Present Status of Fermented Milk Products in Japan

Akiyoshi Hosono

Prof. Emeritus of Shinshu University
Managing Director, Japan Dairy Technical Association

Present Status of Fermented Milk Products in Japan

Akiyoshi Hosono
Prof. Emeritus of Shinshu University
Managing Director, Japan Dairy Technical Association

Fermented milks have been recognized as healthy foods since ancient times, but those using intestinal bacteria such as *Bifidobacterium* and lactic acid bacteria (LAB) are even more valuable from the standpoint of view of maintaining health. They have also now come to be recognized as important in the field of preventive medicine.

Although advances in the medical sciences in the last 50 years have significantly increased the human life span, an unfortunate fact is that many of us are now living long enough to experience chronic disorders such as coronary heart disease, hypertension, osteoporosis, diabetes and cancer. In recent years there has been renewed interest in health promotion and disease prevention by incorporating probiotic bacteria into foods to counteract harmful bacteria in the intestinal tract. Therefore, there are now a wide variety of commercial products containing prospective probiotics that claim health-promoting effects, such reductions in large bowel carcinogens and mutagens, antitumor properties, cholesterol-lowering effects, increased lactose digestion, relief from constipation, stimulation of immunocomponent cells and enhancement of phagocytosis.

Two well-known representative probiotic is LAB and *Bifidobacterium.* Traditional probiotic dairy strains of LAB which have been designated as GRAS (Generally Recognized As Safe) bacteria have a long history of safe use and most strains are considered comestible microorganisms with no pathogenic potential. Accordingly, there is considerable interest in extending the range of foods containing probiotic organisms from dairy foods to infant formulas, baby foods, and pharmaceuticals. In addition, the ingestion of probiotics, prebiotics, and symbiotic as wll as combinations of pro- and prebiotics has recently aroused renewed interest as enhancing the beneficial relationship between the host and intestinal microflora in both healthy and diseased indivisuals.

Non-communicable chronic diseases such as cancer, cerebral hemorrhage, ischemic heart disease, and diabetes mellitus has recently been recognized as adult diseases in Japan as well as other

countries. and are considered to be inevitably associated with aging. These diseases occur as a result of individual life styles. The Japanes Government, Ministry of Health, Labor and Welfare has proposed substituting the term "adult diseases" with "lifestyle-related diseases". It has emphasized the importance of prevention rather than treatment, since the well-known increase in the elderly population in Japan is predicted to result in a variety of socioeconomic problems.

In this lecture on the Present status of fermented milk products in Japan, I will report a strategy for the development of fermented milk products in Japan from the standpoint of view of research in Japan on LAB and *Bifidobacteria.* They could play an important role in preserving human health by controlling intestinal microflora capable of producing toxic effects on the host.

Slide 1

This lecture is delivered on the occasion of the Symposium organized by the Korean Dairy Technology Association: Present Status of Fermented Milk Products in Japan. I will discuss the beneficial health effects of probiotic LAB used as starter cultures in producing fermented milk, based on the research carried out for more than 15 years in Japan.

Slide 2

Cancer is caused by many causes by factors, such as sexual behavior, infection, medical drugs, food additive, tobacco, radiation, UV and diet. Among these factors, diet shares a large portion (33%) of the responsibility for the increasing incidence of cancer as reported by Dole and Peto, 1981.

Slide 3

Here we see data on the number of bladder and kidney cancer mortalities in Japan in 2000. Notice that the incidence of either bladder and kidney cancer is quite differed among areas of Japan in both the male and female population. This fact might be due to different eating habits.

Slide 4

We know that fat, carbohydrate, vitamins and salts are important nutrients for human. However, excess fat consumption may cause breast cancer. Too much carbohydrate may initiate diabetes, which in turn induces some cancers. Eating habits, such as high protein and fat, as well as cooking methods such as heating food at high temperatures (roasting, baking and frying) may form mutagenic compounds.

This is an example of the formation of a mutagenic compound, a nitroso-compound found in pickles and corned beef. Hence, consuming these kind of foods on an empty stomach stimulates the formation of this mutagenic compound.

Slide 5

This slide shows some other mutagenic and carcinogenic compounds which belong to amino acid pyrolysate are produced when high protein foods are subjected to high heat treatments including baking and roasting.

Slide 6

Some plants also may contain natural carcinogens, such as hydrazine in mushroom which may contribute to liver and colon cancer. Caffeic acid in coffee may also cause stomach cancer.

Slide 7

Heavy metal such as high amounts of arsenic compound, especially in well water, play an important role in causing the liver cancers so frequent in Asian countries.

High alcohol levels in some alcoholic beverages also promote esophageal cancer.

Slide 8

In experiments with rats, artificial sweeteners such as saccharin have been shown to cause bladder cancer, while antioxidant BHA promote stomach cancer. The use of agricultural pesticides such as organochlorides proven to cause liver cancer, as well as fungicides found to cause bladder cancer in rat. Should be made to conform to strick government regulations.

Slide 9

Dr. Mitsuoka, Prof. Emeritus at the University of Tokyo has demonstrated the changes in fecal flora with age. Our gastrointestinal-tract is host to 100 million million, which are beneficial (e.g., probiotic lactic bacteria), while some of others are harmful (e.g., pathogenic and toxin-producing bacteria).

We need to balance these microflora to maintain our health. Old people only has few *Bifidobacteria*, and the amount of bad bacteria tend to increase by the age.

