



Inorganic pharmaceutical chemistry

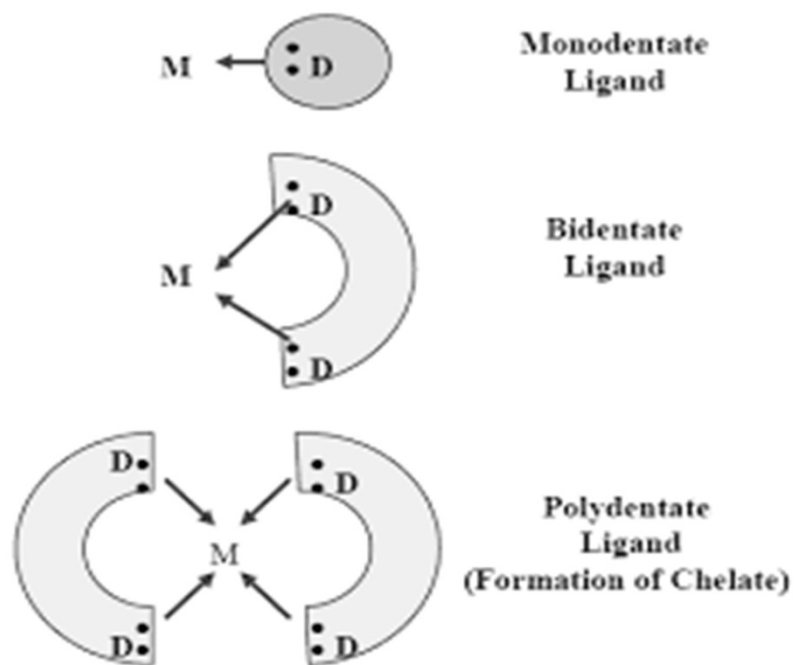
3 stage

lec. 3

Dr-leaqaa

## Complexes & chelating agents:

chelate :- a complex in which a ligand forms a ring that includes the metal atom.



## Characteristics of an Ideal Chelator

- Greater Affinity, Low Toxicity
- Ability to compete with natural chelators
- Ability to penetrate cell membranes
- Rapid elimination of the toxic metal
- High water solubility
- Capacity to form non-toxic complexes
- Same distribution as the metal



In general:

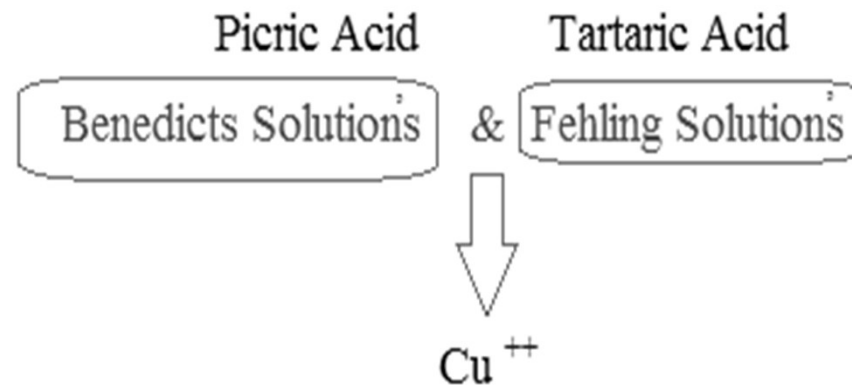
Chelators work by binding to metals in the bloodstream. Once they're injected into the bloodstream, they circulate through the blood, binding to metals. In this way, chelators collect all the heavy metals into a compound that's filtered through the kidneys and released in urine.

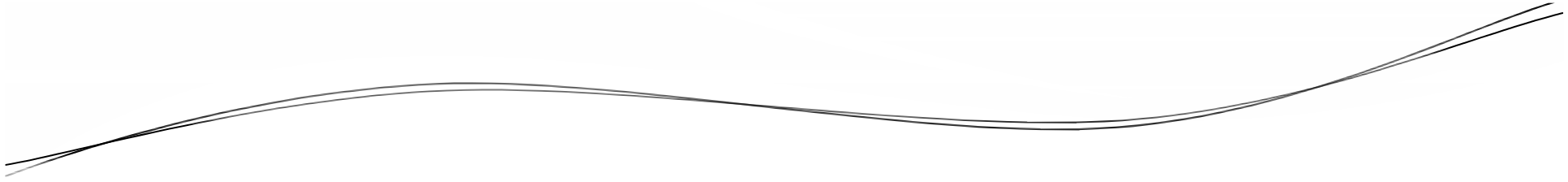
complexes & complexa^ aspects important of chemistry & pharmacy.

some e.g.

1-complexa^ plays an important role in analytical chemistry, e.g.

