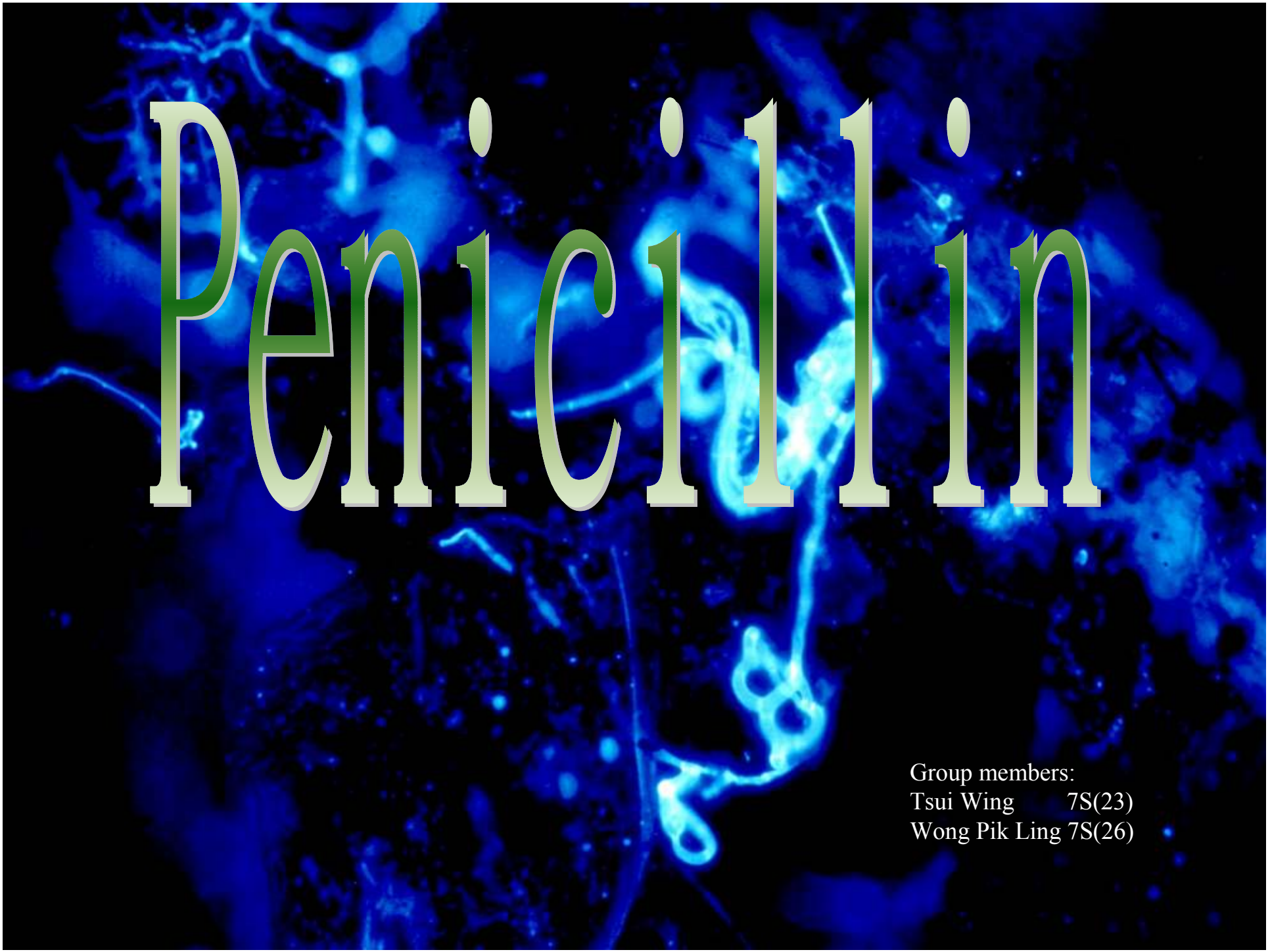


Group members:
Tsui Wing 7S(23)
Wong Pik Ling 7S(26)

