

SUSCEPTIBILITY OF MYCOBACTERIUM TUBECULOSIS TO ISONIAZID & ITS DERIVATIVE

1-isonicotinyl-2-nonanoyl hydrazine

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STUDY APPROACH

- The susceptibility of *M. tuberculosis* to INH was compared to its derivatives, INH9 prepared synthetically.
- The MIC of the drugs was determined using the 1% proportion method.
- Further studies include:
 - •Exposing the cells to INH and INH9 at the MIC level and the effects studied at cellular level.
 - Cellular morphologies and staining characteristics were viewed using a microscope equipped with a Pixera digital camera.
 - Analysis of images were made using Pixera
 Visual Communication Suite Programme.

EXPERIMENTAL:

A) PREPARATION OF 1-ISONICOTINYL-2-NONANOYLHYDRAZINE

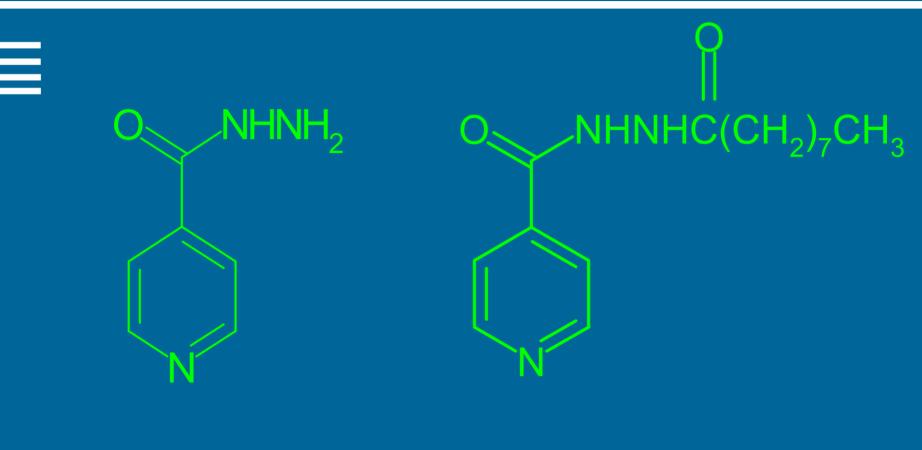
$$C_8H_{17}CO_2H$$
 (1eq) + ClCOCl (10 eq) C₈H₁₇COCl Nonanoic acid oxalyl chloride nonanoyl chloride

 $C_8H_{17}COCI + C_5H_4NCONHNH_2$ (1.1eq) + $C_5H_4NN(CH_3)_2$ (1.2eq) isoniazid 4-dimethylaminopyridine

Stirred 16 hrs Room temperature

1-isonicotinyl-2-nonanoylhydrazine

CHEMICAL STRUCTURES OF INH AND INH9



(a) Isoniazid (INH)

(b) 1-isonicotinyl-2-nonanoyl hydrazine (INH9)

B) DETERMINATION OF MIC

The MIC of the drugs were determined using the 1% proportion method.

Range of concentrations tested: $0.005\mu g/ml - 0.1\mu g/ml$.

MIC was determined as the lowest concentration of the drugs which caused a 10⁻² reduction in viable counts compared to the respective controls.

