ASIAN J TROP BIOTECHNOL
Volume 21, Number 1, June 2024
Pages: 10-25

ISSN: 0216-6887
E-ISSN: 2301-8658
DOI: 10.13057/biotek/c210102

Review: Current perspectives on enzyme applications in medicine, agriculture, and industries

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Manuscript received: 25 February 2024. Revision accepted: 4 May 2024.

Abstract. *Dahiru MM, Abdulhamid AA, Abaka AM. 2024. Review: Current perspectives in enzyme applications in medicine, agriculture, and industries. Asian J Trop Biotechnol 21: 10-25.* The conventional use of chemicals worldwide in different industries has significantly increased, impacting the environment. The need to improve industrial processes led to prospects into enzymes from various sources, including microbial sources to substitute the toxic chemicals and processes with environmentally friendly processes and biodegradable waste products. Enzyme applications are notably getting more attention in medicine, agriculture, and industries, including pharmaceuticals, food, detergents, leather, and cosmetics. They are utilized in these industries to enhance durability of product, shorten process time, improve efficiency and stability, and properly manage waste. Medicine mainly uses them for diagnostic and treatment purposes, including proteases and amylases. The pharmaceutical industries explore the specificity of enzymes to bind target substrates, yielding specific and desired products via reactions, including hydrolysis, acylation, and esterifications. Waste and pathogen treatments, in addition to soil and plant improvements, are the major applications of enzymes in agriculture, employing pectinases, cellulases, and xylanases. In the food industry, amylases are used for starch degradation and dough improvement, while proteases are used for juice beer production clearance. The detergent industry adds enzymes to its formulations, including lipases, proteases, and cellulases, to improve stain removal by modifying fabric fibers to release dirt and soil particles. Enzymes, including proteases and lipases, are used in the leather industry for curing, soaking, dehairing, degreasing, and tanning, in addition to waste elimination. In comparison, an immobilized lipase is utilized in the cosmetic industry to produce retinoids, protein disulfide isomerase, glutathione sulfhydryl oxidase, and transglutaminase are applied in hair waving. Furthermore, developing the cost-effective technique of enzyme immobilization technology further promotes the application of enzymes in these endeavors attributed to their stability and recyclability. Thus, there is a significant improvement in research towards green and eco-friendly applications of enzymes. This review discusses how enzymes have been successfully deployed and utilized in medicine, agriculture, pharmaceutical, food, detergent, leather, and cosmetics industries. Enzymes in these industries exhibited beneficial applications, though the recyclability of the enzymes remains challenging for some endeavors. However, immobilization techniques have been gaining attention which might present a solution to the challenges associated with enzyme reusability.

Keywords: Agriculture, cosmetics, detergent, industries, leather

INTRODUCTION

Enzymes, otherwise called biocatalysts, have for centuries been in use due to their high efficiency and substrate specificity to yield valuable products for several uses (Madhavan et al. 2017; Prasad and Roy 2018). The human body, which comprises cells and tissues, requires a constant supply of nutrients in food containing both plant and animal-sourced enzymes. The most important advantage of enzymes is their chemical and stereoselectivity during catalysis, in which they catalyze and convert specific reactions and substrates into products (Choi et al. 2015; Kaushal et al. 2022). Furthermore, these specificity covers conditions, including temperature and pH, attributed to the optimal functional conditions of their sources, such as microbes (Kaushal et al. 2022); enzyme specificity is a high requirement in industries that use them. Enzymes catalysis de novo reactions in the body, vital for the body's normal functioning, in which food is converted to energy used for synthesis and degradation (Kaur and Sekhon 2012). The inherent characteristics of enzymes to catalyze synthesis, change, or break down molecules are the main reason why they are exploited by several industries and partly due to their most environmentally friendly byproducts (Mata et al. 2010; Huisman and Collier 2013; Kapoor et al. 2017; Madhavan et al. 2017; Sun et al. 2018). Biocatalysts from different sources, including microbial, plant, and animal, have been used in medicine, agriculture, and industries to yield products such as wine, food, and drugs (Gupta et al. 2017; Mariyam et al. 2024). The growing interest in enzyme applications in industries is driven by the increased demand for sustainable and eco-friendly industrial processes (Ranjbari et al. 2019)

Microbial sources especially bacterial and fungal, are the most explored enzyme sources due to the diversity in the optimum conditions to use, ease of production, and optimization (Okpara 2022). Moreover, these sources can be engineered to produce efficient enzymes that withstand harsh conditions, readily on their availability and higher replication rates (Okpara 2022). Different organisms can produce isoenzymes that function in different pH and temperature conditions. These enzymes are utilized in medicine, agriculture, food, pharmaceutical, cosmetics, leather, and detergent industries, with future biotechnologies promoting their advancements and utilization in these industries (Okpara 2022). In those industries, enzymes are crucial in various processes, especially in food industries, exhibiting their significance, with notable examples including alpha-amylase, protease, lipase, pectinase, and glucose oxidase. Moreover, enzymes from microbial sources offer advantages over animal and plant sources, including genetic modification (over-expression of specific genes) and large-scale production via solid-state and submerged fermentation techniques; however, many remain unexplored. Protein engineering provides an avenue to improve and modify enzymes to suit our needs and overcome the challenges associated with the naturally available enzymes including instability to harsh industrial scale conditions (Baweja et al. 2016). These challenges can be lowered by editing specific residues within the enzyme structure via mutation to improve the enzyme's version (Baweja et al. 2016). Moreover, exploring alternative sources of microbial enzymes from natural environments or habitats with extremely harsh conditions offers other alternative methods to obtain industrial stable enzymes (Baweja et al. 2016). Furthermore, some techniques are employed to improve the activities of enzymes and proteins, including rational redesign and random mutagenesis (Baweja et al. 2016). The rational redesign requires the knowledge of the enzyme's mechanism of action and entails reconfiguring the active site of the known 3D structure of the enzyme that has been formulated to achieve the desired product. For the latter, modifications are via direct evolution mimicking the natural evolutionary process, employing variant generation molecular techniques such as chemical agents, error-prone PCR, and repeated oligonucleotide-directed mutagenesis.

