

Dr. MS Reddy's Multiple Mixed Strain Probiotic Therapy

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ABSTRACT

This research article highlights the latest research developments and discoveries with regard to therapeutic uses of Probiotics. Although Probiotics are very popular as the nutritional supplements, the medical field has not fully accepted and understood their therapeutic or healthful benefits. Part of the reason is due to lack of full understanding of the science behind the Probiotics. The recent major breakthrough discovery of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy to treat the hospital associated lethal infections due to Clostridium difficile (C. diff) and Methicillin Resistant Staphylococcus aureus (MRSA) arose a tremendous interest in the field of medicine around the world. This research article is written in a simplified form to explicitly explain about the Probiotics, Multiple Mixed Strain Probiotic Therapy, and the rationale behind such biologically based therapeutics. In addition, the use of Probiotic therapy as a complementary therapy to suppress cancer, integration of Multiple Mixed Strain Probiotics with alternative medicine Ayurveda (Proyurveda) as a whole medical system, and finally the integrated medical approach of using Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy in combination with or without specific antibiotics to cure the terminally ill patients with nosocomial infections has also been thoroughly researched, reviewed and discussed. This article also describes in detail the etiology and pathophysiology of cancer cell proliferation at molecular level. This will enable the reader to partially understand how and where Probiotics can block the cancer cell growth. In addition, detailed explanations are given regarding the legalities and governmental divisions involved in regulating the complementary alternative medicine and integrated health.

INTRODUCTION

Before getting into details of this article, it is imperative to define and explain the meanings of the terminology used. What are Probiotics? What is Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy? What is Complementary and Alternative Medicine (CAM)? What is Integrated Medicine? What is National Center for Complementary Medicine (NCCAM)? What is the National Center for Complementary and Integrative Health (NCCIH)? What is the Office of Alternative Medicine (OAM)? Which category does Probiotics or Probiotic Therapy fall into according to the NCCIH or NCCAM? The following answers are given in a simplified fashion to avoid the confusion, not only in the minds of the consumers but also the practicing physicians and all other medical practitioners including dieticians, naturopaths, chiropractors, and nutritionists etc.

What are Probiotics? According to the Fuller^[1] and also according to the World Health Organization (WHO), the Probiotics are defined as the live microbial supplements that bestow beneficial effects on the host by improving the intestinal microbial balance. Reddy and Reddy^[2] interpreted this, stating that any microorganism, which is nonpathogenic but has significant beneficial effect to improve human/animal health, by restoring the eco-balance in the gastrointestinal tract can be categorized as Probiotic. The term Probiotic is derived from pro meaning "for" and bios meaning "life", which is completely opposite to the term antibiotic (anti-meaning "against" and bios meaning "life").

What is Dr. M.S. Reddy's "Multiple Mixed Strain Probiotic Therapy"? Generally physicians recommend Probiotics (single strain) for the patients to replenish the gastrointestinal microflora, after a long course of antibiotic therapy. Some practitioners

also recommend Probiotics while the patient is undergoing antibiotic treatment. They are not taking into account, whether the Probiotic organisms taken randomly by their patients (either single strain or multiple strains) are implanting in the GI tract or not? The latest false belief in the medical field is that the freeze dried Probiotics ingested (at a very high concentration, irrespective of whether they are single strains or multiple strains) will cure the intestinal infections faster. They have no knowledge on how those Probiotics were prepared and how well they survive in the gastrointestinal tract? Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy is defined as a biologically based therapy comprising several naturally antibiotic and antimicrobial agent resistant strains of Probiotics belonging to different genera and species, along with their growth end products and bacteriocins, to treat the nosocomial or hospital acquired infections. The success of Dr. M.S. Reddy Multiple Mixed Strain Probiotic Therapy is predominantly due to the preformed Nano particles produced by the Probiotic strains in addition to the live Probiotic cultures. The size of individual Probiotic bacterial cell will be in the range of 100 to 200 nm. However when they are grown in a specific nutrient media, these Probiotic cultures produce exo enzymes which will significantly reduce the size of the nutrients (including mineral complexes) to smaller than 100 nanometers, so that they can be transported into the bacterial cell. During this process, due to the enzyme hydrolysis, significant amount of active Nano particles will be generated (10 to 90 nm size) and majority of them will be left in the growth medium. In addition, the Probiotic cultures, by utilizing the hydrolyzed Nano nutrients, will further synthesize (intracellularly) several other Nano compounds which will be excreted into the growth medium. Some of these Probiotic bacteria synthesized Nano particles are bacteriocins. We can safely assume that these synthesized Nano particles should be less than 50 nanometers in size because the bacteria synthesizing them are only 100 to 150 nm in size (to facilitate transport of such particles, out of the cell, through membrane transport system). Consequently the entire growth medium, after fermentation by Probiotic cultures will have significant amount of charged Nano particles (10 to 100 nm in size). In addition, some of the organic acids produced by the Probiotic bacteria will react and decrease the size of the metal salts present in the growth medium to 100 nanometers or less, to transport such metal ions into the cell through membranes. The left over soluble Nano metal ions will be present in the culture medium. Thus the entire growth medium, after the growth of the Probiotics, will have several Nano particles ranging from 10 to 100 nanometers. These Nano particles are small, highly charged, have larger surface area, and act as potent inhibitors against several pathogenic bacteria. To sum it up, in order to classify any technology as a Nano technology, the particle sizes should be less than 100 nanometers. According to this definition, the Probiotic bacterial culture with a size of 100 to 200 nanometer cannot be considered or categorized as Nano technology product. However, the majority of the bacterial growth end products (either left in the medium after Probiotic bacterial enzyme hydrolysis or synthesized and excreted into the growth medium by Probiotics) should qualify as Nano technology products.

Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy is a combination of Nano and microbial technology. It is the most marvelous concept in that 100 to 150 nanometer size bacteria can be constantly producing smaller Nano particles. It has been proven by Dr. M.S. Reddy that the hospital acquired infections due to C. diff and MRSA responded better when Multiple Mixed Strain Probiotics were administered along with their growth end products including the bacteriocins (Nano particles size of less than 100 nanometers). When a fully grown Probiotic culture is subjected to centrifugation, to concentrate the bacterial cells only, the supernatant will have all the Nano particles which are smaller than 100 nm. At the same token the concentrated bacterial culture will have larger particle size (greater than 100 nm). Such a concentrated Probiotic culture cannot be categorized as Nano technology product. This is the reason why the concentrated freeze dried Probiotic cultures could not inhibit C. diff and MRSA-hospital associated infections. This explains why Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy is highly successful to treat or prevent the nosocomial infections because of the presence of abnormal number of Nano particles of size smaller than 100 nm along with the active Probiotic bacteria^[2]. Thus, Dr. M.S. Reddy's Multiple Mixed Strain Probiotics Therapy encompassing several strains of Probiotics belonging to different genera and species along with their Nano particle size (<100 nm) growth end products including bacteriocins, frozen using liquid nitrogen cryogenic technology, should technically qualify to be called Nano technology therapy. Whereas, the Probiotic preparation can be classified as Nano technology product. We can also categorize the Probiotic bacterial cells as continuous Nano particle (less than 100 nm size) generators.

The latest discovery of Dr. M.S. Reddy's "Multiple Mixed Strain Probiotic Therapy" has proved beyond doubt that the liquid nitrogen frozen Multiple Mixed Strain Probiotics along with their bacteriocins and their other prior growth end products, have significantly greater effect in curing the hospital acquired infections than the higher bacterial cell count lyophilized Probiotics^[2]. This novel discovery which took over 47 years worth of basic and applied research by Dr. M.S. Reddy was proven with clinical trials. The discovery clearly revealed that the use of naturally antibiotic resistant Multiple Mixed Strains Probiotics belong to different genera and species is the best way to cure the nosocomial infections, which are infecting over 6,000,000 people, and killing over 100,000 innocent people around the world.