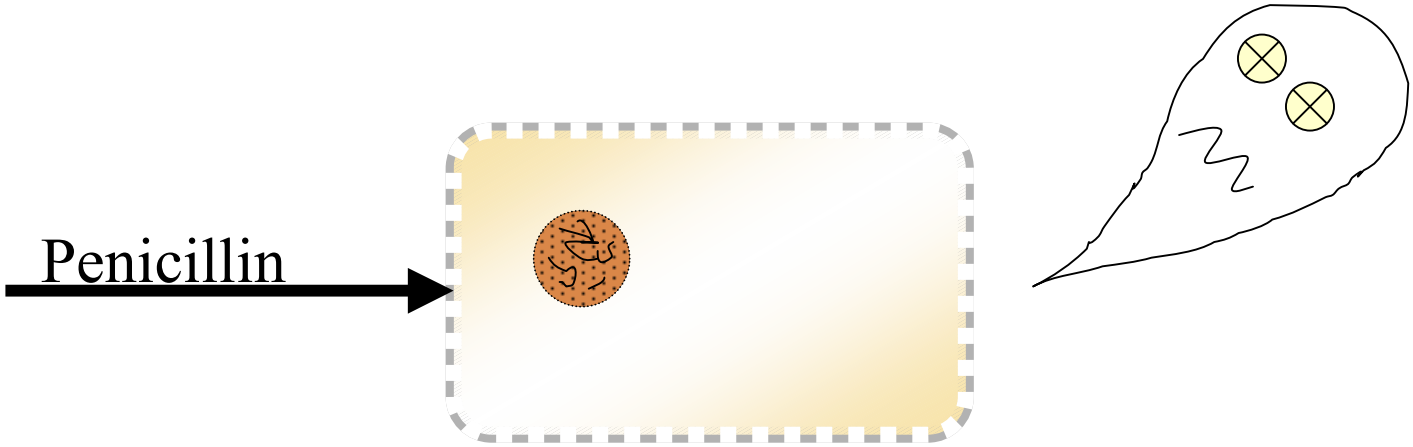
Contents

Introduction

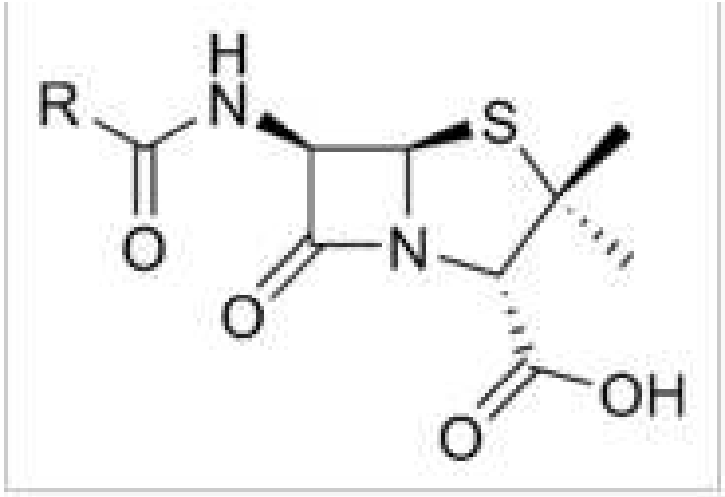
- Penicillin is a group of antibiotics derived from *Penicillium* fungi.
- Penicillin antibiotics are historically significant because they were the first drugs that were effective against many previously serious diseases such as tuberculosis, syphilis, and staphylococcus infections.

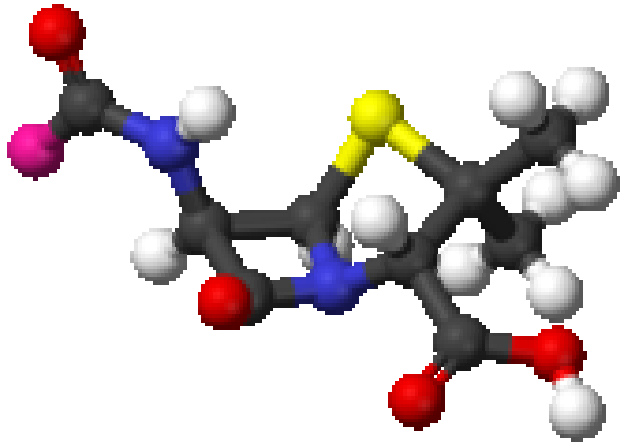
♛ Penicillin V is an antibiotic belonging to the penicillin group of drugs.

♛It works by interfering with the formation of the bacteria's cell wall while it is growing, weakening the wall and killing the bacteria.



