

Biocatalysis for Green Synthesis: Exploring the Use of Enzymes and Micro-Organisms as Catalysts for Organic Synthesis, Highlighting their Advantages Over Traditional Chemical Catalysts in Terms of Selectivity, Efficiency, and Environmental Impact

Pratiksha N Jagtap¹, Pallavi P Somwanshi², Sayali S Nalegaonkar³,
Hanumant N Palkar⁴, Sanyogita D Mungale⁵, Nagnath P Suraywanshi⁶,
Pooja S Shiralkar⁷, Sudarshan J Shinde⁸, Priti R Suraywanshi⁹,
Gokul V Sirsat¹⁰

¹Assistant Professor, Department of Chemistry, Rajarshi Shahu College, Latur (Autonomous)
^{2,3,4,5,6,7,8,9,10}M.Sc. Chemistry, Rajarshi Shahu College, Latur (Autonomous)

Abstract

This study explores the use of microorganisms and enzymes as catalysts for organic synthesis, highlighting the advantages of these catalysts over conventional chemical catalysts in terms of selectivity, efficiency, and environmental effect. This study explains the major advantages of biocatalysis, such as its high selectivity, mild reaction conditions, efficiency, low environmental impact, and compatibility with renewable feedstocks, by looking at several case studies and experimental results. The importance of biocatalysis in advancing environmentally friendly and sustainable manufacturing processes is emphasized

Keywords: Biocatalyst, Green Synthesis, Efficiency, Environmental impact etc.

1. INTRODUCTION:

For many years, enzymes have been used in a wide range of chemical processes [1]. For instance thousands of tons of acrylamide are produced using nitrile hydratases, and enzymes have been a part of detergents for over thirty years [2]. In recent times, there has been a growing trend in the application of proteins as catalysts in the chemical synthesis of more complex compounds, including medications. Because they combine the benefits of a catalyst and a directing group to control selectivity in a single reagent that can also be utilized with other enzymes in a one-pot reaction, enzymes are especially potent [2]. In the last 20 years, numerous attempts at complete synthesis have been made possible by coupled synthetic–enzymatic systems, and the use of enzymes is now standard practice in some process chemistry [3].

Enzymes play Important role in various chemical and metabolic process [1]. Innovative protein engineering technologies that enable quick catalyst activity optimization, such as computational design and laboratory evolution, have propelled biocatalysis in the pharmaceutical sector (Experimentation). Consequently, stringent reaction parameters (Results) can now be satisfied for the effective development of bioprocesses (Applications) within manageable timeframes.

These characteristics include non-physiological reaction settings such high activity on artificial substrates, high temperatures, high substrate concentrations, and resistance to a wide range of pH values and organic solvents [1]. Databases of accessible biocatalysts and their reaction profiles are beginning to be established in addition to protein engineering tools (Reproducibility and data deposition) [2].

The science, technology, manufacture, processing, design, and analysis of materials with diameters ranging from one to 100 nanometres are all included in nanotechnology [3-5]. Nanoparticles, nanotubes, fullerenes, and other forms of nanofibers are examples of nanomaterials. Components of nanoparticles must have three dimensions of no more than 100 nm. Insoluble, physiologically stable materials with one or more exterior dimensions or an interior structure with a size range of 1 to 100 nm are referred as nanomaterials [6-8]. Currently, a wide range of nanoparticles, including carbon, manganese oxide, copper, iron, titanium, silver, palladium, and titanium, are successfully manufactured on an industrial scale.[9].

2. ENZYMES IN GREEN SYNTHESIS:

Chemical researchers have always been interested in enzymes. A hydroxy nitrile lyase was employed by Wohler and Liebig more than 180 years ago to release HCN from a cyanohydrin. The synthesis of (R)-mandelonitrile and mantelic acid was the first enantioselective synthesis ever achieved in 1908 by the reverse process [10]. By this point, Buchner had just won the Nobel Prize in Chemistry for discovering that fermentation could happen without a cell, and Fischer's "lock and key" theory was well accepted. Thus, the stage was prepared for enzymes to become central to the study of chemistry. However, this was surprisingly not how history turned out [11]. Even though there were significant advances in science and industry, many chemists ignored enzymes in their work.

