



Memorandum

NOV 13 2003

Rec'd 11-20-03  
16

Date: \_\_\_\_\_  
From: Interdisciplinary Scientist/Pharmacist, Division of Dietary Supplement Programs  
, Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810  
Subject: 75-Day Premarket Notification of New Dietary Ingredients  
To: Dockets Management Branch, HFA-305

Subject of the Notification: **Lactobacillus plantarum and Fructooligosaccharide  
(FOS) (Gastroplan and Gastroplan CF)**

Firm: Kups International

Date Received by FDA: 2/04/03

90-Day Date: 5/05/03

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and  
Cosmetic Act, the attached 75-day premarket notification and related correspondence for the  
aforementioned substance should be placed on public display in docket number 95S-0316 as  
soon possible since it is past the 90-day date. Thank you for your assistance.

  
\_\_\_\_\_

P drive/ NDI/ NDI File Closeout/DDSP SOP closeout process...

95S-0316

RPT 171



APR 15 2003

8554 '03 NOV 20 P2:04

Mr. Prabbat Garg  
Kups International  
6704 Tomlinson Terrace  
Cabin John, Maryland 20818

Dear Mr. Garg:

This letter acknowledges receipt of your new dietary ingredient notification, dated December 9, 2002 that was originally filed with the Food and Drug Administration (FDA) on December 13, 2002. Subsequently, we requested additional information in accordance with Title 21 of the Code of Federal Regulations (21 CFR) Part 190.6. We received the addendums with this information and informed you that the new effective filing date would be February 4, 2003. Your notification is for the combination of substances, *Lactobacillus plantarum* (ATCC 202195 strain) and Fructooligosaccharide (FOS) under the tradenames, GastroPlan™ and GastroPlan-CF™ and the single substance, *Lactobacillus plantarum* under the trade name of GastroPlan-C™ which you assert to be new dietary ingredients. In a facsimile dated March 6, 2002, you indicated that you wish to withdraw GastroPlan-C™ which contained the single ingredient *Lactobacillus plantarum* from this notification and would file a separate notification for GastroPlan-C.

In accordance with 21 C.F.R 190.6(c), FDA must acknowledge its receipt of a notification for a new dietary ingredient. For 75 days after the filing date (i.e., after February 4, 2003), you must not introduce or deliver for introduction into interstate commerce any dietary supplement that contains *Lactobacillus plantarum* and Fructooligosaccharide.

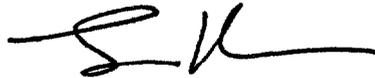
Please note that acceptance of this notification for filing is a procedural matter and, thus, does not constitute a finding by FDA that the new dietary ingredient or supplement that contains the new dietary ingredient is safe or is not adulterated under 21 U.S.C. 342. FDA is not precluded from taking action in the future against any dietary supplement containing these ingredients if it is found to be unsafe, adulterated, or misbranded.

Further, please be aware that under 21 U.S.C. 321(g)(1)(B), if a product is implicitly or expressly represented as being intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease, it may be subject to regulation under the drug provisions of the Act. You may also obtain information on claims that may be made in the labeling of dietary supplements pursuant to 21 U.S.C. 343(r)(6) in the final rule on structure/function claims published in the January 6, 2000 Federal Register (65 FR 1000).

Your notification will be kept confidential for 90 days after the filing date. After May 5, 2003, the notification will be placed on public display at FDA's Docket Management Branch in docket number 95S-0316. Prior to May 5, 2003, you may wish to identify in writing specifically what information in your notifications you believe is proprietary, trade secret or otherwise confidential information, which should not be disclosed to the public.

Please contact Victoria Lutwak at 301 436-2375, if you have any questions concerning this matter.

Sincerely,

A handwritten signature in black ink, appearing to be 'S Walker', written over a horizontal line.

