



MICROORGANISMS FRIEND OR FOE?

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ABSTRACT

Tiny microbial entities had been influenced the world hugely, complex evolutions followed by prokaryotic cell to eukaryotic cell origin. Hitherto, Plague epidemic to the largest death toll from any known non-viral epidemic. Its killed millions people around the world; China lost around half of its population, from around 123 million to around 65 million; Europe around 1/3 of its population, from about 75 million to about 50 million; and Africa approximately 1/8 of its population, from around 80 million to 70 million. In India, plague killed thousands Indians during the British era. Literally microbes had have played an important role on our planet and perhaps cosmos too. Microbe importance can be understood by their role in biogeochemical cycles (nitrogen fixation, carbon cycle, phosphate cycle etc); however, these hidden entities had been responsible for mass mortality among the human and animals. Despite their virulence nature, there is a vigor account of beneficial microbes, that's employed for various human welfare aspects i.e. food, treatment, prevention (vaccination), cosmetic, therapies etc. In this article we tried to highlights their some cons and pros. It is interesting to distinguishing harmful vs beneficial microbes, as they share both negative and positive impact in human lives. Therefore, it's upon our intellect how we interact with them and how we manipulated them. Recent research such as their specific behaviour, communication (Quorum sensing) etc. makes them friendly companion.

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INTRODUCTION

To determine microbes are our friend or not, let's take a small interesting journey of the microbial World. We are familiar about some pathogens that caused mild to life threatening diseases i.e. HIV, swine flu virus, influenza viruses: H1N1, H1N3 and so on. Undoubtedly, we cannot forget swine flu, bird flu outbreaks and more recent lethal Ebola virus attack. Mild to severe food poisoning case reports annually around the world; especially in India several contaminated food born outbreaks engulfed hundreds lives per year. Except pathogenesis, microbes had have played an important role in our lives, various food and pharmaceutical sectors rely on microbial metabolites; wine and beverage completely depends on microbial fermentation. Microbes emerging as the saviour in cosmetic fields, products such as anti wrinkles serum, xanthan gum (thickener for various cosmetic) take places the conventional beauty products. Let's consider their drawbacks before useful aspects.

Plague or Black Death

Plague caused by *Yersinia pestis*; a bacterium, usually infect human and animals, especially rats and transmitted by a rat flea.. The bacterium release a lethal toxin in the human body that cause the life threatening symptoms i.e. fever, headache, gangrene, shock etc. 100% mortality occurred if plague remains untreated. Luckily, now a day effective antibiotic

and vaccines are available to plague. Plague epidemic to the largest death toll from any known non-viral epidemic. Its kill millions people around the world. From 1347 to 1351, the Black Death, a massive and deadly pandemic originating in China, spread along the Silk Road and swept through Asia, Europe and Africa. It may have reduced the world's population from 450 million to between 350 and 375 million. China lost around half of its population, from around 123 million to around 65 million; Europe around 1/3 of its population, from about 75 million to about 50 million; and Africa approximately 1/8 of its population, from around 80 million to 70 million. In India, plague killed thousands Indians during the British era. In 1994, 693 suspected cases and 56 deaths were reported from the five affected Indian states as well as the federal district of New Delhi. These cases were from Maharashtra (488cases), Gujarat (77cases), Karnataka (46cases), Uttar Pradesh (10 cases), Madhya Pradesh (4 cases) and New Delhi (68 cases) [1, 2, 3, 4].

Salmonellosis and Typhoid

Both diseases caused by the bacterium *Salmonella* species. Salmonellosis generally caused by *S. enterica*, symptoms including mild to severe dehydration (*E. Coli*, *Brucella*, and some viruses also cause severe dehydration). While Typhoid caused by *S.typhi*. In 2000, typhoid fever caused an estimated 21.7 million illnesses and 217,000 deaths around the world

[6]. **HIV/AIDS:** (Human immunodeficiency virus /Acquired immunodeficiency syndrome). HIV/AIDS is a global pandemic. As of 2012, approximately 35.3 million people have HIV worldwide with the number of new infections that year being about 2.3 million. Although HIV viruses do not kill the host directly and do not cause any disorders too, but the real culprit is the secondary infection, which is responsible for the mortality in AIDS. The most commonly associated secondary diseases are T.B and cancer that are the main reasons of HIV/AIDS patients death. Why un-curable yet? Certain microbes, including HIVs cause un-curable infection by various complex strategies. In the case of HIV infection, HIV virus hijacks the host immune system by invading immune cells (T- cells) and destroyed host's body defence system on the other hand, as they (viruses) it multiplying with the host cell by an integrated pathway, hence it is make virus more complicated to tackle by any medicine within the host cell. Although more recently, bone marrow transplant and chemotherapies have been proven an effective treatment for HIV [6].

