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# Green Approaches For The Industrial Production Of Active Pharmaceutical Ingredient

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**ABSTRACT:**

*This article's goal was to provide a framework for a bio-based economy by using biomass efficiently from an agricultural standpoint in order to build prospective end goods that could be bio-based (e.g. pharmaceuticals, active pharmaceutical components). We also expand our debate to include the development of bio-based products and biofuels, as well as conservation methods for bioenergy. The essential concepts for creating these by-products were further demonstrated in this review paper. Therefore, the purpose of producing these goods is to enable small-scale farmers to effectively meet the community's demand for bio-based materials and energy. Simultaneously, the development of local markets will create pathways and connections for larger markets. In summary, the review's goal is to investigate the biotechnology techniques' path so that less favoured producers and developing regions might join forces and relieve strain on the biomass production systems.*

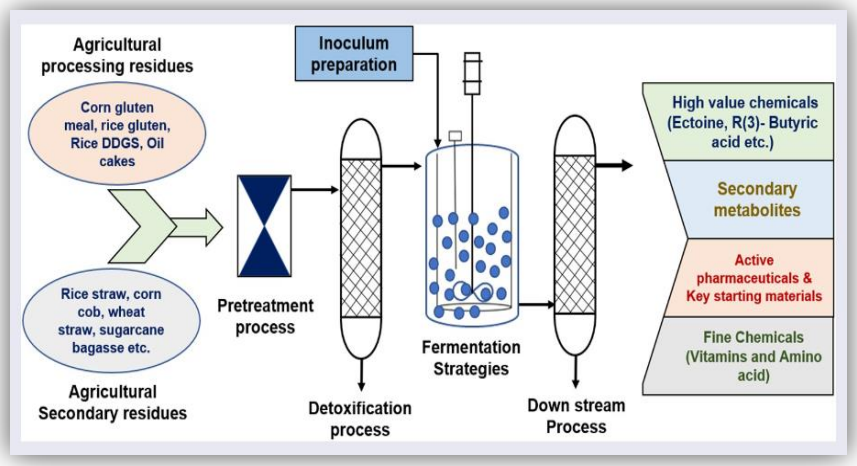


**Fig.1** Biomass Production Systems

**Key word:** API, Strategic Greener Techniques, Energetic life cycle analysis, Environmental Sustainability.

## Introduction

Under the banner of "Green Chemistry," safer product design, production, and application, as well as manufacturing methods, have been major objectives for the past ten years and will continue to progress. After the recession, there was a paradigm change in the usage of novel pharmaceuticals against inexpensive API drugs, which had a favourable effect on the expansion of the API business as a whole. Manufacturers of APIs are using a variety of cutting-edge technologies to keep up with this shift by shortening processing times and increasing output. Strong growth in the biotechnology and generics industries will support the expansion of the global market for active pharmaceutical ingredients (APIs). While current advancements in biotechnology and the continuous study and development of biosimilars are likely to create a huge potential for the API market across the world, the expiry of patented drugs and shift towards the use of low cost API drugs due to economic recession will help to propel the growth of API market, The market for active pharmaceutical ingredients

(APIs) is expanding as a result of advancements in bigeneric medications and high potency APIs. The essential technology for creating environmentally friendly industrial processes for producing active medicinal components is catalysis.

The design of an economical, environmentally friendly, and productive pharmaceutical and API manufacturing process highlights the critical role that catalysis plays. One of the most crucial instruments for the production of fine chemicals and pharmaceuticals at a reasonable cost and with sustainability is probably biocatalysts. Green Chemistry aims to minimise waste as much as possible while increasing the efficiency of synthetic processes, using less toxic solvents, cutting down on the number of stages in the synthetic route, and using less harmful solvents overall. Organic synthesis will thus contribute to the endeavour of sustainable development.1-3 Health and safety will be improved by altering the processes used in organic synthesis not just in small-scale laboratory settings but also in large-scale industrial production processes thanks to the new techniques. The methods include flow reactors, atom-economic multicomponent reactions, solid-supported synthesis, fluorous and ionic liquid-based recycling, reactions in alternative solvents, microwave and ultrasonic reactions, and green catalysis methods such as organo catalysis, supported catalysis, biocatalysis, fluorous catalysis, and catalytic direct C-H bond activation reactions. Prominent developments in solid-state chemistry, micellar catalysis, function-oriented synthesis for natural substances, catalytic asymmetric synthesis, and solid-state chemistry can all be applied to the production of active pharmaceutical components. Active pharmaceutical ingredients (APIs) are chemical-based compounds that are mostly made in Europe, China, India, and the United States. Because of their pharmacological activity, APIs are mostly used in concert with other components to diagnose, treat, alleviate, and cure diseases.

But in recent years, a lot of pharmaceutical companies have begun bringing these materials into their own nations from nations that produce active chemicals. People have employed modern medications to diagnose, treat, prevent, and cure illnesses. Each and every drug is made up of two primary ingredients: the excipient (such as lactose or mineral oil) and the active pharmaceutical ingredient (API), which is the main ingredient and must function chemically and biologically in your body. In a multi-step reaction, a variety of chemical compounds and raw materials are used to create an API. 1-4 Nevertheless, their primary goal is to directly cure the illness by combining inactive forms with their pharmacological activity. Worldwide, people use around one lakh tonnes of pharmaceutical items (for example, up to 24 percent of total pharmaceutical consumption occurs in Europe). Consequently, the production of these APIs has encouraged the release of chemicals into the environment, which has caused pollution to spread. Simultaneously, the massive production of pollution has drawn attention from all around the world, necessitating a rapid change in laws and regulations [1,2].