Another novel aspect of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy is that the physiological condition of the Probiotics and the way they were grown and prepared has significant effect to prevent or cure the nosocomial infections. The Multiple Mixed Strain Probiotics belonging to different genera and species should be paired only after studying their associative growth relationships, for their compatibility, using direct differential plating techniques and individual strain specific bacteriophages. This novel discovery of Dr. M.S. Reddy has uncovered the flaws in the previous Probiotic therapies, which were ineffective. These are presented with explicit details in the publication entitled "development of Multiple Mixed Strain Probiotics

for “Probiotic therapy” under clinical conditions, to prevent or cure the deadly hospital acquired infections due to *Clostridium difficile* (*C. diff*) and methicillin resistant *Staphylococcus aureus* (MRSA),” in the International Journal of Pharmaceutical Sciences and Nano Technology ^[3]. This breakthrough discovery of Dr. M.S. Reddy was awarded the first place in the pharmaceutical arena in 2016 because of its novelty to cure the lethal nosocomial infections and also due to the thoroughness of the research methodology and presentation.

What is Complementary and Alternative medicine (CAM)? CAM is a category of medicine that includes variety of treatment approaches which fall outside the scope of conventional medicine. In this connection, the conventional medicine can be defined as the widely practiced modern traditional western therapy or medicine. If we dissect it further, the CAM can be differentiated into two categories i.e. one is complementary medicine and the other is alternative medicine. The complementary medicine refers to the healing practices and products that work in conjunction with the modern traditional western or allopathic medicine. Whereas, the alternative medicine refers to the practice or medicine, which is not used in conjunction with or as a complement with the traditional medicine. Rather it is used as a substitute for the traditional therapy. Yet, both the complementary medicine and alternative medicine are clumped together, without differentiation into CAM.

What is the Integrated Medicine? Integrated medicine combines the best out of complementary medicine, alternative medicine and the traditional medicine to cure the ailments or diseases. In our opinion, the future is going to be the practice of integrated medicine. What is National Center for Complementary and alternative medicine (NCCAM)? It is a division of National Institute of Health, which governs and defines the categories of the complementary and alternative medicine. The NCCAM recognizes the following four main categories of complementary and alternative medicine.

Mind-body medicine: Which deals with the treatments focused on how our mental and emotional status interacts and affects the body’s ability to function (a classical example is meditation).

Whole medical system: Which originated and practiced for over thousands of years in the Eastern culture (examples are Chinese medicine and Indian Ayurveda) and in the Western culture (homeopathy and naturopathy);

Manipulative and body base practices: which deals with the use of energy fields for promoting healing (magnetic therapy);

Biologically based practices: Which deals with herbs, nutrition, vitamins, dietary supplements, and herbal medicine to promote healing and thus improve health.

What is NCCIH? It is an abbreviation for the National Center for Complementary and Integrative Health, which is same as NCCAM (National Center for Complementary and Alternative Medicine) and OAM (Office of Alternative Medicine). Technically NCCIH, NCCAM, and OAM are all same except the names have been changed over the years. The latest official name (year 2013), which is approved and signed by US President Obama is the National Center for Complementary and Integrative Health (NCCIH). Consequently these names are used interchangeably in this communication, although they all refer to the same department. The question here is, does all these alternative medical treatments considered as legal compliments or substitutes to the traditional western medicine (allopathic medicine)? The answer depends on how they are intended to be used, and which category of NCCAM they come under.

Which one of the above categories of National Center for Complementary and Alternative Medicine does Probiotics and Probiotic therapy belong? Undoubtedly it should be placed under the biologically based complementary and alternative medicine. According to the broad classification of the animal and plant kingdom, Probiotics should come under the plant kingdom. Based on the size of the microorganisms, the mold is the largest followed by yeast, bacteria, and the smallest being virus. The credit of the use of beneficial bacterial cultures as therapeutic agents goes to Nobel Laureate Metchnikoff ^[4]. He has mentioned in his 1907 Nobel lecture that human life can be prolonged if putrefactive bacteria can be controlled in the human gastrointestinal tract with the use of certain nonpathogenic beneficial lactic acid bacteria.

According to the survey conducted by The National Center for Complementary and Alternative Medicine (NCCAM), 40 percent of the adults and 12 percent of the children in the United States of America use and rely on some form of complementary and alternative medicine.

The most common and fatal diseases affecting human beings in the 21st century are as follows:

1. Coronary heart diseases due to arteriosclerosis, hypercholesteremia, and hypertension;
2. Cancer affecting digestive system etc.;
3. Acquired immune deficiency syndrome;
4. Less fatal, but common diseases include stress syndrome, osteoporosis, diabetes, arthritis, premature aging, intestinal diverticulosis, and excess obesity etc.;
5. The hospital acquired infections (nosocomial) due to *Clostridium difficile* (*C. diff*) and Methicillin Resistant *Staphylococcus aureus* (MRSA) etc. affecting over 6 million people annually with over 100,000 deaths.

The allopathic (traditional) practitioners have been treating these diseases with the available pharmaceuticals. If you read the instructions given with each pharmaceutical drug, the list of unwanted side effects are longer than its curative properties. Unfortunately, the side effects of the modern pharmaceuticals are accountable for the 30% of the diseases and the physicians are

forced to treat the symptoms rather than the core cause of the disease due to laws and regulations imposed by the government, legal profession, and the community.

Some alternative medicines, unlike the traditional allopathic medicine treat the whole body in order to alleviate disease. This is called holistic medicine approach. According to Gopal, Americans spent 24 billion dollars out of their pocket in the year 2002 seeking complementary care [5]. This amount has been steadily increasing (perhaps over 200 billion dollars per annum now) and continues to do so because the average American is not content with the care he is receiving from his physician. Probiotic therapy, although is practiced by allopathic practitioners, it is one form of complementary and alternative medicine that is gaining popularity in this decade. In this context, we would like to discuss the details of Probiotics in a simplified scientific manner since the microbiology is not a major subject taught in the medical schools. This article on Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy (complementary and alternative medicine) will be discussed under six different subheadings:

1. Multiple Mixed Strain Probiotics as therapeutic agents;
2. Associative growth relationships of Multiple Mixed Strain Probiotics and other Gastrointestinal microflora in relation to health and disease;
3. Additional benefits of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy, besides preventing or curing the hospital acquired infections.
4. Nano technology based "Multiple Mixed Strain Probiotic Therapy" for cancer suppression;
5. Synergy of Multiple Mixed Strain Probiotics and whole medical system Ayurveda (Proyurveda) - a new complementary and alternative medicine approach;
6. Synergy of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy and allopathic antibiotic therapy-a new integrated medicine approach.

Multiple Mixed Strain Probiotics as Therapeutic Agents

Generally bacteria are associated with a bad connotation of disease production. However, not all bacteria are disease producing i.e. pathogenic. On the contrary, Probiotics are bacteria or micro-organisms that are beneficial to the health of an individual. They are essentially an opposite of antibiotics, which are inhibitory to other bacteria, (including Probiotic bacteria), and the word Probiotic is derived from two Greek words "Pro" and "Bios" meaning "for life". Probiotics are predominately lactic acid producing bacteria. Probiotics are widely present in nature and serve many beneficial functions. They are non-pathogenic, do not produce toxins, and are considered natural and organic. According to the code of Federal Regulations, the U.S. food and Drug Administration has granted them GRAS (generally regarded as safe) status [6]. They can be used in food preparations safely and are used extensively in the manufacture of dairy products. They are also used to improve the health of pets and large animals and thus they indirectly reduce the Zoonotic diseases. One of the earliest discoveries that bacteria can improve human health was by Metchnikoff [4]. Since then, there have been favorable reports about probiotics' utility, including, their innate ability to reduce colon cancer in humans. Also, Russian scientists have reported that daily ingestion of *Lactobacillus bulgaricus* and *Streptococcus thermophilus* bacteria can improve human longevity. Several American scientists have reported that the level of blood cholesterol in humans can be reduced by orally ingesting lactobacillus acidophilus. These Probiotic organisms are believed to exhibit therapeutic effects because of their innate ability to produce lactic acid and other substances that are inhibitory to harmful bacteria. These Probiotic organisms naturally reside in the human intestinal tract, at receptor sites in the ileum, where they create a mildly acidic environment, which is not favorable for the growth and viability of pathogenic microorganisms including viruses. Fuller in 1989 redefined Probiotics as live microbial supplements that bestow beneficial effects on the host by improving the intestinal Microbial balance [1].

