



CSO203: INORGANIC MOLECULES, METALS,
AND MEDICINES

METALS & MEDICINES



Overdose of Metals!

Too much of anything is good for nothing!

Even the Elixir of Life Is a Poison When Exceeds Limits!



Fe Poisoning!

Sources of Iron Poisoning:

- Accidental ingestion of iron supplements, especially by children.
- Overconsumption of iron-containing medications.
- Ingestion of iron-containing household products or industrial substances.

Toxic Effects:

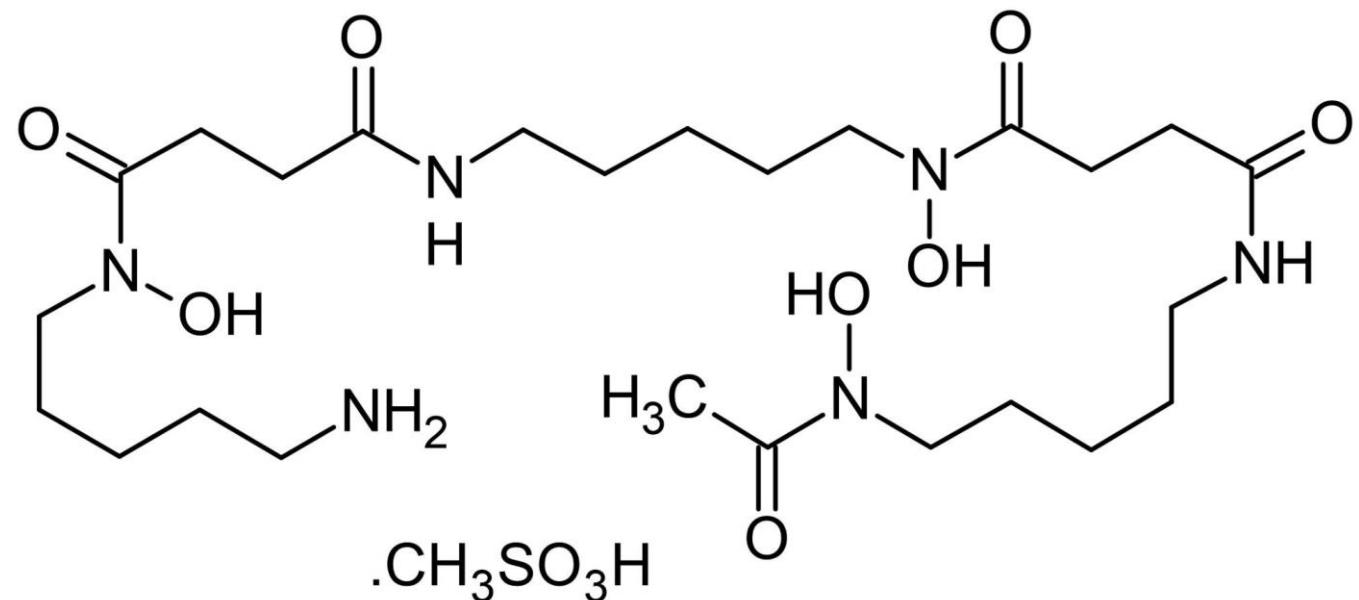
- Iron poisoning can lead to gastrointestinal symptoms such as nausea, vomiting, abdominal pain, and diarrhea.
- In severe cases, can damage the liver, heart, and pancreas, among other organs.
- It can lead to shock, coma, and death.



Fe Poisoning!

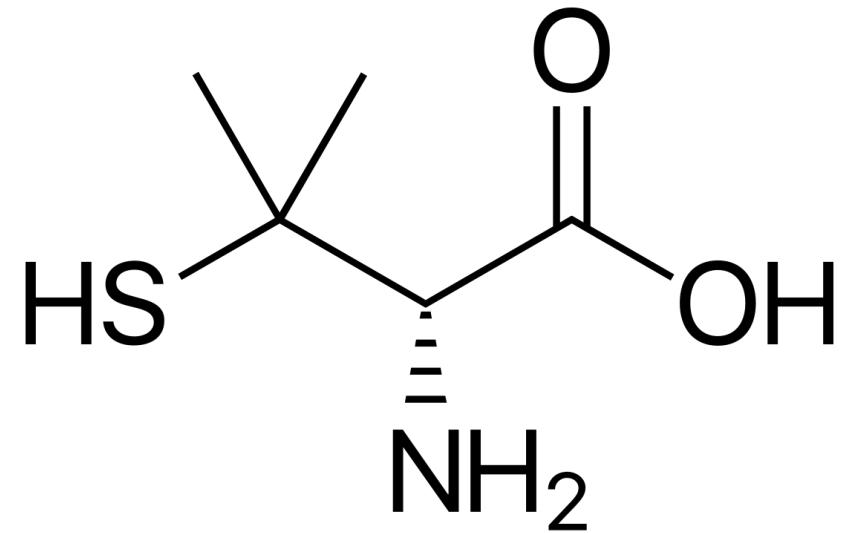
Treatment:

- Supportive care to manage symptoms.
 - In severe cases, iron-chelating agents are used .
 - **Deferoxamine** is a commonly used iron-chelating agent.



Cu Poisoning: Alzheimer's Disease!

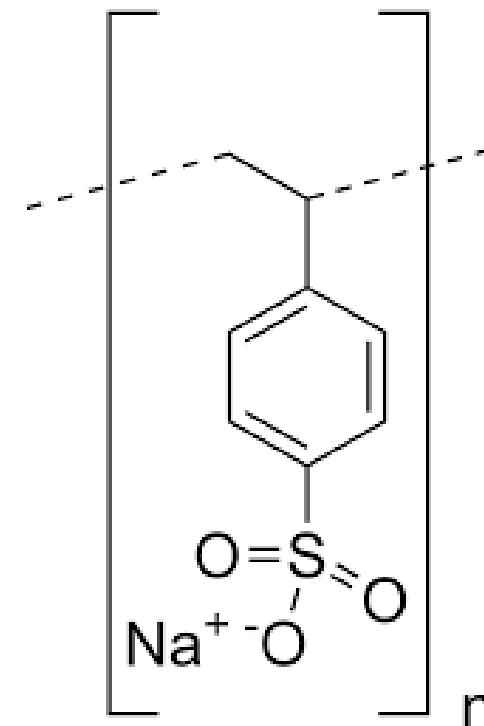
- Increases the accumulation β -amyloid in the brain which is characteristics to Alzheimer's
- Increases ROS production leading to oxidative stress.
- Penicillamine is an example of a chelating agent that can be used.

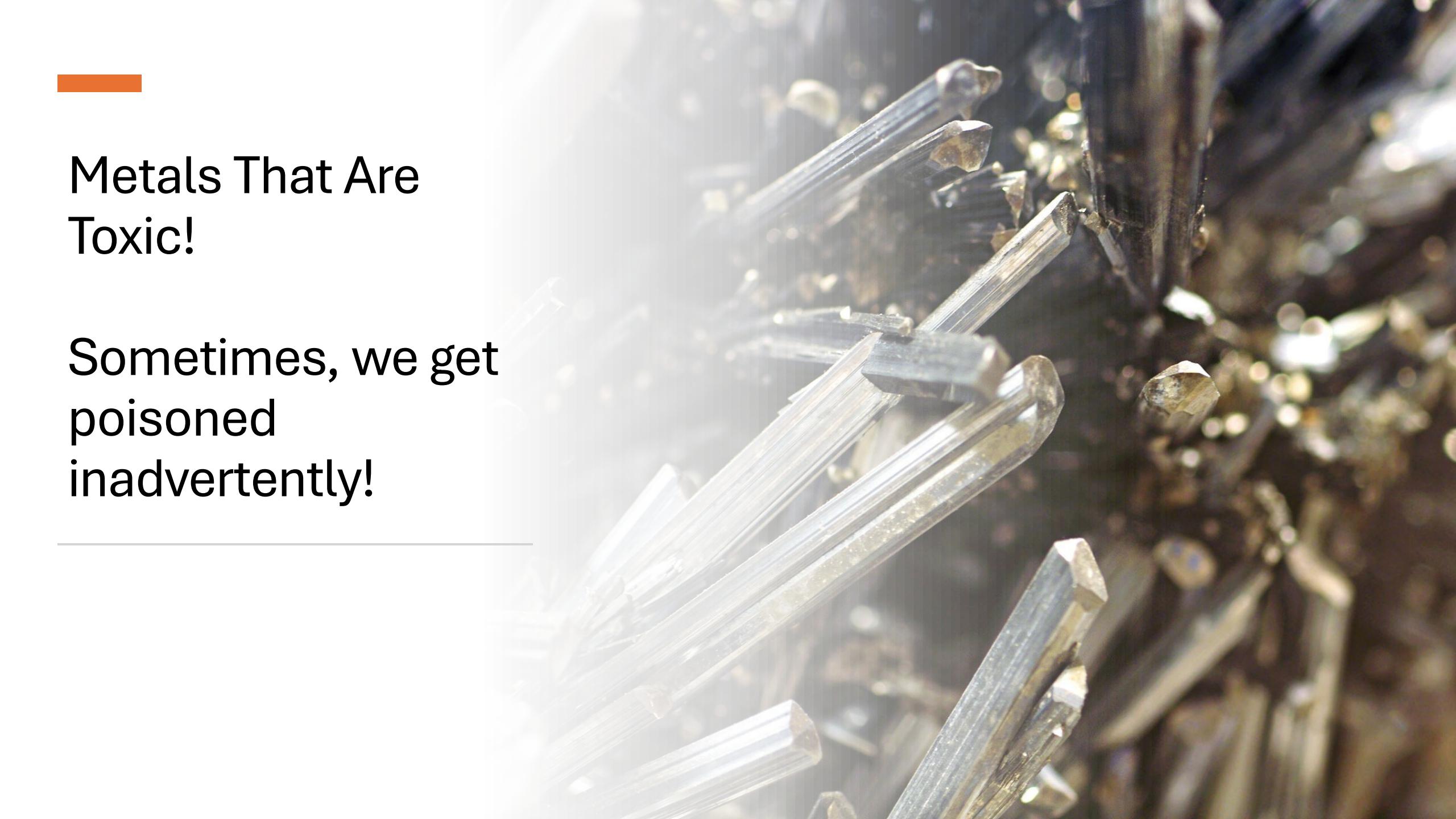


K⁺ Poisoning: Hyperkalemia!

Hyperkalemia is a medical condition characterized by abnormally high levels of potassium in the blood, typically defined as a serum potassium concentration greater than 5.0-5.5 meq/L. While mild hyperkalemia is often asymptomatic, severe elevations, especially above 7 meq/L, can cause life-threatening cardiac arrhythmias, muscle weakness, paralysis, respiratory failure, and even cardiac arrest. The onset of symptoms depends more on how quickly potassium levels rise than on the absolute value. Chronic hyperkalemia patients may tolerate higher levels with fewer symptoms, whereas acute potassium shifts often provoke severe effects.

