BACK

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COVER

Probiotic Manual

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"History of Medicine"

- 2000 BCE
  - Here, eat this root.
- 1000 CE
  - That root is heathen. Here, say this prayer.
- 1850
  - That prayer is superstition. Here, drink this potion.
- 1920
  - That potion is snake oil. Here, swallow this pill.
- 1945
  - That pill is not effective. Here, take this penicillin.
- 1955
  - Oops...bugs mutated. Here, take this tetracycline.
- 1960-1999
  - 39 more "oops"... Here, take this more powerful antibiotic.
- 2000
  - The bugs have won! Here, eat this root.

  Take this one step farther and add:
- 2001
  - Roots are not enough. Here, take this probiotic.

"Probiotics will be to medicine in the 21st century what antibiotics and microbiology were in the 20th"

- Dr. Michael L. McCann MD.

Preface

For years, the 10-metre-long human intestinal tract was like a dark tunnel. Some light had been shed on it by culturing bacteria from the faeces, but the darkness was overwhelming, because about 70 to 90 percent of the bacteria cannot be cultivated in laboratory dishes. These uncultured bacteria remained completely unknown. Microbiologists knew that trillions of microbes live in the gut, but they had no idea which ones. But the situation is changing rapidly. Thanks to new high throughput technologies and matching software. For the last few years, it has become possible to find out which 'species' or 'phylotypes' of bacteria live in our body[1].

Gut flora science is making rapid progress. New technologies such as 16S rDNA screens, metagenomics and metaproteomics are shedding light on the wide diversity of the gut bacteria. Cell, animal and human studies point to the intimate relationship between the immune system and the gut bacteria. And increasing evidence suggests that gut and immune related diseases -such as Crohn's disease, autism, allergy and infections -are associated to a disturbed gut flora[1].

It's not surprising that a growing number of human studies with carefully selected probiotic strains are showing positive results. These studies seem to hold out a promise that some patients will find relief from probiotics[1].

Probiotic strain research is epicentered in Europe and therefore Maknsons has build an association with some of the leading Europeans probiotics researchers and manufacturers to market world class premier probiotic strains in this part of the world. From the same source we have been introducing Resiton™ and Montum™.

We hope that Montum™ – probiotic for children's diarrhea and Resiton™ – probiotic for immune boost, will fulfill in your hands, the axiom - "The key to good health lies in the gut"[2] as evinced by the Nobel Laureate Prof. Elias Metchnikoff, the father of Probiotic therapy.

Montum™ and Resiton™ with your support, no doubt will herald new vistas in medical treatment with Probiotics.

Druk K.
MD Pediatric
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Pharmacist (US licensed)
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Recommended Documentary: **Microwarriors** – the power of probiotics, 2011

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Introduction

At the beginning of the last century, the Russian immunologist and Nobel Laureate Prof. Elias Metchnikoff argued that life long intake of yoghurt containing lactic acid producing microorganisms could explain the differences in length of life between ethnic groups. The idea was that the bacteria in the fermented products competed with microorganisms that are injurious to health[2].

Today it is known that the normal human microflora is important as a barrier against colonization by exogenous pathogenic microorganisms and potentially pathogenic bacteria already present in small numbers in the microflora[3]. The normal microflora influence several biochemical, physiological and immunological features of the host, particularly the gastrointestinal flora, which consists of the most dense and diverse collection of bacteria[4].

Disturbances in the normal microflora can be caused by several things, one being the administration of antimicrobial agents[5]. The normal microflora is also disturbed in infectious conditions of the gastrointestinal tract[6] and also when there is inflammation of the gastrointestinal tract (Ulcerative colitis, Crohn's disease, Chronic pouchitis)[7-10]

Probiotic microorganisms are thought to counteract disturbances and thereby reduce the risk of colonization by pathogenic bacteria[11]. Studies on strains of microorganisms used in probiotic dietary supplements have demonstrated that several strains produce antimicrobial substances such as organic acid, bacteriocins and peptide. In vitro and animal studies have further shown inhibitory effects of probiotic bacteria to be mediated by their interference with the adhesion of gastrointestinal pathogens or with toxins produced by the pathogenic microorganisms. Adjuvant-like effects on intestinal and systemic immunity have also been demonstrated for some strains[12].

A number of clinical trials using various probiotic strains in various gastrointestinal conditions have shown promising results in conditions like infectious diarrhea, antibiotic associated diarrhea, irritable bowel syndrome, inflammatory bowel disease (ulcerative colitis, and Crohn's disease). Some probiotic strains have also shown promising results in boosting immune response.

The Human Normal Flora

From the moment of birth, and throughout our entire lives, we are constantly exposed to microbes. Many contacts will be no more than momentary contacts. A small minority of contacts will lead to infection and disease[13].

In some instances, the microbes that come into contact with humans do not do any harm, and the microbes find conditions suitable for growth. They will persist until the prevailing conditions are no longer favorable. If a microbe persists upon or within its host for only a short period and without becoming established, it forms part of the **transient flora**[13].

Some microbes have become so well adapted to life on humans that upon initial encounter with a new host they thrive and flourish at the particular site of contact. Humans derive great benefit from these microbes. They are our **resident flora**. The resident flora is also known as the **commensal flora**. "*Commensal*" is derived

from the Latin, meaning to share a table. This implies that both partners derive benefit. This is often, but not always, true[13].

A wide variety of microorganisms interact with humans, exploiting a wealth of micro-environments. Certain parts of the body are sterile. These include the solid organs, blood, cerebrospinal fluid, and urine. The lower respiratory tract in health is also sterile. This sterility in an open system is due to the action of the "mucociliary escalator" that sweeps foreign matter back out of the lungs. Exposed sites are colonized by large numbers of microorganism that are highly adapted to their particular environment. These organisms constitute the body's normal flora[13].

In diagnostic microbiology, it is important to distinguish between a patient's commensal flora, and the causative agent of the infection from which they are suffering. This is not always an easy process, since in some cases microbes are normal flora at certain anatomical locations, but are considered pathogens when isolated from other sites[13].

Latent Viruses

Most of the microbes discussed are bacteria, although some fungi and certain protozoa also contribute the human commensal flora. Viruses are a **very** special case. There is still debate concerning the nature of viruses and certainly they are structures that are incapable of autonomous existence. In almost all cases virus infection is entirely to the detriment of the host. Certain viruses, however, have the ability to form **latent infections**. A good example of a virus that causes a latent infection is the herpesvirus, herpes simplex 1 or HSV 1. Although this virus may be highly pathogenic if the circumstances permit, it is so common in humans across the globe as to be regarded almost as normal[13].

Herpes simplex virus infects the vast majority of humans some time during early childhood, and often the primary infection is in-apparent. It infects the mucous membranes around the mouth, and the virus spreads to the trigeminal ganglion. There it enters a latent phase. The virus DNA persists, but there is little or no production of novel virus particles. When the host is subjected to stresses of various kinds, the latent virus can undergo a re-activation. New virus particles are produced, and these spread back to the mucous membranes around the mouth, where they erupt to cause the characteristic "cold sores", suffered by a number of people. Certain individuals are more prone to developing cold sores than others, but the vast majority of people World-wide carry HSV 1 as a latent infection[13].

