INTERACTION BETWEEN NUCLEIC ACIDS AND SOME ANTIBIOTICS

THESIS

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By
IBRAHIM HASSAN KAMAL
Demonstrator of Biochemistry

Supervised By

Prof. Dr. I. R. SHIMI
Professor of Biochemistry

Prof. Dr. NADIA M. ABDALLA
Professor of Biochemistry

Dr. FAHMY T. ALI
Assistant Prof. of Biochemistry

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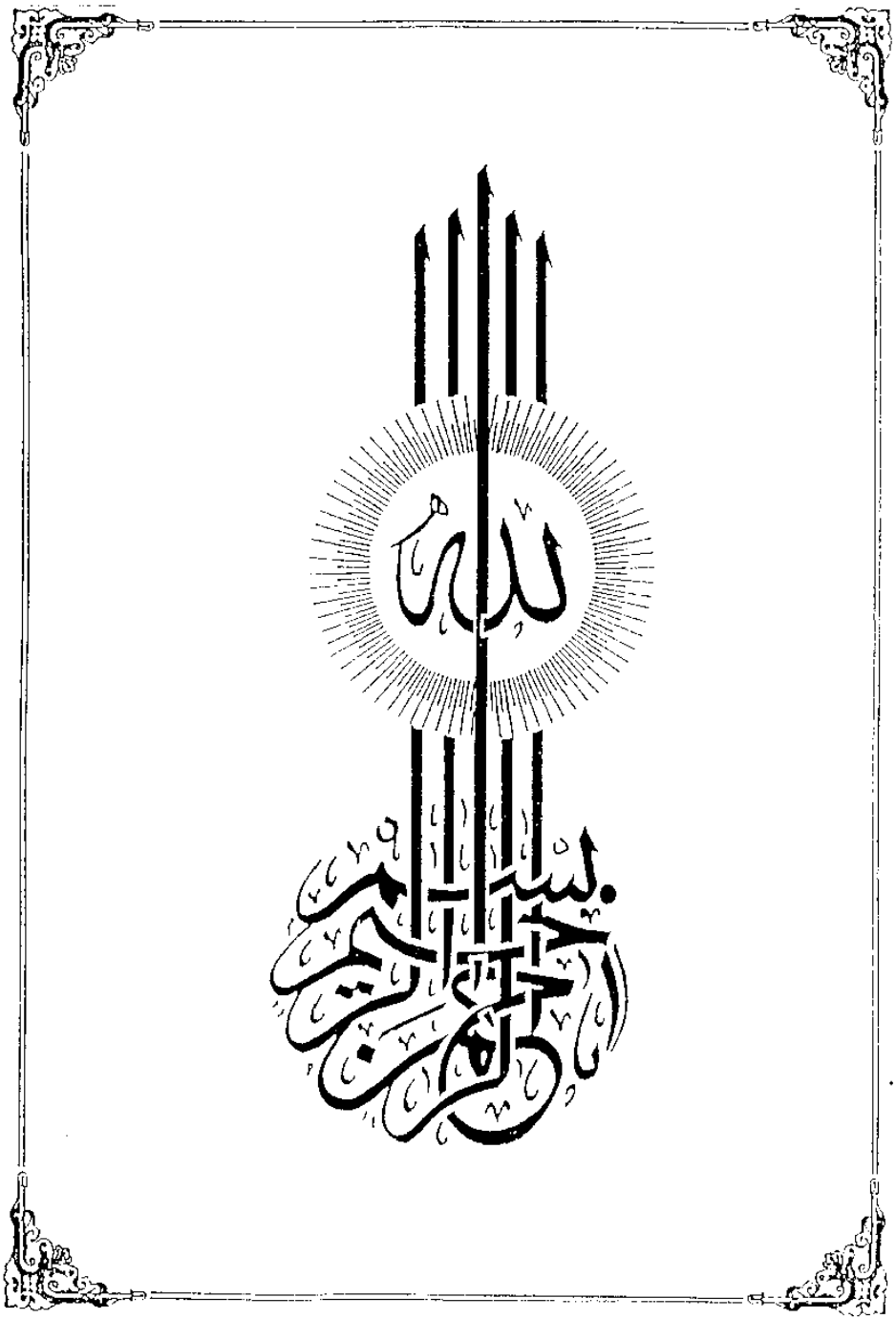

DEDICATION

TO MY BELOVED MOTHER

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PREFACE

More than 100 years have elapsed since the first scientific demonstration of microbial antagonism and four decades since the first clinical use of penicillin. At present, several thousand antibiotics are known and many of them are in practical use. Microbiologists are tempted to consider them to be chemical weapons of microorganisms in their struggle for survival. Biochemists include antibiotics among secondary metabolites with almost unknown purpose for the producing microorganisms. However, together with molecular biologists and geneticists, they find some antibiotics to be useful tools in studying various aspects of cell structure and functions.