Slide 10

Intestinal flora and their metabolites is also influenced by diet, prebiotics, stress and drug consumption. They in turn produce either positive or negative effects on human health by adversely affecting the balance between beneficial microflora and harmful putrefactive microflora. LAB, which has probiotic properties, play important role in maintaining human health. The older the person, the more dominant are the bad bacteria in the composition of intestinal flora, as shown previously by Mitsuoka. Lifestyle choices may also influence the balance of microflora. Consuming foods containing probiotic bacteria e.g., fermented milk products will maintain human health, by stimulating the immune response and reducing the fecal enzyme activity capable of convering procarcinogens into carcinogens.

Slide 11

These are the beneficial effect of intestinal flora :

- They inhibit harmful bacteria and other microflora by producing of antimicrobial components such as organic acids (especially lactic and acetic acid) as well as hydrogen peroxide and bacteriocin in the gastrointestinal tract.
- They perform a scavenging function. LAB have the ability to scavenge the oxygen radicals generated by the presence of superoxide dismutase.
- They stimulate the immune response. The colonization of LAB in the small intestine is an important factor in improving the to bodys immune system. Their adherence to epithelial cells of the intestine helps support the competitiveness of probiotics against pathogenic bacteria. It is thought that lactic acid bacteria enhance the immune system by stimulating the B and T cells of human macrophages.
- Intestinal flora also improve the digestion and absorption of food by producing various kinds of enzymes to help in digesting food and by lowering the pH of the gastrointestinal tract, they may improve bowel movements by speeding up the transport of gastric contents into the intestinal tract.
- They synthesize of vitamins. Some species of LAB have been shown to increase vitamin B complex in fermented foods, while and others synthesize vitamin K in the colon.
  Although such benefits due to good bacteria such as probiotic LAB, some non- pathogenic and non-toxin-producing *E. coli* may also contribute to vitamin B production.

Slide 12

And these are the harmful effects of intestinal flora. The bad bacteria, such as pathogenic and

toxin-producing bacteria, mainly produce putrefactive products such as NH_3, H_2S, indole, amines, phenol and even carcinogens and toxin as their metabolite products. All if them may give rise to various health problems such as diarrhea, constipation, cancer, autoimmune disorder, hepatic carcinoma, hypertension, or may even leave one susceptible to infectious diseases.

Slide 13

Yogurt production is quite simple. Two lactic cultures, *Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *bulgaricus* are the basic yogurt preparation. The addition of one or more probiotic bacteria such as *Lactobacillus acidophilus,* and *Bifidobacteria longum* will result in produce bio-yogurt, which contain viable probiotic bacteria that reach the intestine alive and immediately get to work to improve and maintain our health.

Slide 14

From the late Old Stone Age to the New Stone Age (around 7000-2500 BC), people hunted wild animals for food and domesticated others. Most historians agree that milk was first used in western Asia as indicated by agricultural societies that flourished in this region between 7500 and 5500 BC. The carved relief stone panels of the Sumerians that depicted figures engaged in milking, collecting milk in earthenware pots, filtering cows milk, and making butter provide evidence of such a society.

In 1908, Metchinikoff, a Russian scientist, proposed in his hypothesis on longevity that "There are many useful microbes, amongst which the LAB have an honorable place". Such hypotheses continue to stimulate numerous extensive investigations of the beneficial health effects of fermented milks up to the present day.

Slide 15

The therapeutic effects of fermented milks are now recognized:

1. The nutritious effects of fermented milk components are due to their various nutritional and physiological values such as amino acids and lactose that can promote the production of lactic or acetic acid; and lactic acid that can stimulate gastric secretion and speed up the transport of gastric contents into the intestinal tract as well as lower its pH to inhibit the growth of harmful bacteria, thus preventing constipation.

2. Physiological effects of viable lactic acid bacteria.

- The improvement of bowel movements by is ability to produce abundant lactic and acetic acid

and to lower the pH of the gastrointestinal tract, thus speeding up the transport of gastric contents into the intestinal tract.

- The prevention of lactose intolerance. Most Asian and African populations suffer from lactose intolerance due to a deficiency of enzyme β -galactosidase, resulting in an inability to digest lactose. That undigested lactose is then degraded by intestinal flora, leading to osmotic diarrhea and other symptoms. The consumption of fermented milk containing living LAB could alleviate these symptoms by converting lactose to glucose and galactose via the β 1,4-galactosidase produced by lactic acid bacteria.

3. Physiological effects of fermented milk and LAB cells

- Antimutagenicity. We have extensively investigated the antimutagenicity of fermented milk against various mutagens. Our findings have been published in various international journals. We have found that casein, polysaccharides, and LAB cells were responsible for the antimutagenic activity towards some mutagenic compounds. Other researchers have identified peptides and proteolytic compounds as the components responsible for the antimutagenicity of fermented milk.
- Antitumor activity. Some researchers suggested that the antitumor action of fermented milk may be attributed to the polysaccharides and slimy substances produced by LAB. Others have proposed that such an action is attributable to LAB stimulating the immune system. Still others have proposed mechanisms that reduce the activity of these fecal bacterial enzymes involved in procarcinogen activation, and that also reduce the excretion of mutagens in feces and urine.
- Activation of the immune system. The colonization of probiotic LAB occurs naturally. Their adherence to the epithelial cells of the intestine serves to facilitate the activation of the immune system.
- Cholesterol-lowering action. Many reports have been published on the hypocholesterolemic effects of fermented milk.
- Antipathogenic bacteria. The colonization of probiotic LAB in the intestine enables it to compete with harmful bacteria.

Slide 16

And here we see the formation of cancer cells as they develop through various stages from normal cell into cancer cells.

The initiation of that development involves modification of DNA by chemical carcinogens. Consuming roast beef may trigger initiation due to mutagenic compounds such as Trp-P1 that are formed by roasting beef. The mutagens responsible are called initiators.