Susan Walker, M.D.  
Acting Director,  
Division of Dietary Supplement Programs  
Office of Nutritional Products, Labeling  
and Dietary Supplements  
Center for Food Safety  
and Applied Nutrition



## KUPS International

### Global Business Opportunities

6704 Tomlinson Terrace • Cabin John, Maryland • 20818

Phone: (301) 461-3838 • Fax: (301) 263-9112

Email: KUPSinternational@yahoo.com

March 6, 2003

Ms. Gloria Chang  
Office of Nutritional Products Labeling and Dietary Supplement  
HFS 821, Food and Drug Administration  
5100 Paint Branch Pkwy  
College Park, MD - 20740

Re: GastroPlan Premarket Submission

Dear Ms. Chang:

Thank you for calling me this afternoon regarding availability of the strain from ATCC.

Please let your microbiology personnel know that the *Lactobacillus plantarum* strain we are using in our preparation does not appear in the ATCC catalogue. The ATCC catalogue lists only a small portion of their full depository depending on the demand and popularity of the item. However, they have a much bigger collection with designated numbers, and the party interested in procuring the same should contact ATCC sales and/or technical department to get these items.

To obtain the strain from ATCC you will have to do the following:

1. Call 1-800-638-6597 (or 703-365-2700) and go to SALES or TECHNICAL-help section, give them the ATCC number 202195. ATCC should then be able to advise you on how to procure this *L. plantarum* strain.
2. In case of any problem contact the specialist Tanya Unnally (703-365-2721).

For your review, please use the documents (papers and abstracts) provided to you in triplicate on January 17, 2003 (we had sent two copies of all items per your web site direction in December 2002 and with your advice sent you the third one on January 17). As you have noted correctly, some of them are "abstracts" and although full length papers are not available, these highly relevant and important abstracts have been presented at important national meetings, they are available in *published form* and are cited by others.

As per our discussion, please consider GastroPlan™ and GastroPlan-CF™ as one notification; and we will separately send you three more copies for GastroPlan-C™.

Thank you for your assistance in this matter. Please call me if you need any other details.

Sincerely,

A handwritten signature in black ink that reads "Prabhat". The signature is written in a cursive, slightly slanted style.

Prabhat Garg  
Chief Executive Officer

**KUPS International****Global Business Opportunities**

6704 Tomlinson Terrace • Cabin John, Maryland • 20818  
Phone: (301) 461-3838 • Fax: (301) 263-9112  
Email: KUPSinternational@yahoo.com

January 24, 2003

Ms Gloria Chang  
Office of Nutritional Products Labeling and Dietary Supplement  
HFS 821, Food and Drug Administration  
5100 Paint Branch Parkway  
College Park, MD- 20740.

Re: FOS concentration in GastroPlan™

Dear Ms. Chang:

Thank you for your call in reference to our pre-market notification. Amount of FOS used in GastroPlan™ li products is as follows:

1. GastroPlan™: 150 mg of FOS
2. GastroPlan-C™: No FOS is added in this preparation
3. GastroPlan-CF™: 150 mg of FOS

If you need further information please let us know

Sincerely yours

A handwritten signature in black ink that reads "Prabhat".

Prabhat Garg  
Chief Executive Officer



**KUPS International**

**Global Business Opportunities**

6704 Tomlinson Terrace • Cabin John, Maryland • 20818

Phone: (301) 461-3838 • Fax: (301) 263-9112

Email: KUPSinternational@yahoo.com

January 17, 2003

Ms Gloria Cheng  
Office of Nutritional Products Labeling and Dietary Supplement,  
HFS 821, Food and Drug Administration  
5100 paint Branch Parkway  
College Park, MD- 20740.

Re: GastroPlan Premarket submission by KUPS International

Dear Ms. Cheng:

We really appreciate your call in reference to our pre-market notification. As per your requirement, we are sending you one more copy (third copy) of the notification along with the following information desired by you.

1. *Lactobacillus plantarum* is obtained from American Type Culture Collection (ATCC), Manassas, Va 20108, USA. Tel # 1-800-638-6597.
2. Fructooligosaccharide (FOS) is obtained from American Ingredients, 2929 East White Star Avenue, Anaheim, CA-92806. This is NutraFlora<sup>R</sup> FOS, which has US FDA's GRAS recognition (GRN000044).
3. This product is not targeted towards any particular population and the recommended use is one or two units daily.

If you need further information please let us know.

