INHIBITORS OF PROTEIN SYNTHESIS

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Inhibitors of Protein Synthesis

- Protein synthesis inhibitors are the substances that stops or slow the process of translation (protein synthesis).
- These inhibitors usually act at the ribosomal level.
- Ribosomes are the site of protein synthesis in both prokaryotes and eukaryotes.
- These inhibitors work at different stages of translation such as initiation, elongation and termination.

On the basis of target organisms inhibitor of protein synthesis is categories as follows-

- Acting only on prokaryotes
- Acting on prokaryotes and Eukaryotes
- Acting only on Eukaryotes

Acting only on prokaryotes

- Tetracycline
- Streptomycin
- Chloromphenicol
- Erythromycin
- Rifamycin

Tetracycline

- Semisynthetic antibiotic made by catalytic hydrogenation of chlorotetracycline.
- Chlorotetracycline is obtained from bacteria *Streptomyces aurofaciens*
- It is bind to 30S ribosomal subunit.
- Blocking binding of aminoacyl tRNA to the A site of ribosome.

Streptomycin

- Streptomycin is isolated from soil actinomycete *Streptomyces griseus*.
- Streptomycin is a type of aminoglycoside, binds to the small subunit (30S) of bacterial ribosome.
- It causes misreading of the genetic code at relatively low concentrations and inhibits initiation at higher concentrations.

Chloromphenicol

- Chloramphenicol is isolated from *Streptomyces venezuela*.
- Chloramphenicol is a bacteriostatic antibiotic and its binding is reversible
- Chloramphenicol functions by binding to the A site of the 50S subunit of the ribosome and affects proper binding of the aminoacyl tRNA to the A site and thus inhibits the peptidyl transferase activity.

Erythromycin

- Streptomycin is obtained from *Saccharopolyspora erythraea* (*Streptomyces erythraeus*)
- Erythromycin inhibits protein synthesis by binding to the 23S rRNA molecules (in the 50S subunit) of the bacterialribosome.
- Binds in the exit channel of the ribosomes and thereby inhibits elongation of the peptide chain.

Rifamycin

- Rifamycin indirectly inhibit the protein synthesis.
- Rifamycin block initiation of RNA chains by binding to RNA polymerase (Prevent RNA synthesis).

Acting on prokaryotes and Eukaryotes

- Puromycin
- Actinomycin D

Puromycin

- Puromycin is an antibiotic obtained from *Streptomyces alboniger*.
- Structurally very similar to the 3' end of an aminoacyl tRNA
- It is bind to the ribosomal A site and participate in peptide bond formation, producing peptidylpuromycin .
- It does not engage in translocation and dissociates from the ribosome shortly after it is linked to the carboxyl terminus of the peptide. This prematurely terminates polypeptide synthesis.
- No clinical use due to toxic effect in the host. However, it is used in research especially cell culture research.

Actinomycin D

- Actinomycin D binds to DNA, block the movement of RNA polymerase and subsequently inhibit the synthesis of RNA and protein.

Acting only on Eukaryotes

Inhibitor	Specific Effect
Cycloheximide	cycloheximide blocks the peptidyl transferase (Translocation reaction) of 80S eukaryotic ribosomes
Anisomycin	Block the peptidyl transferase reaction on ribosomes
α-Amaniyin	Block m RNA synthesis by binding preferentially to RNA polymerase II
Diphtheria toxin	Catalyzes the ADP-ribosylation of a diphthamide (a modified histidine) residue of eukaryotic elongation factor eEF2, thereby inactivating it.
Ricin	an extremely toxic protein of the castor bean, inactivates the 60S subunit of eukaryotic ribosomes by depurinating a specific adenosine in 23S rRNA.

Eukaryotic v/s Prokaryotic Translation:

Characteristics	Prokaryotes	Eukaryotes
r-RNA	70S (50s & 30s)	80S (60s & 40s)
Gape b/w transcription & Translation	No	Yes
m-RNA	Non modified/Polycistronic	Having Cap & Tail/Monocistronic
First Amino acid	f-MET	MET
Initiation	3-Factors	9-Factors
Termination	3-Factors	2-Factors (majorly 1)
Duration	Less (20 aa/sec)	More (1 aa/sec)
Modifications	Not common	Yes (PTMs)
Specificity	Polycistronic (Shine Dalgarno Secquence)	Monocistronic