

Yoghurts

november 2002 - Letter N° 10

Health • Nutrition • Flora

& fermented milks

SCIENTIFIC SURVEY . LACTIC ACID BACTERIA . PROBIOTICS

IN THIS ISSUE

- Probiotics and immunity: *presumption of beneficial interaction*
- Prevention of inflammatory bowel diseases: *implication of probiotics*
- Yoghurt and fermented milks: *a strong health identity*
- Stimulation of the chemotaxis of *macrophages*
- Inflammatory process *and safety of lactic acid bacteria*
- Prevention of bacterial diarrhea *by probiotics*
- Benefit of the consumption of probiotics *at the time of a Helicobacter pylori infection*
- International Symposium Program

This survey letter on lactic acid bacteria is produced by the scientific committee of

SYNDIFRAIS

Publishing director

Arnauld de Miollis (Syndifrais)

Scientific coordinator

Brigitte Laurent

Reviewing board,

the Scientific Committee of Syndifrais
Jean Louis Bresson (Hôpital des enfants malades, Paris), Nadine Cerf-Bensussan (Hôpital Necker, Paris), Christine Cherbut (INRA, Centre de recherche en nutrition humaine de Nantes), Robert Ducluzeau (Directeur de recherche INRA), Jean-Marie Eustache (MLC), Irene Lenoir-Wijnkoop (Danone Vitapole), Marie-France Pagerey (Affaires scientifiques et réglementaires, Nestlé France), Patricia Ramos (Yoplait)

Scientific Survey

Judith Benrekassa (Cerin)

Editor



Responsible for the information
Eric Labouze (BIO Intelligence Service)

Writer

Lamy Moulay (BIO Intelligence Service)

edito

Congrilait 2002 : a symposium on yoghurt and fermented milks

Jean-Louis Bresson, Chair of the Scientific Mission of Syndifrais

Newsletter N° 10 provides a first brief survey of the symposium "Yoghurt & fermented milks : benefits of live cultures" devoted to yoghurts and fermented milk, organised by the International Association of Yoghurt and Fermented Milk Manufacturers during the 2002 World Dairy Congress (Congrilait, Paris, 24-27 September 2002).

Eleven renowned specialists from the United States, Europe, Japan and New Zealand covered themes, during the day-long symposium, covering the entire field, from the status of regulations governing industrial production, genomic sequencing of probiotics and their interactions with the host organism, to the analysis of consumers' expectations according to their country and culture.

This day highlighted the richness of this field of research. The scope of fermented milk consumption and production is just as far reaching in time as in space. In fact, fermented milks have been part of some civilisations for a long time, the type of product consumed varying according to geographic areas and cultural practices. However, the effects of milk on, for example, the expression of genes and the functional capacities of ferments still need to be explored.

This meeting was highly successful not only because of the high quality of the presentations, and the richness of the discussions they generated, but also because of the quality of the organisation and warm welcome. We thank the organisation committee, in particular Professors M.E Sanders (USA) and F. Guarner (Spain). The main themes of this day's conferences and debates, and other Congrilait symposia will shortly be available on CD-ROM*.

The meeting was also the opportunity to strengthen our ties with scientific colleagues from other countries, some accepting to contribute to the Mission's activity, in particular by collaborating in this Newsletter.

* For full information concerning the Congrilait CD-ROM you can contact us directly at the following address: syndifrais@syndifrais-syndilait.org.

During the 26th World Dairy Congress that took place in Paris from the 24th and 27th of September 2002, a symposium, chaired by Professor J-L Bresson, was organised on the theme "Yoghurt and fermented milk : benefits of live cultures". This was an opportunity to review the health benefits of these products, in addition to regulatory aspects and consumers' expectations.

We give below insights into two scientific conferences relating to the two themes in the bibliographic selection of this Newsletter: "Probiotics and immunological effects" and "Probiotics and gastro-intestinal health". At quite another level, a third conference, with a wealth of information, was chosen to be included in this Newsletter. It offers an international panorama of consumers' perceptions and expectations in respect to yoghurt and fermented milks. Further informations on this symposium will be available in the next letters.

Probiotics and immunity: *presumption of beneficial interaction*

According to the immunologist Eduardo Schiffrin from Switzerland, intestinal microflora can be considered to be an organ in its own right. In fact, intestinal microflora, made of a wide variety of bacteria, is capable, like an organ, of accomplishing important functions that can be modulated by environmental factors such as nutrition. This organ has the special feature of being acquired after birth since mammals are born without microflora.