Because it is so widespread, and because, at least for the majority of the time it causes so little problem, it has been argued that herpes simplex and other, similar latent viruses may be considered as normal with humans[13].

The Normal Flora of the Skin and Eyes

The skin is a relatively dry environment. It also has an acid pH. It is thus inhospitable for many microbes. Most of the microflora of the skin are Gram-positive bacteria such as the coagulase-negative staphylococci. They can withstand drying better than other microbes[13].

Anaerobic bacteria can live within the pores of the skin. *Propionibacterium acne*

is an example. It metabolizes sebum, releasing free fatty acids. These enhance the anti-microbial environment provided by the skin[13].

The eye has a specialised type of skin. It is kept clean by the washing action and inhibitory factors found in tears. In consequence, few microbes are found on the eye. Some people carry coryneform bacteria on their conjunctivae[13].

The Normal Flora of the Nose and Throat

Many of the microbes that we encounter enter through the nose. Indeed, the nose has an elaborate anatomy and nasal hairs, evolved to prevent potentially dangerous microbes from entering our lungs[13].

The nasal flora resembles that of the skin in many respects. However, the air that we exhale is moist, and this makes the nose a more hospitable environment for *Staphylococcus aureus*, a bacterium that can cause serious infections as well as being a commensal[13].

The oral cavity and throat have a rich and varied microbial flora. There are marked differences between the different surfaces of the oral cavity. The bacteria that attach to the hard enamel of the teeth are different in type from those that colonize the soft tissues that are in intimate anatomical contact with the teeth[13].

There are many anaerobes that live in this area, and protozoa can also frequently be found. Both Gram-positive and Gram-negative bacteria are commonly seen in this area. The predominant bacteria are alpha-haemolytic streptococci. Because they are surrounded by a greenish halo when grown on blood agar they are sometimes known as 'viridans streptococci'. Some people carry pathogenic bacteria as a part of the commensal flora of the throat. These include *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Neisseria meningitidis*[13].

The Lungs - a Special Case

The lungs are exceptional in being a body surface that is kept sterile by numerous defence mechanisms. The beating cilia sweep the mucous secretions back out of the lung, carrying deposited microbes with it. This has been referred to as the mucociliary escalator. Antibodies are present in the lung secretions, and these help to overcome invading microbes. Macrophages, specialised leukocytes, rove over the lung surfaces, engulfing foreign particles, including microbes[13].

The Normal Flora of the Gut

The stomach is considered to be free of a commensal flora. This is because the extreme acid pH at this site is inhibitory. The small intestine is increasingly colonized as it reaches the large intestine. The concentration of bile at the proximal end is inhibitory to many microbes[13].

The faecal flora has been estimated to have a metabolic capacity equal to that of the liver. Obligate anaerobic bacteria, such as those of the genus *Bacteroides*, outnumber the facultatively anaerobic coliforms, such as *Escherichia coli* (the commonest bacterium to grow aerobically from faeces) by at least 100:1[13].

Diet may have a profound effect on the composition of the gut flora. Bottle-fed babies have a faecal flora that is entirely different from that of breast-fed babies. The former resembles the adult faecal flora: the latter is predominantly bifidobacteria.

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The flora of bottle-fed babies breaks own proteins efficiently; the flora of breast-fed babies breaks down sugars. The smell and appearance of the faeces reflect these differences[13].

The Normal Flora of the Urogenital Tract

The genital tract in males is kept sterile by secretions from the prostate gland and by the mechanical washing action of urine. The distal portion may be colonized by a few skin microbes. The female urinary tract is likewise typically sterile. However, the vaginal flora is complex, and is constantly changing[13].

Hormones can profoundly influence the nature of the commensal flora of the female reproductive tract. At birth, maternal hormones are responsible for elevated levels of glycogen in the vagina. This is a good substrate for lactobacilli (also known as Döderlein bacilli), and the vaginal flora of the neonate resembles that of her mother. Quickly the glycogen levels drop, and a flora dominated by enterococci and coliforms develops. At puberty, glycogen returns, and with it the lactobacilli. At the menopause, glycogen wanes, and the flora returns to its pre-pubescent state. These are the gross changes that occur. The vaginal flora is in constant flux through the menstrual cycle as well[13].

The Normal Gastrointestinal Flora and Intestinal Ecosystem

The condition and function of the gastrointestinal tract is essential to our well being. This largely depends on the maintenance of proper balance of the intestinal ecosystem. The human intestinal microflora contributes largely in maintaining a normal balance of the intestinal ecosystem.

The human intestinal microflora is highly important to the host for several reasons. Firstly, microflora benefits the host by increasing resistance to colonization by Potentially Pathogenic Microorganisms (PPMs) ingested through food and water, causing gastrointestinal disorders, as well as by protecting against the overgrowth of already present potentially pathogenic organisms. Another function important to the host is the high metabolic activity of the intestinal flora, helping in the digestion process in the intestine.

They also help in the synthesis of beneficial substances for the host like B-Complex Vitamins and Vitamin K. Indeed, it is now known that the normal gut flora plays an important role in maintaining good health by stimulating the immune system, aiding the digestion and assimilation of food and protecting the host from invading bacteria.

The composition of the gastrointestinal flora differs among individuals, and also during life within the same individual. Many factors, such as diet or climate, aging, medication (especially antibiotics), illness, stress, pH, infection, geographic location, race, socio-economic circumstances, lifestyle can upset this balance[14].

Interactions of the typical intestinal bacteria may also contribute to stabilization or destabilization of the gut flora. A state of balance within the microbial population within the GI tract can be called "eubiosis" while an imbalance is termed "dysbiosis". For optimum "gut flora balance", the beneficial bacteria, such as the gram positive Lactobacilli and Bifidobacteria, should predominate, presenting a barrier to invading organisms. Around 85 % of the intestinal microflora in a healthy person should be good bacteria and 15% bad bacteria.

THE INTESTINAL ECOSYSTEM

The gastrointestinal tract of an adult human is estimated to harbor about 100 trillion viable bacteria. These live bacteria are known as intestinal or gut flora. Viruses, fungi and protozoa can also be present, but these normally form only a minor component of the total resident population of microorganisms in healthy individuals.

The density of microorganisms in the gut flora increases dramatically from 10 - 1,000 CFU/ml in the stomach to 10 - 100 billion CFU/gm in the large intestine[14] and these belong to as many as 400 different species and anaerobic bacteria outnumber aerobic bacteria by a factor of 1000:1. Anaerobic flora is dominated by Bacteroides spp., Bifidobacteria, Lactobacillus, Propionibacteria and Clostridia. Among aerobic and anaerobic bacteria enterobacter, mainly E. coli and enterococci predominate.

The predominant microflora in the GI tract is as follows.