Results: MIC of INH: 0.05 μg/ml

MIC of INH9: $0.025 \mu g/ml$

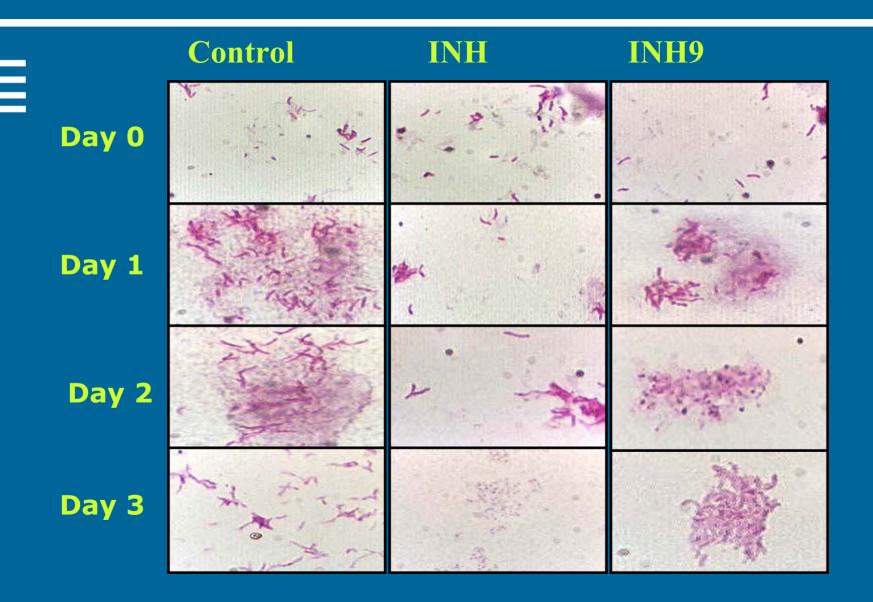
C) EXPOSURE TO INH AND INH9

The drugs were added into the bacterial culture at 3 different stages of the growth cycle:

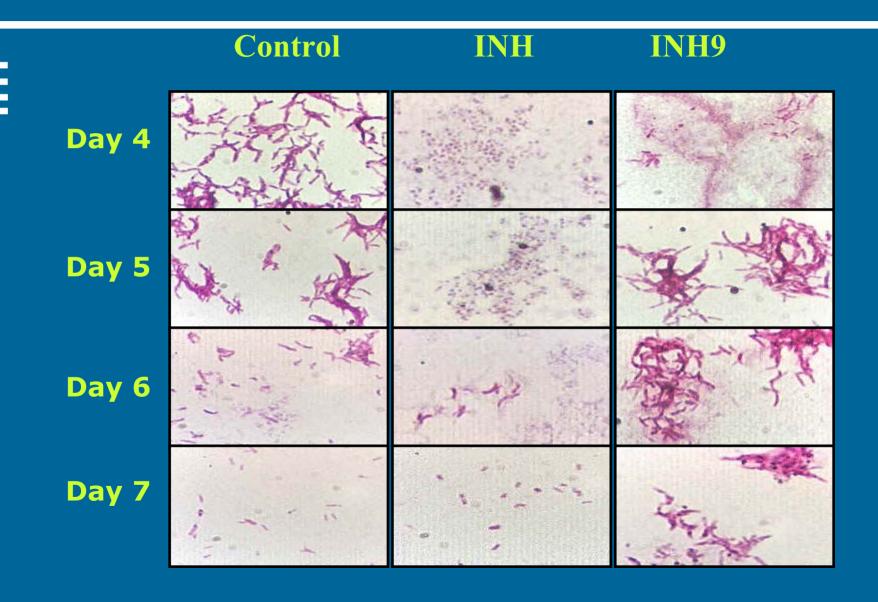
- i. Initial stage,
- ii. After 24 hours, and
- iii. After 72 hours of incubation

Cell samples were harvested daily (for 7 days) for studies on their cellular morphologies and staining properties.

The effects of INH and INH9 on the cellular morphologies of *M* tb H37 Rv; additions at the initial stage of the growth cycle.



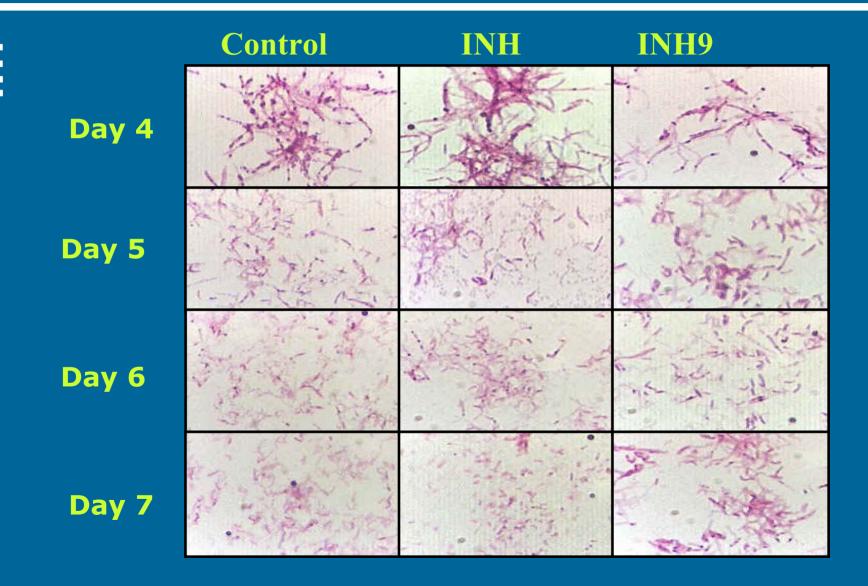
The effects of INH and INH9 on the cellular morphologies of *M* tb H37 Rv; additions at the initial stage of the growth cycle.