We know that certain organisms of the intestinal microflora, such as lactobacilli

and bifidobacteria, participate in the first stages in the maturation of the new born mammal's intestine. These same organisms are also linked to other beneficial effects for the host, such as maintaining intestinal integrity, protecting against pathogenic agents and modulating immunity.

It would appear that the microflora plays a major role in the regulation of intestinal immunity homeostasis and the prevention of inflammation. The contribution of intestinal epithelial cells and microflora to the first line of defence against

pathogenic bacteria and microbial antigens is today recognised.

We note increasing scientific interest in the study of the host's mechanisms of innate immunity response to the different constituents of native microflora. Currently, it is suggested that certain strains of probiotics play a beneficial role in the regulation of intestinal inflammation and perhaps in the host's immunity status.

Prevention of inflammatory bowel diseases: *implication of probiotics*

Inflammatory bowel diseases (IBD) are chronic pathologies with an unknown etiology. The usual therapies mitigate the severity of the acute phases of the inflammation of the intestinal mucous membrane but there is no therapy capable of eradicating these diseases.

Epidemiological observations suggest that there is a link between the establishment of intestinal flora and the risk of developing an IBD. In fact, treatment by broad-spectrum antibiotics reduces the bacterial load and reduces inflammation in people suffering from IBD and in animal models.

Patients suffering from IBD present an abnormal reaction to native bacteria of the intestinal microflora. Constant activation of the intestinal immune

system against these bacteria seems to be responsible for the relapses characteristic of this type of illness.

The fact that the microflora is implicated in these inflammatory diseases leads us to suppose that we could offset these unwelcome effects by compensating for the imbalance of the intestinal microflora by the ingestion of probiotics. Current investigations are seeking to identify the probiotics capable of countering these effects.

The current hypothesis is that probiotics would be capable of exercising an anti-inflammatory activity. The results available are encouraging. For example, it has been shown that colonisation by *Lactobacillus reuteri* is capable of preventing the development of colitis in

genetically sensitive mice. Other studies, using bacteria modified genetically to secrete the anti-inflammatory cytokine IL10, showed a therapeutic effect in a mouse model suffering from colitis. In humans, certain probiotics have an anti-inflammatory activity when they interact with the intestinal mucous membrane.

According to Francisco Guarner of the Digestive System Research Unit at the Vall d'Hebron Hospital in Barcelona, although these results and hypotheses need further investigation, preliminary clinical trials carried out with probiotics in the case of IBD have been encouraging. Today, we can consider probiotics to be a promising tool in the prevention and control of inflammatory bowel diseases.

This scientific letter "Yoghurts & fermented milks" is also available on the following websites:
www.maison-du-lait.com and www.syndifrais.org

Yoghurt and fermented milks: *a strong health identity*

A qualitative study on the perception of yoghurts and fermented milks was carried out in 12 countries by MSM Marketing Research company*.

The approach was based first on expert interviews of dieticians/nutritionists and journalists and secondly on interviews of groups of consumers (young women without

children, women with children under 15 years of age and seniors).

From this study, we will keep in mind the following conclusions. Among food products, yoghurts and fermented milks occupy a privileged position that reconciles two often contradictory trends: the search for so-called healthy food and the appeal of

convenient food products. This status can be explained by the history of yoghurt and fermented milk consumption in the different countries, which can be grouped in four categories (see table below).

Consumption history across countries

Categories	Countries	Consumption origin
"Cultural inventors"	India, Turkey, Sweden, Russia	A strong remaining culture of yoghurts and fermented milks : these products are historically consumed.
"Industrial/ingredient inventors"	Japan, Korea, China	An autonomous development of yoghurt and fermented milks, based on ingredient technology.
"Importers"	Brazil, USA	Yoghurts and fermented milks are totally imported : behaviours differ from country to another.
"Industrial/milk inventors"	France, Germany, Spain	A totally integrated consumption : the industrial production of yoghurts and fermented milks has existed for a long-time.

