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A REVIEW ON: BIOLOGICAL IMPORTANCE OF MICROBES IN FOOD, AGRICULTURE, AND PHARMACEUTICAL INDUSTRY

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ABSTRACT

Biotechnology is the most prominent and rapidly growing segment of the biological sciences that is making its diversified application in sustainable agriculture. Biofertilizers, biopesticides, bioherbicides, bioinsecticides, and many of the other fungal based and viral based insecticides, obtained using microorganisms, are some of the outcomes of biotechnology playing a key role in sustainable agriculture. Many of other important food products are also obtained by microbial fermentation. Different microbes are added to get the desired effect of food at the specific stages of food production process. Pharmaceutical microbiology includes the manufacturing of different pharmaceutical and medicinal products. This review article has a wide overview of microbes mainly used in agriculture, food industries, and pharmaceutical industries.

1. INTRODUCTION

Biotechnology is making the use of microorganisms including fungi, bacteria, and viruses in fields of agriculture, food, and pharmaceutical products. Farmers and researchers are working to make the microbes as pests control agent that is destructive to their crops. Soil microbes, including bacteria and fungi, are essential for decomposing organic matter and recycling dead plant material. In biotechnology and bio manufacturing, these tiny microbes and living cells are like miniature chemical factories that produce the vital products such as amino acids, enzymes, medicines, and food additives. Naturally, microorganisms are used to carry out fermentation processes and for thousands of years man has been using yeasts, molds and bacteria to produce many of food products, that is, bread, vinegar, beer, wine, cheese, and yoghurt, as well as fermented fish, meat, and vegetables by making the use of microorganisms. Microbes are used for the fermentation of different types of food to produce a variety of oriental food products. By making the use of microorganisms in large quantity, numbers of biological preparations have been prepared that have the great importance in field of medicine and pharmacy. .[1]

What are Microbes?

Microbes are also called as the microorganisms. They are the major components of biological systems on the planet earth, which are present everywhere, around us, in the soil, water, air, and both in and on our body. They are also found in other animals and plants. These organisms are so minute and vary in their size and shapes, which cannot be seen by our naked eyes. They can only be seen through the microscope, therefore, they are also referred to as the microscopic organisms. The different types of microbes are:

- Algae
- Bacteria
- Fungi
- Protozoa
- Virus.[2]

Following are some departments where microbes are used:-

AGRICULURE INDUSTRY

Microbial Diversity and Its Interaction With Plant-Soil System

Soil microorganisms like bacteria, algae, fungi, actinomycetes, protozoa and the infective agents such as viruses are the bodies within the massive resources of activities of microscopic diversity. These soil microorganisms perform many valuable functions as well assome harmful impacts. In the soil profile, the impact of soil biota is multifarious and difficult since the same action may be harmful or positive depending on its position . On theother hand, plants show a different range of interactions with these soil-dwelling microorganisms which extends the full variety of biological possibilities (competitive, exploitative, neutral, commensal and mutualistic). However, according to current situation, the alleviating pathogenic effects suchas infection and herbivory are more studied .

As the interactions between plant and microscopic communities are predisposed by various agronomic managements and biological factors predominantly in the present situation of worldwide revolution, the influence of ecological stress aspects must be considered, as they affect proper management of the interactions between crop-microbiome . The soil formation with a high level of soil fertility is a result of more than hundreds of years of soil ―evolution‖ this statement is not surprising due to the complex interactions among microbes and plant-soil system. . The interaction among microbes and plants within the soil system is shown in

Figure 1; Interactions between microbial communities and plant

Beneficial Aspects of Microbes

The soil fertility and its formation from mineral bedrock involves a multifarious interaction of chemical, physical and biological processes. The development rate of the soil is controlled by some factors such as topography, climate, time, bedrock type, plants and microbes that's why the status of nutrients is determined by the quality and identification of microbes in soil . Three types of machines are typically studied and put forward to describe that how microscopic activity can lead to the improvement in plant growth:

a) by manipulating the plant hormonal signaling ;

b) by pathogenic microscopic strain outcompeting or repelling and

c) By increasing soil-borne nutrients bioavailability.

Soil microbes create a link between soil and roots, nutrients recycling, organic matter decomposition and react rapidly to any variations that occur in the ecology of soil by performing as perfect indicators for definite functions in the surroundings of soils . To increase plant yield, a range of non-symbiotic bacteria (Azotobacter, Azospirillum, Bacillus and Klebsiella sp.) and symbiotic bacteria (Rhizobium sp.) are now being used globally (Figure 2) . The living constituents of soil organic matter is microbial biomass. In the meantime, microbes are valuable in reducing the problems that are related to the application of chemicalfertilizers and pesticides, they are extensively being applied in natural agricultural land and organic agriculture . Microbial biomass affects nutrient storage, nutrient transformations, and cycling as the active component of organic matter .

Figure 2: Rhizobium sp and their roles in plant.

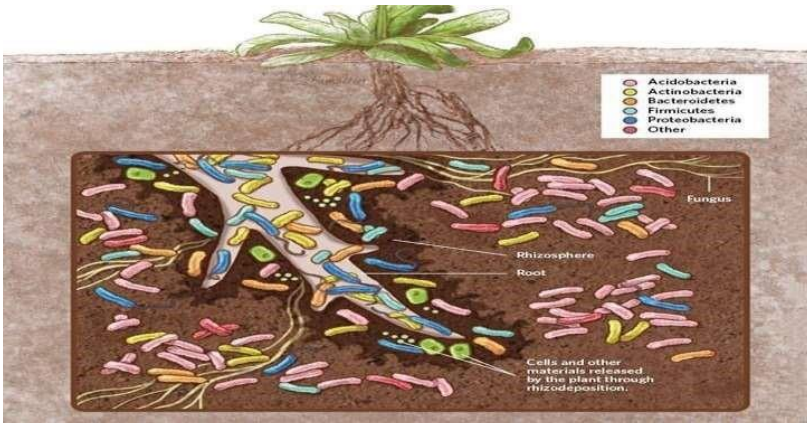
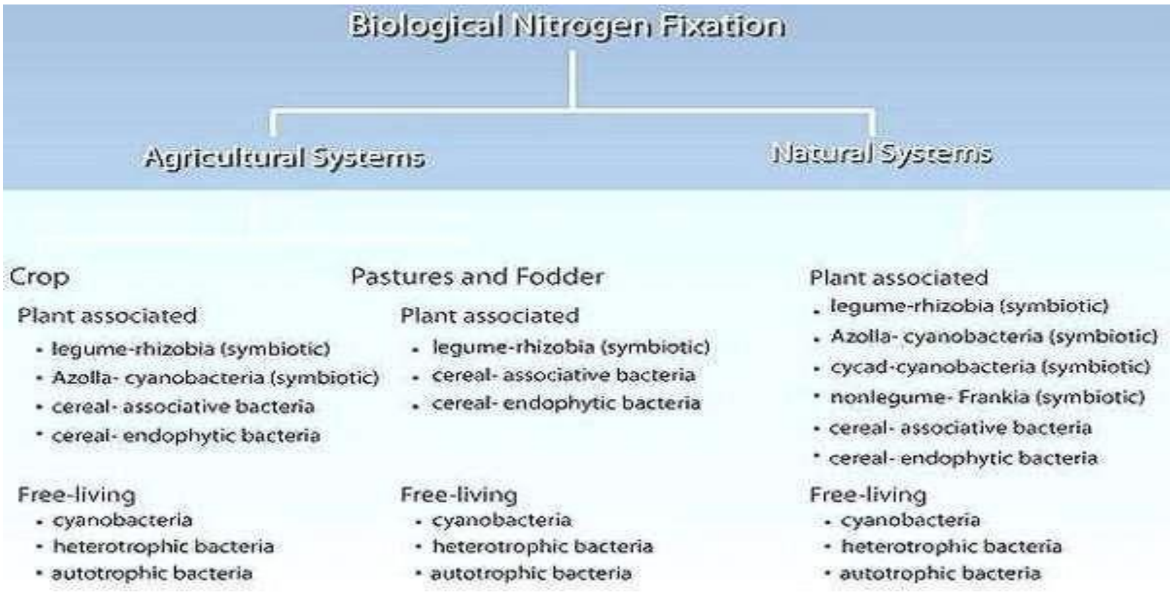


