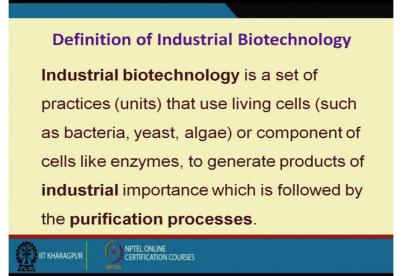
#### Course on Industrial Biotechnology Prof. Debabrata Das Department of Biotechnology Indian Institute of Technology Kharagpur Mod01 Lecture01 Introduction to Industrial Biotechnology

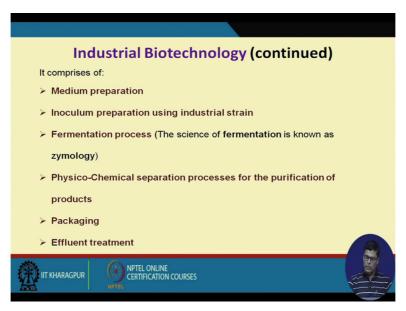
Course that I am going to offer that is industrial biotechnology. It has two components, one is bio biotechnology another is a industrial. Biotechnology again it has the two parts, one is bio another is technology as you that technology basically it is combination of science and engineering. Science tells why it is happening? How it is happening and engineering is the application of science. Basically whatever we develop in the day to day life and when we go for the application the both the combination of science and engineering is required that (()) (0:58) is call technology and bio stands for biological component, if the technology comes through with the help of some biological component we call in biotechnology. An industrial biotechnology basically it is what is in practice in the industry. There is industrial biotechnology.

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Now if you look at the definition of industrial biotechnology, is the set of practices, because what are the different practices we have in the industry to get a purified products as, for example, suppose we want to here what we used the living cells, bacteria, yeast different components, not only the living cells we can use some non-living components also, which is derive from the living of organism as for example, enzymes which is derive from the both plant system, microbial system, animal system which is use for the production of different products.

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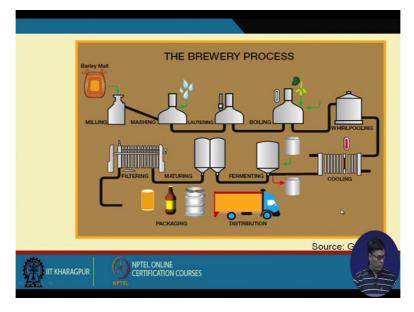


Now industrial biotechnology, it has the it comprises of different components, one is medium preparation and then inoculum preparation using industrial strain. medium preparation plays very important role as we know that media comprises of not only carbon not only a single component, it comprises of carbon source, nitrogen source, minerals and vitamin for the living cells, but for the non-living cells, suppose if we use enzyme we required it particular state, particular pH and temperature to have a particular reaction to get the definite products.

The inoculum preparation usually the industry we use the industrial strain, it is not the this is the specially prepared for the industry and it is it is we consider as a robust strain(())(2:57). Why it is robust strain (())(2:59), because it can has high productivity and I shall discuss more in details in subsequence slides, then it comes to the fermentation process.

Fermentation process is the actually that is when here organism that you know function it has the metabolic pathways (())(3:17) and it produces the (())(3:20) we through the metabolic pathway (())(3:21) the different products and the science of fermentation basically it also known as zymology and then when you get the desired amount desired food and then we go for some physico-chemical separation process to get the purified product when purified product we marketed that should be in the purified form, then after getting this purified product then it undergo packaging where and then for the this is packaging.

Now with this packaging system has been proved (())(3:54) extent for marketing purpose and after that you know that the during the product formation we also generate lot of organic waste that is to be treated. So you know what we call effluent treatment process that we have.

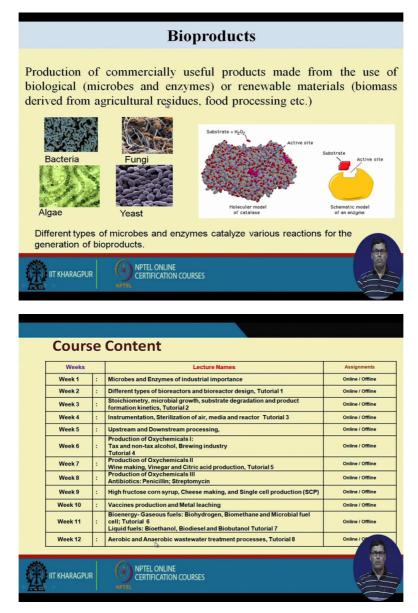


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Now I want to give typical example of the brewing industry, because throughout the world that you know different brewing processes are in practice, we know that we have (())(4:23) we have (())(4:24) in India we produce that allibear (())(4:27) and it comprises the different stage. So as for example molting, then milling then massing then lautering then you have this boiling then you have then whill pooling then cooling fermentation, maturing, filtration then packaging.

