substances, phospholipids, substituted fatty acids, and lipopolysaccharides (Reid et al., 1999). Recently, the activity was shown to affect a broad range of uropathogens (Valraeds et al. 1998) and an active component was found to be a collagen binding protein (Heinemann et al., 2000). Clinical significance of biosurfactants to urogenital infections has to be determined.

Another protective characteristic of urogenital lactobacilli is ability of co-aggregation with uropathogens to block their adhesion and/or displace previously adherent uropathogens on vaginal epithelial cells. Mastromarino et al. (2002) found varying degrees of co-aggregation with *Candida albicans* and *Gardnerella vaginalis* among 10 strains of lactobacilli that were being used in probiotic vaginal tablets. Mechanism of lactobacilli-pathogen co-aggregation and the contribution of these individual antibacterial properties to clinical efficacy are recently unclear.

Same like in the prevention of intestinal disorders, for use as probiotics in the prevention and treatment of urogenital infections, lactobacilli must exhibit adequate antibacterial activity. The most relevant property in this context is the ability to maintain a vaginal pH lower than 4.5. The vaginas of healthy premenopausal women show a pH of 4-4.5 (Merck et al. 2005). A low vaginal pH seems to be important factor in controlling the composition of microbiota. Lactobacilli contribute to vaginal acidity by producing lactic acid and other organic acids (Boris and Barbes, 2000). Valore et al. (2002) reported that the vaginal fluid with the highest levels of antimicrobial activity also contained the highest levels of lactic acid. Except lactic acid, lactobacilli produce additional antibacterial substances, such as bacteriocins and hydrogen-peroxide (Aroutcheva et al., 2001). Different strains of lactobacilli produce varying amounts of these substances. Most lactobacilli are able to produce hydrogen peroxide. Hydrogen peroxide has a toxic potential towards pathogen bacteria but also to the producing bacteria themselves. Its antimicrobial effect is based on its oxidative properties which results in irreversible changes in the microbial cell membrane (Vanderbergh, 1993). Apart from bacteria, in the presence of peroxidase and halide, hydrogen peroxide is toxic toward fungi and viruses (Klebanoff and Coombs, 1991; Klebanoff et al., 1991). Protective effect of hydrogen peroxide - producing lactobacilli against bacterial vaginosis has been observed by several studies (Eschenbach et al., 1989; Hawes et al., 1996; Reid et al., 2001c; Antonio and Hillier, 2003; Uehara et al., 2006). Contrary, the results of some studies showed that hydrogen peroxide could not show any protective effect against some bacteria, fungi and yeasts which cause bacterial vaginosis or vulvovaginitis (Sobel and Chaim, 1996; Rosenstein et al., 1997). In general, according to many biological statements, hydrogen peroxide produced by urogenital lactobacilli could have important antagonistic effect against undesirable microorganisms, but available scientific data have been very opportunistic.

Another important characteristic of lactobacilli is production of proteinaceous bacterial substances which have intraspecies antagonistic effects (Reid, 2010). These substances have been known as bacteriocins. Several lactobacilli produced bacteriocins were isolated from food and raw materials, but it can not be shown yet that vaginal lactobacilli produce bacteriocins (Reid, 2001; Merk et al., 2005). However, bacteriocin-like substances produced by

Table 1. Major deficiencies in some commercial probiotic organisms with respect to their selection for colonizing the urogenital tract and preventing urogenital infections (Reid and Bruce, 2001)
Tablica 1. Osnovni nedostaci nekih komercijalnih sojeva probiotičkih mikroorganizama pri selekciji pogodnih sojeva za kolonizaciju urogenitalnog trakta i spriječavanje urogenitalnih infekcija (Reid i Bruce, 2001.)

Lactobacillus strain* / Soj lactobacilla	Major deficiences[a] / Osnovni nedostaci soja[a]
L. acidophilus SIDU[1]	Poor adhesion to epithelial cells; poor inhibition of pathogen growth and adhesion Slaba svojstva vezivanja na epitelne stanice; slaba inhibicija rasta patogena i njegova vezivanja na epitelne stanice
L. acidophilus NCFM[2]	Poor adhesion to epithelial cells; poor inhibition of pathogen growth; does not produce hydrogen peroxide Slaba svojstva vezivanja na epitelne stanice; slaba inhibicija rasta patogena; ne proizvodi vodikov peroksid
L. rhamnosus GG[3]	Does not have 29-kDa biosurfactant protein that inhibit pathogen binding; weakly produces hydrogen peroxide Ne posjeduje 29-kDa biosurfaktant protein za inhibiciju vezivanja patogena; slab proizvođač vodikovog peroksida
L. casei Shirota[4]	Does not have 29-kDa biosurfactant protein that inhibit pathogen binding; does not produce hydrogen peroxide Ne posjeduje 29-kDa biosurfaktant protein za inhibiciju vezivanja patogena; ne proizvodi vodikov peroksid
L. casei DN-114[5]	Does not have 29-kDa biosurfactant protein that inhibit pathogen binding; does not produce hydrogen peroxide Ne posjeduje 29-kDa biosurfaktant protein za inhibiciju vezivanja patogena; ne proizvodi vodikov peroksid
L. johnsonii LJ1[6]	Does not have 29-kDa biosurfactant protein Ne posjeduje 29-kDa biosurfaktant protein
L. plantarum 299V[7]	Does not have 29-kDa biosurfactant protein Ne posjeduje 29-kDa biosurfaktant protein