The state-of-the-art in enzyme-based ecologically safe organic synthesis is presented in Green Chemistry. The enzyme is always the essential component that makes the chemistry possible and contributes to its greenness [10]. Research on well-established subjects, such as lipases and other hydrolases, is currently ongoing. They are the preferred catalyst for complicated substrates with limited water solubility, as this problem demonstrates. Applications in ionic liquids, dynamic kinetic resolutions, and kinetic resolutions are still highly valuable [12]. However, their use in polymer synthesis—especially when combined with renewable starting materials—might be more intriguing.

Halogenations with enzymes are a relatively recent development, in contrast to lipases. Not only was carbon-carbon bond synthesis a prominent area of study in the past for enzyme-catalysed reactions, but it continues to be so now. Aldolases and ThDP-dependent enzymes have new substrates that propel them into the future and guarantee even greater commercial uses in synthetic processes that are safe for the environment [10].

Enzymatic methods of producing biodiesel have garnered a lot of interest, mostly because they are considered a "green route" in fuel manufacturing [13]. Thus, a sophisticated bibliometric investigation covering the worldwide scientific biodiesel synthesis using immobilized enzymes was carried out. Consequently, publications were located, examined, and categorized in accordance with the substrates, enzymes, supports, immobilization techniques, and reactors that were described. The examined articles

were written by researchers from 748 institutions across 64 different countries, demonstrating the broad interest in these technologies [12]. However, ten countries—China at 23 percent, Brazil at 17 percent, and India at 11 percent—account for more than 80% of all documents published in this field. 67% of the publications mentioned using vegetable oils as basic ingredients. During the last ten years [13].

The extremely pre-organized active site pockets of enzymes, which properly place the catalytic residues for transition state stability, have mostly been credited with their remarkable efficiency in speeding chemical processes. The intrinsic flexibility of the enzyme structure complements this exact arrangement in the active site pocket to optimize the chemical processes [14]. Enzymes could adopt a variety of conformations, and these conformations frequently play crucial roles in equally vital activities, such as the binding of substrates and/or the release of products to resume catalysis. To generate highly pre-organized active site pockets for transition state stabilization, particular amino acid modifications (both in the active site and in distant locations) should be suggested using computational enzyme design techniques [14].

3. MICRO-ORGANISMS AS A CATALYSTS FOR ORGANIC SYNTHESIS:

The use of specific enzymes for chemical transformations, known as biocatalysis, has become a standard technique in organic synthesis and is widely used in industry. The exceptional stereo-, regio-, and chemo selectivity as well as the usually high activity seen in much biotransformation are the outcome of precisely controlling the reaction within the biocatalyst's active region [15]. This control is attained by the catalyst moving subtly, the reagents precisely positioned in relation to one another in a precisely calibrated three-dimensional environment, and the reagents activating interactions with the protein [16].

To create strategies for simultaneously controlling the configurations of several stereogenic centres, the reduction of β -hydroxy ketones to their corresponding 1,3-diols by baker's yeast was studied [17]. It was discovered that the reactions exhibited good diastereoselectivity and were enantiospecific in general. We also took into consideration substrates that have a substituent at the α position of the carbon atom. There was more selectivity shown when the substituent at the α -carbon atom was a member of a ring [17].

In the early stages of biocatalysis, it was thought that transition state stability was primarily responsible for the enzymes' ability to accelerate reaction rates. This theory was disproved, nonetheless, when it was shown that antibodies with the perfect complement structure to the transition state performed noticeably worse than enzymes [18]. It was discovered that transition-state stability alone was insufficient for effective catalysis. Examining an enzymatic catalytic cycle in detail reveals that, in a perfect scenario, many interactions between the substrate and the enzyme govern each step [19].

Both ester hydrolysis and transesterification Lipases and esterase act as catalysts. [22] The synthesis of active pharmaceutical ingredients (APIs) commonly uses the biocatalytic transesterification or hydrolysis of esters, which is mostly utilized in kinetic resolutions and represents a typical approach to generate molecules with excellent optical purity.[23]. It was shown that the application was applicable to both axial and planar chirality molecules in addition to those with central chirality. However, these days, it is not thought that such methods are optimal since the kinetic resolution of a racemic product leads to a 50% loss of the starting material [24]. However, the recycling of the unwanted enantiomer can be included with careful design of the synthetic pathway. Pregabalin production (the active ingredient in the popular medication Lyrica) is one example [25].