So what I want to mean that if you look at the this is the fermentation process, this is the what we you call brewery process and this is before material comes to the brewery process. There are so many units involved we have the molting process, we have milling process, we have massing process, we have lautering process, we have boiling process, we have whill pool the pooling that is process (())(5:14) then we have cooling then it comes to the fermentation. After fermentation it goes to the different separation process (())(5:22) this is call maturation process then we have filtering then packaging can be done in different ways either in the can, in the bottle, cellular barrels (())(5:33) and then it is marketing with the help of some kind of transport arrangements.

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Now this the course I divided into different parts. Now initially I shall restricted myself on microbe the microbes and enzymes for the industrial importance as I have give you some detail information on that, then I shall discuss about different types of bioreactors and bioreactor design and this would be followed by tutorial 1 and stoichiometry is very important part of any kind of fermentation process, because, because the stoichiometry give the material analogy analysis of the system then microbial growths, substrate degradation and product formation kinetics and this will be followed by instrumentation and sterilization of air, media and reactor. Then we I shall discuss the upstream and down-stream processing.

I come (())(6:36) for biochemical block fermentation processes like tax and non-tax alcohol, then brewing industry, wine making industry, vinegars, citric-acid production, penicillin,

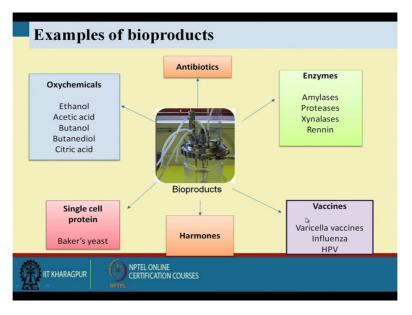
streptomycin, high fructose corn syrup then we have cheese making then single cell protein, vaccine production and metal leaching. We also try to cover this bioenergy, because bioenergy is very important part. Nowadays in because replacing the conventional fossil fuels bioenergical is very important also different bioenergy that is this produce where you in practice nowadays, who are one use the bio methane and another is bioethanol, there largely used biodiesel also used in (())(7:22) industry, I shall discussed about that how it produced and finally I shall discuss about the aerobic and un-aerobic waste water treatment process.

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Bioproducts			
Production of commercially useful products made from the use of biological (microbes and enzymes) or renewable materials (biomass derived from agricultural residues, food processing etc.)			
Bacteria Algae Fungi Fungi Fungi	Substrate = H <sub>2</sub> O, Active site Substrate Citive site Folecular model of catalase		
Different types of microbes and enzymes catalyze various reactions for the generation of bioproducts.			
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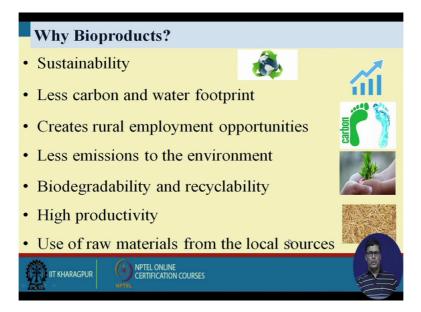
Now how question comes that what are the bio product? Bio production of commercially useful product means from the use of biological as for example microbes and enzymes or renewable materials like biomass is derived from the agricultural residues or food processing. So the different types of microbes and enzyme catalyze the various reaction what about the generation of bio products. So we have bacteria, we have algae, we have fungi, we have yeast that can involve to give produce different type of bio products then we have the enzyme that catalyze (())(8:11) is enzyme(())(8:11) that the that acts on the hydrogen peroxide produce the water and hydrogen molecules.