These beneficial bacteria have an antagonistic effect on pathogenic bacteria, while antibiotics have an antagonistic effect on probiotics. Consequently, when a person is treated with antibiotics, the probiotics residing in the gastrointestinal tract can be inhibited, adding another complexity to the illness. To counteract this problem, some physicians prescribe the use of probiotics following the use of antibiotics in order to restore healthy gastrointestinal flora. Some drug manufactures combine probiotics and antibiotics, although such combinations may be poorly advised (unless they are thoroughly researched) due to the inherent conflicting purposes of the two types. Considerable judgment should be exercised by the physician to prescribe a proper Probiotic by taking into account its physiological and biochemical properties.

Since the Probiotics are natural inhabitants of the human gastro intestinal tract, they have to be maintained in proper balance to bestow good health. The modern foods, with inclusion of preservatives and dyes etc. are not beneficial to the gastro intestinal flora, especially Probiotics. Consequently, in order to maintain and ensure proper gastro intestinal eco flora (Probiotics and the associated flora), continuous or periodic supplementation of proper Probiotic is a must. If the micro flora in the human gastro intestinal tract is eliminated, human being cannot survive.

The following are some of the scientifically proven beneficial effects of Probiotics:

1. They have immune modulatory effect in the human body thus improving the immune system, which is vital for disease prevention as well as cure.
2. Probiotics reduce the incidence of cancer, through reduction of mutagenesis. This is accomplished through competitive inhibition of the non-beneficial micro flora, which produces enzymes that will convert procarcinogens to carcinogens^[7].
3. Probiotics decrease the cholesterol in the body through imbibition, utilization, and through hydrolysis of bile salts^[8].
4. They improve the absorption of calcium in the G.I. tract and also contributes to the reduction of hypertension and Osteoporosis^[9].
5. They decrease the Lactose malabsorption and intestinal discomfort and thus improve digestion.
6. Probiotics improve the intestinal peristalsis and thus reduce the intestinal diverticulosis, constipation etc.
7. Probiotics decrease the bacterial infections in the gastrointestinal tract through nutritional competency and through competitive exclusion of adhesion sites for the pathogenic bacteria.
8. They decrease the virulence of intestinal pathogenic bacteria as well as virus by creating unfavorable pH conditions for the growth and proliferation of these pathogenic organisms.
9. Probiotics synthesize essential vitamins in the G.I. tract. These vitamins serve as co-factors and are essential for enzymatic activities.
10. They improve the digestion of food in the G.I. tract with the aid of their Enzymes (protease, peptidases, amino peptidases, and B-galactosidase etc.) and thus reduce food intolerance and allergies.
11. They reduce the re-infection in bacterial vaginosis.
12. Probiotics increase longevity. It has been reported that Russians who had been routinely consuming Probiotics lived up to 140 years.
13. Probiotics inactivate and also decrease the absorption of the toxins in the gastrointestinal tract.
14. Multiple mixed strain Probiotics inhibit the growth and proliferation of MRSA and *C. diff* infections.
15. Multiple Mixed Strain Probiotics have been proven both to cure as well as treat the hospital acquired (nosocomial) infections^[2].
16. Although it has to be proven through some more research, Probiotics have been attributed to reduce stress through production of certain neurotransmitters.
17. Probiotics produce bacteriocins which are highly effective in inhibiting pathogenic bacteria such as listeria, salmonella and staphylococcus in the gastrointestinal tract.

We have introduced and coined the term “Dr. M.S. Reddy’s Multiple Mixed Strain Probiotic Therapy”, which is unlike regular Probiotic microbial therapy involves selected antibiotic and antimicrobial agent resistant beneficial microbial organisms (Probiotics) belonging to different genera and species as preventative or curative therapeutic agents to control the hospital acquired infections. This discovery is considered novel and can be used as a complementary therapy along with specific antibiotics to protect the patients in terminal illness cases. Some of the therapeutic properties of the Probiotics are gene controlled. These therapeutic genes could either be chromosomal or extra chromosomal (plasmids). The fact that some of the extra chromosomal genes have such therapeutic properties, by coding for specific compound, makes you think that with evolution, these micro-organisms (Probiotics) built these genes (plasmids) to safe guard themselves and indirectly to bestow good health to human beings. It could have taken several years (perhaps over a million years) for bacteria to build such extra chromosomal genes, which will divide and express autonomously. We would like to refer to this as nature’s genetic engineering, in response to the challenges encountered in the process of evolution.

Since the efficacy of Probiotic therapy is linked to the proper Probiotic organisms and also their physiological condition at the time of oral administration, the following selection criteria should be followed by the physician to select desired Probiotic organisms for their maximum therapeutic efficiency: they must be of human origin, since they are highly species specific; they must have high acid and bile stability to survive low pH conditions of stomach and bile salts in the deodinum; they must have adhesion property to stick and colonize on intestinal mucosa to exert immune modulation and competitive exclusion of pathogens etc.; they must be safe and proven clinically that they are non-pathogenic and non-pyrogenic; they must be clinically validated to demonstrate their healthful effects; and finally they must be produced or manufactured by taking into effect the strain stability (plasmid retention), phage resistance, freeze drying or lyophilization survival, their viability upon storage, and free from contamination. Recently it has been discovered that the freeze dried Probiotics are not very effective compared to the liquid nitrogen frozen Probiotics to prevent or cure the hospital acquired infections (nosocomial) due to methicillin resistant *Staphylococcus aureus* (MRSA) and *Clostridium*

difficile (*C. diff*)^[3]. It further illustrates the importance of the suitable manufacturing procedure to produce Probiotic cultures, to maximize their therapeutic potential.

Since some of the therapeutic effects of Probiotics are linked to highly unstable extra-chromosomal plasmid genes, it is extremely important that they must be produced in only highly technical scientific laboratories under the supervision of trained microbiologists and biotechnologists. Several U.S. Gastroenterologists are great believers of Multiple Mixed Strain Probiotic Therapy and have seen dramatic results in their patients. In their experience, the specific strains and viability of such organisms (Probiotics) is the key to obtain faster results in Probiotic therapy. Even the most conservative Gastroenterologists in U.K., Europe and other countries around the world have reported similar results. The most common question asked by several gastroenterologists is as follows: how do I know which Probiotic is good for my patients? Is there a procedure or protocol I can use to select the best Probiotic? We hope, this article is of great help to physicians to answer the above question, so that they will have more confidence to treat their patients using scientifically proven selective Probiotics.

Associative growth relationships of Multiple Mixed Strain Probiotics and Other Gastrointestinal Microflora Relation to Health and Disease

Let us review the microbiological composition of the human gastro-intestinal tract to better understand the role of Probiotics in conjunction with the other commensalistic microbiota. The human gastro intestinal tract harbors a variety of microorganisms, which we can conveniently refer to as gastrointestinal microbial Eco-system. The human stomach content i.e. gastric juice will have only 10 to 100 microorganisms per milliliter or gram. The predominant species of bacteria in the stomach are *Streptococcus*, *Staphylococcus*, and *Lactobacillus* etc. Most of the bacteria are destroyed or inactivated in the stomach due to its low pH.

In the upper portion of the small intestine i.e. duodenum, the bacterial population in the contents range from 1000, to 10,000 per/ml. The bacterial population increases as we go down to the distal part of the ileum to 1,000,000 to 10,000,000 per/ml of the contents^[10]. Whereas, the colon will have 100 billion to 1 trillion bacteria per/ml of the contents^[11]. In the entire colon, the total number of bacteria will be roughly 100 trillion or over. The total number of Eukaryotic cells (cells with definite nucleus) in the human being is roughly 10 trillion. The colon bacterial cell population exceeds ten times more than the total host cell population. According to the literature, the microbial metabolic activity of total colon bacteria is equivalent to that of liver.

