**Applications of Fermentation Technology in Biotechnology: From Food to Pharmaceuticals**

**Introduction:**

Fermentation technology, a process that utilizes microorganisms to produce desired products, has been a cornerstone of biotechnology for centuries. This chapter explores the wide-ranging applications of fermentation technology in various fields, including food and beverage production, pharmaceuticals, biofuels, and industrial biotechnology. By harnessing the metabolic capabilities of microorganisms, fermentation technology has revolutionized numerous industries, enabling sustainable and efficient production of valuable compounds. The technology of fermentation dates back as far as human civilization itself. Over the years, fermentation has evolved from its humble beginnings as a food preservation technology for households to a sophisticated one used to manufacture diverse range of products at the industrial scale [1]. Depending on the product of interest fermentation can be performed in batch mode, continuous mode or in a combinatory, fed-batch mode.

Traditionally, fermentation was employed as a method of preserving and extending the shelf-life of food [2]. It is due to the peculiar flavor and renowned health benefits; fermented foods have become so popular. Their popularity has increased the production and consumption of fermented foods and beverages, globally in the recent years. The scientific community has paid increasing attention to the health benefits of fermented foods and beverages in the last few decades [3]. Apart from its renowned benefits on the gastrointestinal tract, fermented products have also been proven to contain anti-oxidant, anti-microbial, anti-fungal, anti-inflammatory, anti-diabetic and anti-atherosclerotic activity [4]. Probiotics are live bacteria or yeast that supplements the gastrointestinal flora and improves intestinal health, enhances immune response, reduces serum cholesterol levels, lactose intolerance symptoms and prevents gut infections [5]. Despite conventionally being known as the process involving anaerobic conversion of sugar to carbon dioxide and alcohol by yeast, fermentation is now referred to an industrial process used for manufacturing a wide variety of metabolites using microorganisms or mammalian cells in a controlled culture environment. Since a long time, fermentation has been used to produce medically important products such as antibiotics, solvents such as ethanol, intermediary compounds such as citric acid, probiotics such as yoghurt etc. Latest products produced through this process are therapeutic recombinant proteins and DNA, anti-viral drugs, and monoclonal antibodies. In addition to drugs, fermentation is also used to produce materials for commercial use, such as diagnostic kits, drug delivery vehicles and medical devices. As a result, the biopharmaceutical industry continues to grow rapidly thanks to fermentation technology. With the progress in novel technology, it is expected to expand even further in the days ahead [6]. The popularity of industrial fermentation processes has increased in recent years, as they are seen as an important technological asset for reducing our reliance on chemicals and products manufactured from fossil fuels [7]. Industrial food fermentation was possible with the discovery of microorganisms, as it became possible to understand and manage food fermentations. Although fermentation was initially used for food production, it now manufactures food and food supplements (e.g. yoghurt, cheese, pickles), agricultural products (e.g. microbial pesticides), pharmaceutical chemicals (e.g. enzymes, vaccines), industrial chemicals (e.g. acetone, butanol), alcoholic beverages (e.g. beer, wine), analytical products (e.g. citric acid), and biofuels [6]. Thus, over the years fermentation technologies have constantly evolved with advances effectively and the advent of modern sophisticated equipment have addressed the challenges associated with traditional fermentation and progressed with new approaches for fermentation of novel products [8]. As a result of the wide application associated with fermentation technology, in recent times it has witnessed a huge leap in terms of production and consumer acceptance.

**Fermentation Process Overview:**

**1.1. Microbial Fermentation:** The word Fermentation originates from a Latin verb “fevere”, which literally means to boil. During the production of alcohol, the first truly industrial process, the gas bubbles of carbon dioxide appear at the surface of the boiling liquid, which gave the appearance of boiling liquid. Hence, it is named as fermentation. Although fermentation is defined as the anaerobic breakdown of organic substances by microorganisms such as bacteria, yeasts, and fungi. However, this definition is no longer valid since the term industrial fermentation is now used for large- scale cultivation of microorganisms such as yeast, bacteria, and fungi, even though most of them are aerobic, for the conversion of complex substrate into simple compounds which are useful to humans; such as the compounds that have application within the energy production, material, pharmaceutical industries, chemical, and food industries [9], namely for the enzymes production, metabolites, biomass, recombinant technology, and biotransformation product. During fermentation, microorganisms metabolize carbohydrates or other organic substrates, producing energy, metabolites, and desired products. In light of its lower environmental impact and lower operating costs compared to conventional chemical processes, fermentation has attracted attention from the food processing, pharmaceutical, energy, and waste treatment industries. Microorganisms convert raw ingredients into appealing foods with improved shelf life and protection, both biochemically (nutrients) and organoleptically (taste/texture/odour and visual appearance). The final fermented product is dependent on various factors such as temperature, pH, aeration, substrate concentration, and nutrient availability all influence the fermentation process and metabolic processes [10] For the production of primary and secondary metabolites, biotransformation, oil extraction and various other fermentation process high yielding strains of microorganisms are used in order to meet the market demands [11]. Fermentation technology is broadly divided into two parts; viz upstream processing and downstream processing. The initial process of preparing for the fermentation, including selection, screening and improvement of microbial strain, preparation and sterilization of media, inoculum preparation is called as upstream processing. The recovery of the product after the fermentation such as the filtration, extraction, product purification and packing are called as downstream processing.