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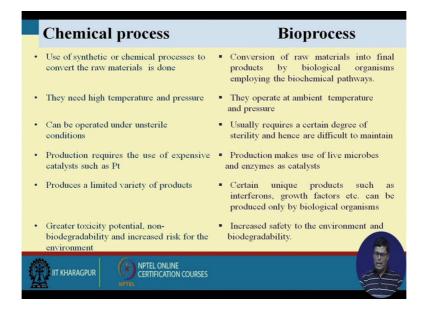
And this is the examples of the bio products that we have I just the talk about the antibiotics that is we have the lot of antibiotics in the nowadays available in the market to cure lot of diseases we have different oxy-chemicals that can be produces the biological means (())(8:37) what is ethanol then acetic acid, butenol and the citric acid. Different enzymes the enzymes can be used not only for the pharmaceutical industry. It can be used for the industrial processes like high fructose corn syrup formation. So we have the amylases we have proteases, xynalases and rennin, then we have vaccine that is nowadays, it is very much important to in the to protect our disease, because different type of vaccines that is usually apply to the babies so that you know they can be free from certain diseases. Hormones that is used particular in the hor (())(9:19) agricultural sector to improve the agricultural goal to a great extent. Then single cell protein like the baker's yeast largely used by the baker industries.

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Now why bio products, the reason is that it is sustainable, because we can use these bio products for longer period of time and second is the less carbon and water footprint that is very much essential for this and it creates rural employment opportunity, because not only is this bio process can be can be applied for the both in the small scale and bigger scales and less emission of the to the emission of pollutant to the environment that is another important. Biodegradability and recyclability. This is very important factors then we have high productivity and lastly we use the raw materials for the from the local sources. So this is different advantages of using bio products while (())(10:16) this is in practice.

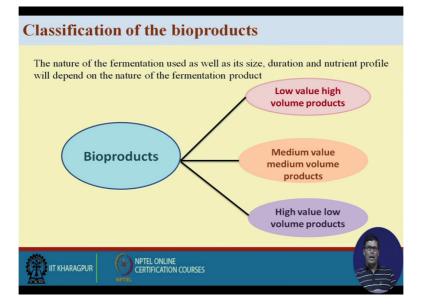
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Now initially we should compare that how this bio process, they compatible with a chemical processes. Now chemical processes one thing I want to tell you in the chemical process that if you want to produce the any kind of chemicals you any kind of product you your if you change the product your raw material will be changes in the chemical process, your product is complicated to your raw material will be complicated, but in the bio process is something different, because the raw material same carbon source can produce the different type of compound, thus (())(10:53) as for example I can give the example of glucose, glucose can be produce ethanol, it can produce citric acid. It can produce lactic (()) (11:03) acid.

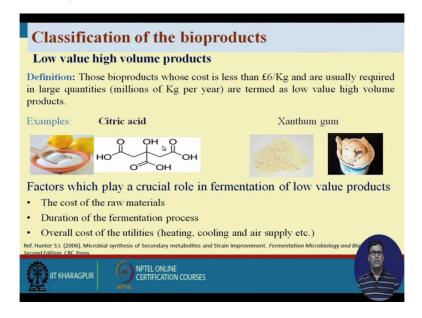
So different type of product formation can be taking place with the help of this this particular bio process and another advantage of the bio process is that it can be operated as the ambient temperature and atmospheric pressure and in the chemical process if you look at is usually operated at high high temperature and high pressure for that **we** we this quite anything to (()) (11:27) and it is easily operated one advantages is that one it is usually operated under (()) (11:34), but biological processes we allow our desire organism to grow in a environment, so your involvement should be sterilized and for the sterility purpose our (())(11:47) that is it is some energy is required to maintain the sterility of the system that is major drawback of this system and it also in the chemical process we required very costly say catalyst like platinum, for biological process we can have in the chemical process, but in the biochemical process we can have wide varieties of product and we have greater toxicity in the chemical process. So it mean itself (())(12:19) is very complicated. In a bioprocess whatever there the they have the effluent generesis (())(12:25) that usually bio degradable.

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Now the bio products they can be available in three different forms, one is here one is call low value high volume product, another is medium value and medium value and medium volume product and high value low volume products.

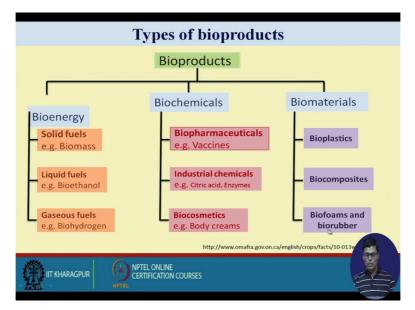
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# **Classification of the bioproducts** Medium value medium volume products Definition: Those bioproducts whose cost is around than £60/Kg and are needed in quantities less than a million Kg per year are termed as medium value medium volume products. Examples: Antibiotics Factors which play a crucial role in fermentation of such medium value products Duration of the fermentation Utility and nutrient cost Ref. Hunter S.I. (2006). Microbial syr NPTEL ONLINE CERTIFICATION COURSES IIT KHARAGPUR **Classification of the bioproducts** High value low volume products Definition: Those bioproducts whose cost is around than £60/mg and are needed in very less quantities (about 1 Kg per year) are termed as high value low volume products. Examples: Human insulin Interferon Nutrient and utility cost is a minor factor and is not critical in such fermentation Major emphasis is on improving the following traits of strain - stability - level of expression - Overall cost of the product ter S.I. (2006). Microbial synthesis of Secondary metabol NPTEL ONLINE CERTIFICATION COURSES