The predominant growth substrates for gut bacteria are of dietary origin, consisting of foods that cannot be absorbed in the upper GI tract (these include resistant starches, dietary fibers, sugars like oligosaccharides, proteins, some specific peptides, and amino-acids).

The principal end products of bacterial fermentation in the colon are short chain fatty acids (SCFA) like acetic, Propionic, and butyric. The others include ethanol, lactate, Succinate, formate, valerate and caproate. Branched chain fatty acids such as isobutyric, 2-methyl butyrate and isovalerate are also formed from the fermentation of the amino acids. Most of the SCFA from bacterial fermentation are absorbed and metabolized contributing to the host energy gain^[11].

The bacterial population in the gut has been adapted through associative growth relationships. There are many factors that interfere with this normal dynamic balance leading to destruction of the entire Eco system and the naturally existing beneficial balance among gut microorganisms. Various factors contribute to this Eco imbalance which include, intake of chemicals and antibiotics etc. Under these adverse conditions, the microflora that are beneficial or health promoters are replaced by pathogenic bacteria like Clostridia, staphylococci, sulphate reducers and certain bacteroid species etc. These pathogenic bacteria predispose the host to a number of clinical disorders including cancer of colon, inflammatory disease, and ulcerative colitis etc. In addition, this shift in eco balance will make the host more vulnerable to infections by transient enteropathogens like *Salmonella*, *Campylobacter*, *Escherichia coli* and *Listeria* etc.

The rapid changes in lifestyles have contributed to this obliteration. Thus, maintenance of balanced beneficial intestinal microflora consisting of *Lactobacillus*, *Bifidobacterium*, etc. *Propionibacterium* and other lactic acid producing bacteria etc. are essential. It raises a very important issue like validity of antibiotic therapy, considering the fatal infections due to some hospital acquired antibiotic resistant bacterial strains such as *Clostridium difficile* (*C. diff*), Methicillin resistant *Staphylococcus aureus* (MRSA), and *Pseudomonas aeruginosa* etc. If high concentration of viable Probiotics is maintained in the G.I. tract, even the antibiotic resistant pathogens can be suppressed.

In our opinion, the microbial Eco-system of the small intestine and colon dictate the overall health and wellbeing of the human. However, the status and normal eco balance of micro-flora is completely ignored and no modern therapy has taken this into account. There are roughly 500 different bacterial species in the gut and they are Saccharolytic, deriving their energy by digesting or degrading the plant cell material. The most common intestinal bacteria are *Bacteroides*, *Bifidobacterium*, *Fusobacterium*, *Clostridium*, *Peptococcus*, *Peptostreptococcus*, and *Eubacterium*. Other genera of bacteria are present to lesser extent. These intestinal bacteria are present in the Lumen, on the surface of the epithelial cells and in the crypts of Lieburkuhn. The metabolic activity of single cell bacterium is significantly higher than the Eucaryotic cell because of its larger surface area. If the human gastro enteric eco balance is altered and wrong kind of pathogenic bacteria dominated the flora, the human health will be in great

danger. This is exactly what is happening with the lethal Nosocomial infections. The best answer to eliminate or reduce these problems is through constant maintenance of large number of Multiple Mixed Strain Probiotics in the gastrointestinal tract.

Additional benefits of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy, besides Preventing or Curing the Hospital Acquired Infections

1. **Immunomodulation:** This is very important and vital activity induced by Probiotics. The immune stimulating activity is attributed to their bacterial cell envelope constituents such as Peptidoglycan. Results of various investigators indicate that Probiotics stimulate the production of antibodies, enhance the systemic activity of Macrophages, increase interferon levels and the number of killer cells. In order to influence the immune system, Probiotics have to activate the lymphoid cells of the gut associated lymphoid tissue, which are diffusely distributed among the epithelial cells and populate the Lamina Propria and submucos^[12]. The immunogenic properties of Probiotic bacteria such as propionic acid bacterium do not reside in extra cellular slime^[13]. Apparently, the cell walls of these bacteria have antigenic properties, rather than their extra cellular slime, further proving the immune modulating effect of Probiotics is a function of their cell wall composition and thus can vary among Probiotics. It is worthwhile to mention that even the dead cells of the Probiotics to some extent can exhibit the immunomodulatory effect because of their cell wall composition.

2. **Reduction of intestinal infections:** These infections are mostly caused by the pathogenic bacteria. Under normal circumstances such pathogenic bacteria are suppressed by the beneficial microflora of the gastrointestinal tract. A group of such beneficial microflora is Probiotics, which have innate ability to out compete the growth of such pathogenic bacteria. It has been documented that the antibiotic induced diarrhea has been successfully controlled by probiotics. *Lactobacillus and Bifidobacterium* have been used in children and adults for therapy of intestinal infections. The mechanism of action of Probiotics to reduce intestinal infections is through competition for gut nutrients, secretion of anti-microbial substances, reduction of pH through short chain fatty acid formation, blockage of adhesion sites for pathogens, blockage of toxin receptor sites, immune stimulation, and attenuation of virulence of unwanted bacteria and virus etc.

3. **Reduction of lactose intolerance:** The lactose sugar is a disaccharide comprising a combination of two simple sugars – glucose and galactose. Lactose sugar can only be hydrolyzed with the aid of enzyme lactase or beta galactosidase. The epithelial cells of the ileum produce the lactase enzyme to hydrolyze the lactose to glucose and galactose. In certain individuals this enzyme lactase is not produced or produced at a miniscule quantity. Since the lactose molecule is not broken down due to lack of the enzyme, such individuals develop the lactose intolerance manifested by symptoms such as excess gas production, intestinal irritation, diarrhea etc. Half of the world population is unable to utilize lactose. Lactose sugar is only present in milk, which is an essential nutrient. The lactose malabsorption can be corrected by probiotics^[14]. The lactic acid producing Probiotics also produce lactase or Beta galactosidase enzyme. In most of the instances the production of lactase enzyme in the Probiotic bacterium is controlled genetically by the extrachromosomal genes or plasmids. When such Probiotic cultures are implanted in the ileum, even if a person is lacking the lactase enzyme, the Probiotic produced lactase enzyme will assist in hydrolyzing the lactose sugar, thus relieving either fully or partially from lactose intolerance. The lactose malabsorption or intolerance is predominantly observed in the older population due to the decreased production of lactase enzyme. Thus the Multiple Mixed Strain Probiotics must be periodically or routinely administered to older population. It has been reported that level of Probiotics decrease as people age due to several physiological factors^[2].

4. **Reduction of coronary heart disease:** Although it sounds unrealistic and questionable regarding how the Probiotic bacteria can assist in reducing the heart diseases, in reality, they do have the intrinsic capacity to improve the cardiac health. The fact that Probiotic supplementation inhibits cholesterol concentrations in the blood and increases the excretion of cholesterol in feces has been well documented^[8,15]. Cholesterol absorption is interfered from the gut partly due to assimilation of cholesterol by Probiotic organisms. In addition, Probiotics (*Bifidobacterium longum*) deconjugate the bile salts with the aid of bile salt hydrolase and thus increases the excretion of free bile salts in the feces. It has a potential to reduce serum cholesterol because the replacement of bile salts would require the utilization of some cholesterol in the body. Thus, the resultant Hypocholesterolemia reduces the incidence of coronary heart disease. In addition, Probiotics improve the absorption of calcium from GI tract by lowering or maintaining the proper pH. Calcium deficiency is one of the prime factors for Hypertension. In addition, Probiotics also inhibit microorganisms, which will convert nontoxic amino acids to toxic amines. Thus the reduction of Hypertension inducing amines (histamine, tyramine etc.) in GI tract due to Probiotics can also be a factor for the reduction of coronary heart diseases.