This typology is also illustrated by definitions which varied across countries. Yoghurt and fermented milks are defined by the consumers via the culture component (in Japan (lactic acid drink), China, Korea, Russia and Turkey), via the milk health benefit (in France, USA, Spain, Sweden, Japan (for yoghurt) and South of India), or via the consumption habits (in Germany, Brasil and North of India).

Unanimously, in all the countries, yoghurts and fermented milks are considered to be

products procuring health benefits thanks to the milk components: calcium, proteins, vitamins, etc., moreover an intuitive link is made between health and fermenting cultures in milk, although knowledge concerning the benefits of lactic acid bacteria is still approximate (except in Asia). Other benefits are also associated with the consumption of yoghurts and fermented milks. Benefits related to digestion are cited, with variations concerning the precise actions. The most informed consumers also cite the role of

fermented milks in strengthening the immune defence system.

Whilst the perception of yoghurts and fermented milks is similar from one country to another, we note that consumer expectations differ slightly (see table below). However, in the majority of countries, consumers are in need of information on fermented milk products (definition, variety, fermentation process, associated effects and benefits).

Consumers expectation in respect to yoghurts and fermented milks

Country profile	Countries	Expected informations
Countries with recent industrial background	India, China	Need information about the relationship between food / body / health, prior to the information on the category.
Countries where the dairy category is strongly developing	Turkey, Sweden, Russia, China, Brazil.	Request for product information: ingredients / components, making process.
Countries where the dairy category is well established	France, Spain, Germany, USA, Japan, Korea	Need of more information about specific effects of cultures on body and health.

Therefore three main points emerge from this study:

- Yoghurts and fermented milks benefit from a strong image of food products that are "good for health". They benefit from a privileged status within the diet and from consumption that is often traditional or culturally well anchored.

- The benefits associated with their consumption are linked to the general concept of "well being" and according to better informed consumers, the benefits are linked to the more specific concept of action on very precise physiological functions.

- Intuitively the consumer establishes a link between dairy cultures and health benefits whilst, at the same time, demanding more information on this subject.

From this information we can conclude thus that yoghurts and fermented milks enjoy a strong, positive identity that can be reinforced even more by more informative communication on the benefits linked to dairy cultures.

* This study was supported by the Centre National Interprofessionnel de l'Economie Laitière (CNIEL) and by International Association of Yoghurt and Fermented Milk Manufacturers.

Stimulation of the chemotactism *of macrophages*

The immunomodulating effects of probiotics are the subject of numerous studies. Some results indicate that lactic acid bacteria would be capable of activating the macrophages and stimulating certain of their functions.

A recent publication (1) attempted to understand whether lactic acid bacteria could modulate the migration of macrophages. The activation of this function provokes the elimination of pathogenic agents at the migration site level. Numerous so-called chemotactic

factors are capable of inducing the migration of macrophages.

The test, carried out *in vitro* with murine macrophages, showed chemotactic activities in the presence of three strains of *L. acidophilus* and all strains of *L. gasseri*. The strongest activity was recorded in the presence of supernatants of *L. gasseri* JCM1131 culture.

A factor involved in chemotactism was isolated from these supernatants and named "gasserokine". The activity of

"gasserokine" was also observed when the test was carried out with human macrophages.

The chemotactism of macrophages induced by a factor produced by *L. gasseri* JCM1131 can be considered as a new feature to be attributed to probiotics.

1 • Kitazawa H, Ino T, Kawai Y, Itoh T, Saito T (2002) A novel immunostimulating aspect of *Lactobacillus gasseri*, induction of "Gasserokine" as chemoattractants for macrophages. *Int J Food Microbiol* 77(1-2), 29-38

Inflammatory process *and safety of lactic acid bacteria*

The cytokines secreted by human enterocytes play a key role in inflammatory processes and in both systemic and mucosal immunity. Since the intestinal microflora is capable of influencing this secretion, we can wonder whether the probiotics are not themselves capable also of playing this role.

The pro-inflammatory cytokines secreted by the epithelium, such as IL6 and IL8, are the markers for the inflammatory response at the level of the intestine. The synthesis of IL6 and IL8 by the enterocytes can be induced by pathogenic enteric bacteria. IL8 amplifies the immune response and provides signals capable of activating the inflammatory response at the early phase of microbial invasion. IL6 plays a dominant role in the acute phase of inflammatory episodes.