The examples there in the low volume products are those, which cost is around 6 pound per kg as for example, citric acid, xanthum gum, this is this is low value product and the high medium value and high medium volume products the cost is the about 60 pounds per kg the examples are different antibiotics like penicillin, streptomycin kanamyne kanamycin usually more costly as compared to penicillin. So this is consider as medium value and medium volume products, but the high value low volume products are human insulin that is largely used nowadays and interferon that is that is in practice this is produce very low volume but the cost is very high.

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Now the bio that bio products can be divided into three different types; one is call bioenergy, biochemicals and biomaterials. Bio I told you that bioenergy we have three different data types one is call solid fuel, another is the liquid fuel and the gaseous fuel. Solid fuel we have the biomass and with the liquid fuel we have bioethanol, biobutenol and gaseous fuel we have bio hydrogen bio methane. So different type of gases we can produce. Biochemicals we have biopharmaceutical, like vaccine can be produce. We have industrial chemicals like we have citric acid, then enzymes then bio cosmetic, like body creams can be produce through cells (())(14:25) and biomaterials we have bioplatic, biocomposit bioplatic nowadays quite highly demanded, because plastic causes the environmental pollution we know it. It is very difficult to biodegrade. So bio plastic has lot of demand in the market, biocomposit that is also largely used and then we have biofoam and bio rubber that can be also produced through this.

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Now if you look at in the biotechnology industrial seen arrow, the India is the among the top 12 biotechnology destinations in the world and ranks second in Asia after china where china is the first then the second is the India in Asia and the last year the growth of the Biotechnology industry about 57.14 percent and is estimated to reach about 11.1 billion dollar by 2017. The bio pharmaceutical segments accounted for the latest revenue. Now here we can see that you know in bio pharmaceutical how they are shearing the line part of these bio products.

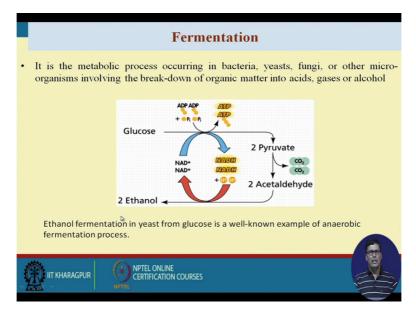
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Oxychemical	Current U.S. Value (\$ millions)
Ethanol	
Ethylene	6,790
Butadiene	1,320
Octane enhancer Industrial	560
11000001101	500
Subtotal	9,050
Ethylene glycol	1,260
Adipic acid	1,030
Acetic acid	620
Isopropanol Acetone	500
Acrylic acid	360
Glycerol	250
1,4-Butanediol	240
Propylene glycol	220
Methylethylketone n-Butanol	210 200
Citric acid	190
Sorbitol	90
Propionic acid	35
Fumaric acid	25
TOTAL OXYCHEMICALS	14,180
	nal Trade Commission, Washington, D.C.

Now this are the different made market values of different products that we have that we have, we have ethanol, we have ethylene glycol, we acetic acid, acetic acid the different type

of chemicals how it is produced through the biological process and their market value is given here.

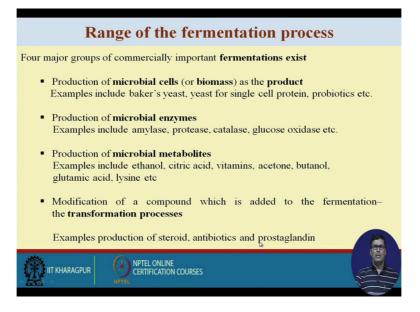
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And this is the examples how this bio products is usually produced, I have given the example of the ethanol, because the alcohol is produced to a great extent, because nowadays because alcohol not only use for the human consumption, but also used in the pharmaceutical sector, also as uses the power alcohol and also it is use as a chemicals install (())(16:23) by the chemical industries.