**1.2. Key Factors in Fermentation:** Several factors influence fermentation processes, including microbial strain selection, nutrient availability, temperature, pH, oxygen levels, and process control parameters.

1. **Microbial strain selection**

Strain refers to the homogenous population of potent microbes. The stain should be high yielding, it should have stable biochemical characteristics, it should be easily cultivable on large scale and should not produce any undesirable substances. Desirable microbial strains can be selected through primary screening and secondary screening techniques. Further, the strain can be improved by either of the following methods: mutagenesis, genetic engineering, natural recombination, regulatory mechanisms or by protoplast fusion.

1. **Raw material:**

The type and quality of the substrate or raw material being fermented play a significant role. Fermentation can utilise a wide range of organic products such as carbohydrates, proteins or fats. The composition, concentration and availability of nutrients in the substrate can impact fermentation efficiency and final product characteristics.

1. **Nutrient availability**

The availability of the nutrients to the microbes is dependent on the composition of the fermentation media. Fermentation media should satisfy all the nutritional requirements of the microorganism and fulfil the technical objectives of the process. The nutrients should be formulated to promote the synthesis of the target product, either cell biomass or a specific substrate. The source, type and nature of carbon and nitrogen source are the most crucial factors determining the success rate of any fermentation process. In order to reproduce, form products, and maintain cells, microorganisms require carbon sources as a source of energy. Traditional carbon sources for microbial fermentations are carbohydrates (such as molasses, malt extract, starch, sulphite waste liquor, cellulose, whey), although alcohol and alkanes can also be used. The type and amount of the product formed depends on the nature of carbon sources and rate of assimilation [12] .Similar to carbon, the source and concentration of nitrogen in the media also plays an important role. Most microorganisms can utilise both inorganic and/or organic nitrogen source. In some cases, nitrogen may have inhibitory effects on the metabolite production whereas in others it may have enhancer effects. The crude forms of nitrogen supplied are usually byproducts of other industries. For example, corn steep liquor, yeast extracts, peptones, soya bean meat are examples of byproducts of other industries. Phosphate is also another basic component of the fermentation media as it is required for the production of nucleic acids and for the production of phospholipids present in the microbial cell membranes. According to the need of the organism and nature of the desired product phosphate must be added in appropriate quantity. For the production of secondary metabolites, some fermentations require specific precursors. Phenylacetic acid is added as a side chain precursor in penicillin production. If a product formation is dependent on the presence of a specific inducer, them it must be incorporated into the culture medium at specific time during fermentation. A metabolic inhibitor reduces formation of other metabolic intermediates and redirects metabolism towards a target product.

It is extremely essential to optimize the fermentation media for the metabolite production prior to the start of semi-pilot/pilot production plans. Optimization techniques should be carried out in order to reduce the time for the process development and to reduce the overall production cost [12].

1. **Temperature and pH**

Temperature and pH are the key factors that directly affect the development of microorganisms as it determines the rate of growth, multiplication, survival and death. Each microorganism has an optimum temperature for its activity. In some cases, temperature control is crucial to prevent the growth of unwanted microorganisms or to promote specific metabolic pathways. To ensure successful fermentation, it is important to monitor and control the pH throughout the process as pH optimisation is crucial for promoting microbial growth, enzyme activity and production of desired fermentation products.

1. **Oxygen levels**

Fermentation can occur both in the presence or absence of oxygen. Aerobic fermentation requires oxygen, while anaerobic fermentation do not require oxygen. The availability or absence of oxygen affects the types of microorganisms that can thrive and produce products during fermentation.

1. **Agitation**

Proper agitation enhances the distribution of nutrients, oxygen and microbial cells and helps to maintain uniform conditions throughout the fermentation vessel, improving fermentation efficiency and preventing the formation of concentration gradients.

**Food and Beverage Industry:**

**2.1. Fermented Foods:** Fermented foods are composed of complex metabolic interactions of the enzymes from raw ingredients that interact with the fermenting microorganisms, resulting in a product with unique physical and biochemical characteristics. When foods are fermented, the nutritional and biochemical quality of the original ingredients alter. Microorganisms play a crucial role in the fermentation process, enhancing flavor, texture, and nutritional quality of the final products. Fermenting microorganisms mainly include lactic acid bacteria (LAB) such as Lactobacillus, *Enterococcus*,  *Streptococcus*, *Leuconostoc* and  *Pediococcus* (Mokoena,2017) *and* yeasts and molds viz. *Debaryomyces*, *Kluyveromyces*, *Saccharomyces*, *Geotrichium*, *Mucor*, *Penicillium*, and *Rhizopus* species [14], [15]*.*  Fermentation not only makes the food safer for consumption but also reduces the energy consumption when cooking [16], [17]. Several advantages can be attributed to fermented foods [4], [18]:

1. The shelf life of fermented foods is longer than that of their original counterparts
2. Enhanced of organoleptic properties. For example, cheese in comparison to its raw substrate, milk, has more enhanced organoleptic properties.
3. For obtaining raw materials that are free of harmful/unwanted ingredients. For example, Cyanide content in garri is reduced during preparation of cassava, and the flatulence factors in soybeans are removed by fermentation.
4. Higher antioxidant properties in fermented foods. For example:  yogurt consist of higher antioxidant properties compared to milk, as the proteolysis of milk proteins releases biopeptides such as α-casein, α-lactalbumin, and β-lactoglobulin.
5. Cooking time period of fermented foods is greatly reduced compared to non-fermented counterparts.
6. Fermenting microorganisms enhances the nutritional properties of fermented foods. For example, Yeast increases the nutritional value of bread and garri. Fermented foods exhibit several beneficial effects on health by reducing blood cholesterol levels, protecting against pathogens, increasing immunity, osteoporosis, fighting carcinogenesis, diabetes, allergies, obesity and atherosclerosis, and alleviating the symptoms of lactose intolerance [19].Fermentation is used in the production of various fermented foods and beverages, including yogurt, cheese, idli, dosa, sauerkraut, kimchi, soy sauce, bread, fermented vegetables (mustard, pickles, and turnips), fermented fruits, non-alcoholic beverages (boza), cereal-based fermented foods (tarhana), beer, wine, vinegar, etc. Starter cultures of (LAB) and other microorganisms are used in the production of fermented beverages, dairy, meat, and vegetable products. It is the production of lactic acid and other organic acids that produces the preservation effect, which lowers pH and prevents harmful and spoiling organism growth [20]. Fermented foods are also rich in proteins. Due to all these advantages of fermented foods, it has gained its importance in recent past, attracting the interest of consumers which drastically raised the market size.

**2.1.1. Fermented milk and milk products**

Fermented milk constitutes an important part of human nutrition due to its hypotensive, hypo-cholesterolemic and antimicrobial effects [21]. In order to protect the nutritive value of milk and improve the shelf life most of the milk based fermented food are produced from LAB. Lactic acid fermentation enhances protein solubility and some micronutrients and amino acids' availability [22] Traditionally, fermented foods such as yogurt are prepared using microorganisms based on raw materials and local practices where, curdling of milk may be induced by adding several different curdling agents or by adding a small amount of preformed curd, with subsequent incubation at a warm temperature [23], [24]. Yogurt, a potential source of probiotics is a coagulated fermented dairy product obtained by the lactic acid fermentation of milk [25]. Fermented dairy products such as cheese offer high energy values, high fat, protein, calcium and vitamin B content. Combined with the vitamins, minerals and bioactive peptides cheese prevents against several diseases due to its anti-carcinogenic and anti-obesity characteristics [26]. Unpasteurized milk is fermented into koumiss, a slightly alcoholic fermented beverage [27], [28]. The distinctive sour and alcoholic flavour of kousmiss is the result of both lactic acid fermentation and alcohol fermentation [4], [29]. Kefir is an ancient fermented milk drink with a sour, acidic, and mildly alcoholic flavor with creamy texture. Due to its pleasing organoleptic characteristics in addition to anti-hypertensive, anti-carcinogenic, hypocholesterolemic, anti- inflammatory, anti-mutagenic, anti-allergenic, anti-bacterial, anti-diabetic, anti-oxidant, and probiotic effects, it has become a focus of interest in recent years [30].

**2.1.2. Fermented Meat and Meat Products**

Meat fermentation is one of the earliest and most prevalent type of fermentation [31]. Several biochemical, microbiological, and chemical processes are involved in the production of fermented meat, and as a result of these changes, fermented meat products acquire their distinctive taste, colour, aroma, and odour [4]. Examples of fermented meat products are Sucuk (Turkish fermented dry sausage), fermented sausage, pastırma, Nham, salami, Fermented fish products such as fish sauce, Suan yu, bagoong, paak [32], [33]

**2.1.3. Fermented Fruit and Vegetable Products**

Globally, fermented fruits and vegetables such as pickled cucumbers, sauerkraut, and kimchi are indispensable components of human nutrition [34], [35]. The fermentation of fruits and vegetables is mainly lactic acid fermentation which involves the oxidation of carbohydrates to carbon dioxide, alcohol, and organic acids that inhibit pathogen and spoilage microorganisms [36], [37]. Mexican pulque is made by fermenting juices from the cactus plant (Agave) and it is the oldest alcohol-containing beverage on America’s continent [38].

