

Microbial Biotransformation of Chemical Compounds to Obtain Commercially Useful Drugs-An Industrial Management Basis

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ABSTRACT: There's a lot of really fun stuff you can do in the world of microbiology. The big buckets are academia, pharma, agriculture, biotech, and medical. Obviously, there's overlap in the focus, but generally, academia is focused on research and discovery, while pharma, agriculture, and biotech are more focused on innovation and commercialize solutions to problems. As I mean it here, medical refers to microbiology labs in hospitals and contract labs diagnosing infectious diseases. Those are the major fields microbiologists likely find themselves in.

I started ZBiotics because I liked the idea of innovation and developing novel solutions to existing problems, but rather than join an existing biotech or pharma company, I thought it would be fun to pursue my own ideas. It was a thrilling proposition for me to take something out of my own head and try to build it into something that people are going to use in their day-to-day lives!

Biotransformation is a process by which organic compounds are transformed from one form to another to reduce the persistence and toxicity of the chemical compounds. This process is aided by major range of microorganisms and their products such as bacteria, fungi and enzymes. Biotransformations can also be used to synthesize compounds or materials, if synthetic approaches are challenging. Natural transformation process is slow, nonspecific and less productive. Microbial biotransformations or microbial biotechnology are gaining importance and extensively utilized to generate metabolites in bulk amounts with more specificity. This review was conceived to assess the impact of microbial biotransformation of steroids, antibiotics, various pollutants and xenobiotic compounds.

KEYWORDS: biotransformation, chemical, compounds, pollutants, xenobiotics, metabolites

I. INTRODUCTION

It is not the first company that Ulrich Rabausch had made a start on, but it is the first to which the microbiologist from the University of Hamburg has devoted his professional career. The company is occupied with the production of health-promoting, cosmetically active ingredients for the cosmetics industry. "I've always found the business side of things to be exciting," says Rabausch, who already in his student days dipped his toe into business founding with the creation of the firm FrutAmazon. The company is now history, but the interest in commerce remained, leading him to supplement his studies in microbiology with a minor in Business Administration. When he chanced upon an ad for the third 'Innovation Academy biotechnology' in the summer of 2012, he was immediately convinced: "The format of the event sounded promising. I wanted to give it a try."

Drug biotransformation is carried out by combination of phase I and phase II reaction (1). Phase I: In phase one reaction drugs undergo oxidation, reduction and hydrolysis to which convert them into an intermediate: a) active drug into inactive drug, b) prodrug into active drug, c) sometimes it forms compound which retains same property of parent drug. During phase one some drug become water soluble and eliminates out but some drug does not acquire enough water solubility hence undergo phase II reaction (2). Phase II: Phase II reaction also called as conjugate reaction convert the intermediate into nontoxic compound by attaching molecules present in the body to reactive site of phase I product and as a result its solubility increase and it is then eliminated out of body (3)

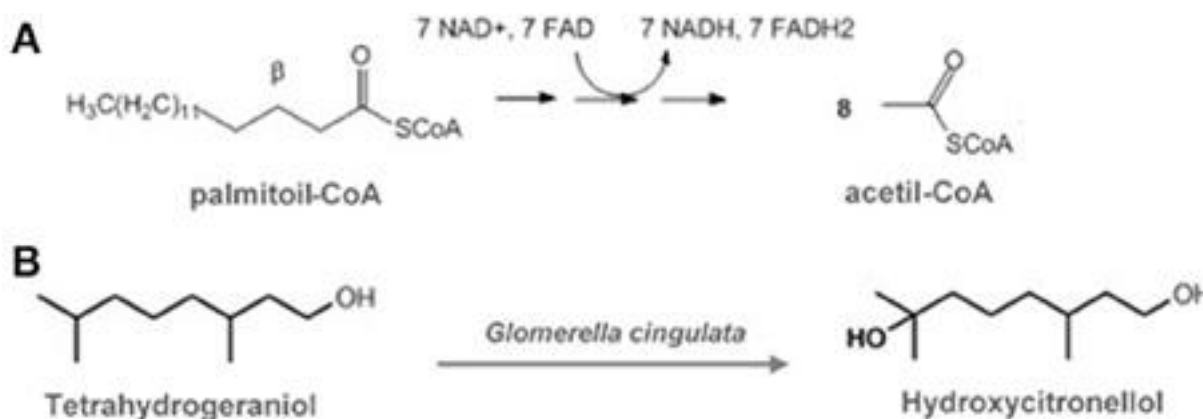
Biotechnology might contribute to the discovery of molecules with antifungal properties by microbial biotransformation procedures. Authors present some aspects of (1) microbial biotransformation of herbal medicines and food; (2) possibility of major and minor molecular amendments in existing molecules by biocatalysis; (3) methodological improvements in processes involving whole cells and immobilized enzymes; (4) potential of

endophytic fungi to produce antimicrobials by bioconversions; and (5) *in silico* research driving to the improvement of molecules.