Sincerely yours

Prabhat Garg  
Chief Executive Officer



**Global Business Opportunities**

6704 Tomlinson Terrace • Cabin John, Maryland • 20818  
Phone: (301) 461-3838 • Fax: (301) 263-9112  
Email: KUPSinternational@yahoo.com



## Pre-Market Notification for a New Dietary Ingredient

Date: December 09, 2002

To

Office of Special Nutritional Products Labeling  
and Dietary Supplements  
5100 Paint Branch Parkway  
College Park, MD 20740

From  
KUPS International,  
6704 Tomlinson terrace,  
Cabin John, Maryland 20818

Dear Sir/Madam,

KUPS International is submitting a pre-market notification to the Food and Drug Administration pursuant to the Code of Federal Regulations, 21CFR190.6. This application is to notify Center for Food Safety and Applied Nutrition, the intent of Kups International to contract manufacture and market the products, GastroPlan, GastroPlan-C and GastroPlan-CF, which contains *Lactobacillus plantarum* (ATCC 202195 strain) and Fructooligosaccharide (FOS) as new dietary ingredients. As per the requirements, Kups International will restrain marketing these products for at least 75 days from the date of application and acceptance.

We are enclosing two copies of Pre-Market Notification application for your reference. Please contact us if you need more information or have any queries.

Sincerely,

Prabhat Garg  
Chief Executive Officer  
(301) 461-3838 (voice); (301) 263-9112 (fax)  
PrabhatG@kupsinternational.com

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## **1. Name of new Dietary Ingredients:**

*Lactobacillus plantarum* ATCC 202195  
Fructooligosaccharride (FOS)

## **2. Names and Addresses of the Manufacturer and Supplier:**

GastroPlan™ line of products are formulated and packaged for **KUPS International**, 6704 Tomlinson Terrace, Cabin John, Bethesda, MD 20818, at:

Functional Foods Inc.,  
470, Rt. 9, Englishtown,  
New Jersey - 07726

*Lactobacillus plantarum* is manufactured and lyophilized at:

Rhodia Inc.,  
3322, Vondron Road,  
Madison,  
Wisconsin - 53716

Fructooligosaccharide is obtained from:

American Ingredients,  
2929 East White Star Ave, Anaheim  
California – 92806

## **3. Dietary Supplement Description:**

### **3.1 Products Name:**

#### **3.1.1 GastroPlan™**

Each capsule/tablet/lyophilized powder sachet of GastroPlan dietary supplement will contain approximately 2-8 billion colony-forming units (CFU) of *Lactobacillus plantarum* and 150 mg of FOS together with binders/excipients.

#### **3.1.2 GastroPlan-C™**

Each capsule/tablet/lyophilized powder sachet of GastroPlan-C dietary supplement will contain approximately 20-80 billion colony forming units (CFU) of *Lactobacillus plantarum* together with binders/excipients.

### **3.1.3 GastroPlan-CF™**

Each capsule/tablet/lyophilized powder satchet of GastroPlan-CF dietary supplement will contain approximately 20-80 billion colony-forming units (CFU) of *Lactobacillus plantarum* and 150 mg of FOS together with binders/excipients.

### **3.2 Recommended Use:**

One or two units daily.

Fructooligosaccharide & *Lactobacillus plantarum* help maintain a healthy digestive tract by replenishing and maintaining the natural balance of microflora in the intestine.

## **4. Product Description:**

The Genus *Lactobacillus* comprises of Gram positive bacteria known to produce lactic acid. These lactic acid bacteria in general, are rod shaped, non-motile and microaerophilic or anaerobic in nature. Lactic acid bacteria are considered harmless, non-pathogens and are given "generally recognized as safe" (GRAS) status (Lee and Salminen, 1995) in different countries. *Lactobacilli* are used in the food industry in various food fermentations, food preservation (Stiles 1996) and when added as cultures are considered safe and do not pose a health risk to humans (Holzapfel et al., 1995). These bacteria play a very important role in the intestine of humans by breaking down food particles into components which help in the absorption of essential nutrients. Donohue and Salminen, 1996 have investigated and reported the safety of lactic acid bacteria. It has been shown that certain Lactic acid bacteria species are beneficial to humans and their inclusion in the diet may benefit human health (Gorbach, 1990; Rafter, 1995; Scheinbach, 1998). These microorganisms are referred to as "probiotics".