**2.1.4. Fermented Beverages**

The beverage industry is one of the fastest growing segments of the food fermentation since modern health-conscious consumers worldwide recognize them as refreshing, convenient, and healthy products, as well as probiotic vehicles that could improve well-being and reduce the risk of chronic and degenerative diseases [39]. Therefore, fermented beverages are becoming increasingly popular throughout the world because of their health-promoting properties. Additionally, non-dairy probiotic fermented beverages have been developed from whey, soy milk, cereals and vegetable and fruit juices, in addition to traditional beverages [40]. In the production of fermented beverages and foods, Saccharomyces cerevisiae plays a central role [41] as in the history of mankind, yeast has been the most important factor in producing alcoholic beverages and economically important of all biotechnologies [42]. There are several different types of sugar-containing materials that can be used to make fermented beverages, including cereals, fruits and vegetable juices, tea, and milk. Thus, the fermented beverages obtained from different sources includes the following: wine from grapes, beer from barley, kefir from kefir grains, cider from apples, sake from rice, mead from honey, and other fermented beverages like probiotics. Traditional Turkish fermented beverages most commonly consumed include non-alcoholic beverages such as kefir, ayran, shalgam juice, boza, and hardaliye [43]. Acetic acid bacteria (AAB) is commonly found in fermented beverages such as lambic beer, water kefir, kombucha, and cocoa [44]. Supplementation of carrot juice fermented with *Lactobacillus rhamnosus* GG LGG (DFCL) could favourably regulate blood glucose, insulin, antioxidant capacity [45]. In the course of time, various fermented beverages have been developed from various food matrices, offering consumers diverse alternatives to introduce bioactive components in their daily diet. Throughout the evolution of fermentation, scientific and technological advances have played a crucial role, from selecting and using specific starter cultures to improving their performance through the application of novel technologies, resulting in products with improved nutritional properties and characteristics [46]**.** It is anticipated that fermented beverages will gain prominence in the functional food markets, in the coming era, as a result of recent advancements [47].

**2.2. Probiotics:** Fermentation is employed to produce probiotic products containing live beneficial microorganisms. The term probiotic refers to a single strain or mixture of different strains of live microorganisms that benefit the host, either directly or indirectly, by improving its intestinal microbial balance. Probiotics are commonly classified by a widely accepted broad definition, proposed by a Joint Expert Consultation of the Food and Agricultural Organization of the United Nations (FAO) and the World Health Organization (WHO) as “a live microorganism that confers health benefits to its host when consumed in an adequate amount” [48]. Probiotics contribute to gut health, enhance digestion, and boost the immune system. In order to derive the health benefits conferred by probiotics, humans consume fermented foods, as they are the major source of probiotics [49]. Fermented foods rich in probiotics are fermented dairy products like yogurt, cheese and fermented milk. Apart from the fermented dairy products, probiotics are also available in the form of capsules, pills and tablets [50]. In addition to these, non-dairy functional foods are seen as a wise alternative for vegans and individuals with lactose intolerance [51]. Among this plethora of options rich in probiotics, the dominant source of probiotic are the dairy products [52] especially yogurt as they have a relatively low pH environment for the survival of probiotic bacteria. There are two genera of probiotic microorganisms that make up most of their composition: *Lactobacillus* and *Bifidobacterium.* Among which Lactic acid bacteria (LAB) are commonly used as probiotics. LABs perform dual function; they act as both probiotic delivery vehicles as well as starter culture for fermentation [53]. In general probiotics not only serve as a starter culture but also imparts many distinctive functional and sensory characteristics to the product (for instance, improved aroma, taste, and textural characteristics) [54], in addition to conferring many health-promoting properties [55]. The primary health benefits derived from probiotics include improved balance of gut microbiota that helps in alleviating resistance against gastrointestinal infections by strengthening the gut barrier function, increasing immunity, inhibiting the growth of pathogenic bacteria, preventing irritable bowel syndrome and diarrhoea, improving assimilation of serum cholesterol etc [56]. In order to derive the health benefits conferred by probiotics, strains of probiotics are incorporated in products such as yogurt, cheese, fermented milk and ice cream [57]. A probiotic fermented milk is made of fermented milk that has been inoculated with probiotics [58]. The probiotics in fermented fruits and vegetables with lactic acid bacteria can help to prevent certain diseases such as cirrhosis and diarrhoea, while antioxidants found in fermented fruits and vegetables can help prevent degenerative diseases caused by harmful free radicals [59]. Hence, probiotics have gained significant prominence in the last few decades [57]. Essentially, there are three steps involved in the manufacture of a probiotic product:

 (a) The starter culture is chosen based on its ability to reach a particular niche within the host's gastrointestinal tract, colonize it, and confer the probiotic action;

(b) Evaluation of the starter culture from a technological perspective, which is based on the starter culture's ability to propagate successfully and maintain viability at industrial levels and functionality after a series of processing steps; and

(c) Incorporating probiotic cultures into products as starters or adjunct cultures. Probiotic strains tools of several strains were characterized using predictive microbiology using whole genomes to provide information related to their properties as probiotics [60], [61].