Emerging trends show the exploitation of enzyme immobilization techniques in bioprocessing and catalysis, reccently gaining attention (Kaushal et al. 2022; Mohidem et al. 2023). This technique overcomes the challenges encountered using free enzymes, including instability, poor shelf-life, and sensitivity to harsh conditions of industrial processes (Razzaghi et al. 2018; Liu and Dong 2020). Free enzymes are not immobilized; thus, they are free reaction, medium, and cheaper than their immobilized counterpart. However, enzyme recovery for the free enzyme technique has been reported to be challenging (Ribeiro et al. 2011). This cost-effective technique allows enzyme recovery from the reaction mixture, preventing enzyme degradation and allowing reusability (Mohidem et al. 2023). The application of these techniques, including adsorption, entrapment, and cross-linking, improves enzyme properties, such as stability and reusability (Jesionowski et al. 2014; Cao et al. 2016; Cipolatti et al. 2016; Mehta et al. 2016; Grigoras 2017; Mohidem et al. 2023). These methods rely on the nature of the substrate, enzyme employed, and operating conditions for optimum output (Chauhan 2014; Mohidem et al. 2023). The advantages, including high output and efficiency of these techniques, are considered to identify a suitable one for high product specificity (Chauhan 2014; Jesionowski et al. 2014). Furthermore, a comparable catalytic activity was reported previously for both immobilized and bound enzymes (Ge et al. 2023). Additionally, immobilized enzymes offer advantages over free enzymes, including reusability and stability towards reaction conditions (Somu et al. 2022). Thus, a perfect eco-friendly substitute for both conventional catalysis and free enzyme techniques. Notably, advancement in the immobilized enzyme technology is the nanocarriers in the form of encapsulated enzymes further enhancing enzyme reusability and stability to harsh conditions (Cao et al. 2016; Mehta et al. 2016; Grigoras 2017; T.sriwong and Matsuda 2022; Aziz and Abdel-Karim 2023). Moreover, encapsulation is a dose-release control, leading to extended enzyme use (Aziz and Abdel-Karim 2023). Although previous studies highlight the applications of enzymes in different endeavors, emphasizing their advantages over conventional techniques, more research gaps open more opportunities to explore, notably the enzyme immobilization technique, which has been gaining attention recently. The emergence of new applications in enzyme technology is reported in the present study. The present review is focused on the applications of enzymes in medicine, pharmaceutical, agriculture, food, detergent, leather, and cosmetics industries regarding how these enzymes have been utilized to improve different processes to improve industrial processes from toxic chemicals and processes to environmentally friendly processes and biodegradable waste products.

MEDICINE AND PHARMACEUTICAL INDUSTRIES

Medical application of enzymes considers enzymes' therapeutic and diagnostic roles, including alleviating enzyme deficiencies, improving the immune, detoxifying, aiding digestion, and detecting some substances in body fluid levels (Meghwanshi et al. 2020). The use of enzymes in medicine can be singly or combined with other drugs or vaccines to work synergistically (Mane and Tale 2015). Several ailments, such as metabolic and genetic disorders (fibrosis conditions, ocular pathologies), infectious diseases with antibiotic-resistant capabilities, cancer, cardiovascular diseases, and digestive problems, have been reported as targets of enzyme therapy (Gupta et al. 2017; de la Fuente et al. 2021). These enzymes are administered due to their specificity and high affinity, though sometimes they present challenges, including immune response to their presence, short life, and difficulty reaching their targets (Lenders and Brand 2018; de la Fuente et al. 2021). These

challenges hamper the potential application of enzymes, which must be improved for effective application in this endeavor. Although the ELISA technique has been well implemented in the medical field, emerging techniques such as microarray have recently gained attention (de la Fuente et al. 2021). Additionally, angiotensin-converting enzyme 2 has been studied as a potential option for COVID-19 therapy (de la Fuente et al. 2021). Typical examples of enzymes used to treat metabolic disorders include amylase, lipase, and protease (Mane and Tale 2015). Enzymes play key roles in therapeutic medicine; a typical example is using RNases in chemotherapy; antitumor activity of RNase from *Bacillus licheniformis* (baliface) has also been reported (Sokurenko et al. 2016). Moreover, another lysozyme, RNase U, was reported to exert antiviral activity via selective degradation of viral RNA and is regarded as a potential anti-HIV drug candidate (Lee-Huang et al. 1999). A chondroitin sulfate ABC endolyase chemonucleolysis therapy for cervical and lumbar intervertebral disc herniation yielded positive results. It was regarded as a novel approach for many treatments, attributed to its high nucleus pulposus specificity (Ishibashi et al. 2019).

Enzymes diagnose different medical conditions, including diabetes and other health disorders. Typical examples are glucose oxidase for glucose, urease and glutamate dehydrogenase for urea, lipase, carboxyl esterase, glycerol kinase for triglycerides, urate oxidase for uric acid, creatinase, and sarcosine oxidases for creatinine (Le Roes-Hill and Prins 2016; Singh et al. 2016). Glucose oxidase combined with catalase is utilized in test kits, notably biosensors, to detect and estimate glucose levels in biological fluids (Khatami et al. 2022). Cholesterol oxidase has been implicated in the detection of cholesterol, while putrescine oxidase is employed for detecting biogenic amines, such as putrescine, a marker for food spoilage (Le Roes-Hill and Prins 2016). Enzymes are also utilized as therapeutic drugs in ailments characterized by enzyme deficiencies, problems associated with digestion, and diagnostic procedures, such as ELISA and diabetes test kits (Mane and Tale 2015). Another enzyme benefit with medical applications is proteases with several subclasses with different uses. Alkaline protease produced by *B. subtilis* has some therapeutic properties, such as fibrin degradation, and is suggested to have future anticancer potential (Jaouadi et al. 2011). In another study, oral administration of combined aceclofenac and the proteolytic enzymes bromelain and papain via supplementation to patients with lower back pain led to a significant decrease in alkaline phosphatase and serum creatine with prolonged beneficial effects (Naeem et al. 2020). Elastoterase immobilized on bandages has been used for burns and wound treatments (Palanivel et al. 2013; Harish and Uppuluri 2018). Tyrosinase is involved in melanogenesis and the production of L-Dihydroxy phenylalanine (L-DOPA), a precursor for dopamine synthesis, used for the management of Parkinson's disease and control of myocardium neurogenic injury (Zaidi et al. 2014). Enzymes applied in medicine are the target for removing cytotoxic substances from circulation, anticoagulants, and disorders arising from metabolic deficiencies (Kaur and Sekhon 2012).

Adenosine deaminase (pagadamase), which was the first enzyme utilized to treat an inherited immune disorder, acts by cleaving excess molecules of circulating adenosine, thereby reducing the immune toxicity associated with a high level of adenosine (Tartibi et al. 2016; Fejerskov et al. 2017). Pagadamase cleaves the enzyme leading to an increase in the half-life of ADA and decreasing the immune response due to the bovine origin of the enzyme. Another enzyme, α-galactosidase, is vital for digestion and breaks down α-galactoside residues in carbohydrates, with its absence leading to gastrointestinal disturbances. However, this enzyme is now supplemented in food to remedy its absence (Shang et al. 2018). The deficiency of lysosomal acid lipase is associated with metabolic disease; Wolman disease has been reported to be remedied via sebelipase alfa, a recombinant form of the enzyme (Pastores and Hughes 2020). Other recombinant replacement therapies include porphobilinogen deaminase, sacrosidase, and lactase administered for acute intermittent porphyria (Fontanellas et al. 2016), congenital sucrase-isomaltase (Puntis and Zamvar 2015), and lactase deficiencies (Catanzaro et al. 2021), respectively. Chronic total occlusion characterized by coronary artery blockage leads to collagen plaque buildup, obstructing blood flow to the heart. However, catheter administration of type IA collagenase from *Clostridium histolyticum* digest the collagen plagues (Strauss et al. 2003). Moreover, collagenase is employed in fasciotomy to remove the fibrotic fascia of the fingers and palm (Degreef 2016). Furthermore, it is applied in the degradation of fiber plaques associated with Peyronie's disease (Randhawa and Shukla 2019). Tumor cells are linked with increased amino acid metabolism for survival and proliferation. PEGylated kynureninase was reported to exhibit anti-tumor activity via a prolonged depletion of the L-tryptophan metabolite, kynurenine, which can be readily eliminated. Additionally, the enzyme reversed the immune-suppressing effect of interferon-γ-inducible indoleamine 2,3-dioxygenase (Triplett et al. 2018).