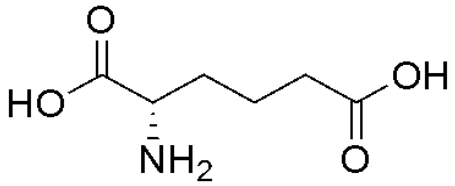
♚The molecular formula of it is R-$C_9H_{11}N_2O_4S$, where R is a variable side chain with its structural formula as shown below.



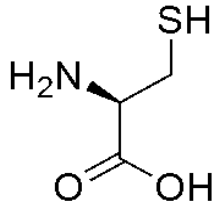


Penicillin core structure. "R" is variable group.	Penicillin core structure, in 3D. Purple is variable group.

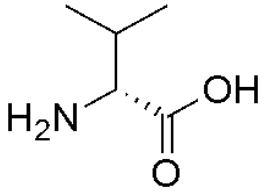
Penicillin-biosynthesis



L-Amino-adipic acid

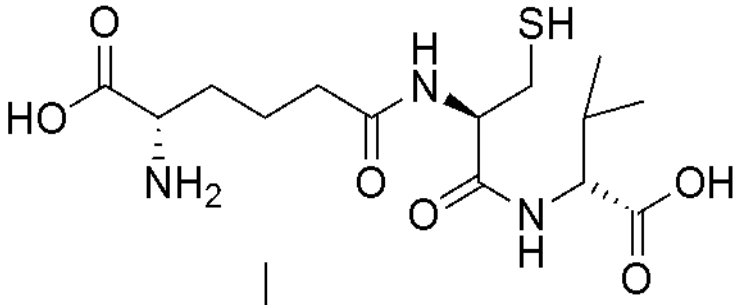


L-Cysteine

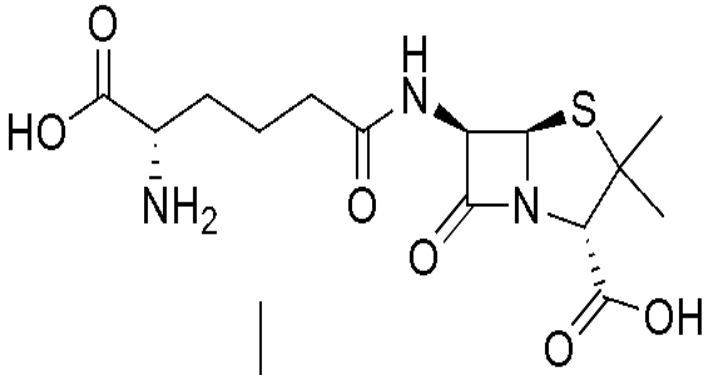


D-Valine

ACV-Tripeptide

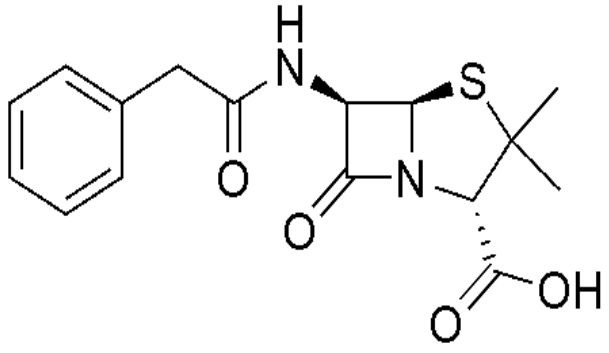


Isopenicillin N



Cephalosporines

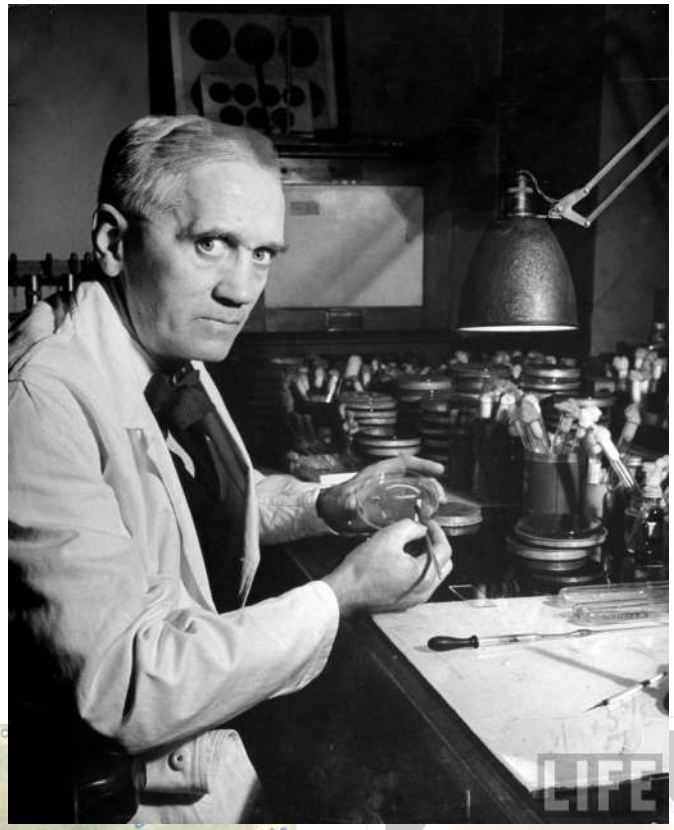
Penicillin G



Stages of development:

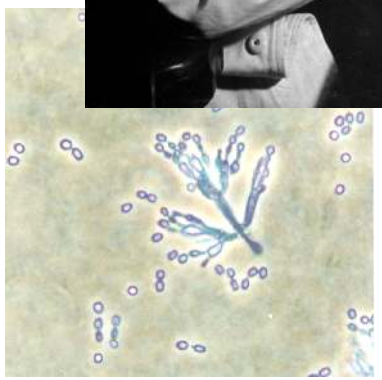