Promotion is the next step toward carcinogenicity. Once DNA has been modified by chemical carcinogens, the presence of tobacco smoke and salt act as promoters that may hasten the process.

Progression involves the development of mutations, mutations, which is the penultimate stage in the formation of cancer cells.

Cancer is the leading cause of human mortality in our time. Diet plays an important role in our high incidence of cancer. It is reported that a diet with high fat and cholesterol greatly promotes the secretion of bile acids into the intestinal tract resulting in rectal cancer. Malnutrition could also change the balance of intestinal flora by stimulating the growth of harmful bacteria which produce fecal bacterial enzymes, which in turn form carcinogens and can even produced toxin. Moreover, ingestion of mutagen as promoter supports cancer formation. Consuming fermented milk which contains probiotic bacteria may support the antimutagenic activity also to prevent cancer.

Slide 17

Among the numerous methods for detecting mutagenic substances, one of the most widely used is "The Ames Test" named after Prof. B. N. Ames of the University of California. *Salmonella typhimurium* TA 98 and TA 100 are commonly used with the addition of S-9 mix for detecting the mutaginicity of samples. Even though the genotype of these two strains is the same, their mutation types are different. Strain TA 98 forms revertant mutants from histidine (his^+) to histidine non-requiring (his^-) types by frameshift mutation, while strain TA 100 forms by base-exchange mutation.

Slide 18

Salmonella typhimurium TA 98 could not be used to evaluate the mutagenicity of samples containing histidine such as milk and milk products. In order to overcome this drawback, we introduced a streptomycin-dependent strain, a mutant strain of *Salmonella typhimurium* TA 98. Moreover, this strain has an other advantage it does not require an expensive S-9 mix for an assay of mutagenicity.

Among several streptomycin-dependent strains, we found SD 510 was the most sensitive to various mutagens. As I mentioned earlier, this strains could be used in assessing samples containing histidine such as milk and fermented milk, and does not require an expensive S-9 mix.

Slide 19

An assay of the antimutagenicity of LAB towards mutagenic nitroso compounds and aflatoxin showed that some strains of dadih lactic bacteria, i.e., R-63, R-62 and R-48 achieved an almost 100% inhibition of the mutagenicity of nitroso-diethylamine, while 3 strains of *L. acidophilus* demonstrated a 50~75% inhibition towards the mutagenicity of N-nitrosoguanidine. Significant

reductions in the mutagenicity of aflatoxin B1, B2 and G1 by the cells of *L. acidophilus* LA-2 and *L. rhamnosus* Lcr 101 were also observed.

As for the antimutagenicity of various strains of *Lactobacillus acidophilus* towards mutagenic MNNG, from this slide we can see that its antimutagenicity varied among different strains over a range of 26.0~77%.

Slide 20

A study has also been conducted on the effects of supplemented fermented milk on human fecal mutagenicity. Six male volunteers were selected on the basis of general health, absence of constipation, and higher fecal mutagenicity. Each subject was given 200 ml of *Lactobacillus acidophilus* LA-2 fermented milk per day for 7 days. Fecal samples were collected before and after the intake of fermented milk, and fecal mutagenicity was analyzed by the Ames test. The result showed that the fecal mutagenicity of the six volunteers was significantly reduced after 7 days of consuming fermented milk (200 ml/day), as indicated by a reduction in the number of revertant colonies.

Slide 21

I would now like to discuss our findings on the binding properties of LAB cells with mutagens and carcinogens.

Slide 22

One possible mechanism underlying the antimutagenicity of LAB is by the direct binding of the mutagens to cell walls of LAB. As shown in this figure mutagens such as Trp-P1, Trp-P2 and Glu-P1 that belong to heterocyclic amines are commonly found and isolated from cooked or heated high protein foods. An *in vitro* binding assay with HPLC convincingly demonstrated the binding ability of bacterial cells of *Lactococcus lactis* subsp. *lactis* with those mutagens.

Slide 23

Comparing the binding properties of viable and dead cells of *Lactococcus lactis* subsp. *lactis* revealed the binding ability of dead cells with Trp-P1 is slightly lower than that of viable cells.

Slide 24

Now we come to another probiotic property of LAB, namely, its hypocholesterolemic effect.

Slide 25

Hypercholesterol patients both men and women are on the increase in Japan. In fact, during the decade 1990~2000 that increase has been dramatic. In Japan the number of CHD patients has also increased from time to time. This slide shows that the 64~74 age was the most susceptible to CHD.

Slide 26

Two mechanisms underlying the hypocholesterolemic action of LAB have been proposed: cholesterol binding to bacterial cells, and deconjugation of bile salts. Direct binding of dietary cholesterol to bacterial cells in the small intestine before cholesterol has been absorbed. As for the deconjugation of bile salts they are excreted more rapidly and blind more readily to bacteria and dietary fiber than conjugated bile acids. As a consequence, more cholesterol is needed to synthesize new bile acids, which in turn reduces the total cholesterol in the body. This shows that various strains of LAB each has different abilities in binding cholesterol as well as in deconjugating bile salts.

Slide 27

We investigated the effects of milk products fermented by the probiotic strain *Bifidobacterium longum* BL1 on blood lipids in humans. 32 subjects with total serum cholesterol ranging from 220 to 280 mg/dl were randomly assigned to two treatments: 1) intake of a low-fat yogurt drink prepared with ordinary yogurt starters *S. thermophikus* and *L. delbrueckii* subsp. *bulgaricus* (P-group) and, 2) intake of a low-fat liquid yogurt prepared with those two ordinary yogurt starters plus *B. longum* strain BL1 (B-group). After an intake for 4 wk at 3 × 100 ml/day, a reduction in total serum cholesterol was observed in approximately half of the B-group subjects, with a particularly significant decrease among subjects with moderate hypercholesterolemia. However, serum lipid concentrations in the P-group subjects remained almost stable during the experimental period.