Asparaginase, an effective enzyme for managing acute lymphocytic leukemia, has been reported previously (Gupta et al. 2017). Asparagine is a normal nonessential amino acid synthesized in the body; however, tumor cells are short of the enzyme aspartate-ammonia ligase required for the synthesis of asparagine (Radadiya et al. 2020; Wang et al. 2021). Administration of asparaginase doesn't affect normal cellular concentration but leads to a decrease in the extracellular concentration of asparagine, preventing its entry into tumor cells. Hyaluronidase cures heart attack and increases in activity of enzymes such as aldolase, malic dehydrogenase, and isomerase due to myocardial infarction (Chowdhury et al. 2017). Lytic enzymes from isolated bacteriophages effectively treat drug-resistant strains of bacteria and remove dead skin from burns (Gurung et al. 2013). Collagenase has also been reported to facilitate the healing mechanism due to skin burn by removing dead cells, thus working synergistically with antibiotics (Ostlie et al. 2012). Lysozyme as an antimicrobial agent has also

shown potential against HIV (Chan et al. 2006). Extracts isolated from fungi, consisting of amylase, proteases, and cellulases, have been applied to prevent dyspepsia and flatulence as they break down indigestible fiber in food such as cabbage (Fieker et al. 2011). Nattokinase has been previously reported to demonstrate beneficial effects in cardiovascular ailments, including preventive and treatment effects, and is regarded as an alternative cardiovascular disease therapy (Chen et al. 2018). Congenital sucrase-isomaltase associated with the indigestion of sucrose has been reported to be remedied by the administration of *Saccharomyces cerevisiae* β-fructofuranoside fructohydrolase, otherwise called sacrosidase which aids in the digestion of sucrose (Lwin et al. 2004; Matta et al. 2018). Phenylketonuria, characterized by the deficiency of phenylalanine hydroxylase, has been reported to be treated using phenylalanine ammonia-lyase produced from a recombinant yeast, which aids in the digestion of phenylalanine in the gastrointestinal tract (Wallig et al. 2017).

Lysosomal storage diseases present a group of inherited and rare pathologies associated with either lysosomal enzyme deficiencies or molecular transport alterations. Notable examples include Hunter's syndrome, Fabry's disease, and Gaucher's disease. Iduronate 2-sulfatase, which catalyzes the breakdown of glycosaminoglycans dermatan- and heparan-sulfate, is deficient in Hunter's syndrome, accumulating metabolites in tissues and organs. This impairs physical and mental development, which can be improved by intravenous enzyme administration (Whiteman and Kimura 2017; Mohamed et al. 2020; Ueda and Hokugo 2020). Another deficient enzyme associated with lysosomal storage disease (Fabry's disease) is the α-galactosidase A, which leads to cellular accumulation of metabolites, potentially leading to renal and cardiac failures (Chan and Adam 2018; McCafferty and Scott 2019; Azevedo et al. 2021). However, intravenous administration of α-galactosidase A ameliorates symptoms (El Dib et al. 2016). β-glucocerebrosidase cleaves the β-glucosidic linkage of glucocerebroside, an intermediate in glycolipid metabolism. Genetic mutation in the gene for the enzyme results in a lysosomal disease known as Gaucher's disease, characterized by the accumulation of excess glucocerebrosides (Erdem et al. 2018). In Gaucher's disease, the glucocerebrosidase enzyme deficiency leads to the buildup of lipids in the liver, spleen, and bone marrow with symptoms including swelling of these tissues, anemia, and thrombocytopenia. Similarly, exogenous intravenous injection of the enzyme improves the enzyme level (Charrow 2009; Shemesh et al. 2015). Additionally, administration of exogenous α-L-iduronidase, N-acetylgalactosamine-6-sulfate sulfatase, arylsulfatase B, β-glucuronidase, α-D-mannosidase, tripeptidyl peptidase 1 and acid α-glucosidase presents potential treatment alternatives for Hurler's syndrome (Tolar and Orchard 2008; Bie et al. 2013), Morquio syndrome type A (Regier and Tanpaiboon 2016; Lee et al. 2022), Maroteaux-Lamy syndrome (Harmatz et al. 2017), Sly syndrome (Harmatz et al. 2018; Wang et al. 2020), α-mannosidosis (Ceccarini et al. 2018; Lund et al. 2018), Batten disease (Brudvig and Weimer 2022) and Pompe's disease (Kishnani and Beckemeyer 2014; Bellotti et al. 2020), respectively.

The pharmaceutical industries achieved large-scale enzyme production via fermentation using bacteria and fungi strains *Escherichia coli*, *B. subtilis*, *Aspergillus oryzae*, and *A. niger* that give high enzyme yield (Brahmachari et al. 2016; Yang et al. 2017). The ability of enzymes to specifically bind to their target substrate and transform it into a desired useful product is heavily exploited by pharmaceutical industries (Choi et al. 2015). The major targets of enzymes in pharmaceutical industries include hydrolysis, diacylation, acylation, group protection and deprotections, esterification, and others (Meghwanshi et al. 2020). In these industries, enzyme application highly relies on substrate and product specificity, including stereo-, regio-, and chemo-selectivity (Choi et al. 2015). Pharmaceutical synthesis often produces undesirable and environmentally toxic products and harsh process conditions, including high temperatures, which are significantly lowered or abolished in enzyme-catalyzed routes (Choi et al. 2015). Biocatalysts, especially those of microbial origins, are utilized by these industries due to their high specificity and affinity for their substrate which are transformed into specific products under optimum conditions. Enzyme-catalyzed reaction pathways reduce the requirement of harsh chemicals to speed up reactions or the need to apply high temperatures. Thus reducing risk and improving the safety of the processes (Choi et al. 2015). Enzymes are utilized to produce important precursors and intermediates such as amines, alcohols, carbonyl, and carboxylic acid derivatives required for synthesizing different pharmaceuticals via various processes (Wu et al. 2021). A novel β-glucosidase obtained from *Pseudomonas lutea* combined with *S. cerevisiae* was reported to efficiently convert the conversion of cellobiose to ethanol at 4℃ with 91.42% efficiency via simultaneous saccharification and fermentation. The technique was considered energy-saving compared to the commercial β-glucosidase (Tiwari et al. 2014).