Lead compound discovery

The discovery of penicillin is attributed to Scottish scientist Alexander Fleming in 1928.



♛On September 28 1928, Fleming noticed a petri dish containing Staphylococcus plate culture he had mistakenly left open, which was contaminated by blue-green mould.

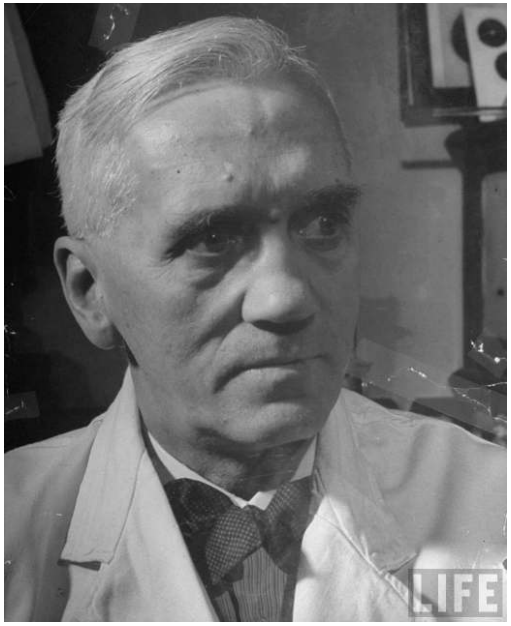
♛There was a halo of inhibited bacterial growth around it.



Fleming concluded that

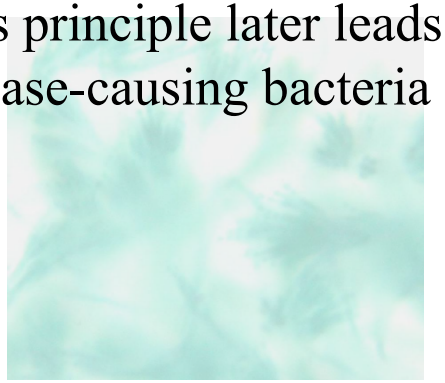
- the mould was releasing a substance that was

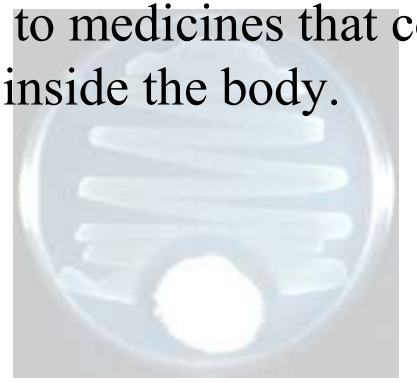
  - repressing the growth and
  - lysing the bacteria.

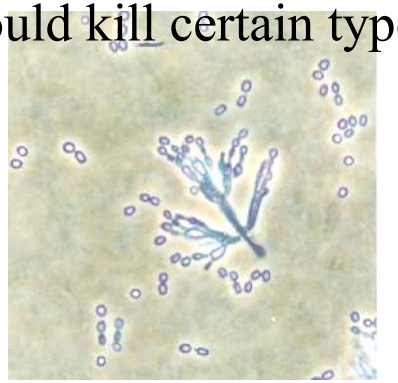


He grew a pure culture and discovered that it was a Penicillium mould, now known to be Penicillium notatum.