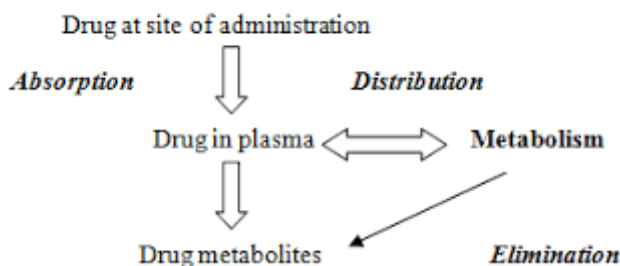
II. DISCUSSION

Microbial metabolism is composed of two major processes; primary metabolism, which is responsible for cellular function, and secondary metabolism, which uses pre-existing metabolic pathways to produce substances from endogenous intermediates to allow better adaptation of the organism to the environment (4). Primary metabolism consists of reactions associated with energy generating, biomass production, and essential cell components. Events such as glycolysis, oxidative phosphorylation, and the Calvin-Benson cycle (in algae and photosynthesizing bacteria) are examples of typical sets of reactions of primary metabolism.

In contrast, secondary metabolism involves important events for adaptation to environmental conditions. In general, it generates low molar mass metabolites that are not essential for growth but that offer some advantages and may sometimes have medical/veterinary/agricultural/industrial importance. They include antibiotics, pigments, anti-tumor agents, etc. They have unusual structures and are normally synthesized during the late phase of cell growth (5).



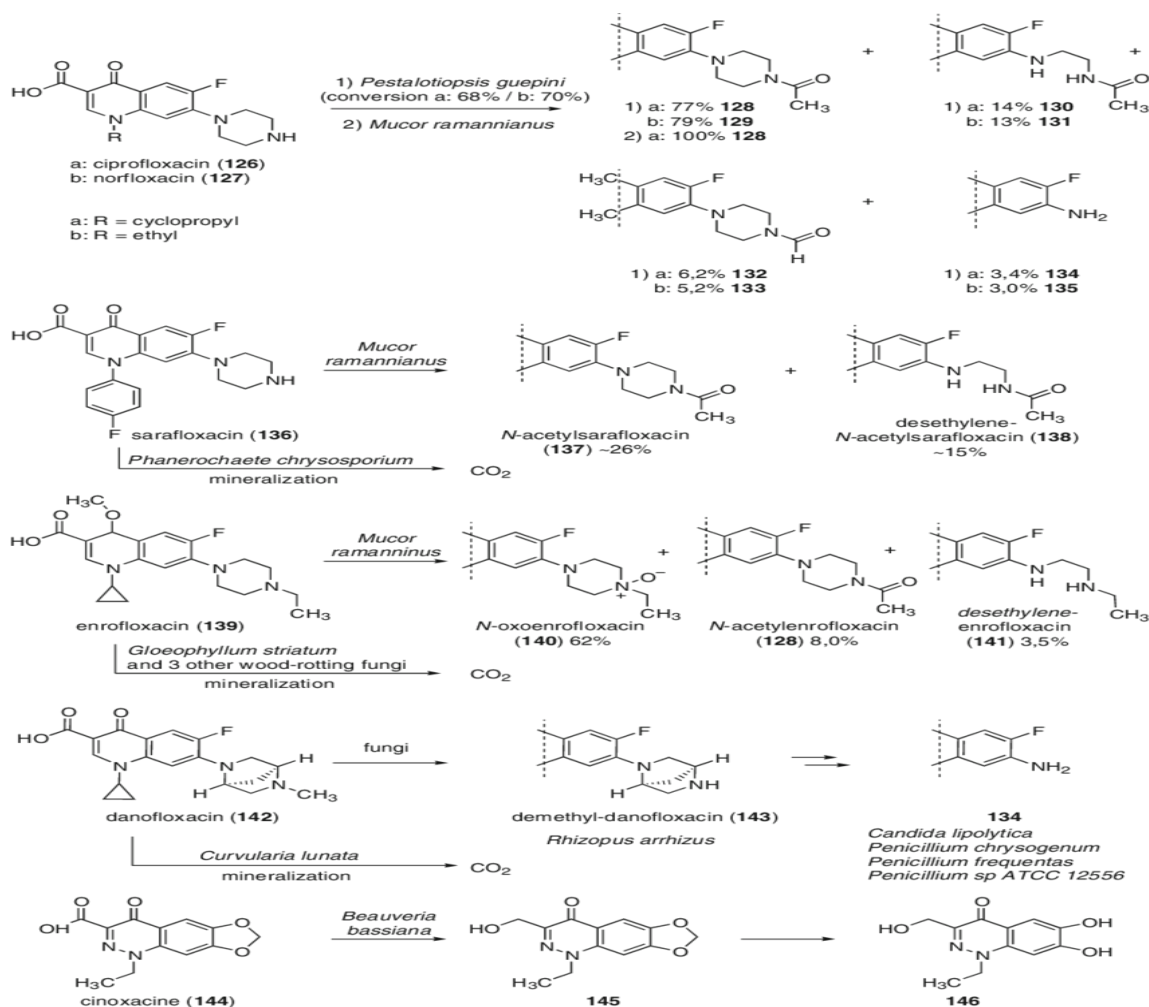
- (A) Typical multi-step metabolic reactions, with deep alterations on carbon skeleton (in this case, fatty acid oxidation). (B) Typical one-step biotransformation reaction, with minor punctual alterations on carbon skeleton (6).
- (B) A reasonable research design for the prospecting of new antifungal drugs under the above stated conditions involves the following:
- (C) (1) The *in silico* analysis of existing molecules for possible new couplings to different targets;
 - (D) (2) The *in silico* identification of necessary changes in the precursor molecule for effective coupling on targets;
 - (E) (3) In the absence of new discoveries, the biotransformation of various candidate substrates for obtaining new molecules;
 - (F) (4) The recognition of which organisms or isolated enzymes may modify structural precursor molecules to yield enantiomerically pure antifungal molecules based on the theory of enzyme promiscuity;
 - (G) (5) The *in silico* evaluation of toxicity for newly developed antifungal molecules;
 - (H) (6) The process of scaling up with environmentally friendly inputs to test the economic viability.



