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Industrial Catalytic Production Process of Erythromycin

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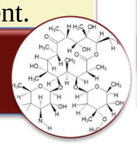
INTRODUCTION & AIM

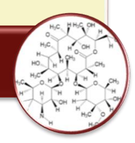
Erythromycin OVERVIEW

- What is Erythromycin?
- Erythromycin is an antibiotic discovered in 1949. Is it produced by Saccharopolyspora erythraea and is used as an alternative to penicillin, particularly in case of allergy. It has improved stability, delivery, and potential antiviral applications, including COVID-19 treatment.



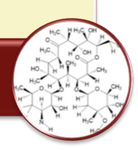
Erythromycin IMPORTANCE

- Why should we discuss it?
- The need for optimized industrial production is essential. Erythromycin's synthesis advances through catalysis, purification, and sustainability. It is used in treating respiratory, skin and systemic infections.



Erythromycin AIM

- What is the purpose of the study?
- Refining fermentation and enzymatic processes, lead to optimization of industrial synthesis. Catalytic performance and economic efficiency are boosted. Metabolic bottlenecks in the biosynthetic pathway are overcome.



METHOD

Production

- Yield and cost-effectiveness is enhanced due to optimization of pH, temperature, and nutrients with the Saccharopolyspora erythraea HOE107 strain.
- Al the targeted modifications increase methylmalonyl-CoA, relieving TCA cycle bottlenecks and all in all enhancing efficiency.

Catalytic System

- Structural Analysis: Cytochrome's P450eryF's 3D structure-haem orientation and substrate pocket geometry essential for 6S-hudroxylation of 6 DEB are revealed through analytical techniques (Figures 1,2).
- Enzyme Optimization: Targeted modifications enhance catalytic turnover and specificity, improving production efficiency.

Purification

- Isolation erythromycin A is achieved by advanced crystallization methods (antisolvent, evaporative, reactive), reducing contaminants.
- This boosts purity and reduces processing costs.

Waste

- Sustainability is ensured through hydrolysis of fermentation residues that reduces chemical oxygen demand.

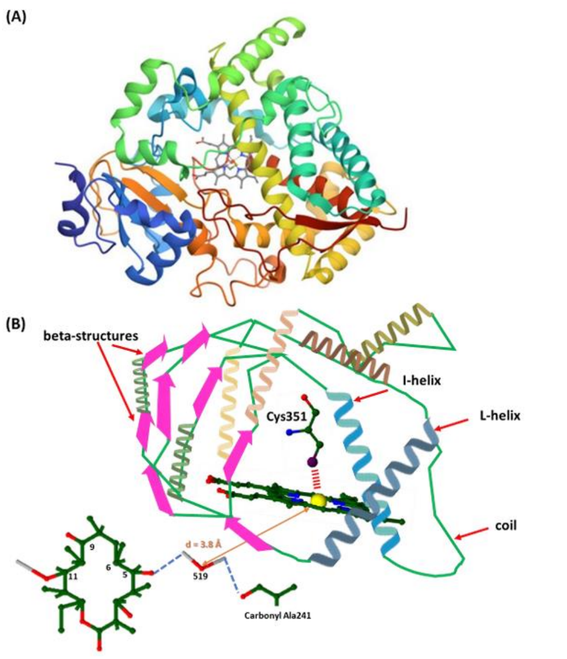


Figure 1: (A) Cytochrome P450eryF general 3D structure (downloaded by the RCSB PDB (Protein Data Bank)). (B) The alpha/beta structure of cytochrome P450eryF in detail. In figure (A), alpha helices are represented by ribbons of different colors on the right side, while beta-structures with coils on the left are depicted with orange arrows.