- Moderate to severe hyperkalemia can lead to muscle weakness, numbness, tingling, or paralysis.
- Cardiac symptoms may include irregular heartbeats (arrhythmias) and, in severe cases, cardiac arrest.
- Kayexalate is an ion-exchange resin that works by exchanging sodium ions for potassium ions in the gastrointestinal tract. (only for moderate cases)

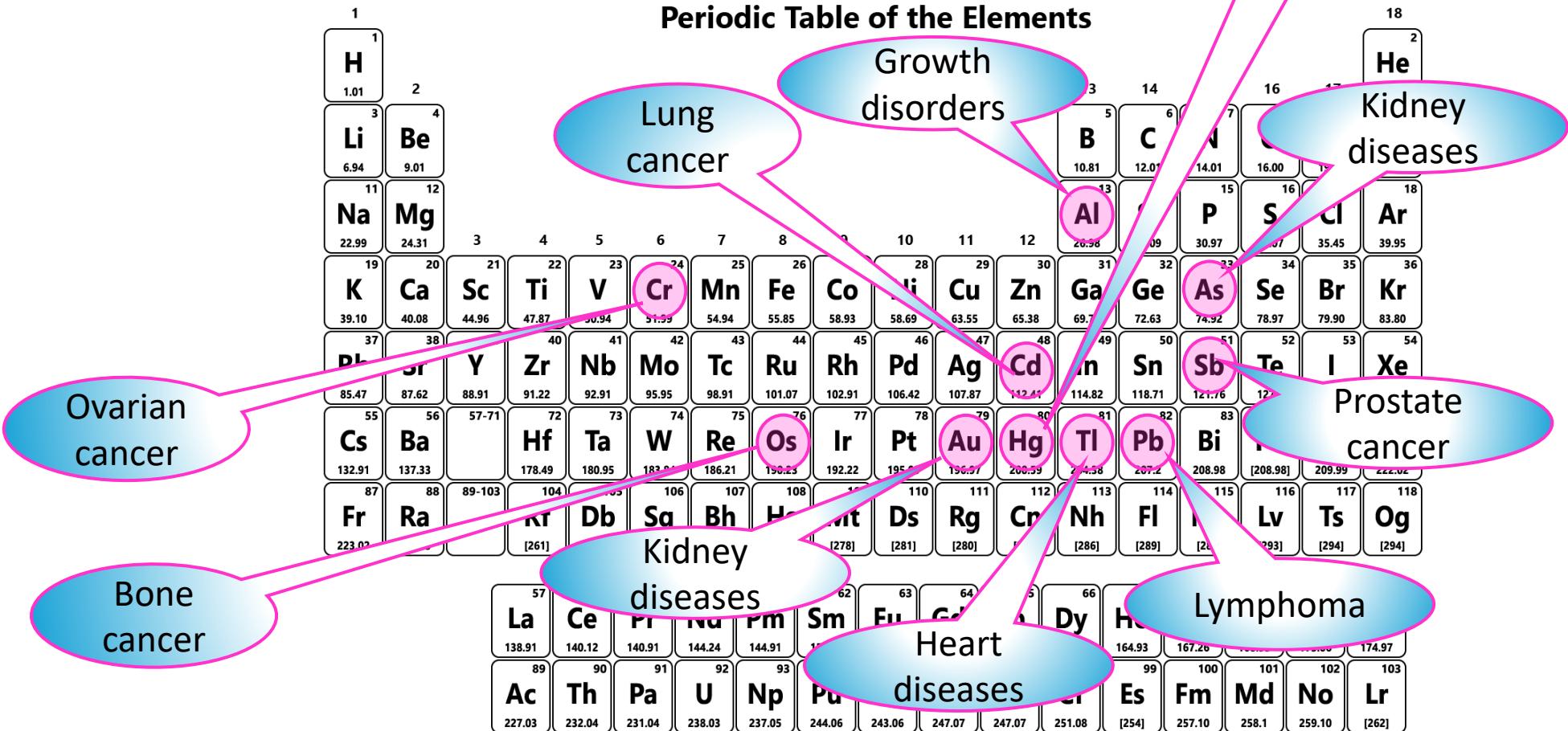




Metals That Are Toxic!

Sometimes, we get
poisoned
inadvertently!

Metals That Can Kill Us!



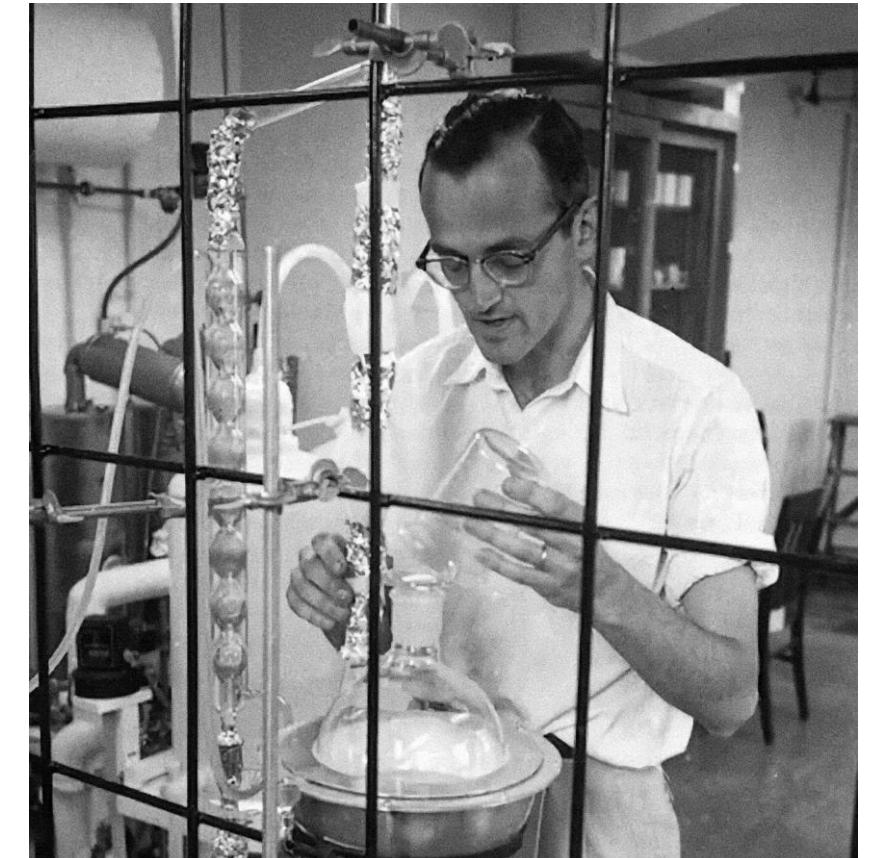
Inadvertent Intake of Toxic Metals!

- Pb(Et)_4 was used to improve the octane rating of gasoline.
- The **octane rating** of gasoline is a standard measure of the fuel's ability to resist "knocking" or premature detonation during combustion in an internal combustion engine. The higher the octane rating, the more compression the fuel can withstand before detonating.
 - Hence Pb in air, land, and water is omnipresent
 - Poses extreme health risks and proven cases of deaths
 - The case against **Nestle®** for Pb in **Maggi**



Dr. Clair Cameron Patterson and his struggles in determining the age of the Earth

- A legend who calculated the Earth's age and took on the powerful lead industry.
- Determined the age of earth around 1940s wasn't close enough.
- Patterson tried it with Zircon
 - Zircon has U238 which decays into Pb at a known rate!
- No matter how careful he was, his samples were continually contaminated with high conc. of Pb.
- He couldn't trust any of his readings.
- Created the first clean room and calculated the age of the earth (~4.55 billion years).
- **Shocking discovery:** Pb was ubiquitous in the environment at levels far beyond what should be naturally present.



Patterson's fight against lead (Pb) contamination:

- One of the most significant environmental battles in modern history.
- Patterson's 1965 paper, "*Contaminated and Natural Lead Environments of Man*", provided undeniable evidence that industrial activities (especially leaded gasoline) had massively increased Pb levels in the environment and human bodies.
- The lead industry, particularly **Ethyl Corporation**, aggressively tried to discredit him.
- Patterson was **blacklisted from receiving funding** from organizations like the U.S. Public Health Service and the American Petroleum Institute.
- His relentless advocacy led to the **1970s Clean Air Act amendments** and the eventual **ban on leaded gasoline** in the U.S. by 1996.
- **Lead levels in Americans' blood dropped by over 80% as a result.**

The Most Important Scientist You've Never Heard Of

By [Lucas Reilly](#) | May 17, 2017



Michael Rogalski | Michael Rogalski



The Enemies that Patterson Faced!

- These firms took several aggressive steps to discredit Clair Patterson and protect the billion-dollar **tetraethyl lead (TEL) industry**.
- Blocking Research Funding
- Exclusion from Advisory Panels
 - replacing him with scientists funded by Ethyl and other pro-lead organizations.
- Attacking His Scientific Credibility
 - Industry-backed researchers published papers arguing that Patterson's work was flawed
 - Claimed that lead in the environment was **naturally occurring** and had no connection to leaded gasoline.
- Promoting a “Safe Lead” Narrative
- **Robert A. Kehoe**, a toxicologist funded by the lead industry, was one of the most prominent defenders of **tetraethyl lead (TEL)** and even **ingested lead himself** to convince the public it was safe.
- **Thomas Midgley Jr.**, the leaded gasoline inventor, poured tetraethyl lead on his hands and **inhaled its vapors for 60 seconds** during a press conference to prove it was harmless.



Midgley's Legacy: A Scientist Who Was Consumed by Money and Pride!

- Invented TEL
- Invented Freon® (CFCs)

Legacies:

- Environmental historian J. R. McNeill opined that Midgley "had more adverse impact on the atmosphere than any other single organism in Earth's history"
- Fred Pearce, writing for New Scientist, described Midgley as a "**one-man environmental disaster**"
- Time magazine included both TEL and CFCs on its list of "**The 50 Worst Inventions**"



The lawsuit against Nestle® for Pb in Maggi

- Food Safety and Standards Authority of India (FSSAI) found Maggi® samples containing excessive Pb.
- Nestlé India addressed by conducting independent testing and providing evidence that Pb was within limits.
- Central Food Technological Research Institute (CFTRI) confirmed Nestlé's findings.

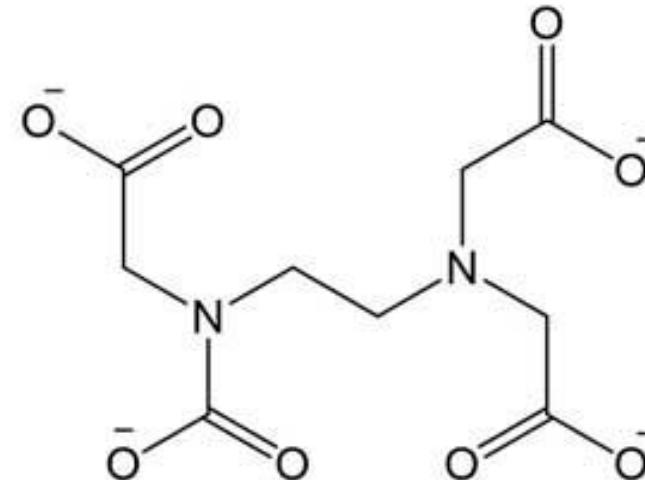


Nestle® argued, there is no clean room at FSSAI to do this test reasonably because Pb is ubiquitous!

A close-up photograph of two hands clasped together, symbolizing support or rescue. The hands are positioned in the lower right quadrant of the frame, with one hand resting on top of the other. The background is dark and out of focus.

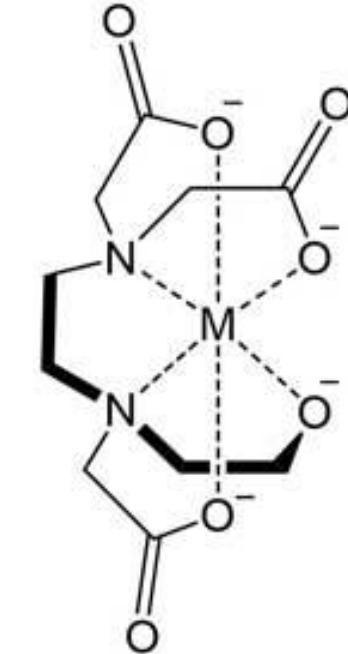
Chelation Therapy to The Rescue!

What Is Chelation?



Fully deprotonated EDTA

M
M = metal

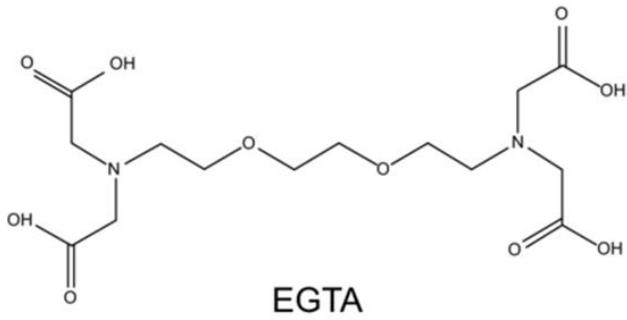


"Metal-EDTA complex"

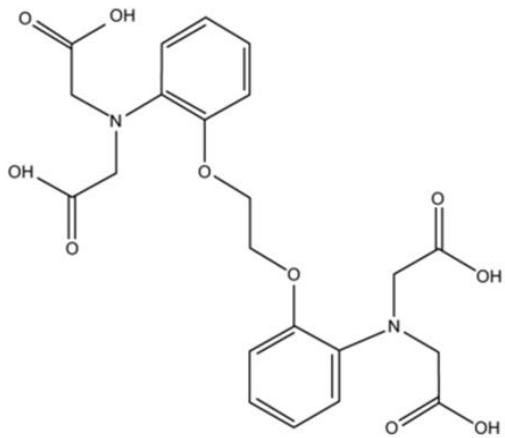
- The term "chelation" is derived from the Greek word "**chele**," meaning **claw**, reflecting the way the chelating agent wraps around the metal ion.