BIOTRANSFORMATION OF XENOBIOTICS

EXAMPLE OF BIOTRANSFORMATION OF ANTIBIOTICS

The absence of a lag period in the bioconversion of chloramphenicol by spores and the pronounced influence of the pH of the medium on this reaction strongly suggested that chloramphenicol acetyltransferase (CAT) is located at or near the surface of the spores of *Streptomyces griseus*. A two-hour exposure of spores to dilute solutions of β -mercaptoethanol or surfactants resulted in significant decrease in activity even in the presence of glucose as an energy source. However, the inclusion of any of the reagents in the reaction mixture neither influenced the conversion activity nor the spore viability. These treatments did not reveal any cryptic activity for CAT in the spores. In addition, more drastic treatment of the spores with ethylenediaminetetraacetate (EDTA) or with concentrated salt solutions did not reduce the activity nor significantly affect the spore viability. Considering the modes of action of β -mercaptoethanol and the surfactants, a combination of disulfide bridges and lipoprotein interactions may be responsible for the binding of CAT to the surface of the spore. Moreover, results of acid treatment of intact spores indicated that most of CAT activity, if not all, is located at the spore surface. Incorporation of 14 C-acetate by cell-free extracts of *Streptomyces griseus* clearly showed that CAT selectively catalyzed the formation of chloramphenicol-3-acetate at an optimum pH of 6.5. The shape of the pH-activity curve in cell-free extracts is essentially identical to that of the enzyme in intact spores and is additional evidence that the enzyme is located at the spore surface.