The racemic API was produced by the first generation of synthesis, and many recrystallization cycles were needed to produce the pure enantiomer. Various biocatalytic methods, such as enzymatic reductive amination and enzymatic C-C reduction, were thoroughly examined to offset the loss of the inactive

enantiomer [25]. The last method makes use of lipase from *Thermomyces lanuginose* (commercial lipase called Lipolase).[20] Chemical preparation of a cyan-diester as a racemate resulted in its transformation in a kinetic resolution to the enantiomerically [21].

Many of the microbes are also used in the organic synthesis reactions and it is very easy to use microbes in Organic and green Synthesis and it is also ecofriendly and Hazzard free to use them. In Recent Years, the use of green Chemistry is encouraging the use of biocatalysts which are basically Micro-organisms, and these can reduce the use of most of the chemical and traditional Day to day use catalysts. Many of the Microorganisms like yeast are used in Bio fermentation Process to increase alcohol production by safe and Secure way without damage to reactant and Get desired Product.

4. ADVANTAGES OF GREEN CATALYST OVER CHEMICAL CATALYSTS:

Biocatalysts are becoming indispensable instruments in chemistry because of new methods and technologies [23]. Previously limited to laboratory use, biocatalysis can now be applied on an industrial scale, with the result that complex molecules can be synthesized efficiently. Biocatalysis opens new Ave Biocatalysis has evolved, and thanks to the development of new technologies, its application has been accelerating significantly in the modern era. The enzymatic production of esters using lipases was invented in 1916. [4], and the application of microbial extracts led to a first breakthrough. Invertase immobilization was described in the same year [5], while Novo Nordic in Denmark produced proteases on a large scale in 1960.

The 1970s saw a significant advancement in biocatalysis due to scientific advancements in molecular biology. The second revolution in biocatalysis occurred in 1980 when cloning and gene expression made it possible to market a large range of enzymes. Information for research and can solve chemo-selectivity and efficiency issues that traditional chemistry is unable to address.[22]

To contribute to the wide range of global sustainability, chemists, pharmacists, medicinal chemists, and chemical engineers can build procedures, protocols, and synthetic techniques using the framework that green (sustainable) chemistry offers. green artificial environments, in particular Space [23].

The cornerstone of green chemistry is catalysis. By creating environmentally friendly catalysts, green solvents, using microwave and ultrasonic radiation, solvent-free methods, grinding, and chemo-mechanical techniques, synthetic chemists can overcome the drawbacks of conventional synthesis, including slow reaction rates, hazardous solvents and catalysts, and lengthy reaction completion times [24]. A member of the class of nitrogen-sulfur-containing heterocycles with a variety of pharmaceutical and medical uses is 1,2,4-thiadiazole, a preferred structural Modification [25].

Heterocyclic pharmacophore-based bioactive therapeutic medicines are synthesized using green chemistry synthetic techniques and are very important in medicinal and pharmaceutical chemistry [30]. Many isomeric forms of the adaptable heterocyclic thiadiazol rings, including 1,2,3-, 1,2,4-, 1,2,5-, and 1,3,4-, have significant therapeutic efficacy against a range of disorders. The 1,2,4-thiadiazole scaffolds are a notable class of core heterocyclic structures with five members that contain nitrogen and sulfur [31]. They are of great interest due to their role as a structural component of biologically active molecules, serving as a useful intermediate in medicinal chemistry and a component of clinical drugs [31].

5. SELECTIVITY OF GREEN CATALYST OVER CHEMICAL CATALYSTS:

Depending on how many steps the catalytic reaction goes through, synthetic processes can use either homogenous or heterogeneous catalysis. Heterogeneous catalysis involves two or more phases, whereas

homogeneous catalysis is a single-phase reaction that is often liquid/liquid. One of the many benefits of using homogeneous catalysts is that they can lower reaction temperatures, which saves energy [32]. Greater specificity and fewer undesired byproducts are typically produced at lower temperatures. As a result, these catalysts offer a completely safe synthesis, reduce energy costs, and increase yields and purity. The necessity to separate and retrieve the catalyst is one of its main drawbacks, though [33]. The creation of active sites by the attachment of metal complexes with a specific chemical composition to support surfaces is a crucial component of heterogeneous catalysis [32]. Among the issues with heterogeneous catalysts are: The lifespan of heterogeneous catalysts is significantly shortened by high working temperatures. Elevated temperatures hasten the deactivation process, diminish the selectivity of the catalysts, and impede their capacity to generate substantial yields [33].