\*2 solu^s employed in identifical^ of reducing substances (sugar):





\* Also chelating agent can be effectively used in cases of heavy metal poisoning.

in addition to their usefulness in toxicological problems such as these, they are also being used to treat certain metabolic disorders where metals such as Fe, Cu are accumulated in abnormal amounts in various tissues.

e.g. Chelating agents:

# 1- ~~CaNa<sub>2</sub> Edetate: U.S.P.XVIII~~

Ca disodium versenate ,Ca disodium ethylenediaminetetracetate

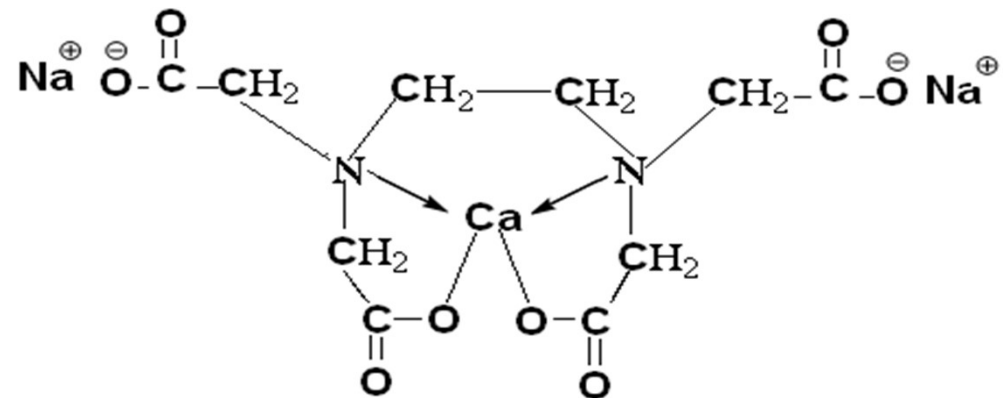
\*  $\Delta$ is cpd. Is a mixture of dihydrate & trihydrate.

\* odorless,slightly hygroscopic,stable in air , freely soluble in water

\* pH of an aq.sol. is (.) 6.5-8.

-High affinity for Pb, Zn,Cd,Mn, Ni, Cu

MOA: removes the metals by exchanging with Ca<sup>2+</sup>





Uses:

1- ttt of heavy metals poisoning, primarily  $\wedge$ at caused by pb[plumbism], it employed in poisoning by Cu, Ni, Cd, Zn, Cr & Mn, but it no value in ttt of toxicities produce by Hg, As or Au.  
Mech.?

2- EDTA prepara $\wedge$ s have a strong affinity for Ca,  $\wedge$ erefore disodium ca form is used to avoid inducing hypoglycemic states .





Rout of administra<sup>^</sup>:

\*I.V. inj.(official Ca disodium Edetate inj.U.S.P.XVIII,contains not less <sup>^</sup>an 180 mg & not more <sup>^</sup>an 220 mg of cpd. In each ml.

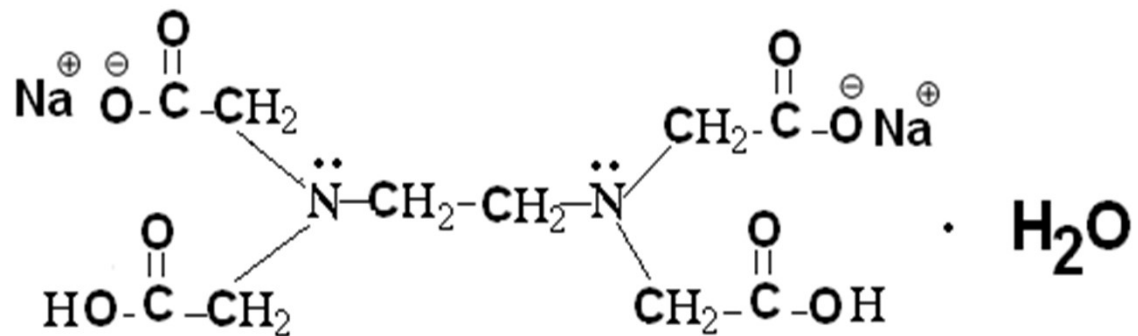
\*I.M.-----is employed sometimes in diagnosis of metal poisonings

2- Disodium Edetate:U.S.P.XVIII [Na<sub>2</sub>EDTA]--  
 disodium ethylenediaminetetraacetate

\* providing aq.sol.of pH (.) 4&6.

\*its chelate ^ same metals as diNaCa form.

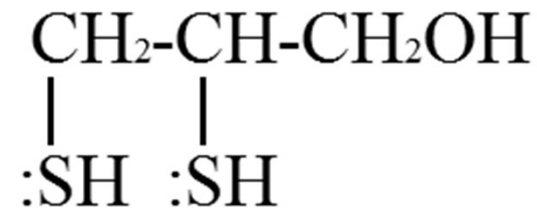
\*by use ^is agent----- ^ hypocalcemia during such  
 therapy is exists.