**Pharmaceuticals and Biologics:**

**3.1. Antibiotics and Pharmaceuticals**: The cultivation of specific microorganisms and optimization of fermentation conditions enable the efficient production of therapeutic compounds. Antibiotics are an important group of bioactive compounds produced by different microorganisms during fermentation process, having the ability to selectively kill or inhibit the growth of harmful pathogenic microorganisms at very low concentrations [62]. They are secondary metabolites produced during the idiophase. Antibiotics are widely used round the world for the prevention and treatment of diseases [63]. With industrialization and globalisation, population is increasing at a rapid rate, leading to the increased consumption of antibiotics. Hence production of a cost-effective method for the antibiotic production is inevitable in order to meet the rising demands [64]. Many antibiotics, such as penicillin, streptomycin, and tetracycline, are produced through fermentation. Since it has been estimated that less than 1% of antimicrobial agents have any medical or commercial value despite the wide variety of antibiotics that are known, screening of useful antibiotics is an important step for antibiotic production at large scale. Antibiotics are generally produced at the industrial scale using agro-wastes, such as sawdust, corn cobs, rice hulls and groundnut shell. Agro-wastes are used as they are rich in bioactive compounds. Different agricultural are used for the production of different antibiotics. Oxytetracyline was produced with SSF by consuming groundnut shell as a raw material with strain of *Streptomyces rimosus* [65] . This method of production of oxytetracycline was also supported by [66] and [67]. Agro-wastes are also used in the construction of antibiotic, such as neomycin [68]. Of the different agro-industrial wastes tested, coconut oil cake and ground nut shell produced the most antibiotics. In recent studies, solid state fermentation (SoSF) was used to produce neomycin, oxytetracycline, and rifamycin. Hence, antibiotics can be produced efficiently by fermenting agro-waste using appropriate fermentation techniques. In order to reduce the operational cost and increase the yield, strain improvement is carried out for the large-scale production of antibiotics from microbial fermentations [62]. In addition to strain improvement, use of agricultural residues as low-cost carbon source the cost of antibiotic production can be significantly reduced. The first antibiotic produced through microbial fermentation was Penicillin from *Penicillium notatum,* in which wheat bran and sugarcane bagasse are used as substrate under high moisture content (70%)*.* Mixed cultures of actinomycetes and fungi produced penicillin in Solid state fermentation (SSF). Today, SSF is more widely used than Submerged fermentation (SmF) as a result of the development of proper substrates due to the production of constant and high quantity antibiotics in SSF. Some common antibiotics produced from SSF are Cephamycin C, Cyclosporin A, Penicillin, Neomycin, Iturin, and Cephalosporins. Through fed-batch system most antibiotics are produced, such as teicoplanin [69]daptomycin [70] tylosin and β-lactams [71]. Monobactams, cephalosporins and penicillin together they are known as β-lactam antibiotics. Any research and development program aiming to manufacture fermentation products on a large scale usually ends with scaling up the fermentation process [72]. Although antibiotics can be synthesized by synthetic processes as well, microbial fermentation remains the only practical way to produce this valuable drug [73]. Since (a) the purity of the active substances depends on which fungal or bacterial strain produces the antibiotic; (b) the raw materials that are utilized, including the quality of water in which the strains grow, may also vary; (c) the conditions under which strains are processed may vary; and (d) the extraction and purification processes may have limited selectivity [74]. Due to the drastic advances made in exploring the sector of antibiotic production, regulatory networks and its intracellular and environmental signals, have made it possible to discover and overproduce novel antibiotics. At present, genetic engineering is playing a vital role in strain and fermentation improvement to hasten the process of discovery and development of new antibiotics as effective drugs [75].

