

Bactalk

WINTER 2012

International Probiotics Association Newsletter | Issue 008

Can Probiotics Help
With Kidney Stones?

Probiotics May Help
Break Down Carbs

“Good” Bugs, “Bad” Bugs
and Autism

Lactobacillus Role in
Menopausal Symptoms

Bactalk Newsletter

Winter 2012

—

DIRECTOR GENERAL

Ioannis Misopoulos

ADMINISTRATION MANAGER

Nevena Krstić

EXECUTIVE BOARD

PRESIDENT

George Paraskevacos

Harmonium Int'l.

VICE PRESIDENT

Nancy Hamren

Springfield Creamery/
Nancy's Yogurt

TREASURER

Michael Shahani

Nebraska Cultures

SECRETARY

Peter Rothschild

Biogaia

PAST PRESIDENT

Scott Bush

Message from the President



Dear IPA Members,

I have always viewed anniversaries as bitter sweet. The time to ponder what just passed and what the future holds, sounds like a case of auld lang syne brewing! But in all seriousness looking back as we complete our first year of activity, the newly elected executive officer team of the IPA and myself, can assure you we have a firsthand feel of the 14th century proverb, time and tide wait for no one."

It has been quite a busy year for all of us. We hit the ground running at the turn of 2011 with a visit to Health Canada and a preview of the monograph revisions being planned – finally announced this past September they sent the industry running with some of the requirements on that monograph and new labeling standard.

Also early in the year, following our rebranding and logo change, the marketing activities also ramped up with the completion of trademarking the IPA's new tagline "The Global Voice of Probiotics®" and initiating the development work for the IPA World Congress web site, being held in Los Angeles April 2012. Also launched early first quarter was the probiotic documentary "Micro warriors" a film which IPA and its members participated in targeting primarily end users and consumers.

We also firmly implanted the IPA Scientific Advisory Board thanks to Dr. Frederic Durmont, who was able to get acceptance from top medical professionals with expertise in different areas of healthcare to be IPA's scientific and independent advisors. It will be the first year of a functional SAB committee to run alongside an already functional Regulatory Affairs committee that Svend Laulund has been spearheading from last year.

This year also saw the hiring of IPA's second employee Nevena Krstić as our Administration Manager – fresh out of university with a degree in law has transitioned into the role like a seasoned veteran. Supporting and working in tandem with Ioannis Misopoulos our Director General – both have been hard at work making the IPA the most globally recognized probiotic association.

Other than having global membership, we also became certifiably international as we held our first ever IPA board meeting in Geneva

Switzerland, during the Vita Foods EU conference. Since 2010 we also continued our two board meets a year initiative by reconvening during the Supply Side Las Vegas show in October as well.

Insofar as addressing the various government agencies, our Regulatory Affairs committee was hard at work, first off with the Position paper regarding probiotics. This was submitted to the FDA in collaboration with EFFCA and IFAC – we were ahead of the curve on this one since this was pre NDIN guidance announcement, May 2011. Following which this position paper was re-submitted alongside the IPA's official position regarding the NDIN guidance from the FDA at the deadline earlier this month. Currently we are working on a comment paper for Health Canada and their Probiotic monograph and abbreviated labeling standard.

IPA also actively participated in the new regional standard initiative for Ayrar on behalf of the Turkish government that Codex is in the process of discussion. Moving along with Codex, we also have been working on bringing a proposal forth, asking them to revisit the definition of what is a health benefit in relations to fermented foods and supplements.

IPA visited Asia this year in a call to reinforce presence in that region of the world with current membership and ended up signing on a new company as well. At IPA'S 2010 Supply Side West board meet we had announced targeting 5 new member companies to the board for 2011 – we signed on 12.

The upcoming year 2012 is looking to be an exciting one; with all the new initiatives we are working on and of course this is an IPA World Congress year. I took a look back at the 2010 WC which attracted participants from 37 countries, looking at this year's programs we are expecting to have another sold out event with as many if not more country participants. Do not forget to mark your calendars for the IPA World Congress on April 20th and 21th in Universal City Los Angeles.

