Biocatalysis : An Innovation in Chemistry

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Abstract -

Modern single-step reactions with one or two substrates have been a key strategy these days for a cost-effective and sustainable industrial process. The discovery and introduction of new biocatalytic reactions into industrial practice has been a breakthrough innovation. Biocatalysis is the use of microorganisms or enzyme preparations to catalyze chemical transformations. Several enzymes have the capacity to fold into three-dimensional structures and thus, help in achieving high reaction rates.

Key words - Substrate, sustainable, biocatalysis.

Introduction -

Diastase was the first enzyme to be discovered in the year 1833[1] .It was followed by discovery of other hydrolytic enzymes such as pepsin and invertase[2]. The term enzyme was coined in 1877 by Wilhelm Kühne[3]. Enzymes are very effective catalysts.They carry out several co-ordinated chemical reactions involved in the biological processes of living beings. In comparison with chemical catalysts, enzymes exhibit the unique property of substrate and reaction specificity that promotes only one reaction with the respective substrate and ensures the synthesis of a specific biomolecular product without the concomitant production of by-products.

Biocatalysis is the utilisation of biological systems or their parts to catalyze chemical reactionsespecially chemical transformations on organic compounds. Both enzymes that have been isolated and the enzymes still residing inside living cells are being used for this process[4,5,6]. Organic synthetic processes that generate minimum waste and avoid the use of toxic and/or hazardous materials form the basis of sustainable development[7] because the major causes of waste in organic synthesis are the use of

stoichiometric inorganic or organic reagents and solvents in multi-step synthesis[8]. Therefore, the use of biocatalysis in industrial synthetic chemistry is gaining popularity.

Examples of Biocatalysts -

Hydrolases and redox biocatalysts are the most prominent categories of biocatalyst used in industrial biotransformation reactions. The earliestbiocatalytic conversion known to mankind is the manufacture of ethyl alcohol from molasses, the mother liquor left after the crystallisation of cane sugar from concentrated cane juice. This transformation is brought about by the enzyme 'invertase' which converts sucrose into glucose and fructose and finally by the enzyme zymase which converts glucose and fructose into ethyl alcohol. It is well known that most of the antibiotics have been prepared using enzymes (enzymatic fermentation). One of the most common examples is the biocatalytic conversion of Penicillin into 6-APA by the enzyme 'Penacylase' (one step process). The major six classes of enzymes are - oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases.

Recent Advances -

The synthesis of biologically active molecules or active pharmaceutical ingredients (APIs) requires manipulation of stereogeniccenters and functional groups like alcohols, amines. Pharmaceutical industry has been widely usingbiocatalysis for API manufacturing. Several biotransformation processes in the pharmaceutical industry use biocatalysts, for e.g. chiral alcohols using alcohol dehydrogenases, the synthesis of atorvastatin using ketoreductases (KREDs) or sitagliptin production by transaminases (TAs)[9,10]. Following table enumerates a few of the recently developed biocatalytic synthetic reactions of APIs.

ENZYME	SOURCE ORGANISM	BIOCATALYST	SUBSTRATE	PRODUCT	REFERENCE NO.
ATP-dependent amide bond synthetaseMcbA	Marinactinosporather motolerans	Isolated enzyme	4-Chlorobenzoic acid; 4-(2-aminoethyl) morpholine	Moclobemide	11
Carboxylic acidreductase CARmm-A	Mycobacterium marinum	Isolated enzyme	3,4,5-trimethoxycinnamic acid; piperazine acetic acid pyrrolidine	Cinepazide	12
SpRedAm-R3-V6	Streptomyces purpureus	Isolated enzyme	Isopropyl 3-oxocyclobutane-1-carboxylate; monomethyl amine	Isopropyl 3-(methylamino) cyclobutane-1-carboxylate (abrocritinib key intermediate)	13
Lysine dioxygenase (KDO)	Catenulisporaacidiphila	Isolated enzyme	l-Lysine	(3S)-3-Hydroxy- l-lysine	14
Terpenecyclase (AacSHC)	Alicyclobacillusacidocaldarius	Isolated enzyme	Geranyl acetone	γ-Dihydroionone	15
Norcoclaurine synthase (tfNCS)	Thalictrumflavum	Cell lysate	Aromatic β-amine; ketone	Tetrahydroisoquinolines	16

Conclusion -

Biocatalysis has contributed to the safe, quick and sustainable production of high-value chemicals and pharmaceuticals.In future, genome mining and synthetic DNA technologies,desktop DNA printing, cell-free protein expression, enzyme immobilization and analysis will be enabling more intensive and productive access to natural substances with the help of biocatalytic transformation reactions.

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