Figure 3: Types of microorganisms involved in BNF at a glance.



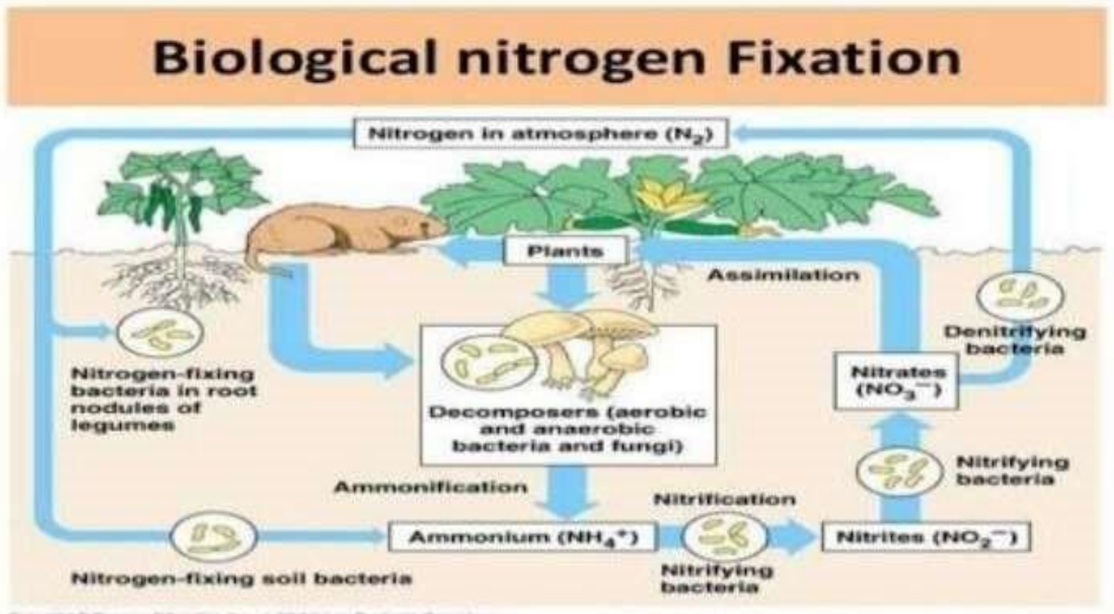


Figure 4: Biological nitrogen fixation cycle

The soil production and soil fertility may increase by both fungi and bacteria with organic matter. According to an estimation, soil with the weight of one gram may comprise 200 m hyphae of fungal and 6,000–50,000 species of bacteria and the bulk of them are considered to be favorable for soils as well as plants. By controlling the source of obtainable nutrients to pathogens valuable microbes can overturn the growth of phytopathogens in a variability of ways such as contending for space and nutrients . It also helps in plant growth promotion as well as phytopathogen suppression and causes mineral uptake from the soil, nutrient achievement and organic matter decomposition.[4]

Nitrogen-Fixing Bacteria

Nitrogen plays an important role in the production of food and promotes plant growth, it is also essential for the synthesis of cellular enzymes, chlorophyll, proteins, RNA and DNA. Nitrogen is provided through the fixation of symbiotic interaction of atmospheric N2 by nitrogenase in rhizobial bacteroids for the nodulating legumes. In agriculture currently, 65% of the nitrogen is utilized through the process of biological nitrogen fixation and will remain to be vital in upcoming sustainable systems of crop production. Favorable plant mutualistic symbionts comprise multifunctional arbuscular mycorrhizal (AM) fungi and the nitrogen- fixing bacteria. The diverse genera of bacteria collectively named "rhizobia" are capable to fix nitrogen in mutualistic symbiosis with plants legume . It should be stated that nitrogenase genes are existing in miscellaneous microbial taxa concerning the taxonomy of nitrogen- fixing symbioses. Significant biochemical reactions of biological nitrogen fixation occur mostly through the symbiotic relationship of legumes with nitrogen-fixing microbes that alters elemental nitrogen into ammonia and that non-leguminous plants have been recognized to host nitrogen-fixing microbial strains of bacteria possibly indicating that other plant microorganism mixtures (not just legumes and Rhizobia) could be correspondingly optimized to indorse N2- fixation. Other bacteria (actinomycetes) belonging to the genus Frankia form nitrogen-fixing nodules on the root of the so-called ―actinorhizal‖ plant species having a great environmental significance [37-40]. The

Group of microorganisms involved in biological Nitrogen Fixation is shown in Figure 3 and process of BNF is given in Figure 4.

Conclusion:

In nutrients cycling within the soil microorganisms play a vital role and and all the beneficial microbes are located around the root zones of the plant. Microorganisms are the indicator of soil health as well as soil productivity. The presence of organic matter within the soil is itself nothing until or unless beneficial microorganism's act on it and convert it into available form (humus) by releasing the different types of enzymes. Manipulating the interaction between plant and microbes is leads to an increase in plant growth as well as soil health within the ecofriendly environment. Therefore, it is concluded that soil health and crop production can only be improved by soil microbes.[5]

2. FOOD INDUSTRY

There are many useful applications of microbes in the food industry. They influence the quality, availability and quantity of food. Microorganisms are used to change one substance to another which is used as food, such as milk to yoghurt and cheese, sugar to wine and bread.