The present study is mainly devoted to examine some effects of the selected antibiotics on DNA.

In the present thesis, thermal denaturation of DNA is carried out with the selected antibiotics to explore their possible action on DNA. Some antibiotics decreased the thermal denaturation and some increased it. The absorption spectrum of DNA was also examined.

From the various antibiotics tested on the salmon testis DNA, the neomycin was chosen for its significant effect on the thermal denaturation and the absorption spectrum of salmon testis DNA.

The antibiotic neomycin significantly affects DNA by forming an antibiotic-DNA complex under certain conditions of concentration, incubation and temperature.

ABBREVIATIONS

ATP = Adenosine Triphosphate

CTP = Cytidine Triphosphate

DNA = Deoxyribonucleic Acid

GTP = Guanosine Triphosphate

mM = Millimolar

MIC = Minimum Inhibitory Concentration

ml = Milliliter

N = Normal

nm = nanometer

O. D. = Optical Density

RCF = Relative Centrifugal Force

RNA = Ribonuclei Acid

r.p.m. = Revolution per minute

Temp. = Temperature

T_m = Transition temperature, Melting Temperature

TTP = Thymidine Triphosphate

ug = Microgram

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INTRODUCTION

INTRODUCTION

Antibiotics are among the most widely prescribed drugs in both human and veterinary medicine. Furthermore, they are used to protect plants against bacterial and fungal diseases, to decontaminate the shells of eggs, and to improve weight gain and feed conversion in a variety of animals. More antibiotics, in addition, have been essential tools in the elucidation of specific cellular functions. Nowadays, antibiotics have a considerable role in genetic engineering.

Antibiotics are low molecular weight microbial metabolites that, at low concentration, inhibit the growth or even destroy other microorganisms. The term low molecular weight substances refers to molecules of at most a few thousand daltons.

The term antibiosis was coined by Paul Vuillemin in 1889 and was used by him in a broad sense, referring to all instances where one species destroys the life of another to preserve or maintain its own.

The term antibiotic was introduced by Waksman et al., in 1942 to designate a chemical substance of

microbial origin which has the property to inhibit the gorwth of microorganisms (bacterio-static). Waksman in 1947 added that antibiotics might also destroy bacteria and other microorganisms i.e., bactericidal. Most antibiotics are primarily bacteriostatic in their action, that they do not appear to inhibit the metabolic processes of treated microorganisms except where subdivision and growth are concerned. Some antibiotics are bactericidal i.e., irreversibly destroy the metabolic processes of the susceptible cell.

Umezawa in 1956 introduced the following definition "Antibiotics are chemical substances which are produced by microorganisms and have the capacity in dilute solutions to inhibit the growth of other miroorganisms and in some situations to destroy them".

A broader definition was presented by Bendict and Langlyte, according to which antibiotic is a substance derived from or produced by a living organism capable of inhibiting the life processes of microorganisms in small concentration (Glasby, 1976).

Most antibiotics are products of the secondary metabolism of three main groups of microorganisms:

eubacteria, actinomycetes and lower fungi. Only a few antibiotics are produced by higher fungi, algae and plants and they generally show low activity and low specificity. The actinomycetes, especially genus Streptomyces produce the largest number and the great variety of the tumour antibiotics. More than 3000 different antibiotic substances have been isolated from this important group of microorganisms. The lower fungi produce approximately 700 antimicrobial substances. The eubacteria, mainly spore-forming bacilli (Bacillus) and members of the genus Pseudomonas, produce now up to about 400 antibiotic substances (Lancini and Parenti, 1982).

Antibiotics are characterized by selective antibacterial spectrum: some of them affect primarily Gram-positive bacteria; others are active on Gram-negative forms; and still others only on certain fungi and yeasts. A few antibiotics inhibit both Gram-positive and Gram-negative bacteria and if they also affect such intracellular organisms as those of psittacosis, lymphogranuloma, and the rikettsiae, these antibiotics are termed "broad spectrum" antibiotics (Ender , 1940; Huebner et al., 1946; and Roth & Schulick, 1951).