*Commercial strains; producers: SIDU Enterprises[1], Rhodia[2], Valio[3], Yakult[4], Actimel[5], Nestle[6], Probi[7]
*Komercijalni sojevi; proizvođači: SIDU Enterprises[1], Rhodia[2], Valio[3], Yakult[4], Actimel[5], Nestle[6], Probi[7]
[a]deficiences were determined on the basis of in vitro experiments/[a]nedostaci utvrđeni nizom in vitro eksperimenata

different strains of urogenital lactobacilli could be described and isolated (McGroarty and Reid, 1988; Okkers et al., 1999). Boris and Barbes (2000) cited that bacteriocin-like substances do not fit into the typical criteria for bacteriocins and are incompletely defined. They normally have a broader spectrum of antimicrobial activity than bacteriocins and can inhibit a wide range of Gram-positive and Gram-negative bacteria (McGroarty, 1993). Antagonistic action of mentioned substances against *Clostridium sporogenes*, *Clostridium tyrobutyricum*, *Listeria inocua*, *Propionibacterium* species, *Escherichia coli*, *Enterococcus* species and *Candida albicans* was proved by the results of *in vitro* studies (McGroarty and Reid, 1988; McGroarty, 1993; Okkers et al., 1999; Aroutcheva, 2001; Kaur et al., 2002; Rodriguez et al., 2003).

Oral administration of probiotic lactobacilli for prevention and treatment of urogenital infections: clinical evidence

It is well known and scientifically confirmed that some selected probiotic strains applied directly to the vagina can colonize and compete against uropathogens, and reduce the risk of urogenital infections (Reid et al., 1995; Sobel, 1999). Possibil-

ity to prevent and treat urogenital infections by oral ingestion of probiotics represents a major advance in care of women urogenital health, because it could be a major step in the right direction for patients as it potentially allows the self administration of therapy (Reid et al., 2001a; Marelli et al., 2004). Moreover, oral ingestion of probiotics provides easy medical treatment of pregnant women with BV, or women in developing countries, where there is a high risk from sexually transmitted diseases infestation (Reid et al., 2001a). From all of these reasons, it is very interesting for food industry to produce certain products with potential protective role for urogenital tract. Is it real and possible? A number of positive scientific evidences about beneficial effects of selected probiotic lactobacilli oral ingestion for prevention and treatment of urogenital infections have been reported in last 15 years. The results of many recent clinical studies show that oral ingestion of selected lactobacilli strains (especially *L. rhamnosus* GR-1, *L. fermentum* RC 14 and *L. crispatus* CTV-05) has been successful in urogenital tract (Reid and Burton, 2002; Reid et al., 2003b; Merck et. al., 2005; Barrons and Tassone, 2008). According to Reid et al. (2003b), oral ingestion of these probiotics could provide alteration of vaginal flora, prevent and obstruct urogenital infections, as well as protect against recurrence of urogenital infections. This is very important fact, but the problem is more complex if we try to produce some fermented or non fermented dairy food containing probiotic lactobacilli, which have potential protective properties for the urogenital tract of consumers. A number of questions and dilemmas could be raised: How these urogenital-effective strains of lactobacilli grow in milk? What are the inhibiting factors for their growth in milk? In what form these urogenital-protective strains could be storage and what is the best way to inoculate them to milk? Which adequate concentration of probiotic cells product must contain to be effective as protective for urogenital health? What is with their viability in product during storage? Is the abundance of fermented products on market really reliable? Are the selected probiotic lactobacilli strains from fermented food equally effective like these from pharmaceutical preparations?

Antagonistic effect of commercially available probiotic *Lactobacillus* strains against uropathogens have been proved in a number of *in vitro* studies, same like their ability to colonize epithelial cells of vagina (Chan et. al., 1985; Sieber and Deitz, 1998; Reid, 2000; Reid et al., 2001c; Gardiner et al., 2002; Antonio and Hillier, 2003; Barrons and Tassone, 2008). However, the results of many clinical examinations gave very controversial results. Conflicting findings of studies with the same lactobacilli strains raise questions about the design of these studies and emphasize the need for additional clinical researches whit this strains. For example, Colodner et al. (2003) reported that *Lactobacillus* GG did not prevent UTI when it was applied orally by fermented food, and failure to reduce subsequent ascent of the uropahnogens to the bladder. Opposite, group of Finish researches in a study of 185 women with 5-years UTI-free history found that the subjects consuming the *Lactobacillus* GG drinks, at least three times per week, had fewer episodes of UTI compared to those women not receiving probiotics (Kontiokari et al., 2001). Reid (2000) reported that the application of *L. acidophilus* NCFM strain to humans might be effective in urogenital tract if applied directly to the vagina, but not by oral ingestion, whereas the results of Neri et al. (1993) clearly show beneficial effect of consumption of yoghurt with incorporated *L. acidophilus* cells on BV status of 84 women in first trimester of pregnancy.