Proximal small intestine	Lactobacilli + Enterococcus faecalis (10^5 - 10^7/ml of fluid)
Distal small intestine	Lactobacilli + Enterococcus faecalis + Coliforms + Bacteroides (10^8 bacteria/ ml of fluid)

Colon Bacteroides + Bifidobacteria (10^{11} bacteria / ml of fluid)

Composition of the Human Gastrointestinal Microflora[15]

Nunber of microorganisms (CFU/ml or CFU/g)

MICROORGANISMS	STOMACH	JEJUNUM	ILEUM	COLON
Total Count	0 - 10^4	0 - 10^5	10^4 - 10^8	10^{10} - 10^{12}
AEROBIC MICROORGANISMS				
Streptococcus	1 - 10^3	0 - 10^4	10^2 - 10^4	10^3 - 10^5
Enterococcus	rare	0 - 10^2	10^2 - 10^4	10^5 - 10^{10}
Staphylococcus	0 - 10^2	0 - 10^3	10^2 - 10^5	10^4 - 10^6
Enterobacteria	0 - 10^2	0 - 10^3	10^2 - 10^7	10^2 - 10^{10}
Yeasts	0 - 10^2	0 - 10^2	10^2 - 10^4	10^2 - 10^5
ANAEROBIC MICROORGANISMS				
Peptostreptococcus	1 - 10^3	0 - 10^3	10^2 - 10^6	10^{10} - 10^{12}
Bifidobacterium	0 - 10^2	0 - 10^4	10^3 - 10^9	10^8 - 10^{11}
Lactobacillus	0 - 10^3	0 - 10^4	10^2 - 10^5	10^6 - 10^8
Clostridium	rare	rare	10^2 - 10^4	10^6 - 10^8
Eubacterium	rare	rare	rare	10^9 - 10^{12}
Veillonella	0 - 10^2	0 - 10^3	10^2 - 10^4	10^3 - 10^6
Fusobacterium	0 - 10^2	0 - 10^3	10^3 - 10^4	10^6 - 10^8
Bacteroides Fragilis	rare	0 - 10^3	10^3 - 10^7	10^{10} – 10^{12}

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Establishment of Intestinal Microflora in the New Born Infant

Fetuses are sterile in the womb, but beginning with the birth process, infants are exposed to microbes that originate from the mother and the surrounding environment including breast milk or formula[16]. The infant tends to acquire the flora swallowed from the vaginal fluid at the time of delivery. Because vaginal flora and intestinal flora are similar, an infant's flora may closely mimic the intestinal flora of the mother[17].

Another factor affecting the intestinal flora of the newborn is delivery mode. A normal vaginal delivery commonly permits transfer of bacteria from the mother to the infant. During cesarean deliveries, this transfer is completely absent. These infants commonly acquire and are colonized with flora from the hospital's environment and, therefore, their flora may differ from maternal flora. Thus infants delivered by cesarean section are colonized with more anaerobic bacteria, especially Bacteroides, than vaginally delivered infants. Clostridium perfringens is the anaerobic bacterium most frequently isolated after cesarean deliveries. When colonized, cesarean delivered infants less frequently harbor E. coli, and more often Klebsiellae and Enterobacteria[18].

The initial colonizing bacteria also vary with the food source of the infant. In breast fed infants, Bifidobacteria account for more than 90% of the total intestinal bacteria. The low concentration of protein in human milk, the presence of specific anti-infective proteins such as immunoglobulin A, lactoferrin, lysozyme, and oligosacharides (Prebiotics), as well as production of lactic acid, cause an acid milieu and are the main reasons for its bifidogenic characteristics. In bottle-fed infants, Bifidobacteria are not predominant[19]. Instead enterobacteria and gram negative organism dominate because of a more alkaline milieu and the absence of the prebiotic modulatory factors present in breast milk.

The establishment of an intestinal microbial ecology is very variable at the beginning but will become a more stable system similar to the adult microflora by the end of the breastfeeding period.

Mechanisms by which the normal intestinal flora protects the host against intestinal disease

a. Production of inhibitory substances

Bacteria of the normal gut flora produce a variety of substances that are inhibitory to both gram positive and gram negative bacteria. They produce antimicrobial compounds (bacteriocins), volatile fatty acids, organic acids, and lactic acid, which reduce the intestinal pH. These compounds reduce the number of viable pathogenic organisms in the gastrointestinal tract[20, 21].

b. Blocking of adhesion sites

The gut microflora competes directly with gut pathogenic organisms for epithelial attachment sites in the gastrointestinal tract, thereby preventing attachment and colonization of the GI tract by the potentially pathogenic organisms[20, 21].

c. Competition for nutrients

The gut microflora competes directly with gut pathogenic organisms for the essential nutrients necessary for survival and multiplication, thereby inhibiting the growth and multiplication of potentially pathogenic organisms[20, 21].

d. Stimulation of immunity

The underlying mechanisms of immune stimulation by the gut microflora are not well understood. However, local gut immunity enhancement by the gut microflora may be one possible mechanism of inhibiting growth of potentially pathogenic microorganism[20, 21].

Probiotics

Bacteriotherapy

isplace pathogenic organisms. It is an alternative and promising way of combating infections[22].

What are Probiotics?

The word probiotic is derived from the Greek meaning "for life". A probiotic by general definition is a "Live microbial feed supplement, which beneficially affects the host by improving the host's intestinal microbial balance". Probiotics are generally mono or mixed cultures of live microorganisms which otherwise form the major component of the gut microflora (e.g. lactobacilli, bifidobacteria). Probiotics, when ingested, beneficially affect the host by improving the properties of the indigenous microflora[14].

Ingestion of Probiotics beneficially affects the host by:

a. Replenishing the depleted gut microflora, which may have occurred due to use of antibiotics, illness, stress, travel or lifestyle changes.

b. Improving the properties of the indigenous microflora.

Probiotic bacteria are generally, though not exclusively, lactic acid bacteria and include:

1. Lactobacillus species like Lactobacillus acidophilus, L. casei, L. bulgaricus, L. plantarum, L. salivarius, L. rhamnosus, L. reuteri,
2. Bifidobacterium species like Bifidobacterium bifidum, B. longum, B. infantis.
3. Saccharomyces boulardii (yeast).
4. Streptococcus thermophilus.

The desirable properties of a probiotic dietary supplement are[23]:

1. Must be of human origin and be able to inhabit the small and large intestine
2. Exert a beneficial effect on the host by helping in proper digestion and assimilation of nutrients and synthesis nutrients like B complex Vitamins, and Vitamin K for the host (man)
3. Be non-pathogenic and non-toxic

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4. Contain a large number of viable cells
5. Be capable of surviving (should not be killed by gastric juice and bile acids) and metabolizing in the gut
6. Remain viable during storage and use
7. Be antagonistic to pathogens

Health benefits offered by Probiotics are[21,24]:

1. Offers increased resistance to establishment of infection by potentially pathogenic organisms in the intestine.
2. Decreased duration of diarrhea (antibiotic associated, travelers', infective).
3. Use in Lactose Intolerance (promotion of intestinal lactose digestion).
4. Helps boosting immunity against viruses, bacteria and fungi.
5. Increased nutritional value (better digestibility, increased absorption of vitamins and minerals).
6. Regulation of gut motility (constipation, irritable bowel syndrome).
7. Maintenance of mucosal integrity of the intestine.
8. Reduction in serum cholesterol concentration.
9. Reduction in Allergy.
10. Prevention of Colon Cancer.
11. Reduction in carcinogen/co-carcinogen production.