Here's wishing everyone a great holiday period with all your families, and friends for a healthy and prosperous 2012 – see you all in LA.

*Thank you and best regards,
George*

UNLIKE MEN, ALL PROBIOTICS ARE NOT CREATED EQUAL

A broad understanding of the benefits of probiotics has been limited, like much of complementary medicine, by hypothesis-drive research. One of the founding principles of the American Declaration of Independence is that *all men are created equal*. Much research into the effects of probiotics on human health has taken a similar philosophical approach in the selection of organisms for clinical trials. Little mechanistic data have been available for application into study design. Thus, despite the increasing demand for probiotics on the basis of their beneficial effects on gastrointestinal health, there are more hypotheses than experimental data on the molecular mechanisms of probiotic action. And in fact, one of the challenges has been to recognize that all probiotics are not created equal, as has been demonstrated by whole genome sequencing of an increasing number of accepted probiotic strains. A recent report characterized a probiotic-derived soluble protein, revealing a mechanism of prevention and treatment effects of probiotics in the setting of intestinal inflammatory diseases. A *Lactobacillus rhamnosus* GG (LGG)-derived soluble protein, called p40, was purified, cloned, and shown to ameliorate cytokine-induced apoptosis in intestinal epithelial cells through activation of the EGF receptor and a down-stream target, Akt. Expression of this protein is relatively restricted even among lactobacilli. By using special hydrogel beads to deliver intact p40 to the colon the authors showed reduced intestinal epithelial apoptosis and preserved barrier function in the colon epithelium in an EGF receptor-dependent manner, thereby preventing and/or treating intestinal inflammation in several mouse models

of colitis. Thus, this research supports the idea that development of probiotic-derived factors as potential therapies health and disease prevention and treatment.

This issue of Bactalk addresses evidence of specific biological effects of different probiotic strains in different clinical settings. Most people are well aware of the purported benefits of probiotics on gastrointestinal health. Recent exciting research has revealed the potential clinical applications of probiotics for diseases of other systems that are associated with altered microbiota leading to dysbiosis in two major locations of the human body, the gut and the vagina.

Autism spectrum disorders is a multifactorial disease. Increasing evidence indicates that alterations of microbiota in the gut might contribute to symptomatology and/or severity of symptoms in autistic children. Clinical studies suggest that gastrointestinal dysfunction is often associated with increased irritability, tantrums, aggressive behavior, and sleep disturbances in children with autism. Probiotic treatment has been shown to restore the microbial balance in the intestine, to relieve gastrointestinal problems and to attenuate immunological abnormalities in these patients. However, better-controlled clinical trials are needed to investigate whether probiotic treatment can lead to improved behaviors in children with autism.

It is well known that the microbiota plays an important role in regulating healthy vaginal

homeostasis, including maintaining the pH balance and excluding pathogens. A recent study focusing on identifying the microbiome of postmenopausal women and detecting epithelial gene expression associated with atrophy revealed *Lactobacillus iners* and *L. crispatus* were found to be the most abundant bacteria in healthy woman. However, lactobacilli were absent or depleted in post-menopausal women. An inverse correlation was found between Lactobacillus ratio and dryness and an increased bacterial diversity in women experiencing moderate to severe vaginal dryness. Genes involved in maintenance of epithelial structure and barrier function were down regulated, while those associated with inflammation were up regulated in menopause women with vaginal dryness and atrophy. Based on these findings, probiotics may have clinical efficacy for menopause symptoms. However, since probiotic function is strain specific, selection of correct probiotic strains based on a mechanistic understanding of the host and microbial responses will be important for the design of future studies.

These and findings in other conditions, such as infant cow's milk allergy and necrotizing enterocolitis challenge us to understand the unique basis for responsiveness (or non-responsiveness) to the application of probiotics in human disease. The sooner we understand why all probiotics *are not created equal*, the sooner we will be able to declare the basis for their efficacy in promoting human health.

CAN PROBIOTICS HELP WITH KIDNEY STONES?