Chelating Agents!

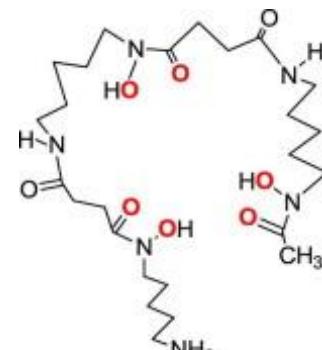
Ligands with two or more donor atoms!



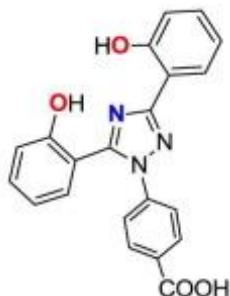
EGTA



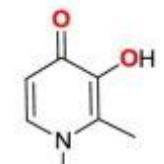
BAPTA



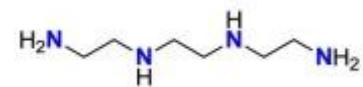
DFO-B



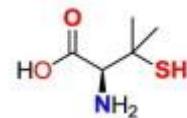
Deferasirox



Deferiprone



Trientine



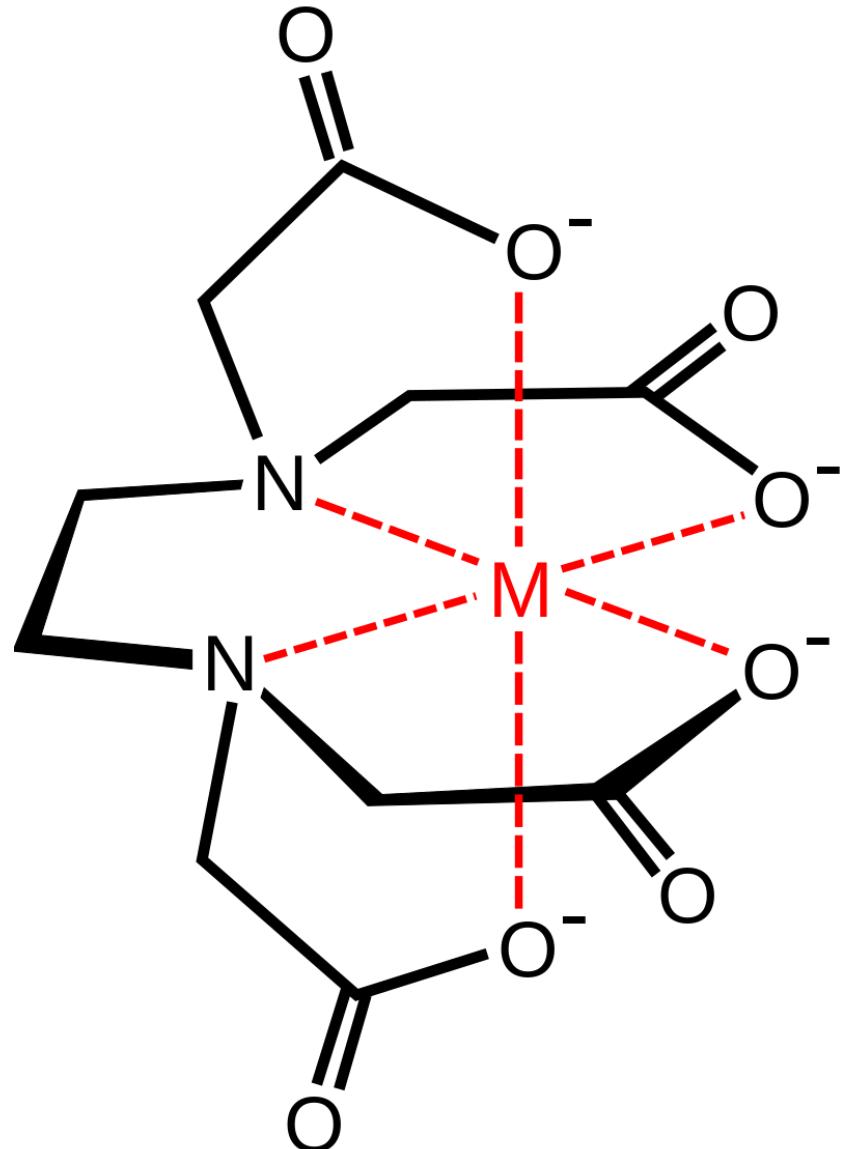
D-penicillamine



EDTA

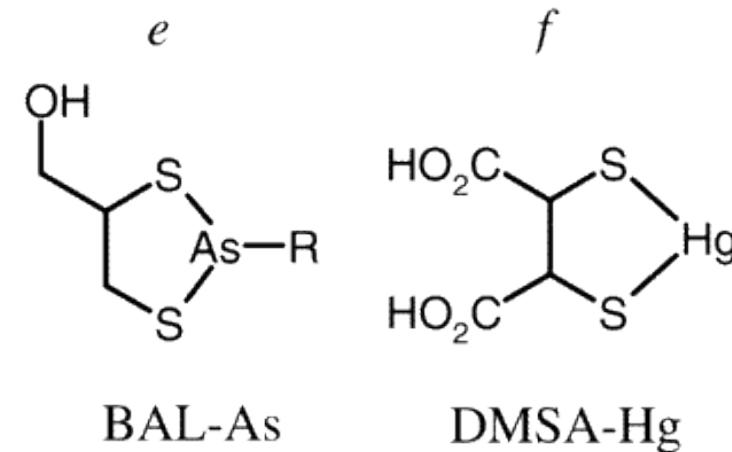
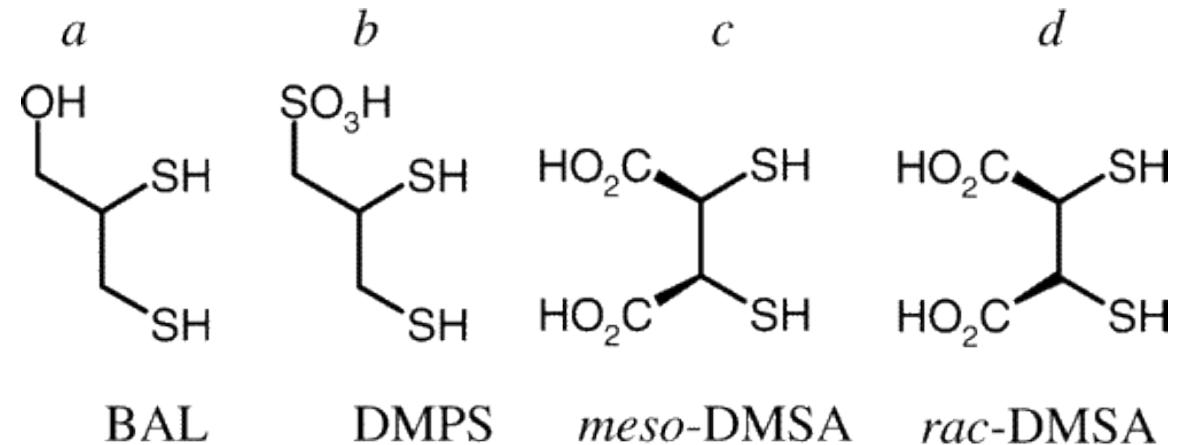
The Chelation Therapy:
Treating $\text{Pb}^{2+/4+}$, Al^{3+} , $\text{Cu}^{+/2+}$,
 Zn^{2+} , Mg^{2+} , etc. Poisoning!

M = $\text{Pb}^{2+/4+}$, Al^{3+} , $\text{Cu}^{+/2+}$, Zn^{2+} , Mg^{2+} , etc.

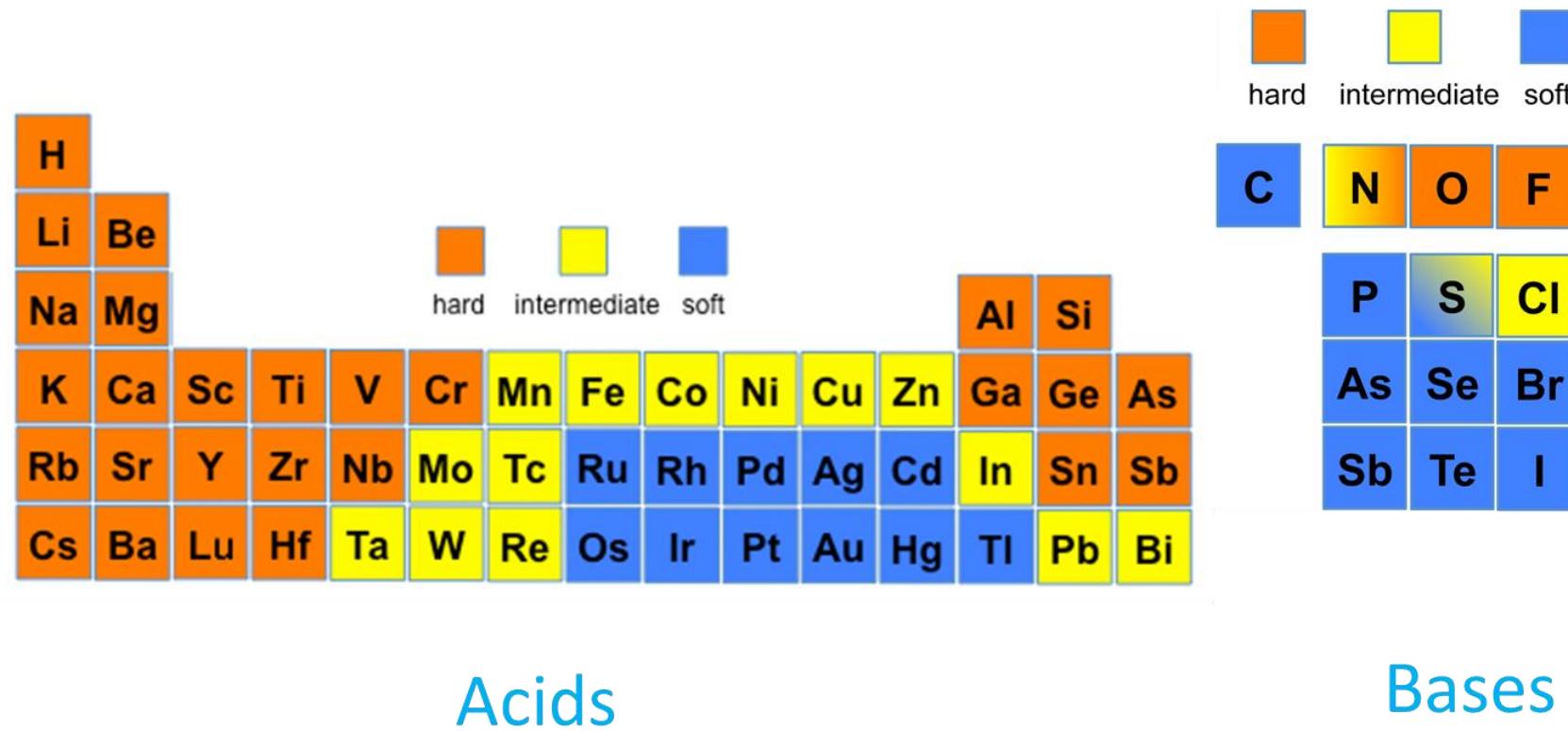


The Chelation Therapy: Treating Hg & As Poisoning!