5. **Suppression of *Helicobacter pylori*:** *Helicobacter pylori* is a gram-negative spiral shaped bacterial pathogen that colonizes in the area between the mucous layers of stomach and gastric epithelium. It avoids low pH of stomach by establishing neutralized micro niches through generation of ammonia from urea via its surface bound Urease enzyme. It is now recognized as the causative agent for chronic gastritis, which is a major factor for causing gastric and duodenal ulcers, gastric atrophy and gastric cancer^[16,17]. Gastric Carcinoma is the most common cause of cancer in developing countries and the second most common cause of cancer mortality worldwide. The International agency for research on cancer (1994) has classified *H. Pylori* as Group I Carcinogen, a definite cause of Gastric Adenocarcinoma in humans. This is the first pathogenic bacterium to be classified as such. Published research data indicate that even *H. Pylori* can be inactivated or suppressed with the use of proper Probiotics. The

possible mechanism of inhibition may be through the activity of bacteriocins and other non-specific peptides and other undefined inhibitory substances produced by Probiotics ^[3].

6. **Reduction of cancer:** It has been well documented that several strains of Probiotics play significant role in suppressing the lethal colon cancers. Although it is difficult to prove in vivo, Probiotics undoubtedly assist in reducing some of etiological factors involved in cancer cell proliferation. The dietary intake of cultures of *Bifidobacterium longum* has significantly suppressed the development of Azoxy methane induced aberrant cryptic foci (ACF) formation in colon. Later recently the same group of scientists elucidated the ability of the Probiotic strain to inhibit incidence of colon tumors ^[18]. The fecal (bacterial) enzymes by reacting with some substrates can produce Carcinogens or tumor promoters in the gut. Please refer to review by McIntosh ^[19]. Tumor inhibition by Probiotics may proceed through diverse mechanism. The probable mechanisms are: Immunostimulation, Antimutagenicity, and modulation of intestinal bacterial enzymes that convert Procarcinogens to Carcinogens through microbial competitive inhibition. More details are presented in different section in this article.

Nanotechnology based “Multiple Mixed Strain Probiotic Therapy” for Cancer Suppression

In this section of the research review, we will be discussing about the Etiology of cancer including the current statistics mechanism of cancer cell propagation, mutagen and the mechanism of induction of mutagenesis, and finally the effect of Probiotics on reduction of cancer through suppression some of the non-beneficial microflora which produce enzymes capable of converting procarcinogens to carcinogens. Specific details are also given on how such fecal microbial enzymes convert procarcinogens to carcinogens. We have outlined the genesis of cancer in a simplified scientific fashion so that the reader can appreciate how Probiotics can minimize or prevent cancer by reducing the conversion of procarcinogens to carcinogens.

Some of the non-Probiotic type gastrointestinal flora will convert procarcinogens to carcinogens. Some of the end products of the digestion are procarcinogenic. For example the end products of digestion of beef and other meat products may be more procarcinogenic than vegetables. The procarcinogenic material may not cause cancer. However, if it is acted upon by certain microbial enzymes in the G.I. tract, it will be converted to carcinogen. Probiotics, by their innate nature, suppress the growth of these undesirable enzyme producing non-Probiotic bacteria and thus reduce the chances of converting procarcinogen to carcinogen. The following are some of the fecal (bacterial origin) enzymes that are responsible for production of carcinogens, and tumor promoters: beta glycosidase; beta glucuronidase; steroid 7 alpha dehydroxylase; nitro-reductase and nitrate reductase; azoreductase; and tryptophanase.

Beta glycosidase: Human diet contains many plants Glycosides mainly flavonoids, which are poorly digested and are passed to colon where the bacterial enzyme Beta Glycosidase hydrolyses to take sugar moiety for energy requirement and leave the aglycone. Some of these plant-derived aglycones are mutagenic ^[20,21].

Beta glucuronidase: The ingested carcinogens are absorbed from the intestines and are detoxified in liver in conjugation with glucuronic acid. The inactivated Glucuronidates are more polar – water-soluble and get excreted in the urine. But these can also pass to the aqueous medium of the bile and gets excreted into the intestines where these are converted back to the parent carcinogens by bacterial enzyme Beta Glucuronidase. The carcinogen is once again absorbed from the intestines into portal circulation and takes part in the enterohepatic cycle. This process increases the persistence of carcinogen in the body. *E. coli* and *Clostridium* Spp. have the highest Beta Glucuronidase activity ^[20,21].

Steroid 7 alpha dehydroxylase: Diet high in fat increases the risk of colon cancer. High fat intake induces the secretion of bile salts that play a part in the emulsification and thus improve digestion of fat. Bile salts are deconjugated by certain bacterial Glucuronidases to primary bile acids. The inducible, Steroid 7 Alpha Dehydroxylase present in some Eubacteria and *Clostridium* eliminate hydroxyl groups from primary bile acids mainly colic acid, and chenodeoxy colic acid, to produce secondary bile acids such as deoxycholic acid and lithocholic. These secondary bile acids are genotoxic and comutagenic, thereby increasing the cell proliferation, which is risk factor for colon cancer ^[20,22]. Studies in humans have shown that patients with colon cancer excrete more secondary bile acids ^[3].

Nitro reductase and Nitrate reductase: The common industrial pollutants are aromatic and heterocyclic nitro compounds. Bacterial nitro reductase reduces them to N nitroso and N hydroxyl compounds before conversion to aromatic amines. The intermediate and end products of this reaction are mutagens. Nitrates are common food contaminants. Bacteria can reduce nitrates to nitrites, which can cause mutations and chromosomal damage. The Nitrites also combine with amino compounds to form nitrosamines, which are mutagenic and carcinogenic ^[20].

Azoreductase: Azo dyes are commonly used to color foods, drinks, and cosmetics. These are reduced to aromatic amines and azo compounds in the intestines by the azoreductases of the bacterial origin. These aromatic amines and azo compounds are mutagenic and carcinogenic.

Tryptophanase: The bacterial enzyme tryptophanase convert non-carcinogenic acid tryptophane to Indole, which is a known carcinogen. Certain aerobic and anaerobic bacteria through fermentation produce carcinogens such as, phenol and para cresol, from the amino acid tyrosine.

All of the above fecal enzymes are produced by non-Probiotic bacteria in the G.I. tract and they can be suppressed by maintaining a healthy population of Probiotics through periodic ingestion or Multiple Mixed Strain Probiotics [3].

Etiology of Cancer

The recent world's statistics on Etiology of cancer indicate the following: 30% of the cancers are due to tobacco consumption: 35% of the cancers are due to over eating or improper diet with high fat, too few vitamins and minerals, and low fiber: 17.5% are due to pathogens especially viral infections such as Epstein bar virus, Human Papilloma, Hepatitis B or C, etc.: 5% are due to Hereditary causes i.e. inherited genes with carcinogenic properties. The rest of 12.5% are due to the other unknown factors [23]. We would like to take a guess that 50% of the unknown could be due to the side effects of the modern drugs. Our strong feeling is that this unknown etiological factor of cancer may be due to the side effects of the modern prescription or over the counter drugs and also due to pollution. If we tighten this arena, we are down to only one factor i.e. unavoidable cancer due to hereditary factors, which amounts to only 5%. With all the modern scientific advances we are making in the genetic research, sooner or later a cure can be found even for pathological hereditary factors. It goes to prove that human being, due to lack of knowledge, created 95% of this cancer disease and it can be eliminated or reduced significantly through scientific knowledge, and modest life style changes [7].

Since 35% of cancer is due to over eating or improper nutrition, it is worth looking into this area. No matter what, indirectly 35% of the cancer is linked to the Gastro-intestinal tract. Our knowledge of nutrition has brought significant awareness to our food habits. Also, diagnostic tests improved the awareness of the disease onset. Our knowledge about digestive enzymes and hormones is superb. However, our knowledge about the dynamics of the gastrointestinal microflora and their influence on health is not at all adequate. In addition to understanding and practicing the nutrition principles we have to concentrate on understanding the associative growth relationships of microorganisms of the Gastro intestinal tract. We have to come to a point of taking into account the effect of any administered drug and its adverse effects on the GI tract flora. The biggest discovery in the twentieth century was the recognition of Probiotics as possible saviors of disease. The twenty first century is for the application of Probiotics to reduce the cancer and other potential molecular and metabolic diseases.

