

Aspects of Biochemical Engineering
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Lecture – 05
Bioproducts And Their Market Values

Welcome to my course on aspects of biochemical engineering. Now today in the last 2 classes last couple of classes I discussed microbiology and biochemistry which is very essential as far biochemical engineering is concerned. We should understand that microbiology that deals with mostly the what are the different microbes, what is the classification of microbes. And biochemistry major mostly deals with what are the different bio molecules present in the living systems, and how we take part in different reactions. Now this particular lecture I deals with that what are the different bio products that is and their market value. Because what do you mean by bio products?

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Definition of Bioproducts

Bioproducts are usually produced from the
living cells (such as bacteria, yeast, algae)
or non-living materials like enzymes or
biomass.

Now, if you look at the bio products are usually produced from the living cells, such as bacteria, yeast and algae. Because different type of living cells that can produce the bio product. Not only living cells it can be produced from non-living cells also. Like enzymes or biomass, it can produce. I can I have you see that here that living system we call about the, we talk about the bacteria yeast and algae. And non-living cells we enzymes and the biomass that we have.

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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
Fungi
Algae
Yeast

Substrate
Active site
Substrate
Active site

Molecular model of catalase
Schematic model of an enzyme

Different types of microbes and enzymes catalyze various reactions for the generation of bioproducts.

<http://www.dehidalnews.com/news/1/coordn-component-in-yeast-made-but-home-brew-plates-still-not-feasible-1438640479/>
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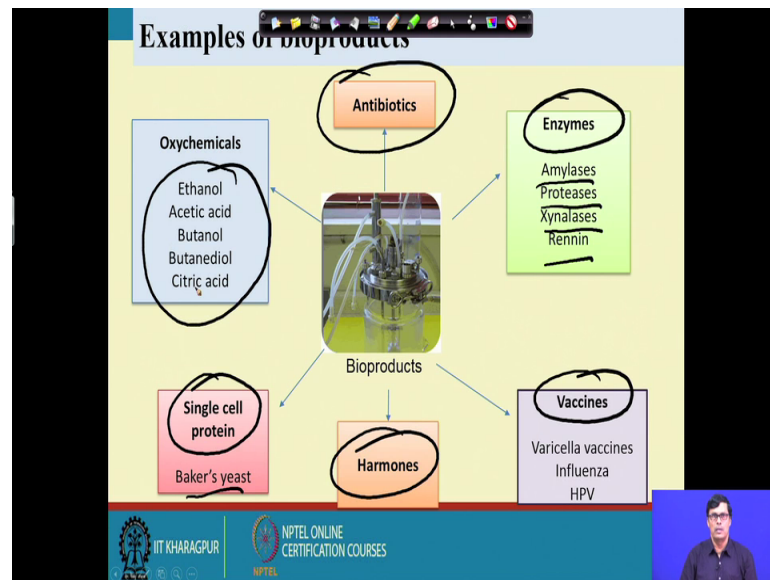
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Now, the bio products we have production of the commercially useful product made by the use of biological microbes or renewable material. So, bio products not only mean that you know that which is produced by the living system, but the if we use some kind of biomaterials for the production of some useful product, that also we considered as a bio products.

So, here I can see that, I can show you that what are the living organisms already we discussed, we have bacteria, we have we have bacteria, we have this bacteria. And then we have algae, then fungi, yeast that it largely used for the formation of different useful products. Now if you look at the enzymes, that you know that I have given the example of catalase enzyme. Now catalase enzyme is mostly present in the aerobic organism.

What is the aerobic organism, I told you before that organism, microorganism usually take the oxygen, which is dissolved in the fermentation media. And this fermentation when they take the oxygen it forms some kind of superoxide, like hydrogen peroxide or some superoxide. So, they should have some enzyme which can discrete degrade this the superoxide molecule. The catalysis is one type of this of that enzyme that can degrade the H_2O_2 to H_2O plus O_2 and this O_2 can be used by the organism for their metabolic purpose.