- Ligands with multiple S atoms as donors are used
- The same ligands can also be used for the poisoning of
 - Au^+
 - Ag^+
 - Cd^{2+}
 - Pb^{2+}
 - Sn^{2+}



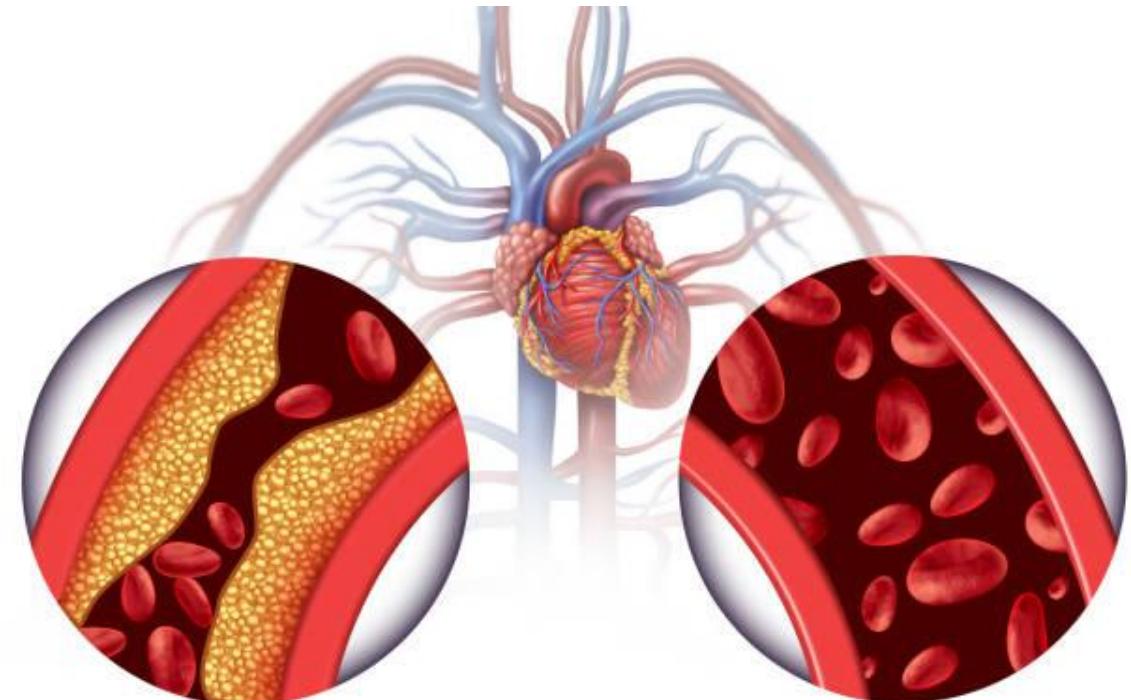
The Chelation Therapy: How to Choose the Chelating Agent?



Atherosclerosis: The Chelation Therapy!

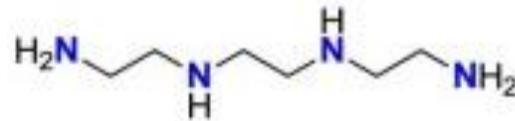
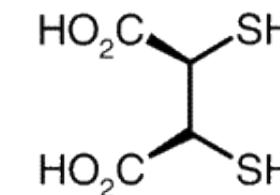
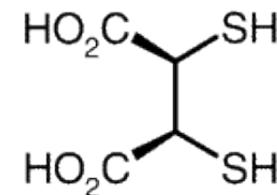
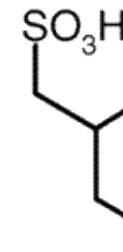
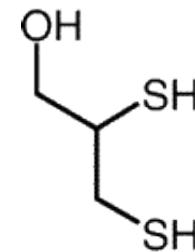
- A treatment method where different chelating agents were used to improve cardio-vascular health.
- Plaques are said to built up in connection with Ca^{2+} ions
- Hence, they can be removed with a chelating agent.
- Extra caution should be exercised as it could lead to dangerously low levels of other essential metals too if unsupervised.

Atherosclerosis is a chronic disease where plaques, consisting of fats, cholesterol, **calcium**, and other substances, build up inside arterial walls, causing narrowing, hardening, and reduced blood flow.



The Chelation Therapy: Choose the Appropriate Chelating Agent!

- Ru^{3+}
- Al^{3+}
- Ag^+
- Ca^{2+}
- Ru^{6+}
- Sn^{2+}
- Mn^{2+}
- Mn^{4+}



Trientine

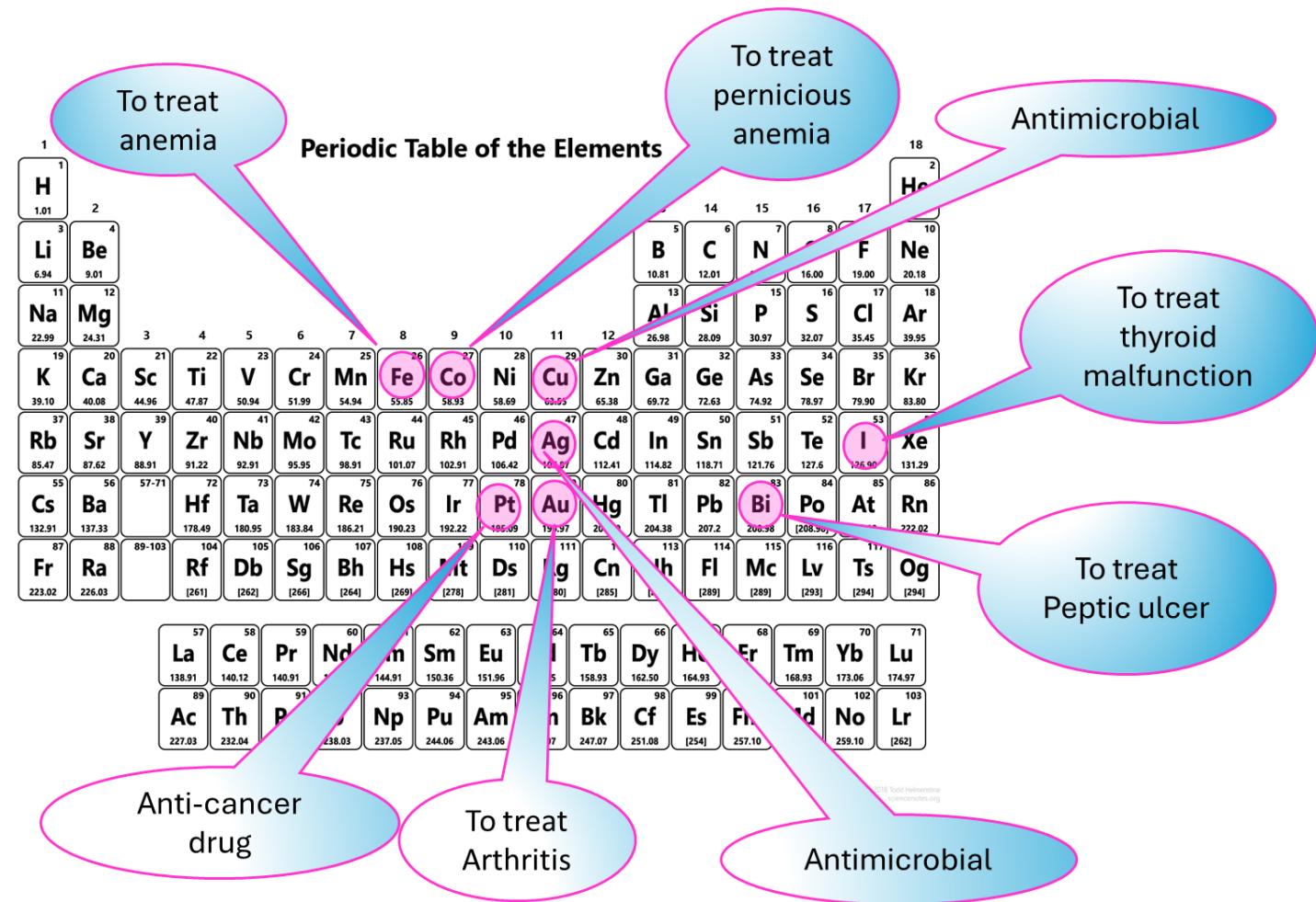


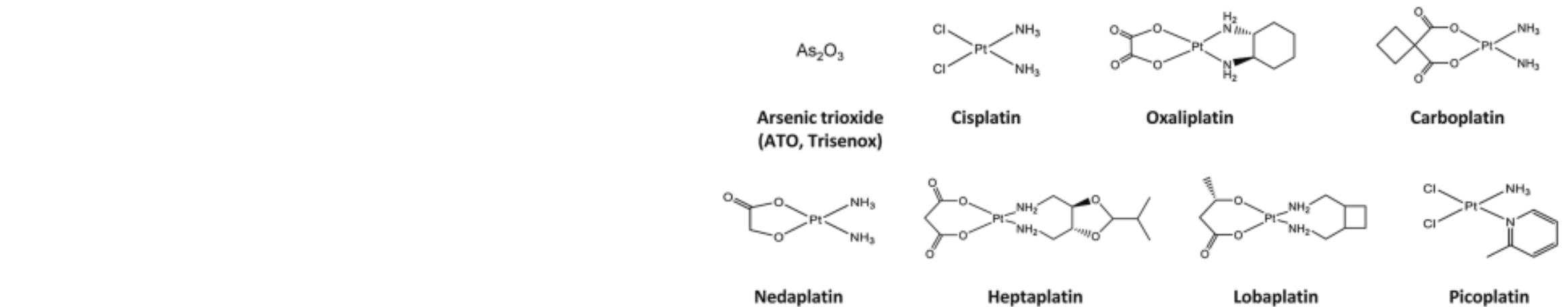
D-penicillamine



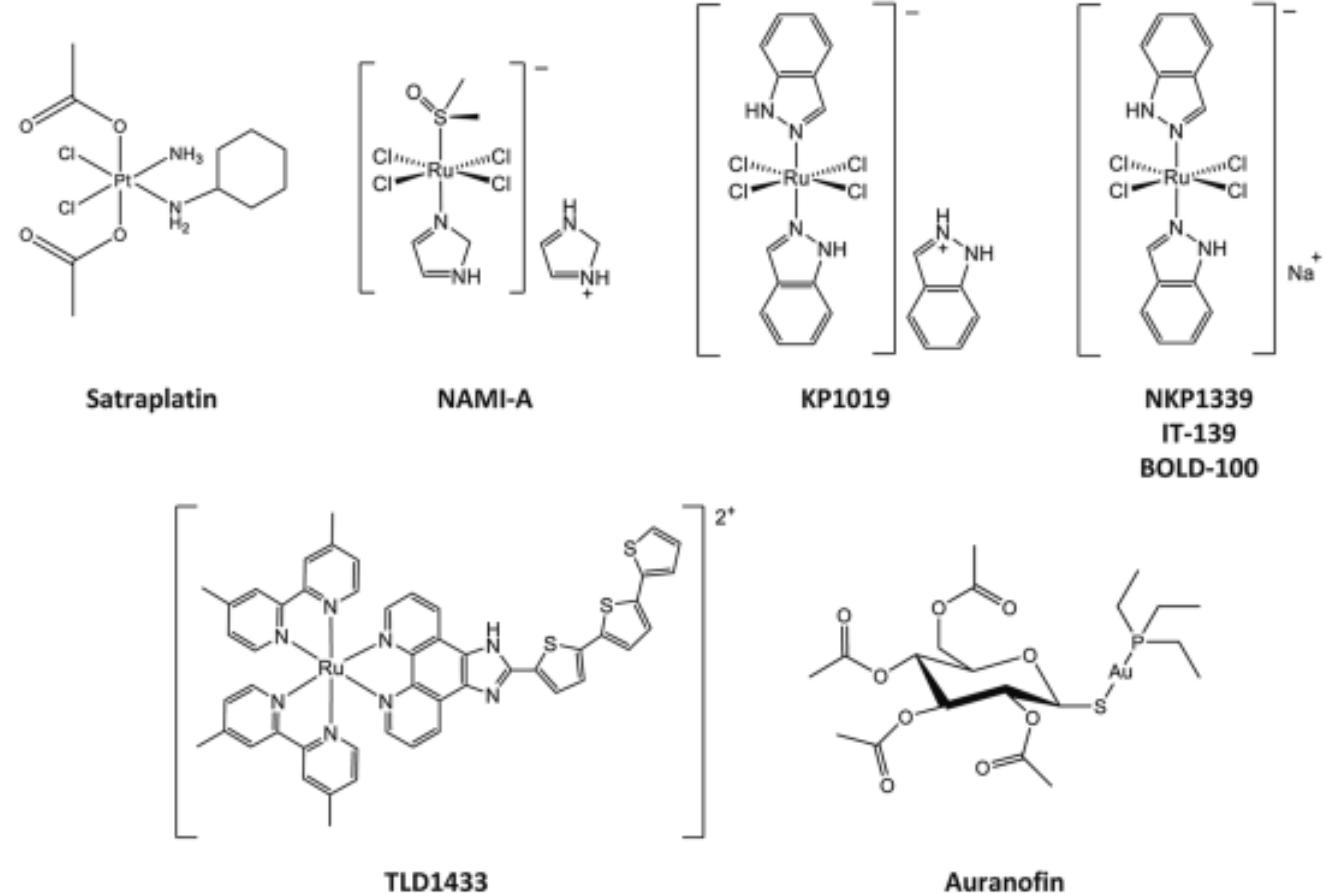
EDTA

Metals with Notable Therapeutic Properties!