Bioweapon or bio-terror

Some pathogens have also been used as the bio –weapon or bio-terror. For instance concentrated *Bacillus anthracis* spores were used for bioterrorism in the 2001 anthrax attacks in the United States, delivered by mailing postal letters containing the spores It is indicated that infectious diseases remained top most human health threats so far[7].

Food spoilage and Contamination

India is the second major producer of fruits and vegetables and ranks next to Brazil and China respectively, in the world. It contributes 10 percent of world fruit production and 14 per cent of world vegetable production. Fruits and vegetables are more prone to spoilage than cereals due to their nature and composition, and this spoilage occurs at the time of harvesting, handling transportation, storage, marketing and processing resulting in waste. Efficient management of these wastes can help in preserving vital nutrients of our foods and feeds, and bringing down the cost of production of processed foods, besides minimizing pollution hazards. According to India Agricultural Research Data Book 2004, the losses in fruits and vegetables are to the tune of 30 per cent.

perishable horticultural produce serve as an effective tool for getting better return to the produce and also help in avoiding wastage both at production site and distribution centers, which will help in regulating the market infrastructure. Like any other food, fruits and vegetables are also prone to microbial spoilage caused by fungi, bacteria, yeast and moulds. A significant portion of losses of fruits and vegetables during post-harvest period is attributed to diseases caused by fungi and bacteria. The succulent nature of fruits and vegetables makes them easily invaded by these organisms. Besides attacking fresh fruits and vegetables, these organisms also cause damage to canned and processed products. Many serious post-harvest diseases occur rapidly and cause extensive break down of the commodity, sometimes spoiling the entire package. It is estimated that 36 % of the vegetable decay is caused by soft rot bacteria. Similarly fruit rot in aonla and other soft fruits caused by fungi is also very destructive. As far as vegetables are concerned, naturally the source of infection is from the field, water used for cleaning the surface, contact with equipment and storage environment. The most common pathogens causing rots in vegetables and fruits are fungi such as *Alternaria*, *Botrytis*, *Diplodia*, *Monilinia*, *Phomopsis*, *Rhizopus*, *Pencillium*, *Fusarium*, etc. Among bacteria *Ervinia*, *Pseudomonas*, etc. cause extensive damage[11] on the other hand various contaminated food born outbreaks reported in India frequently (table 1).

Beneficial Microorganisms

Microbes shared both negative and positive characteristics. Beneficial microbes generally do not cause any harm to their host. They remained either in mutualism or neutralism. In the case of mutualism they provide some benefit to their host and also get some benefit from their host while in the case of neutralism both host and microbe remained neutral to each other. Despite pathogenesis, there are several microbes which play a crucial role in our lives. Common microflora that prevent or halt pathogenic microbes, secretes some vitamins and enzymes to maintain human health also. In the past few decades, microbes have been proven their importance in health and pharmaceutical fields. Now a days antibiotic to food supplements, and essential vitamins produced by

Table 1 Bacterial Food born outbreaks in India (1980-2016).

Places	Incidences	Victims	Pathogen	Food
Party	3	98	<i>Salmonella Paratyphi A Var Durazoo; S.aureus; V. parahaemolyticus</i>	Veg food Coconut balls Fish and meat sandwiches[12]
Mess	1	76	<i>E. coli serotype 020</i>	Dinner[12]
Home	2	5	<i>Salmonella spp.</i>	Stale rice, Chicken[12]
Feast	2	303	<i>Yersinia enterocolitica Salmonella weltevreden and Vibrio fluvialis</i>	Butter milk Mutton- ghogni[12]
Religious	2	164	<i>ceremony Vibrio fluvialis Shigella sonnei</i>	Bread and vegetable curry Food item not identified[12]
Military establishment	2	78+43	<i>Salmonella spp.</i>	Frozen food Potato bitter gourd vegetable contaminated by rodents[12]
Marriage party	2	800	<i>Vibrio vulnificus Shigella sonnei</i>	Fish Food, item not identified[12]
School	2	135	<i>E. coli, Staph. Spp.</i>	Soyabean milk Bhalla
Hostel	2	184	<i>Salmonella weltevreden Salmonella weltevreden</i>	Fish Food item not identified[12]
Educational institution	1	150	<i>Salmonella enteritidis</i>	Kheer[12]
Hospital	10	10	<i>Salmonella wein</i>	Poultry products[12]
Slum area	1	103	<i>Salmonella typhi</i>	Yogurt and sweets[12]
Tea Garden	1	72	<i>Salmonella weltevreden</i>	Contaminated drinking water[12]
Funeral reception	1	44	<i>Vibrio parahaemolyticus</i>	Food item not identified[12]

'Taking estimated production of fruits and vegetables in India at 150 million tones, the total waste generated comes to 50 million tones per annum. The post-harvest technologies for

manipulating their primary and secondary metabolites. Vaccine was the first microbial weapon used against microbial infection, as an immunization.