A Brief Description of Behavior of Cancer Cells and the Genetic Changes, which Bring about Cancer

1. **A Cancer cell propagates itself through avoiding the programmed cell death i.e. Apoptosis:** Before a cell divides its genes are examined for defects to prevent mutation. Should the genetic defects proved irreparable, the surveillance proteins instruct the damaged cells to self-destruct, a process called Apoptosis. Since cancer cells go through large number of mutations, they somehow short-circuit this natural control mechanism of apoptosis.

2. **Imitating growth signals:** Cell in an organ replicate thru signals from the body that transmit to the cell nucleus through complex chain of signals. Cancer cells give themselves the signals to proliferate without interference.

3. **Colonization and spread:** A range of contact molecules and messenger substances ensures that the cells cannot leave their native tissue without permission from their neighbors. Cancer cells violate this and leave their native tissue and colonize on body tissues. This is called Metastasis.

4. **Unbridled proliferation:** A normal cell divides an average 52 times before genetic programs instruct it to commit self-destruction. Cancer cells on the other hand are immortal and extend their lifetime indefinitely.

5. **Deceiving the immune system:** The immune system generally recognizes mutated cells and destroys them. Cancer cells can trick themselves to skip the destructive effect of the immune system.

6. **Abnormal blood vessel formation i.e. angiogenesis:** The abnormally growing cancer tissue elicits the angiogenetic factor, forcing the surrounding tissue to generate new blood vessels to supply the blood and thus gets continued supply of oxygen and essential nutrients. When once the angiogenesis is established, it is impossible to halt the cancer tissue growth.

7. **Ignoring the contact inhibition:** The cancer cell exhibits impaired contact inhibition. This impaired contact inhibition enables malignant growths to develop within the community of cells.

Mutagen, Mutation and Metastasis

We want to summarize briefly, how a mutagen can induce mutation in intestinal cell and transforms mutation to Metastasis?

1. Under the normal circumstances, the individual stem cells are constantly dividing at the base of each Villus. The daughter cells then migrate up the Villus to its tip. Since the intestinal mucous membrane is constantly eroded, the stem cells have to produce daughter cells constantly to replenish the eroded mucous membrane.

2. When a Carcinogen is absorbed through mucous membrane, mutation takes place due to damage of the genetic material

in the cell. This step involves malfunction of the APC gene on chromosome 5, which controls the migration of daughter cells from the base to the tip of the villus.

3. The next stage, villi start to grow more rapidly. This is because of second mutation in RAS gene (an oncogenic gene). The cell starts to divide autonomously, instigating irregular cell growth.

4. The tumor starts to grow in size into benign polyps. In some cases, a third Mutation takes place on chromosome 18. Then the stage of uncontrolled growth begins.

5. The center cells of the prolifically growing tumor starts to die due to the shortage of oxygen and nutrients.

6. The cells, which survived in the tumor, go through fourth mutation on Chromosome 17. Since P53 gene mechanism is shut off at this stage, the mutated cells do not undergo self-destruction i.e. apoptosis.

7. The malignant tumor gradually grows out of control and forces the surrounding tissues to connect it to adjacent blood vessels, ensuring a steady supply of nutrients.

8. The next stage, tumor becomes irreversibly malignant and goes through another mutation to obtain the behavior of metastasis. The metastasis now takes place in the liver. The tumor over-rides the body's immune mechanism and also develops resistance to cell toxins developing within its mass. Ultimately the malignant tumor kills the host.

If you analyze the entire mechanism, the cancer starts with one cell through mutation. If mutagens are reduced or eliminated in the body, cancer can be controlled. Mutagen can be reduced if proper Multiple Mixed Strain Probiotics are administered (along with their growth end products and bacteriocins) and make them colonize in the gastro intestinal tract. In our opinion, proper diet and Multiple Mixed Strain Probiotic therapy is the wave of the future to eliminate the mutagenesis, which is the starting point of cancer. Any reduction of intestinal pH due to Probiotics will alter the other non-beneficial microbial flora activity, bile solubility, and decrease the transit time to eliminate the carcinogen producing fecal bacterial enzymes and thus reduce the conversion of procarcinogens to carcinogens. Now you can appreciate the significance of the Multiple Mixed Strain Probiotics to prevent or treat some of the gastrointestinal associated cancers.

While running the clinical trials (on curing the osteoporosis and osteopenia), several physicians and hospitals reported as a syrendipous observation that certain cancer patients recovered very quickly and responded very well to the cancer treatment, when the bioavailable calcium and other major and minor minerals (with the inclusion of Probiotics) were administered simultaneously (along with traditional cancer treatment) as part of the treatment modality^[9]. The only explanation that can be given to this positive effect is that, either the bioavailable calcium and other minerals (manufactured by IMAC) along with the milk derived smaller peptides and Probiotics have inhibitory effect on the cancer cell proliferation or cancer cells inhibition was enhanced significantly by the bioavailable calcium and other minerals along with Probiotics in conjunction with the conventional cancer treatment. In this connection we would like to point out that the Probiotic bacteria synthesized Nano particles, which are highly active, may act as synergistic compounds to complement or enhance the efficiency of the traditional cancer therapy. The size of the typical Probiotic *Streptococcus* bacterium is 0.5 to 1.0 micrometer. A micron is one millionth of a meter. When such an organism is challenged to grow in a bacteriological medium with various concentrations of minerals and large molecular weight proteins, it will structurally alter the minerals and proteins etc. to protect itself from metal toxicity through reduction and also to break the complex proteins to smaller peptides and amino acids for easy assimilation. In addition, the organism will also synthesize smaller peptide bacteriocins and other Nano particles, which have therapeutic effects. Bacteriocins produced by Probiotics are extremely inhibitory to the growth and proliferation of the several pathogenic bacteria^[3]. The Nano meter is one billionth of a meter and such small Nano particles are extremely active due to their large surface area and ease of penetration into cells. It explains partly the reason for the speedy recovery of some of the cancer patients (observed by physicians) when bioavailable calcium Probiotic mixture is administered through oral route in addition to the traditional cancer therapy.

The bioavailable calcium and other minerals derived from the milk source, and Multiple Mixed Strain Probiotics come under biologically based practices (specifically under the category of nutrition and dietary supplements), according to the National Center for Complementary Integrative Health (NCCIH). Thus they can be given as complement (as a part of integrative therapy) along with the traditional cancer therapies. Once again this is the novel intention of NCCIH to encourage such complementary integrative health approach to protect the people from hard to treat diseases such as cancer.

Synergy of Multiple Mixed Strain Probiotics and Whole Medical System Ayurveda (Proyurveda)- A New Complementary and Alternative Medicine Approach

Can Multiple Mixed Strain Probiotic therapy be construed as an approved complementary alternative medicine all by itself or does it have to be in conjunction with other treatment modalities? To answer this question, we would like to discuss about the science of Proyurveda, (Probiotics + Ayurveda), which is a derivative of the popular and ancient alternative medicine Ayurveda.

Proyurveda is a combination of Probiotics and Ayurveda. A brief description is given regarding the philosophy of Ayurveda and its synergistic effect with Probiotics. We want to point out to the reader that some of the terminologies used in Ayurveda are derived from Sanskrit language. Thus we made every effort to give simplified explanation of the meaning such Sanskrit words.

