INTRODUCTION

The antitubercular activity of such drugs as INH, PAS, and thiosemicarbazone is affected by the ability of the compounds to form complexes with Cu$^{2+}$. The Cu$^{2+}$ complex of PAS was later found to be as active as PAS, but the effectiveness of both substances is enhanced by excess Cu$^{2+}$ (89). The Cu$^{2+}$ as well as the Fe$^{2+}$, Co$^{2+}$, Mn$^{2+}$, and Cr$^{2+}$ complexes of PAS are less tuberculostatic than the pure compound. Other investigators reported that Co$^{2+}$ enhances (103), and that the majority of metallic ions tested suppress (17), the antitubercular activity of PAS. The toxicity of Cu$^{2+}$ or Hg$^{2+}$ for frog heart tissue is suppressed by PAS (28) but the Fe$^{2+}$ complex is more toxic towards mice than is PAS itself (39). INH and PAS, thiosemicarbazone suppresses the toxicity of Cu$^{2+}$ and Hg$^{2+}$ towards isolated frog heart tissue (28).

Metalloantibiotics-III

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Abstract

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

Key words: Metal ions, antibiotics

Aspergillic acid

The antimicrobial activity of aspergillic acid is suppressed by Fe$^{2+}$ and enhanced by Bi$^{3+}$. The potency of the compound is also enhanced by Co$^{2+}$, Ni$^{2+}$, Zn$^{2+}$, and As$^{3+}$, but to a lesser extent than by Bi$^{3+}$ (46, 47). Goth (45) has postulated that aspergillic acid is antitubercular because of its ability to chelate Fe$^{2+}$ which he observed to be essential for growth of mycobacteria.

Usnic acid

Johnson et al. (57) have suggested that usnic acid may owe its antitubercular action to inhibition of phosphorylation reactions, because antimicrobial concentrations of the compound suppress oxidative phosphorylation of rat liver and kidney homogenates.
Miscellaneous antimicrobial compounds

Compounds whose Antimicrobial Activity is Influenced by Metallic Cations. The inhibitory effect of penicillin and bacitracin on the growth of Micrococcus pyogeneis enhanced by Co2+, (104); and the inhibition by 2,3-dimercaptopropanol nitroso-2-naphthol to inhibit growth of gram positive bacteria is suppressed by Fe2+ and slightly enhanced by Cu2+ and Co2+; Ni2+, Zn2+, and Mn2+ are inactive.

Kojic acid

Inhibits P. fluorescens (but not B. subtilis) more strongly in the presence of certain concentrations of Al+++, Cu++, or Fe2+; similarly, Stove (100) noted that metal derivatives of kojic acid are better fungicides than is the nonchelated substance.

The ability of actidione to inhibit growth of Saccharomyces cerevisiae is suppressed by oxalate; and the growth inhibitory action of juglone towards B. subtilis is strongly enhanced by Hg2+ and Co2+, moderately enhanced by Al++, Ni++, Cu2+, Zn2+, and Mn2+, and suppressed by citrate, tartrate, and oxalate.

(British anti-Lewisite) of the binding of penicillin by whole cells is counteracted by Co2+ and Mn2+ (30). Bacitracin has been observed to be precipitated by salts of heavy metals and to be partially inactivated by British anti-Lewisite (11). Mg2+, Mn+++, Ca++, and Fe,+++ suppress the ability of polymyxin to inhibit Pseudomonas aeruginosa; a Mg2+:drug ratio of 400:1 is required for maximum activity of Mg2+ (73). The ability of novobiocin to inhibit gram negative bacteria is suppressed by Mg2+& and, to a lesser extent by Ca2+, Sr4+, and Ba3+ (19, 117). Co2+ slightly enhances the ability of chloramphenicol to inhibit growth of B. subtilis. An analogue of chloramphenicol, 3,4-dichlorophenylserine, is inert against strains of Enterobacteriaceae but prevents sporulation of Aspergillus niger by the irreversible binding of essential Cu2+ (108). The ability of 1-

A-Picolinic acid

When tested with B. subtilis, is suppressed strongly by Co2+ or Ni2+ and moderately by Cu2+.
or Zn\(^{2+}\). With \(P.\) fluorescens, the ions are inactive except for Cu\(^{2+}\), which possesses slight reversing ability. However, the toxicity of high concentrations of Co\(^{2+}\) towards cells of each species is suppressed by \(\alpha\)-picolinic acid (118). Previous studies demonstrated that Co\(^{2+}\), but not Cu\(^{2+}\), suppresses the antitubercular activity of \(\alpha\)-picolinic acid hydrazide (34) and that Cu\(^{2+}\), Fe\(^{2+}\), Mn\(^{2+}\), and Mg\(^{2+}\) suppress the inhibition of metallo-enzymes of rice plants by \(\alpha\)-picolinic and fusaricnic (5-butylpicolinic) acids (102).

The ability of cycloserine (oxamycin) to inhibit growth of \(B.\) subtilis is suppressed by citrate, tartrate, oxalate, phosphate, or EDTA, whereas the antagonism of the substance towards growth of \(P.\) fluorescens is suppressed only by Cu\(^{2+}\) (118).

Antagonism of morin towards \(B.\) subtilis is, like that of cycloserine, suppressed by citrate, tartrate, or oxalate; the inhibition by morin of \(P.\) fluorescens is suppressed strongly by Co\(^{2+}\), and to a lesser extent by Fe\(^{3+}\), oxalate, or phosphate (118).

The activity of patulin is suppressed by Mn\(^{2+}\), Ca\(^{2+}\), and Ba\(^{3+}\), and slightly enhanced by Sb\(^{+}\), Co\(^{2+}\), Cd\(^{2+}\), Ni\(^{2+}\), and Zn\(^{2+}\).

REFERENCES