MIC OF SOME NEWLY DEVELOPED ANTIMICROBIALS AGAINST COMMON URINARY AND BLOOD PATHOGENS

THESIS

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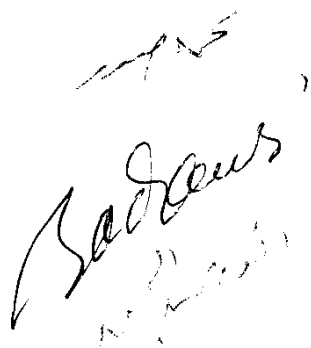

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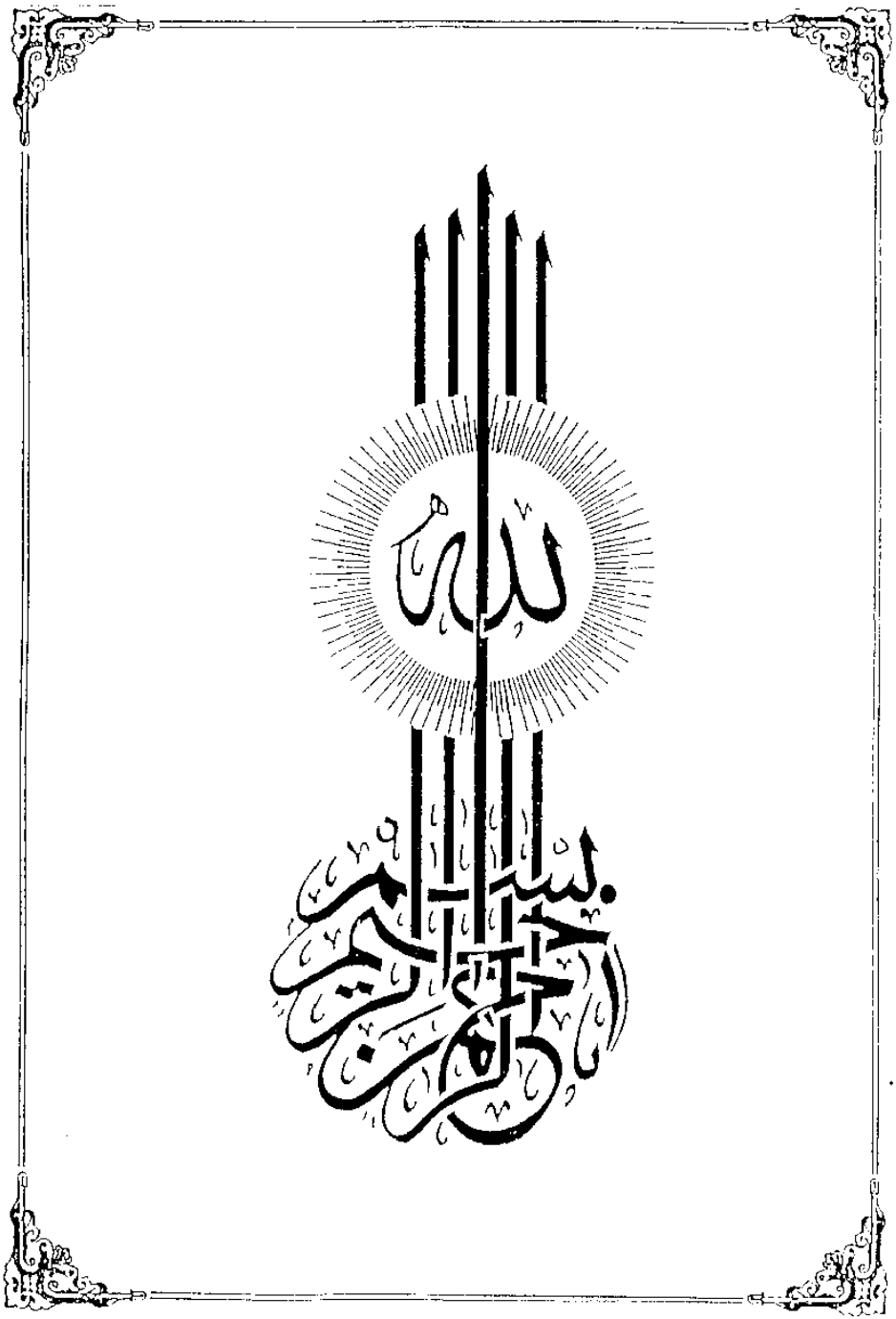

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PROTOCOL OF THE THESIS

Protocol Of Thesis

Background:-

The continuous emergence of resistant bacterial strains to the present antibiotics and the continuous change in the pattern of pathogens necessitate search for new antimicrobials and continuous evaluation of the sensitivity pattern to the continuously developing chemotherapeutic agents.

Aim Of The Work:-

To study the minimal inhibitory concentration of some newly developed antimicrobials against common pathogens encountered in infections nowadays.

Material And Method:-

Patients selected for the study are those with:

a- Serious urinary tract infection that requires hospitalization.

b- Microbial blood invasion.

Who are admitted to a department of medicine during 12 months.

They will be studied by following methods:-

1- Isolation, identification of pathogenic organisms from urine or blood sample.

2- Estimation of MIC_{50} of the isolated organism to some newly developed antimicrobial agents.

FOREWORD

Foreword

The battle against infection continues unabated. Despite tremendous advances in the development and production of antimicrobial agents, doctors the world over are discovering that microscopic organisms are not only persistent in their varied attacks on man, but are also using novel means of fighting back against attempts to eliminate them. No clinician can afford to ignore the problem of bacterial resistance to antibiotics, for it threatens every established therapeutic and prophylactic regimen at his disposal. And well recognized pathogens are being joined in the arena by some apparently new elements, whose arrival is frequently a source of great confusion and distress (Meredith, 1984).