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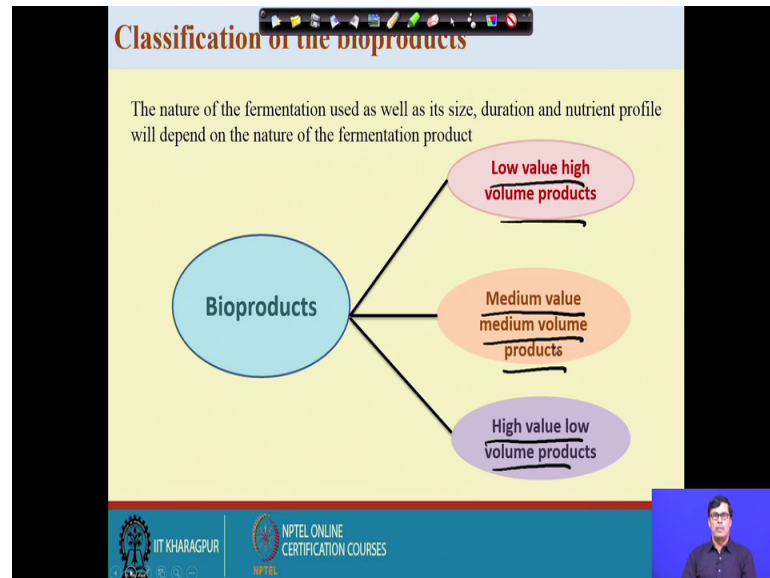
So, this is how it here it is shown that. Now what are the different bio products that we have in the market. We have different bio products as for example, we have I told you that I mentioned that there are different antibiotics that is we have in the market. Particularly, if you if you look at the history of the bio products, that you know that first antibiotics that has been marketed in the world that is the penicillin. And penicillin is kind of antibiotics it is active against the gram-positive bacteria.

Then we have enzymes. The enzymes we have amylase, we have protease, xynalase and the rennin is largely used in the different industry. As for example, amylase is we have been largely used in the in the beer making industry, the amylase and protease they are largely used in the beer making industry. Then rennin is used in the chin making industry. And in the vaccine, we have a that is used for the several purpose in the in to in our day to day life I can give the example of polio vaccine, this is this is a vaccine due to the invention of this vaccine the infection of polio has been removed to a great extent.

Then hormone is largely used in the agricultural sector for the growth of the plant as well as in the animals also sometimes we use the hormone in the living in the human beings also used for some rectification of some diseases we use something. And then a single cell protein, that is used as the source of a protein, because as you know that the microorganism they grow very fast as compared to plants and other materials.

So, it can be used as a very good source of protein. And again, kind of example we have that is the baker yeast. And finally, I want to tell this bio the processes can be used for the production of different oxy chemicals. And this has ethanol acetic acid butanol butanediol silencer citric acid the different type of products we can produce through this process.

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Bio products can be classified in 3 different ways. One is called low value high-volume products. And then medium value and medium volume products. And high value low volume products.

Now, what do you mean by that? Now I can give a typical example. Suppose when we talk about the citric acid industry, and citric acid is produced by using a *Aspergillus niger* from cane molasses. And this is the voluminous product. Because then huge amount of product and concentration of this citric acid may be may be 10 to 11 percent. So, you know that we can we can we use as a bulk production. We can I can give the example of ethanol. Ethanol when produced in the fermentation broth the concentration may vary from 10 to 14 or 15 percent. And this we produce in the bulk. So, this is the low volume low value and high-volume products. Low value with respect to the per unit cost of the product is very low. And high volume means a amount of product that is very high. That high work with c 2 g bio chemicals and where we used to produce 4 to 5 tons of citric acid per day. Now medium volume and medium value and medium

volume products we mean that if the cost of production I can give very typical example in the coming slide.

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Classification of the bioproducts

Low value high volume products

Definition: Those bioproducts whose cost is less than £6/Kg and are usually required in large quantities (millions of Kg per year) are termed as low value high volume products.

Examples: Citric acid Xanthum gum

Chemical structure of Citric acid:
OC(CC(=O)O)C(=O)O

Factors which play a crucial role in fermentation of low value products

- The cost of the raw materials
- Duration of the fermentation process
- Overall cost of the utilities (heating, cooling and air supply etc.)

