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Biocatalysis:

Leveraging nature's catalysts in pharmaceutical development

Reviewed by:
Dan Stark
Group Leader (R&D)

Introduction

Enzymes are considered nature's catalysts. They are found in all living organisms and aid in specific natural processes such as digestion and DNA replication. Over the years, various industries have found ways to apply enzymes to synthetic chemistry, finding ways to harness their catalytic activity in a controlled environment. In fact, although people have used enzymes in brewing for thousands of years, they didn't know what enzymes were or understand that they could be isolated until the 1800s.

As the scientific field advanced, the application of enzymes expanded far beyond brewing, with scientists only beginning to realise the full potential of enzymes in the late 20th century. As they developed the ability to evaluate an enzyme's suitability for various processes, biocatalysis, the use of enzymes to speed up chemical reactions, began to gain traction. Today, biocatalysis is employed within a diverse set of industries, including pharmaceuticals, biotechnology, food and beverage, nutraceuticals, cosmetics, waste treatment, and more. Today, it is estimated to have over several hundred commercial applications.

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For pharmaceutical development, biocatalysis can be particularly compelling as it offers superior enantio-, regio- and chemoselectivity to chemical catalysis, whilst maintaining other benefits such as efficiency and cost-effectiveness. Furthermore, enzymes mostly work under very mild conditions, though there are exceptions that work under harsh conditions.

In this article, we will closely examine the growth of biocatalysis in pharmaceutical development, the power of enzyme immobilisation to overcome some of biocatalysis' key challenges, and why Sterling's partnered approach to biocatalysts provides solutions for our customers.

Did you know?

The global biocatalysis market is expected to reach $1.86 billion by 2031.[1]

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Why biocatalysis applications are expanding in pharma and beyond

If enzymes are naturally occurring and have been used for centuries, why is the widespread use of biocatalysis in manufacturing relatively new? The primary reason is that advances in technology have enabled far more widespread access to natural enzymes, as well as the controlled optimisation of natural enzymes for greater catalytic efficiency. This, coupled with more widespread awareness of biocatalysis' compelling advantages, are collectively responsible for the technology's rapid growth.

Let's take a closer look.

Over the past 20 years, next generation DNA sequencing has revolutionised genomic research. Ultra-high throughput capabilities have allowed genetic material to be read faster than ever before.

Furthermore, inventive methods of DNA manipulation have allowed enzymes to be customised in a highly controlled manner. These methods include directed evolution and protein engineering, which now make it possible for enzymes to be tailored and optimised for a given chemical reaction. In 2018, American chemical engineer Frances Arnold was awarded the Nobel Prize in chemistry for her work in directed enzyme evolution.

Finally, the expanding field of enzyme immobilisation has yielded highly efficient, robust and stable heterogeneous biocatalysts; tackling some of the key challenges related with the use of enzymes at scale.

Coupled with enzyme commercialisation, four compelling advantages have driven the growth of biocatalysis:

- **Efficiency**: In one example, the enzyme carbonic anhydrase was shown to catalyse the hydration of 4 million molecules of CO_2 per second, approaching the limit of turnover dictated by diffusion.
- **Cost effectiveness:** Biocatalysis avoids the need for scarce precious metals and eliminates the cost of removing them.
- **Sustainability:** Biocatalysis aligns with key green chemistry principles, like using renewable resources and generating residues that are not environmentally harmful.
- **Customisation:** In one example, scientists were able to produce the HIV drug islatravir using solely enzymes, five of which were engineered.

Immobilisation for enzyme optimisation and risk mitigation

In spite of its promising benefits, the pharmaceutical industry has been relatively slow to adopt biocatalysis in drug development until recently. Three main concerns with utilising enzymes have included their high upfront costs, challenges detecting and separating them from products, and their sensitivity to changes in the reaction environment.

The question, then, is what can be done to alleviate these key concerns when incorporating biocatalysis into pharmaceutical development?

In a customer project at Sterling, a lipase was immobilised onto 15 different immobilisation media, with significant retention of enzyme activity.