What is Ayurveda? According to the National Center for Complementary and Integrated Health, Ayurveda is an approved alternative medicine, since it has been practiced for 1000's of years. Ayurveda is composed of two words i.e. Ayus and Veda. Ayus stand for "life" and Veda means "knowledge". The Ayurvedic clinician deals with the body, mind, behavior, environment, diet and patient's consciousness or inner awareness. Ayurvedic treatment is aimed at preventing and eliminating disease, consequently prolonging life with excellent health. The Ayurveda is roughly 5,000 years old and it originated in India. The scientific logic behind Ayurveda has been misinterpreted and misunderstood. Ayurveda has been categorized under alternative medicine and is being practiced widely in India and several parts of the world. The difference between Western medicine (allopathy) and Ayurveda is that Western medicine interprets the health and disease on the material of the body (physical), whereas Ayurveda relies on the body's non-material substrate, consciousness or inner awareness (soul).

The modern allopathic medicine modality assumes that the human body can be explained by material reductionism, which segregates consciousness (soul) from material world (physical body). This can be termed as objective science. In contrast, Ayurveda views human body as an abstract pattern of intelligence, which does not segregate consciousness (soul) from material world (physical body). It goes to prove that the philosophy of Ayurveda is in tune with the unified field theory of the modern physics. Ayurveda also uses combination of herbs to treat ailments. The belief is that herbs will have the active principle come into contact with nutrients and buffers. Such a preparation will not give any side effects when consumed because the active therapeutic principle is naturally buffered. Generally, Ayurvedic preparations are formulated by blending several complementary herbs. The idea is to counteract the adverse effect of one herb with the other. Consequently the host will not have any side effects from the herbal medications. Ayurvedic preparations are excellent for treating chronic diseases. According to Dr. Hari Sharma, M.D., professor emeritus of Ohio State University (personal communication), some of the Ayurvedic herbs have been proven to reduce angiogenesis during cancer progression, thus retarding the growth of cancer.

A Complementary Alternative Medical Science, Using Probiotics Along with Ayurvedic Medications "Proyurveda" and Its Effect on Improving Health and Longevity

According to Ayurveda (science of life or long life), 85 percent of the diseases are due to improper digestion either at the gastrointestinal level and/or at the cellular level. The Sanskrit term used in Ayurveda to denote the end product(s) of poor digestion is "ama". This "ama" plays a key role in inducing disease due to its interaction with the aggravated doshas and thus facilitates itself (ama) to adhere to areas of the human body in which it did not belong. The doshas are expressions of the unified field (the inner most core of one's own being and experience). According to Ayurveda, the doshas are divided into three i.e. Vata, Pitta and Kapha, on the basis of the natural individual constitution of the human being. Since doshas are the subtle expressions of the unified field, the ultimate cause of disease is losing physical body's connection to the unified field. According to Ayurveda, such a disconnection will aggravate the body's natural state of internal balance (dosha). An interaction of such aggravated natural state of internal balances (doshas) and "ama" (the end products of poor digestion) are the causes for both the acute and chronic diseases such as heart disease, cancer, arthritis, etc.

Thus, Ayurvedic treatment is aimed at reducing or eliminating the "ama", improving OJAS (overall wellbeing of the person) and also pacifying the aggravated doshas to bring them to their natural state of balance. This can be accomplished through proper diet, digestion, positive lifestyle and herbal remedies and meditation. Ayurvedic pharmacology utilizes the synergistic cooperation of substances as they co-exist in natural sources (natural health foods). Ayurveda considers herbs as the concentrated repositories of nature's intelligence and when used in proper combinations can express that intelligence in the body to cure an ailment. In the modern pharmacological terms, intelligence of herb is nothing but the active therapeutic compound in the herb, and its intelligent expression- in the body is the therapeutic effect.

In our opinion the Probiotics, which are the beneficial bacterial cultures which co-exist in nature (all natural) are also concentrated repositories of nature's intelligence and when used along with the therapeutic herbs can enhance the expression of their own intelligence as well as the intelligence of herbs in the human body, to enhance the immunity and other physiological process such as digestion and metabolism of the body etc. to cure or prevent the disease. In our opinion, taking Ayurvedic science into account, Probiotics can significantly reduce "ama" and also pacify the doshas associated with diet and digestion when administered in combination with proper therapeutic herbs and thus improve "ojas" (overall wellbeing of the person) and longevity.

Even though, Ayurveda has been around for 5000 years, the awareness and therapeutic effects of the natural Probiotics was discovered only in the early part of the twentieth-century. These beneficial bacterial cultures always associated with the plants or herbs in the nature and were ingested knowingly or unknowingly along with the herbs. Ayurvedic pharmacology concentrated on herbs, but did not pay much attention to the beneficial microorganisms associated with the herbs. We cannot blame them because, formal microbiology is only roughly 150 to 200 years old science. As civilization progressed, the modern practices

of agriculture and sanitation greatly improved. However, these modern practices partially or totally destroyed these naturally beneficial microorganisms associated with medicinal herbs and thus made them less effective as therapeutic agents. That could be one of the reasons why the popularity of Ayurvedic drugs came down in light of Allopathic drugs, even though Ayurvedic drugs did not exhibit any unwanted side effects. Everybody accepted the fact that Ayurvedic drugs are relatively slow acting and thus are primarily used for treating the chronic ailments. Now it is proven that this theory is wrong. A recent discovery, which led to U.S. patent #6,080,401 clearly proved that herbs and Probiotics have a beneficial synergy and together their therapeutic values are greatly enhanced. Using this discovery, ADFAC Labs of India have developed over 100 Ayurvedic drugs (Proyurveda-Probiotics + Ayurveda) and successfully used them to treat both the acute as well as chronic diseases. ADFAC Labs Pvt. Ltd. has demonstrated that the combination of "Ayurvedic drugs with properly prepared Probiotics" is the best way to improve the efficiency of Ayurvedic drugs, to cure the ailments, without any side effects, at a significantly faster pace than Ayurvedic herbs alone. ADFAC India Pvt. Ltd. have conducted in depth clinical studies, using over a million human subjects, to study the Proyurvedic drug efficiency in relation to Ayurvedics and Probiotics themselves, in a span of over 15 years. None of the patients reported any adverse side effects using Proyurveda drugs or nutritional supplements [24,25].

The beneficial properties of the Probiotics contribute to the health of the G.I. tract and overall health of an individual. This health promoting property of Probiotics can be greatly elevated when administered along with proper herbs [24]. Ayurveda insists that reduction or elimination of the toxic end products of improper digestion is vital for curing disease. Probiotics definitely reduce the GI tract disease through their natural enzymatic systems, physiological process, and natural therapeutic properties. In other words, proper modulation of digestion must be a prime factor for improved health. Probiotics can modulate the digestive system variations towards normality by working in conjunction with the gastric enzymes, G.I. tract associated micro flora, and end products of the gastric and intestinal enzyme digestion of food. These digestive modulation properties of Probiotics can be greatly enhanced with the aid of Ayurvedic herbs because of the symbiosis. Perhaps Ayurvedic herbs act as Prebiotics and when administered along with Probiotics. This combination improves efficiency of both Probiotics as well as Prebiotics (herbs) through symbiosis. A Prebiotic is a non-digested food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species in the gastro intestinal tract that can improve host health. It has also been reported that Probiotics survive for a long time when capsulated along with herbs. Such a Probiotic culture not only survives for a long time but also exhibits excellent adhesion and therapeutic properties in the human G.I. tract. The possible explanation for this survival is the anti-oxidation properties of the herb which improves the survival of the Probiotics during storage and subsequently in the G.I. Tract. This explains why in the nature these Probiotics associate with herbs and plants.

To sum it up, Ayurvedic herbs work excellent in conjunction with Probiotics to cure acute or chronic diseases at relatively faster pace, but without any adverse side effects. The Proyurveda products and its philosophy can be used in conjunction with an allopathic treatment, as a complementary alternative medicine. In our opinion, this is the wave of the future in the health care industry throughout the world. This once again proves the good intentions of the United States National Center for Complementary Integrative Health (NCCIH), under the direction of the National Institute of Health (NIH), to integrate several medical therapies, to improve the health of the people.