Key Events in the History of Food Microbiology :

- **7000 BCE –** Evidence of fermentation used by the ancient Babylonians to produce beer. Fermented drinks have long been considered safer to consume than local water supplies, which can be contaminated with water-borne diseases such as cholera from sources such as raw sewage. Even today, in underdeveloped countries without access to modern sanitation this is still the case. Wine would not appear until 3,500 BCE.
- **3000 BCE –** The first recorded manufacture of cheese and butter by the Egyptians and the Sumerians. As these are fermented foods, they are also much safer to consume than milk, their raw counterpart. Several ancient cultures were also learning to use salt as a preservation technique around this time.
- **1000 BCE –** Preservation of shrimp in the snow by the Romans as well as smoked and fermented meats.
- **1665 –** Francesco Redi demonstrates that maggots are the larval stage of flies with an experiment that helped to disprove the spontaneous generation theory which had held sway since ancient times. Further experiments by Schwann and Spallanzani were carried out in the next two centuries, although the doctrine of spontaneous generation persisted.
- **1683 –** Anton van Leeuwenhoek, the discoverer of the microbial world, examined and described bacteria by using a recent invention: the microscope. His scientific observations and reports were widely published by the newly formed Royal Society in England, leading to the formation of the field of microbiology.
- **1857 –** Louis Pasteur (from whose name we get the term pasteurization) demonstrates that microbes cause the souring of milk. Further experiments by Pasteur demonstrated that heat destroyed microbes in wine and beer, and that fermentation was caused by microbial activity. He also discovered that different types of fermentation were caused by different micro-organisms.
- **The late 1800s** – Legislation to protect food quality starts to be enacted by several governments.
- **The 1920s –** A severe outbreak of botulism, which is caused by the microbe *C. Botulinus* prompts the U.S. canning industry to adopt conservative heat treatment processes which reduced the survival of botulism significantly. To date, since adopting these processes, there have only been 5- 6 known cases of botulism. The dairy industry, responding to several outbreaks of diseases such as brucellosis, also started to enact stringent microbial-based reforms.

The application of microbiological standards to the food industry has continued unabated since then, with more legislation and the development of processes that ensure the safety of food having been enacted and developed over the intervening decades.[6]

Fermented Dairy Products:

Fermented milk is produced by inoculating pasteurised milk with specific culture of microorganisms. The different fermented dairy products include yoghurt and cheese.

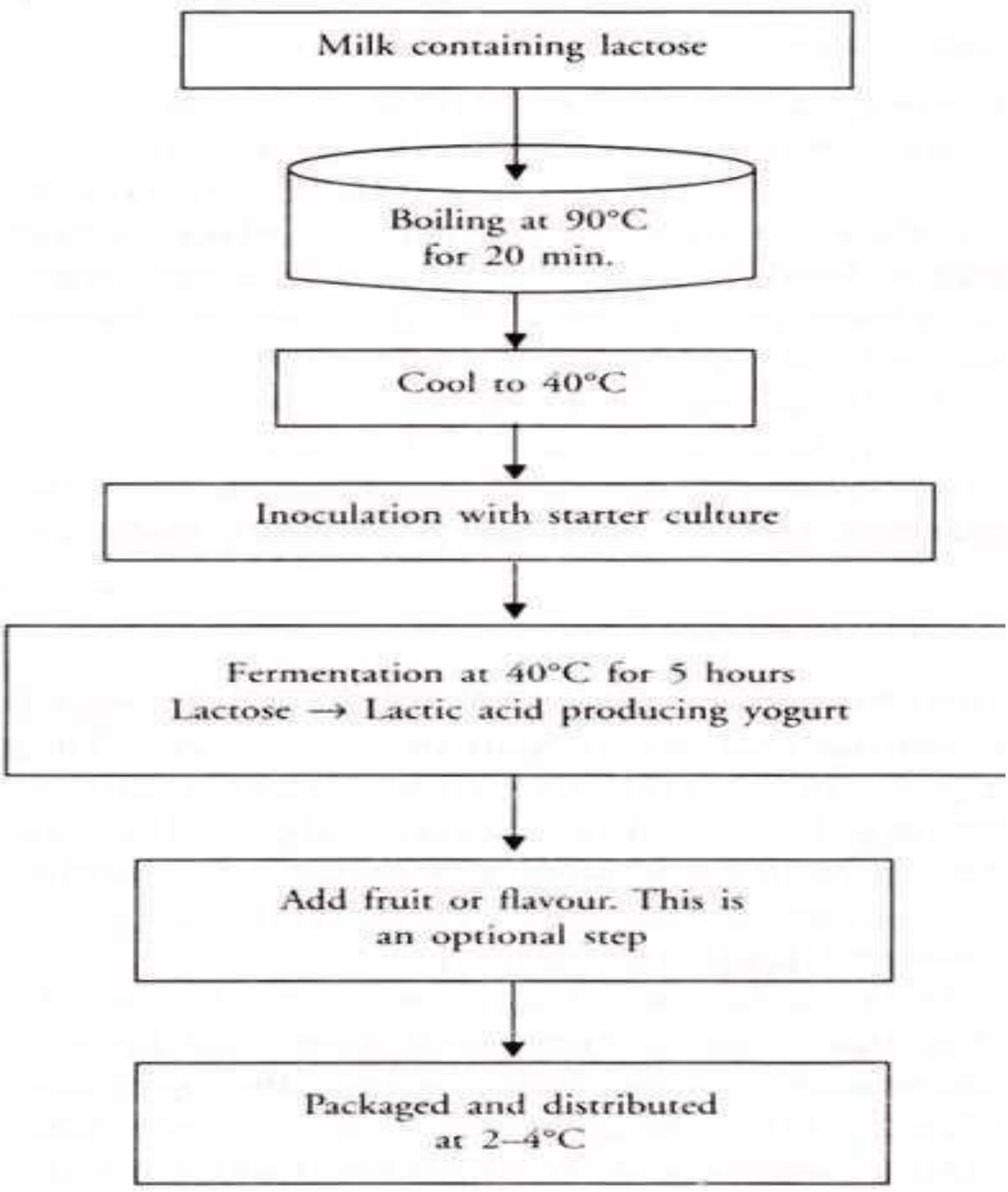
Bacteria is used in Yoghurt Making:

Yoghurt is a dairy product which is produced by the bacterial fermentation of milk.

Most commonly, cow's milk is used, though it can be made from any kind of milk. It can be prepared from a variety of milk including whole, skimmed, dried, evaporated or semi-skimmed milk.

The milk sugar, i.e. lactose is fermented into lactic acid by the friendly bacteria, Streptococcus salivarius, S. thermophilus and Lactobacillus bulgaricus. These bacteria are collectively known as lactic acid bacteria or LAB. The bacteria feed on the lactose and release lactic acid as a waste product

The steps involved in yoghurt making are illustrated in Fig. 5:



The acid cause the curdling of the milk protein, casein into a solid mass called curd. The gel like texture and taste of yoghurt is due to the fermentation of lactose to lactic acid. The increased acidity (pH = 4-5) also prevents the proliferation of other potentially pathogenic bacteria.

Both unpasteurised and pasteurized milk may be used for yoghurt making. The use of unpasteurised milk maintains the healthy balance of bacteria and enzymes of milk in its unprocessed state under very carefully controlled temperature and environmental conditions. To ensure complete fermentation two or more different bacteria may be used together.

Yoghurt is often sold sweetened and flavoured, or with fruit added at the bottom.

The flavour varies in different countries.

a) Lassi is yoghurt-based beverage in India and is consumed either salty or sweet. Salty lassi is usually flavoured with ground- roasted cumin and black pepper powder, while the sweet variety is served with lemon, mango or other fruit juice.

b) A lassi-like, salty drink called ayran is popular in Turkey and Bulgaria and is prepared by mixing yoghurt with water and salt.