Immune modulator: Several microbial species regularly expose, enhance the specific immunity of the host despite the promote pathogenesis or any debility like Bifidobacterium [8]. The human body contains approximately 10^{14} bacterial cells, It is estimated that 500 to 1,000 species of bacteria live in the human gut like Firmicutes and Bacteroidetes dominate but there are also *Proteobacteria*, *Verrumicrobia*, *Actinobacteria*, *Fusobacteria* and *Cyanobacteria*. The mass of microorganisms is estimated to account for 1-3% total body mass. These microbes called as human microbiota or microflora. Especially skin and mucosal membrane microflora compete with the pathogens and halt their growth [9].

Probiotic: A true gut friend, some species of *Lactobacillus* as the therapeutic agent. *Lactobacillus* species naturally found in Yoghurt (Just like Dahi in India) and human gut. *Lactobacillus* found to be effective to stop diarrhoea as well as colon- cancer in human. Probiotic based several food products also available in the market.

Antibiotic associated diarrhoea: In a meta-analysis of trials that used live organisms to prevent diarrhoea associated with antibiotics shows that probiotics may be effective in preventing antibiotic associated diarrhoea. We had only a small number of trials in our meta-analysis, and it should be noted that the different antibiotics used in the trials may have altered the risk of patients getting diarrhoea and their response to the probiotics. Although probiotics have been used to prevent or treat diarrhoea of other causes—namely traveller's diarrhoea and infantile infectious diarrhoea—we did not include trials that investigated probiotics in these indications; however, most of these studies showed positive results, and some reviews have been encouraging [17].

Aging hypothesis

Institute in Paris, proposed the hypothesis that the aging process results from the activity of putrefactive (proteolytic) microbes producing toxic substances in the large bowel. Proteolytic bacteria such as clostridia, which are part of the normal gut flora, produce toxic substances including phenols, indols, and ammonia from the digestion of proteins. According to Metchnikoff, these compounds were responsible for what he called "intestinal autointoxication", which would cause the physical changes associated with old age [13].

It was at that time known that milk fermented with lactic-acid bacteria inhibits the growth of proteolytic bacteria because of the low pH produced by the fermentation of lactose. Metchnikoff had also observed that certain rural populations in Europe, for example in Bulgaria and the Russian steppes, who lived largely on milk fermented by lactic-acid bacteria were exceptionally long lived. Based on these observations, Metchnikoff proposed that consumption of fermented milk would "seed" the intestine with harmless lactic-acid bacteria and decrease the intestinal pH, and that this would suppress the growth of proteolytic bacteria. Metchnikoff himself introduced in his diet sour milk fermented with the bacteria he called "Bulgarian Bacillus" and found his health benefited. Friends in Paris soon followed his example and physicians began prescribing the sour-milk diet for their patients [13].

Novel Source of Nutrient: Various fermented products, i.e. tofu, kefir, kumis, yoghurt even bread also a produce and flavoured by microbes. Several fungal and bacterial species

used commercially to make vitamins and proteins related food supplements and tonics by the pharmaceutical companies.

Faecal therapy: The original modern hypothesis of the positive role played by certain bacteria was first introduced by Russian scientist and Nobel laureate Élie Metchnikoff, who in 1907 suggested that it would be possible to modify the gut flora and to replace harmful microbes with useful microbes [14].

Antibiotics: As an Indian idiom "Iron cut the iron", truly followed by the microbes as they still remained a vast and novel source of antibiotics. The world first antibiotic Penicillin was isolated from a fungal species *Penicillium notatum*. In the present scenario a number of bacterial and fungal species used to make broad spectrum antibiotics.

In a recent study, *Lactobacillus* sp. strain GG, which was isolated from the feces of a normal person, produced a substance with potent inhibitory activity against a wide range of bacterial species. It inhibited anaerobic bacteria (*Clostridium* spp., *Bacteroides* spp., *Bifidobacterium* spp.), members of the family Enterobacteriaceae, *Pseudomonas* spp. *Staphylococcus* spp., and *Streptococcus* spp., as demonstrated by a microbiological assay; however, it did not inhibit other lactobacilli. The inhibitory activity occurred between pH 3 and 5 and was heat stable. Bactericidal activity against *Escherichia coli* was demonstrated at a dilution of 1:128. The inhibitory substance was distinct from lactic and acetic acids. It had a low molecular weight (less than 1,000) and was soluble in acetone-water (10:1). Because of these characteristics, the inhibitory material could not be considered a bacteriocin; it most closely resembled a microcin, which has been associated previously with members of the family Enterobacteriaceae [16].