Slide 28

Most studies found that LAB could improve the immune system by the activation of macrophages. Once activated, macrophages could then stimulate the B cells to secrete antibodies and T cells. LAB are also able to modulate the production of cytokines and produce natural killer (NK) cells against cytotoxicity. Other studies reported an immuno-activating activity of LAB by the modulation of interleukins 1, 2 and 6, tumor necrosis factor (TNF) alpha, and interferons (IFNS) alpha, beta and gamma. All of those immunomodulatory effects of probiotic LAB originate from

the ability of lactic bacteria to colonize and adhere to the epithelial cells of the intestine.

Slide 29

Here are some recent Japanese studies on the cellular immune responses of LAB and *Bifidobacterium*. Please note that LAB facilitate the activation of the immune system in a variety of ways.

Slide 30

There have been many studies on the effects of LAB on hypertension, cholesterolemia and cancer. However, their antidiabetic effects have hardly been investigated. We have recently studied the antidiabetic effects of *Lactobacillus* GG on streptozotecin-induced diabetic rats. Neonatally streptozotecin-induced diabetic (n-STZ) rats were given food containing *Lactobacillus* GG cells or a control diet from 9 to 18 wks of age. The GG cells significantly lowered the blood hemoglobin (HbA_{1C}) level and improved glucose tolerance in those n-STZ rats ($p<0.05$).

Slide 31

Yazawa et al. have recently published a very interesting paper suggesting that *Bifidobacterium longum* might be used as a delivery system for gene therapy of chemically induced mammary tumors. In their experiments, all rats (n=19) at 6 wk of age are administered 10 mg of 7, 12-dimethylbenzanthracene (DMBA) in 1ml of sesame oil by intragastric gavage once a week for two wks. By 23 wks after the first dose of DMBA, 89% (17/19) of rats had developed mammary tumors. Those rats were injected bacilli intravenously and daily administered DMBA intraperitoneally. This shows that the bacilli were detected in tumor tissues only but not in normal tissues, including those of the liver, spleen, kidney and lung.

Slide 32

Prof. Fuller, a British microbiologist, proposed the term "Probiotics", which may be defined as deliberately digested, health-promoting live bacteria that beneficially affect the microbial intestinal balance of the host.

Antibiotics play an important role in treating various infections and diseases caused by viruses, bacteria and other microorganisms. However, we have recently faced serious problems concerning the resistance of certain bacteria and other pathogens, and the risk to patients from a change in the balance of intestinal flora, resulting in diarrhea.

The application of probiotics is the answer to such problems. Probiotic causes no resistance to certain microorganism in the host gastrointestinal tract. In fact, when administered to the host, they will colonize, grow and quickly exert their beneficial effects. Probiotics also improve balance of intestinal flora by increasing the number of beneficial microflora while reducing the number of harmful ones.

Slide 33

Since most foods and medicinal products are directly concerned with human health and survival, Japans Food Sanitation and Pharmaceutical Laws strictly prescribe that such products shall be free of impurities and sanitary conditions. Under the Food Sanitation Law, the Ministry of Health, Labor and Welfare established a "Nyuto-shorei", which is a government order for the regulation of wholesome milk and milk products.

Slide 34

The most popular current world wide trend is the use of functional foods to improve health. The functional food movement started in Japan in 1991. The Japanese government adopted legislation concerning Foods for Special Health Uses (FOSHU). Now more than 400 products have received approval to be labeled FOSHU foods. More than 30% of such foods are LAB drinks and fermented milk products. Consumers are demanding foods that provide specific health benefits. Food, pharmaceutical, and biotech companies are spending billions of dollars in research and development to take advantage of those demands.

Slide 35

Here you see some fermented milk products approved as FOSHU foods that are now commercially available.

In 2001, we have also successfully developed dadihi yogurt by the addition of one strain of *Lactobacillus casei* subsp. *casei* 027, and this product is also commercially available as shown in this slide.

Slide 36

Once we have established *in vitro* and *in vivo* probiotic LABs, the next step will be to conduct studies on dose-response, the mechanisms underlying probiotic and symbiotic effects and human studies to confirm the effectiveness of probiotic LAB. After completion of these studies, the

production of commercial fermented milk will finally get underway.

Slide 37

The production of fermented milk in Japan will tend to increase overtime. In fact, fermented milk products are becoming more and more popular in Japan. This figure shows the production figures in Japan from 1994 to 2003. The production of fermented milk has currently reached more than 91 hundred thousand liters.

Slide 38

This illustrates why chemoprevention is better and less costly than chemotherapy to combat certain cancers and infectious diseases. It is better to engage in chemoprevention by consuming probiotic LABs before the disease becomes severe, rather than to attempt to cure the disease by chemotherapy.

Food is no longer considered as merely providing sufficient nutrients, but also as giving the consumer a feeling of satisfaction and well being. Diet also controls and modulates various functions in the body, thus contributing to maintaining good health and reducing the risk of some diseases. Probiotic (viable beneficial bacteria, mainly LAB) and health-promoting non-digestible (prebiotic) ingredients are being commercially marketed, especially in developed countries. Currently, research and development are focused on both a foods probiotic and prebiotic properties. Moreover, the synergistic effect of the combination of probiotic and prebiotic ingredients in improving as well as maintaining human health has been given top priority by research workers in the field of nutrition.