Ref. Hunter S.I. (2006). Microbial synthesis of Secondary metabolites and Strain Improvement. Fermentation Microbiology and Biotechnology, Second Edition. CRC Press.

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Then I say I hope it will be clear, that that if you look at a low volume and high low value high volume products, we mean that the cost of if the cost of product is 6 pound per k g of products. This is a car, we mean 6 pound per kg we call it, then examples as I told you this is citric acid which is nothing but the tri carboxylic acid. Largely used for our day to day requirement. And factors that affecting the crucial low value products is the cost of raw materials. Duration of the fermentation process and overall cost of the heat releases. And the utilities means heating, cooling and air supply. Those are the different utilities that is that depends on the cost of production.


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Classification of the bioproducts

Medium value medium volume products

Definition: Those bioproducts whose cost is around $\text{£}60/\text{Kg}$ 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 synthesis of Secondary metabolites and Strain Improvement. Fermentation Microbiology and Biotechnology, Second Edition. CRC Press

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Now medium value high volume products, we have that whose cost is around 60 pound per kg. This is the and examples are different antibiotics. I have given the examples of penicillin who is largely used in our day to day life for the for killing the gram positive bacteria, because when we have some kind of injury, we have some kind of pulse formation and this pulse formation can be rectified with the help of penicillin. And factors affecting this process is the duration of fermentation and utility of the utility and the nutrient costs. Because we know as for example, that in case of penicillin production we required not only carbon source, like glucose, but also it nitrogen source as a constable occurred, but also it conveyed requires some kind of precursor like fennel acetic acid and phoenix acetic acid.

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Classification of the bioproducts

High value low volume products

Definition: Those bioproducts whose cost is around that £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

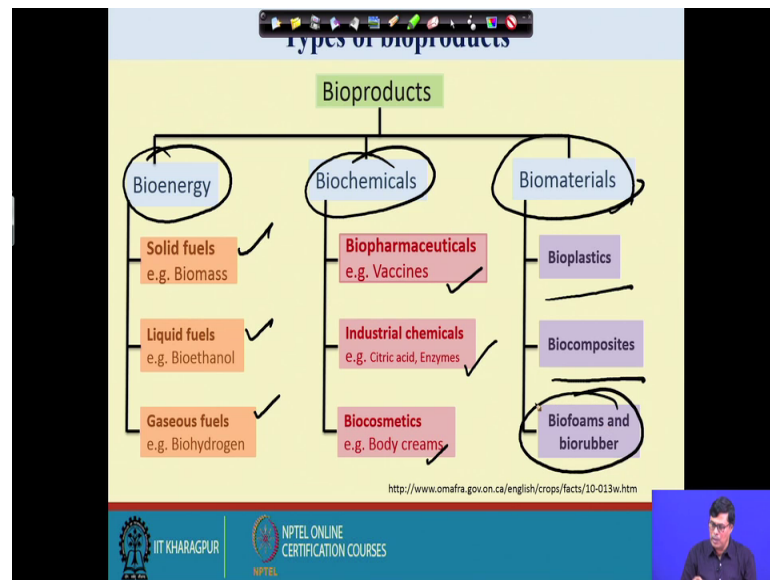
- Nutrient and utility cost is a minor factor and is not critical in such fermentation
- Major emphasis is on improving the following traits of strain
 - stability
 - level of expression
 - Overall cost of the product

Ref. Hunter S.I. (2006). Microbial synthesis of Secondary metabolites and Strain Improvement. Fermentation Microbiology and Biotechnology, Second Edition. CRC Press

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Now, high value low high value low volume products we have if you and cost is more than this is 60 pound per milligram of products. And examples are human insulin. As you know that we have as the time passes on more and more people they are infected by suffering from diabetes, and they used to take this insulin. And insulin is produced by using recombinant DNA technology, and this is very costly. So, this is this cost is a is lies in between the 60 pound per milligram. It is usually produced about one kg of product per year. And another important example is the interferon. The major emphasis for improving that this strength is the stability level of expression and overall cost of the product. Because since this is it is a recombinant protein. So, we that label of expression that plays very important role.