Thus, pharmaceutical corporations are endorsing the use of bacteria or yeast in microbial fermentation, taking into account the adverse effects of these chemical channels that produce API [3,4].Similarly, during the past ten years, there has been a growing trend towards the microbial-based manufacture of recombinants, and these manufacturings are responsible for the FDA's authorization for usage in humans. To compound the issue, microbial-based biopharmaceuticals generated returns of around $100 billion in 2017 and the industry is growing at a significant rate (6% CAGR) [5,6]. It is anticipated that the market for pro-tein medications derived from fermentation will grow from $44 billion to $60 billion by 2020. Likewise, the projected demand for vaccines and peptide hormones, which were $10–19 billion and $10–19 billion, respectively, is anticipated to reach $18–28 billion [7,8]. Pharmaceutical businesses that produce biopharmaceutical products today, including Bayer, AbbVie, Biocon, GlaxoSmithKline, Eli Lilly, Sanofi, and Merck, rely on microbial systems and partnerships. In contrast to conventional approaches, the focus of this review is on the recent and contemporary advancements in the chemical route of biomass processing, with a particular emphasis on the production of APIs. These active ingredients in pharmaceuticals and veterinary products can be manufactured or natural chemicals. Certain chemical-based active substances are made by risky chemical processes. Because of their uncontrolled exposure to the environment, their widespread production, use, and disposal are becoming dangerous for people, waterways (particularly drinking water), and other biobased life [3-5,7,9]. Additionally, throughout the past ten years, these chemicals have been found in ground water, drinking water, and waste water at trace amounts ranging from nanograms to micrograms [4, 6–9].

A recent investigation revealed the widespread presence of around 18 APIs in Lake Victoria, Uganda, with a concentration of 5600 ng L−1. Thus, it has been determined that these APIs are glo-bal pollutants. These chemical compounds are formed from numerous chemical components, most of which are initiated from a single intermediate, rather than from a single source of reaction [11]. In addition, a number of intermediates are created along the way to turn any raw material into an API. During their progressive engineering, which uses large reactors, these many reactions typically go through lengthy purification channels [12]. Before these APIs are supplied to the pharmaceutical companies, they undergo a subsequent purity check. Among the principal biomasses used to produce the chemicals are the

carbohydrates, which make up around 95% of all organic compounds on Earth. These are essentially used to produce more goods through chemical or fermentation change. Typically, biomass takes the form of feedstock and includes starch, cellulose, hemicel-lulose, pectin, and lignin [13]. During the earlier days of conventional processing, the vibrant chemical industry would typically use starch and other feedstocks high in carbohydrates as a raw material. Undoubtedly, various products in the form of che-mical and polymers can be generated by using any alteration in the procedure (fermentation) in order to achieve the desired derivative.

The application of this cellulosic biomass (lignocellulosic) has more of an inclination towards fuel production, which is greater than the conversion to xylose and glucose, despite the unease surrounding the use of starch between the food-based and chemical sectors [14–16]. Since lignocellulose makes up the majority of the biomass on Earth, all crop residue, including wheat and rice straw, sugarcane bagasse, and maize husk fibres, is categorised under it [4]. These crops are composed of lignocellulosic material, which is a combination of cellulose, hemicellulose, and lignin. These lignocellulosic materials undergo a variety of processing methods, such as chemical, thermal, or biological ones, and are transformed into chemicals, sugars, or ethanol [17–19].

However, pretreatments such as hydrolysis, delignification (using sulfuric acid), alkaline treatment, high-temperature steaming, and pressure-based homogenization are typically needed to break down these lignocellulosic materials and distort their organised and structured plant-based structure [20–25]. Consequently, these lignocellulosic materials can be easily transformed to the required intermediates following the use of pretreatments. To exploit the potential applications of lignocellulosic materials and minimise production processes or costs while maintaining environmental safety, we must overcome certain technological and economic obstacles [9].

Several published reports concentrate on the production of ethanol instead of other products [26, 27]. Because of this, the number of life cycle assessments (LCAs) that can produce numerous products is restricted. However, the majority of bio-based fuels and bioresources produced under the same roof of the enterprises are still not a promising alternative from an environmental or economic standpoint [28].

A specific example of this is the biorefinery system based on forestry [29]. Simultaneously, several important elements have been identified in relation to the environmentally preferred performance for the production of bioethanol and biodiesel. A broader and better-suited spectrum is required to carry out the united production of chemicals [30]. However, there are still significant pricing gaps that need to be filled in order to create large-scale biorefineries. Moreover, the chemical characteristics of biomass may not always be advantageous for raw materials derived from biomass; as a result, existing enterprises find it difficult to adopt new technology [31].

Additionally, 192,000 tonnes of propionic acid and its related esters are produced annually, and they are used in the chemical industry for a variety of purposes, including the manufacture of thermoplastics, solvents in paints and resins, and animal feed [32]. Furthermore, its production can be increased for the fermentation of sugar and glycerol from the perspective of a biorefinery [33]. Additionally, it is predicted that the economic conversion of glucose to propionic acid will be 15% lower than the conversion of glycerol. Similarly, another related forthcoming feasibility is to use glycerol fermentation to produce 3-hydroxypropionic acid, a crucial chemical building component [34]. Second, it can be changed into acrylic acid, which has superior environment-based functioning when compared to 3-hydroxypropionic acid. Simultaneously, researchers at the National Renewable Energy Laboratory have reported on the creation of a novel pre-treatment for the clarification of lignin and sugars generated from chemical nature. This pre-treatment uses an organic solvent in addition to water [25, 35]. Furthermore, the development of sophisticated technologies in the modern era (such as enzymatic and genetic engineering) has created new opportunities for the production of innovative industrial goods like plant-based APIs using raw materials [4, 6]. The idea of a biorefinery has evolved as a result of the chemical companies that generate APIs using biomass as a renewable raw material. This concept can be used to replace chemical-based manufacturing with the production of various bioproducts [8,10].