This principle later leads to medicines that could kill certain types of disease-causing bacteria inside the body.

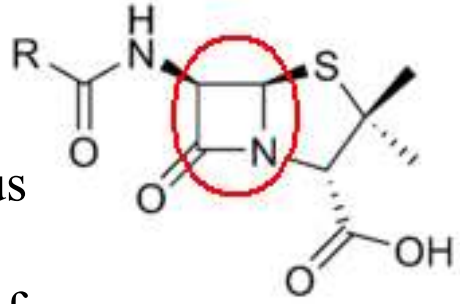






Molecular modification

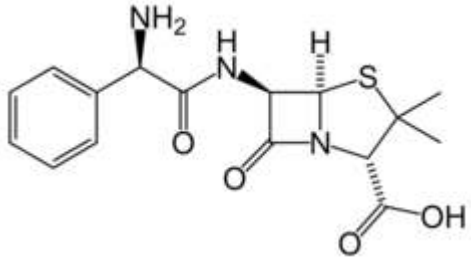
Penicillins are characterized by a structural feature known as a Beta-Letam ring



This four-membered ring makes the molecule thermodynamically unstable, thus accounting for the trouble that scientists had when working on it in the beginning of this century.

This ring is also easily hydrolyzed in the presence of acid;

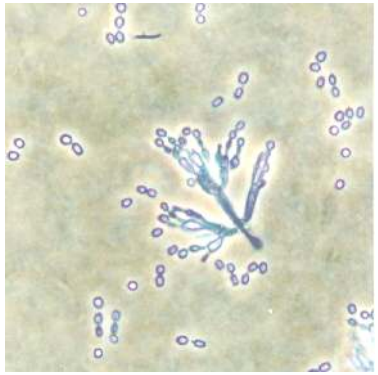
therefore Penicillin derived from natural sources needs to be modified during manufacturing for oral administration, so that it will not be destroyed in the stomach.



(Ampicillin)

-Formulation development

There are various routes of administration of penicillin. Each route requires different types of formulation. Each of them has different advantages and disadvantages.



Benzylpenicillin, commonly known as **penicillin G**, is the gold standard penicillin.

♖ Penicillin G is typically given by a parenteral route of administration (not orally)

♗ because it is unstable in the hydrochloric acid of the stomach.

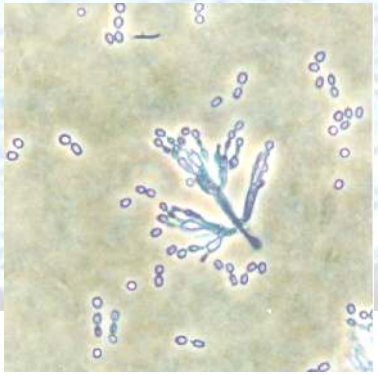
♝ Since the drug is given parenterally, higher tissue concentrations of penicillin G can be achieved than is possible with phenoxymethylpenicillin.

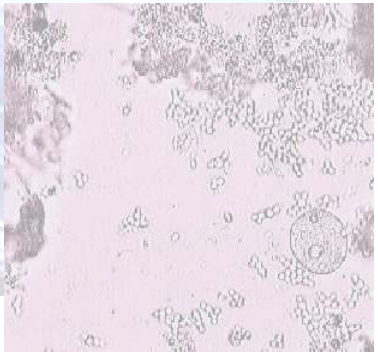
♝ These higher concentrations translate to increased antibacterial activity.

Phenoxymethylpenicillin, commonly known as **penicillin V**, is the *orally active* form of penicillin.

- It is less active than benzylpenicillin,

- and is appropriate only in conditions where high tissue concentrations are not required.





Procaine benzylpenicillin (rINN), also known as **procaine penicillin**, is a form of penicillin which is a

combination of benzylpenicillin and the local anaesthetic agent procaine.

Following deep intramuscular injection, it is slowly absorbed into the circulation and hydrolysed to benzylpenicillin —

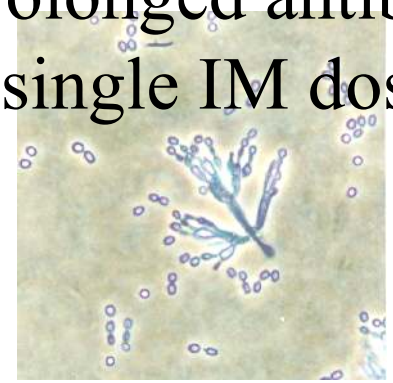
- thus it is used where prolonged low concentrations of benzylpenicillin are required.