3- Dimercaprol (BAL) : U.S.P.XVIII

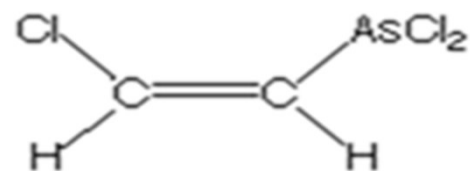
(2,3-dimercapto-1-propanol)

\*is an effective chelating agent for heavy metals such as As,Sb ,Hg & Au.



\*antidote to lewisite(arsenic war gas).

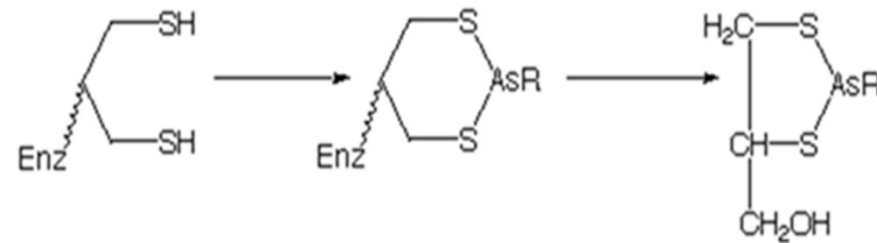
\*SH ligands of dimercaprol compet with –SH enz.



Lewisite

these heavy metals form strong bonds to the sulfur atoms in dimercaprol

\*[Stable mercaptides]



\*[Compete with thiol grp.for binding M ion,which then excreted in the urine].

\* dimercaprol-metal chelate tend to dissociate in acid media?



Also use:

- \* for ttt of Au & Hg poisoning .

- \*Use to improve the excretion of Pb & cu (wilson's disease)

- Contraindicated in Fe & cd or Se poisoning(b- resulting complexes have greater renal toxicities than do free metal.

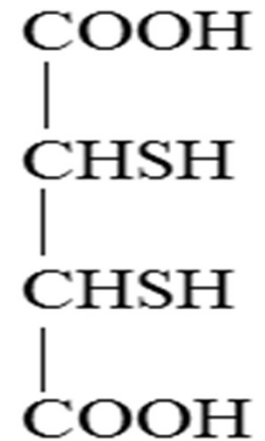
4- DMSA (Succimer)  
(2,3-dimercaptosuccinic acid)

-Dimercaprol analogue

water soluble, less toxic, orally effective

\* for Pb poisoning

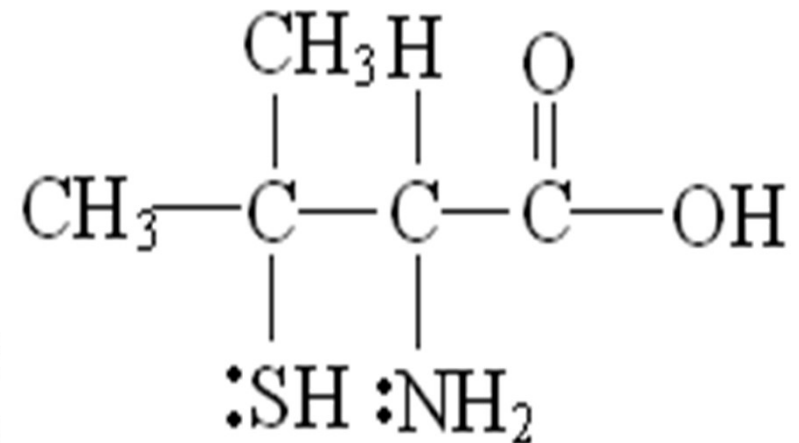
- As, Hg, Cd



5-Penicillamine:

D-β,β-Dimethyl cysteine (D-isomer, more potent)

-used for Cu, Fe, Hg & Au poisoning.



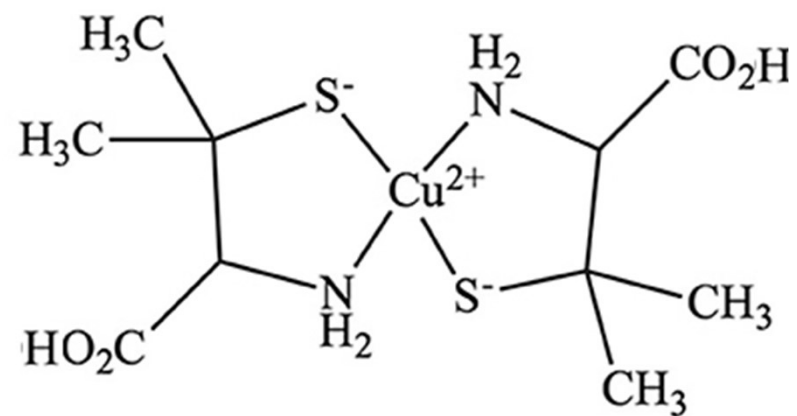
-Use to improvement Cu ε  
hepatolenticular degenrati

- to chronic Pb poisoning.