A good example of the application of enzymes in the pharmaceutical industry is in the manufacture of sitagliptin, used to treat type II diabetes. Sitagliptin is a dipeptidyl peptidase-4 inhibitor that prevents the blood-retinal barrier increase and inhibits diabetes-induced tight junction disassembly (Gonçalves et al. 2018). Conventionally, this drug is produced by a rhodium-based catalyst through hydrogenation of enamine at high pressure to produce sitagliptin at 97% enantiomeric excess (Sheldon 2011). However, engineered R-selective transaminase from *Arthrobacter* sp. can produce the drug through the conversion of prositagltiptin ketone to sitagliptin with more than 99.95% enantiomeric excess (Sheldon 2011). Furthermore, (R)-3-amino-4-(2,4,5-triflurophenyl) butanoic acid, an intermediate for the drug synthesis is synthesized in dual steps initially requiring the conversion of β-ketoester to β-keto acid by *Candida rugosa* lipase followed by its subsequent conversion *Ilumatobacter coccineus* ω-Transaminase to its equivalent β-amino acid (Kim et al. 2019). A route was previously proposed for the synthesis of the neuroactive drug pregabalin, which exerts

anticonvulsant, pain-killing, and anti-anxiety effects used to treat epilepsy, anxiety, and social phobia (Martinez et al. 2008; Chen et al. 2011; Marouf 2018). Here, lipolase, which belongs to the class of lipase, is employed to synthesize by hydrolyzing selectively and separating the *S*-enantiomer intermediate from the *R*-enantiomer to pregabalin via decarboxylation (Martinez et al. 2008; Chen et al. 2011). The conventional route, bisphosphine rhodium, and nitrilase are employed for the asymmetric synthesis of (S)-3-cyano-5-methylhexanoate. However, both routes are neither cost-effective nor eco-friendly (Hoge et al. 2004; Xie et al. 2006; Zheng et al. 2014). The new route was reported to be more efficient and cost-effective than the classic route by increasing product yield by up to 40-45% with a purity of up to 99.5% and reducing waste generation by 20% (Zheng et al. 2014).

Alcohols with chirality are important precursors and intermediates in the pharmaceutical industries, taking advantage of their chiral moieties for drug synthesis (Prier and Kosjek 2019; Hollmann et al. 2021). Dulox alcohol, which is the precursor for the synthesis of the antidepressant drug Duloxetine, was reported to be synthesized by alcohol dehydrogenase from *Lactobacillus brevis* and EbN1 strain from *Aromatoleum aromaticum* (Leuchs and Greiner 2011). A new route was proposed for (*S, S*)-reboxetine succinate synthesis used for managing the late stage of development of fibromyalgia acting as an antidepressant (Krell et al. 2005; Hayes et al. 2011). Synthesis of this drug requires acetylation of a diol intermediate, whereas, in the conventional route, this process is accompanied by generating unwanted products due to poor enantioselectivity and inefficiency (Choi et al. 2015). In the new route, lipase B from *Candida antarctica* is used, which allows for acetylation of the diol intermediate with good enantioselectivity, resulting in 99% yield and 98% regioselectivity and enzyme recovery and reuse. Thus, a cost-effective route (Hayes et al. 2011). Xemilofiban which is an antiplatelet agent, is synthesized via enantioselective acylation of ethyl 3-amino-5-(trimethylsilyl)-4-pentynoate mediated by *E. coli* penicillin G amidohydrolase to yield the *S*-isomer which act as a chiral synthon for xemilofiban synthesis (Topgi et al. 1999). Nanokitanase employed as a cardiovascular drug, is a bacteria serine protease that demonstrated improved activity and stability as a therapeutic agent following modification via site-directed mutagenesis (Weng et al. 2015). Similarly, Harobin, another serine protease, exhibited improved anti-fibrinolytic and anti-thrombosis activities following genetic modifications. The mutant was hypothesized to be a therapeutic candidate for thrombosis and hypertension due to its high expression and activity level (Li et al. 2017). Furthermore, *Bacillus pumilus* serine alkaline protease employed for harsh conditions due to its high catalytic activity, thermoactivity, and pH stability demonstrated a shifted optimum temperature from 65°C to 75°C and increased activity following its genetic mutation (Jaouadi et al. 2010).

In the conventional synthesis of bicyclic proline, an intensive process requires an excess of metal-based oxidant and reductant through 8 reaction steps. The enantioselective, MAO-catalyzed (monoamine oxidase) synthesis of the intermediate is an attractive alternative that might reduce operation time and waste generation (Li et al. 2012b). However, there has been research for the scale-up of a monoamine oxidase (MAO)-catalyzed process for enantiomerically pure desymmetrization of a bicyclic proline intermediate. This is an important precursor in synthesizing boceprevir, an NS3 protease inhibitor used to treat chronic hepatitis C infections (Kjellin et al. 2018). The MAO-catalyzed method is more convenient and faster, generating less waste (Li et al. 2012b). The properties of MAO are improved through a series of protein engineering through subsequent evolution and mutation. Bisulphate is added to alleviate its inhibition while capturing the imine compounds. Significant improvements in MAO activity, solubility, and thermostability are achieved through protein engineering via 4 rounds of evolution involving random mutations and subsequent screening for desired phenotypes. Adding bisulfate to the MAO-catalyzed process to capture imine compounds mitigated its irreversible inhibition (Li et al. 2012b).

Table 1. Enzymes in medicine and pharmaceutical industries

Enzymes	Applications
Amylase, lipase, and protease	Treatment of metabolic disorders (Mane and Tale 2015)
RNases	Chemotherapy (antitumor) (Sokurenko et al. 2016)
Glucose oxidase, urease, glutamate dehydrogenase, lipase, carboxyl esterase, glycerol kinase, urate oxidase	Diagnostic purposes (Le Roes-Hill and Prins 2016; Singh et al. 2016; Khatami et al. 2022)
Proteases, tyrosinase, pagadamase, β-glucocerebrosidase, α-galactosidase, asparginase, hyaluronidase, collagenase	Therapeutic purposes (Ostlie et al. 2012; Gurung et al. 2013; Chowdhury et al. 2017; Fejerskov et al. 2017; Erdem et al. 2018; Shang et al. 2018; Khatami et al. 2022)
R-selective transaminase	Sitagliptin production (Sheldon 2011)
Lipolase	Pregabalin synthesis (Martinez et al. 2008; Marouf 2018)
Alcohol dehydrogenase	Duloxetine and statin production (Leuchs and Greiner 2011)
Lipase B	Reboxetine succinate synthesis (Krell et al. 2005; Hayes et al. 2011)
Monoamine oxidase	Boceprevir production (Li et al. 2012b)
Penicillin acylase	Penicillin analogs production (Martens and Demain2017)
Lipase	Sitagliptin, retagliptin, and evogliptin production (Kim et al. 2019)
Leucine dehydrogenase and glucose dehydrogenase	Boceprevir, atazanavir, and telaprevir production (Li et al. 2014; Patel 2018)