NutraFlora® (Fructooligosaccharide commonly known as FOS) is one of the purest, and most concentrated form of short-chain fructooligosaccharides (scFOS™) available in the market. These short chain oligosaccharides (also called "prebiotics", are found in breast milk and as a natural component in many fruits, vegetables, and grains. However, one needs to consume a large amount of fruits and vegetables (for example (eat 6 bananas, 4 onions, or 95 Clives of garlic) daily to get the same amount of scFOS™ found in just one gram of FOS. Studies show that just one gram (1/4 teaspoon) of FOS included in daily diet could help in staying healthy.

## 5. Product Safety:

***Lactobacillus plantarum*** is commonly found in dairy products, sauerkraut, and pickled products and as the most common and predominant species in the human intestinal tract (Ahrne et al., 1998, Hammes and Tichaczek, 1994) and is considered to be a friendly bacterium. It is a facultative anaerobic bacterium, which produces lactic acid as a main product from carbohydrates ([www.wellnessadvocate.com](http://www.wellnessadvocate.com)). *Lactobacillus plantarum* is one of the *Lactobacillus* bacteria listed as probiotics. According to Fuller, 1991, probiotics are live microbial feed supplement, that beneficially affect the host by improving its intestinal balance. Fermentation with *Lactobacillus plantarum* is used to preserve various vegetables such as cucumbers, cabbage and is typically related with pickles and sauerkraut. Several clinical and scientific studies using *Lactobacillus plantarum* in different parts of the world have shown its safety and beneficial effect in multiple disease states.

Bukowska et al (1998) studied 30 Polish males averaging aged about 42 years having a moderately high serum cholesterol. During a period of six weeks, half of the males were given *Lactobacillus plantarum* in 200ml (ProViva™) per day and the other half were given a placebo (rose hip drink) with no *Lactobacillus plantarum*. The aim of this study was to observe if there was any decrease in the total and the LDL cholesterol without affecting the levels of the (protective) HDL cholesterol. At the end of the study it was found that the control group showed no change in blood lipids, glucose or fibrinogen. While, the Pro Viva™ group showed a 7.3% and 9.6% fall in total cholesterol and LDL cholesterol respectively. There was no change found in the HDL cholesterol level. They also observed a 13.5% reduction in serum fibrinogen for this group.

In the Swedish study, *Lactobacillus plantarum* significantly decreased the subjective experienced bloating during the treatment of 52 inflammatory bowel syndrome (IBS) patients. The pain was significantly decreased in both the groups, but the decrease was more rapid and pronounced in the group, which was given *Lactobacillus plantarum*. Twelve months after the treatment, the patients given *Lactobacillus plantarum* in the study still experienced a better overall gastrointestinal function than the patients of the placebo group (Nobaek et al., 2000).

Levy (1997) has shown that *L. plantarum* helps in the eradication of *Clostridium difficile* from chronic carriers, and it also prevents diarrhea during chronic antibiotic use. The studies were done using *Lactobacillus plantarum* 229v in 15 children, for the period of 3 to 52 weeks, with Antibiotic associated diarrhea. Seven of these children were being recurrent *Clostridium difficile* infection.

Chlebcewicz-Szuba et al (1999) observed similar results in their study with antibiotic associated diarrhea. They treated 8 children with antibiotic associated

diarrhea and 25 others with acute diarrhea. The children were given 2-3 doses of *Lactobacillus plantarum* in ProViva™ (30-50ml doses for children less than 2 years and 50-100ml per dose for those over 2 years). The symptoms were resolved in 3 to 4 days of treatment and with no side effects.

Mack et al (1997) studied two immunocompromised patients with *Clostridium difficile* colitis. They were treated with antibiotics, but the symptoms resumed when the therapy was discontinued. However, when they were given the antibiotic and *Lactobacillus plantarum* 299v on a daily basis the patients recovered within two to three days.

Several other scientific studies involving *in vitro* and animal models have shown a wide spectrum of health-promoting effects of *L. atobacillus plantarum* ranging from induction of intestinal enzymes to suppression of inflammatory cytokines, and serious necrotic disease conditions of the intestinal tract. Selected studies are listed in section 5.2 (below).