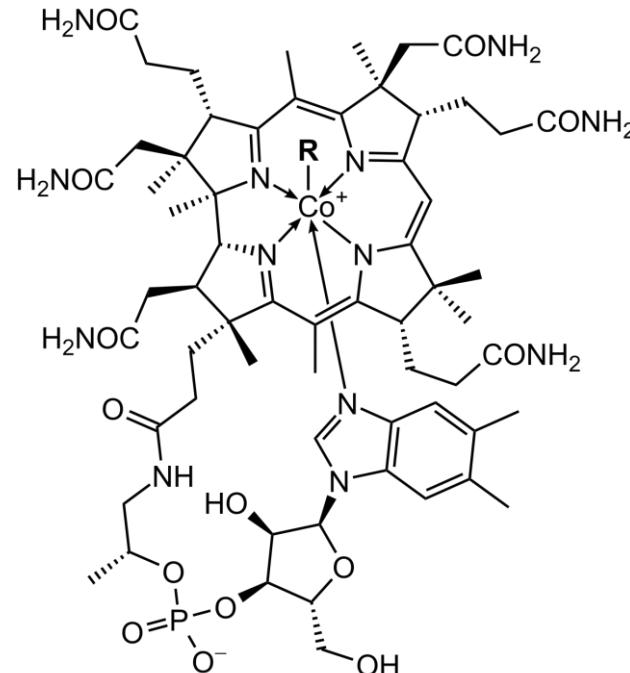
Overview of approved or clinically investigated metal drugs.



Lack of Co Leads to (Pernicious) Anemia

1. Mild Fatigue / Weight Loss
2. Racing Heartbeat
3. Dizziness
4. Tingling Skin
5. Shortness of breath
6. Arm and leg weakness

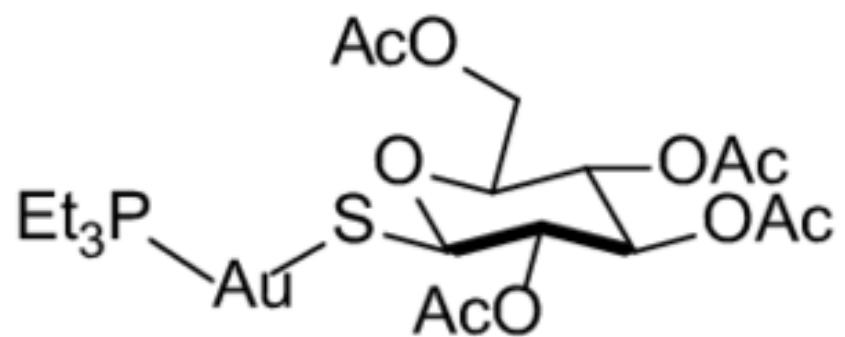
- Lack of B12 will cause anemia
- With certain mutation, the small intestine lose its ability to generate X-factor (the protein responsible for the absorption of B12 to the system) leading to pernicious anemia.



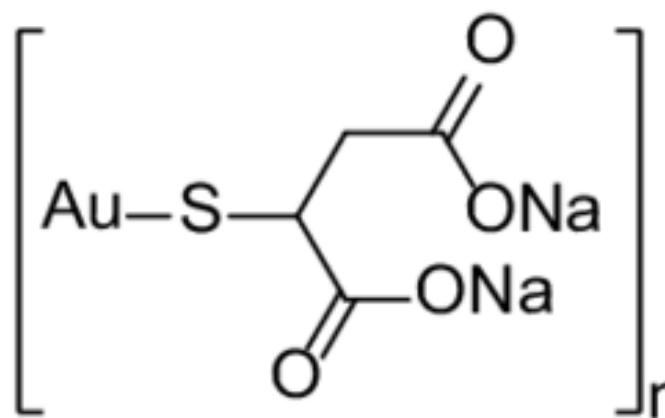
$\text{R} = 5'$ -deoxyadenosyl, CH_3 , OH , CN

Rheumatoid Arthritis and Au- Complexes!

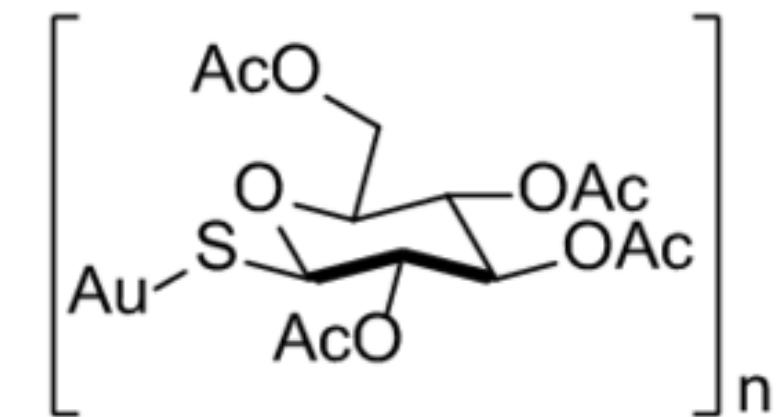
- An autoimmune disease attacking bone joints
- Inflaming the connectives



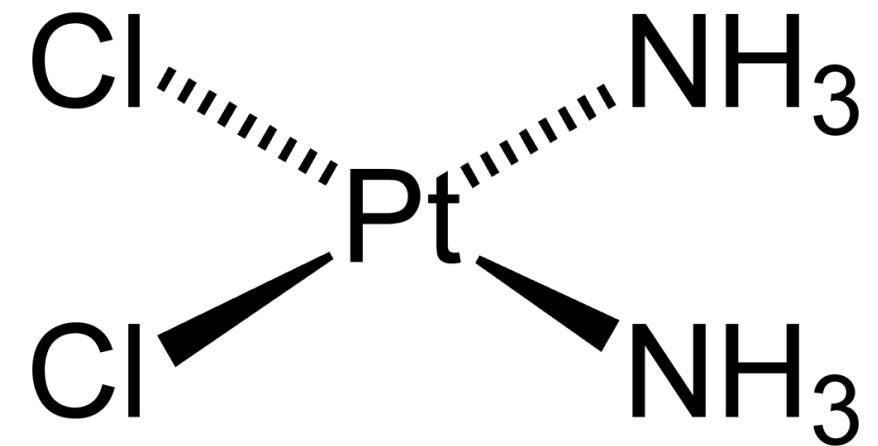
Auranofin



Myocrisin



Solganol



Cis-Platin: The
wonder Drug That's
Saving Millions!

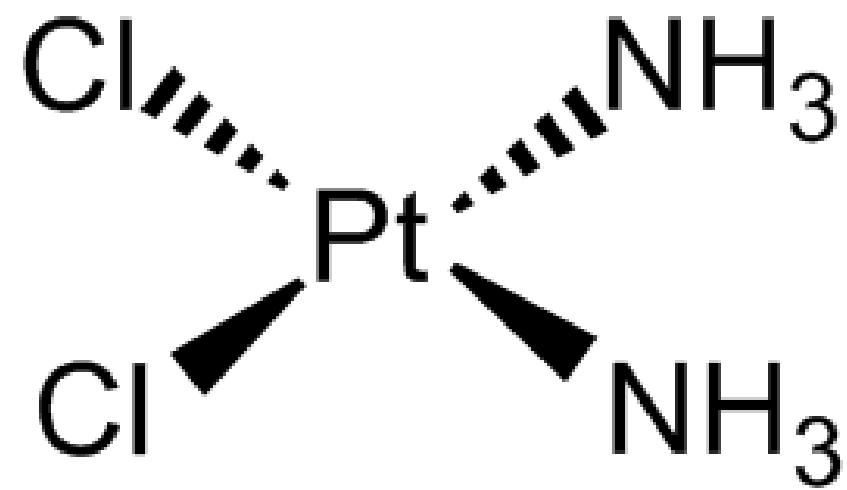


Cis-Platin

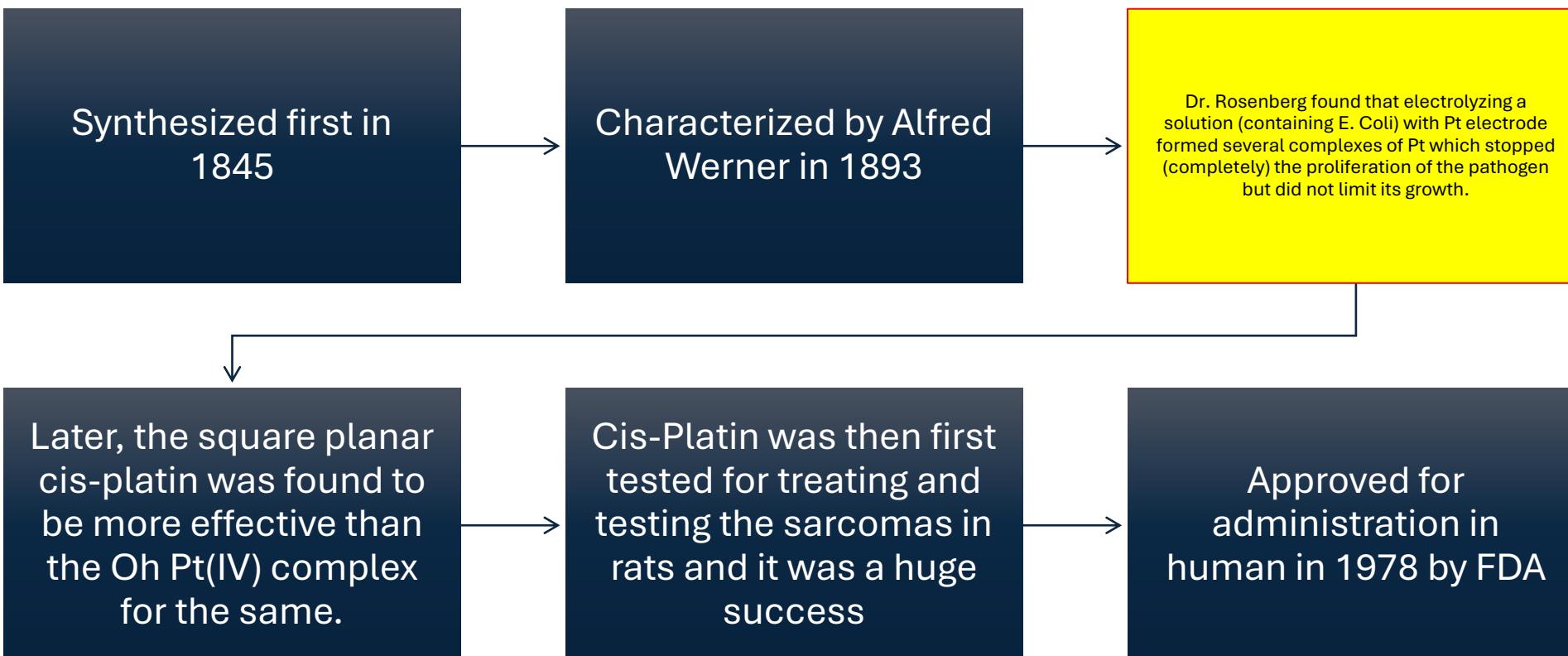
Added to WHO's essential medic list

It is used to treat

- testicular cancer
- ovarian cancer
- cervical cancer
- bladder cancer
- head and neck cancer
- esophageal cancer
- lung cancer
- mesothelioma
- brain tumors and neuroblastoma



The Accidental Discovery of Bioactivity of Cis-Platin!