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Now, if you look at the general category of bio product, you know we can have 3 different categories. One is we considered the bio energy, we have bio energy as well as we consider it can be available in both the forms. Both 3 forms we have one is that solid fuels and the liquid fuels and the gaseous fuels. Now solid fuels we have biomass we have different biomass we can bond the biomass we can get the energy. But the problem with the solid biomass is the transportation problem, but liquid and gaseous fuel has the added advantage, because we can easily transport the liquid or gaseous fuel on 1 place to other very easily. Now and the different bio chemicals if you look at we have in the pharmaceuticals industry we have vaccines in industrial chemicals we have citric acid and enzymes.

And bio conservative we have body creams. This is a lot of bio products now it is used as a cosmetic industry so that carcinogenic property of the pure chemicals can be reduce to a great extent. Now biomaterials we have we have used in the industry we have bio plastic, I have I can give the example of that poly lactic acid which is largely used in the pharmaceutical industries, bio compost which has lot of lot of application in our agricultural sector. As you know due to use of inorganic fertilizer, the fertility of the soil that reduces a great extent by using the bio compose, it is possible to retain the particle character of the soil. And fertile character of the soil depends on the water retention property of the soil. Because plant is too take that nutrient through the process of

diffusion through their roots, and bio form and bio rubber this is another the biomaterials we have.

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The diagram illustrates the fermentation pathway. It starts with Glucose, which is converted to 2 Pyruvate. This step involves the conversion of ADP to ATP. Pyruvate then undergoes decarboxylation to form 2 Acetaldehyde and CO₂. Acetaldehyde is further reduced to 2 Ethanol, a step that involves the conversion of NAD⁺ to NADH. Handwritten chemical structures are provided for Pyruvate (CH₃C(=O)COOH), Acetaldehyde (CH₃CHO), and Ethanol (CH₃CH₂OH).

Ethanol fermentation in yeast from glucose is a well-known example of anaerobic fermentation process.

<https://ethanol-overview.wikispaces.com/1.+Ethanol+.+An+Aromatic+Compound>

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Now this is how fermentation is carried out, this is if you look at the; then I showed you this (Refer Time: 12:14) pathway, one mole of glucose produces 2 moles of pyruvic acid. And then this pyruvic acid, what is the formula pyruvic acid? This is CH₃COOH. Now when it undergoes decarboxylation reaction it forms acetaldehyde, acetaldehyde formulated CH₃CHO. And then when it is further reduced, it will form CH₃CH₂OH. So, this is the difference how the ethanol formation takes place, and throughout the world most of the country they are producing the ethanol through the biological process just to replace the gasoline.

Because gasoline usually produced through the fossil fuels which has limited result.

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Industrial fermentation processes

Four major groups of commercially important fermentations exist

- Production of **microbial cells** (or **biomass**) as the **product**
Examples include baker's yeast, yeast for single cell protein, probiotics etc.
- Production of **microbial enzymes**
Examples include amylase, protease, catalase, glucose oxidase etc.
- Production of **microbial metabolites**
Examples include ethanol, citric acid, vitamins, acetone, butanol, glutamic acid, lysine etc.
- Modification of a compound which is added to the fermentation—the **transformation processes**
Examples production of steroid, antibiotics and prostaglandin