**Fructooligosaccharides (FOS)** are short chain oligosaccharides are naturally found in variety of vegetables, grains and fruits including artichoke, asparagus root, onion, wheat, rye, banana, tomatoes, and garlic. These short chain oligosaccharides are also found in breast milk. NutraFlora™ FOS is one of the purest, and most concentrated form of short-chain fructooligosaccharides currently found in the market and is used in GastroPlan™. This concentrated form provides a powerful fiber effect without bulk or grit commonly found in other fiber products. NutraFlora™ has U.S. FDA GRAS recognition (GRN000044). FOS is a food source for the friendly bacteria that are present in our digestive system. These bacteria, such as *Lactobacillus* and *Bifidobacteria* are considered friendly and they help digest food and boost body's resistance to infection and diseases. FOS passes through the stomach without being digested and it is used as a food source for these friendly bacteria when it reaches the lower intestine. As these friendly bacteria use FOS and multiply, they provide a number of health benefits - such as improving the absorption of calcium and magnesium. They also help create an unfavorable environment in the digestive system for most harmful bacteria to survive. These harmful bacteria, such as *E. coli* and *Clostridia*, have been know to produce toxins that can have negative health consequences. Helping the body fight these harmful bacteria is one of the key ways that FOS helps the body stay healthy. Harmful bacteria cannot use FOS. Selected references and scientific studies (abstracts) using FOS are given below section in 5.3.

Currently, several probiotic products available in the world market use the combination of *Lactobacillus plantarum* and FOS in their formulation.

### **5.1 Dietary supplements available in the market with *Lactobacillus plantarum*:**

There are already products available, in USA and abroad, with *Lactobacillus plantarum* as an ingredient. Some of the products are mentioned below.

1. FutureCeuticals *Lactobacillus plantarum* – N46.4, Futureceuticals, Santa Rosa, CA 95401
2. Proviva, Probi AG, Lund, Sweden.
3. Bio-Culture 3000, Bio-Energy Systems, ([www.bioenergysystems.com](http://www.bioenergysystems.com))
4. Plantadophilus, Transformation Enzyme Corporation (TEC), Houston, TX 77042.
5. Probiotic LP299V, Probi AG, Lund, Sweden.
6. Kirkman's Pro-immune support, Kirkman laboratories, Lake Oswego, Oregon 97035
7. Plantadophilus, Enzyme Essentials LLC, Houston, TX 77007
8. Plantadophilus, Advanced Athletic Performance, Frederick, MD 21701

There are many other products where *Lactobacillus plantarum* is used as a mixture with other probiotics bacteria. Few examples are given below:

1. FloraFood, AIM International. ([www.aimnaturally.com](http://www.aimnaturally.com))
2. Friendly Colonizer powder, Elixia Ltd., Albuquerque, NM 87112.
3. TH-1 Probiotics, Jarrow Formulas™, Los Angeles, CA 90035.
4. PB 8, Nutrition Now<sup>R</sup>, Bloomington, IN 47407.

### **5.2 Scientific Studies for *Lactobacillus plantarum*:**

1. "Oral Bacteriotherapy as Maintenance Treatment in Patients with Chronic Pouchitis: A double-Blind, Placebo-Controlled Trial". Paolo Gionchetti et al., *Gastroenterology*, 2000, 119:305-309.
2. "Alteration of Intestinal Microflora Is Associated with Reduction in Abdominal Bloating and Pain in Patients With Irritable Bowel Syndrome". Soren Nobaek et al., *The American Journal of Gastroenterology*, 2000, Vol. 93, No 5: 1231-1238.
3. "Probiotics and Immune Response". Susanna Cunningham-Rundles et al., *The American Journal of Gastroenterology*, January Supplement, 2000, Vol. 95, No 1: S22-S25.
4. "Probiotics inhibit enteropathogenic *E. coli* adherence in vitro by inducing intestinal mucin gene expression". David R Mack et al., *American Journal Physiology*, 1999, 276: G941-G950.