Important Probiotic Species

Lactobacilli and Bifidobacteria are Gram positive lactic acid producing bacteria that constitute a major part of the normal intestinal microflora in humans and animals. They play an important role in resistance to colonization against exogenous, potentially pathogenic organisms. They are essentially lactic acid producing bacteria. The lactic acid helps in reducing the pH in the intestine and thereby creates an environment, which is not conducible for growth of pathogenic organisms (pathogenic intestinal organisms prefer an alkaline environment for growth and proliferation).

Lactobacilli are Gram positive, non-spore forming rods or coccobacilli. They have complex nutritional requirements, aerotolerant or anaerobic, acidophilic and are found in habitats rich in carbohydrate containing substrates such as the human intestinal mucosal membrane[15]. They predominantly colonize the upper and lower small intestine.

LACTOBACILLUS ACIDOPHILUS:

This natural inhabitant of the intestines also lives in the mouth of vagina. Its main site occupation is the small intestine. Its major roles are:

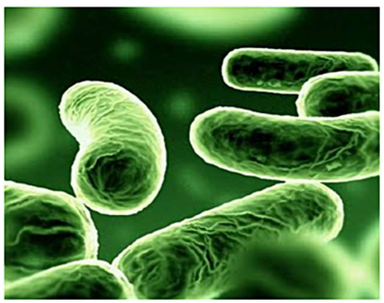
< Preventing colonization by hostile microorganisms such as yeast competing with them for attachment sites and nutrients

- Producing lactic acid (out of carbohydrates) which helps to maintain the correct environment for digestion, by suppressing hostile organisms (other bacteria and yeasts)
- Improving the digestion of lactose (milk sugar) by producing the enzyme lactase
- Assisting in the digestion and absorption of essential nutrients from food
- Destroying invading bacteria (not all the strains of L. acidophilus can do this)
- Slowing down and controlling yeast invasions such as Candida albicans

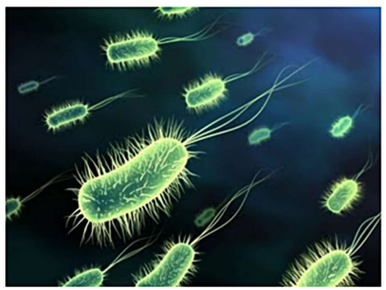
LACTOBACILLUS CASEI

Lactobacillus casei is beneficial bacteria that are found naturally in both the mouth and intestines of human beings. Lactobacillus casei, more commonly referred to as L. casei, is a harmless, nonpathogenic microorganism that has been widely recognized for the attributes and properties it possesses that have been found to be beneficial to the human body:

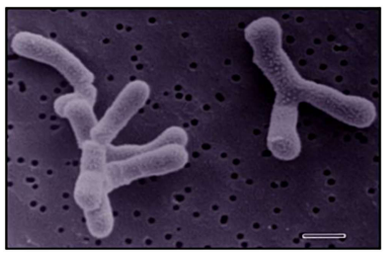
- L. casei is a type of bacteria that helps protect the human body from disease and illness by restricting the growth of various types of harmful bacteria that cause infection and be detrimental to an individual's health.
- It produces lactic acid which helps lower pH levels in the digestive system and impedes the growth of harmful bacteria.
- It is able to improve and promote digestion.



Lactobacillus casei



Lactobacillus acidophilus



Bifidomacterium

- Some strains of the bacteria help control diarrhea, while other strains have an anti-inflammatory effect on the gut.
- Other advantageous effects include reducing lactose intolerance, alleviating constipation, and even modulation of the immune system.
- Because friendly bacteria are vital to proper development of the immune system, to protection against microorganisms that could cause disease, and to the digestion and absorption of food and nutrients ensuring that the body has an appropriate amount of L. casei inhabiting the body is important.

LACTOBACILLUS BULGARICUS:

This extremely useful friendly bacteria is not a resident of the human body, but a 'transient'. Once it enters the body through food (yogurt, for example) it remains for several weeks before being passed, but while in the body it performs useful tasks. L. bulgaricus is a yogurt culture, as is the other main yogurt-making culture, Streptococcus thermophilus, and is therefore found in some yogurts and cheeses if they have not been sterilized to kill their bacterial cultures – to enhance shelf life – after manufacture; it performs a number of useful roles, such as:

- Some strains produce natural antibiotic substance.
- Some strains have been shown to have anti-cancer properties.
- They enhance the ability to digest milk and its products by producing the enzyme lactase, which is absent or deficient in almost half the adults on earth, and many children. Especially if they are of Asian, African or Mediterranean genetic stock.
- Because they produce lactic acid (as do all bacteria which have as the first part of their name 'lactobacillus'), they help to create an environment which encourages colonization by the bifidobacteria (they are therefore known as 'bifidogenic' bacteria) and L. acidophilus by helping to prevent colonization by other, undesirable microorganisms.

Some additional (usually useful) lactobacilli found in the digestive tract include:

- L. plantarum – are transient bacteria of the intestine, found in dairy products, sauerkraut, pickled vegetables; manufactures lactic acid.
- L. brevis –are transient bacteria of the intestine, found in dairy products (especially kefir, a fermented milk drink); manufactures lactic acid.
- L. caucasicus (known as L. kefir) are transient bacteria of the intestine, found in kefir grains and drinks; manufactures lactic acid (as well as alcohol and carbondioxide). It therefore inhibits undesirable bacteria.

BIFIDOBACTERIUM BIFIDUM:

These friendly bacteria inhabit the intestines – with a greater presence in the large intestine (the colon) then the small intestine. They also live in the vagina. In breastfed babies together with B. infantis and B. longum they from 99 per cent of the flora of the intestines, but gradually reduce in numbers with age.

Their major roles are:

- Preventing colonization by hostile microorganisms by competing with them for attachment sites and nutrients

- Preventing yeasts from colonizing the territories which they inhabit
- Helping to maintain the right levels of acidity in the digestive tract to allow for good digestion
- Preventing substances such as nitrates from being transformed into toxic nitrites in our intestines
- Manufacturing some of the B-vitamins
- Helping detoxify the liver

BIFDOBACTERIUM LONGUM:

This is a natural inhabitant of the human intestines and vagina. It is found in larger numbers in the large intestine than the small intestine. Together with other bifidobacteria, this is the dominant organism of breast feed infants (making up 99 per cent of the micro flora). In adolescence and adult life the bifidobacteria are still the dominant organisms of the large intestine (when health is good). Among its main benefits are:

- Preventing colonize by hostile microorganisms by competing with them for attachment sites and nutrients
- Producing of lactic and acetic acids, which inhibit invading bacteria
- Helping in weight gain in infants by retention of nitrogen
- Preventing harmful nitrites being formed from nitrates in the digestive tract
- Manufacturing B-vitamins
- Assisting in liver detoxification.

BIFIDOBACTERIUM INFANTIS:

This is a natural inhabitant of the human infant's digestive tract as well as of the vagina, (in small numbers). Its presence is far greater in the gut of breast fed infants compared with bottle-fed infants. Among its main benefits are:

- Preventing colonization by hostile microorganisms by competing with them for attachment sites and nutrients.
- Production of lactic and acetic acids, which inhibit invading bacteria.
- Helping in weight gain in infants by retention of nitrogen.
- Preventing harmful nitrites being formed from nitrates in the digestive tract.
- Manufacturing B-vitamins.