In India, Bulgaria and Turkey yogurt is prepared at home using a small amount of plain active culture yogurt as the starter culture. The milk is boiled to kill undesirable microbes. It is cooled to about 40°C. A tablespoon of starter culture is added and mixed thoroughly. It is left undisturbed for about 6 hours.[7]

Molds :

The term mold is applied to certain multicellular, filamentous fungi whose growth on foods is usually readily recognized by its fuzzy or cottony appearance. Generally molds are concerned in the spoilage of foods; moldy or mildewed food is considered unfit to eat. On the other hand some of molds are used in manufacture of different foods and are ingredients of some foods. Some kinds of cheese are mold- ripened (e.g. Roquefort, Camembert). Molds are grown as feed and food and are employed to produce products used in foods, such as amylases and other enzymes for bread making or citric acid used in soft drinks. Molds are major contributors in the ripening of many oriental foods. A species of Bothrytis cinerea, is responsible for the noble rot of grape. Molds are used for production of several antibiotics.

Morphological Characteristics:-The gross appearance of a mold growing on a food is often enough to indicate its genus. Some molds are fluffy, others are compact. Some look velvety on the upper surface, some dry and powdery, and others wet or gelatinous. Pigments in the mycelium—red, purple, gray, black, etc.—are also characteristic. Some molds are restricted in size, but others seem limited only by the food or container. Macroscopically the mold consists of a mass of branching, interwined filaments called hyphae (singular hypha), and the whole mass of these hyphae is known as a mycelium. Hyphae may be classed as vegetative or fertile based on their biological function. The vegetative hyphae or growing hyphae are concerned with the nutrition of the mold and the fertile ones with the production of reproductive parts. The hyphae of some molds are full and smooth, but the hyphae of others are characteristically thin and ragged. A few kinds of molds produce sclerotia (singular sclerotium) which are tightly packed masses of hyphae, often thick-walled, within the mycelium. These sclerotia are considerably more resistant to heat and other adverse conditions than the rest of the mycelium and for this reason may be important in some processed food products. With microscopic study, further details of molds may be recognized. In the group of molds called septate the hyphae are divided by cross-walls into cells.

The hyphae of the nonseptate group consist apparently of cylinders without cross walls. The reproductive parts or structures of molds are the spores, which are mainly asexual. Such spores are produced in large numbers and are readily spread by air. Spores that settle on favorable substrates can initiate a new phase of growth and develop into a new mycelium.

Physiological Characteristics:- In general, molds require less moisture than bacteria and yeasts. Molds differ considerably among themselves as to optimum water activity and range of water activity for germination of spores. The minimum water activity for spore germination has been found to be as low as 0.62 for some molds and as high as 0.93 for others. Each mold has an optimum of water activity and a range of water activity for growth.

The reductions of UNESCO – EOLSS SAMPLE CHAPTERS FOOD QUALITY AND STANDARDS – Vol. III - Microorganisms Important in Food Microbiology - Radomir Lasztity ©Encyclopedia of Life Support Systems (EOLSS) water activity below the optimum for a mold delays the germination of the spores and reduce the growth rate. Most molds grow well at ordinary room temperatures and are classified as mesophilic. The optimum is for most molds between 25 and 30 o C. Nevertheless it should be noted that some molds grow fairly well at temperatures of freezing or just above, and others can grow slowly at sub-zero temperatures. Molds require free oxygen for growth. This is why molds grow on the surface of contaminated food. Most molds grow over a wide range of pH, but some are favored by acid foods such as the majority of fruits.

Classification of Molds and Molds of Industrial Importance:- It is beyond the scope of this article to discuss in detail the complicated system of classification of molds. In the following only genera of industrial importance will be shortly overviewed.

Genus Mucor (Mucor racemosus, Mucor rouxii). Mucors are involved in the spoilage of some foods and in the manufacture of others e.g. oriental fermented foods.

Genus Rhizopus. Rhizopus nigricans, sometimes called „bread mold‖, is very common and is involved in the spoilage of many foods such as berries, fruits, vegetables, bread, etc. Genus Aspergillus. The members of this genus are very widespread. Many are involved in the spoilage of foods and some are useful in preparation of fermented foods. Many groups and hundreds of aspergillus species are known.

Aspergillus niger is the leading species important for food microbiologists.

Selected strains are used for commercial production of citric and gluconic acids.

Genus Penicillium. This is another widespread genus important in foods.

Penicillium expansum, a green spored species, causes soft rot of fruits.

Penicillium camemberti with grayish conidia, useful in the ripening of Camembert cheese, and Penicillium roqueforti, used in ripening of blue cheeses, are also weel known members of this genus.

Genus Bothrytis. The species Bothrytis cinerea causes the noble rot of grape in some wine producing areas such as Tokay (Hungary).

Genus Alternaria. Molds of this genus are common causes of the spoilage of foods.

Alternaria citri, Alternaria tenuis and Alternaria brassicae are the common species.

Genus Neurospora (Monilia). The species of this genus grow on various foods.[8]

Bacteria and Fungi are used in Cheese Making:

Cheese is prepared by inoculating milk with a starter culture containing specific microorganisms. Cheese is a solid food made from the milk of various animals, most commonly cows. Milk from goat, sheep, reindeer and water buffalo may also be used. There are several types of cheese.

Fermentation of milk leads to lactic acid production, which sours the milk. This leads to coagulation of milk protein, casein. The solid part of the milk produced by coagulation is known as curd and the liquid is known as whey.

The curds can be separated and pressed into desired shape and whey is used as food source for yeasts, which in turn can be processed as cattle feed and is rich in protein and vitamins. The cheese can be matured or ripened by the addition of bacteria or fungi or both. The bacteria added reduce the pH, alters texture and develops a flavour.

Coagulation can be controlled using rennet tablets, which contains the enzyme rennin. Rennin is an enzyme present in the stomach of Calves but now is also available in genetically engineered bacteria. Coagulation can also be done using acids such as vinegar or lemon juice.

Depending on the nature of the organism added, cheese is of the following types:

a) Cheddar cheese is prepared by the addition of bacteria to enhance its flavour and texture.

b) The use of mould fungi produces Roquefort cheese and blue cheese

c) A combination of both bacteria and fungi produces camembert cheese.

d) Swiss cheese is prepared by the addition of Propionibacterium sharmanii. The big holes in the cheese is because of the production of large amounts of CO_2.

The natural colour of cheese ranges from off-white to yellow. Herbs and spices may also be added to the cheese. Other factors that contribute to a different flavours and styles of cheese are different levels of milk fat, variations in length of aging, different processing treatments and different breeds of cows, sheep or other mammals.