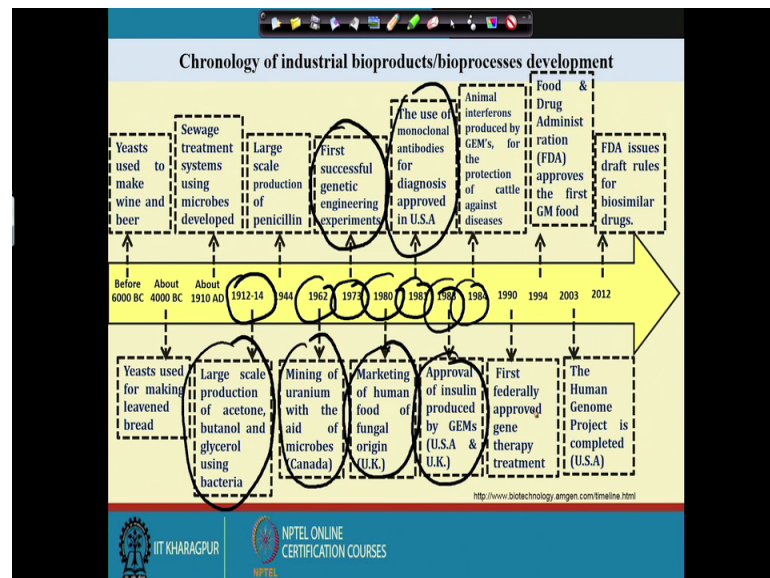
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Now, industrial fermentation process the 4 major groups; that is, very commercially important for the permutation exist. The production the microbial cells or biomass. As the product when bio mass itself acts as the product, I told you the bakers is the industry the baker's yeast is used in the in the bread making industry largely used. And this can be used as a single cell protein as a source of protein, and also probiotic. It is used because probiotic is very important now a days and sometimes, we want because in our system in a metabolic system we might be aware we have some desirable organism that is required in our metabolic system so that our system then can walk in a proper manner.

So nowadays lot of industry there producing probiotics. And which is largely recommended by the doctor for giving our digestion problem. Now and there are 7 microbial enzymes, we have like amylase, protease, catalase and glucose oxidase. Besides that, you know iii told you this is not only used in the in the food or pharmaceutical industry. This also used in the detergent sector. Because particularly protease enzyme in the when we have some kind of stain in our cloth. You know, that if we use some protease enzyme that the stain will go. Before use this protease enzyme it will go. That is help for removing the strain. This is, then we have different middle metabolic microbial metabolites that is used I told you this is we have ethanol. Then we have a citric acid vitamin, acetone, butanol, glutamic acid, lysine.

Different types of bio chemicals we can use for our different requirement. Now here I want to stress one point that whatever bio whatever chemicals we require in our day to day life most of the chemicals can be produced through the biological means. But in practice, these are not in practice the reason is that the concentration of this bio chemicals in the fermentation broth is so small our recovery cost is so high that we cannot compete with the with the chemical process. So, we do research just to improve upon the process. So, that concentration of these chemicals increases. So, the recovery cost can be reduced to some extent. So, that we can compete with the chemical process. So, in that way that you know that is that is the one disadvantage we have with a biochemical process that the concentration of the product. If we can increase the concentration of the product, then and only then we can we can reduce our recovery cost and we can compete with the chemical process.

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Now, here I want to show you one very interesting thing that, what is the chronological development of the different bio product and bio processes we have. And if you look at our this is we are talking about the history, that how different bio products formation take place. Now if you look at the before if you 6000 BC, before christ that we have mostly the yeast is used to make wine and beer. So, that is the startup of the bio products. Then yeast is then 4000 BC yeast is used for making the leavening breads. This is then in one 1910 AD, then we have used this or process for the sewage treatment using the microbes developed. Now here I want to point out again that waste we have it has been observed

by the central pollution control board, that most of the chemical and biochemical industry, they pose some kind of environmental pollution problem toward water stream to a great extent.

And more than 70 percent of the this wastewater treatment processes are controlled through the biological means. Because the reason is that if you use the biological process, your microorganism can utilize the soluble organics very easily, and convert it to carbon dioxide and cell mass. And since the cell mass is the insoluble mass, you can easily separate it out. This is the major advantage of that. That is why it is largely used in the in the case of the waste water treatment process. Then 1912 to 14 loss scale production of acetone butanol and glycerol using the bacteria that take place.

And then 1962 that the mining of uranium with the aid of microbes that take place. Now here let me stress one thing that the bio leaching, that plays the important role as far as per the industry is concerned. Particularly, in case of the woods where the main the metal concentration is very low. Now if the old content metal contrary rode contemplate very less amount of metal, our that recovery cost is very high. So, we usually it is it is recommended they should go through the bio leaching process so that the insoluble that material can be solubilized in the liquid form. And then from the liquid plum, we can purify we purify the product very easily. And then 1973 first successful genetic engineering experiments that take place.