Antibiotics have been in clinical use for only 46 years, yet despite the large number now available, bacterial resistance has emerged to most of them. When the sulfonamides, synthetic antibacterials, were introduced in the 1930s, they were widely and successfully used to treat gonorrhoea and certain streptococcal infections. But it was not long before the sulfonamides became largely ineffective against those infections. In gonorrhoea, which is transmitted exclusively by person to person contact, resistance emerged and was spread rapidly by patients and their contacts. The widespread use of sulfonamides to prevent streptococcal infections and rheumatic fever soon caused resistant strains of streptococci to emerge, which proved fatal in many cases.

In both of these instances the subsequent availability of penicillin was effective. But in gonorrhoea the original marked susceptibility of the causative organism gradually declined; strains with greater resistance appeared, needing larger doses of penicillin for a cure, and the degree of failure grew. In the last few years strains of gonococci completely resistant to penicillin have emerged.

Streptococci, on the other hand, have presented a different picture. In the early 1970s apart of certain strains being less sensitive to penicillin, this group of organisms has remained highly susceptible to the antibiotic. But in 1978 outbreaks of penicillin resistant Streptococcus pneumoniae occured in two large hospitals in Johannesburg. Fortunately such strains have not become widespread (Clayton, 1980).

Penicillin was the first highly effective antibiotic against staphylococcal infections. But by 1948 as many as 50 per cent of strains in hospitals were found to be resistant, a very serious problem at the time. It was an example of resistance developing through therapeutic selection. The staphylococcal population had always contained a few penicillin - resistant cells but at first they were not enough to pose a treatment problem. But getting rid of the sensitive staphylococci by the widespread use of the antibiotic created an environment in which the resistant cells were able to multiply and become dominant (Clayton, 1980).

Methicillin-resistant strains of Staphylococcus aureus have spread extensively in many countries and some strains are only sensitive to vancomycin (Kean, 1984). Gram-negative bacilli for example Serratia marcescens, are often resistant to several antibiotics including gentamicin and related aminoglycosides.

Resistance is commonly associated with the widespread use of an antibiotic particularly if used topically. Multiple resistance not only increases the problem of treating patients, but also the cost of the therapy. The possible reasons for the emergence of multiple antibiotic resistance throughout the world include the following:

1- Free availability of antibiotics in some countries, including our country, without the necessity of a prescription from a medical or a veterinary practitioner.

2- Poor prescribing practice, consisting of over or inappropriate use and unnecessarily prolonged therapy.

3- Wide spread use of antibiotics in animal feeds.

4- Cross-infection with antibiotic-resistant bacteria in hospitals and in animal husbandry. Resistance tends to develop slowly in individual patients on treatment, but once it has emerged the resistant strain can then spread to many other patients in the same environment.

5- Plasmid consists of extrachromosomal DNA capable of controling resistance to four or five or more antimicrobial agents. The plasmid, or part of a plasmid, can spread, usually by conjugation, to other organisms of the same or other species and sometimes to organisms of different genus.

This means that resistance in organisms of the normal flora, like Escherichia coli, can spread to enteric pathogens such as Salmonella typhi. Resistance to ampicillin and chloramphenicol has already emerged in Salmonella typhi in countries where these antibiotics are readily available to the general population. Some plasmids are particularly transmissible and one in particular is responsible for penicillinase production in E. coli, Haemophilus influenzae and Neisseria gonorrhoea (Ayliffe, 1985).

One plasmid can control resistance to several agents. For example carbenicillin-resistant Pseudomonas aeruginosa was eleminated from a burn unit in Birmingham by avoiding the use of carbenicillin, ampicillin, tetracyline and kanamycin (Lowbury et al., 1972). Stopping the use of only one, for example carbenicillin, would have failed as the other three agents, due to selection would have maintained the plasmid in strains of bacteria in the unit.

Obviously, the problem of bacterial resistance means there must be continuous vigilance to ensure that any change in the resistance pattern is recognized and the appropriate antibiotic is selected for the treatment.

So it is likely that the main impetus to the discovery of new antibiotics is the continuous emergence of resistant microoganisms and their prevalence allover the world.

When antibiotics are used to treat an infection, a favorable therapeutic outcome is influenced by numerous factors. However, in simple terms, success is dependent on achieving concentrations of the antimicrobial agents at the site of infection sufficient to kill or to inhibit the micro organisms. That is to say, the choice of a proper antimicrobial agent depends on a balance between two factors.

First, the concentration of the drug at the site of infection.
Second, the lowest concentration of the drug that is sufficient to inhibit or to kill the microorganism. That is the MIC, the subject of the present study.

OVERVIEW ON THE DIFFERENT GROUPS OF ANTIBIOTICS

Overview On The Different Groups Of Antibiotics

Most of the antibacterial antibiotics belong to one of these seven structural classes: The first member of each class was discovered and isolated in the year opposite to the name of the class.

1. B- Lactams	1940
2. Aminoglycosides	1944
3. Chloramphenicol	1947
4. Tetracycline	1948
5. Macrolide	1950
6. Lincomycin	1955
7. Ansamacrolide	1957

(Clayton, 1980)

B-Lactam Antibiotics

This group of antibiotics shares a general mechanism of antibacterial action and is characterized by the presence of 4-membered B-lactam ring which is responsible for their action.

They include the following:-

1) Penicillins	2) Cephalosporins	3) Oxapenams
4) Penems	5) Carbapenems	6) Monocylic B-lactams (Monobactams)