Many of the catalysts are causing impact on environment and on the Product Quality and Increasing the purification Steps and Getting much more time for Reaction Yield [33]. The Selectivity of the green catalysts impacts abnormally on the yield of the reaction and gives ecofriendly and more potent product for the Reaction to be Produced. The Range of Selectivity of Green Catalysts is impactful as compared to the Other Chemical Catalysts [34]. Antibody catalysts are another type of biocatalyst that are often used [36]. The specificity and selectivity of antibodies correlate with the structure of the antigen needed to provide the immune response. Antibodies can be created against any molecule with a surface structure. They bind with ligands (antigens).

Many chemical processes that are conducted stoichiometrically rely on methods that are frequently expensive, ineffective, and detrimental to the environment. As a result, there is an ardent desire to develop and use safer and more effective methods. Within this framework, catalysis is currently regarded as a distinctive and essential cornerstone of green chemistry, and among the most advanced instruments in organic synthesis for the creation of numerous excellent compounds and useful materials. It has made chemical transformations more sustainable by opening new avenues. Green-catalyzed organic reactions have made significant contributions to the reduction of undesirable side products and the improvement of desired synthesis steps by improving selectivity.

6. ENVIRONMENTAL IMPACT OF GREEN CATALYST OVER CHEMICAL CATALYSTS:

chemical designing pioneers built the primary large-scale plants, clearing the way for the fabricating of hundreds of thousands of items, counting fills, fertilizers, and drugs, that have been essential to human improvement. Nevertheless, the overwhelming dependence on fossil assets in these forms has brought about extreme natural and wellbeing impacts. A later investigation of around 500 chemicals uncovered that the generation of more than 99% of them transgresses the secure working space of at slightest one of the seven planetary boundaries assessed, especially climate alter, sea fermentation and alter in biosphere keenness, and hence can be regarded unsustainable [12]. The current straight economy demonstrates, in which as it were roughly 7% of extricated assets from normal capital are reused, compounds the natural burden. These challenges have contributed to the move into the Anthropocene age, characterized by human-induced natural changes, and have made constraining worldwide warming to 1.5 °C inside this century an impressive challenge [32].

1-allyl-3-methylimidazolium chloride, 1-butyl-3-methylimidazolium chloride ([BMIM]Cl), sodium dicyanamide, sodium thiocyanate, silver nitrate, sodium nitrate, chloroauric acid, 1-ethyl-3-methyl-(EMIM), 1-butyl-3-methyl-(BMIM), 1-octyl-3 methyl (OMIM), 1-decyl-3-methyl-(DMIM), 1-dodecyl-3-methyl- dodecyl MIM), 1-ethyl-3-methyl imidazolium salts, etc. can be used as ionic liquids as a

solvents [37]. Which affects lesser in the Environmental Crisis and Helps to Sustainable Development. Catalysis plays a crucial role in the environmentally friendly synthesis of chemicals. By replacing traditional synthetic pathways with environmentally friendly alternatives, we can significantly reduce the production of unwanted by-products, co-products, potential wastes, and pollutants. Catalysts have the potential to streamline the synthesis process by minimizing the number of steps typically involved in conventional methods [37]. The utilization of catalysts in chemical synthesis not only contributes to the development of safer technologies but also enables the production of safer chemicals [38].

7. ACKNOWLEDGEMENTS:

Put applicable sponsors acknowledgements in this section; do not place them on the first page of your paper or as a foot-note. Guide's name may be put either here or on the first page. Other supportive people's names can be mentioned in this section.