And this is very important the reason is that through the genetic engineering it is possible to get the very useful products, I have given the example of insulin and that is that is largely used for safeguarding our that diabetes disease. And not only that we use we use this for hepatitis b and other vaccine also, we produce with the help of the genetic manipulation techniques. Then in 1980 that human food marketing of human food of fungal origins. That, that is another because we here I want to stress one thing, that since we are we are living in a vastly populated country, or you know other country also it is same applicable that you know a time will come our agricultural land will not be sufficient to keep the food to our people. In that case we shall have to find out better utility of the food. And for the better utility of the food we do we shall have to enrich our the quality of the food.

I can give a typical example that if you consider the and the vegetable protein, the utilization efficiency of the vegetable protein is about 10 percent. And if we because this is the reason is that that that you know that essential amino acids present in the in the in the vegetable protein, we not preferred, because there is some one or 2 essence a lamina acid. It might be lacking I can give the example of the rice protein it lacking of lysine enzyme. So, if we add lysine to this rice then a utilization efficiency of the rice protein will increase to a great extent. So, those are the things we shall have to look into. So, this small amount of product, if it is small amount food we take that will give the better impact in our body. So, our food consumption will reduce to a great extent. Then 1981 the use of molecular and antibody for diagnostic purposes that approved by USA 1983 approval of insulin produced I ii have already discussed. Then 1984 we have the interference products and other products that has been shown here.

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List of industrially important enzymes and their applications	
Enzymes	Applications
Proteases	Food processing, Detergent industry, Health Care etc.
Lipases	Dairy and food processing industries
Cellulases	Biofuel industries for the breakdown of cellulose
Isomerases	used to convert glucose syrup into fructose syrup
Xylanases	Used in the paper processing industry
Ligases and Nucleases	Molecular biology
Rennin	Cheese making
Pectinase	Food processing (fruit pulp processing)
β -glucanase	Brewing industries
Trypsin	Pharmaceutical industry
Tannase	Elimination of tannin

Now, let me they give you the examples of list of different important enzymes and their applications. As for example, that if you look at protease enzyme I was talking about. This is used in the food processing industry, detergent industry and healthcare. Now particularly I can tell you that in the I have already discussed about how coat is used in the detergent industry, healthcare particularly when the day to day life when we take food a little bit higher amount of food in our system. Then our system may be overburden or during the examination or during the disease, during the infection of a particular patients, the enzyme secretion of the body is not proper, then doctor

recommended some kind of the enzymes from outside so that it help in the digestion process. And food processing industry also; it is now it has lot of use.

Then lipase is as you see it is used in the dairy industry, and for improving the product food products and also the food processing industry is largely used. The cellulose they largely used for the bio fuel industry breakdown because it has been found that the lignocellulosic material, might be the best raw materials for the production of biofuels, because the raw material cost will be say will be very less as compared to any other biomass. So, by using this cellulose is cellulose enzyme it is possible to degrade the use the cellulose molecule for getting this biofuels. Then isomerase that use for the conversion of glucose fructose glucose to fructose syrup, as you know the fructose is more sweeter than glucose, then xynalase is used for paper making industry.

Then lie ligase and nucleus used in the monomer molecular biology, rennin is use is cheese making industry for precipitation of the proteins. Then pectin is enzyme that food processing industry food pulping processing beta glucan is that is used in the brewing industry. The trypsin is you in the pharmaceutical industry, and tennis is use for the elimination of tannin.

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Product	Current world sales (US\$ million)
Therapeutic proteins and monoclonal antibodies	170000
Antibiotics	26000
Amino and organic acids	12000
Industrial Enzymes	5000
Vitamins	3000
Fine chemicals, secondary metabolites	11000

Christoph Wittmann and James C. Liao, Industrial Biotechnology, Products and Processes, Wiley VCH, 2016

The these are the different industry that we can we can have then other bio products the market value, because I can I can give you it is the way. Unfortunately, I do not have the all bio product market value, but some major market value products is given here.