The human body is designed to prevent humans from digesting cellulose, which certain foods such as fruits and vegetables contain, because they lack the enzyme cellulase as found in other mammals. Microbes such as *B. licheniformis* and *Trichoderma reesei* produce cellulases sold commercially to blend enzymes under different brands (Jayasekara and Ratnayake 2019). Penicillin acylase produced by yeast, bacteria, and fungi breaks penicillin into 6-amino penicillanic acid, offering an advantage over the conventional method for synthesizing 6-amino penicillanic acid (Brahmachari et al. 2016). This is faster and more cost-effective, especially considering the enzyme immobilization techniques (Brahmachari et al. 2016; Zhang et al. 2017; Meghwanshi et al. 2020). Penicillin acylase also catalyzes the condensation of the β-lactam nucleus with the appropriate D-amino acid while producing other penicillin analogs (Martens and Demain 2017). Furthermore, penicillin acylases were previously reported to be employed in synthesizing semisynthetic penicillin, a more stable with better pharmacological properties than penicillin G and V. Moreover, they are a better alternative against antibiotic-resistant microbial targets (Grulich et al. 2016). This process is achieved by condensing the β-lactam nucleus with the suitable D-amino acid. Synthesis of the carbacephalosporin antibiotic Loracarbef was also reported *via* kinetic enantioselective acylation of azetidinone intermediate catalyzed by penicillin G acylase (Cainelli et al. 1997). Moreover, Glutaryl-7-ACA hydrolase catalyzes a key step in synthesizing 7-aminocephalosporanic acid, a vital intermediate for β-lactam antibiotic synthesis (Groeger et al. 2017). Lipase from *C. rugosa* plays a crucial role in the conversion of β-ketoester to β-keto acid, which is converted to the corresponding β-amino acid (R)-3-amino-4-(2,4,5-triflurophenyl) butanoic acid (3-ATfBA) by ω-Transaminase (ω-TA) from *I. coccineus*. This is a vital intermediate in the production of sitagliptin, retagliptin, and evogliptin (Anjibabu et al. 2016; Kim et al. 2019).

Two key enzymes, leucine dehydrogenase, and glucose dehydrogenase from Exiguobacterium sibiricum and Bacillus megaterium, respectively, synthesize L-tert-leucine. L-tert-leucine is the chiral backbone for the production of antiviral drugs boceprevir, atazanavir, and telaprevir, which are potent inhibitors of Hepatitis C genotype 1 protease, HIV protease, and Hepatitis C NS3-4A serine protease, respectively (Li et al. 2014; Patel 2018). Leucine dehydrogenase converts trimethylpyruvic acid to L-tert-leucine, while glucose dehydrogenase regenerates NADH from NAD+ to continue the process. The intermediates of the hypolipidemic drug statin which is also employed as a prevention strategy for cardiovascular diseases are enzymatically synthesized in *E. coli* host by alcohol dehydrogenase (KleADH) from *Klebsiella oxytoca* and ketoreductase of *Acinetobacter calcoaceticus* for t-butyl 6-chloro-(3R,5S)-dihydroxyhexanoate and (3S,5R)-dihydroxy-6-(benzyloxy) hexanoic acid, ethyl ester, respectively (Patel 2009, 2018). Table 1 summarizes the applications of enzymes in the medicine and pharmaceutical industry.

AGRICULTURE

Enzymes have a very wide range of applications in agriculture, such as soil and plant improvement, waste treatment, and treatments against pathogens (Gupta and Seth 2020; Kumar et al. 2023; Mariyam et al. 2023; Kim et al. 2024; Kumar et al. 2024). Application of different cellulase and pectinases is common in agricultural practices, such as promoting plant growth through rhizobacteria rather than chemical fertilizers (Asmare 2014; Mori et al. 2014), thus decreasing fertilizers. Although such microbes' exact mode of action is not yet understood, certain fungi species are also used to improve yield (Jayasekara and Ratnayake 2019). Both fungi and bacteria used in agriculture can produce cellulase, and possible synergy is suspected between cellulase and antibiotics (active against plant pathogens) to improve plant growth and development (Jayasekara and Ratnayake 2019). Among the cellulolytic microorganisms, there have also been reports of soil improvement through soil decomposition and nutrient accessibility. However, as mentioned earlier, no supporting evidence exists for such a mechanism.

During animal feed formulation, some enzymes are added to improve the quality of livestock feed to break down non-nutritional and harmful feed components (Singh et al. 2016). A notable example is the enzyme addition to improve the overall protein quality of feed. Xylanases are used during feed formulation to improve fiber content and degrade arabinoxylan, cellulose, and hemicellulose by hydrolyzing them to easily digestible form. Thus, improving digestion by both ruminant and non-ruminant animals (Bhat 2000). Amylases were also previously reported to be used during animal feed pretreatment to improve digestibility (Sivaramakrishnan et al. 2006). Enzymes used in poultry include phytase (used in cereal-based feed to liberate phosphorus), proteases (degrade protein in feed), amylases, and gluconases (Selle and Ravindran 2007; Adrio and Demain 2014). Phytase acts on phytic acid to liberate phosphorus, an important mineral for bone formation in growing animals (Selle and Ravindran 2007). This enzyme liberates phosphate in situ, eliminating the need to add phosphorus as a feed supplement, subsequently reducing the cost (Jarvie et al. 2015; Scanlon et al. 2018).

The enzyme keratinase are hydrolase groups that disrupt keratin's disulfide hydrogen bonds (Kalaikumari et al. 2019). They are utilized in animal waste treatments, which constitute plenty of keratins that would have been left undegraded due to their complexity, leading to environmental pollution if untreated. This enzyme converts such waste into simple biodegradable substances (Hossain et al. 2017). Keratinase is also utilized in the degradation of feathers from poultry which contains keratin structure accounting for 5% of the body weight and is a rich source of proteins for feed and food. Thus, it can be degraded into feed and food by the keratinolytic process (Lasekan et al. 2013). Although these enzymes directly affect feed, they are also useful for reducing feed costs and increasing meat yield (Adrio and Demain 2014). The application of

enzyme-immobilized carrier nanomaterials and agro-waste was recently reported to show promising results with a potential for exploration attributed to their reusability, stability, and improved enzyme activity (Mohidem et al. 2023). Moreover, previous studies showed improved enzyme activities and recyclability using agro-waste carriers, including rice husk and onion skins (Ganonyan et al. 2021; Spennato et al. 2021; Khataminezhad et al. 2023). In another study, different enzymes were reported employed in bioremediation processes, including dehydrogenase, oxygenase, esterase, and laccase (Cirino and Arnold 2002; Park et al. 2006; Bhatt et al. 2021). Sobucki et al. (2021) reported the implication of soil enzymes in the ecosystem's normal function, including soil mineralization, plant decomposition, and nutrient cycling. These enzymes include cellulase, protease, phosphatases, and arylsulfatase, contributing to carbon, nitrogen, and phosphorus cycles to maintain soil ecology (Sobucki et al. 2021). The agricultural applications of enzymes are summarized in Table 2.

FOOD INDUSTRY

Enzyme use in the food industry has been on the rise for centuries due to the ease of use and the inherent characteristics of enzymes that make them specific regarding product yield. Key applications in the food industries include protease, amylase, lipases, and glucanases. Globally, enzymes are employed in different food industries, including dairy, brewery, meat, baking, juice and beverages, vegetable processing, dietary supplements, oils, and fats (Robinson 2015). Alpha-amylase is used in the baking industry to improve the quality of bread and degrade the starch in wheat flour into small dextrins to improve the activity of yeast during dough fermentation (Singh and Kumar 2019). Another significant application of α-amylase is beer and fruit juices clarification and the pretreatment of animal feed to improve fiber digestibility (Singh and Kumar 2019). During beer production, amylases hydrolyze starch into smaller particles easily fermented by *S. cerevisiae* to produce beer and for clarification (Okpara 2022). The qualities of acidic proteases, including stability and activity around acidic pH, are exploited in manufacturing digestive aids, soy sauce, and seasonings (Razzaq et al. 2019). Furthermore, these proteases are crucial in manufacturing beer and fruit juices for clearing the mixtures (Zhang et al. 2010). Alkaline protease immobilized on mesoporous silica and mesoporous ZSM-5 zeolite materials was reported to increase the catalytic properties of the enzyme (Kumari et al. 2015). Moreover, the technique presented a novel bioprocess approach for milk coagulation to produce cheese. Gluten-reduced beer was previously produced from chitosan cross-linked immobilized *A. niger* prolyl endopeptidase, exhibiting improved thermal stability with comparable activity to the free enzyme. The result revealed a decreased gluten level from 65 mg/kg to 15 mg/kg after 10 hours of treatment (Benucci et al. 2020). In another study, fungal amylase covalently immobilized on a chitosan-containing cellulose exhibited improved resistance to pH inactivation and increased thermal stability up to 350% in addition to an augmented stability of the enzyme compared to its native counterpart. Moreover, the enzyme for the hydrolysis of barley malt demonstrated an increased product yield by a factor of 1.5 (Raspopova and Krasnoshtanova 2016).