STREPTOCOCCUS THERMOPHILUS:

These are transient (non-resident) bacteria of the human intestine which together with L. bulgaricus is a yogurt culture, also found in some cheeses. It performs a number of useful roles, such as:

- Some strains produce natural antibiotic substances.
- They enhance the ability to digest milk and its products by producing the enzyme lactase.
- They produce lactic acid, thereby helping to create an environment which encourages colonization by the bifidobacteria and L. acidophilus, and discourages colonization by other, undesirable microorganisms.

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STREPTOCOCCUS FAECIUM:

This is a natural resident of the human intestine. It is found in human feces as well as on some plants and insects. Its characteristics include:

- It is used as a part of the manufacture of cheeses (in some dairies, not all).
- Its potential benefits to humans remain a possibility but not a certainty.
- It manufactures lactic acid from carbohydrates and so enhances the environment for colonizing friendly bacteria.

STREPTOCOCCUS FAECALIS:

This is a resident to the human intestine which is known as an enterococcus. It is found in faece, some insects and some plants. Its characteristics include:

- The manufacture of lactic acid from carbohydrates, thereby enhancing the environment for colonizing friendly bacteria.
- The production of substances called amines which can be toxic. Tyramine, for example, is associated with migraine headaches, and histamine with allergic and inflammatory reactions.
- Has been associated with urinary tract infections.
- Overall there is little evidence that S. faecalis is beneficial for humans; on balance it would seem to have a harmful potential.

SACCHAROMYCES BOULARDII

Saccharomyces boulardii belongs to the yeast species. It is non-pathogenic and non-colonizing. It is considered as transient yeast in the human intestines, which means that it does not set up residence in the mucosal membrane of the intestinal tract like the lactobacillus and bifidobacteria. As it travels to the intestines, this yeast has the ability to aggressively displace species of pathogenic yeast and bacteria and at the same time it does not harm the normal intestinal flora. S. boulardii is described as a probiotic which has the ability to beneficially affect the delicate balance of the intestinal bacteria, and also has the capacity to prevent or reduce the effects of harmful pathogenic organisms. The mechanism of probiotic action is probably by production of acetic and lactic acid, which lower the intestinal pH and thereby inhibiting the growth of pathogenic yeast and bacteria. This also encourages a good environment for the intestinal resident bacteria (lactobacillus and bifidobacteria). There are some reports in medical literature of infections (septicemia) in immunocompromised patients after treatment with S. boulardii.

Prebiotics

Prebiotics are range of non-digestible dietary supplements, which modify the balance of the intestinal micro flora, stimulating the growth and / or activity of beneficial organisms and suppressing potentially deleterious bacteria.

These supplements include lactulose, lactitol, a variety of oligosaccharides (especially fructooligosaccharides or FOS), and inulin. In particular, Prebiotics promote the proliferation of bifidobacteria in the colon. Some of them also help in promoting the proliferation of lactobacilli in the small intestine to a certain extent.

To be effective, Prebiotics should escape digestion in the upper gut, and reach the

large bowel, and be utilized selectively by a restricted group of microorganisms that have been clearly identified to show health promoting properties (e.g. lactobacillus, bifidobacteria).

Antibiotics and the Ecologic Damage of Intestinal Flora:

It is known that the normal human micriflora is important as a barrier against colonization by exogenous pathogenic microorganism and potentially pathogenic bacteria already present in small numbers in the microflora. The normal microflora influence several biochemical, physiological and immunological features of the host. Disturbances in the normal microflora can be caused by several things, one being the administration of antimicrobial agents. Even when used appropriately antibiotics badly damage the ecology of the intestinal flora. As a result it facilitates development of wide range of conditions including[24]:

- Digestive and bowel problems
- Depressed immune function
- Liver disease
- Elevated cholesterol levels
- Gynecological symptoms
- Increased risk of bladder infections
- Serious arthritic conditions

Infectious Diarrhea

Infectious diarrhea that occurs in children and adults are due to infection with bacteria, viruses or protozoa. Children are more prone to viral infection of the gastrointestinal tract, whereas adults are more prone to bacterial and protozoan infection of the gastrointestinal tract.

In viral diarrhea the most common pathogen is Rotavirus. This virus leads to loss of absorptive surface of the intestines thereby resulting in diarrhoea[25]. The diarrheal stools may be small to large volume and watery in nature. Usually viral diarrheas are self-limiting in nature, lasting for 5-7 days, in which time the Rotavirus is shed from the gastrointestinal tract through the stools. Treatment is replenishing the lost fluids from the gastrointestinal tract either by oral rehydration therapy (ORS) or by intravenous infusion of fluids depending on the severity of fluid loss.

In bacterial diarrhea, the pathogens often involved are E, coli, Salmonella Sp., Shigella Sp., and V. cholerae[25]. In infection due to some E. coli and V. cholera the diarrhea is due to the action of certain toxins secreted by them. In infection due to Shigella Sp., the diarrhea is due to invasion of the GI tract by the bacteria. Treatment of diarrhea due to bacterial infection is by use of the appropriate antibacterial agent. The bacteria mentioned above are potentially pathogenic organisms, which tend to displace the friendly bacteria that constitute the normal GI flora and thereby try to colonize the GI tract, causing infection and diarrhea.

PROBIOTICS AND INFECTIOUS DIARRHEA

Numerous probiotic agents have been studied for the management of diarrheal diseases in both children and adults. Probiotic works against Salmonella, Shigella,

E. coli, Clostridium difficile and Rotavirus and could be used in preventing other enteric infections[26]. A combination of two well documented probiotics strains of Lactobacillus paracasei subspecies paracasei CRL 431 and Lactobacillus acidophillius LA5 colonizes in the intestine and prevent colonization of opportunistic and pathogenic microorganisms. This, thus, helps control children's diarrhea of varying etiologies[27-33]. Lactobacillus paracasei subspecies paracasei CRL 431 and Lactobacillus acidophillius LA5 inhibited the growth of Shigella by 91% in 14 hours[34]. Some probiotic agents like Lactobacillus GG have been shown to reduce the duration of acute viral diarrhea (rotavirus induced diarrhea) in children, when used therapeutically. The use of other agents, particularly Bifidobacteria, in way of supplementing the regular feed of infants may have an effect as prophylactic agent against acute diarrheal disease. An immunological mechanism may be responsible for the beneficial effects[35]. It has been shown that supplementation of infant formula with Bifidobacterium bifidum and Streptococcus thermophilus can reduce the incidence of acute diarrhea and rotavirus shedding in infants admitted to hospital[36].

In human large intestine Bifidobacteria are a numerically important group of microorganisms which are considered to exert a range of biological activities related to host health. It has been suggested that the mechanism of inhibition carried out by Bifidobacteria is related to the fermentive production of acids such as acetate and lactate. Studies showed that eight species belonging to the genera Salmonella, Listeria, Campylobacter and Shigella, as well as Vibrio cholerae were all affected. These results show that Bifidobacteria are able to exert more than one mechanism of inhibition, which may be of importance with regard to protection against gastroenteritis[37].