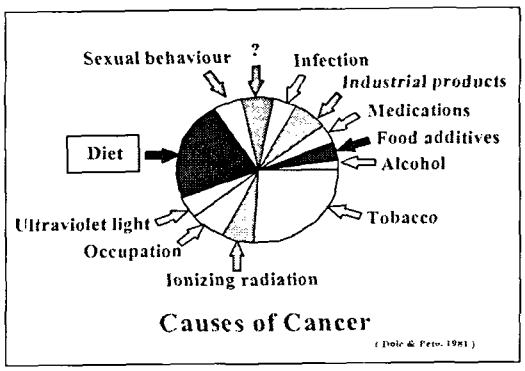
Slide 39

Thank you for your kind attention.

Present Status of Fermented Milk Products in Japan

Akiyoshi Hosono, Ph.D.
Professor Emeritus, Shinshu University

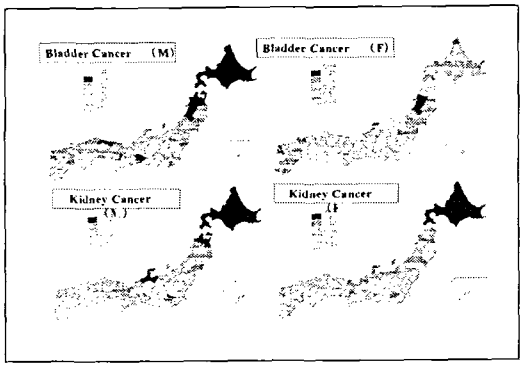
Slide 1



Causes of Cancer

(Doll & Peto, 1981)

Slide 2

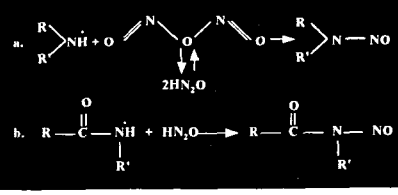


Slide 3

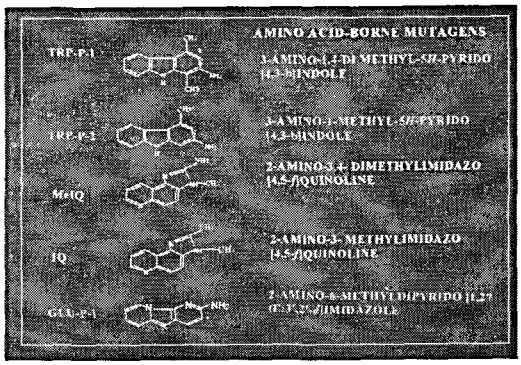
N-nitroso compounds

Produce by reaction of nitrite in foods with amines under acidic conditions. N-nitroso compounds are causative factors in cancers of various organs

Amines / Amides + Nitrite → N-Nitroso compounds



Slide 4



Slide 5

Plant carcinogens

Plants	Carcinogens	Tumor (rats)
Cycad	Cycasin	Liver, Colon
Bracken	Putakiroside	Colon
Butterbur scape	Putasitenine	Liver
Mushroom	Hydrazines	Liver, Colon
Coffee bean	Caffeic acid	Stomach

Slide 6

Metals

Arsenic compounds promote liver cancer in rats administered with carcinogenic compound(s).

Occurrence of skin and liver cancers is generally high in persons who usually drink well water containing much arsenic in parts of China.

Ethyl Alcohol

Ethyl alcohol is known to be a promoter of *esophageal cancer* in rats.
Epidemiological study shows that cancer of the esophagus frequently occurs in heavy drinkers and smokers lot.

Slide 7

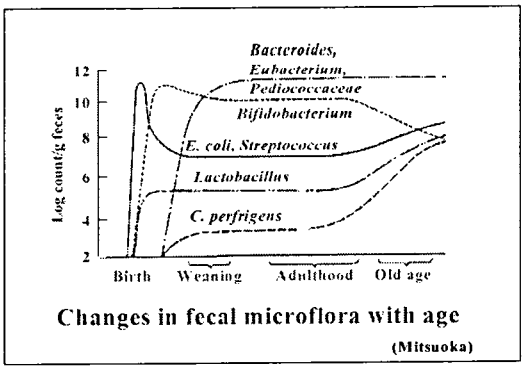
Food additives

a. **Saccharin:** bladder cancer (rats ?)
b. **BHA:** stomach cancer (rats)
c. **Diethylstibestrol (hormone):**
liver cancer, breast cancer etc. (rats)

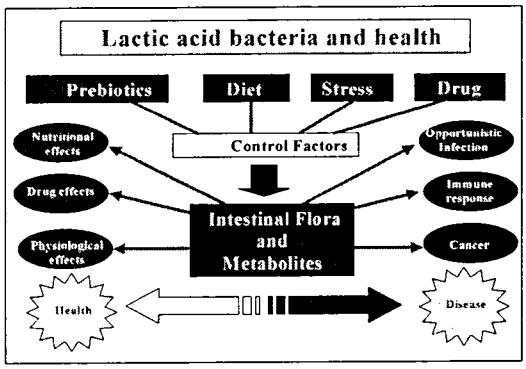
Pesticides

a. **Organochlorides**
Dieldrin, Chlorden, DDT, α-BHC
liver cancer (rats)
b. **Fungicides**
Sodium *o*-phenylphanate: bladder cancer (rats)