Table 1 summarises the major classes of cheese:

Class of cheese	Type
White mold cheese	Camembert
Blue mold cheese	Roquefort
Red surface bacteria cheese	Limburger
Hard-grating cheese	Parmesan
Cheese with eyes	Swiss
Pasta filata cheese	Mozzarella
Hard cheese	Cheddar
Semi-hard cheese	Double Gloucester, Edam and Gouda
Soft, unripened cheese	Cottage cheese, Hoop cheese
Whey cheese	Ricotta cheese, Mysost, Brunost cheese
Sour milk cheese	Harzer

Cheese is sold in the form as slices or in blocks or as a thick fluid. In addition, there is a class of cheese known as processed cheese or cheese food. Processed cheese is similar to cheese, but contains emulsifying salts acting as stabilisers. Heat treatment during the manufacturing process gives processed cheese a mild flavour.[9]

Other Fermented Foods:

Some important food produced in whole or in part by microbial fermentation are pickles, sausages, etc. Different microorganisms are added to specific stages of food production to produce the desired effect. Moulds are used for the fermentation of rice to produce a variety of oriental foods.[10]

Yeast is used for Making Bread:

Yeast is a fungus that feeds saprotrophically. The enzymes secreted by the yeast cell, digest food that contains sugar and minerals. Yeast is used to make bread. When yeast is added to raising flour and water, carbon dioxide is produced which gets trapped in the dough prepared from the flour.

The dough rises and bread is made. The flour is usually made from wheat and contains starch. Starch is the energy source for the yeast. The flour also contains a protein called gluten, which forms sticky stretchy threads as the yeast works on the sugar. The threads trap the carbon dioxide and make the dough rise well.

Some commercial uses of yeast are shown in Table2:

Types of yeast	Product	Uses
Saccharomyces cerevisiae	Beer, Wine, Bread, Baker's yeast	Baking industry and brewing industry
Saccharomyces rouxii	Soy sauce	Food condiment
S. cerevisiae	Ethanol	Fuel, solvent
Eremothecium ashbyi	Riboflavin	Vitamin supplement

Baker's Yeast:

Yeast is used as leavening agent in baking since earlier times. The most commonly used species is Saccharomyces cerevisiae because of its ability to ferment sugar in the dough vigorously and to grow rapidly. The carbon dioxide used during the fermentation is responsible for the leavening or the rising of the dough. The procedure of mass production of Baker's yeast is elaborate under controlled conditions of pH, temperature conditions. [11]

Microorganisms as Food – Single Cell Protein:

Algae, yeasts and bacteria can be grown in large quantities to yield a cell crop which is rich in protein known as single cell protein. The protein may be used for human consumption or as animal feed. It may be a useful source of minerals, vitamins, fat and carbohydrates. The composition of the different SCP depends upon the organism and the substrate on which it grows.

The advantages of using microorganisms as a food source are:

a) They grow very fast and do not need much space as conventional crops.

b) They grow on a wide range of cheap, waste products of agriculture and industry such as petroleum products, methanol, ethanol, sugar, molasses, waste from paper mills etc. The secondary advantage is that they help in recycling the materials and thereby clean up the wastes.

c) They are high yielding. In a growth medium of 1000 lb of yeast in one day, many tonnes of protein is produced. This is about 10-15 times greater than soyabean and about 25-50 times greater than corn.

d) The protein content of the cells is very high. Yeast cells have a protein content as high as 40-50%; for algae the range is 20- 40%.

e) The proteins of the microorganism contain all the essential amino acids.

f) Some microorganisms, particularly yeasts, have high vitamin content.

g) Factors, such as climate do not affect them, since they do not occupy large areas of land.

Pruteen was the first major SCP to be produced. It was produced by a bacterium, Methylophilus methylotrophus. Methanol was used as a source of energy and the temperature was maintained at 30-40°C and pH at 6.7.

Methanol + Nitrogen + Mineral salts + Oxygen $\longrightarrow$ SCP + CO_2 + Heat energy + Water

Pruteen synthesis

Pruteen was rich in essential amino acids and has high vitamin content. It is twice as nutritious as soyabean meal and was used as an animal feed.

Some disadvantages of using SCP:

a) The high nucleic acid content causes intestinal disturbances. It can also lead to an increase in the uric acid in the blood that will eventually lead to gout. Additional processing can be done to reduce the nucleic acid content, but this would increase the cost.

b) Bacterial cells have small size and low density, which makes harvesting from the fermented medium difficult and costly.

c) The taste is not acceptable for many persons. Individual taste and customs make microorganism unattractive as a food to some individuals.[12]

Chocolate production:- by yeast and bacteria Chocolate is produced with the help of microbes. Chocolate is actually obtained from the seeds of cacao trees. These seeds are present in white fleshy pods of cacao trees For the removal of the seeds out of these pods, the pods are fermented first with naturally occurring microbes mainly includes yeasts and bacteria, that is, Lactobacilli and Acetobacter. The raise in temperature during fermentation process is occurred and products obtained by these microorganism, that is, the ethanol produced from yeast, kill the beans, and become contributor in flavoring of the chocolate. In chocolate, fermentation is the process that produces aromas, flavor, and rich colors. There are two stages involved in this process, that is, alcoholic fermentation and acetic acid fermentation. In this process, first, the sugar is converted into alcohol in the cocoa pulp by yeast activity.

Then, bacteria oxidize the alcohol and produce acetic acid.[13]

WINE AND BEER

Without doubt the first use man made of micro-organisms was in the conversion of the juice of grapes and other fruits to wine. This natural process, which prolonged the length of time a fruit product could be kept, was employed wherever fruit was available. Over 100,000,000 gallons of wine is now being produced every year in the United States. Yeasts are naturally present on the stems and skins of grapes and on most other fruits as well. When the berries are crushed, the yeasts multiply rapidly in the juice, forming carbon dixoide and alcohol from the sugar. If the proper control is exercised over the fermentation, almost all other micro-organisms can be prevented from growing in the material. Most scum or surface-growing forms can be eliminated by sealing the product from the air and allowing the carbon dioxide formed by the yeast fermentation to sweep all of the oxygen out of the container. In making champagne, the carbon dioxide is retained in the liquid by keeping the container stoppered; a pressure of as much as 120 pounds per square inch is developed. In order to insure a good clean fermentation, most wineries inoculate the must or juice with a pure culture of wine yeast, which gets a head start on the other micro-organisms and prevents an undesirable type of fermentation. Most wine yeasts grow well in acid solutions and at temperatures slightly below the optimum for the growth of most bacteria. Where low temperatures are not available treatment with sulfur dioxide or pasteurization of the must is often employed. Yeasts are tolerant of concentrations of sulfur dioxide that will kill most spoilage organisms. When all of the sugar of the must has been converted to alcohol, the yeasts die for lack of food and because of the killing action of the alcohol. Light wanes contain up to 14 percent of alcohol by volume, but 16 or 17 percent may be obtamed by natural fermentation when the juice has a very high sugar content. By special methods of feeding the yeast an alcohol content as high as 21 percent has been attained. Wines stored in casks should be sealed from the air to prevent spoilage, and spoilage organisms in bottled wines can be killed by pasteurization. Beer is made by a yeast fermentation of malted cereal grain extracts. The sugars are converted to carbon dioxide and alcohol as in the wine fermentation, but the percentage of alcohol produced in beer is very much lower. In the case of beer the carbon dioxide is retained in the product under considerable pressure. This not only adds to the palatability but aids in the preservation of the product. Since the acidity of the beer is relatively low there is danger of souring by the action of the lactic acid bacteria unless the proper precautions are taken. Most present-day beer is pasteurized in order to insure its keeping quality in the bottle or can.[14]

