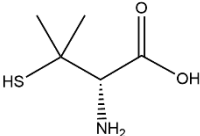
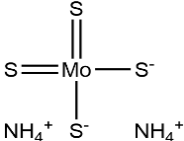
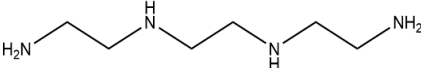
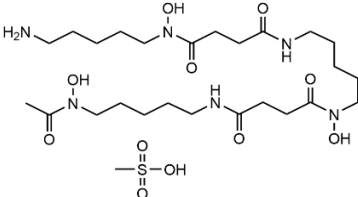
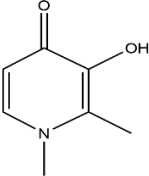
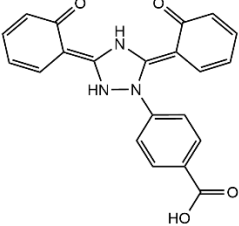
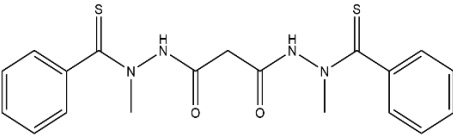
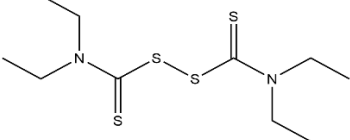
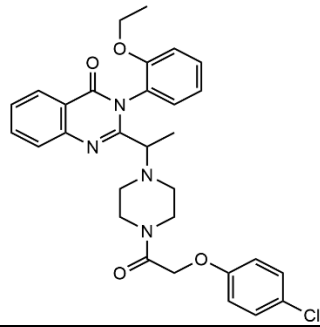


Supplementary table

Table S1: Chemical properties of key metal modulating agents

Chemical name	Structure	Activation/ Metabolism	Coordination (binding) groups	Related Metal(s)
Chelators				
D-Penicillamine		Directly active; forms stable complexes.	Thiol (-SH), Amino (-NH ₂), Carboxylate (-COO ⁻)	Cu(I/II), Zn(II), Pb(II)
Ammonium Tetrathiomolybdate (ATTM)		Directly active; sequesters copper in a stable tripartite complex with albumin.	Sulfide (S ²⁻)	Cu(I/II)
Trientine		Directly active; chelates free copper.	Amino (-NH ₂)	Cu(II)
Deferoxamine (DFO)		Directly active; high-affinity iron chelator.	Hydroxamate	Fe(III), Al(III), Cu(II)
Deferiprone (DFP)		Directly active; orally active iron chelator.	Hydroxypyridinone	Fe(III), Al(III), Cu(II)
Deferasirox (DFX)		Directly active; orally active iron chelator.	Triazole / Phenolate	Fe(III)
Ionophores				
Elesclomol		Binds extracellular Cu(II); reduced to Cu(I) upon cellular uptake, leading to cytotoxic ROS.	Thiocarbonyl (C=S), Hydrazine	Cu(II/I)
Disulfiram		Metabolized to diethyldithiocarbamate (DDC); DDC chelates copper to form a cytotoxic complex.	Dithiocarbamate (-N(C(S)S))	Cu(II)
Ferroptosis inducers				

Erastin

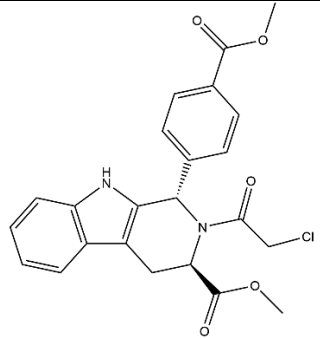


Directly active. Inhibits system x_c^- and directly targets mitochondrial voltage-dependent anion channels.

Pharmacological inhibitor (not direct metal binding)

Pathway is Fe(II) -dependent

RSL3

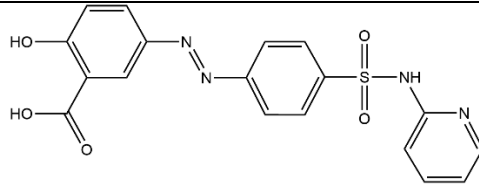


Directly active. Covalently inhibits glutathione peroxidase 4 (GPX4).

Electrophile; reacts with selenocysteine active site of GPX4

Pathway is Fe(II) -dependent

Sulfasalazine (SAS)



Prodrug; metabolized to 5-aminosalicylic acid and sulfapyridine. Inhibits system Xc^- .

Pharmacological inhibitor (not direct metal binding)

Indirectly affects Fe/Cu via redox balance