For the manufacture of green chemicals, APIs, and key starting materials (KSMs), which fall under a broad category, renewable resources are ideal sources to use as a substrate. As a result, the pre-sent assessment fully addresses the significant advancements and opportunities for lignocellulose as a feedstock that have arisen recently in the capacity of renewable biomass as a leading basis for chemicals and their linked compound products.

## 2. Environmental issues associated with the production of API chemicals through chemical route

These days, an increasing number of API-producing businesses are being pushed to take a more environmentally friendly route in an effort to decrease waste generation (particularly with regard to chemicals and solvents that are by-products) because of the environmental threat posed by pollution [36, 37]. While businesses that produce APIs are constantly searching for more efficient and cost-effective approaches, the actual number of steps required to produce API must be decreased if waste generation is minimised [38]. Since the main need for the creation of solvents or chemicals generated to produce a single pure molecule of API is fewer and less tan-gible stages. Similarly, manufacturers must use nonhazardous solvent types that can yield efficient and effective results in addition to reducing the number of stages [39, 40]. Thus, to achieve the results on greener guidelines, manufacturing companies should hire contract development officers (CMOs) and then use contract development and manufacturing organisations (DCMOs) to further pass their product through their services. This way, the formulation of the API process can be planned out early on with the aid of additional screening to prevent unavoidable changes or alteration in the later stage. This can be achieved by adhering to the scale-up processing protocols in the pilot plants, where careful supervision is required to assess quality control and assessments on a regular basis. However, establishing a kilo lab of this kind could provide problems for good manufacturing practises (GMPs), which call for careful oversight and a well-planned budget. Additionally, by taking these steps, we may lessen the production of byproducts and the exploitation of raw materials [41, 42].

Simultaneously, innovative organic synthesis techniques have been used in the past year to produce pharmaceutical items, strengthening the medical industry by lowering the number of accidents, diseases, and fatalities. Nevertheless, pharmaceutical chemists' efforts will be in useless if we simultaneously worsen the environment in order to accomplish this goal. As a result, the green chemical route is highly preferred for reducing the terrible effects on the environment. It is commonly known that the solvent disclosed by GlaxoSmithKline accounts for 80% of the waste produced by the pharmaceutical industry as byproducts [43]. Therefore, air pollution and other pollutants will be produced by the large-scale production of contaminated sol-vents. These methods can only be accomplished by using sustainable tools. In order to make the procedures threat-free, these tools require nib-to-nib strategy-based research, which entails the following actions. The important elements that can reduce environmental problems to the barest minimum are the methods by which biomass-generated feedstocks are produced, their bioconversion pathways, the use of specific safe chemicals, and standardised methods of technical processing. Comparably, the continuing use of biosubstrates while consuming nonrenewable resources and the integrated biorefinery idea can both significantly protect the environment [44]. To meet these requirements, the LCA methodology—which included a thorough evaluation of the processes and products from beginning to end—must be convinced.

## 3. Method of biomasses conversion in APIs synthesis

Environmentally friendly methods are currently gaining a lot of popularity for turning biomass into active pharmaceutical ingredients. By going in this direction, we can slow down the rate of global warming. In terms of fermentation, there are several methods that can transform lignocellulosic biomass into active pharmaceutical ingredients (APIs).

### 3.1.Chemical approach

Chemical conversions are the processes that convert biomass into value-added chemicals (furfural, levulinic acid, etc.) at high temperature and pressure conditions and in the presence of catalysts (phosphoric, hydrochloric, and sulfuric acids) [38–40, 44–46]. Even so, low yield is a constant source of significant obstacles to commercialization. Therefore, a variety of creative techniques have been used to convert biomass into chemicals in order to close the gap between the obstacles. Similarly, the Northwest National Laboratory described a unique approach that involved the use of modified carbon-based catalysts that were broadened to change sugar and organic acids [44–48]. Moreover, zeolites have been used to convert biomass into APIs, and their effectiveness in this process has been demonstrated [47, 49]. This is because zeolites have selective sizes and shapes and have demonstrated their potential as catalysts. Furthermore, it was discovered that silica-based catalysts are strong and consistent in their ability to convert glucose to sorbitol [46]. The investigation encompassed not only novel catalysts but also novel pathways and their potential for selective conversion of significant chemicals, such as hydroxymethyl furfural synthesis [48, 50].

Meanwhile, it was also claimed that acetic acid may be produced from biomass utilising supercritical water and hydrothermal processing [49–53]. Furthermore, from 1, 4-diacids and 1,3-propanediol, certain chemical intermediates (3-hydroxypropionic acid) also form and promote the creation of final stage products such as tetra-hydro furan (THF) and gamma-butyrolactone [50–52]. Certain monosaccharides, such as glucose and xylose, can undergo bioconversion in order to change into various chemicals, which is a method of chemical processing. Consequently, it was also said that supercritical water and hydrothermal processing may be used to create acetic acid from biomass [49–53]. Moreover, specific chemical intermediates (3-hydroxypropionic acid) from 1,4-diacids and 1,3-propanediol develop and aid in the synthesis of final stage products such tetra-hydro furan (THF) and gamma-butyrolactone [50–52].