Synergy of Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy and Allopathic Antibiotic Therapy a New Integrated Medicine Approach

Earlier [3], after running the clinical trials using the combinations of freeze dried Probiotics and antibiotics, have reported that such a combination therapy was ineffective [24]. In their study they have used antibiotics [24] which are not only effective against the pathogenic bacteria but also equally effective in inhibiting the beneficial Probiotics used as part of treatment modality.

Recently in the year 2016 they [2] have discovered that using the naturally antibiotic resistant (for specific antibiotics) Multiple Mixed Strain Probiotics belonging to different genera and species along with their bacteriocins and their growth end products (both specific and nonspecific Nano particles) prepared by freezing in liquid nitrogen, cured with 100% efficiency the lethal hospital acquired infections due to *Clostridium difficile* (*C. diff*) and Methicillin resistant *Staphylococcus aureus* (MRSA). The principle here is that if the *C. diff* and MRSA pathogenic bacteria are resistant to several antibiotics but responds only to antibiotics bacitracin and vancomycin (perhaps 60 to 70% of the time), consequently administering Probiotics which are sensitive to bacitracin and vancomycin to cure these infections will be ineffective. Instead, if we use the Probiotics, which are naturally resistant to bacitracin and vancomycin along with antibiotics bacitracin and vancomycin, such a combination therapy of, using Probiotics along with these antibiotics can cure the nosocomial infections quickly and effectively. While running these clinical trials Reddy and Reddy have discovered that Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy was very effective (without even using vancomycin and bacitracin) to cure the *C. diff* and MRSA infections [3]. They have also discovered that under certain circumstances, when the patients were severely ill and almost to the point of dying, using antibiotics vancomycin and bacitracin (antibiotic therapy) as a complement to Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy proved to be the most successful treatment approach. It is very well documented and accepted by several physicians that the antibiotic therapy alone using bacitracin and vancomycin is not reliable to cure these nosocomial infections. In other words, it is a hit or miss therapeutic approach.

It goes to prove that Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy, although categorized under NCCAM or

NCCIH as the biologically based complementary alternative medicine; under certain circumstances, it can be integrated with the allopathic medical practice of antibiotic therapy to completely cure the deadly lethal hospital associated infections. We do understand the earlier concern of the medical community questioning the efficacy of the Probiotic therapy as a complement to antibiotic therapy, since Probiotics are sensitive to such antibiotics. However, the breakthrough discovery of Dr. M.S. Reddy, using the naturally antibiotic resistant multiple Mixed Strain Probiotics along with their bacteriocins and Nano particles, frozen using liquid nitrogen, has given a total comfort to the medical community^[3]. Such a therapeutic approach further confirms the good intentions of the United States National Center for Complementary Integrative Health (NCCIH). When a particular therapy is not one hundred percent effective, there is nothing wrong in looking into the complementary and alternative medical approaches, which are legal and controlled by the National Center for Complementary Integrative Health, which is in turn under the wing of the National Institute of Health (NIH).

CONCLUSION

Prior to the discovery of antibiotics, the Nobel Laureate Metchnikoff, in the early 1900's came up with an idea about using beneficial microorganisms to counteract the pathogenic bacterial infections^[4]. His concept did not go too far due to lack of perfect understanding of the physiology of both the beneficial microorganisms as well as the pathogenic bacteria. After the discovery or isolation of bacterial virus (bacteriophage) for the first time in the history in 1907, the attention of the medical researchers tuned towards using the specific bacteriophages as therapeutic agents, which can infect and lyse or kill the pathogenic bacteria. However, after long standing research, they have discovered that the bacteriophage is highly specific and can infect and lyse or kill only the genetically related specific strains only. Bacteriophage activity is not broad spectrum. In other words, they are species and strain specific. Since the bacterial infections were due to several different serotype bacterial strains, using bacteriophage as a therapeutic agent became unsuccessful and thus the research in this arena was discontinued.

After Nobel Laureate Dr. Alexander Fleming, for the first time in the history, came up with a great discovery of antibiotic penicillin, the entire medical community in the world started using the penicillin to cure the pathogenic bacterial infections. The first antibiotic penicillin was introduced into medical commerce in the mid 1940's and became widely accepted as the popular antibiotic therapy. At the time of introduction of "antibiotic therapy" in mid-1940's, the scientific world never realized that the pathogenic bacteria (once sensitive to penicillin) can mutate and develop resistance to antibiotic penicillin. In fact, it did happen and the "antibiotic therapy" turned out like chance therapy, rather than choice therapy to cure the infections. As the old saying goes, "the problem breeds solution", the scientists involved in pharmaceutical sciences started to develop second generation antibiotics which can inhibit the penicillin resistant pathogenic bacteria. This battle of new development of antibiotics vs. the continuously mutating bacteria to resist such antibiotics went on for decades. Finally the multiple antibiotic resistant pathogenic bacteria (superbugs) evolved and they started to cause the lethal infections and deaths in humans as well as in animals. One such example is Nosocomial or hospital acquired infections due to *Clostridium difficile* (*C. diff*) and Methicillin Resistant *Staphylococcus aureus* (MRSA). These infectious organisms exhibit the broad spectrum antibiotic resistance and are infecting over 6,000,000 people (it could be more) in the world and killing over 100,000 innocent people. This became a great concern to world health organization (WHO), and they are already in the process of issuing orders to discontinue the unscrupulous use of antibiotics, due to a scare of several pathogenic bacteria developing the antibiotic resistance and subsequently passing such resistance to other bacteria.

The next best alternative is the use of beneficial nonpathogenic Probiotic bacteria to inhibit the pathogens. This research started in the mid 1900's and surprisingly only handful of scientist were involved. Dr. M.S. Reddy started his research in late 1960's and discovered that several of the beneficial nonpathogenic Probiotic bacteria used for making the dairy products were naturally resistant to several antibiotics. Dr. M.S. Reddy's research continued for over 47 years and finally for the first time he came up with a breakthrough discovery of using Multiple Mixed Strain Probiotics as therapeutic agents to cure the multiple antibiotic resistant hospitals associated infections due to *C. diff* and MRSA. The details of this breakthrough discovery were published in 2016^[3].

In this current article, we have outlined the significance of Probiotics as alternative and complementary therapeutic agents. For example in 2000's^[24], for the first time in the world, we were able to combine the Probiotics with other approved pharmaceutical and Ayurvedic drugs to speed up the therapy without any side effects. Since then, some pharmaceutical companies have developed medical products with the inclusion of Probiotics^[26,27]. The latest Dr. M.S. Reddy's "Multiple Mixed Strain Probiotic Therapy" can also be used in conjunction with the antibiotic therapy (using specific antibiotics such as vancomycin and bacitracin etc.) to cure the infectious diseases, without altering the gastrointestinal microbial eco balance. The end products of the Probiotics, such as bacteriocins and other Nano particles will have maximum therapeutic effect in conjunction with the live Probiotic bacterial cells. The Multiple Mixed Strain Probiotic Therapy of Dr. M.S. Reddy is a classic example of modern Nano technology since Probiotics produce abundant amount of the therapeutic Nano particles which are extremely effective in not only inhibiting pathogenic bacteria but also benefiting the host (to improve health) at the cellular and tissue level in the entire body.

We have also presented specific details on the genesis of cancer and how Probiotics can reduce such terminal diseases. The alternative and integrative medical approach to treat the incurable diseases is the wave of the future. The medical community and pharmaceutical industry should view this in an optimistic way to arrive at newer technologies to put an end to the human mystery due to several incurable diseases. We are very positive, this article is of immense help to physicians to understand the

myriad uses of integrating Probiotic therapy as a complement with other therapies. Finally, Dr. M.S. Reddy's Multiple Mixed Strain Probiotic Therapy without limitation, can also be used to treat other diseases such as Irritable Bowel Syndrome (IBS), Crohn's disease, Intestinal diverticulosis, Colitis, certain Cancers, and also the Helicobacter pylori infection (which is the root cause for gastric carcinoma) etc.

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