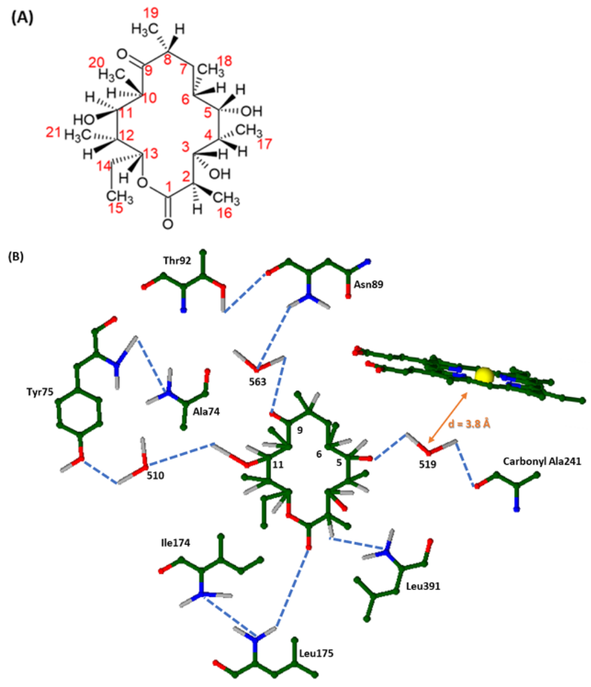


Figure 2: P450eryF substrate, 6-deoxyerythronolide, and numbering system. (B) 6-DEB in the active site. Red = oxygen, blue = nitrogen, green = carbon, yellow = iron (II). Cyan dashed lines show hydrogen bonds. Water molecules Wat510, Wat519, and Wat563 play roles, with Wat519 possibly being the proton donor in O2 cleavage (3.8Å from iron).

RESULTS & DISCUSSION

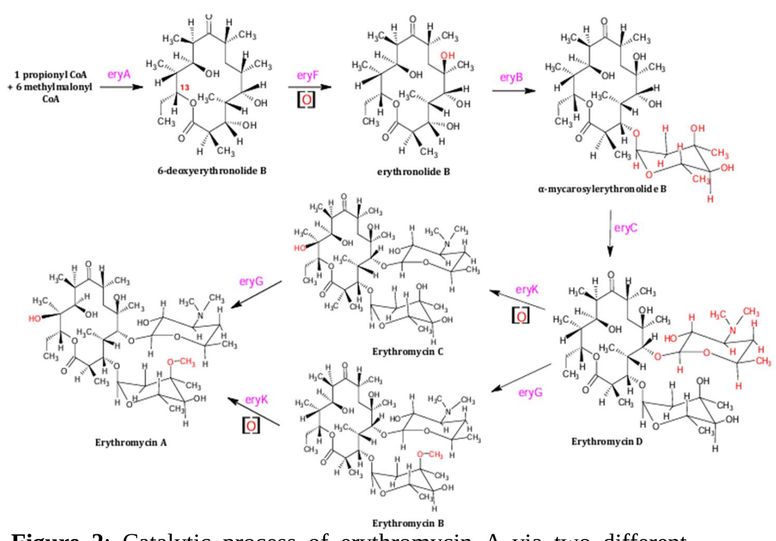
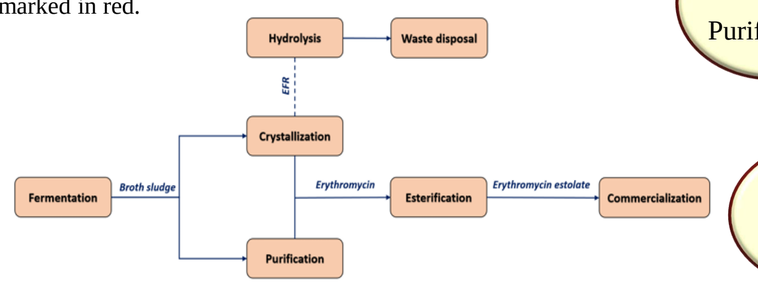


Figure 2: Catalytic process of erythromycin A via two different means (the oxidation reaction is displayed using [O]). The catalysts of all reactions are depicted in pink, and all transformations are marked in red.

Catalytic Mechanism
P450eryF converts 6-DEB into erythronolide B, a key erythromycin precursor.

Yield & Efficiency
Modifications and waste management enhance production.

By-Products
By- product erythromycin B and especially toxic C require removal.



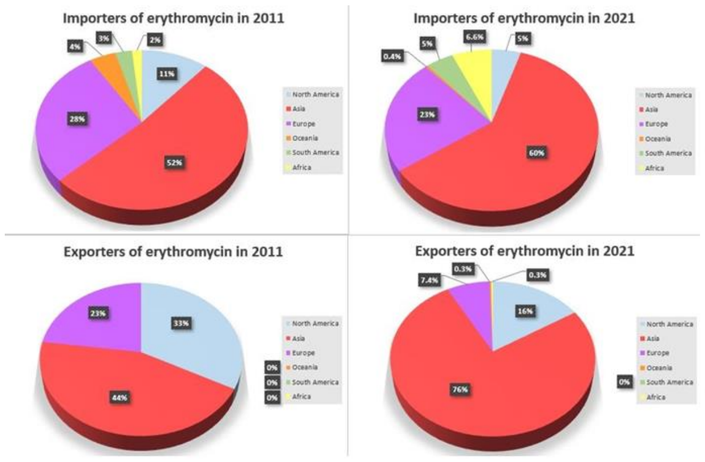
Challenges in Purification

Erythromycin A is separated from the toxic by-products. Three crystallization methods-antisolvent, evaporative, and reactive.