In the beverage industry, amylases are employed to hydrolyze polysaccharides in raw juice to improve juice extraction, clarification, and yield (Sivaramakrishnan et al. 2006). Lipase and xylanase improve dough stability and conditioning, while glucose oxidase and lipoxygenase achieve dough strengthening and whitening. Aspartame is a popular artificial sweetener synthesized from L-aspartic acid, which itself is synthesized by adding ammonia to fumarate by aspartase. L-aspartate-α-decarboxylase is utilized to produce L-aspartic acid, a precursor for the synthesis of β-alanine through decarboxylation (Qian et al. 2018). Food industries exploit the acyl groups, transferring the ability of lipases from esters to other nucleophiles to give end products flavors and aromas (Sá et al. 2017). Lipases are continuously utilized in baking industries in the manufacture of bread, where aeration is a requirement that contributes to the quality of the end product. Egg whites are used during baking, which affects the dough by reducing dough quality; lipases are employed to hydrolyze the lipids in the egg whites to improve quality and act as a preservative to the finished product (Okpara 2022); here, phospholipases that degrade phospholipids in flour with a low tendency to generate off-flavors are used. In another study, *Rhodothermus marinus* extremophile lipase covalently immobilized on chitosan was employed to synthesize aroma ester methyl acetate with potential application to improve food flavors (Memarpoor-Yazdi et al. 2017). Moreover, the enzyme's catalytic activity was retained; up to 78.6% of the initial activity for up to 60 minutes post-incubation at 70°C and pH 8.5 with 67% recovery of the immobilized enzyme compared to the free enzyme (22%). Additionally, the enzyme showed stability to high temperatures and organic solvent with potential application for organic synthesis in harsh industrial conditions.

Table 2. Agricultural applications of enzymes

Enzymes	Applications
Cellulase	Promoting plant growth (Jayasekara and Ratnayake 2019)
Xylanases	Feed formulation (Bhat 2000; Sivaramakrishnan et al. 2006)
Keratinase hydrolases	Poultry waste degradation and feed formulation (Hossain et al. 2017)
Phytases	Feed formulation of cereal-based feed to liberate phosphorus (Selle and Ravindran 2007; Adrio and Demain 2014)
Proteases	Protein degradation in feed formulation
Amylases	Feed pretreatment to improve digestibility (Sivaramakrishnan et al. 2006)
Dehydrogenase, oxygenase, and esterase	Bioremediation processes (Cirino and Arnold 2002; Park et al. 2006; Bhatt et al. 2021)

Table 3. Enzymes in food industries

Enzymes	Applications
Alpha-amylase	Bread, juice, and beer production (Singh and Kumar 2019)
Lipase and xylanase	Dough stability and strengthening (Qian et al. 2018)
Glucose oxidase and lipoxygenase	Dough whitening (Qian et al. 2018)
Aspartase	Synthesis of aspartame (Qian et al. 2018)
Lipases	Flavoring (Sá et al. 2017) and preservation (Okpara 2022)
Laccase	Discoloration, stabilization, and flavoring (Singh and Kumar 2019)
Glucoamylase	Dough stalling and appearance and beer production (Okpara 2022)
Proteases	Flavoring and cheese production (Allegrini et al. 2017)
β-galactosidase	Probiotic production (Panesar et al. 2013; Fernández-Lucas et al. 2017)
Papain	Protein hydrolysates production (Elavarasan and Shamasundar 2016)
Pectinases	Color and aroma improvement in beverages (Kårlund et al. 2014)
Cellulase and xylanases	Fruit juice extraction (Garg et al. 2016)
Naringinase	Debittering agent (Gallage et al. 2014)
Pepsin and renin	Cheese production (Qureshi et al. 2015)
Transglutaminase	Milk protein polymerization (Okpara 2022)
Catalases	Preservative (Röcker et al. 2016)

Another application of phospholipases is seen in cake baking, where there is the stabilization of bubbles on egg yolk lipids within the batter due to the availability of a bubble-batter interface created by the monoacylglycerols (Borrelli and Trono 2015). Laccase is applied in discoloration, haze, wine stabilization, baking, and flavoring during food processing (Singh and Kumar 2019). During baking, laccase oxidizes and improves the dough's and baked products' strength, enhancing crumb structure and increasing softness and volume. Glucose oxidase is employed during production to produce D-glucono-δ-lactone, an additive that improves color development, flavor, and texture and acts as a preservative (Khurshid et al. 2011). Glucose oxidase also increases bread size during baking (Ge et al. 2020). In wine production, it is added to decrease the alcohol level in wine (Röcker et al. 2016). Glucoamylase is another enzyme of microbial origin used for dough stalling in the baking industry to improve the quality and appearance of bread (Okpara 2022). Additionally, this enzyme is employed in beer production to produce light beer via addition to the wort during fermentation (Blanco et al. 2014).

Proteases have a broad operational temperature (10-80°C), which favors their applications in the processing of cheese and dairy products and enhances the quality of bread, baked goods, and crackers (Singh and Kumar 2019). A typical example is aminopeptidases, which significantly improve the flavor of fermented milk products. Proteases are also applied during cheddar production to lower the time for cheese aging by accelerating flavor modifications via the enzymatic breakdown of proteins (Allegrini et al. 2017). Microbial alkaline protease is used in synthesizing highly nutritive protein hydrolysate preparation used in food preparation for infants, drug production, and fortification of soft drinks and juice (Mótyán et al. 2013; Singh et al. 2016). Probiotics beneficial to the gut's health by stimulating bacteria growth can also be enzymatically produced in the form of non-digestible dietary supplements. A typical example is galactooligosaccharides, which are used as a low-calorie sweetener and are synthesized via simultaneous transgalactosylation and hydrolysis of lactose by β-galactosidase (Panesar et al. 2013; Fernández-Lucas et al. 2017). Moreover, β-Galactosidase finds its use in the dairy industry, exhibiting significant activity improvement of up to 99% in the enzyme immobilization technique with potential application in lactose hydrolysis in milk or whey (Panesar et al. 2010). In another study, β-galactosidase immobilized on silica/chitosan support exhibited high stability with potential dairy industry application (Ricardi et al. 2018). Moreover, operational stability was observed after 200 hours of continuous use on a fixed-bed reactor with up to 90% activity. The proteolytic enzyme papain from papaya has been identified as a key enzyme in fish industries, minimizing pollution by converting the waste from these industries to protein hydrolysates employed as flavor enhancers and food supplements (Elavarasan and Shamasundar 2016). Proteases are utilized for the hydrolysis of protein hydrolysates into free amino acids to synthesize antioxidants against the autoxidation of linoleic acid (Gómez-Guillén et al. 2011).