Antihypertensive potential: Peptides derived from α_{s1} - and β -caseins by the *Lactobacillus helveticus* CP790 proteinase were investigated for their inhibitory activities against angiotensin I-converting enzyme. The antihypertensive effect of casein hydrolysates in strain SHR spontaneously hypertensive rats was also investigated. Both α_{s1} and β -casein hydrolysates inhibited this enzyme. Some of these peptides showed enzyme inhibitory activity, and one of them from β -casein inhibited the enzyme greatly; the concentration of an angiotensin I-converting enzyme inhibitor needed to inhibit 50% of the enzyme activity was $4 \mu\text{M}$. The hydrolysate of casein demonstrated antihypertensive activity in spontaneously hypertensive rats at an orally administered dosage of 15 mg/kg of body weight. Milk fermented with *L. helveticus* CP790, containing about .3% peptides, also showed antihypertensive activity in SHR rats with 5 ml/kg of body weight (15 mg of peptide/kg); however, the milk fermented with *L. helveticus* CP791, a variant defective for proteinase activity, did not show this activity. Results suggested that the peptides liberated from casein by the proteinase in the culture medium showed antihypertensive effect in SHR rats [15].

Hepatoprotective (against fatty liver) effect

In a study, Ob/ob mice, a model for nonalcoholic fatty liver disease (NAFLD), develop intestinal bacterial overgrowth and overexpress tumor necrosis factor α (TNF- α). In animal models for alcoholic fatty liver disease (AFLD), decontaminating the intestine or inhibiting TNF- α improves AFLD. Because AFLD and NAFLD may have a similar

pathogenesis, treatment with a probiotic (to modify the intestinal flora) or anti-TNF antibodies (to inhibit TNF- α activity) may improve NAFLD in ob/ob mice. To evaluate this hypothesis, 48 ob/ob mice were given either a high-fat diet alone (ob/ob controls) or the same diet + VSL#3 probiotic or anti-TNF antibodies for 4 weeks. Twelve lean littermates fed a high-fat diet served as controls. Treatment with VSL#3 or anti-TNF antibodies improved liver histology, reduced hepatic total fatty acid content, and decreased serum alanine aminotransferase (ALT) levels. These benefits were associated with decreased hepatic expression of TNF- α messenger RNA (mRNA) in mice treated with anti-TNF antibodies but not in mice treated with VSL#3. Nevertheless, both treatments reduced activity of Jun N-terminal kinase (JNK), a TNF-regulated kinase that promotes insulin resistance, and decreased the DNA binding activity of nuclear factor κ B (NF- κ B), the target of IKK β , another TNF-regulated enzyme that causes insulin resistance. Consistent with treatment-related improvements in hepatic insulin resistance, fatty acid β -oxidation and uncoupling protein (UCP)-2 expressions decreased after treatment with VSL#3 or anti-TNF antibodies. In conclusion, these results support the concept that intestinal bacteria induce endogenous signals that play a pathogenic role in hepatic insulin resistance and NAFLD and suggest novel therapies for these common conditions [20].

Anticancer agents

The role played by lactic acid bacteria in various biological functions of the host has been extensively reported. During the last two decades, numerous studies have demonstrated the anticarcinogenic properties of lactic acid bacteria and great emphasis has been laid on the antitumour activity exerted by yoghurt and by milks fermented with *Lactobacillus acidophilus* has demonstrated that, in mice fed with fermented colostrum, the growth of experimentally induced tumours was inhibited, but only in animals dosed before the onset of tumour growth. The antitumour effect was exerted by the presence of lactic acid bacteria by components of their cell wall, or by products formed as a consequence of the fermentation process were able to isolate a dialysable antitumour component from yoghurt. That demonstrated in mice dosed with *L. acidophilus* there was a decrease in the incidence of the colon cancer induced by 1,2-dimethylhydrazine dihydrochloride. The intraperitoneal administration of *L. casei* inhibited tumour growth in both syngeneic and allogeneic mice. The effect depended on the dose and on the time of administration of *L. casei*; the antitumour activity was effective only in pre-treated animals [18].