But first, I want to point out therapeutic proteins and monoclonal antibodies largely market in the world market. This is it is about 170,000 million us dollar. Presently, we have in the market. Antibiotics we have 20,000 us dollar. Then then we have amino acid and organic acid we have 12,000 us dollar. Industrial enzyme we 5,000 us dollar. And vitamins we have 3,000 us dollar. Fine chemicals and secondary metabolize we have 11 thousand us draw million us dollars. So, these are the this clearly indicates the potentiality of bio products in the global market.

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Product	Annual production (tons)
Bioethanol	26,000,000
L-Glutamic acid (MSG)	1,000,000
Citric acid	1,000,000
L-Lysine	350,000
Lactic acid	250,000
Vitamin C	80,000
Gluconic acid	50,000
Antibiotics	35,000
Feed enzymes	20,000
Xanthan	30,000
L-Threonine	10,000
L-Hydroxyphenylalanine	10,000
Nicotinamide	3,000
Vitamin F	1,000
Aspartame	600
L-Methionine	200
Vitamin B12	12
Provitamin D2	5

Gavrilescu M, Chisti Y. Biotechnology—a sustainable alternative for chemical industry. Biotechnol Adv. 2005;23:471–99.

Now, other than that a global production of the different specific product in the market is also given here. Now if you look at that bioethanol that is you now it is producing about 26,600, 26 lacks actually, that 2060 lakhs that is tons. You know, that use amount of 26 into 10 to the power 6 tons of this bioethanol is produced. Then glutamic acid is one thousand a thousand tons then citric acid also thousand tons. The lysine is the 350 thousand tons. Lactic acid is to 250 thousand tons. Vitamin c 80 thousand tons, this is a gluconic acid is 50 thousand tons, antibiotic is 35 thousand tons. Then that feed enzymes is the enzymes can be used as you, know I told you it can be used for a medicinal tonic that is feed enzymes is about 20,000 tons. That xanthan, it is about 30,000 tons and threonine is kind of amino acid this is 10,000 tons.

Then nicotinamide this is 3,000 tons, vitamin f 1,000 tones as then other products is given here. So, this indicate that you know that much then amount of production of this

bio products and the market value of the bio products is significantly a high in the world market.

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Product	Market (US\$ million)
Erythropoietin	6803
Insulin	4017
Blood clotting factors	2585
Colony stimulating factor	2181
Interferon beta	2087
Interferon alpha	1832
Monoclonal antibody	1751
Growth hormone	1706
Monoclonal antibody	1152
Plasminogen activator	642
Interleukin	184
Growth factor	115
Therapeutic vaccines	50
Other proteins	2006

Gavrilescu M., Cristil Y. Biotechnology—a sustainable alternative for chemical industry. Biotechnol Adv 2005;23:471–89.

The market value some pharmaceutical products are given here. You see the here through 14 this is 6803 million us dollar. Insulin is 4017 us million us dollar. Those blood clotting factors, then plot running factors. So, we know that during some kind of the sable attacks and other things the blood clotting take place, those who are largely used then in the colony simulation factored interferon beta interferon alpha monocular antibiotic growth hormone monoclonal antibodies that that plasminogen activator. And interleukin growth factor therapeutic vaccine and other protein. So, all these market values are given here. And that because main purpose are given this value, the just to give you an overall impression that different bio products has occupied significantly in the world market. So, in this particular presentation I try to tell you that what are the different bio products we have.

And bio products mainly divided into 3 different ways, the low value high volume products, medium value medium volume products, and high value low volume products. So, that purely depends on the cost of the products. We have seen that in case of low value high volume products the cost of the product lies within the 6th pound per kg of the products. Now in case of medium value and medium volume products the cost of the products is within 60 pound per kg of the products. But in case of high volume and low

value products, we have 60 pound per milligram of that product. So now difference the different examples I have given as far this products are concerned also. I try to find point out that what are the different market values of this particular bio products we have. And what is the deal what are the different uses of the bio products in the in the in our day to day life. And what is the amount of bio product that has been marketed in the world market. I hope this will give you the overall ideas on the bio products.

Thank you very much.