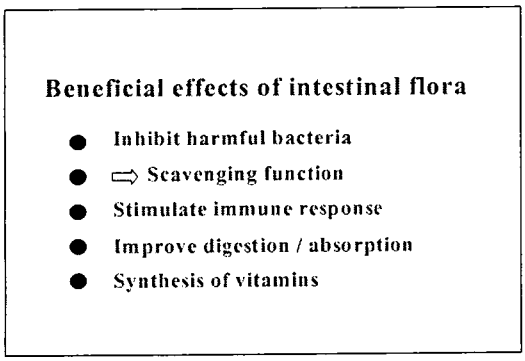
Slide 8



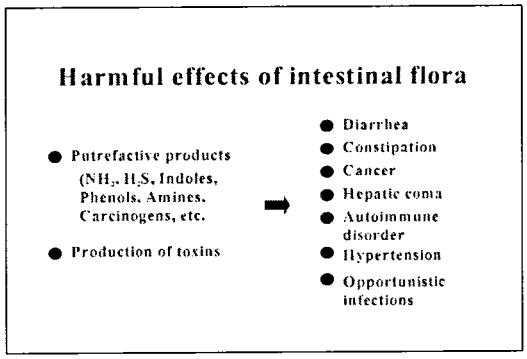
Slide 9



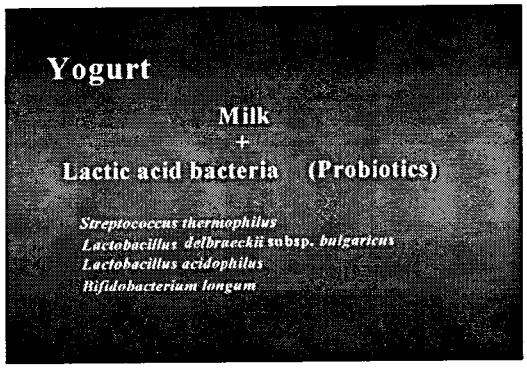
Slide 10



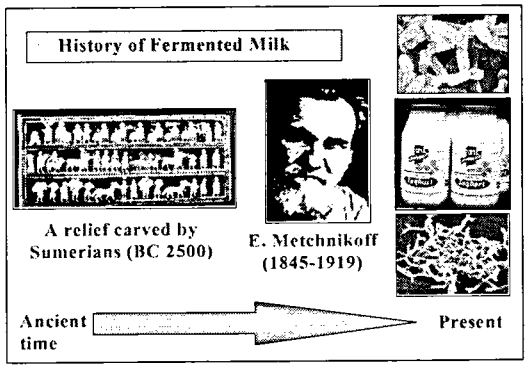
Slide 11



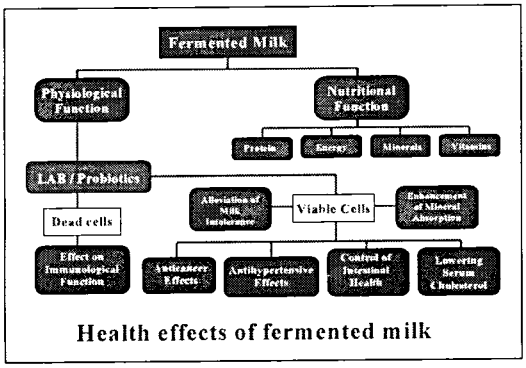
Slide 12



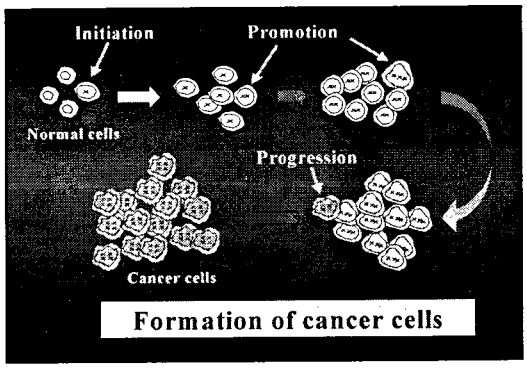
Slide 13



Slide 14



Slide 15



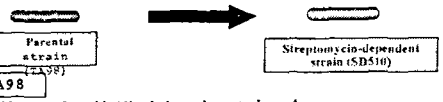
Slide 16

Genotypes of Ames strains

Salmonella typhimurium	Genotypes				
	LPS	DNA repair	Plasmid pkM 101	Marker screened	Mutation type
TA 98	rfa⁻	uvB⁻	+	His D	Frame-shift
TA 100	rfa⁻	uvB⁻	+	His G	base exchange

Slide 17

Characteristics of streptomycin dependent strain (SD 510) from *Salmonella typhimurium* TA 98



TA98

① Mutation from histidine independence to dependence
② Experimental procedures are very complicated to a sample containing histidine

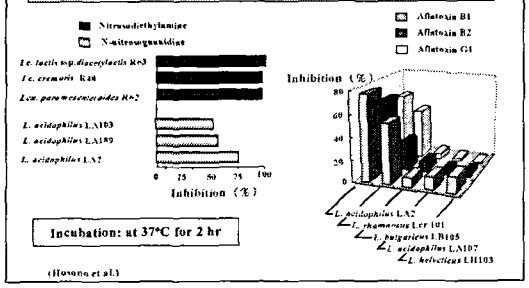
SD510

① Mutation from streptomycin independence to dependence
② Available in wide varieties of samples and simple procedures for assay
③ Higher sensitivity than the parental strain
④ Expensive S-9 mix for assay not required

(Hosono et al.)