Now if you look at the how it is produce how the ethanol is produce by the fermentation industry, the by we can form if you take the example of simple compound like glucose or sucrose, sucrose when hydrolyze sugar when hydrolyze it produce fructose and glucose and glucose and fructose, they will undergo (())(16:47) which produce the pyruvic acid and pyruvic acid then it converted to acetaldehyde then to ethanol. So this is the biochemical pathways how it produce the ethanol through the fermentation process.

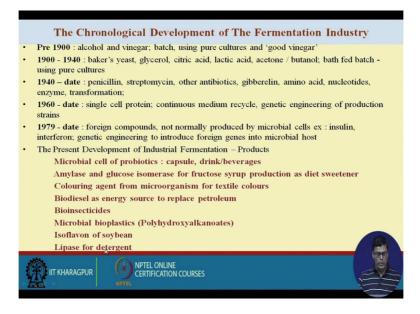
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Now the range of fermentation process 4 major groups of commercial important fermentation exist, the one is the production of the microbial cells as the product; examples include the baker's yeast, of for single cell protein and probiotics. This is the this is one types and second is the production of microbial enzymes, the enzymes as I told you that enzymes not only use for the pharmaceutical sectors but also it is for the industrial purpose to for the detergents we use this and also for the production of high fructose corn syrup we produce that.

Also, it is used for the here the bio sensor formation of the bioreactors sensors. Production of microbial metabolites, we have several I just I giving the example of ethanol beside that we have citric acid, vitamins, acetone, butenol and glutamic acid, lysine etcetera. The modification of a compound which is added to the fermentation with the transformation process that can be used to a great extent as the as for example the steroid, antibiotics and prostaglandin that we used.

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Now there is very interesting seen arrow that how this bio product development has been develop in the chronological order if you look at pre 1900 that the alcohol with the vinegar this is usually produce through the batch fermentation process, then in between 1900 and 1940 the baker's yeast, glycerol, citric acid, lactic acid, acetone, butenol, that is usually produce through the fed batch fermentation process, then 1940 on the to up to date that we have several antibiotics in the market like penicillin, streptomycin other antibiotics we have gibberellin, this kind of (())(19:08) growth hormone then we have amino acid, nucleotides, enzymes and transformation takes place.

Then 1960 whereas onwards we have single cell protein that continuous medium cycle genetic engineering of productions (())(19:25) strains. Then 1979 to onwards, we have following compounds not normally produce microbial cells as for example insulin, interferon, genetic engineering to introduce the foreign gene into microbial host. This is largely in practice. The present development of industrial fermentation products is the microbial cell of probiotic in the that is use in the form of capsule, in the form of drinks, beverage, amylase and glucose glucose isomerase for high fructose corn syrup production that is mostly use in the western country.

Coloring agent from microorganism for the textile what we considered as natural colored then we have biodiesel as the energy source to replace the petroleum then bio insecticides we know nowadays we have lot of problem with the pesticides and pesticides is such a chemicals, which I keep on accumulating (())(20:25) system (())(20:26) never goes out of your system and has (())(20:29) property. So if we use the bio insecticides this is the basically

the that the protein molecules that can be easily biodegraded. So we did not cause any kind of pollution problem, then we have microbial plastic, bio plastics then isoflavon soybean lipase for detergent.

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List of industrially important microbes			
Products	Microbes		
Bakery, beer, wine	Saccharomyces cerevisiae		
Yoghurt, kefir, probiotics	Lactic acid bacteria		
Soy sauce	Aspergillus oryzae, Zygosaccharomyces rouxii		
Tempeh (Deep-frying fermented soya beans)	Rhizopus oryzae		
'Topoi'	Hansenula, Saccharomyces		
Acetic acid	Acetobacter aceti		
Citric acid	Aspergillus niger		
Lactic acid	Lactobacillus delbrueckii		
Nata Nata	Acetobacter xylinum		
Pickles, sauerkraut	Lactic acid bacteria		
Glutamic acid	Corynebacterium glutamicum		
Lysine	Brevibacterium lactofermentum		
Penicillin	Penicillium chrysogenum		
'Oncom' (Foods fermented using mold, similar to Tempeh)	Neurospora sitophila 🖙		
Angkak	Monascus purpureus		
MTEL NPTEL	http://agroindustriindonesia.blogspot.in/2010/10/agroindustry-of-fermer		

Then a list of industrial importance microbes which is involve for the production of different type of products is listed in this table and we find that in the baker industry that we use the saccharomyces cerevisiae. This use the saccharomyces cerevisiae also use for the production of beer and wine, then we have lactic acid bacteria, it produce the yoghurt and we have kefir and probiotics. We have then Asepergillus oryzae is used Soy Sauce formation, tempeh deep frying fermented soya beans, the rhizopus oryzae. So different type of product that has been listed here that is then penicillin chrysogenum that is used for penicillin production process.