3.2.Biotechnological approaches

The biotechnological pathway investigated the use of organisms or biocatalysts (enzymes) to convert biomass into useful compounds. In summary, it is regarded as one of the simplest, most straightforward, and most practical processes for turning biomass into industrial goods [4]. Biological conversions are generally milder than chemical conversions, which need high temperatures and pressures. Nevertheless, the idea behind these biotechnologically based conversions is not new, since yeast and bacteria have long been utilised to manufacture a variety of widely used compounds, such as acetone-butanol, citric acid, ethanol, lactic acid, etc. [56,57].Recently, there has been interest in the benefits of using biocatalysts to transform renewable resources into chemicals due to their selectivity, lower by-product generation time, and increased product yield.

We are unable to generate a wide range of products, despite some limits in the fermentation process caused by different variations in the microbes' route [6]. Simultaneously, there's a big need for innovative processing methods to expand the product line. Therefore, using technologies based on genetic engineering and recombinant DNA technology, which may modify gene coding and bring about the needed alterations for the metabolism of sugar, is the only option to provide variety and overcome

**Table 1:** Summery Of Chemical Product

| S. no. | Name of chemicals | Substrate name | Microbe's name | Production process strategy | Yields | Reference |
|---|---|---|---|---|---|---|
| 1. | Diosgenin | Dioscorea zingiberensis | Mixed culture of *Trichoderma reesei* and *Aspergillus fumigatus* | Solid-state fermentation | 95.82% | [69] |
| 2. | Glutathione | Spent coffee grounds | *Millerozyma farinosa* | SmF | | [70] |
| 3. | 2,5-furan dicarboxylic acid (FDCA) | Lignocellulosic biomass | Chemical route | Catalyzed synthesis | 75% | [71] |
| 4. | Glucaric acid | Corn stover | *Gluconobacter oxydans* | Two-stage fermentation | 8.7 g/L/h | [72] |
| 5. | Glutamic acid | Rice straw | *Bacillus subtilis* NX-2 | Solid-stage fermentation | 73.0 g /L | [73] |
| 6. | Itaconic acid | Glucose | *Aspergillus terreus* | SmF | 146 g/L | [74] |
| 7. | 1,2-Propendiol | Cellobiose | Beta-glucosidase-expressing *E. coli* | SmF | 1.48 g/L | [75] |
| 8. | 2,4-Butanediol | Soy hull hydrolyzate | *K. pneumoniae* | SmF | 21.9 g/L | [76] |
| 9. | Isoprene | Poplar (*Populus* spp.) | Recombinant technology | - | - | [77] |
| 10. | Lactic acid | beechwood | *Lactobacillus delbrueckii* sp. *bulgaricus* | SmF | 51.6 g/L | [78] |
| 11. | Ectoine | Rice straw hydrolyzate | *Halomonas elongata.* | SmF | 377 mmol/ kg FW | [79] |
| 12. | R(3)-Butyric acid | Glucose, xylose, and arabinose | *E. coli PPA652ara* | SmF | 1.38 g $g^{-1}$ dry cell | [80] |

The constraints of biotechnological routes [58]. Likewise, modified Escherichia coli proved useful for the production of the compounds (catechol and adipic acid) from glu-cose. Recombinant Saccharomyces yeast converts glucose and xylose present in cellulosic biomass into ethanol [59].

Additionally, compounds made from biomass can be produced using entire cells and immobilised enzymes. Huang and Yang [60] generated fumaric acid from glucose and maize starch by rotating the fibrous matrix of immobilised Rhizopus oryzae cells. Hames et al. [61] have patented the technology of converting biomass hydrolyzate into chemicals by absorbing it on solid metal oxide support utilising a microbial process with compounds made from lignin and fermentation inhibitors to increase yield.

For this reason, attempts have been made continuously to modify enzymes and living things in order to manufacture the needed compounds, especially from renewable sources. The conversion of biomass into higher-value compounds through biological processes is favoured by high yield, selectivity, and low waste streams. However, a number of obstacles stand in the way of the ongoing biologically based changes (such as increased energy needs, slower production rates, and constant stirring) that prevent the intended outcomes from being achieved in bulk [3, 6].

In order to convert saccharides into chemical-based byproducts during the fermentation process, biorefineries are significantly necessary [62–64].

In this way, the raw materials were encouraged to completely degrade into unalloyed sugar solutions and generic feedstocks. After that, microorganisms are employed in a fermentative medium to generate surplus metabolic product. As a result, these metabolic products can also be used to convert large molecules via chemical or biological processes. Nevertheless, arabinitol, aspartic acid, fumaric acid, glutamic acid, levulinic acid, succinic acid, sorbitol, 2,5-furandicarboxylic acid, 3-hydro-xybutyrolactone, and 3-hydroxy-propionic acid are the essential 12 molecules that have been identified as the most advantageous for use in the conversion of biomass [65,66]. It was suggested that the above-mentioned chemicals could be produced more effectively through fermentation using a glucose-based medium and genetically modified microorganisms. These microorganisms would be used to enhance the chemical conversion of saccharides derived from biomass molecules, specifically glucaric acid, levulinic acid, 2,5-furandicarboxylic acid, and 3-hydroxybutyr-olactone [67, 68]. Table 1 provides a summary of several significant bioactive molecules that are derived from various biomasses [69–80].

