

Chalmers, J. H. Toxicity of antibiotics

and other drugs to *Neurospora*.

In a search for agents suitable for isolating cytoplasmically-inherited drug-resistant mutants, a number of antibiotics, antibacterials, respiratory inhibitors and compounds known to induce the "petite" phenotype in yeast were examined. Toxicity tests were performed in 2 ml's of Vogel's Medium N in 4-inch stationary test tubes. Sucrose at 2% (w/v) was used as a fermentable carbon source; sodium acetate at 40 millimolar or glycerol at 2% was employed as a non-fermentable substrate. The pH of the drug-containing media was either pH 5.8-6.5 (low pH) or pH 7.5-8.5 (high pH), and the growth rate of 74A was found to be reasonably good over this entire range. Germinating conidia of five-day-old cultures of 74A were added to a final concentration of approximately 10^6 conidia/ml, and the cultures were incubated at 34° for 5 days. The concentrations of the drugs given in Table 1 [following page] are either those which permitted no visible growth in 5 days, or the highest concentrations which, for technical reasons, were tested.

In general, aminoglycoside antibiotics are ineffective, except for kasugamycin and paromomycin. Macrolides are toxic only at the higher pH and show little discrimination between fermentable and non-fermentable carbon sources. In fact, a good portion of the differences seen between the two carbon sources and the two pH's is probably due to the differences in growth rate observed under these conditions in the absence of any drugs.

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The symbols and abbreviations used in the table on the following page are given below:

Symbols

M Molar
- - - No measurement
* Amount of drug/ml of medium
> Growth still observed at this conc
~ Approximate limit of growth
+ Solubility limit of drug
± Drug is unstable
γ Microgram

Abbreviations

ATA Aurintricarboxylic Acid
CCCP Carbonyl Cyanide m-Chlorophenyl Hydrazone
DMSO Dimethyl Sulphoxide
H O Q N O 2-Heptyl-4-hydroxy-quinoline-N-oxide
PAHS Polyamidohydrostreptin
TTFA Thenoyl trifluoroacetone
TTC Triphenyl tetrazolium Chloride

Table 1. Inhibitory Concentrations of Drugs for Neurospora

	Low pH Carbon Source		High pH Carbon Source	
	Fermentable	Non-fermentable	Fermentable	Non-fermentable
Acriflavin	> 5 γ *	5 γ	---	---
Actinobolin	> 1 mg	1 mg	> 1 mg	1 mg
Attractylate, K	> 1 mg	> 1 mg	---	---
Amicetin	> 5 mg	2 mg	> 1 mg ⁺	> 1 mg ⁺
Amobarbital	> 1 mg	> 1 mg	---	---
Amphotericin B	> 1 γ	1 γ	> 1 γ	1 γ
Antimycin A	> 10 γ	\sim 1 γ	> 1 γ	< 10 γ
ATA	> 5 mg ⁺	> 5 mg ⁺	---	1 mg ⁺
Azide, Na	\sim 10 ⁻³ M	\sim 10 ⁻³ M	---	---
Benzyl alcohol	> .08%	> .08%	---	---
Bluansomycin	> 20 mg	> 20 mg	> 20 mg	> 20 mg
Brilliant Green	2 γ	2 γ	---	---
Carbomycin	> 5 mg	---	---	---
CCCP	1 γ	1 γ	1 γ	1 γ
Chloramphenicol	> 4 mg	4 mg	---	---
Chloroquin Phos.	---	> 1 mg ⁺	---	---
Chlorpromazine	\sim 50 γ	50 γ	---	---
Clindamycin	---	---	1.5 mg	1.5 mg
CoCL ₂ ·6H ₂ O	> 2 mg	---	---	---
Crystal Violet	1 γ	1 γ	---	---
Dicoumarol	> 5 mg ⁺	> 5 mg ⁺	> 5 mg ⁺	> 5 mg ⁺
DMSO	> 2%	> 2%	---	---
Dinitrophenol	\sim 10 ⁻³ M	\sim 10 ⁻³ M	---	---
Erythromycin	> 5 mg	> 5 mg	5 mg	5 mg
Ethidium Bromide	> 10 γ	5 γ	---	---
Fusidic Acid	---	> 5 mg ⁺	---	> 5 mg ⁺
Gentamycin	> 20 mg	> 20 mg	> 20 mg	20 mg
Gramicidin D	>100 γ ⁺	>100 γ ⁺	>100 γ ⁺	>100 γ ⁺
HOONO	> 1 mg	> 1 mg	---	---
Janus Green B.G.	1-2 γ	1 γ	---	---
Kanamycin	> 20 mg	> 20 mg	> 20 mg	> 20 mg
Kasugamycin	> 20 mg	5 mg	---	---
Lincomycin	> 20 mg	> 20 mg	> 20 mg	> 20 mg
Malachite Green	1 γ	1 γ	---	---
Mikamycin	> 2 mg ⁺	---	---	---
Nalidixic Acid	>200 γ	100 γ	>200 γ	>200 γ
Neamine	> 20 mg	> 20 mg	> 20 mg	> 20 mg
Neomycin	> 20 mg	> 20 mg	> 20 mg	20 mg
Oleandomycin	> 20 mg	> 20 mg	> 20 mg	20 mg
Oligomycin	> 10 γ	10 γ	> 10 γ	10 γ
Ouabain	---	---	> 5 mg	> 5 mg
Oxytetracycline	> 1 mg [±]	> 1 mg [±]	---	> 1 mg [±]
Pararosaniline	> 10 γ	10 γ	---	10 γ
Paromomycin	> 10 mg	5 mg	5 mg	5 mg
Pentachlorophenol	5 γ	5 γ	5 γ	5 γ
PAHS	10 γ	5 γ	> 10 γ	> 10 γ
Pyronine B	100 γ	100 γ	100 γ	100 γ
Pyronine Y	>500 γ	>500 γ	---	---
Quinine SO ₄	1 mg ⁺	1 mg ⁺	1 mg ⁺	1 mg ⁺
Rifampicin	---	> 1 mg ⁺	---	> 1 mg ⁺
Rotenone	> 1 mg	> 1 mg	---	---
Rutamycin	>200 γ	25 γ	100 γ	25 γ
Safranine	100 γ	100 γ	---	---
Spectinomycin	> 20 mg	> 20 mg	> 20 mg	> 20 mg
Spiramycin	> 5 mg	> 5 mg	> 5 mg	5 mg
Staphylomycin	> 4 mg ⁺	---	---	---
Streptogramin	> 2 mg ⁺	---	---	---
Streptomycin	> 20 mg	> 20 mg	---	> 20 mg
Tellurite, K	> 1 mg	---	---	---
Tetracycline	> 1 mg [±]	1 mg [±]	> 1 mg [±]	> 1 mg [±]
TFA	>100 γ	100 γ	---	---
Thiomycetin	> 4 mg ⁺	---	---	---
Thiostrepton	---	---	> 1 mg ⁺	> 1 mg ⁺
Trimethoprim	> 5 mg ⁺	\sim 5 mg ⁺	---	---
TTC	> 1 mg	> 1 mg	---	---
Tyrothricin	50 γ	50 γ	50 γ	50 γ
Valinomycin	> 10 γ	10 γ	10 γ	10 γ
Vernamycin $\beta\alpha$	> 5 mg ⁺	> 5 mg ⁺	> 5 mg ⁺	> 5 mg ⁺
Viomycin	> 20 mg	> 20 mg	> 20 mg	> 20 mg