A number of similar opportunistic episodes have been noted in scientific literature. However, some positive and optimistic scientific data have to be referred. The results of the randomized clinical observations have emphasized beneficial effects of therapy with probiotic milk (food) to health status of women with BV or vulvovaginal candiasis (VC) (Neri et al., 1993; Reid et al., 2001a; Demirezen, 2002; Jeavons, 2003; Reid et al., 2001b; Reid et al., 2003b; Anukam et al., 2006; Falagas et al., 2006). Clinically controlled ingestion of probiotic lactobacilli from fermented food influenced greatly on a reduction of vaginal infections and improves the overall urogenital health of tested women subjects. Moreover, clinically controlled therapy with probiotic dairy food, used separately or combined with appropriate antibiotcs; influenced frequently to total absence of BV and VC after proper treatment period (Anukam et al., 2006; Falagas et al., 2006). Lesser than in case of BV and VC, positive role of probiotic lactobacilli oral ingestion was scientifically confirmed for the prevention of UTI. In

a randomized, open-label study, Kontiokari et al. (2001) observed that consummation of dairy probiotic drink and cranberry-lingoberry juice influencing on reduction of risk of reccurance UTI. The both type of probitic drinks were commercially available.

Selection of *Lactobacillus* strains and their related probiotic products for urogenital applications has also great importance, but additional limitations appear. There is need to select probitic strains on the basis of functional attributes in urogenital tract, and based on this, a particular culture (or mix of cultures) should be chosen for certain application. Commercial strains which have been usually used in dairy (food) industry have some serious deficiencies to be effective in urogenital tract (Table 1). On the other hand, growth kinetics and viability of urogenital-effective *L. rhamnosus* GR-1 and *L. fermentum* RC 14 in milk or some other food substrate has been poorly investigated.

Finally, the dose required for probiotic lactobacilli to impact vaginal, or urinary tract flora must be clearly defined. Findings of Reid et al. (2001b) indicate that a daily oral dose of 10^8 viable probiotic lactobacilli (GR-1 and RC-14), can restore and maintain the urogenital health of a women. However, it is clear from this paper content that this "therapeutic dose" could be valid only for these two lactobacilli strain.

Conclusions

Different strains of lactobacilli have different potential to be effective against pathogens in urogenital tract. Their efficacy has been based on their characteristics, but also on their bahaviour in urogenital tract. Although many of their characteristics required to confer protection of urogenital tract have been identified *in vitro*, evidence of their expression *in vivo* is scant and the relative significance of each is unknown. Production of so called "biotherapeutics" products for oral consummation is very complex field and requires a number of further investigations and probes prior to. Proper selection of a strain, proof of concept, and efficacy of product must be clearly formulated. Such products are a great opportunity, because they provide a major step in the right direction for patients as they potentially allow the self administration of therapy. Incorporation of urogenital-effective *L. rhamnosus* GR-1 and *L. fermentum* RC 14 to food, as well as processing of their fermentative products, needs to be additionally investigated and processing parameters must be determined.

Prevencija urogenitalnih infekcija oralnim unosom probiotičkih laktobacila

Sažetak

Laktobacili su dio standardne nepatogene normalne urogenitalne mikroflore, koji djeluju kao barijera protiv kolonizacije nepoželjne (patogene) mikroflore. Prema rezultatima mnogih *in vitro* studija probiotički laktobacili u urogenitalnom traktu mogu djelovati putem sljedećih mehanizama: adhezija na stanice urogenitalnog trakta, natjecanje s patogenima za adhezivna mjesta, produkcija biosurfaktanata, koagregacija s patogenima, produkcija antimikrobnih supstancija (organske kiseline, vodikov peroksid i bakteriocini) i stimulacija imunološkog sustava. U urogenitalnom traktu samo nekoliko sojeva laktobacila, od 80 sojeva laktobacila koji su izolirani iz probavnog i urogenitalnog trakta, ima terapijska svojstva. U kolonizaciji epitelnih stanica vagine i sprječavanja adhezije patogena najuspješnijom se pokazala kombinacija bakterija *Lactobacillus rhamnosus* GR-1 i *Lactobacillus fermentum* RC-14. Rezultati niza kliničkih studija potvrdili su blagotvorni učinak oralnog unosa probiotičkih laktobacila. Međutim, najveći broj komercijalno dostupnih *Lactobacillus* sojeva, koji se uobičajeno koriste za fermentacije u mljekarskoj industriji, ukoliko se unesu oralno imaju limitirano zaštitno djelovanje u urogenitalnom traktu.

Ključne riječi: probiotički laktobacilli, urogenitalne infekcije, oralni unos, zaštitni učinak

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