Travelers' Diarrhea

This is a form of infectious diarrhea due to intestinal infection with the bacteria belonging to Shigella Sp. It is most prevalent in third world countries and affects tourists traveling to the third world[38]. Transmission of infection is from man to man through the faeco-oral route. Infection is transmitted on fingers and by flies and does not require heavy contamination of food or water. Shigella organism first multiplies and colonizes in the upper small intestine and latter localizes to the large intestine. Travelers' diarrhea could be prevented by a regular prophylactic intake of a Prebiotic and a Probiotic which contain beneficial bacteria like lactobacillus and bifidobacterium that colonize the small and large intestines and therefore prevent multiplication and colonization of the shigella sp[37]. The intake of probiotic could start one week prior to onset of journey and continued throughout the journey. It could be then stopped one week after returning from the journey.

Antibiotic Associated Diarrhoea

Any antibiotic can cause diarrhea. The most common antibiotics that frequently cause diarrhea are[39]:

1. Ampicillin and Amoxycillin group of drugs.
2. Macrolides (e.g. Erythromycin)
3. Cephalosporins
4. Clindamycin

5. Penicillins other than Ampillicin and Amoxycillin
6. Quinolones
7. Sulphonamides

The common underlying factor in antibiotic associated diarrhoea is the alteration in the composition of the normal bacterial intestinal flora due to the action of antibiotics. This alteration of the normal bacterial intestinal flora makes the GI tract susceptible to superinfection by fungus (Candida) or by a bacteria Clostridium difficile, which causes a condition known as pseudomembranous enterocolitis[39].

Fungal diarrhea commonly occurs due to super infection with the fungus Candida Sp. The fungus alters the absorptive surface of the GI tract thereby resulting in diarrhea[39].

Pseudomembranous Enterocolitis is caused by superinfection with Clostridium difficile[39]. It is an inflammatory disease of the small and large intestines, which occurs after antibiotic exposure. Use of antibiotics leads to change in normal intestinal flora, which allows Clostridium difficile to establish in the GI tract and proliferate. Symptoms of diarrhea and crampy abdominal pain can occur any time from the first to the third week of antibiotic therapy. It can also occur after 4- 6 weeks of stopping antibiotic therapy. This condition is treated with either Metronidazole or Vancomycin[39].

Both the above conditions arising due to use of antibiotics and alteration in the normal gut flora may be prevented by oral supplementation with Probiotics along with antibiotics so as to maintain the normal bowel flora. In this way, antibiotic associated diarrhea can be prevented and treated[35].

Bifidobacteria and lactobacilli are gram-positive lactic acid producing bacteria constituting a major part of the intestinal microflora in humans. Administration of antimicrobial agents may cause disturbance of their colonization by potential pathogens. To maintain or reestablish the balance in the flora, supplements of intestinal microorganisms, as Probiotics, mainly bifidobacteria and lactobacilli, have been successfully used[15].

Inflammatory Bowel Disease

Inflammatory bowel disease encompasses.

1. Ulcerative colitis
2. Crohn's disease

The etiology of these conditions is not known. There is an increased risk of development of these conditions, if there is a positive family history[40]. It mainly affects young adults in the age group of 20-40 years.

In ulcerative colitis the inflammation involves the rectum and the colon. In Crohn's disease, the inflammation involves the small and large intestine. Patients present with symptom of diarrhea or dysentery, which is present for weeks or months. The diagnosis is confirmed by performing a colonoscopy and biopsy. Patients are treated with drugs like sulphasalazine, steroids, immunosuppressive agents[40].

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Supplementation with Probiotics, in addition to the above mentioned therapy, helps to mitigate the symptoms. This is because it has been shown that patients with inflammatory bowel disease have a compromised bowel flora due to presence of inflammation. Supplementation with probiotics helps to normalize the bowel flora and thereby minimize the symptoms. It has also been shown that normalizing the bowel flora helps to bring down the degree of inflammation in the bowel. On a more chronic basis, it has been suggested that some Probiotics can help maintain remission in the inflammatory conditions like ulcerative colitis[41].

Bifidobacterium counts have been shown to be decreased in the intestine in Crohn's Disease. Digestive bacterial microflora plays a major role in the pathogenesis of Crohn's disease. Bifidobacteria are regarded as beneficial for the host. The reduction in bifidobacteria is responsible for decreased beta-D-galactosidase activity. Thus oral administration of prebiotic that promotes their growth might have potential therapeutic interest[42].

Irritable Bowel Syndrome

Patients with Irritable Bowel Syndrome most commonly report with symptoms of abdominal pain and altered bowel habit[43] (change in frequency and consistency of stools). Most commonly patients report of abdominal pain which is eased after bowel movement. They can also present with abdominal distention, passing mucus per rectum and experience a feeling of incomplete evacuation.

Irritable Bowel Syndrome is a diagnosis of exclusion, after investigations have ruled out the presence of any bowel disease. The exact etiology of this condition is not known. The basic pathophysiology is alteration in bowel motility and transit[43]. It is also possible that most of the patients with Irritable Bowel Syndrome have an underlying anxiety disorder.

Management of Irritable Bowel Syndrome begins with reassurance and psychological support to the patients. Tranquilizers or anxiolytics may help in patients who are highly apprehensive[43]. Dietary advises to avoid food items that aggravate the symptoms also help. Recently it has been shown that supplementation with Probiotics help in relieving the symptoms of Irritable Bowel Syndrome. This may be due to the fact that the bowel flora may be altered in Irritable Bowel Syndrome.

The fecal microbial population in Irritable Bowel Syndrome has been studied and statistical analysis of the results showed a decrease of Coliforms, Lactobacilli, and, to a lesser extent Bifidobacteria, as compared to control healthy individuals[44].

Restoring the balance of bowel flora by supplementing with Probiotics, the symptoms are minimized, and well being is enhanced. More over studies have suggested that Probiotics are as effective as anti-spasmodic drugs in the alleviation of irritable bowel syndrome[41].

Lactose Intolerance & Recurrent Aphthous Ulcers

Lactose Intolerance is a condition, commonly seen in children, but not common in adults, due to the absence or deficiency of an intestinal enzyme, lactase. Lactase is an enzyme that digests the sugar lactose commonly present in milk and milk products. In the absence of the enzyme lactase, lactose is not digested and its presence in the GI tract lumen results in osmotic diarrhea. The patient has intolerance to milk and milk products and present with abdominal bloating, abdominal cramps and diarrhea, on consuming milk and milk products.

Lactose intolerance could be

1. Congenital - absence or deficiency of enzyme lactase since birth.
2. Acquired - decrease in enzyme lactase due to GI infection or antibiotic use which disrupt the normal bacterial flora that help in formation of lactase in the intestine,

It has been shown that oral supplementation with lactase and / or probiotics can help to mitigate the condition of Lactose Intolerance.

Recurrent Apthous Ulcers

This condition is characterized by appearance of recurrent superficial ulcers or fissures in the mucosa of the mouth. It is a painful condition that has a tendency to recur, each episode lasting from 8-14 days. The exact etiology of this condition is not clear. Stress appears to play a role. These conditions are often treated with B-complex/multivitamin supplementation, Probiotics, and antiseptic or tetracycline mouth-wash.