Vaccine: A vaccine word originated from the Latin “Vacca” means Cow (To the honour of Edward Jenner, who studied and developed the first vaccine from the cow). The vaccine is the attenuated or weakened microbial cells that commonly injected (some time orally as a polio vaccine) in the host to prevent from later or future infection of the same microbes. Vaccines basically worked on the immune system provoke. In the past few decades vaccination programme saved millions of lives around the world. Recently polio has been eradicated completely from India. Although, hepatitis and rabies like lethal diseases also need to be mass vaccination and complete eradication from our country, as like the first world countries.

Weight management: Claims that some lactobacilli may contribute to weight gain in some humans; Although, remained controversial [19].

In a study efficacy of probiotics in reducing the incidence and severity of necrotizing enterocolitis (NEC) in very low birth weight (VLBW) infants was evaluated. The infants in the study group were fed with Infloran (*Lactobacillus acidophilus* and *Bifidobacterium infantis*) with breast milk twice daily until discharged. Infants in the control group were fed with breast milk alone. Infloran as probiotics fed enterally with breast milk reduces the incidence and severity of NEC in VLBW infants [21].

Cosmetic: Botulinum toxin (BTX) produced by the bacterium *Clostridium botulinum* widely used for cosmetic applications and in various medical aspects. Injection of botulinum toxin can be used to prevent development of wrinkles by paralyzing facial muscles [10].

Traditional Indian fermented food

Fermented foods such as idli and dahi were described as early as 700 BC. At present, there are hundreds of fermented foods with different base materials and preparation methodology. Each fermented food is associated with a unique group of microbiota, which increases the level of proteins, vitamins, essential amino acids and fatty acids (see table no.2)[22]. Foods like idlis, dosas, dhoklas, wadas and kadhi are some of the lactobacillus fermented cereals and legumes that are commonly consumed in India. The fermented foods increase the absorption of vital minerals from gastrointestinal tract, thus preventing mineral deficiencies. Bread, fish sauce, wine and beer are some of the yeast-based fermented food beverages. Experts say that probiotic foods improve immunity, aids in better digestion, absorption of calcium and prevention of allergies. They also help in treating diarrhoea.

Table 2 Popular Indian Fermented foods and associated microbial species (Gupta, Saxsena *et al.*).

Fermented food	Ingredients	Place	Microbial species
Rabdi (rabadi)	Flour of barley, pearl millet, corn or soybean and country buttermilk	Rajasthan	<i>Bacillus</i> and <i>Micrococcus</i> sp.
Kulu	Wheat flour, buttermilk	Himachal Pradesh	<i>Lactobacillus</i> sp.
Idli	Rice, black gram dhal, table salt, fenugreek seeds	South India	<i>L. mesenteroides</i> , <i>E. faecalis</i> , <i>P. cerevisiae</i>
Dosa	Rice, black gram dhal (either raw or parboiled rice), table salt	South India	<i>L. mesenteroides</i> , <i>E. faecalis</i>
Dhokla	Bengal gram dhal, rice and leafy vegetables	Gujrat	<i>L. fermentum</i> , <i>L. mesenteroides</i> , <i>E. faecalis</i>
Chilra or Iwar	Wheat/barley, buckwheat flour and starter material Treh	North India	Not reported
Sinki	Radish root	North-east India	<i>L. casei</i> , <i>L. brevis</i> , <i>L. plantarum</i> , <i>L. fallax</i> ,
Kinema	Soybeans	Darjeeling, Sikkim	<i>E. faecium</i>
Kanji	Carrot or beet root, rice, mustard	North India	<i>L. pentosus</i> , <i>L. paraplantarum</i> , <i>L. plantarum</i>

If a pregnant woman consumes probiotic food like a month before her delivery, this will help prevent the new born infant

from contracting allergies to some extent. Also, if infants who are six months and older are given probiotic food it helps to build their immunity [22].

CONCLUSION & DISCUSSION

On the basis of above instances, microbe seems to be shared approximately equal characteristics, whether favourable or not. Microbial outbreaks have been caused harm to economy and health. Food contamination and spoilage is the biggest health concern for us; on the other hand some pathogens tend to resist conventional medicine, and might be triggers life threatening conditions, for instance antibiotic resistant tuberculosis remained major challenge in India. On the other hand microbes being employed in various human welfare aspects, especially in health sector i.e. insulin production, anti ageing agent, anticancer, immune modulator, digestive, hepato protective and many gastrointestinal ailments. However, some harmful species are also being used to obtain desirable products, by attenuating, weakening, and plasmid modification. Therefore it's upon our intellect how we interact with them and how we manipulated them. Recent research such as their specific behaviour, communication (Quorum sensing) etc. makes them friendly companion.

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