CHARACTERIZATION OF STREPTOMYCIN RESISTANT MUTANT OF *Corynebacterium acetoacidophilum* ATCC21476

by
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Thesis Submitted
in fulfilment of the requirements of the degree of
DOCTOR OF PHILOSOPHY
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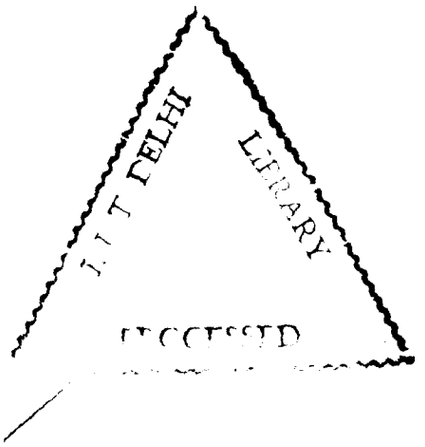

CERTIFICATE

This is to certify that the thesis entitled **"Characterization of streptomycin resistant mutant of *Corynebacterium acetoacidophilum* ATCC21476"** *being submitted by* **Goutam Karan** *to the Indian Institute of Technology, Delhi, for the award of Degree of* **Doctor of Philosophy,** *is a bonafide research work carried out by him under my supervision and guidance. The results obtained in this thesis have not been submitted to any other University or Institute for the award of any other degree or diploma.*

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Dedicated to
my
Parents

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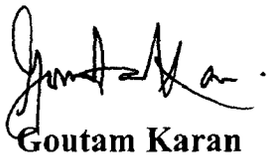

Goutam Karan

ABSTRACT

Antibiotics have hitherto been the magic bullets for the cure of innumerable life threatening diseases and the trend continued quite unhindered until the appearance of multiple drug resistant pathogens. The situation is quite alarming thus necessitating discovery of newer drugs to contain this menace. Although extensive study is being conducted on the isolation and characterization of organisms showing resistance to diverse antibiotics, these are mostly isolated from patients. One of the major reasons for such resistance is believed to be indiscriminate use of antibiotics in the treatment of diseases. Concern for human health has also led to the understanding of such resistance among pathogenic organisms e.g by conjugation, transduction, transposition by elements such as integrons. However, the problem is not limited to pathogens only, though they attract maximum attention. Extensive use of antibiotics in agriculture and animal husbandry has widened the limit of dissemination of resistance which includes many nonpathogenic organisms.

The present study is, therefore, aimed at understanding of mechanisms of streptomycin resistance exhibited by a spontaneous mutant of *Corynebacterium acetoacidophilum*, a nonpathogenic soil bacterium. This

mutant shows high level of resistance to streptomycin (MIC 10mg/ml) and is distinct from other spontaneous mutant of the same organism. The biochemical and molecular biological studies with the mutant have identified the gene and revealed that the resistance is due to the enzymatic modification of the antibiotic. Sequence comparison of the resistance and sensitive genes has also been done to understand the difference between the two at the molecular level. The absence of a 'T' towards the 5' end of the gene of the sensitive strain vis-a-vis the resistance gene introduced quite a few stop codons in the former thus rendering it nonfunctional. The resistance gene showed high degree of sequence similarity with streptomycin resistant genes of plasmids of several pathogenic organisms besides the plasmid pCG4 of a related corynebacteria, *Corynebacterium glutamicum*.

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