INTRODUCTION

A strong affinity of tetracycline and oxy- and chlortetracycline for metallic ions was reported by Albert (3, 8) who observed the formation of drug-metal complexes of 1:1 and, as the pH is raised, of 2:1. The cations tested (in the order of decreasing stability of the drug-metal complexes) were: Fe++, Al+++ , Cu2+ , Ni++, Fe++, Co2+, Zn2+, and Mn2+. The iron complexes of the tetracyclines are red, the Cu2+, and Ni2+ complexes are green, and the Al3+, Co2+, Zn2+, and Mn2+ complexes are yellow. In contrast, Oxford (77) was not able to obtain colored complexes of chlortetracycline with Zn2+ or Mn2+ but did observe stable yellow complexes with Cu2+, Ni2+, Co2+, Mg2+, Ca2+ and Sr4+. The tetracycline structure contains numerous sites at which chelation with metallic ions might occur. Perhaps the most important sites lie along the system marked by atoms 1 through 7 which consists

Metalloantibiotics-I

KISHU TRIPATHI¹ and SHOBHA KULSHRESHTHA²

¹Professor, Surya College of Pharmacy, Lucknow (India)
²Head, Department of Pharmacology, SN Medical College, Agra (India)

(Received: February 12, 2008; Accepted: April 04, 2008)

ABSTRACT

Metal ions after forming complexes with an antibiotic alters the antimicrobial activity of an antibiotic alone.

Key words: Metal ions, antibiotics.
essentially of two 1,3 diketones with two of the keto
groups in the enol form. Such monoenoils in 1,3
diketones chelate with metallic ions very readily to
form six-membered. In each ring, the two atoms
that bind the metallic ion are oxygen atoms (23):

The tetracycline compounds have been
described as uncouplers (21) and inhibitors (107) of
oxidative phosphorylation and inhibitors of
respiration (91, 99, 106), fatty acid oxidation,
arginine catabolism (55), nitro reduction (92, 93,
94), and adaptive enzyme formation (15).

Effect on Enzyme Systems

Scheme 2

The possibility that metallic ions might enhance the
activity of the drugs was during the series of growth
tests described above. Moderate enhancement was
observed with low concentrations of Mn2+ or with
high concentrations of Fe+ with P. aeruginosa
(112,113). Previously, chlortetracycline had been
found to be enhanced by similarly low
concentrations of Mn+1 in its antibiotic effect against
C. cucullus (65). The resistant strains tested to date
include a strain of M. pyogenes whose average
minimum inhibitory concentration of tetracycline and
oxy- and chlortetracycline is 120 pg per ml and a
strain of Penicillium notatum which requires 750 pg
per ml of the drugs for suppression of growth. Fe2+
and Mg2+ are active with the bacterium and Fe+H
with the fungus.

8-hydroxyquinoline

Molecular Structure and Affinity for Metallic
Cations of seven isomeric mono-hydroxyquinolines,
only 8-hydroxyquinoline (oxine) can chelate metallic
ions (9, 90): observed that the Cu2+, Ni2+, Cd++,
and Ag+ compounds of 8-hydroxyquinoline are as fungistatic as oxine itself; and Manten et al. (67) reported that neither Zn+, Cu++, Mn2+ nor Mo2+ suppresses the toxicity of oxine toward Aspergillus. Other investigators reported that Cations Cu2+ and Fe2+ enhance antifungal activity (10) and that conalbumen suppresses the antibacterial action of 8-hydroxyquinoline (36). Gram positive bacteria are more susceptible to oxine than are gram negative species and trace amounts of Co2+ excess amounts of Fe++ suppress the activity of 8-hydroxyquinoline against the former organisms whereas Fe2+, Zn2+ or Cu2+ suppress the toxicity of oxine towards the latter bacteria. Furthermore, with Micrococcus pyogenes, an increase in the concentration of 8-hydroxyquinoline results in a paradoxical decrease in toxicity. Subsequent studies revealed that small concentrations of Fe2+ Cu2+, or Cd2+ are required for toxicity towards gram positive species and that a 2:1 oxine-Fe- molar ratio is maximally toxic.

REFERENCES