- in ttt of gold dermatitis .

- ttt of cystinurea & cystine stones.

- aspect was proposed ability of SH grp. to reduce Cu(II) in tissues to Cu(I). a probable str. of complex is:







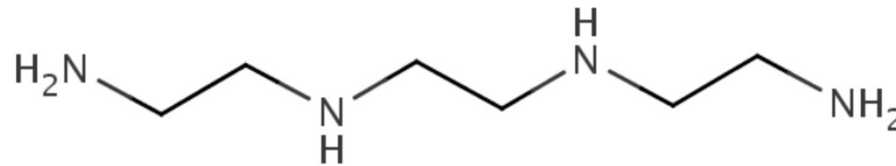
\*usual rout is orall---penicillamine capsules r- official in  
U.S.P.XVIII

Doses:usual oral dose in 250 mg 4 time a day.

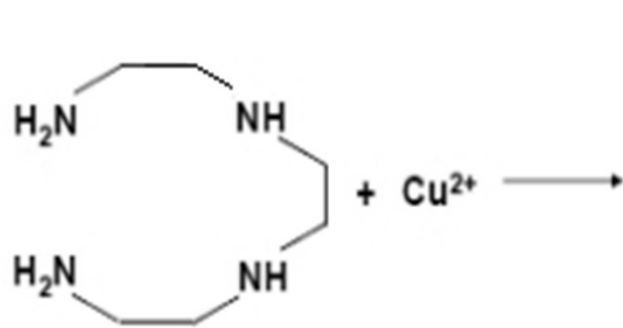
exchang resin is frequntly employed during ^erapy.

Prep.:Cuprimine<sup>®</sup> capsules containing 250 mg for oral admi.

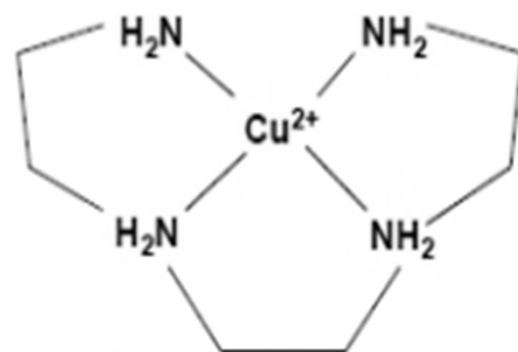
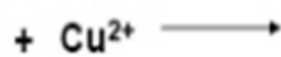
Trientine(triethylene tetramine):  
cupriuretic agent



- N,N'-Bis(2-aminoethyl)ethane-1,2-diamine
- \* chelates Cu and is used in wilson's disease
- less potent but safer than penicillamine



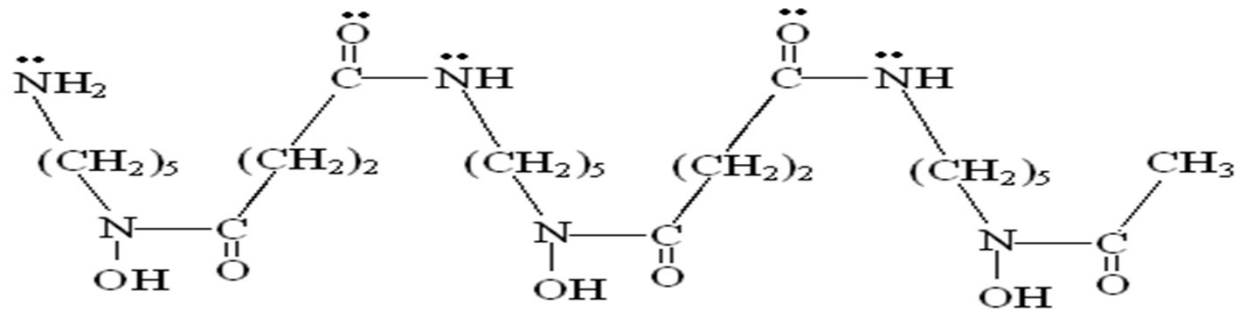
**Trientine**



**Trientine-copper complex**

Deferoxamine mesylate:

-for acute Fe(+3) toxicity.



-high affinity for Fe(III) ,not for Fe(II)

\* used for ttt of iron storage disease  
(Hemochromatosis)

its polydentate ligand with a particular affinity for Fe(III) ions= Oh complex