Diverticular Disease of Colon

Diverticular disease of colon is an acquired disorder. The basic pathology in this condition is the presence of small out pouching of the mucosa of colon forming diverticuli (diverticulosis). This condition is seen predominantly in elderly patients, especially those suffering from constipation. The diverticuli sometimes harbour PPMs, thereby resulting in the overgrowth of PPMs in the diverticuli. This results in an inflammatory process whereby there is inflammation in the surrounding region in the colon resulting in symptoms of abdominal pain and abnormal bowel movements. This condition is known as diverticulitis. Treatment is with antispasmodic agents and high fiber diet. Probiotics help in inhibiting over growth of PPMs and therefore symptoms of diverticulitis.

Post Operative State

In surgery there is an element of stress, intake of altered diet, use of wide spectrum antibiotics, all of which tend to alter the normal bowel flora. In surgeries involving the bowel there is an additional element of trauma to the bowel which contributes additionally in altering the normal bowel flora.

The altered bowel flora gives rise to production of increased flatus (abdominal bloating), and altered bowel movement (constipation). Abdominal discomfort can be relieved postoperatively by use of Probiotics to normalize gut flora.

Probiotic and Immune Health

A number of *in vivo* studies in animals and humans have demonstrated that probiotic bacteria may modulate the immune response and increase antibody titers against enteric infections by bacteria (*S. typhimurium*, *Shigella*, *E. coli*, *Clostridium difficile*, Cholera-toxin) or viruses (rotavirus-induced diarrhea)[26]. Although the term "probiotic" is not limited to health effects concerning the gastrointestinal tract, some studies have examined the effect of probiotics on systemic infections, or virus infections concerning organs other than the gastrointestinal tract, respectively. Lykova et al observed enhanced immunity (T/B-cell immunity, NK-cells, ?-Interferon) in children

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with acute respiratory tract infections consuming a bifidobacteria preparation. A randomized, controlled study demonstrated that long-term consumption of the probiotic strain *Lactobacillus rhamnosus* GG (LGG) was associated with reduced absence from day-care centers due to common gastrointestinal and respiratory tract infections in otherwise healthy children.

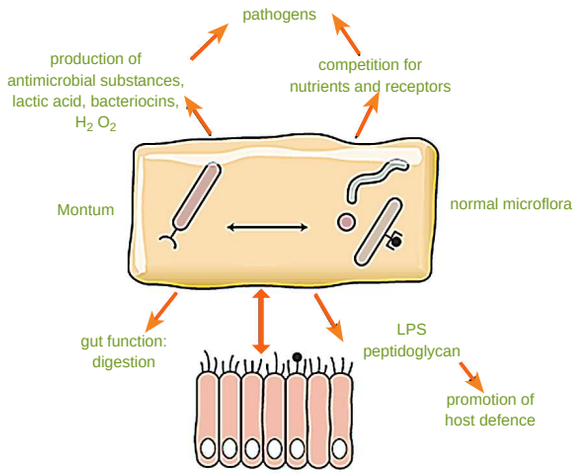
Orally ingested probiotic bacteria may modulate the immune response and increase antibody titers against enteric infections by bacteria or viruses. Even though positive effects of probiotics on respiratory tract infections have been reported, overall only few studies have examined effects on virus infections concerning organs other than the gastrointestinal tract. An study conducted with an aim to investigate whether and how probiotics affect the immune response to a standardized enterovirus challenge (polio) and infections not limited to the gastrointestinal tract in healthy adults. With this aim a method was design. In a randomized, controlled and double-blind study 64 volunteers consumed for 5 weeks chemically acidified clotted milk without bacteria or with 10^{10}/serving *Lactobacillus rhamnosus* GG or *Lactobacillus casei* CRL431 added. In the second week subjects were vaccinated orally against polio 1, 2 and 3. Polio virus neutralizing serum activity, the primary parameter, was determined by the standard neutralization test (WHO) before and three times after vaccination. Polio-specific IgA, IgG and IgM were detected by ELISAs. The result was very encouraging. Probiotics increased poliovirus neutralizing antibody titers (NT) and affected the formation of poliovirus-specific IgA and IgG in serum. The maximum increase after immunization was about 2, 2.2, or 4-fold higher, respectively, for NT, IgG or, IgA, in volunteers consuming probiotics instead of placebo. No consistent difference was noted between bacterial strains. It was concluded that probiotics induce an immunologic response that may provide enhanced systemic protection of cells from virus infections by increasing production of virus neutralizing antibodies[26].

Product Description:

Montum™

Probiotic for Children's Diarrhea

According to WHO, around 4 billion cases of diarrhea occur every year among children. WHO recommends probiotic therapy in children's diarrhea. Probiotic strains restore the balance of protective intestinal microflora and thus help controlling diarrhea. Clinical studies proved that a combination of two well-documented probiotics strains of Lactobacillus paracasei subspecies paracasei 431 and Lactobacillus acidophilus LA5 colonize in the intestine and prevent colonization of opportunistic and pathogenic microorganisms. This, thus, helps controlling children's diarrhea of varying etiologies. Montum™ contains *Lactobacillus paracasei ssp paracasei* and *Lactobacillus acidophilus* probiotics strains that colonize in the intestine and fight against harmful microbes. Montum™ reduces the incidence of diarrhea and also the risk of antibiotic side effects, including diarrhea. It also provides faster recolinization of healthy flora of the intestine after antibiotic treatment. Montum™ is a dietary supplement containing potentially beneficial bacteria. In order to provide health benefits Montum™ has been developed in accordance with the WHO guidelines.



Montum™ prevents colonization of opportunistic and pathogenic microorganisms and fights against them by producing antimicrobial substances: lactic acid, bacteriocins and H2O2.

Montum™ and the normal microflora interact with the host in metabolic activities (Gut function –digestion) and immune function (promote host defense by releasing LPS peptidoglycane).

Ingredients:

Each sachet of Montum™ contains 1.0g (> 3 billion CFU) of a standardized powder consisting of freeze-dried cultures of *Lactobacillus paracasei* subspecies *paracasei and Lactobacillus acidophilus*.

Indications:

- Montum™ is indicated for the treatment, management and prevention of acute and chronic infectious diarrhea of non specific origin.
- Montum™ is also indicated for antibiotic associated diarrhea and travelers' diarrhea.
- Daily use of Montum™ reduces the risk of rotavirus diarrhea and has a protective effect against acute diarrhea and travelers' diarrhea.
- Montum™ can be co-prescribed with ORS, antibiotics, anti-fungal, anti-protozal, or anti-viral products.

Contraindication:
There is no specific contraindication associated with Montum™

Dosage and Administration:

The usual recommended dosage of Montum™ for children and adults is 1-2 sachets a day. Consuming Montum™ everyday for long term helps maintaining balanced

intestinal flora and thus ensures a healthy intestine. If required up to 8 sachets of Montum™ can be recommended. If recommended with an antibiotic, Montum™ should be taken 2-3 hours before or after the anti-biotic administration. Contents of the sachet can be taken directly into the mouth or mixed with some normal water, cold beverage or soft food.