In one study, thirty strains of lactic acid bacteria were selected for their ability to adhere to Caco-2* cells and for their aptitude to stimulate the secretion of pro-inflammatory cytokines by this same cell line (2). Whether live or heat-inactivated lactobacilli or the *Lactobacillus* GG strain (which presents a strong affinity for epithelial cells) are considered, it has been shown that the bacteria adhere in a strain-dependent way to the Caco-2 cells and that this contact has not induced the production of IL6 and IL8. There does not, therefore, appear to exist any correlation between the capacities of adhesion to Caco-2 cells and induction of cytokines for the lactobacilli tested.

These results indicate that the adherent lactic acid bacteria interact with the human epithelium in a way that differs from that of infectious agents. They can adhere to epithelial cells without activating any inflammatory response, characterised by high levels of IL6 and IL8. The absence of these signals suggests that the immune system responds differently to lactic acid bacteria or pathogenic agents.

In another study (3), Italian researchers at the University of Bologna explored the interactions between epithelial cells and the mix of probiotics contained in VSL#3**. The authors measured the presence of IL8 in the supernatants of cultures of HT29/19A human epithelial cells. These cells are cultivated in the presence of different doses of cell debris or extracts of each of the VSL#3 strains or the non-pathogenic *E. coli* Nissle 1917 strain. It has been shown that none of the lactic acid bacteria contained in VSL#3 induced the production of IL8. On the other hand, the *E. coli* Nissle 1917 cell extracts and debris induced the production of IL8 in a dose-dependent way.

The results of these two studies suggest that the Gram-positive lactic acid bacteria and *E. coli* Nissle 1917 bacteria interact differently with the host cells. It would appear that the VSL#3 probiotic mixture is not recognised as an "inflammatory stimulus" by the epithelial cells, at least not in this *in vitro* model.

According to the authors, it seems that lactic acid bacteria appear to be incapable of inducing an inflammatory response in the human enterocytes cultivated *in vitro* and these results underline, to a certain extent, the safety of the lactic acid bacteria used as probiotics.

* Caco-2 cells are cultured cells originated from human colon epithelium.

** VSL#3 is a probiotic mixture that contains the following strains : *L. plantarum* MB452, *L. bulgaricus* MB453, *L. casei* MB455, *L. acidophilus* MB443, *B. breve* Y8, *B. longum* Y10, *B. infantis* Y1, *S. thermophilus* MB455 and *L. casei* subsp *rhamnosus* GG.

2 • Morita H, He F, Fuse T, Ouweland AC, Hashimoto H, Hosoda M, Mizumachi K, Kurisaki J. (2002) Adhesion of lactic acid bacteria to Caco-2 cells and their effect on cytokine secretion. *Microbiol Immunol* 46(4), 293-7

3 • Lammers KM, Helwig U, Swennen E, Rizzello F, Venturi A, Caramelli E, Kamm MA, Brigidi P, Gionchetti P, Campieri M. (2002) Effect of probiotic strains on interleukin 8 production by HT29/19A cells. *Am J Gastroenterol* 97(5), 1182-1186.

Prevention of bacterial diarrhea *by probiotics*

Enteropathogenic infections are very widely found diseases. It is currently known that the gastro-intestinal microflora acts as a barrier against the enteropathogens. However, the mechanisms by which the native microflora exerts this protective effect, in particular against cell damage caused by these enteropathogens, are still being studied.

In order to better understand these mechanisms, an INSERM* team chose to examine the activity of *Lactobacillus acidophilus* LB (of human origin) in an *in vitro* model. The lactobacilli represents the human intestinal flora and the pathogenic agent, inducing diarrhea and cell damage, was *E. coli* (Afa/Dr DAEC) C1845. The Caco-2/T7 cells, cultivated *in vitro*, were chosen as the model of the human intestinal epithelium (4). The study aimed to analyse the modifications undergone by the brush border, both structural (analysis of actine F

deterioration) and functional (analysis of the modification in the activity of sucrase-isomaltase and dipeptidylpeptidase IV hydrolases, of glycosylphosphatidylinositol anchored to phosphatase alcaline and of the fructose carrier). The anti-bacterial activity was examined by measuring the viability of *E. coli*. The distribution of the cytoskeleton proteins and the functional proteins at the level of the brush border was analysed by confocal microscope after marking by immunofluorescence. The drop in the viability of *E. coli* (free in the culture medium or adhering to the Caco-2/TC7 cells) was observed after contact with the supernatants of the lactobacilli culture.