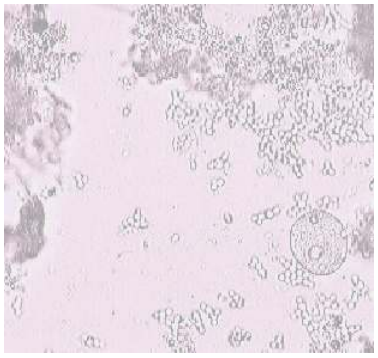
- This combination is aimed at reducing the pain and discomfort associated with a large intramuscular injection of penicillin.

- It is widely used in veterinary settings.

Benzathine benzylpenicillin (rINN) is a form of penicillin also known as **benzathine penicillin**.

- It is slowly absorbed into the circulation, after intramuscular injection, and hydrolysed to benzylpenicillin *in vivo*.
- It is the drug-of-choice when prolonged low concentrations of benzylpenicillin are required and appropriate,
- allowing prolonged antibiotic action over 2–4 weeks after a single IM dose.

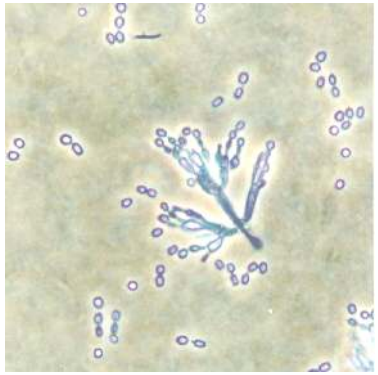




-Safety test and human trials

- Penicillin can cause allergy independent of the used dose.
- Therefore, patients should receive a test before use.

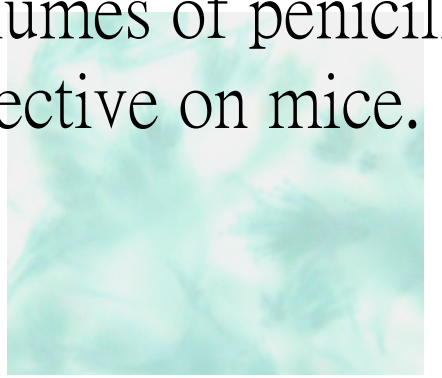
In 1930 Cecil George Paine, a pathologist at the Royal Infirmary in Sheffield, attempted to use penicillin to treat sycosis barbae but was unsuccessful, probably because the drug did not penetrate the skin deeply enough.

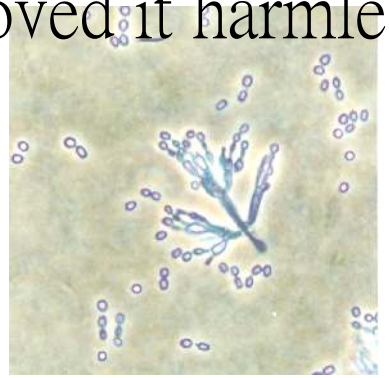


Moving on to ophthalmia neonatorum, he achieved the first recorded cure with penicillin, on November 25, 1930. He then cured four additional patients of eye infections, failing to cure a fifth.

In 1939, Australian scientist Howard Florey and a team of researchers made significant progress in showing the bactericidal action of penicillin.

Their attempts to treat humans failed due to insufficient volumes of penicillin, but they proved it harmless and effective on mice.






Approval for marketing

When the drug has passed all the phases of the clinical research, the pharmaceutical company of penicillin needs to make a formal appliction to the regulatory authority for approving the use of the drug in the market.

The application must include results and analyses from the tests of the drug on both animals and humans, as well as a description of how the drug was manufactured.

The appliction must provide sufficient information for the regulatory authority to make several critical decisions, including

- whether the drug is safe and effective and
- whether its benefits outwigh its risks,
- whether the drug’ s labelling information is appropriate,
- and whether the manufacturing methods used to make the drug are adequate for ensuring purity and integrity of the drug.

1945

Penicillin Amendment requires FDA (Food and Drug Administration) testing and certification of safety and effectiveness of all penicillin products. Later amendments extended this requirement to all antibiotics.

January 26, 1971

The NADA 46-668 **Procaine G Penicillin** was originally approved as safe

Reference:

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