Slide 18

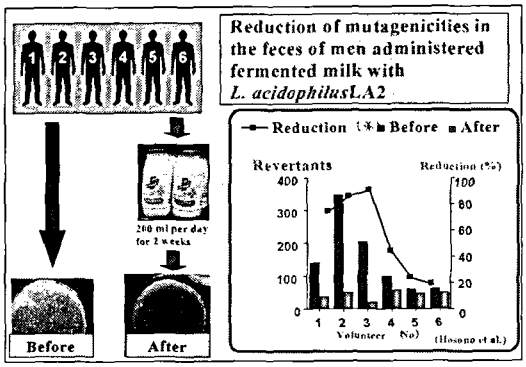
Antimutagenicity of lactic acid bacteria against various carcinogens



(Hosono et al.)

Slide 19

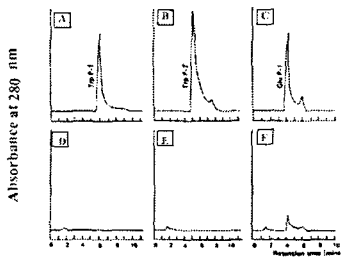
Reduction of mutagenicities in the feces of men administered fermented milk with *L. acidophilus* LA2



Slide 20

Binding properties of lactic acid bacterial cells to mutagens and carcinogens

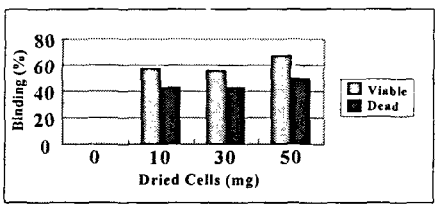
Slide 21



Binding properties of *Lactococcus lactis* subsp. *lactis* cells for various mutagenic compounds

(Hosono et al.)

Slide 22



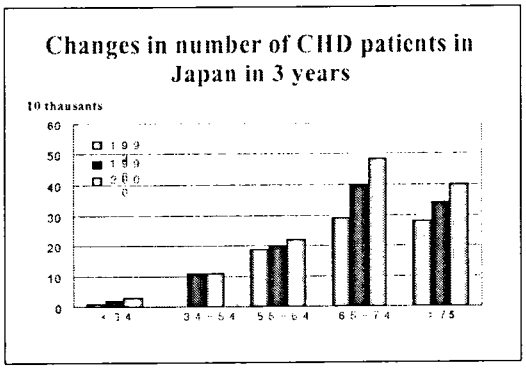
Binding properties of *Lc. lactis subsp. lactis* cells for Trp-P1

(Hosono et al.)