5. "Immunomodulatory effects of *Lactobacillus plantarum* colonizing the intestine of gnotobiotic rats". M. V. Herias et al., Clin Exp Immunol, 1999, 116: 283-290.
6. "The Effects of Lactobacillus Strains and Oat Fiber on Methotrexate-Induced Enterocolitis in Rats". Yilei Mao et al., Gastroenterology, 1996, 111: 334-344.
7. "Probiotics in foods not containing milk or milk constituents, with special reference to *Lactobacillus plantarum* 299v<sup>1-3</sup>". Goran Molin, Am J Clin Nutr, 2001, 73(suppl): 380S-385S.
8. "*Lactobacillus plantarum*: Immunomodulation in the inflamed Colon Through T cell and Macrophage IL – 10 synthesis". Shri Pathmakanthan, et al., Gastroenterology, 2001, 120(suppl): No. 1662, A-322.
9. "Disaccharide and Junctional Protein Induction by *Lactobacillus plantarum* in Cultured Intestinal cells". Xiaoling Cui et al., Pediatric Research, 2001, 49(suppl): No.4, 1990 poster 8.
10. "Lactobacillus plantarum PP-217 Blocks Bacteria-Induced Tissue Injury in a Weanling Rabbit Heal Loop Model of Necrotizing Enterocolitis". Pinaki Panigrahi et al., Pediatric Research, 2000, 47(suppl): No.4, 2501 poster.
11. "Differential Immune Responses to Probiotic and pathogenic Bacteria in Normal and Colitic Patients". Shri Pathmakanthan et al., Digestive Disease Week, San Diego, California, May 21-24, 2000: A-140, 726.
12. "Lactobacillus plantarum 299v in the Irritable Bowel Syndrome: A Randomized, Double-Blind, Placebo-controlled Crossover Study". John K DiBaise et al., Digestive Disease Week, San Diego, California, May 21-24, 2000: A-614, 3163.
13. "Mechanisms of Colonic Epithelial Protection by *Lactobacillus plantarum*". Shri Pathmakanthan et al., Digestive Disease Week, San Diego, California, May 21-24, 2000: A-823, 4236.
14. "Effect of Butyrate and *Lactobacillus Plantarum* on Cytokine Expression in Caco-2 Cells". Linhuang Han et al. Peds. Res. (Suppl), 2001. 49(4): p. 115A

### 5.3 Scientific Studies for Fructooligosaccharide (FOS):

1. "Fructo-oligosaccharide supplementation: effects on metabolic, endocrine and hematological traits in veal calves". Kaufhold J, Hammon HM, Blum JW Division of Nutritional Pathology, University of Berne, Switzerland, J Vet Med A Physiol Pathol Clin Med 2000 Feb;47(1):17-29
2. "Influence of a synbiotic mixture consisting of Lactobacillus acidophilus 74-2 and a fructooligosaccharide preparation on the microbial ecology sustained in a simulation of the human intestinal microbial ecosystem (SHIME reactor)", Gmeiner M, Kneifel W, Kulbe KD, Wouters R, De Boever P, Nollet L, Verstraete W Department of Dairy Research and Bacteriology, University of Agriculture, Vienna, Austria, Appl Microbiol Biotechnol 2000 Feb;53(2):219-23