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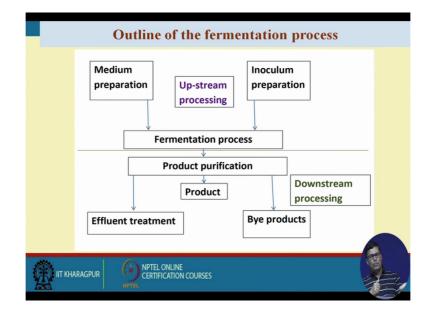
Outline of the fermentation process			
	Medium preparation Up-stre process Fermentation Product pur Product pur Effluent treatment	n process	
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List of industrially important enzymes and their applications			
Enzyme	25	Applications	
Protease	25	Food processing, Detergent industry, Health care etc.	
Lipases		Dairy and food processing industries	
Cellulase	25	Biofuel industries for the breakdown of cellulose	
Isomeras	ses	used to convert glucose syrup into fructose syrup	
Xynalase	5	Used in the paper processing industry	
Ligases a	nd Nucleases	Molecular biology	
Rennin		Cheese making	
Pectinas	e	Food processing (fruit pulp processing)	
β−gluca	anase	Brewing industries	
Trypsin		Pharmaceutical industry	
Tannase		Elimination of tannin	
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Now we have list of industrial important enzymes and their applications as for example proteases, the lipase, cellulases, isomerase, xynalases, ligase and nucleases, rennin, pectinase, beta glucanse, trypsin and tannase, because this is lot of enzymes that is used and I have given you the protease use in the food processing industry and the desire also in the detergent industry particular for removing the kind of strain that has been attached to the (())(22:20) that can be easily removed with the help of protease enzyme as for example, the blood can be degraded with the help of protease enzyme and different health care, it can be used.

Health care as for example that is used protease enzyme is used. Lipases it has lot of use in the dairy and food processing industries. Cellulose, nowadays for used in the biofuel industry for the breakdown of cellulose. Isomerase used for the conversion of glucose to fructose as

we know that fructose is the 10 times sweeter than glucose. So that is why that is used in the (())(23:01) industry to a great extent, we have lipase ligase and nuclease that is used in the molecular biology. The rennin is used for the cheese making industry. Pectinase in the food processing industry, trypsin is used in the pharmaceutical industries.

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Now finally I want to tell you that if you look at the industrial Biotechnology processes, it broadly it can be divided into 2 parts, one is we call it upstream processing another is the downstream processing. Upstream processes comprises of medium preparation, inoculum preparation and the fermentation process. So the different things that is involve as for example medium preparation medium I told you media comprises of carbon source, nitrogen source, minerals and vitamin that we mix in a tank then we have we shall have to sterilize it that is call medium sterilization. Then most of the fermentation process, they are operated aerobically and most of them so they are mostly operated aerobically, so we required air and air should be sterilized then inoculum preparation that is also very important that inoculum is usually prepared with the help of industrial enzyme, then this whole unit where we have including the fermentation process we call it upstream processing.

In the downstream processing that is nothing but the product purification, because I told you whenever we market any kind of product, that should be in the purified form, we cannot market the product, because we know that if you look at the chemical catalog, we have two type of products that is available, one is call that analytical grade chemicals or that is commercial grade chemicals. Analytical grade chemicals usually 99.9 percent purity and the commercial grade chemicals it might be 94, 90 percent 94 percent like this and if you look at

the cost difference of this particular chemical is used may be your analytical chemical, it is 4 times costly at then the commercial grade chemicals.

So with the purity of the chemicals is very important I can give the example of the penicillin production industry. Penicillin is the marketed in the 2 different forms in the form of capsule, in the form of injection fluid. Now injection fluid, it should be 100 percent free from contaminance, we could use directly injected to our blood. In a blood pH is 7. So any kind of contamination is there, the immunity your body your see our system will be affected, so it should be 100 percent free from contaminance, but when we take the antibiotics in the form of capsule, it goes through your stomach and when it goes through your stomach (())(25:45) here the stomach we know the our pH is 2 even some contamination is there your stomach pH will take care the contamination problem. So this is the things we are we are going to cover in this course I hope it will be very helpful to you all, thank you.