Kidney stones, one of the most painful urologic disorders, have plagued humans for most of recorded history. Unfortunately, kidney stones are still one of the most common disorders of the urinary tract. According to the U.S Department of Health and Human Resources, kidney stones account for almost 3 million visits to health care providers and more than half a million people go to emergency rooms for kidney stone issues each year in the United States alone. There is currently no cure for kidney stones, but according to recent literature, it has been suggested that probiotics may provide some solutions to prevent kidney stones.



The incidence of kidney stones has been linked with various intestinal diseases due to alterations in the metabolism of oxalate, calcium, and uric acid. The most common stones are made up of a build-up of calcium oxalates. Since humans lack the enzymes needed to metabolize oxalate waste products, they are usually eliminated through excretion in urine, by forming insoluble calcium oxalate and elimination in feces, or oxalate degradation by gastrointestinal microorganisms. Kidney stones are caused by the formation of hard lumps composed of these waste products that remain in the urine because they could not be eliminated by the body. The stones form over time and travel down through the urinary system. During the process, the stones can damage the urinary tract, cause infection, disturb the flow of urine, and cause severe pain.

The discovery of oxalate-degrading bacteria within the human gastrointestinal tract has led to a flood of research regarding the role of probiotics in the management of chronic calcium oxalate kidney stones.

Abratt and Reid reviewed the research regarding probiotic use to manage kidney stones in 2010 in the journal, *Advances in Microbiology*. They found that *Oxalobacter formigenes* and *Lactobacillus* and *Bifidobacterium* species are the best studied in this regard.

The South African scientists concluded, "Clinical trials investigating reduced

hyperoxaluria through administering *O. formigenes* or its enzymes show a promising trend, but the data need confirmation through larger scale, well-controlled trials."

The authors also suggested further investigations are needed to determine whether there is a direct link between the lack of these beneficial, oxalate-degrading bacteria and increased oxalates in the urine and also whether their absence is a risk factor for kidney stones.

Furthermore, studies that can connect microbial numbers, oxalate metabolism, molecular analysis of the regulatory genes involved, and the ability of the bacteria to survive in the gut are crucial elements in finding suitable probiotics for treating kidney stone disease, the researchers believe

According to another recent review in the Indian Journal of Urology, researchers looked into the possible role that probiotics may provide in treating and preventing kidney stones. The researchers reviewed 137 articles and cited 53 in their review.

Overall, the authors maintained, "Due to lack of good-quality prospective interventional trials it is essential to test the findings of pathophysiological understanding and epidemiological evidence. Role of probiotics and phytochemicals needs special attention for future research."



PROBIOTICS MAY HELP BREAK DOWN CARBS

Researchers from the University of Washington in St. Louis, Missouri investigated the effects of probiotics found in yogurt on gastrointestinal flora in identical twins. The article appeared in the journal, *Science Translational Medicine*, in October, 2011. This recent study found that yogurt administered to identical twins did not actually colonize their gut microbiota, but in a follow-up investigation conducted on mice they found the probiotic culture affects how they digested carbohydrates.

Previous research led by Dr. Gordon in 2006 in the journal, *Nature*, had investigated the gut microbiota of obese and lean subjects. The team found that when the obese group lost weight they exhibited the same gut flora landscape that their leaner counterparts exhibited. This finding infers a microbial etiology to obesity.

The team of researchers analyzed the stool samples adult female identical twin pairs through repeated sampling 4 weeks before, 7 weeks during, and 4 weeks after ingestion of a commercially available fermented milk product (FMP) containing subspecies of the following: *Bifidobacterium animalis*, two strains of *Lactobacillus delbrueckii*, *Lactococcus lactis*, and *Streptococcus thermophilus*.

In addition, gnotobiotic mice containing model human gut flora whose genomes contain predicted genes were studied before and after they were treated the fermented milk product.

The results of the study showed no significant changes in the gut microbial species composition in the feces of humans and minimal changes in the mice consuming the FMP. ↩

However, the molecular analysis revealed that introducing the FMP strains into mice results in significant changes in expression of enzymes involved in carbohydrate metabolism. *Bifidobacterium animalis* showed to be the dominant persistent member of the FMP consortium.