**3.2. Recombinant Proteins and Biologics**: In order for mankind to survive, therapeutic proteins must be produced at a large scale to treat diseases at a large scale. The production of recombinant proteins has been made possible by recent progress in recombinant DNA technologies that can be used as therapeutics, vaccines, and diagnostic reagents. Fermentation technology plays a pivotal role in the production of recombinant proteins, including therapeutic enzymes, hormones, vaccines, and monoclonal antibodies. Microorganisms or cell cultures are genetically engineered to express and produce these complex molecules at the laboratory scale as well as in large-scale settings. For smaller biologics (e.g., peptides, proteins, cytokines, growth factors, plasmid DNA, nucleic acids, single-domain antibodies, peptibodies and non-glycosylated antibody fragments), microbiological fermentation in bacteria, yeast, or fungi is generally preferred as the processing time required in these cases are typically much shorter, and media costs can be significantly lower than those associated with cell culture. The use of microbial fermentations in manufacturing recombinant proteins results in faster development, higher yields, and higher quality products, reduced variation between batches, better scalability, and lower production costs .For industrial production of recombinant proteins of therapeutic and prophylactic importance it is essential to develop bioprocessing strategies such as the use of high-throughput devices for effective bioprocess optimization and of disposable systems, continuous upstream processing, continuous chromatography, integrated continuous bioprocessing, Quality by Design [76]. Recombinant insulin produced from Escherichia coli was of the first recombinant pharmaceutical protein to receive approval for its clinical use in the early 1980s by microbial fermentation. Since then, this field has witnessed many advances. Novel cell factories are produced for large scale production of therapeutic proteins through high throughput analysis techniques (the so-called — omics approaches) and integrative approaches (systems biology) [77]. Several studies have demonstrated that Escherichia coli is the ideal host for the production of non-glycosylated proteins as it offers various advantages over yeast and other expression systems. This is primarily due to its ease of handling and simple upstream process (USP), which allows it to be used in the production of recombinant proteins in large quantities at cost-effective prices [78]. Saccharomyces cerevisiae and Pichia pastoris are the second and third most favorable microbial systems, respectively for the production of recombinant proteins after E.*coli* [79]**.** Chinese hamster Ovary (CHO) cells are the fourth most popular host mammalian system as it contributes for the production of around 70% recombinant proteins [80]. Over the last decade the commercial production of recombinant therapeutic proteins including monoclonal antibodies (mAbs) have undergone a sea change improvement in terms of implementation of various novel technologies [81]

**Biofuels and Renewable Energy:**

**4.1. Ethanol Production**: In recent years need for fossil fuels such as petrol and diesel has increased several folds, as a result biofuels are in high demand. This is due the fact that biofuels are an excellent substitute of fossil fuels. Fermentation is used in the production of biofuels such as bioethanol, a renewable and sustainable alternative to fossil fuels. Various biofuels produced from biodegradable and waste materials leading to zero waste concept are biodiesels (produced from vegetable oils, re-used wax, or creature fats), bioethanol (alcohol produced by fermenting sugar and starch crops such as corn), butanol, biohydrogen etc [82]. Biofuel are an excellent substitute for fossil fuels their nontoxic, sulfur-free, biodegradable nature, originating from the renewable sources [83]. Moreover, they have the potential of bringing control to the ever-increasing problem of greenhouse gas emissions due to the burning of petroleum fuels. [84]. Furthermore, biofuels are increasingly being used in transportation, heat, and power developments that require renewable energy sources [83]. The most significant benefit of biofuels is that they are a renewable source of fuel mostly derived from agriculture and essential harvesting, woods, and residue streams [85]–[87]. Biofuels are a kind of energy fuels derived from the organic sources (comprehensively depicted as biomass) created by the plants and living things, which can be grown and harvested over and over again. They are mostly derived from agricultural and essential harvesting, woods, and residue streams, which are utilised to substitute non-renewable energy fuels [85]–[87]. The most common types of biofuels are biodiesel, which is derived from vegetable oils, recycled wax, or animal fats, bioethanol, which is derived from the fermentation of sugar and starch crops like maize, and biogas [83].  Depending on the biomass used by the fermentation technologies four generations of biofuel production technologies have been developed. First-generation biofuels are produced from various food crops such as starch, sugars, animal fats, and vegetable oils. Second-generation biofuels are produced from the non-edible portion of crop and biological waste matter mainly lignocellulosic biomasses. Third-generation biofuels are produced from specially engineered energy crop such as algae or food waste biomass. Fourth-generation biofuel is a pretty novel idea, which aims to capture the carbon dioxide (CO2) at every stage of the biofuel production and dispose it back to earth [84],[88]. The creation of biofuels from beneficial agro-industrial leftovers, such as rice straw, sweet potato waste, sawdust, potato waste, corn stalks, sugarcane bagasse, and sugar beetroot waste, has been demonstrated in prior studies [89], [90]. Biomass, such as sugarcane, corn, rice straw, sweet potato waste, sawdust, potato waste, and sugar beet waste is fermented to produce ethanol through the action of yeast or bacteria. Fermentation is a very promising approach for the conversion of food waste into biofuels. Different biotechnologies are able to turn food waste into biofuels through anaerobic digestion, aerobic digestion, and microbial fermentation processes such as biomethane, biohydrogen, bioethanol, and biodiesel [91]. In the production of biofuel, a wide range of raw materials has been used, depending on the availability of biomass, cost-effectiveness, and their geographic location. The use of lignocellulosic biomass as a raw material has attracted the attention of many researchers all over the world compared to any other raw material [92]. Lignocellulosic biomass for the production of second-generation biofuels was investigated in various studies [93], [94].The production of biofuels could be based on a variety of lignocellulosic residues such as straws, crop residues, wood pellets, wood chips and agro-waste [95] . Due to the low price, availability throughout the year and wide distribution geographically, lignocellulosic biomass is considered not only the most feasible option for biofuel production but also for fossil fuel replacement since these raw materials do not compete with food crops and have the significant potential of bioethanol productivity [96]. Lignocellulosic materials have been used in many research studies to make bioethanol [97], [98]. Reference [99] discussed the use of agricultural wastes to produce second-generation bioethanol. They concentrated on the utilisation of various agro-industrial wastes' lignocellulosic content. Thus, for the production of biofuels, the lignocellulosic-derived biofuels are not only cost effective but also an eco-friendly and alternative source of energy for upcoming future. Due to rapid population influx and industrialization in most of the developing countries, the demand for low-priced energy source is extremely high. High demand for energy fuels can be met by using economical agricultural residues for the production of biofuels. Using the yeast *Saccharomyces cerevisiae* bioethanol was producedfrom vegetable’s waste by fermentation [100]. They made use of common vegetable scraps including onion peel, potato peel, and carrot peel. Producing bioethanol might be the best alternative to eating agricultural waste. In India, where banana pseudo stem is widely available as a waste, using banana stem as a substrate for the synthesis of bioethanol is a good alternative. So, a better method to meet the need for energy while preserving limited resources is to produce valuable biofuels out of cheap, environmentally friendly agricultural waste. Hence, our reliance on woody biomass from forests is reduced by the use of agricultural residues, helping to reduce deforestation[101]. To address the industrial demand for renewable energy, metabolic engineering is pushing the boundaries of what is possible by creating microbial chassis for biofuel bio-foundries. [102]. Metabolic engineering can be used to get beyond these obstacles in the biofuel production routes, which have revolutionised the standards for producing both conventional and advanced biofuels. By changing the molecular mechanisms linked to the metabolic pathways that produce fuel, this method seeks to improve the metabolic performance of microorganisms. [102]. Hence, biofuels have gained a great deal of interest because of their environmentally-friendly and nontoxic nature. Industrialization and commercialisation require propelling lab-scale cycles of biofuels to improve yields and productivities [83].