This study has shown that the protection against the deterioration induced by *E. coli* on the different structural and functional proteins of the brush border was observed when the epithelial cells were exposed to

the supernatant of the lactobacilli culture. Thus, in the cultured enterocytes, the *L. acidophilus* LB strain of human origin was capable, via its metabolites excreted in the culture medium, to prevent the deterioration of the brush border induced by the pathogenic strain *E. coli* C1845. On the basis of this result, it is possible to make the hypothesis that the presence of *L. acidophilus* LB in humans, as a member of the native flora or as an ingested probiotic, could be useful for the prevention of bacterial diarrhea.

* (French Institute of Health and Medical Research)

4• Lievin-Le Moal V, Amsellem R, Servin A L & Coconnier M F (2002)

Lactobacillus acidophilus (strain LB) from the resident adult gastrointestinal microflora exerts activity against brush border damage promoted by a diarrhoeagenic *Escherichia coli* in human enterocyte-like cells. Gut 50, 803-811.

Benefit of the consumption of probiotics

at the time of a Helicobacter pylori infection

The link between infection by *Helicobacter pylori* and the development of duodenal and gastric ulcers has been recognised in recent years. Because the usual antibiotic treatments are not always effective and are often associated with secondary effects, it will be necessary to develop alternative treatment methods. Because some strains of lactic acid bacteria are known to inhibit *in vitro* the growth of *H. pylori*, an alternative treatment could be the consumption of probiotics.

The results of a clinical trial conducted by a research team at the University of Alberta in Canada showed the absence of efficiency of a fermented milk for the eradication of *H. pylori* (5). This study concerned 27 women who tested positive for *H. pylori* but were asymptomatic. These volunteers were taking no medication at the time of the trial. At the beginning of the study the endoscopies revealed no sign of ulceration or erosion. The fermented milk was consumed during 30 days, 524 ml per day. It contained the following probiotic strains: *L. casei* 03, *L. acidophilus* 2412, *L. acidophilus* ACD1, *L. bulgaricus* and *Streptococcus thermophilus*.

A month after the consumption of fermented milk was halted, 26 of the 27 volunteers remained positive for *H. pylori* (dosage carried out by the expired urea 13C test). It would, therefore, appear that the consumption of fermented milk was not effective in eradicating the pathogen.

The use of probiotics for the eradication of *H. pylori* has been studied by various

teams. Michetti *et al* (6) demonstrated a partial effectiveness linked to the administration of supernatants of *L. acidophilus* La1 culture to volunteers. Another study reported that the administration of fermented milk with *L. acidophilus* during a period of 2 months eradicated *H. pylori* in 6 out of 14 volunteers (7). Sakamoto *et al* (8) showed that the consumption of fermented milk containing *L. gasseri* OLL2716 eliminated *H. pylori* infection. In two other clinical trials (9, 10) the probiotics were administered during and after treatment with antibiotics. It would appear that the administration of probiotics was not effective in totally eradicating *H. pylori*. On the other hand, the reduction of secondary effects linked to the antibiotics was noted (11).

The role of lactic acid bacteria, or products of their metabolism present in the fermented milks, in the treatment of the *H. pylori* infection requires further clinical studies to be clarified. Thus, whilst it is not certain that taking probiotics alone is sufficient to eradicate *H. pylori*, it would appear that the choice of a therapy combining probiotics with antibiotics could offer an efficient alternative both for fighting against the pathogen and countering the secondary effects engendered by the antibiotics.

One aspect that could be explored is the development of a better combination of probiotics/antibiotics. This implies determining the minimum effective dose of antibiotics and the strain of probiotics

that is the most effective to minimize the antibiotics side effects.

5• Wendakoon C, Thomson A & Ozimek L (2002)
Lack of therapeutic effect of a specially designed yoghurt for the eradication of *Helicobacter pylori* infection. Digestion 65, 16-20.

6• Michetti P, Dorta G, Wiesel PH, Brassart D, Verdu E, Herranz M, Felley C, Porta N, Rouvet M, Blum AL, Corthesy-Theulaz I (1999).
Effect of whey-based culture supernatant of *Lactobacillus acidophilus* (johnsonii) La1 on *Helicobacter pylori* infection in humans. Digestion 60(3), 203-9.