These experiments reflect another level of understanding the effects of oral probiotic use and on gut function.

"GOOD" BUGS, "BAD" BUGS AND AUTISM

Autism Spectrum Disorder (ASD) affects 1 out of 110 children in the United States, according to the Centers for Disease Control. Studies in Asia, Europe, and North America have identified individuals with an ASD with an approximate prevalence of 0.6% to over 1%. There is a growing body of knowledge that implicates gastrointestinal dysbiosis as a possible inducer of the disease. Recent research is attempting to connect the dots between gastrointestinal complaints, autism and probiotics.

In the November 2011 issue of *Nutrition*, Polish scientists investigated the level of D-arabinitol (DA) and the ratio of D-/L-arabinitol (DA/LA) in the urine of children with autism. D-arabinitol is a five-carbon sugar alcohol that is a metabolite of most pathogenic *Candida* species, and it has been associated with invasive candidiasis and other gastrointestinal diseases which are common in this population.

The subjects were given probiotic therapy and the changes in DA/LA after probiotic treatment in urine samples of children with autism were recorded. The participants were also monitored for changes in behavioral markers as well.

The probiotic supplementation was found to correlate with a significant decrease in DA and DA/LA in autistic subjects and led to a significant improvement in ability of concentration and carrying out orders.

The authors concluded, "The use of probiotics seems to be helpful in reducing the level of DA and the ratio of DA/LA in the urine of children with autism."

Another study featured in the March 2011 issue of *BMC Gastroenterology*, an American group of researchers compared gastrointestinal flora and other markers of gastrointestinal status from stool samples of children with ASD as well as healthy subjects.

The objective of this study was based on the data that children with autism have been reported to have gastrointestinal problems that are more frequent and more severe than in children that do not have an ASD.

The gastrointestinal markers were assessed from stool samples of 58 children with ASD and 39 healthy typical children of similar ages. The researchers from Doctors Data and the University of Arizona included bacterial and yeast culture tests, lysozyme, lactoferrin, secretory IgA, elastase, digestion markers, short chain fatty acids (SCFA's), pH, and blood presence.

Gastrointestinal symptoms were also assessed via questionnaire and autistic symptoms were assessed with the Autism Treatment Evaluation Checklist (ATEC).

The authors found that gastrointestinal symptoms were strongly correlated with the severity of autism. When comparing the different biomarkers between the two groups of children, the children with ASD had much lower levels of total short chain fatty acids as well as lower levels of species of *Bifidobacter* and higher levels of species of *Lactobacillus*. Lysozyme was somewhat lower in children with autism as well. Other markers of digestive function were similar in both groups whether they were treated with probiotics or not.

Overall, the research team found that gastrointestinal symptom severity strongly correlate with autism severity. The authors report, "it is possible that autism symptoms are exacerbated or even partially due to the underlying gastrointestinal problems." Further investigation into probiotic use as well as understanding the role of the endogenous microbial landscape is warranted.

LACTOBACILLUS ROLE IN MENOPAUSAL SYMPTOMS

The quest to help alleviate post-menopausal symptoms has been muddled due to conflicting arguments and data on the use of hormone replacement therapy. A common symptom associated with menopause is vaginal dryness. Most often this is due to atrophy of the vaginal tissue as a result of a persistent decrease in estrogen. It is known that the resident microbes play a key role in maintaining vaginal health by promoting an optimal pH and staving off pathogenic bacteria. Interestingly, it is not common to see the role of microbiota as a target in literature pertaining to these commonplace menopausal symptoms.

A recent study in the journal Plos One sought to identify the bacterial landscape of post-menopausal women with and without vaginal dryness and symptoms of atrophy. The Canadian group of researchers also aimed to examine any differences in tissue gene expression associated with atrophy. Thirty-two postmenopausal women were included in the study to identify the vaginal microbiota. The results of the study indicated that the microbiota profiles were relatively stable over 10 weeks.

The authors also found, "an inverse correlation between Lactobacillus ratio and dryness and an increased bacterial diversity in women experiencing moderate to severe vaginal dryness."