In the beverage industry, pectinase preparations decrease maceration time by enzymatically breaking pectin and bringing about quick dissolution, improved aroma, color, and product (Kårlund et al. 2014). During juice processing, cellulases, pectinases, and amylases soften fruits by hydrolyzing cellulose and hydrocellulose found in fruits and vegetables to improve the procedures. Thus enhancing yield and cost-effectiveness (Garg et al. 2016). The main sources of cellulase for industries are made up of cellulase from fungi and bacteria, including *A. niger*, *T. reesei*, and *B. licheniformis* (Yadav et al. 2020). Cellulase and pectinase enhance juice yield, cloud stability, and texture. During debittering, enzymes such as Naringinase and lemonade degrade bitter substances in citrus juice (Bhardwaj et al. 2019). Esterases are another class of enzymes employed to synthesize ferulic acid, the precursor of vanillic acid used to improve flavor and taste in the beverage industry (Gallage et al. 2014). The beverage industries also utilize xylanases to hydrolyze hemicellulose and improve juice extraction, clarification, and yield (Bhardwaj et al. 2019). In another study,

pectinases immobilized on polyvinyl alcohol gel were tested for fruit juice clarification. The immobilized enzyme demonstrated stability to low pH with 20% initial activity retention after eight cycles of reuse, decreasing the turbidity of apple juice up to 80% after 3 cycles (Cerreti et al. 2017). Laccases from fungal sources are employed in the brewery industry to remove haze from beer and wine via phenol oxidation improving the appearance and acting as a preservative by removing oxygen from beer (Okpara 2022). In juice making, laccases clarify and increase yield (Yin et al. 2017). Pectinases mainly produced by fungi are employed in the cocoa industry to increase yield, improve flavor and aroma, and decrease processing time at the curing stage of wet processing (Oumer 2017; Okpara 2022). Additionally, pectinases are employed in coffee production to remove the mucilage layer of the cocoa beans (Oumer 2017), while in tea production, they are used to remove pectin from the leaves to enhance fermentation time (Suhaimi et al. 2021). In baking, enzymes improve the text, color, softness, and appearance of crumbs and increase shelf life. These enzymes are used for the product's consistency; a typical example is amylase, which softens the dough and enhances shelf life (Singh et al. 2016).

Another key enzyme in the baking industry is xylanase, which is employed to hydrolyze arabinoxylan in wheat to solubilize and make it extractable thereby improving the qualities of the dough (Courtin and Delcour 2002). Additionally, a recombinant form of this enzyme produced by *Pichia pastoris* was reported to decrease the sugar content of bread (de Queiroz Brito Cunha et al. 2018). Glucoamylases are used in breaking down maltose for utilization during fermentation, leading to a rise in the dough for bakeries and the production of ethanol in beer or wine (Raveendran et al. 2018). Laccases are used to cross-link milk proteins in skimmed milk, thus improving the quality of the yogurt (Struch et al. 2016). These enzymes are also used to produce soy sauce and light beer. Probiotics are not digestible, hence their usage in enhancing the bacteria growth in the gut (Choi et al. 2015). Lipase enhances the flavor and shelf-life extension of bakery products (Adrio and Demain 2014). In another study, lipase immobilized on α-lactalbumin nanotube carriers remarkably increased the enzyme's activity (by up to 68%) and catalytic efficiency and promoted free fatty acids and flavor release (Guan et al. 2021). Enzymes are employed in the dairy industry to enhance the organoleptic properties (flavor, aroma, and texture) and yield increase. Diary enzymes, including lactases, lipases, proteases, and catalases, produce cheese, milk, and yogurt (Qureshi et al. 2015). Milk coagulation is achieved during cheese production by combining pepsin and chymosin, known as rennet. Proteases are also used to produce cheese and decrease allergic reactions to milk. People who are unable to take milk due to lactose intolerance can now take milk due to the use of lactase, which breaks down lactose, thus promoting the digestibility and sweetness of milk (Qureshi et al. 2015). Transglutaminase from bacterial sources (Okpara 2022) is another vital enzyme of the dairy industry that is added to polymerize milk proteins to improve the quality of some dairy products (Kieliszek and Misiewicz 2014). Catalases act as a preservative that removes peroxide and oxygen from milk, wine, and other food products to prevent rancidity, thereby acting as a preservative (Röcker et al. 2016). Table 3 summarizes the enzymes utilized in the food industry.

DETERGENT INDUSTRIES

The enzymes used in the detergent industry are on the rise due to their stain-removal ability. Fabrics made up of cotton are cleaned with cellulases by modifying the fibers within the fabric to remove dirt and soil particles within the fabric, thus brightening and softening it (Jayasekara and Ratnayake 2019). A recent advance has shown the use of different enzyme formulations to increase cleaning efficiency. A typical example is the combination of lipase, cellulase, protease, and amylase used to clean blood, fats, lipids, and carbohydrates from surgical equipment (Jayasekara and Ratnayake 2019). Alkaline yeast lipases are preferable in a cold wash than those from bacteria and molds due to their suitability for lower temperatures, hence, being used as components of detergents. Moreover, applying enzyme immobilization techniques significantly improves the yield of the efficiency and catalytic effect of the enzyme formulations in detergents. Immobilized serine protease, esperase retained its catalytic activity following 20 minutes of incubation in anionic and non-ionic surfactants, while the free enzyme lost 50% of its activity (Vasconcelos et al. 2006). The immobilized enzyme exhibited a superior stain removal effect from cotton than the free enzyme, with no recorded damage to wool. In addition, *Bacillus* sp. NPST-AK15 alkaline protease immobilized on hollow core-mesoporous shell silica nanospheres retained its catalytic efficiency for twelve consecutive reaction cycles. Although the catalytic temperature of both the immobilized and free enzyme remained at 60°C, an insignificant pH change from 10.5 to 11.0 was observed for the immobilized enzyme with a 1.5-fold increase in substrate affinity and enhanced organic solvent stabilities (Ibrahim et al. 2016).