3. "A computer-controlled system to simulate conditions of the large intestine with peristaltic mixing, water absorption and absorption of fermentation products", Minekus M, Smeets-Peeters M, Bernalier A, Marol-Bonnin S, Havenaar R, Marteau P, Alric M, Fonty G, Huis in't Veld JH TNO Nutrition and Food Research Institute, Zeist, The Netherlands, *Appl Microbiol Biotechnol* 1999 Dec;53(1):108-14
4. "Caecal fermentation and energy accumulation in the rat fed on indigestible oligosaccharides", Sakaguchi E, Sakoda C, Toramaru Y Laboratory of Animal Nutrition, Faculty of Agriculture, Okayama University, Japan, *Br J Nutr* 1998 Nov;80(5):469-76
5. "Short-chain fructo-oligosaccharide administration dose-dependently increases fecal bifidobacteria in healthy humans", Bouhnik Y, Vahedi K, Achour L, Attar A, Salfati J, Pochart P, Marteau P, Flourie B, Bornet F, Rambaud JC INSERM U 290, Fonctions intestinales, metabolisme et nutrition, Hopital Saint-Lazare, 75010 Paris, France, *J Nutr* 1999 Jan;129(1):113-6
6. "Plasma lipids and fatty acid synthase activity are regulated by short-chain fructo-oligosaccharides in sucrose-fed insulin-resistant rats", Agheli N, Kabir M, Berni-Canani S, Petitjean E, Boussairi A, Luo J, Bornet F, Slama G, Rizkalla SW Department of Diabetes and INSERM U341, Hotel-Dieu Hospital, 75004 Paris, France, *J Nutr* 1998 Aug;128(8):1283-8
7. "In vitro fermentation of carbohydrate by breast fed and formula fed infants", Parrett AM, Edwards CA Department of Human Nutrition, Glasgow University, *Arch Dis Child* 1997 Mar;76(3):249-53
8. "Protective effect of dietary fructo-oligosaccharide in young rats against exocrine pancreas atrophy induced by high fructose and partial copper deficiency", Taper HS, Delzenne N, Tshilombo A, Roberfroid M Department des Sciences Pharmaceutiques, Universite Catholique de Louvain, Brussels, Belgium, *Food Chem Toxicol* 1995 Aug;33(8):631-9
9. "Effect of fiber source on short-chain fatty acid production and on the growth and toxin production by *Clostridium difficile*", May T, Mackie RI, Fahey GC, Cremin JC, Garleb KA Dept. of Animal Sciences, University of Illinois, Urbana, *Scand J Gastroenterol* 1994 Oct;29(10):916-22
10. "Gaseous response to ingestion of a poorly absorbed fructo-oligosaccharide sweetener", Stone-Dorshow T, Levitt MD, *Am J Clin Nutr* 1987 Jul;46(1):61-5

## 6. References (Cited in the Body of the Text):

- Ahrne S et al, "The normal Lactobacillus flora of healthy human rectal and oral mucosa". J. of Applied Microbiology, 1998, 85:88-94.
- Bukowska H, Pieczul-Mroz J, Jastrzebska M et al "Decrease in fibrinogen and LDL-cholesterol levels upon supplementation of the diet with Lactobacillus plantarum in subjects with moderately elevated cholesterol". *Atherosclerosis*. 1998, 137 437-8.
- Chlebcewicz-Szuba W, Birkenfeld B, Piusinska K, Rudnicki J (1999): Administration of Lactobacillus plantarum 299v in children with acute diarrhoea and during prolonged antibiotic treatment. (*paper in preparation*).
- Donohue, D.C. and S. Salminen. "Safety of probiotic bacteria". *Asia Pacific J. Clin. Nutr*, 1996, 5:25-28.
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- Hammes, W.P. and P.S. Tichaczek. "The potential of lactic acid bacteria for the production of safe and wholesome food". *Z. Lebensm. Unters. Forsch.* 1994, 198:193-201.
- Holzapfel, W.H., R. Geisen, and U. Schillinger. "Biological preservation of foods with reference to protective cultures, bacteriocins and food-grade enzymes". *International J. Food Microbiol.* 1995, 24:343-362.
- Lee, Y.K. and S. Salminen. "The coming age of probiotics". *Trends in Food Sci. Technol.* 1995, 6:241-245.
- Levy J. "Experience with a juice beverage containing live Lactobacillus plantarum (LP) 299v; a promising adjunct in the management of antibiotic-related and other G-I disturbances". (*Poster presented to the American Gastroenterological Association, 1998. 11-14 May, Washington DC*).
- Mack DR, Abromowitch M, Ramey L et al (1997): "Short course antibiotics with probiotics for *Clostridium difficile* colitis in immunocompromised patients". (*Poster at the North American Soc for Paediatric Gastroenterology and Nutrition, Toronto*).
- Nobaek S, Johansson M-L, Jeppson B (1998): "Administration of a rose-hip soft drink containing oats fermented with Lb plantarum DSM9843 (299v) in patients with IBS". (*Poster presentation*).
- Rafter, J.J. "The role of lactic acid bacteria in colon cancer prevention". *Scand. J. Gastroenterol.* 1995, 30:497-502.
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