



الجمهورية العربية السعودية
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المضادات الحيوية (BCH 476)

Antibiotics

Lecture 3-4

When and why antibiotics are produced?

Lect No.	Topics
3-4	<ul style="list-style-type: none">•When & why antibiotics are produced from microorganisms?•The concept of trophophase & idiophase.•Primary and secondary metabolism in relation to antibiotic production.•Ecological role of antibiotics in nature.•Antibiotics in regulation of metabolism.•Role of antibiotics in differentiation of producing microorganisms.

When and Why antibiotics are produced?

- **Production of antibiotics has been mostly studied in submerged batch cultures.**
- The process can be divided into two phases:
 - 1-Trophophase** (feeding and growth phase) in which a rapid consumption of nutrients and growth occurred. A lot of new cells are produced and the growth rate can be monitored either by cell count or by measuring the increasing DNA content.
 - 2- Idiophase** (cease of growth and increase production of antibiotics). It can be monitored by decreased RNA synthesis and drop in respiratory activity.

When and why antibiotics are produced? Cont

In bacterial cultures, the separation between the trophophase and idiophase is clearly observed by observing the growth throughout cell counter, **but in filamentous actinomycetes and fungi**, there is no clear cut between the two phases .

We may distinguish between the two phases in filamentous organisms by estimating the dry cell weight or by estimating the DNA contents.

Primary metabolism and its products

- **The primary metabolism:**

The process in which primary metabolites are synthesized. It is the summation of a series of enzyme-catalyzed reactions (**both degradative & synthetic**) which provide the organism with its energy, its synthetic intermediates and other macromolecules such as nucleic acid, protein, polysaccharides and lipid.

Secondary metabolism and its products

- The term **secondary metabolites** is borrowed from plant physiology to indicate products that are not essential for plant growth. It is considered by physiologists as products for the protection of plants.
- Sometimes, secondary metabolites are called “**idiolites**” because they are produced during idiophase of growth.

Secondary metabolism and its products (cont.)

- Secondary metabolism involves **only synthetic pathway** to give secondary metabolites which play no obvious role in the economy of the organism.

Reasons of antibiotic production

What is the importance of antibiotic production for the producing microorganism?

Many studies CLAIMED many functions for the production of antibiotics as secondary metabolites from microorganisms:

BUT THEY ARE NOT CORRECT REASONS

The mostly discussed explanations were:

- Evolutionary relics (why not?)
- Waste products of normal metabolism (why not?)
- Concentrated food storage as starch and lipids (why not?)
- Fragments of digestion of large molecules (why not?)
- Product of detoxification processes.

Reasons of antibiotic production

Recently, the following functions are proposed for the role of antibiotics in their producers:

- 1- Ecological role in nature
- 2- Role of antibiotics in regulation of metabolism
- 3- Role of antibiotics in regulation of differentiation and morphogenesis of the producing microorganisms.

1- Ecological roles of antibiotics for the microorganism that produce it

- **Are antibiotics produced in nature or only in lab?**
 - It is proved that antibiotics can be produced by micro-organisms in normal ecological conditions (out of lab conditions)
- **Do antibiotics have a function when produced naturally?**
 - Some antibiotics may have a protective effect on the organism producing them and play an important role in the ecology of actinomycetes.
 - Antibiotics are important for differentiation and maturation of microorganism
- **Is one function that of inhibiting or killing competing organism in nature?**
 - Yes some antibiotics producing microorganisms resist the deleterious effect of their antibiotics but in contrast, these antibiotics protects their producing microorganisms against the microbes or actinomycetes in vicinity.

2- Role of antibiotics in regulation of metabolism of its producer

Many possible or presumed effect of antibiotics on its producing microorganisms are discussed:

- Some antibiotics inhibit DNA, RNA, or protein synthesis in their producers.
- Some antibiotics interfere with energy metabolism.
- Some changes the membrane functions, transport across membranes or even inhibit cell wall synthesis of the cell that produce it.

How do antibiotic-producing microorganism avoid suicide?

- Many possible mechanisms are discussed to explain “**How do antibiotic-producing microorganisms avoid suicide**”:
 - In some microorganisms, the sensitivity against antibiotic is high in the growth phase (trophophase) and decreases during antibiotic synthesis phase (idiophase).
 - In other antibiotic producing microorganisms, this organisms lack the target structure for the antibiotic attack.
 - Some other organisms protect it selves by modifying the ribosome (target for antibiotic) by adding methyl group to one of its subunits (23S), hence the antibiotic cannot attack the ribosome.

How do antibiotic-producing microorganism avoid suicide? (cont.)

- Some microorganisms modify the antibiotic it selves by converting it into harmless compound.
- Other microorganisms defend itself against its antibiotics by accumulating it away from the target molecule. For example it stores antibiotic in the cell wall area which is impermeable, so the antibiotic cannot reach the site of protein synthesis in the cytoplasm.
- Finally, some microorganisms inactivate their antibiotics.

3- Role of antibiotics in regulation of differentiation and morphogenesis of the producing microorganisms

- One cannot generalize a role of antibiotics in regulation of differentiation and morphogenesis of the producing microorganisms because the different mechanisms exist in different type of microorganisms (bacteria, actinomycetes, fungi, etc).

Summary

- Certain antibiotics might be considered as means of struggle with a competing organism, others as regulators of metabolic processes of the producers themselves and yet others as factors regulating or accompanying processes of differentiation and morphogenesis.