Shri. Shivaji Science College, Amravati

(NAAC Accredited with Grade 'A')

Seminar on

"Chloramphenicol"

Submitted by :

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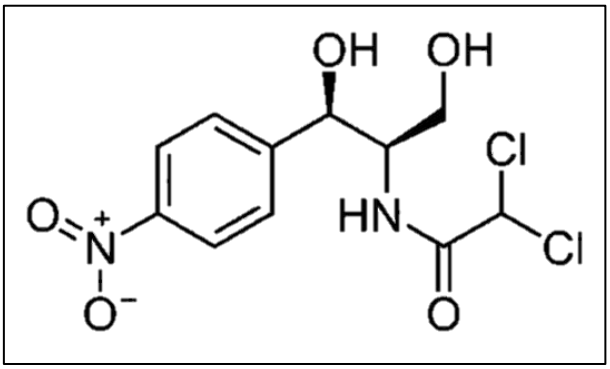
History :

- Chloramphenicol was obtained from the Streptomyces Venezuela and organism first isolated in 1947.
- Introduced into clinical practise in 1949 under the trade name chloromycetin. It was the first antibiotic to be manufactured synthetically on large scale.
- It was the first man made antibiotics.
- It is isolated from the soil.
- Used in chemotherapy.

Introduction :

- Chloramphenicol was obtained from the Streptomyces Venezuela.
- It was soon synthesized chemically and the commercial product now it all synthetic.
- It has a nitrobenzene substitution which is probably responsible for the antibacterial and the intensity bitter taste.
- chloramphenicol is primarily bacteriostatic through high Concentration have been shown to exert cidal effect on same bacteria.
- chloramphenicol was highly active against salmonella including s. typhi, but it is strain resistant.
- It is more active than tetracyclines against H. inFluenzene, B. pertussis, and Klebsiella, N. meningitidis and anaerobes including Bacteria fragillis. It is less active against gram positive cocci, spirochetes, certain Anterobacteriaceae Spirochetes and chlamydia.
- Chloramphenicol is the yellowish while crystalline solid antibiotics.
- Its aqueous solution is quits stable stands on boiling but it needs protection from light.

Structural Formula :



- Chloramphenicol has a simple structural mode up of Nitrobenzene ring it is consist of two components :
  - Nitra group GNO_2
  - Dichloraacetyl group

Pharmokinetics :

- It remains unbounded to protein and is a small molecule.
- It is extremely lipid soluble and penetrates effectively into all tissues of the body including brain.
- It is distributions is not uniform, with highest concentrations found in liver, and kidney, with lowest in the brain and cerebrospinal fluid.
- Concentration in brain is around 30% to 50%.
- Duration – Typhoid 8-10 days, meningitis 7-10 days, brain abscess up to 4 weeks
- Absorption – Radially absorbed with peak plasma concentrations after 1 to 2 hrs.
- Distribution – Distribution is not uniform. It is widely distributed into tissues and enters the breast milk, protein binding so.
- Excretion – via the urine, via the bile (3%), via the faeces (1% as inaction form), 1.5 – 2 hrs.
- Concentration – In brain and cerebrospinal fluids around 30% to 50%.

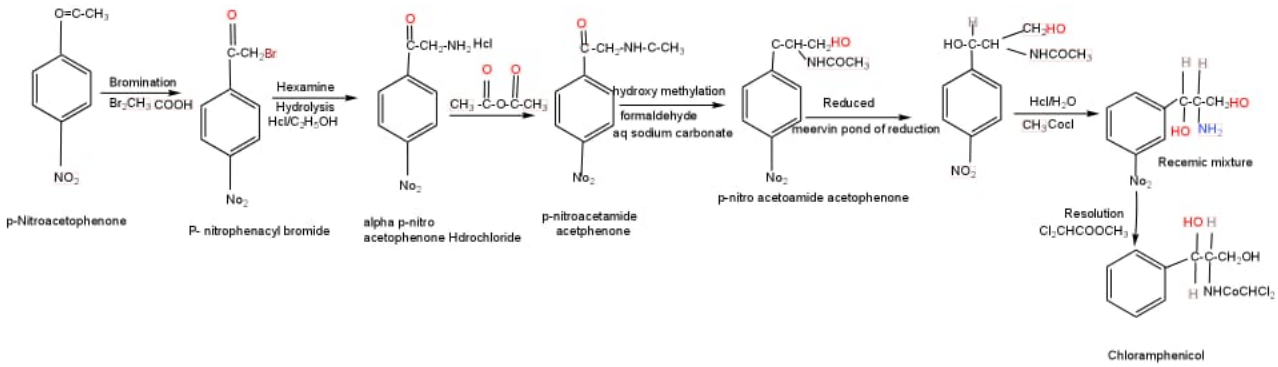
Mode of Action :