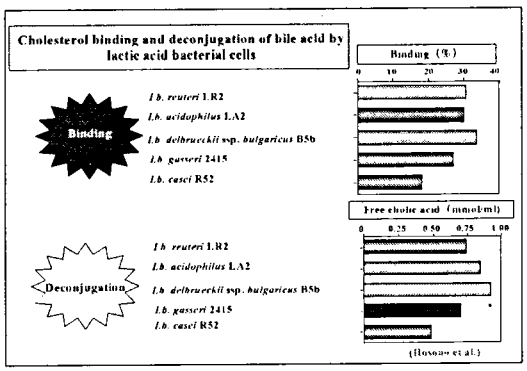
Slide 23

Serum cholesterol-lowering effect of lactic acid bacteria

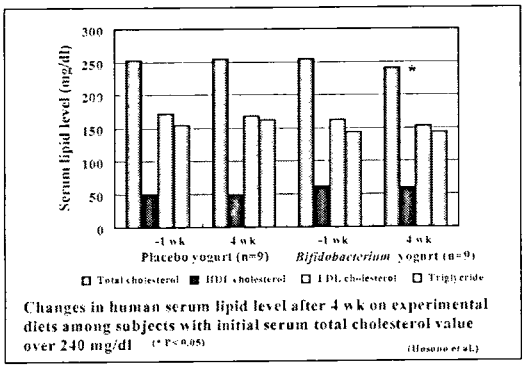
Slide 24



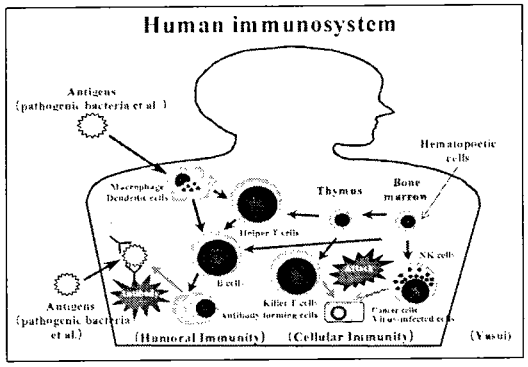
Slide 25



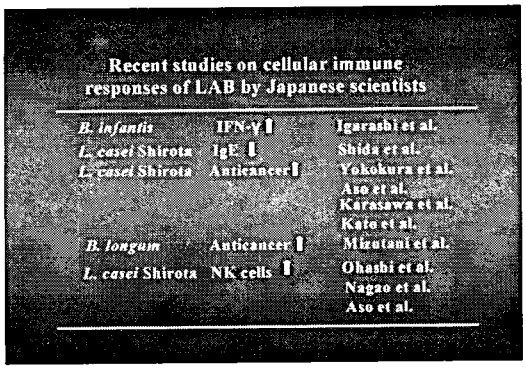
Slide 26



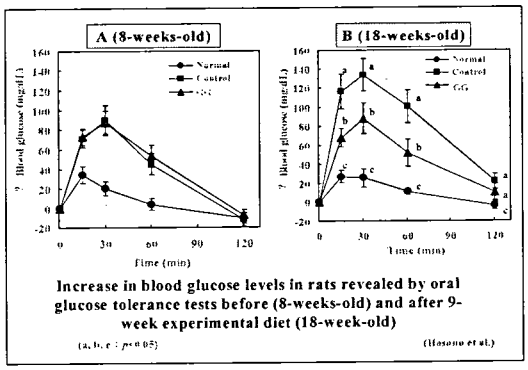
Slide 27



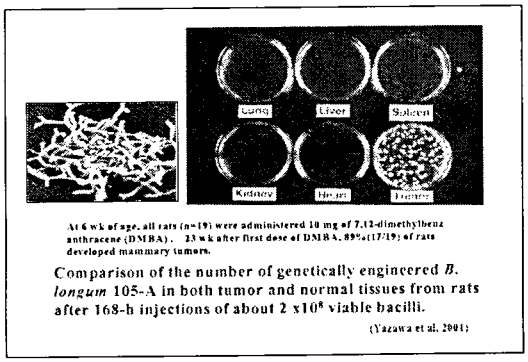
Slide 28



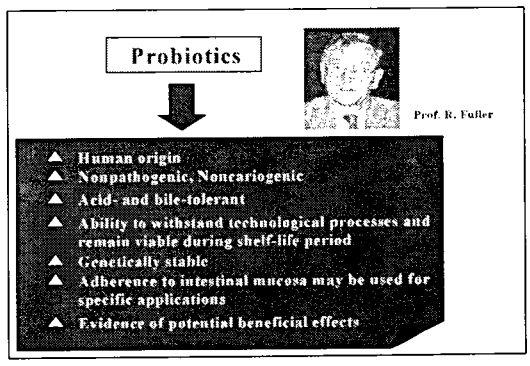
Slide 29



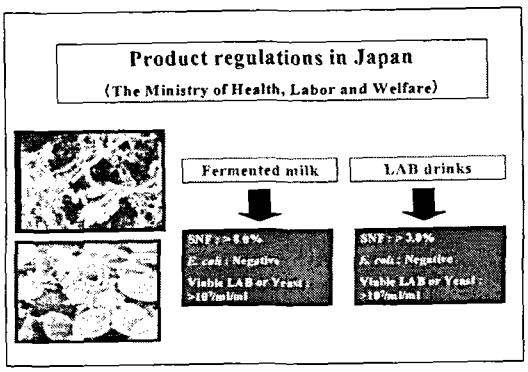
Slide 30



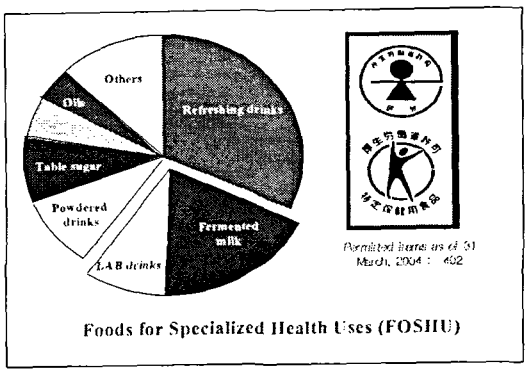
Slide 31



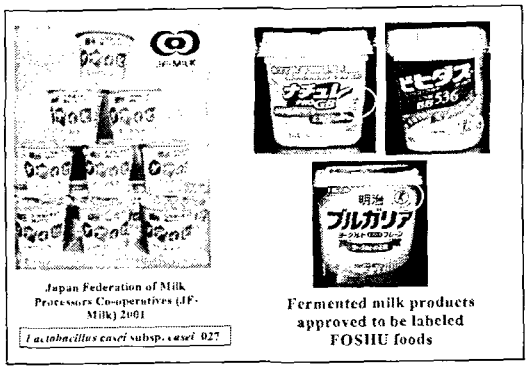
Slide 32



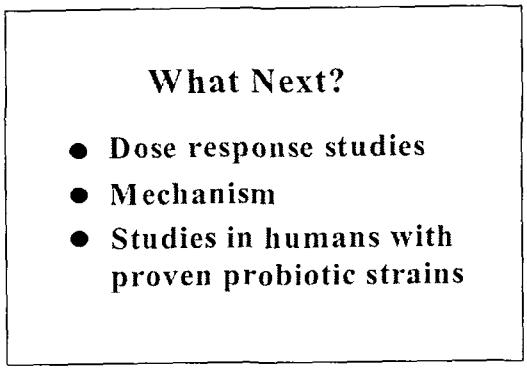
Slide 33



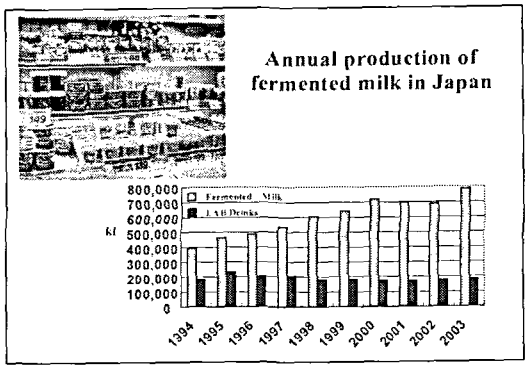
Slide 34



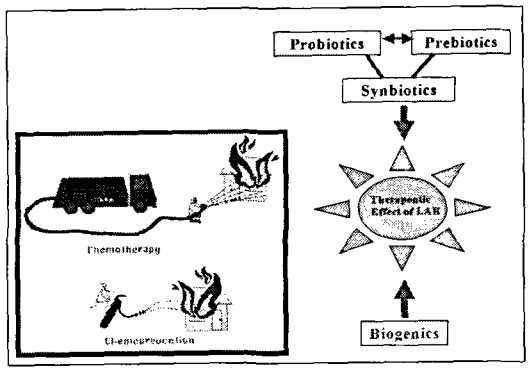
Slide 35



Slide 36



Slide 37



Slide 38

Slide 39