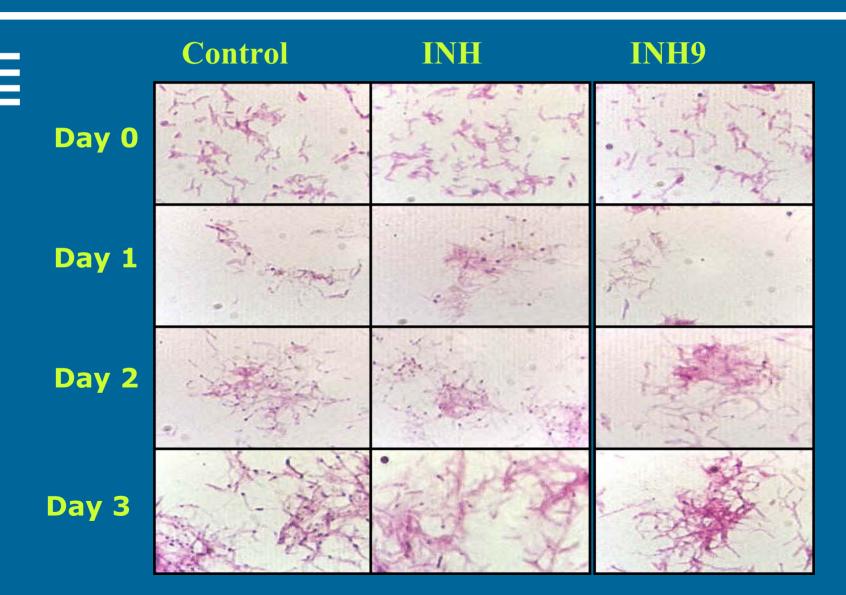
The effects of INH and INH9 on the cellular morphologies of *M. tb* H37 Rv; additions after 24 hrs of incubation in the growth cycle.

Control INH INH9 Day 0 Day 1 Day 2 Day 3

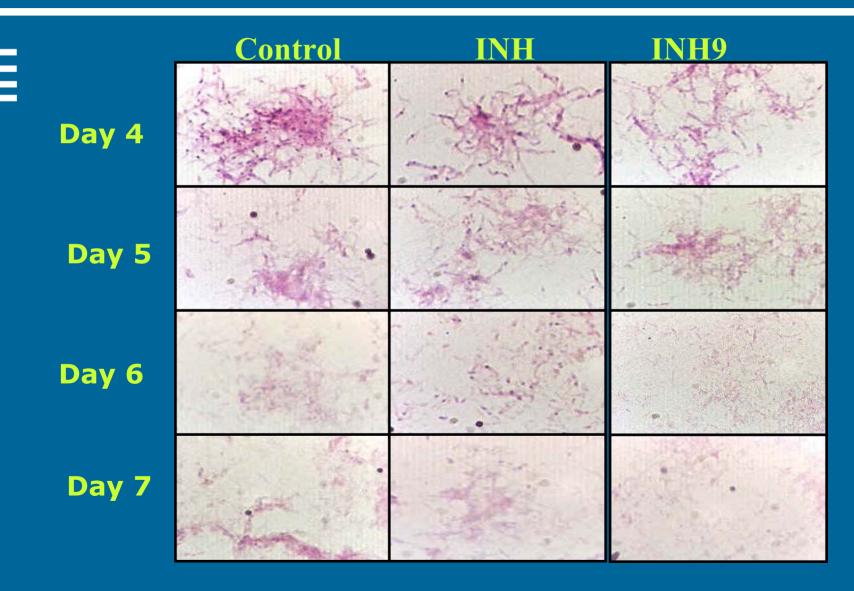
The effects of INH and INH9 on the cellular morphologies of *M. tb* H37 Rv; additions after 24 hrs of incubation in the growth cycle.



The effects of INH and INH9 on the cellular morphologies of *M. tb* H37 Rv; additions after 72 hrs of incubation in the growth cycle.



The effects of INH and INH9 on the cellular morphologies of *M. tb* H37 Rv; additions after 72 hrs of incubation in the growth cycle.



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