3.3.Metabolic approach for API production

The branch of metabolic engineering is one of the empowering skill of science that has an eminentrole in the expansion and progress of cell factories to further produce pharmaceuticals, fuels, chemi-cals, and food ingredients via following the route of microbial fermentations [69]. With the development and expansion of genetic engineering, it is likely now much more feasible to produce small protein-based molecules via fermentation, such as insulin and several growth hormones. At the same time, metabolic engineering made it possible to turn tiny microorganisms into cellular factories by using cheap raw materials like sugars generated from biomass to produce chemicals and fuels [81–84]. Numerous industry applications of cutting-edge bioprocesses for transforming feedstock into agriculturally based products were demonstrated in the literature reviewed by Hong et al. [81]. The Dutch multinational company DSM has investigated one of its several biotech routes for the synthesis of the antibiotic cephalexin, having previously done so for the chemical conversion of penicillin.

A similar joint venture between Novozymes and Cargill aims to create a bio-based process for the production of 3-hydroxypro-pionic acid. Nevertheless, by employing an isobutanol synthesis method, Gevo has expanded the biofuel potential. Furthermore, Amyris has improved upon a yeast-based fermentation process to produce farnese, which can be used to produce biodiesel or transformed into the widely used chemical squalene.

It has been observed that submerged strains of Streptomyces clavuligerus generate CA. Thus, Ser et al. [85] have investigated several different strains in an effort to boost production. In order to manufacture CA, S. clavuligerus has also been cultivated using glycerol, the most widely accessible carbon source, which has been reported to increase the cultivation up to fivefold [86–88]. According to recent research, Saccharomyces cerevisiae is a big cell factory that produces vibrant industrial products [81]. In a similar vein, our team is also working on this yeast to produce butanol so that it can be used in the pharmaceutical business and for the manufacture of biofuels (like biodiesel). Numerous theoretical investigations have elucidated the potential of cell factories in generating an extensive array of compounds, such as malic acid, glycerol, and lactic acid [85,89–91]. Furthermore, isoprenoids are becoming increasingly polymorphic, suggesting the synthesis of additional bioactive substances by the use of unique enzymes that may be investigated for chimeric pathways

[91]. Due to these factors, a great deal of attention has been paid to increasing the microbial production of isoprenoids by relocating relevant genes and adhering to a plant-based pathway with some important genetic modifications of the leader sequence [92].

## 4. Some important types of API chemicals

4.1.Shikimic acid

Shikimic acid is widely utilised in the pharmaceutical sector to synthesise chiral building blocks. Oseltamivir, an antiviral medication based on shikimic acid, is used to treat influenza patients as well as prevent them from getting sick (A, B). Additionally, shikimic acid is essential to the creation of Tamiflu, an anti-influenza medication [93–97]. However, producing a greater quantity of Tamiflu is considered risky. The synthesis phases of this drug reaction include potentially explosive chemistry, therefore careful handling is necessary due to the moderate reaction conditions. Since it is expected that catabolite repression controls the transport systems of shikimic acid, methyl-α-D-glucopyranoside, which mimics glucose, was added to the culture medium to reduce the uptake of shikimic acid by E. coli that can synthesise it [97]. Quinic acid production was minimised throughout, ranging from 0.09 to 0.01 mol/L, as a result of methyl-α-D-glucopyranose being substituted for glucose. When methyl-D-glucopyranoside was added, the yield of shikimic acid increased from 28 to 35 g/L, whereas the yield of glucose initially increased from 0.14 to 0.19 mol/L. Strains of E. coli that blocked the first three steps of the Pittard and Wallace aromatic amino acid pathway can be used to measure aromatic amino acids and aromatic vitamins using shikimicacid [95]. Shikimic acid is currently produced by the Swiss pharmaceutical company Roche using fermentative methods on E. coli [90].

The creation of several bioproducts during the synthesis of shikimic acid, however, is the main cause for concern. Numerous researches have found that limiting the carbon source during the fermentation of shiki-mic acid results in the formation of a significant number of bioproducts. On the other hand, if the medium is refilled with a high carbon source, a high shikimic acid buildup results. It has been discovered that growth conditions that are carbon-rich and phosphate-limiting favour the development of shikimate over byproducts, and that restricting carbon growth causes the formation of byproducts [98]. This is related to the inhibition of the aromatic amino acid pathway following the synthesis of shikimiate-3-phosphate (S3P). Bacterial phosphatases were responsible for the conversion of S3P into shikimic acid. Draths et al. [99] discovered that in logically modified E. Coli strains, the disruption of the K and L genes (which encode shikimate kinase I and II) and the amino acid pathway in these strains resulted in the most advanced metabolic engineering production of shikimic acid. Moreover, whey, a dairy waste product, can be a useful source of glucose extract due to enzymatic whey hydrolysis [100]. This glucose could be used as a starting material to make shikimic acid.

4.2.Succinic acid

In addition to being present in beer, coal, meat, eggs, honey peat, molasses, fruits, urine, and plants, succinic acid, also known as butanedioic acid (C4H6O4) or amber acid, is a frequent metabolite in microbes, animals, and plants. Since its initial purification from "amber," the ancient, fossilised resin of ancient trees and conifers, in 1546, it has been widely used. By breaking down acetaldehyde, the most hazardous metabolite of alcohol, it has been reported to be able to cure hangovers from alcohol. Medicinal uses for succinates often include sedatives, antispasmers, antirheoters, contraceptives, potassium ion inhibitors, and antioxidants. pp. 101–103. It has been acknowledged that succinic acid's linear saturated structure offers a promising intermediate for the synthesis of highly relevant compounds related to industry. Applications for succinic acid are numerous and include waste gas cleaning, plating, photography, food, medicine, agriculture, textiles, plastics, cosmetics, and radiation dosimetry. It is used as feedstock in esterification reactions to produce a variety of commercial chemicals, including polybutyrate succinate (PBS) and polyamides [104,105]. The newest use of succinic acid is in the production of "Bionelle," a biodegradable plastic that is succinicacid and 1,4-butanediol ester, by Tokyo, Japan's Showa Highpolymer Co., Ltd. In [106]