VINEGAR:-The first step in any vinegar process is the production of alcohol as in making wine or beer. Cider vinegar is produced from fermented cider, while wliite or distilled vinegar may be made from the alcohol distilled from fermented mashes, molasses, or other saccharine materials. After fermentation, the alcohol is converted to acetic acid by an oxidation process carried on by acetic acid bacteria. Whereas the yeast fermentation is carried out in the absence of air, the conversion of the alcohol to acetic acid can be carried out only in the presence of air. In the old barrel method the acetic acid bacteria are allowed to grow on the surface of the alcohol solution, while in the generator process the alcoholic solution is allowed to trickle down through towers filled with shavings, pumice, rattan, or other filling material. Millions of gallons of vinegar are produced each year by this use of micro-organisms in these two relatively simple processes.[15]

3. PHARMACEUTICAL INDUSTRIY

ROLE OF MICROORGANISM FOR PHARMACEUTICAL PRODUCT

The important products that manufactured by microorganism in pharmaceutical industry is described below-

VACCINE

A vaccine is a biological preparation that improves immunity to a particular disease. A vaccine typically contains an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as foreign, destroy it, and "remember" it, so that the immune system can more easily recognize and destroy any of these microorganisms that it later encounters.

There are several types of vaccines in use. These represent different strategies used to try to reduce risk of illness, while retaining the ability to induce a beneficial immune response.

Types of Vaccine Killed

Some vaccines contain killed, but previously virulent, micro-organisms that have been destroyed with chemicals, heat, radioactivity or antibiotics. Examples are the influenza vaccine, cholera vaccine, bubonic plague vaccine, polio vaccine, hepatitis A vaccine, and rabies vaccine.

Attenuated

Some vaccines contain live, attenuated microorganisms. Many of these are live

viruses that have been cultivated under conditions that disable their virulent properties, or which use closely related but less dangerous organisms to produce a broad immune response. Although most attenuated vaccines are viral, some are bacterial in nature. They typically provoke more durable immunological responses and are the preferred type for healthy adults. Examples include the viral diseases yellow fever, measles, rubella, and mumps and the bacterial disease typhoid. The live Mycobacterium tuberculosis vaccine developed by Calmette and Guérin is not made of a contagious strain, but contains a virulently modified strain called "BCG" used to elicit an immune response to the vaccine.

Toxoid

Toxoid vaccines are made from inactivated toxic compounds that cause illness rather than the micro-organism. Examples of toxoid-based vaccines include tetanus and diphtheria. Toxoid vaccines are known for their efficacy. Not all toxoids are for micro-organisms; for example, *Crotalus atrox* toxoid is used to vaccinate dogs against rattlesnake bites.

Subunit

Protein subunit – rather than introducing an inactivated or attenuated micro- organism to an immune system (which would constitute a "whole-agent" vaccine), a fragment of it can create an immune response. Examples include the subunit vaccine against Hepatitis B virus that is composed of only the surface proteins of the virus (previously extracted from the blood serum of chronically infected patients, but now produced by recombination of the viral genes into yeast), the virus-like particle (VLP) vaccine against human papillomavirus (HPV) that is composed of the viral major capsid protein, and the hemagglutinin and neuraminidase subunits of the influenza virus. Subunit vaccine is being used for plague immunization.

Conjugate

Conjugate – certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g. toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen.

This approach is used in the *Haemophilus influenzae* type B vaccine.

Valence

Vaccines may be *monovalent* (also called *univalent*) or *multivalent* (also called *polyvalent*). A monovalent vaccine is designed to immunize against a single antigen or single microorganism. A multivalent or polyvalent vaccine is designed to immunize against two or more strains of the same microorganism, or against two or more microorganisms. In certain cases a monovalent vaccine may be preferable for rapidly developing a strong immune response.[16]

ANTIBODY

An antibody (Ab), also known as an immunoglobulin (Ig), is a large Y-shaped protein produced by B-cells that is used by the immune system to identify and neutralize foreign objects such as bacteria and viruses. The antibody recognizes a unique part of the foreign target, called an antigen. Each tip of the "Y" of an antibody contains a paratope (a structure analogous to a lock) that is specific for one particular epitope (similarly analogous to a key) on an antigen, allowing these two structures to bind together with precision. Using this binding mechanism, an antibody can *tag* a microbe or an infected cell for attack by other parts of the immune system, or can neutralize its target directly (for example, by blocking a part of a microbe that is essential for its invasion and survival). The production of antibodies is the main function of the humoral immune system.

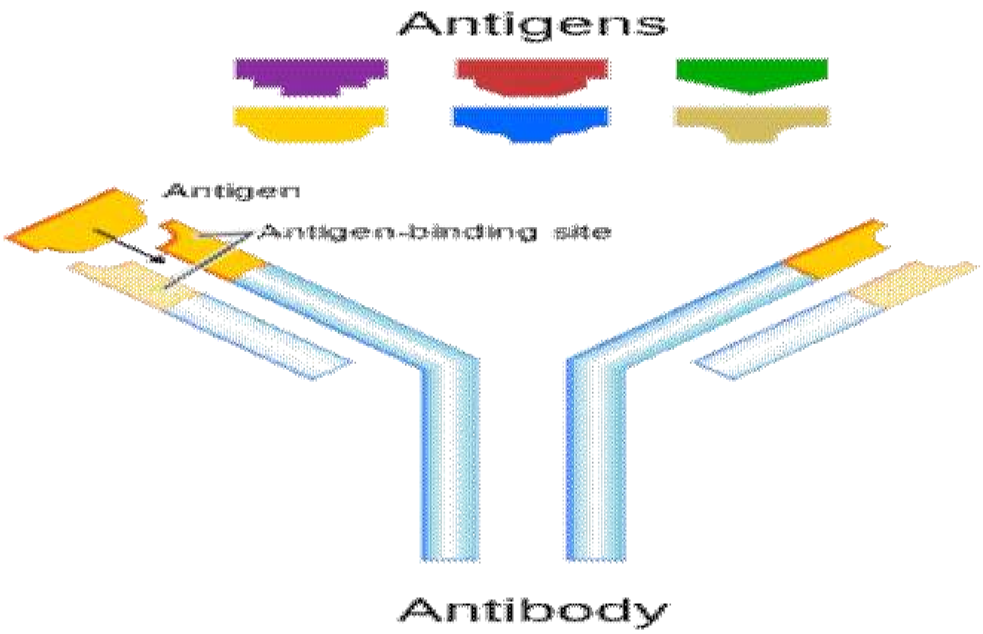


Fig :6 Antibody

Antibodies are glycoproteins belonging to the immunoglobulin superfamily; the terms antibody and immunoglobulin are often used interchangeably. Antibodies are typically made of basic structural units—each with two large heavy chains and two small light chains. There are several different types of antibody heavy chains, and several different kinds of antibodies, which are grouped into different isotypes based on which heavy chain they possess. Five different antibody isotypes are known in mammals, which perform different roles, and help direct the appropriate.[17]

ANTIBIOTICS

An antibacterial is an agent that inhibits bacterial growth or kills bacteria. The term is often used synonymously with the term antibiotic(s). Today, however, with increased knowledge of the causative agents of various infectious diseases, antibiotic(s) has come to denote a broader range of antimicrobial compounds, including anti-fungal and other immune response for each different type of foreign object

Fig 7:- Antibiotics

The term *antibiotic* was first used in 1942 by Selman Waksman and his collaborators in journal articles to describe any substance produced by a microorganism that is antagonistic to the growth of other microorganisms in high dilution. This definition excluded substances that kill bacteria, but are not produced by microorganisms (such as gastric juices and hydrogen peroxide). It also excluded synthetic antibacterial compounds such as the sulfonamides. Many antibacterial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units.