- Chloramphenicol inhibits bacterial protein synthesis by transferring with 'transfer' of the elongating peptide chain to the newly attached. Aminoacyl t-RNA at the ribosome m-RNA to the acceptor site for amino acid incorporation most probably, by acting as a peptide analogue, it prevents formation of peptide bonds.
- At high doses, chloramphenicol may inhibit the mammalian mitochondrial protein synthesis.
- Chloramphenicol is rapidly and completely absorbed after oral administration.

Physiochemical properties :

- It is a yellowish white crystalline solid but aqueous solution is quite stable.
- It stands boiling, but needs protection from light.
- The nitrobenzene moiety of chloramphenicol is probably responsible for the antibacterial activity which produces intensity bitter taste.

Synthesis of Chloramphenicol :



p-Nitroacetophenone

P- nitrophenacyl bromide

alpha p-nitro acetophenone Hdrochloride

p-nitroacetamide acetphenone

p-nitro acetoamide acetophenone

Adverse effects :

- Bone morrow depression – chloramphenicol cause of a plastic anaemia, agranulocytosis thrombocytopenia or pancytopenia.

  a. Non-dose related idiosyncratic reaction.
  b. Dose and duration of therapy related myelosuppression.

a) Non-dose related idiosyncratic reaction -

- Rare (1 in 40,000) , unpredictable, but serious, often, fatal and has a genetic basis occurs after repeated courses.
- Aplastic anaemia is the most common with higher mortality.
- Many victims after sometimes develop leukaemia's.

b) Dose and duration of therapy related myelosuppression –

- A direct toxic effect, predictable and probably due to inhibition of mitochondrial enzyme synthesis in the erythropoietic cells.
- Reversible without long-term sequelae liver and kidney disease predisposes to such toxicity.
- Gray baby syndrome (also termed Gray or grey syndrome) is a rare but serious side effect that occurs in new born infants.
- In these syndromes the skin became pale blue in colour and Lethargic eyes.

Symptoms :

- Loss of appetite.
- Vomiting.
- Ashen gray colour of the skin.
- Hypotension (low blood pressure).
- Cyanosis (blue discolouration of lips and skin).
- Hypothermia.
- Cardiovascular.
- Abdominal distension.
- Irregular respiration.
- Increased blood lactose.

Precautions :

- Before taking it, tell your doctor or pharmacist if you are allergic to it.
  - If you have certain medical conditions :
    - A bone marrow
    - A family history of blood disorder known as dyscrasias.
  - If you have certain eye infection :
    - Use any other eye drop and use contact lenses.
    - Dry eyes syndrome and any eye injury.

Warmings :

- For eye drops should be used with caution by :
  - People with eyesight problems.
  - Eye injury.
  - Dry eye syndrome.
- Using contact lens :
  - People with history of liver disease & blood disorder.
  - With history of kidney disease.
  - Should not used children under 2 years (eye drop).

Storage :

- For eye drops :
  - Store it in a refrigerator between 2 degree and 8 degrees. Store it in original packages to protect from Light.
  - Don’t store above 25 degrees Celsius.

Chloramphenicol dosage :

- Over dose :
  - Over dose with eye drops is unlikely to constitute a hazard & no specific treatment is required. If you think you might have accidently taken more than the recommended dose of it, contact your doctor.
  - In case of medical emergencies always dial 1122.
- Missed dose :
  - If your miss a dose, take it as soon as you remember. If it is near the time of next dose then skip the missed dose and resume your usual dosing schedule. Do not double the dose to catch up.

Reference :

- Introduction of Medicinal chemistry : Graham l. Patrick
- Medicinal chemistry : A Kar.

Thank you…!