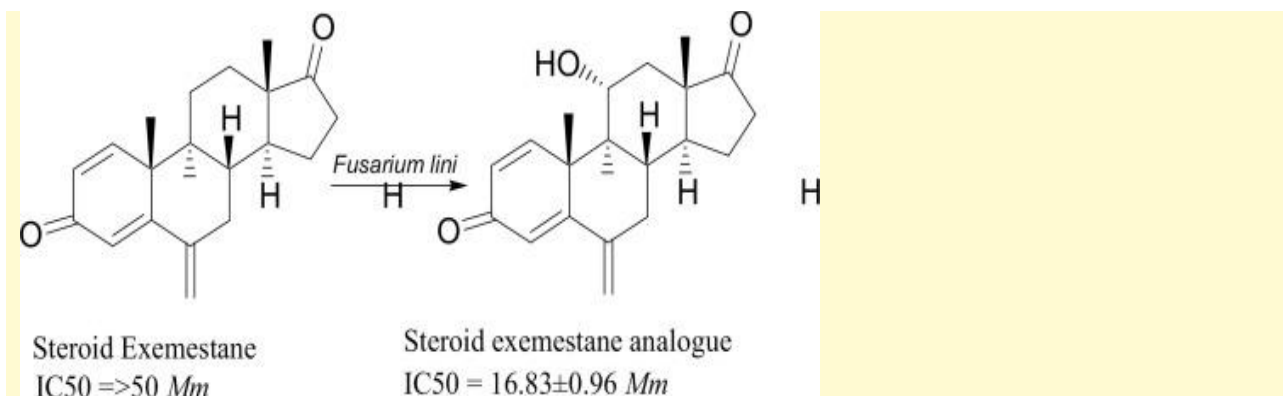


Degradation of fluoroquinolone and related antibiotics by fungi

EXAMPLE OF BIOTRANSFORMATION OF STEROIDS

The microbiological transformations of steroids have been an essential chemical tool used for the preparation of many intermediaries and in the generation of new drugs, where chemical functionalization-hydroxylation, Baeyer-Villiger oxidation, reduction, isomerization, Michael additions, and condensation reactions can be carried out in different positions of the steroid skeleton in *chemo*-, *regio*-, and *stereoselective* ways, being very complicated or even impossible

by the classic chemical methods. Currently, any stereogenic center of the steroid skeleton can be specifically hydroxylated stereoselectively. Nowadays, *biohydroxylations* in C-11 α , 11 β , 15 α , and 16 α are industrially carried out via a microbial hydroxylation with good yields and enantiomeric excess (8). Below are some of the microbiological transformations performed on different natural and synthetic steroids [7].



A number of new applications of stereoselective biotransformations are appearing in the literature. A small sample of these have been presented in this report to represent a form of bioprocessing used for many decades. This type of bioprocessing is finding an increasing use in the pharmaceutical industry as it strives for lower levels of toxicity in its products and, also, in the chemical industry as it begins to redefine itself as a more environmentally friendly and efficient sector. The ability of the ubiquitous and versatile microbe to rapidly adapt to changing environments has now made it a target as a synthetic tool for production of novel building blocks.

III. CONCLUSION, SCOPE AND SIGNIFICANCE

Microbial resolution of racemic mixtures of chemical precursors or final products has already been established. Microbial transformation or biocatalysis has proven to be a valuable tool in production of pharmaceutical intermediates, in particular enantiomerically pure compounds. In some of the cases, solubility of the reactants and or products in the reaction mixture employing enzymes or microbial cells remains a critical problem to be solved. Furthermore, stability of microbial enzyme(s) could be a problem in the chemical environment suited for chemical reaction.(9,10)

Developments in microbial biotransformation technology, including new and more stable enzymes, improvement of existing enzyme systems using site-directed mutagenesis and search for novel microorganisms with desired enzymatic properties will further advance the application of chemoenzymatic synthesis in organic chemistry.

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REFERENCES

1. Ahmad, S., Garg, S.K. and Johri, B.N. (1992) *Biotechnology Advances* **10**: 1-67.
2. Ahmad, S. and Johri, B.N. (1992) *Applied Microbiology and Biotechnology* **37**: 468-469.
3. Ahmad, S., Roy, P.K., Khan, A.W., Basu, S.K. and Johri, B.N. (1991) *World Journal of Microbiology and Biotechnology* **7**: 557-561.
4. Ahmad, S. and Johri, B.N. (1993) *Indian Journal of Chemistry (Sec. B)* **32B**: 76-69.
5. Alphanh, V. and Furstoss, R. (2000) *Journal of Molecular Catalysis B: Enzymatic* **9**: 209-217.



6. Andreas, L. and Filho, M.V. (1999) Current Opinion in Biotechnology **10**: 595-603.
7. Azerad, R. and Buisson, D. (2000) Current Opinion in Biotechnology **11**: 565-571.
8. Berrie, J.R., Williams, R.A., Smith, K.E.(1999) Journal of Steroid Biochemistry and Molecular Biology **15**:153-65.
9. Hudlicky, T. and Thorpe, A.J. (1996) Chemical Communication 1993-2000.
10. Hudlicky, T., Tian, X., Konigsberger, K., Maurya, R., Rouden, J. and Fan B. (1996) Journal of American Chemical Society **118**: 10752-10765.