7• Mrda Z, Zivanovic M, Rasic J, Gajin S, Somer L, Trbojevic S, Majoros J, Petrovic Z. (1998)
Therapy of *Helicobacter pylori* infection using *Lactobacillus acidophilus*. Med Pregl 1998 Jul-Aug;51(7-8):343-5

8• Sakamoto T, Igarashi M, Kimura K, Tagaki A, Miwa T & Koga Y (2001)
Suppressive effect of *Lactobacillus gasseri* OLL2716 (LG21) on *helicobacter pylori* infection in humans. J Antimicrobial Chem 47, 709-710

9• Armuzzi A, Cremonini F, Ojetti V, Bartolozzi F, Canducci F, Candelli M, Santarelli L, Camarota G, De Lorenzo A, Pola P, Gasbarrini G & Gasbarrini A (2001)
Effect of *Lactobacillus* GG supplementation on antibiotic-associated gastrointestinal side effects during *helicobacter pylori* eradication therapy : a pilot study. Digestion 63, 1-7

10• Felley C, Corthesy-Theulaz I, Blanco Rivero JL, Sipponen P, Kaufmann M, Bauerfeind P, Wiesel P, Brassart D, Pfeifer A, Blum A & Michetti P (2001)
Favourable affect of an acidified milk (LC1) on *Helicobacter pylori* gastritis in man. Eur J Gastroenterol hepatol 23, 25-29

11• Syndifrais (2001) Yaourts & Laits Fermentés n° 5, p. 2.

International Symposium Program
“Yoghurt & Fermented Milks: benefits of live cultures”
 September 25th, 2002

Introduction : Prof Jean-Louis Bresson - Necker Hospital, France

Session 1. From Traditional to Modern Fermented Milks

Chair Prof Zdenko Puhan - Institute of Food Science, Switzerland

Four Generations of Fermented Milks - Prof Zdenko Puhan - Institute of Food Science, Switzerland

Present Diversity of Products - Prof Ramesh C.Chandan - Global Technologies Inc, United States

Trends and Evolution of Fermented Milks - Prof Tsuneo Hirahara - ILSI, Japan

Session 2. Regulatory Context/ Consumer

Chair Dr Allan Anderson - New Zealand Dairy Research Institute, New Zealand

Consumer Perception and Expectations - MSM - International Research Company, France

The rationale behind Health Claims Regulation - Mrs Sabine Nafziger - CIAA, Belgium

Health benefits of Probiotics and Regulatory requirements - Dr Pramod Gopal - New Zealand Dairy Research Institute, New Zealand

Session 3. Benefits of Live Cultures: Practical Implications of Scientific Data

Chair Prof Mary Ellen Sanders - California Polytechnic State University, United States

Milk and Lactic Acid Bacteria: influence of the dairy environment on gene expression and culture functionality - Prof Todd Klaenhammer - North Carolina State University, United States

Probiotics in Inflammatory bowel Diseases - Prof Francisco Guarner - Hospital General Vall D'Hebron, Spain

Host Cell Interactions - Dr Eduardo Schiffrin - Nestlé Research Centre, Switzerland

Live Cultures and Cancer - Prof Ian Rowland - University of Ulster, Northern Ireland

Session 4. Panel Discussion: Assets and diversity of Live Yoghurt and Fermented Milks

Concept and definition of Probiotics - Prof Gertjan Schaafsma - TNO - Department of Human Nutrition - The Netherlands

Panel discussion

Chair

Pr M.E.Sanders, California Polytechnic State University - United States

Pr F.Guarner, Hospital General Vall D'Hebron - Spain

Pr J.-L.Bresson, Necker Hospital - France

Dr A. Anderson, New Zealand Dairy Research Institute - New Zealand

M.P.Levieil, Nestlé - France

M.J.-F.Molle, Danone Group - France

Pr Z.Puhan, Institute of Food Science - Switzerland

Pr G.Schaafsma, TNO - Department of Human Nutrition - The Netherlands

Your suggestions and comments will draw all our attention. Please send them to :

SYNDIFRAIS

42 rue de Châteaudun • 75314 Paris Cedex 9

Tél. 01 49 70 72 30 • Fax : 01 42 80 63 90

e.mail : syndifrais@syndifrais-syndilait.org