Drug Interaction:

There is no specific drug interaction associated with Montum™

Safety and Side Effects:

Montum™ is safe to use. It contains friendly bacteria that colonize in the intestinal tract and do not enter into the systemic circulation. In clinical studies no noticeable side effects have been noted which may be related to Montum™.

Storage Condition:
Store in a cool dry place. Protect from moisture, freezing, excessive heat and sunlight.

Presentation:
Each box contains 10 Sachets.

Manufactured by: BIOFARMA
Italy

Manufactured for: MAKNSONS
Pakistan

(MTM PI: 0311P)

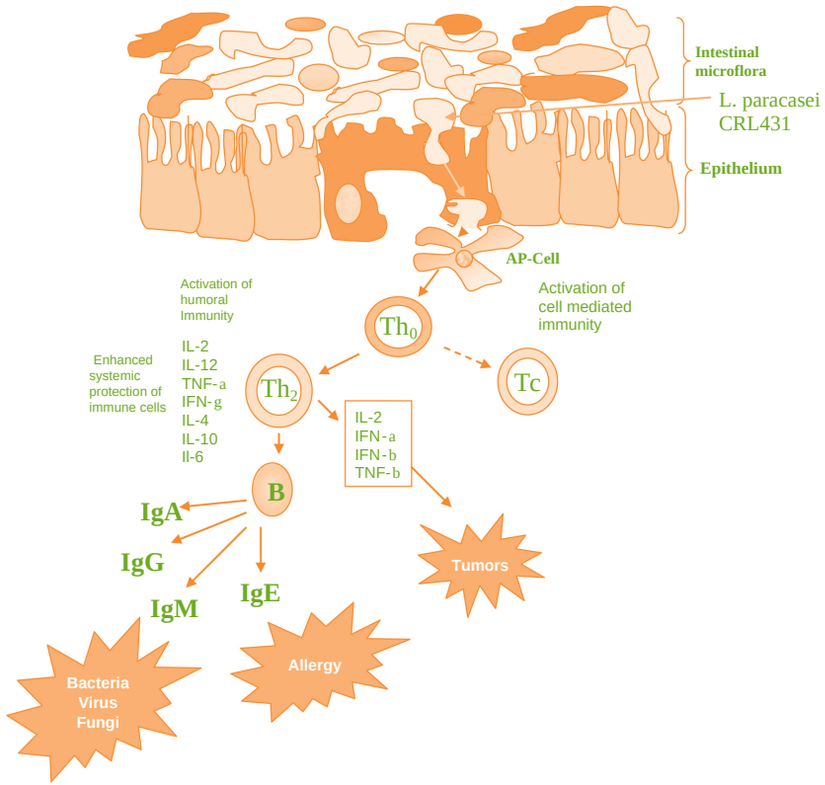
Product Description:

Resiton™

-Probiotic for immune boost

80% of the body's immune cells are located in the gastrointestinal system. Studies revealed that Lactobacillus paracasei subspecies paracasei CRL431 induced an immunologic response that provided enhanced systemic protection of cells from virus infections by increasing the production of virus neutralizing antibodies by 2 to 6 times more. It is equally effective against bacterial and fungal infections. Resiton™ contains Lactobacillus paracasei subspecies paracasei, clinically proven probiotic strain that colonizes in the intestine and strengthens the natural defense of the body, and stimulates the immune system. Resiton™ is a dietary supplement containing potentially beneficial bacteria. In order to provide health benefits Resiton™ has been developed in accordance with the WHO guidelines.

How Resiton™ Boost Immunity[26, 45]



Ingredients:

Each sachet of Resiton™ contains 1.0g (>3 billion CFU) of a standardized powder consisting of freeze-dried cultures of *Lactobacillus paracasei* subspecies *paracasei*.

Indications:

- Resiton™ is recommended for the management, treatment and prevention of infections caused by viruses, bacteria or fungi of non-specific origin.
- Resiton™ can be used in conjunction with vaccines, including Polio vaccine to increase the production of virus neutralizing antibodies.
- Resiton™ is recommended for the prophylaxes of cold and flu symptoms.
- Resiton can be recommended in allergic conditions
- Resiton can be prescribed for atopic eczema
- Resiton can also be recommended in other secondary immunity deficiency symptoms

Contraindication:

There is no specific contraindication for Resiton™

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Dosage and administration:

The usual recommended dosage of Resiton™ for children and adults is 1-2 sachets a day. Consuming Resiton™ everyday for a long term helps maintain balanced intestinal flora and thus ensures good health. If required up to 8 sachets of Resiton™ can be recommended. If recommended with an anti-biotic, Resiton™ should be taken 2-3 hours before or after the anti-biotic administration. The contents of each sachet can be taken directly into the mouth or mixed with some normal water, beverage or semi liquid food.

Drug Interaction:

There is no specific drug interaction associated with Resiton™

Safety and Side Effects:

Resiton™ is safe to use. It contains friendly bacteria that colonize in the intestinal tract and do not enter into the systemic circulation. In clinical studies no noticeable side effects have been noted which may be assumed as Resiton™ related.

Storage Condition:

Store in a cool dry place. Protect from moisture, freezing, excessive heat and sunlight.

Presentation:

Each box contains 10 sachets.

Manufactured by:
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WHO Guidelines for Selection of Probiotics

Food and Agriculture Organization of United Nation (FAO) and World Health Organization (WHO) guidelines for selection of Probiotics[27, 28]:

1. Genetically identified strain.
2. Shelf life viability
3. Survivability in the gut

Montum™ and Resiton™ provide what WHO guides...in bacteriotherapy

1. Since probiotic properties are strain related, the strain identification (genetic typing) should be performed[27, 28].

The strains in Montum™ and Resiton™ using DNA fingerprinting and RNA sequence analysis, is genetically identified bacteriotherapy thus provides the genetic stabilized probiotic strains of:

- Lactobacillus paracasei ssp. paracasei
- Lactobacillus acidophilus

Therefore, Montum™ and Resiton™ ensure the same species with same efficacy during production, batch after batch and year after year.

2. Shelf life viability— to ensure that any given culture maintains the beneficial properties; the viability and probiotic activity must be maintained throughout storage of product containing probiotic[27, 28].

Montum™ and Resiton™ are genetically identified bacteriotherapy of Lactobacillus paracasei ssp. paracasei and Lactobacillus acidophilus have been cultured, lyophilized and packed in special environment—temperature controlled, humidity controlled and oxygen controlled.

Therefore, it prevents loss of bacteria due to temperature, humidity and thus assuring shelf life viability throughout 24 months.

3. Survivability of probiotics throughout the gut—in order to survive passage through the stomach and exposure to bile, the probiotic product should be consumed in a vehicle that allows them to survive the GI passage[27, 28].

Montum™ and Resiton™ are genetically identified bacteriotherapy of Lactobacillus paracasei ssp. paracasei and Lactobacillus acidophilus provided in unique polysaccharide matrix technology— in stomach polysaccharide matrix forms gel in the acidic environment of stomach, thus preventing viable bacterial count loss. This gel then dissolves at pH 6.4 in duodenum and bacteria released at the desired site of action.

Therefore, there is no loss of Montum™ and Resiton™ strains in stomach and bile and thus ensure colonization in the gut.

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