**4.2. Biogas Generation**: Anaerobic fermentation of organic waste materials, such as agricultural residues, animal manure, and food waste, produces biogas.  As a flexible source of energy, biogas can be used to produce heat, power, biomaterials, and transportation fuels, as well as contribute significantly to control environmental pollution [103]. Biogas, primarily composed of methane, serves as a renewable energy source for electricity generation and heat production. The principal constituent of biogas includes CH4 (60%) and CO2 (40%) [104]. Biogas can be a useful means of achieving a number of goals relating to waste, environment, and energy management. To replace fossil fuel in an environmentally sustainable way, biogas production is the most crucial prerequisite. Biogas can be created at landfills, wastewater treatment facilities, and agricultural biogas plants under controlled conditions [105]. In spite of numerous routes of renewable energy sources available, due to the enormous supply of lignocellulosic biomass, biogas generation holds an unparalleled position. As a result, researchers from all around the world are working diligently to create low-cost, sustainable methods of producing biogas for use in power, heat, and transportation [103]. By 2050, it is anticipated that the share of renewable energy in total energy consumption will rise to 55%-75%, with an emphasis on geographic self-reliance. Thus, the expanding field of renewable energy sources should include biogas plants as facilities that transform waste into electricity. A key technology for renewable energy is the production of compressed biogas or renewable natural gas from organic residues using anaerobic technology [106]. The efficient conversion of organic materials in biomass under the assimilation of anaerobic bacteria is known as biomass anaerobic fermentation, which finally creates economically valuable methane and some carbon dioxide that can be burned to produce electricity. Due to a number of disadvantages associated with traditional anaerobic fermentation such as long fermentation time and low gas production rate, wide application of this method for biogas production is limited. The high temperature anaerobic fermentation technology has higher gas production efficiency and can kill a large number of pathogenic microorganisms compared to the medium temperature anaerobic fermentation. Hence, high temperature anaerobic fermentation technology is highly efficient and cost-effective [107] . It was shown that C. autoethanogenum might act as a biocatalyst to ferment CO2 from synthetic biogas supplemented with H2 to produce ethanol and acetate as biogas upgrading technologies [108]. In anaerobic fermentation to produce methane, duckweed has excellent methane production potential and can take the role of lignocellulosic plants [107]. Another investigation into the production of biogas utilising a variety of agricultural waste products from diverse sources and two weeds, Typha angustifolia L. and Eichornia crassipes Solms, was conducted [109]. The use of biogas as a sustainable fuel appears to be the path of rising relevance when taking into account the benefits to the environment and the economy. Utilizing waste to create biogas is undoubtedly in keeping with the circular economy movement [105]