REFERENCES:

1. Bell, E.L., Finnigan, W., France, S.P. et al. Biocatalysis. *Nat Rev Methods Primers* 1, 46 (2021). <https://doi.org/10.1038/s43586-021-00044-z>
2. Yamada, H. & Kobayashi, M. Nitrile hydratase and its application to industrial production of acrylamide. *Biosci. Biotechnology. Biochem.* 60, 1391–1400 (1996).
3. Sheldon, R. A., Brady, D. & Bode, M. L. The hitchhiker's guide to biocatalysis: recent advances in the use of enzymes in organic synthesis. *Chem. Sci.* 11, 2587–2605 (2020).
4. Koivisto, A.J.; Aromaa, M.; Mäkelä, J.M.; Pasanen, P.; Hussein, T.; Hämeri, K. Concept to Estimate Regional Inhalation Dose of Industrially Synthesized Nanoparticles. *ACS Nano* 2012, 6, 1195–1203. [CrossRef] [PubMed]
5. Som, C.; Berges, M.; Chaudhry, Q.; Dusinska, M.; Fernandes, T.F.; Olsen, S.I.; Nowack, B. The Importance of Life Cycle Concepts for the Development of Safe Nanoproducts. *Toxicology* 2010, 269, 160–169. [CrossRef] [PubMed]
6. Galanie, S., Entwistle, D. & Lalonde, J. Engineering biosynthetic enzymes for industrial natural product synthesis. *Nat. Prod. Rep.* 37, 1122–1143 (2020).
7. Mäkelä, J.M.; Keskinen, H.; Forsblom, T.; Keskinen, J. Generation of Metal and Metal Oxide Nanoparticles by Liquid Flame Spray Process. *J. Mater. Sci.* 2004, 39, 2783–2788
8. Scott, T. A. & Piel, J. The hidden enzymology of bacterial natural product biosynthesis. *Nat. Rev. Chem.* 3, 404–425 (2019).
9. Cushen, M.; Kerry, J.; Morris, M.; Cruz-Romero, M.; Cummins, E. Nanotechnologies in the Food Industry—Recent Developments, Risks and Regulation. *Trends Food Sci. Technol.* 2012, 24, 30–46
10. Enzyme catalysis in organic synthesis Toshiyuki Itoh and Ulf Hanefeld DOI:10.1039/C6GC90124G (*Green Chem.*, 2017, 19, 331-332)
11. Goldsmith, M. & Tawfik, D. S. Enzyme engineering: reaching the maximal catalytic efficiency peak. *Curr. Open. Struct. Biol.* 47, 140–150 (2017).
12. Enzymes in Green Chemistry: The State of the Art in Chemical Transformations <https://doi.org/10.1016/B978-0-444-64114-4.00005-4>.
13. Privett, H. K. et al. Iterative approach to computational enzyme design. *Proc. Natl Acad. Sci. USA* 109, 3790–3795 (2012).
14. Warshel, A. et al. Electrostatic basis for enzyme catalysis. *Chem. Rev.* 106, 3210–3235 (2006).