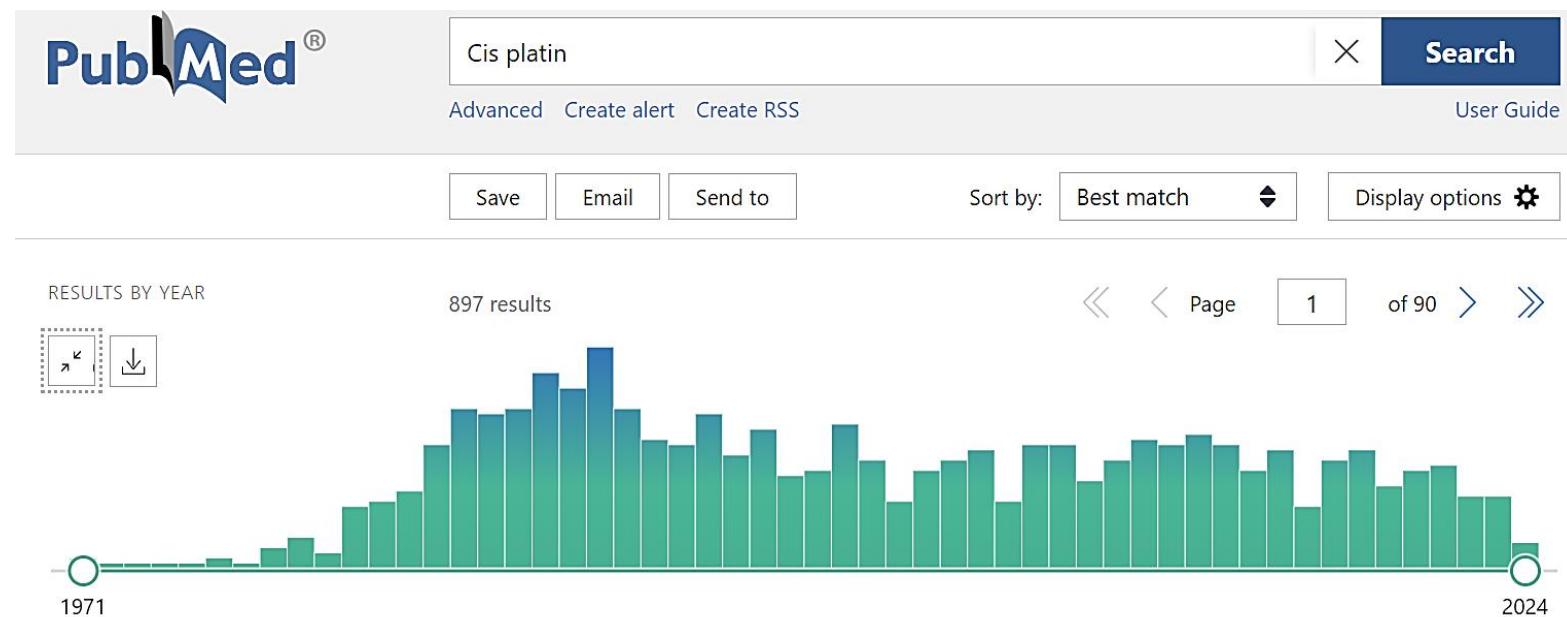


Barnett Rosenberg

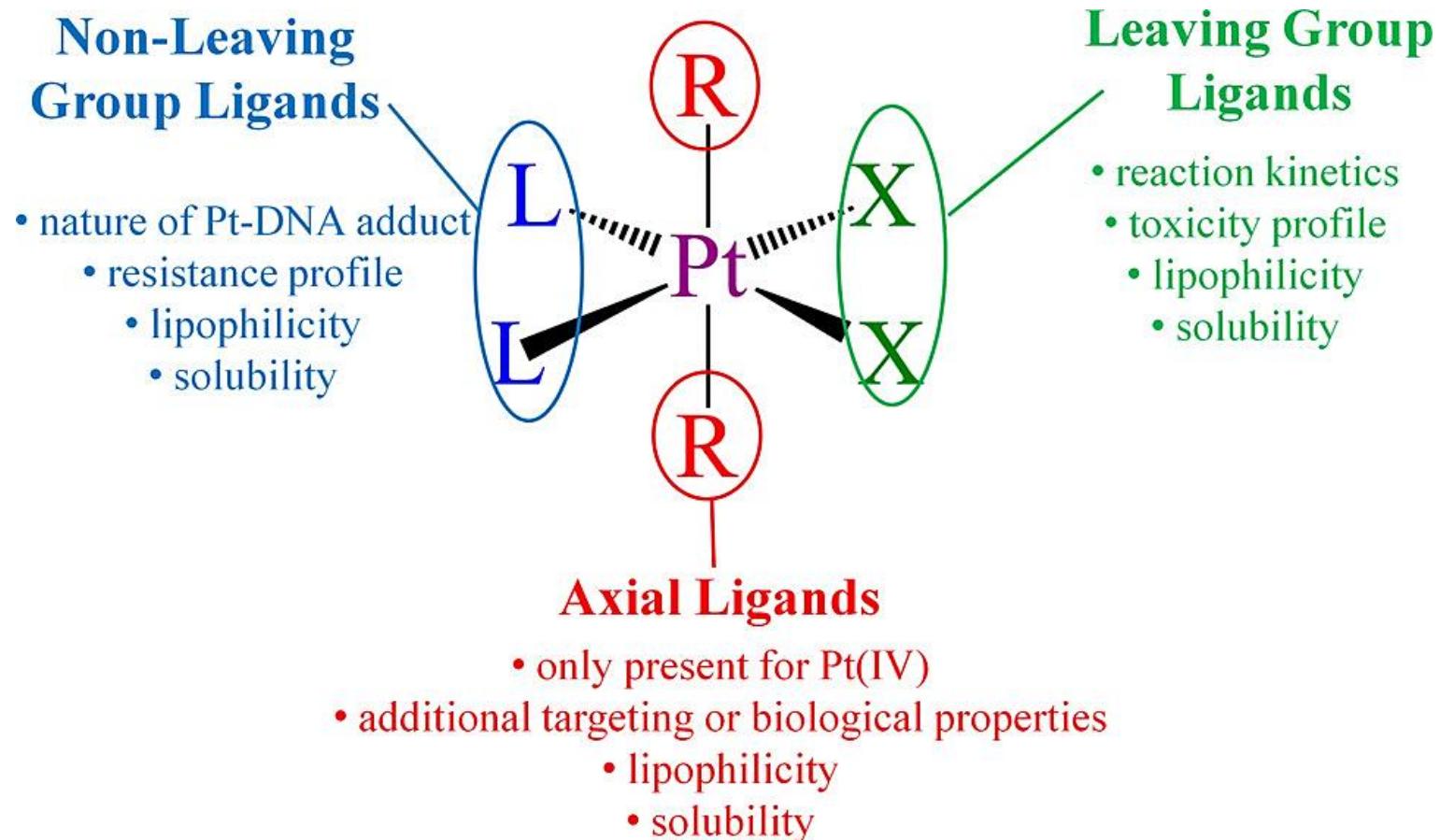
Michigan State University, USA

Research on Cis-platin over the years

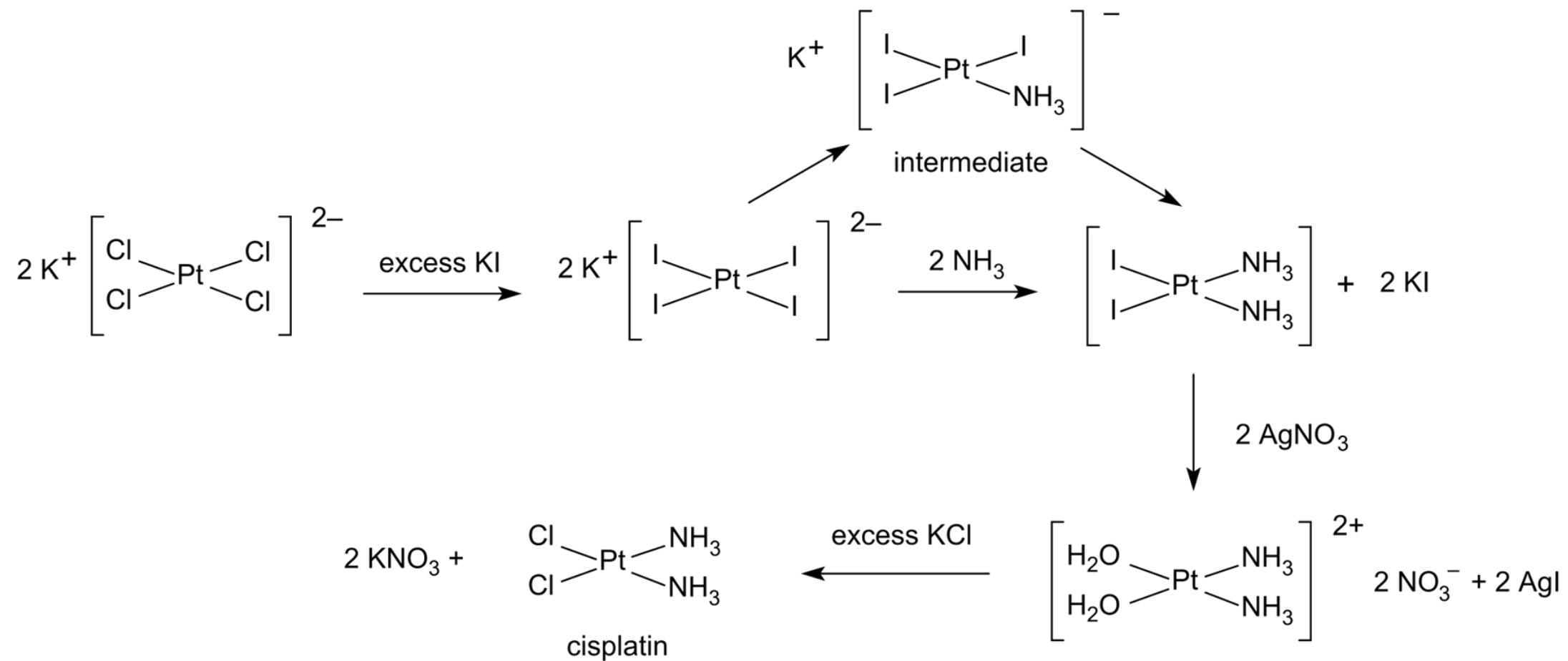
- Approved for clinical use in **1978**.
- Between 2020 and 2022, approximately 10,000 papers per year were published.
- Estimates suggest it has contributed to saving **millions** since its clinical approval in **1978**.