**Industrial Biotechnology:**

**5.1. Enzyme Production**: Enzymes are efficient, sustainable and greener substitutes to the chemicals used for the industrial processes. They are the flexible biocatalysts that have the power to significantly alter the food sector and lignocellulosic biorefineries [110]. Fermentation is utilized to produce a wide range of enzymes used in various industries, including detergent, textile, paper, and biofuel production. Microorganisms are engineered to overexpress specific enzymes, resulting in high yields and cost-effective production. Enzyme-catalysed reactions offer various advantages; since these reactions are specific, produce less and low toxic by-products There are economic and environmental benefits to immobilizing and reusing enzymes, and these benefits can be achieved through enzyme inactivation [111]. There are several different applications of enzymes, including technical applications, food processing, biofuel production, and organic synthesis in pharmaceuticals and cosmetics [112]. In the detergent industry, enzymes are used to break down proteins, fats, and starches in order to soften the fabric and improve colour. In the pulp and paper industry, amylases, cellulases, and xylanases are used to reduce the viscosity of mixtures, improve product softness and increase brightness [113]. Enzymes used in the dairy industry for the manufacture of cheese and production of lactose-free dairy products are lipases and lactases. Amylases are an important group of carbohydrate hydrolytic enzymes that are used for improving the stability of the dough in bakery industry and also for clarifying fruit juices in juice industry [114]. A number of enzymes are used in the production of bioethanol for the breakdown of lignocellulose, including cellulases, hemicellulases, and xylanases [115]. In order to manufacture enzymes, enzyme cultivation is the most important technique. The collection of enzymes is made possible with both fungi and bacteria when fermentation is done on appropriate substrates. Enzymes are produced through both submerged and solid-state fermentation. Enzymes cultivated from fungus are generally produced through solid state fermentation as they require less water potential, whereas bacterial enzyme production is best produced through submerged fermentation [116]. However, recent studies have shown that bacterial enzyme production could also be achieved by solid state fermentation. Many commercial sectors have been contemplated with the use of enzymes, such as the pharmaceutical industry (production of biopharmaceuticals, e.g., L-Asparaginase and collagenases), leather industry (peptidases) degradation of plant biomass (cellulases, esterases, xylanases, and ligninases) bioremediation (oxidoreductases) [117].Well known enzymes produced from bacteria are amylase, cellulase, xylanase, and L-asparaginase. Several species of fungus, Aspergillus, have been isolated from this process, which is an industrially important enzyme-producing process. In the past, *Aspergillus* is used as model microorganism used to produce fungus enzymes as it is the largest fungal source of enzyme [118]. In the agroindustry, many microorganisms that decompose lignocellulosic material are being investigated as producers of enzymes useful in enzymatic hydrolysis of the lignocellulosic material [119]. Worldwide, lignocellulolytic enzymes account for 20% of commercially available enzyme sales and have applications in textile, food, animal feed, paper, biofuel, and pharmaceutical industries [120]. Engineering tools can be used to improve the strains of enzymes produced. Purity, catalytic efficiency, specificity, and expression yield of engineered enzymes are improved thanks to altered amino acid sequences and the use of promising protein engineering tools like directed evolution, rational design, and computational methods [121]. Thus, in the field of biotechnology, microbial enzyme production provides an invaluable resource which has a wide application.

**5.2. Specialty Chemicals and Fine Chemicals:** Fermentation enables the production of specialty chemicals and fine chemicals, including organic acids, amino acids, vitamins, and bioactive compounds. Microbial strains are optimized to generate high-value products with desired properties. Many industrial production methods rely on model organisms such as *Saccharomyces cerevisiae* and *Escherichia coli* due to their robust and desirable traits [122]. The industrial biotechnology industry has grown into a significant manufacturing tool for fuel-grade ethanol, organic acids, and bulk amino acids, though most items are still specialized products for food and pharmaceuticals [123].Common organic acids produced through solid state fermentation are Gallic acid, citric acid, fumaric acid, kojic acid, and lactic acid. some agro-industrial wastes which are proven to be very resourceful substrates for production of citric acid in solid state fermentation (SSF) are wheat bran, de-oiled rice bran, sugarcane, coffee husk, pineapple wastes, kiwi fruit peels, grape pomace, and apple. For the production of citric acid from *Aspergillus*, pine apple waste was used as substrate. Secondary Metabolites are mostly produced from Fungus. Gibberellic acid is a secondary metabolite produced by a fungus in its stationary phase through solid state fermentation using wheat bran as substrate. Nicotinic acid, vitamin B12, thiamine, riboflavin, and vitamins B6 are the water-soluble vitamins produced on SSF with the help of different species of *Rhizophus* and *Klebsiella*, which is well-known producer of vitamin B12.

**Conclusion:**

Fermentation technology serves as a versatile and powerful tool in biotechnology, offering diverse applications in food production, pharmaceuticals, biofuels, and industrial biotechnology. Without a doubt, fermentation is a crucial and vital processing technique used to create new food products. It also emphasizes the significance of fermentation as a multifaceted and sustainable process for the production for the production of wide range of products. This chapter underscores the crucial role of biotechnology in harnessing microbial fermentation for the benefit of society, paving the way of innovative and eco-friendly solutions to address global issues. By harnessing the metabolic capabilities of microorganisms, fermentation facilitates sustainable production processes, leading to the development of valuable compounds, renewable energy sources, and innovative solutions. Continued advancements in fermentation technology hold immense potential for addressing global challenges and shaping a more sustainable future.

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