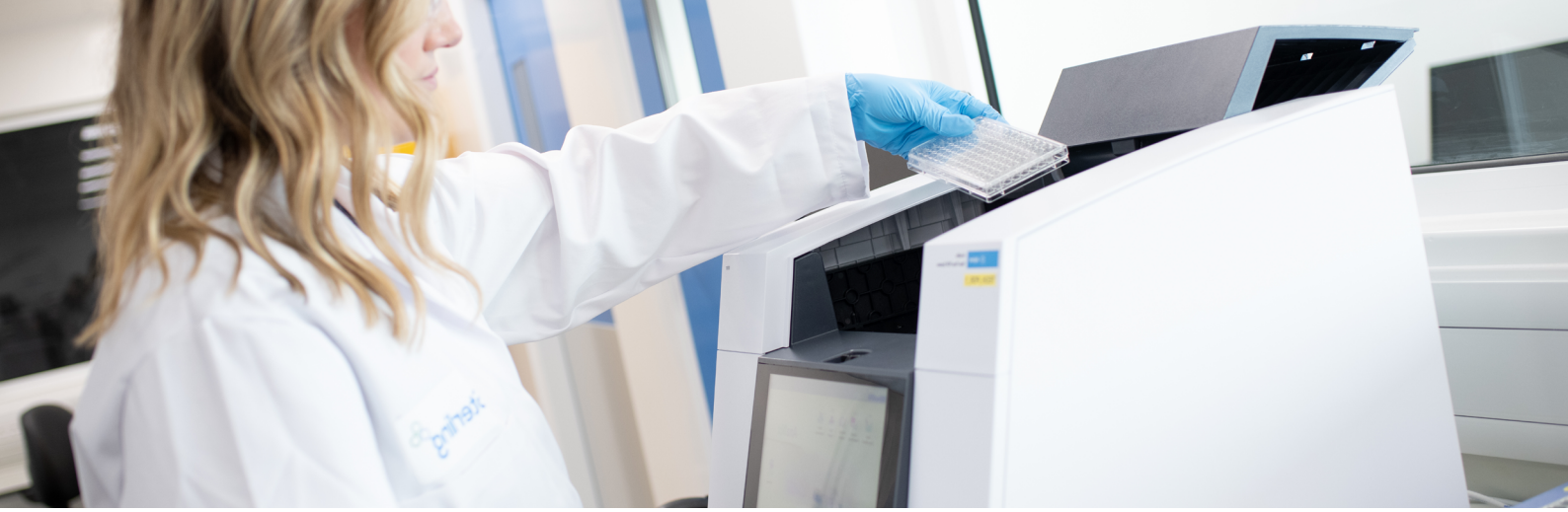
Enzyme immobilisation, or the practice of affixing to or encapsulating an enzyme within a heterogeneous solid support, presents a promising solution to all these major challenges. There are a number of methods for immobilisation, including adsorption, ionic bonding, covalent bonding etc.; and immobilisation supports or "media" are most often polymers or inorganic materials, such as polyacrylates or silica.

When attached to a solid, the stability of an enzyme to conditions such as temperature, pH and organic solvent content can be significantly improved. In one example, an immobilised α-chymotrypsin was shown to be 1,000 times more active in a methanolic environment compared to its free enzyme counterpart.

Secondly, immobilisation can help to ensure product purity. Attachment to a solid makes the enzyme easier to separate from the desired drug after the reaction is complete. Commonly used methods of enzyme recovery include simple filtration or centrifugation. Pharmaceutical developers can take comfort in knowing that their end products have been purified through these reliable and cost-effective methods.

Finally, because free enzymes are challenging to separate and isolate from completed reaction mixtures without enzyme denaturation, they are often only used once before disposal. This is inefficient and wasteful, diminishing the cost-effectiveness of biocatalysis for the pharmaceutical sector and other industries.

As immobilised enzymes can be readily separated and stored, however, they may be recycled and reused over many batches to reduce overall costs. Immobilised lipases, for example, have been recycled over 20 times on a current customer project here at Sterling, without significant diminishment of enzyme activity.



Case study: Dual enzyme cascade for benzoic ester

Let's take a closer look at enzyme screening and immobilisation through the lens of a project at Sterling.

The challenge:

Develop a dual-enzymatic cascade reaction for a complex benzoic ester while ensuring efficiency and yield

The solution:

Screened 50+ enzymes, ran a retro SAR study, used in silico modelling, and tested 15 immobilisation media

The outcome:

Identified enzymes with strong activity against structurally similar compounds, and demonstrated strong activity across a variety of immobilisation media

In this project, one of Sterling's biocatalysis teams investigated a dual enzyme cascade reaction for a highly substituted benzoic ester. Using the augmented enzyme panel available on site as well as sourcing from Sterling's partner biologic suppliers, they initially screened over 50 enzymes for two-step conversion, yielding a few weak hits. These were further evaluated against 22 structural analogues. The team was then able to perform a retro structure-activity relationship (SAR) study to pinpoint additional enzymes from literature that showed activity against compounds of high structural similarity, and ultimately identify more hits that were effective for the two-step conversion. This also allowed the team to understand key interactions the compound had with each enzyme active site.

The biocatalysis team went on to model the enzymes in silico for crystal structure characterisation and active site resolution, gathering data to optimise the enzymes through directed evolution or protein engineering as necessary.

The free enzyme was ultimately tested across 15 immobilisation media using a variety of affixation techniques, including ionic bonding, absorption, and covalent bonding. These studies demonstrated significant activity retention across many of the immobilisation media, indicating that a number of viable routes could be used.

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Sterling's partnered approach to biocatalysis

At Sterling, we have decades of experience working with complex chemistries, including the use of enzymes. We are committed to continually embracing new technologies that have the power to bring significant advantages to the API development and manufacturing process.

We have over 50 years of experience taking novel chemistry from the laboratory to industrial scale. We grant you full ownership over the IP that results from the enzyme screening and development process, and we couple our enzyme expertise with full cGMP manufacture of APIs and intermediates.

Lastly, we are a Partnership Development and Manufacturing Organisation (PDMO®). Our differentiated commitment to transparency and simple, collaborative ways of working is instrumental to providing our customers peace of mind as they embrace biocatalysis.

Our Technology and Innovation Programme underscores our commitment to continual innovation and improvement. In addition, to complement and expand our own capabilities, we have carefully selected experienced partners to maximise value throughout the entire biocatalysis process, from suitability screening to full scale-up.

Visit sterlingpharmasolutions.com/contact to speak to an expert

1 | ReAnIn (2026). Biocatalysis Market Size & Share Analysis - Growth Trends and Forecast (2025-2032). https://www.reanin.com/reports/biocatalysis-market

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