Different Components of a Pt-Based Anti-cancer Drug

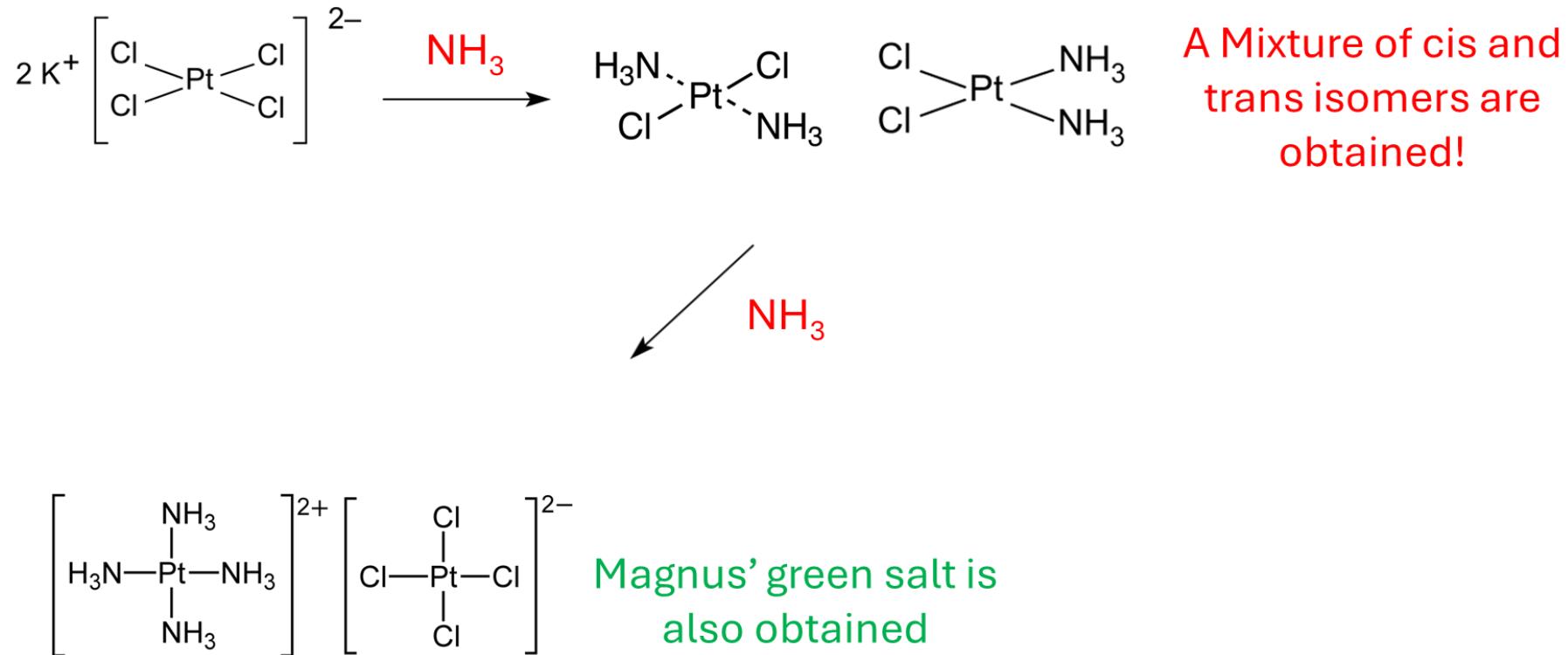


Cis-Platin: The Synthesis (Dhara's Method)!



Cis-Platin: The Brilliance of Dhara's Method!

- If KI is not used!

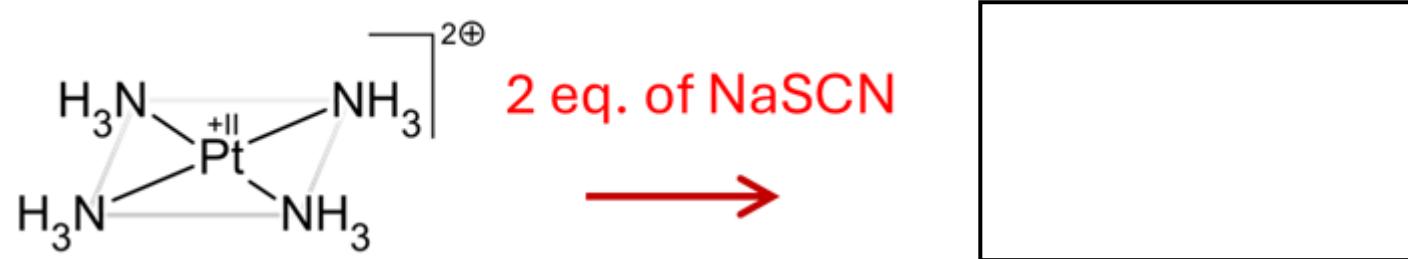


What is this “Trans-Effect?”

“Ability of a ligand to make the ligand opposite to it leave or be replaced in a complex with ease”

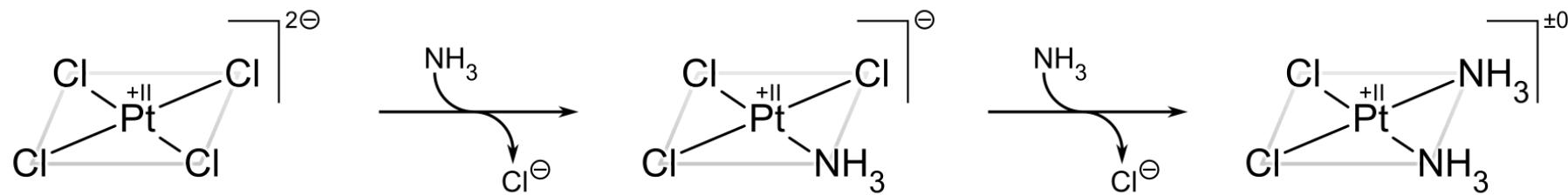
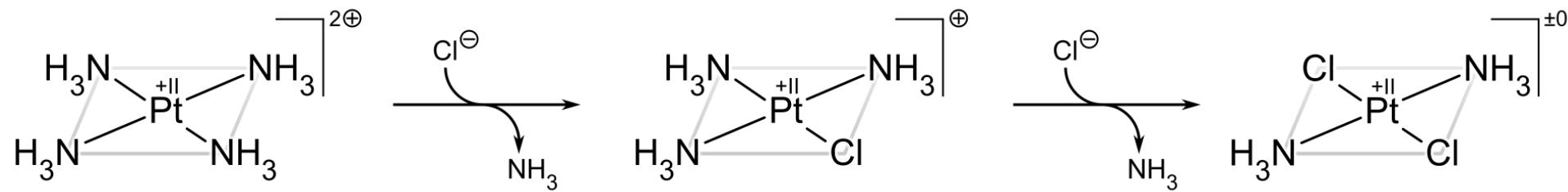
- Electronic structure and the extent and ways of orbital overlap govern this phenomenon
- In general, smaller, highly charged, less polarized, sigma donors exert poor trans effect
- In contrast, larger, polarizable, pi-acceptors exert extreme trans effect
- Observed for both *Oh* and *Sp* complexes but pronounced well with the later.

The *Trans-Effect* Series!

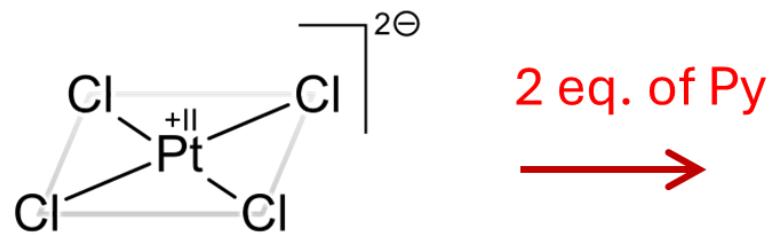


F^- , H_2O , $\text{OH}^- < \text{NH}_3 < \text{py} < \text{Cl}^- < \text{Br}^- < \text{I}^-$, SCN^- , NO_2^- , $\text{SC}(\text{NH}_2)_2$, Ph^-
 $< \text{SO}_3^{2-} < \text{PR}_3$, AsR_3 , SR_2 , $\text{CH}_3^- < \text{H}^-$, NO , CO , CN^- , C_2H_4

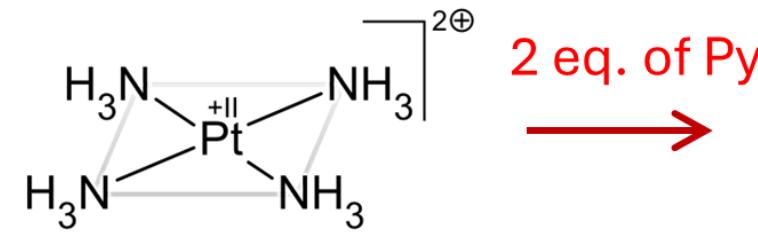
What is this “Trans-Effect?”



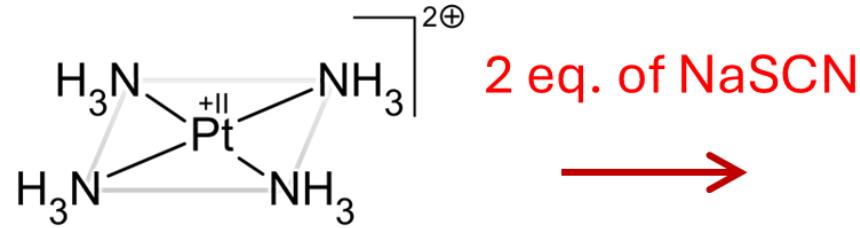
“Trans-Effect”: Predict the Products!