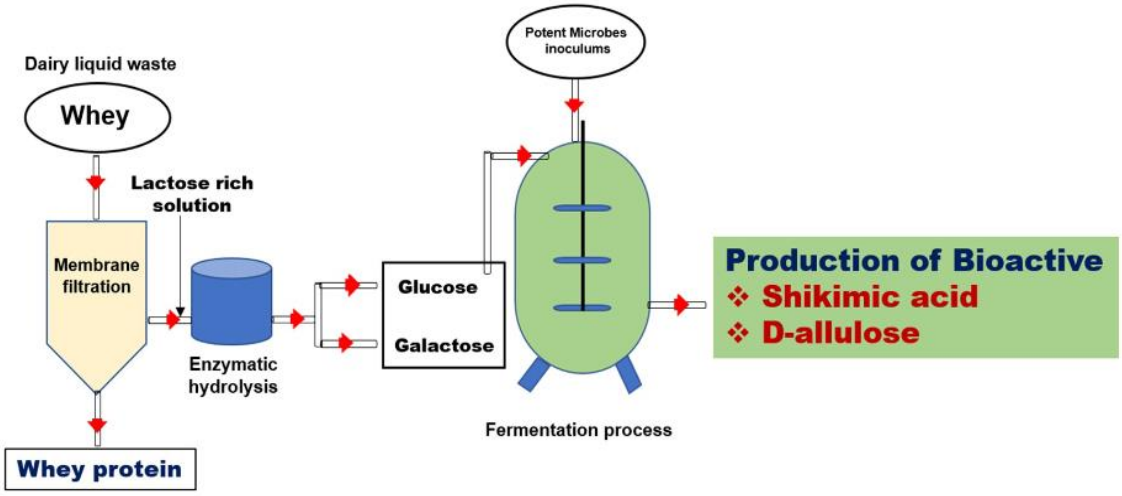


**Figure 2:** Systemic prestation of utilization of dairy waste for the production of APIs

This is mostly because the cost of the chemicals needed to convert maleic anhydride into succinic acid has decreased its industrial applications [107]. Furthermore, lignocellulosic biomass and petroleum products are hydrolyzed to produce succinic acid for commercial use (Figure 2), which raises environmental concerns [108]. Green technology is currently leading the chemical industry to limit pollution from petrochemical processing and solve supply chain problems by basing hydrocarbon production on an environmentally friendly, renewable carbohydrate economy [108,109].

4.3.Erythritol

Around the world, this sugar-based alcohol is recognised as a low-calorie sweetener. Many fruits and fermented foods naturally contain erythritol [110]. It is typically produced from glucose through fermentation (using food-grade osmophilic yeast and Moniliella pollinis, yeast), which ferments the glucose and produces erythritol [111]. It is almost entirely non-caloric (approximately 60–70%) and does not raise blood sugar levels or promote tooth decay at the same time. Erythritol can be produced by fermenting glucose using food-grade osmo-philic yeast. approximately (of roughly 60–70%) a non-caloric sugar that does not promote tooth decay or change blood sugar levels at the same time. Osmo-philic yeast suitable for food. After being taken out of the fermentative broth, erythritol is purified; the resulting crystalline product has 99% purity. Because of its unique digestive metabolism, it does not cause any gastric-related negative effects [112]. Because erythritol can be found in food, the US population's daily consumption of erythritol is estimated to be 80 mg. Erythritol has been verified to be present in both human and animal bodily fluids. Both human plasma and animal foetal blood contain amounts of about 1.2 mg/L. Erythritol concentrations in human urine range from 10 to 100 mg/L [113]. However, renowned countries as Japan and the United States have already marked it as zero- calorie sugar, wherea, European regulations cur-rently label it under nearly low calorie sugar (~0.24 kcal/g).

4.4.Clavulanic acid

Clavulanic acid is a popular medication that is reasonably priced. It is utilised in the battle against Figure 2. Systematic illustration of lignocelluosic biomass generation of succinic acid.bacterial resistance to β-lactam antibiotics, and it is also listed on the World Health Organization's essential medicinal list. Olive pomace oil (OPO) is an industrial waste product from olive oil that has been investigated as a substituted carbon source for S. clavuligerus's clavulanic acid production. Taran et al.'s work on OPO was conducted in [114]. It was discovered that olive pomace oil was six times more affordable than glycerol. According to estimates, OPO can be utilised in place of a carbon source to produce clavulanic acid.

But it was found that OPO can also be used as a possible supply of carbon (Figure 3). Similar to this, Efthimiou et al. [115] discovered that S. clavuligerus forms olive oil, which serves as a unique carbon and energy source to aid in the production of clavulanic acid. The outcomes demonstrated that yields and production are comparable to those explained by complex media containing oil. The concept of distinct metabolic pathways for converting the substrate into the intended product was illustrated by the variance in the recoverable yields.

When employing S. clavuli-gerus to produce clavulanic acid, glycerol and arginine, a nitrogen source, are the typical carbon sources [116–118]. When oils, such as olive oil, are employed to produce antibiotics in bacteria, complex culture media containing carbon has been used [119, 120].