The nature of lipids makes fatty stains difficult to remove from fabrics and glassware. These stains might easily be removed at high temperatures; however, washing at a lower temperature is favored. Lipases in laundry and dishwashing detergents remove fatty stains such as butter, margarine, fats, fat-containing sauces, salad oil, soups, human sebum, or certain cosmetics. Several thermostable lipases have been successfully used as detergent additives (Naganthran et al. 2017; Tang et al. 2017). Lipase isolated from *Bacillus methylotrophicus* was previously reported to show thermostability at a broad pH range, making it a good alternative for the detergent industry for the removal of grease, oil, and other oily stains (Sharma et al. 2017). Mannans are frequently used as thickening agents or stabilizers in ice cream, chocolate, ketchup, and personal care products. Mannan-containing soils also easily adsorb to the cellulose fibers of cotton fabrics by hydrogen bonds and are difficult to remove. Mannanases are specifically

supplemented with detergent to remove mannan-based dirt from clothes (Chauhan et al. 2012). Pectinases in detergents break the pectin backbone in pectin-based stains caused by fruits, vegetables, sauces, jams, and jellies for easy removal from fabrics during a wash. Thus, pectin-based stains and pectinase detergents are used (Sarmiento 2015). In another study, lipase immobilized on woolen fabric demonstrated enhanced oily stain removal after staining with olive oil after 24 hours of room temperature storage. Furthermore, an 80% activity was retained following storage of the immobilized woolen fabric for more than 80 days in pH 8.5 of tris buffer in a refrigerator (An et al. 2014). Similarly, lipase immobilized on arylamine glass beads showed promising results in oil stain removal without considerable activity loss after 100 cycles (Sharma et al. 2008).

The specificity of the enzymatic effect reduces damage to fabrics and surfaces notably associated with chemically synthesized detergent (Singh et al. 2016). A typical example is dishwashing detergents, often containing varying degrees of amylase and lipase intended to remove starch food deposits and fats and oils, respectively (Li et al. 2012a; Sarmiento 2015). *Laceyella sacchari* TSI-2 α-amylase immobilized on diethylaminoethyl cellulose via glutaraldehyde crosslinking showed high operation stability, increased shelf-life, and improved solvent stability, exhibiting high efficiency in removing starch stains from cotton (Shukla and Singh 2016). Although the pH optima remains intact, the temperature optima and thermal stability changed from 60 to 70°C, while the pH stability of the immobilized enzyme changed from 6 to 7.

LEATHER AND COSMETICS INDUSTRIES

In the leather industry, challenges include preparing the leather and eliminating waste. The conventional leather processing method entails using toxic chemicals, generating and releasing pollutants with significant environmental effects, including total solids accumulation in water bodies and oxygen deprivation (Kanagaraj et al. 2020). These challenges can be lowered by applying enzymes that offer an eco-friendly, efficient, and cost-effective alternative. Enzymes are used to enhance the quality of the leather and also minimize waste (Adrio and Demain 2014). Enzymes facilitate procedures and enhance leather quality at different stages in leather processing, such as curing, soaking, liming, dehairing, bating, pickling, degreasing, and tanning (Mojsov 2011). These enzymes include alkaline proteases, neutral proteases, and lipases. Proteases, lipases, and amylases are used in the dehairing process to preserve the hair, which is a challenging step in leather preparation. This excludes the conventional use of chemicals like amines and limes (De Souza and Gutterres 2012). Therefore, to make leather soft during soaking, alkaline proteases eliminate nonfibrillar proteins (composed of aggregated protein structures that don't form fibrils) from leather (Singh et al. 2016). Different enzymes are being investigated for their application in leather processing, such as the soaking step, including chondroitinases, hyaluronidases, phospholipases, amidases, and lignocellulases (Kanagaraj 2009). In the conventional method, the dehairing process entails using lime sulfide, leading to sulfide contamination. However, enzyme technology employs proteases, which eliminate this dehairing problem. Ugbede et al. (2023) reported the dehairing process of animal skin using *B. subtilis* and *A. flavus* proteases in a medium containing hair, feathers, and agro-waste. Moreover, both enzymes exhibited 71.5% and 94.8% recovery with 1.5 and 2.0 fold purifications, respectively. Moujehed et al. (2022) reported a chemical-free alternative for degreasing sheep skins using *Yarrowia lipolytica* LIP2 lipase. Here, 6 mg of lipase/kg of raw skin was used for the degreasing in 15 minutes at pH 8 and 30°C, yielding superior quality leather compared to the chemically treated.

Enzymes are also utilized in the cosmetic industry. An example is using an immobilized enzyme technique applied to lipase to synthesize retinoid's water-soluble derivative, used in skin care products (Gurung et al. 2013). The use of superoxide dismutase in sunscreen cream, mouthwash, and toothpaste as free radical scavengers was previously reported (Li et al. 2012a). Damages such as those caused by microbes are minimized by superoxide dismutase. Protein disulfide isomerase, glutathione sulfhydryl oxidase, and transglutaminase are applied in hair-waving (De Souza and Gutterres 2012). In another study, *Marasmiellus palmivorus* VE111 laccase produced after hydrolysis and alcoholic fermentation in a medium of lignocellulosic residues of *Araucaria angustifolia* degraded almost 33% of melanin in 8 hours, using vanillin mediator (Polesso et al. 2022). It demonstrates potential eco-friendly applications for producing anti-hyperpigmentation skin care products. A combined laccase and natural phenol redox mediators cocktail effectively degraded eumelanin from *Sepia officinalis*, offering an alternative to traditional skin whitening agents (Gigli et al. 2022). Moreover, the combined cocktail demonstrated a synergistic effect and degrading eumelanin sub-units better than single-mediator counterparts. In another study, cetstearyl stearate, a widely employed substance in the cosmetic and hygiene personal industry, was enzymatically synthesized *via* esterification of stearic acid and cetostearyl alcohol with high conversion values of 99% (Holz et al. 2018). Moreover, the optimum reaction condition was 75°C, 1:1.5 acid to alcohol molar ratio, 600 mmHg vacuum, and 760 rpm agitation. At the same time, the final product characterization showed acidity index, iodine index, hydroxyl index, and saponification index values of 0.6 mg KOH g^{-1}, 0% of iodine absorbed/g of the sample, 17.06 mg KOH.g^{-1}, 133.68 mg KOH g^{-1}, respectively. The *C. antarctica*, lipase B, was used to synthesize amphiphilic fatty amides from linoleic acid and salicylic acid in a solvent-free process at 65°C and reduced pressure (50 mbar) with high conversion rates, up to 95% via aminolysis reactions (Mouad et al. 2016). Furthermore, adjusting the enzyme concentration showed an increased yield of fatty amide 3 from 30% to 88%. Thus, this result demonstrates that a solvent-free enzymatic synthesis is an attractive method for producing

fatty amides with potential applications in the cosmetic industry.

CONCLUDING REMARKS

Conventional industrial processes employ chemicals for production, leading to increased environmental toxic waste accumulation, inefficiency, and high cost. The application of enzymes presents a link for transformation into eco-friendly industrialization, minimizing the environmental impact and providing efficient and cost-effective techniques. Although using enzymes offers a better alternative to conventional methods, there are also shortcomings associated with enzymes, including short life, instability to harsh industrial bio-processing conditions, and reusability. However, biotechnology technology advancement presents opportunities to overcome these shortcomings via genetic engineering and enzyme immobilization technology. The use of enzymes on a commercial scale is applied in different endeavors, encompassing medicine, agriculture, and industries, to improve efficiency and sustainability processes. This brings about processes under mild conditions with lesser energy requirements due to the environmentally friendly and biodegradable nature of enzymes and their byproducts. Thus, enzymes will continuously be employed in industries due to their low cost and safety for both individuals and the environment, leading to higher performance and improved production processes with lower environmental influence.

ACKNOWLEDGEMENTS

The authors express their gratitude to the Departments of Pharmaceutical Technology and Science Laboratory Technology, Adamawa State Polytechnic, Nigeria for institutional support.

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