With advances in medicinal chemistry, most of today's antibacterials chemically are semisynthetic modifications of various natural compounds.[4] These include, for example, the beta-lactam antibacterials, which include the penicillins (produced by fungi in the genus *Penicillium*), the cephalosporins, and the carbapenems. Compounds that are still isolated from living organisms are the aminoglycosides, whereas other antibacterials for example, the sulfonamides, the quinolones, and the oxazolidinones—are produced solely by chemical synthesis. In accordance with this, many antibacterial compounds are classified on the basis of chemical/biosynthetic origin into natural, semisynthetic, and synthetic. Another classification system is based on biological activity; in this classification, antibacterials are divided into two broad groups according to their biological effect on microorganisms: bactericidal agents kill bacteria, and bacteriostatic agents slow down or stall bacterial growth.[18]

PROBIOTICS

Probiotics are live bacteria that may confer a health benefit on the host. In the past, there were other definitions of probiotics. The first use of the word ―Probiotic‖ as microorganisms that have effects on other microorganism was accredited to Lilly and Stilwell (1965), expressed as follows: Substances secreted by one microorganism that stimulate another microorganism. Later, the definition was greatly improved by Fuller in 1989, whose explanation was very close to the definition used today. Fuller in 1989 described probiotics as "live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance". He stressed two important facts of probiotics: the viable nature of probiotics and the capacity to help with intestinal balance. Alternative expert review indicates there is insufficient scientific evidence for supplemental probiotics having a benefit. Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics, but certain yeasts and bacilli may also be used. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures, such as in yogurt, soy yogurt, or as dietary supplements. Probiotics are also delivered in fecal transplants, in which stool from a healthy donor is delivered like a suppository to an infected patient. [19]

Table 3: Source of Probiotics and Effect on Body

Strain	Claimed potential effect in Body
Bacillus coagulans GBI-30, 6086	May improve abdominal pain and bloating in IBS patients. Mayincrease immune response to a viral challenge.
Bifidobacterium animalis subsp. lactis BB-12	May have an effect on the gastrointestinal system.
Bifidobacteriu longu subs m infantis m p. 35624	Possible fro abdomin pain/discomfort, an relief m al bloating d constipation.
Lactobacillus acidophilus NCFM	Shown in one study to reduce the side effects of antibiotic therapy.
Lactobacillus paracasei St11 (orNCC2461) Lactobacillus johnsonii La1 (= Lactobacillus LC1, Lactobacillusjohnsonii NCC533)	May reduce incidence of H. pylori-caused gastritis and may reduceinflammation.
Lactobacillus plantarum 299v	May affect symptoms of IBS.
Lactobacillus reuteri ATCC 55730(Lactobacillus reuteri SD2112)	Evidence for diarrhea mitigation in children, decreased crying in infantile colic, H. pylori infection, antibioticassociated side-effects, fever and diarrhea in children and number of sick days in adults.
Lactobacillus reuteri Protectis (DSM 17938, daughter strain of ATCC 55730)	Evidence for shortened duration of diarrhea in children, decreased crying in infantile colic, reduced risk of diarrhea in children, may affect constipation and functional abdominal pain in children.

Lactobacillus reuteri Prodentis(DSM 17938/ATCC 55730 and ATCC PTA 5289 in combination)for oral health	Evidence for effect on gingivitis and periodontitis,[103][104][105][106] preliminary evidence for reduction of oral malodor, evidence for reduction of risk factors for caries.
Saccharomyces boulardii	Good evidence for treatment and prevention of antibiotic-associateddiarrhea and acute diarrhea.
Tested as mixture: Lactobacillus rhamnosus GR-1 & Lactobacillus reuteri RC-14	In one study, oral ingestion resulted in vaginal colonisation andreduced vaginitis.
Tested as mixture: Lactobacillus acidophilus NCFM & Bifidobacterium bifidum BB- 12	Preliminary evidence for reduced C. difficile–associated disease.

ENZYME PRODUCTION

There is a large number of microorganisms which produce a variety of enzymes. Enzymes differwith respect to substrates. Some of the microorganisms producing enzymes are listed in Table-

Table 4:-Microorganisms producing enzymes

	Microorganisms	**Enzymes**
Bacteria	Bacillus cereus	Penicillinase
	B. coagulans	a-amylase
	B. licheniformis	a-amylase, protease
	B. megaterium	Penicillin acylase
	Citrobacter spp.	L-asparaginase
	Escherichia coli	Penicillin acylase, b-galactosidase
	Klebsiella pneumoniae	Pullulanase
Actinomycetes:	Actinoplanes sp.	Glucose isomerase
	Aspergilus flavus	Urate oxidase

Fungi:	A. niger	Amylases, protease, pectinase, glucose oxidase
	A. oryzae	Amylases, lipases, protease
	Aureobasidium pullulans	Esterase, invertase
	Candila lipolytica	Lipase
	Mucor micheli and M. pusillis	Bennet
	Neurospora crassa	Trysinase
	Penicillium funiculosum	Dextranase
	P. notatum	Glucose oxidase
	Rhizopus sp.	Lipase
	Saccharomyces cerevisiae	Invertase
	S. fragilis	Invertase
	Trichoderma reesei	Cellulase

VITAMIN PRODUCT

Table 5:Microbial and enzymatic processes for the production of fat-soluble vitamin

Vitamin	Enzyme (Microorganism)	Method
Vitamin E and K_1 side chains	multiple enzyme system (*Geotrichum candidum*)	enzymatic conversion from (*E*)-3-(1′,3′-dioxolane-2′-yl)-2-butene-1-ol
[(*S*)-2-methyl-γ-butyrolactone] [(*S*)-3-methyl-γ-butyrolactone] [(*S*)- or (*R*)-β-hydroxy-isobutyric acid]	reductase bakers' yeast, (*Geotrichum* sp., etc.) multiple enzyme system (*Candida* sp., etc.)	asymmetric reduction of ethyl-4,4-dimethoxy-3-methylcrotonate stereoselective oxidation of isobutyric acid
Vitamin K_2	multiple enzyme system (*Flavobacterium* sp.)	conversion of quinone- and side chain-precursors to the vitamin
Arachidonic acid	fermentation (*Mortierella alpina*)	fermentative production from glucose
Dihomo-γ-linolenic acid	fermentation (*Mortierella alpina*)	fermentative production from glucose by a Δ5-desaturase-defective mutant
Mead acid	fermentation (*Mortierella alpina*)	fermentative production from glucose by a Δ12-desaturase-defective mutant
Eicosapentaenoic acid	multiple enzyme system (*Mortierella alpina*)	Δ17-desaturation of arachidonic acid or conversion from α-linolenic acid