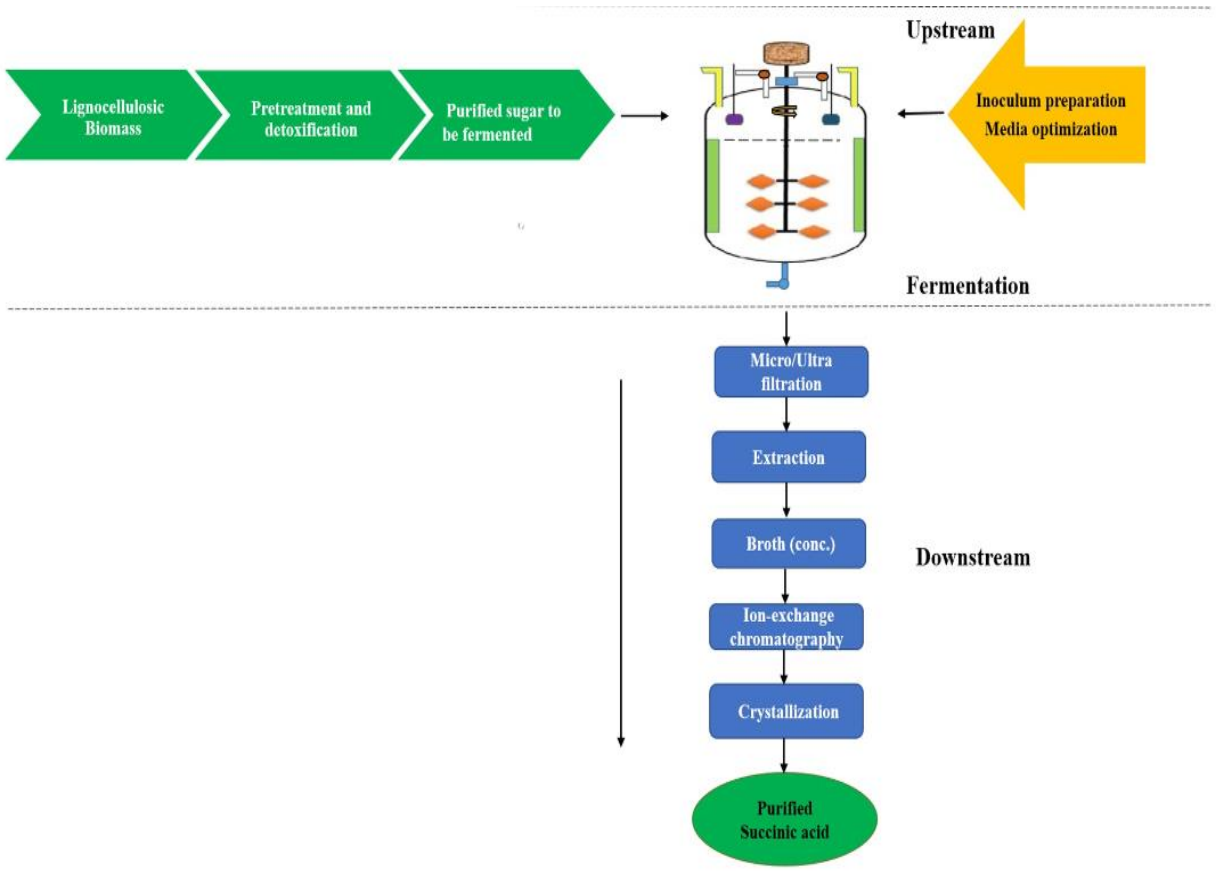


**Figure 3:** Sysremic representation for the production of succinic acid using lignocelluosic biomass

4.5.Cephalosporin (7-aminocepahlosporanic acid) antibiotics

These are derived from cephalosporin and are regarded as important medications that are effective in treating bacterial infections and illnesses. The cephalosporins' heterocyclic moiety has recently produced a wide variety of medications. Among the β-lactam antibiotics based on cephalosporins that have been marketed are cefdinir, cefotaxime, cefuroxime, and ceftriaxone [121]. The most recently created and efficient medications for treating severe infections caused by Staphylococcus aureus that are resistant to methicillin are ceftobiprole and its variants. Cephalosporin C is the most acceptable starting material that can be acquired in the required amount at a fair cost through microbial fermentation, and it can be used to begin the synthesis of 7-amino-cephalosporanic acid (7-ACA). Additionally, cephalosporin C is a direct precursor that causes 7-ACA to develop byamide bond cleavage [122].

4.6.Rifampicin

Known as "Wonder Drugs," rifamycin is an antibiotic with a broad spectrum of applications and a high demand in medication therapy for humans. It prevents the spread of a wide variety of pathogens, such as viruses, bacteria, and eukaryotes [123, 124]. Ragi bran was used to optimise the usage of a mutant strain of Amycolatopsis mediterranei OVA5-E7 in solid-state fermentation (SSF) for the synthesis of rifamycin SV (1310 mg/ 100 gds) utilising inexpensive agro-industrial by-products [125]. By adding deoiled cotton cake (10% w/w) to substrate with a pH of 7.0, 80% moisture content, an incubation temperature of 30°C, and a 25% v/w inoculum percentage for nine days under solid state fermenter conditions, the yield can be increased even further to 197 g/kg of dry substrate.