Genetic Engineering Strategies

Genetic tailoring in Saccharopolyspora erythraea can deactivate genes that reduce erythromycin production.

Figure 3: Flow chart of erythromycin production.



Industrial Trends and Global Production

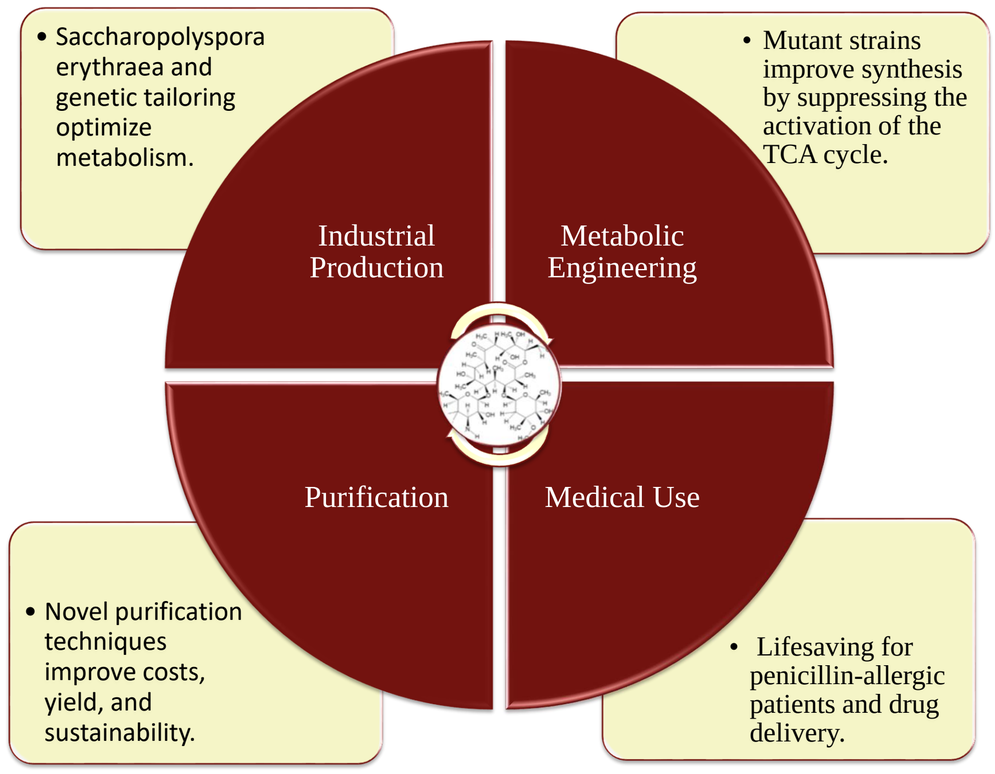
Asia, South America and Africa have increased Erythromycin production, whereas Europe and North America have experienced declines.

Market expansion

Future market expansion relies on advancements in optimization of biotechnological engineering and process.

Figure 4: Importers and exporters of erythromycin throughout the years 2011–2021

CONCLUSION



- Saccharopolyspora erythraea and genetic tailoring optimize metabolism.
- Mutant strains improve synthesis by suppressing the activation of the TCA cycle.
- Novel purification techniques improve costs, yield, and sustainability.
- Lifesaving for penicillin-allergic patients and drug delivery.

FUTURE WORK / REFERENCES

Improve the efficiency of industrial production.

Reduce by-products and waste.

Expand medical applications

Guengerich, F.P. Cytochrome P450 Enzymes. Am. Sci. 1993, 81, 440–447.

OMURA,T.Recollection of the Early Years of the Research on Cytochrome P450. Proc. Jpn. Acad. Ser. B Phys. Biol. Sci. 2011, 87, 617–640

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