15. Galanie, S., Entwistle, D. & Lalonde, J. Engineering biosynthetic enzymes for industrial natural product synthesis. *Nat. Prod. Rep.* 37, 1122–1143 (2020).
16. Acetti D, Brenna E, Fuganti C, Gatti FG, Serra S (2010) Baker's yeast reduction of β -hydroxy ketones. *Eur J Org Chem* 2010:142–151
17. Asymmetric Reduction of α -Amino Ketones with a KBH_4 Solution Catalyzed by Chiral Lewis Acids Peng He, Haifeng Zheng, Xiaohua Liu, Xiangjin Lian, Lili Lin, Xiaoming Feng.
18. Patel, R. N. Biocatalysis for Synthesis of Pharmaceuticals. *Bio-org. Med. Chem.* 2018, 26, 1252–1274.
19. Seddigi, Z. S.; Malik, M. S.; Ahmed, S. A.; Babalghith, A. O.; Kamal, A. Lipases in Asymmetric Transformations: Recent Advances in Classical Kinetic Resolution and Lipase–Metal Combinations for Dynamic Processes. *Coord. Chem. Rev.* 2017, 348, 54–70.
20. Pamies, O.; Backvall, J. E. Combination of Enzymes and Metal Catalysts. A Powerful Approach in Asymmetric Catalysis. *Chem. Rev.* 2003, 103, 3247–3262
21. Google Search: Chemical Catalysis versus Biocatalysis
22. Varma, S.R. Greener and Sustainable Trends in Synthesis of Organics and Nanomaterials, *ACS Sustainable Chemistry & Engineering*. *ACS Sustain. Chem. Eng.* 2016, 4, 5866–5878.
23. Matsuo, J.; Tsuchiya, T.; Odashima, K.; Kobayashi, S. Lewis Acid Catalysis in Supercritical Carbon Dioxide. Use of Scandium Tris(heptadecafluorooctanesulfonate) as a Lewis Acid Catalyst in Diels-Alder and Aza Diels-Alder Reactions. *Chem. Lett.* 2000, 29, 178.
24. Zhu, Y.; Carpenter, K.; Ching, C.; Bahnmüller, S.; Chan, P. (R)-Binap-Mediated Asymmetric Hydrogenation with a Rhodacarborane Catalyst in Ionic-Liquid Media. *Angew. Chem. Int. Ed.* 2003, 42, 3792–3795
25. Ross, S.D.; Finkelstein, M.; Petersen, R.C. Solvent effects in the reactions of N-Bromo succinimide with toluene, fluorene and acenaphthene; Evidence for a polar mechanism in propylene carbonate. *J. Am. Chem. Soc.* 1958, 80, 4327–4330.
26. Bennett, J.S.; Charles, K.L.; Miner, M.R.; Heuberger, C.F.; Spina, E.J.; Bartels, M.F.; Foreman, T. Ethyl lactate as a tunable solvent for the synthesis of aryl aldimines. *Green Chem.* 2009, 11, 166–168
27. Jordan, A.; Hall, J.G.C.; Thorp, R.L.; Sneddon, F.H. Replacement of less-preferred dipolar aprotic and ethereal solvents in synthetic organic chemistry with more sustainable alternatives. *Chem. Rev.* 2022, 122, 6749–6794.
28. Shaik, B.B.; Seboletswe, P.; Mohite, B.S.; Katari, K.N.D.; Bala, D.M.P.; Karpoor math, R.P.; Singh, P.P. Lemon juice: A versatile biocatalyst and green solvent in organic transformations. *Chemistry Select* 2022, 7, e202103701.
29. Tahghighi, A.; Babalouei, F. Thiadiazoles: The appropriate pharmacological scaffolds with leishmanicidal and antimalarial activities: A review. *Iran. J. Basic Med. Sci.* 2017, 20, 613–622.
30. Romagnoli, R.; Baraldi, G.P.; Carrion, D.M.; Cruz-Lopez, O.; Preti, D.; Tabrizi, A.M.; Fruttarolo, F.; Heilmann, F.; Bermejo, J.;
31. Estevez, F. Hybrid molecules containing benzo[4,5]imidazo-[1,2-d][1,2,4]thiadiazole and α -bromoacryloyl moieties as potent apoptosis inducers on human myeloid leukaemia cells. *Bioorg. Med. Chem. Lett.* 2007, 17, 2844.
32. Huheey J.E. (1996), Incorporating Environmental Issues into the Inorganic Curriculum, *Designing Chemistry for the Environment*, ACS symposium series 626, New York, 251pp
33. Gates B. C. Koningsberg D.C. (1992) *Chemtech* 300-307.
34. Simpson M., Wei J. and Sundaresan S. (1996), Kinetics of Zeolitic Solid Acid-Catalyzed Alkylation

- of Isobutene with 2-butane. Green Chemistry, Designing Chemistry for the Environment, ACS symposium series 626, New York, 251pp.
35. Huheey J.E. (1996), Incorporating Environmental Issues into the Inorganic Curriculum, Designing Chemistry for the Environment, ACS symposium series 626, New York, 251pp.
36. Anastas P.T. and Warner J.C. (1998), Green Chemistry. Theory and Practice, Oxford University Press, New York, 234pp.
37. Somorjai G.A. (1992). In: Perspective in Catalysis Thomas J.M., Zamaraev K.I. Eds; Blackwell Scientific Publications: Oxford, 542pp.
38. Dekamin, M.G.; Karimi, Z.; Latifidoost, Z.; Ilkhanizadeh, S.; Daemi, H.; Naimi-Jamal, M.R.; Barikani, M. Alginic acid: A mild and renewable bifunctional heterogeneous biopolymeric organo catalyst for efficient and facile synthesis of polyhydroquinolines. Int. J. Biol. Macromol. 2018, 108, 1273–1280.



Licensed under [Creative Commons Attribution-ShareAlike 4.0 International License](https://creativecommons.org/licenses/by-sa/4.0/)