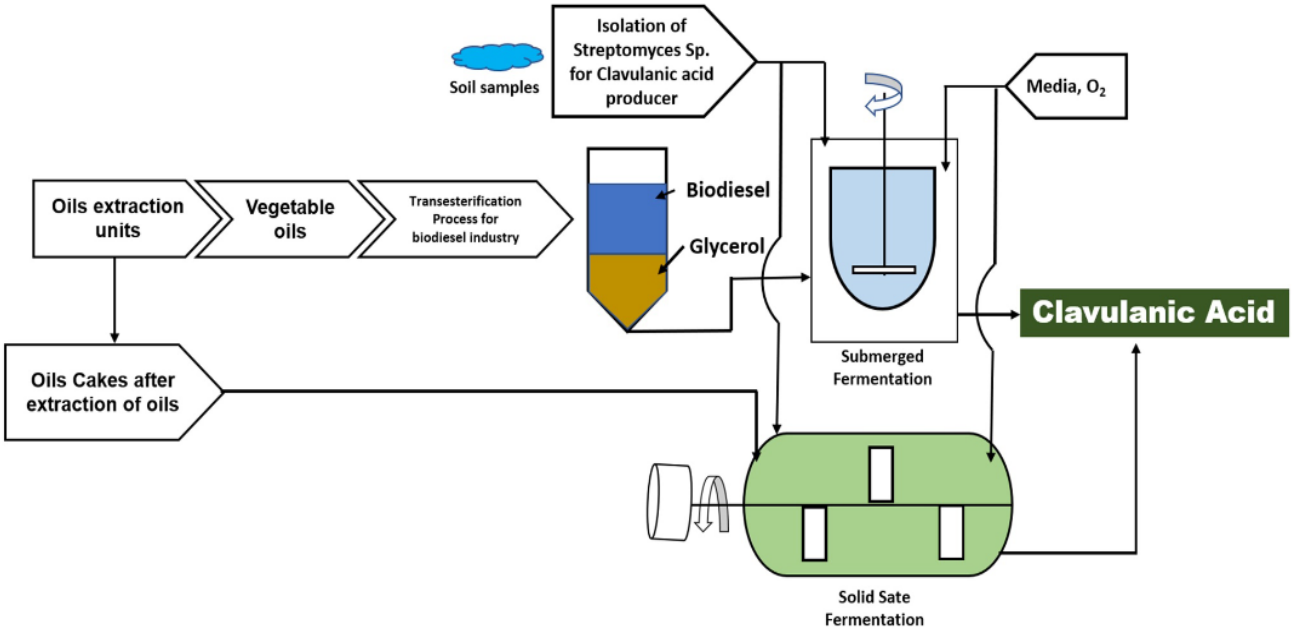


**Figure 4:** Utilization of processing residues (oil cake and glycerol) from oil extraction and biodiesel production industry for clavulanic acid production through fermentation approach

4.7.Pregabalin

An effective anticonvulsant, pregabalin is prescribed to treat neuropathic pain, fibromyalgia, and seizure disorders [126]. The asymmetric synthesis of the stereo isomeric structure, or (S)-enantiomer, has gained significant importance in the pharmaceutical sector due to its recognised pharmacological action with pregabalin [127]. Key intermediary of (S)-pregabalin, (S)-3-cyano-5-methylhexanoic acid, has been asymmetrically synthesised using chemo- and biocatalytic processes. There have been reports of the asymmetric synthesis of (S)-3-cyano-5-methyl-hexanoate, with 98% and 97% of excellent enantio-meric yield from nitrilase [129] and bisphosphine rhodium [128]. Despite the fact that both routes were undesirable from an economic and environmental standpoint [130].

4.8.Ectoine

Microorganisms that are grown in a medium containing a high concentration of salt generate primary metabolites that aid in their adaptation to harsh environments. Ectoine is the name of the principal metabolite [131]. Ecoine is a type of amino acid that is generally produced by bacteria that are halophilic. Ectoine is a premium substance that is frequently utilised in medications and cosmetics. Moreover, lignocellulosic biomass and processing residues can be used to create ectomyin. Ectoine production is currently costly because of the increased cost of the substrate. The low cost of the substrate being used to produce ectoine is another area of interest for many studies. After at least nine cycles, 7.4 g/L of ectoin were successfully recovered from fermentation broth utilising bacterial milking procedures produced by Halomonaselongata [132]. The productivity of the process was 0.22 g/L/h. Using the halophilic bacteria H. elongata (DSM 142T) in batch fermentation of 15% (w/v) NaCl, ectoin was produced on an industrial scale [133]. Cells were then separated, and ecoin extract was extracted from these cells using hypoosmotic shock.

**FUTURE PROSPECTIVES:**

As per the latest Pike research, by 2020, the $100 billion green chemical and engineering business will be dominated by one third in Asia, resulting in a $30–40 billion industry. One of the biggest Asian markets, India, is quickly implementing green engineering and chemistry techniques because to the rapidly evolving circumstances of today, including: sociocultural changes, regulatory agencies' enforcement consciousness, business seeing the opportunity, the government

understanding its part, and so forth. That change in the current dynamics creates enormous prospects worth over $5 billion in the entering India's developing green chemical and engineering business in the next five to ten years.

## CONCLUSION:

"Organic synthesis," the focus of science on synthesising substances in the lab, includes the pharmaceutical industry's hunt for small molecules with biological activity. A practical synthesis of the discoveries from the biological sciences and the chemical sciences, including information on the target molecule and the mechanisms behind disease, forms the basis of rational drug discovery for small molecule treatments. The development of a more practical and economical process for producing novel therapeutic scaffolds is aided by the application of microwave chemistry and green chemistry, as well as the rational drug discovery principles and other tactics like diversity- or natural product-based drug discovery. It is also evident from the literature that more often a combination of one or more of these strategies can help abridging the ‗valley of death'. The examples, presented here, although not exhaustive, may help the pharmaceutical society in presenting an outlook to appreciate the new trends and techniques.

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