In the healthy subjects, *Lactobacillus iners* and *Lactobacillus crispatus* were found to be abundant.

In the subjects that experienced symptoms, there a down-regulation of human genes involved in maintenance of vaginal epithelial tissue structure and function, and those genes associated with inflammation were up-regulated.

The significance of this study was that, contrary to previous thought, not all post-menopausal women experience a decrease in beneficial flora as a result of estrogen depletion.

About the Author: Helen Davakos, ND, DC, is board-certified in naturopathic and chiropractic medicine, and serves in a variety of professional roles including consultant, clinician, and educator. Dr. Davakos is the Vice President of the Illinois Association of Naturopathic Physicians. She lectures and writes about health and wellness for nationally recognized, professional and community organizations.

Probiotics in the News

Here is what is trending about Probiotics recently:

Probiotics May Prevent Antibiotic-Associated Diarrhea in Children,
Natural Standard Blog, November 16, 2011
<http://naturalstandard.com/news/news201111028.asp>

Probiotic Ice Cream Shows Oral Health Potential: Study,
Nutraingredients-usa.com, December 1, 2011
<http://www.nutraingredients-usa.com/Research/Probiotic-ice-cream-shows-oral-health-potential-Study>

Probiotics Help with Brain Injury, United Press International, December 2, 2011
http://www.upi.com/Health_News/2011/12/02/Probiotics-help-with-brain-injury-outcome/UPI-69731322877162/

If You're Tired or Constipated, This "Unusual Treatment" May Help,
FoodConsumer.org, December 5, 2011
http://www.foodconsumer.org/newsite/Nutrition/Supplements/probiotics_1205110845.html

Probiotics as Medicine, The Daily Star, December 9, 2011
<http://www.thedailystar.net/newDesign/news-details.php?nid=213021>

News from the IPA Office

It has been a particularly nice year for IPA, as our President described on his message addressing the membership, IPA has hit several milestones including the hiring of a new Administration Manager along with having new functional committees addressing issues and being proactive on the global regulatory environment. 2012 will be bringing a lot more new exciting things for our members and new educational initiatives will be in place as we are striving to bring information that you would like to see from us. In 2011 we released the first ever high quality documentary named Microwarriors which targeted consumers and we will continue being on the same path in 2012. Stay tuned by frequently visiting our website www.internationalprobiotics.org for information and to obtain documents of interest.



2 0 1 2

During the last few months we have spent a lot of time designing and confirming speakers from around the world for the next IPA World Congress which will take place on April 20th – 21st 2012 at the Hilton Universal City in sunny Los Angeles, California. We are hoping you will share our excitement for this event which will feature topics ranging from consumer, healthcare, regulations and science. This meeting is also endorsed by the American Gastroenterology Association (AGA). For more information please visit our website www.ipaworldcongress.com and register today. Do not delay, once all spots gets filled out registration will close.

On behalf of the entire IPA Team, I would like to wish everyone wonderful holidays and a Happy and Prosperous 2012 – Looking forward to seeing you in LA!

Ioannis Misopoulos, *Director General*

BOARD OF DIRECTORS

Rob Hurlbut
Attune Foods

Peter Rothschild
Biogaia

Claude Chevalier
BioK+

Henrik Dalboege
Chr. Hansen

Scott Bush
Danisco

Steve Sikorski
Futureceuticals

Mike Bush
Ganeden

George Paraskevacos
Harmonium Int'l.

Frederic Durmont
Institut Rosell/Lallemand

Jarrow Rogovin
Jarrow Formulas

Natarajan Ranganathan
Kibow Biotech

Hishashi Matsumura
Morinaga Milk Co

Michael Shahani
Nebraska Cultures

Tim Gamble
Nutraceutix

Barbara Miller
P&G

Peter Cartwright
Probiotics Int

Nancy Hamren
Springfield Creamery/Nancy's Yogurt

Dr. S.K. Dash
UAS Labs

Ted A. Nordquist
Whole Soy & Co.

Ryoichi Akahoshi
Yakult Honsha