Table 6 :Microbial and enzymatic processes for the production of water-soluble vitamins and coenzymes

Vitamin, Coenzyme	Enzyme (Microorganism)	Method
Vitamin C (2-Keto-L-gulonic acid)	2,5-diketo-D-gulonic acid reductase (*Corynebacterium* sp.)	enzymatic conversion of 2,5-diketo-D-gluconate obtained through fermentative process to 2-keto-L-gulonic, followed by chemical conversion to L-ascorbic acid
Biotin	fermentation (*Serratia marcescens*)	fermentative production from glucose by a genetically engineered bacterium
	multiple enzyme system (*Bacillus sphaericus*)	conversion from diaminopimelic acid using the biotin biosynthesis enzyme system of a mutant of *B. sphaericus*
Pantothenic acid (D-Pantoic acid)	lactonohydrolase (*Fusarium oxysporum*)	resolution of D,L-pantolactone to D-pantoic acid and L-pantolactone by stereoselective hydrolysis
Coenzyme A	multiple enzyme system (*Brevibacterium ammoniagenes*)	conversion by enzymatic coupling of ATP-generating system and coenzyme A biosynthesis system of *B. ammoniagenes* (parent strain or mutant) with D-pantothenic acid, L-cysteine, and AMP (or adenosine, adenine, etc.) as substrates
Nicotinamide	nitrile hydratase (*Rhodococcus rhodochrous*)	hydration of 3-cyanopyridine
Nicotinic acid	nitrilase (*Rhodococcus rhodochrous*)	hydrolysis of 3-cyanopyridine to form corresponding acid (nicotinic acid) and ammonia

BACTERIOCINS

Bacteriocins are peptides that can be more readily engineered than small molecules, and are possible alternatives to conventional antibacterial compounds. Different classes of bacteriocins have different potential as therapeutic agents. Small-molecule bacteriocins (microcins and lantibiotics) are similar to the classic antibiotics; colicin-like bacteriocins possess a narrow spectrum, and require molecular diagnostics prior to therapy. Limitations of large-molecule antibacterials include reduced transport across membranes and within the human body. For this reason, they are usually applied topically or gastrointestinally.[20]

CHELATION

Chelation of micronutrients that are essential for bacterial growth to restrict pathogen spread *in vivo* might supplement some antibacterials. For example, limiting the iron availability in the human body restricts bacterial proliferation. Many bacteria, however, possess mechanisms (such as siderophores) for scavenging iron within environmental niches in the human body, and experimental developments of iron chelators, therefore, aim to reduce iron availability specifically to bacterial pathogens.[21]

ANTIMICROBIAL COPPER ALLOY SURFACES

Copper-alloy surfaces have natural intrinsic properties to effectively and quickly destroy bacteria. The United States Environmental Protection Agency has approved the registration of 355 different antibacterial copper alloys that kill E. coli O157:H7, methicillin-resistant Staphylococcus aureus (MRSA), Staphylococcus, Enterobacter aerogenes, and Pseudomonas aeruginosa in less than 2 hours of contact. As a public hygienic measure in addition to regular cleaning, antimicrobial copper alloys are being installed in healthcare facilities and in a subway transit system.[22]

PHAGE THERAPY

Phage therapy is the use of viruses that infect bacteria (i.e. phages) for the treatment of bacterial infections. Phages are common in bacterial populations and control the growth of bacteria in many environments, including in the intestine, the ocean, and the soil. Phage therapy was in use in the 1920s and

1930s in the US, Western Europe, and Eastern Europe. However, success rates of this therapy have not been firmly established, because only a limited number of clinical trials testing the efficacy of phage therapy have been conducted. These studies were performed mainlyin the former Soviet Union, at the Eliava Institute of Bacteriophage, Microbiology and Virology, Republic of Georgia. The development of antibacterial-resistant bacteria has sparked renewed interest in phage therapy in Western medicine. Several companies (e.g., Intralytix, Novolytics, and Gangagen), universities, and foundations across the world now focus on phage therapies.

One concern with this therapeutic strategy is the use of genetically engineered viruses, which limits certain aspects of phage therapy. [23]

ANTIMICROBIAL ACTIVITY AND DISINFECTION

Another major focus of pharmaceutical microbiology is to determine how a product will react in cases of contamination. For example: You have a bottle of cough medicine. Imagine you take the lid off, pour yourself a dose and forget to replace the lid. You come back to take your next dose and discover that you have indeed left the lid off for a few hours. What happens if a microorganism "fell in" whilst the lid was off? There are tests that look at that. The product is "challenged" with a known amount of specific microorganisms, such as E. coli and C. albicans and the anti-microbial activity monitored.

Pharmaceutical microbiology is additionally involved with the validation of disinfectants, either according to U.S. AOAC or European CEN standards, to evaluate the efficacy of disinfectants in suspension, on surfaces, and through field trials.

MEDICAL DEVICES

Microbiology plays a significant role in medical devices, such as fluorescent fusion, which are used for fast and precise detection of pathogens in tissue samples. It is a technology for carrying out immunofluorescence studies that may be applied to find specific cells in complex biological systems.[24]

COSMETIC MICROBIOLOGY

According to International Microbiology, microbial contamination of cosmetic products is a matter of great importance to the industry and it can become a major cause of both product and economic losses. Moreover, the contamination of cosmetics can result in them being convertedinto products hazardous for consumers.

The water and nutrients present in cosmetics make them susceptible to microbial growth, although only a few cases of human injury due to contaminated cosmetics have been reported.

More often, microorganisms are the cause of organoleptic alterations, such as offensive odors, and changes in viscosity and color.[25]

4. CONCLUSION

Industrial microbiology includes the use of microorganisms to manufacture food or industrial products in large quantities. Numerous microorganisms are used within industrial microbiology; these include naturally occurring organisms, laboratory selected mutants, or even genetically modified organisms (GMOs). Currently, the debate in the use of genetically modified organisms (GMOs) in food sources is gaining both momentums, with more and more supporters on both sides. However, the use of microorganisms at an industrial level is deeply rooted into today's society. The following is a brief overview of the various microorganisms that have industrial uses, and of the roles they play.

The relationship between microbes, the human microbiome, diet, and food safety has played a critical role in the development of the modern food industry with its plethora of choice and variety and the consequent improvements in our overall quality of life.

Our knowledge of just how this complex balancing act contributes to the development of human society through the most basic of means, our food, has continued to develop over the last several thousand years. From the earliest fermentation of beer and production of bread to the probiotic foods which have been appearing on supermarket shelves over the last two decades, the application of microbiology to the food industry will certainly continue well into the future.

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