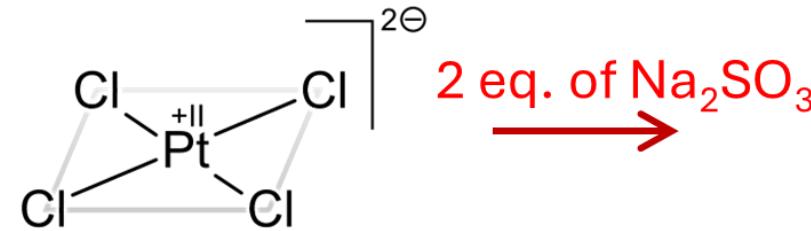
2 eq. of Py
→



2 eq. of Py
→

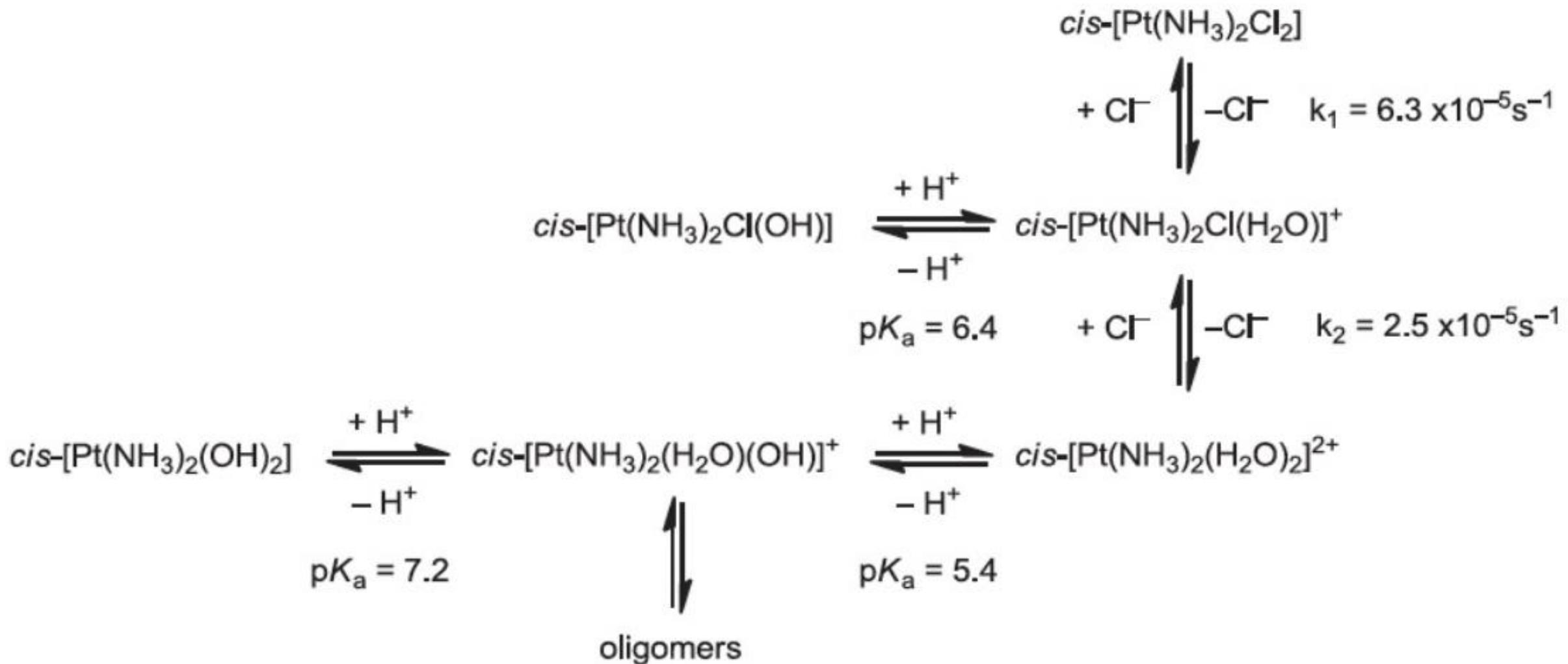


2 eq. of NaSCN
→

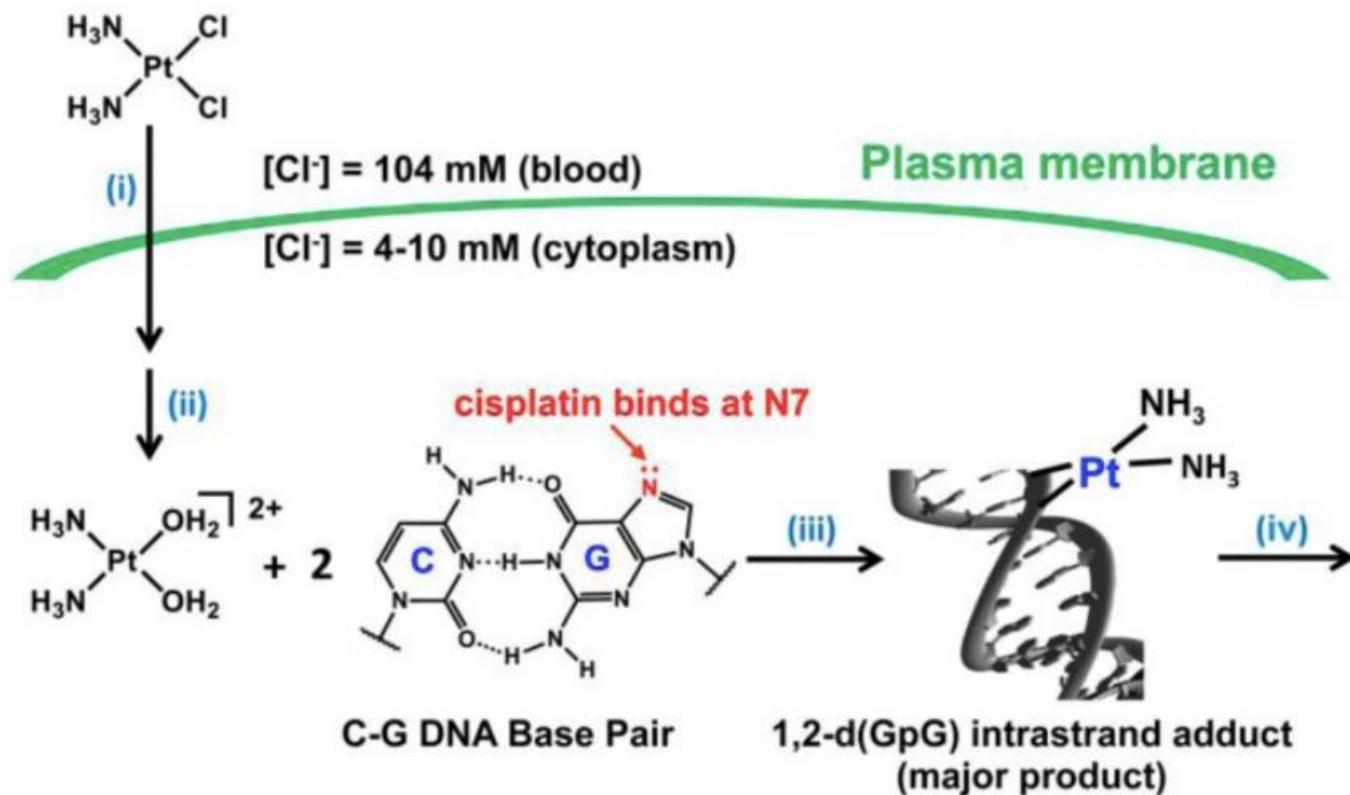


2 eq. of Na_2SO_3
→

Mechanism of Action



Mechanism of Action

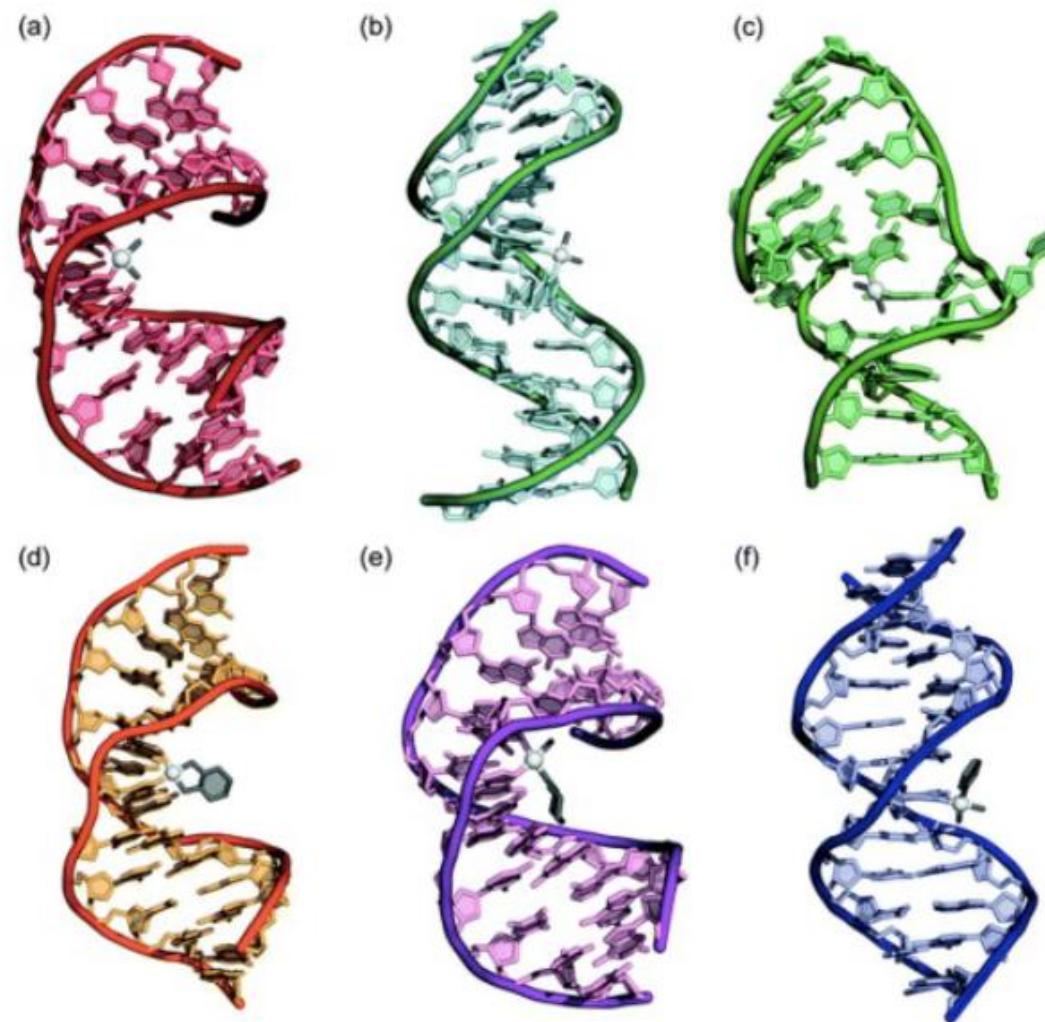


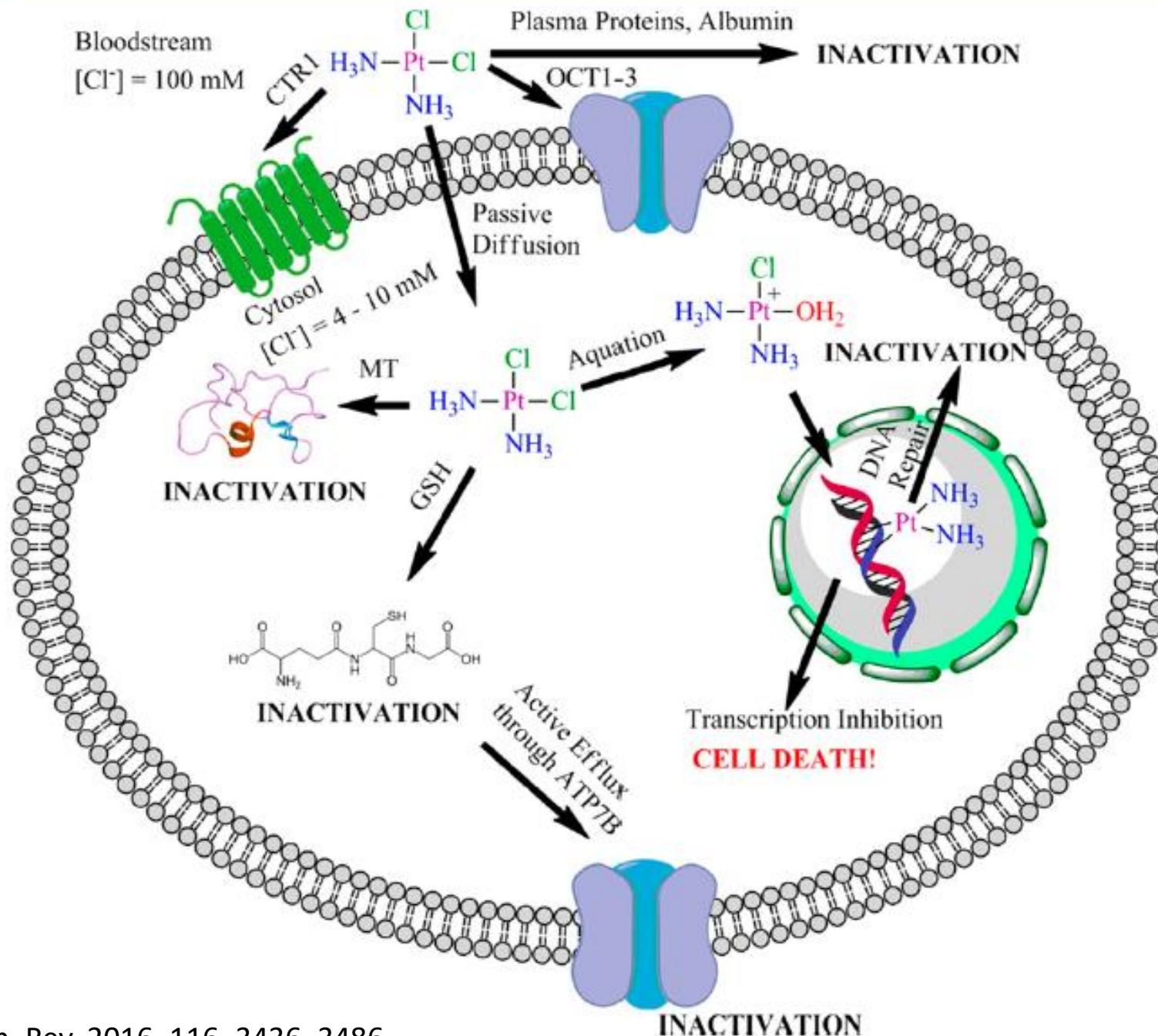
The four steps of the mechanism of cisplatin and, by extension, related platinum anticancer drugs. (i) Cellular uptake, (ii) aquation/activation, (iii) DNA binding, and (iv) cellular processing of DNA lesions leading to apoptosis

Cytotoxicity and Resistance mechanism

The structures of double-stranded DNA adducts of different platinum anticancer agents as determined by X-ray crystallography or NMR spectroscopy.

- (a) Cisplatin 1,2-d(GpG) intrastrand cross-link (PDB 1AIO).
- (b) Cisplatin 1,3-d(GpTpG) intrastrand cross-link (PDB 1DA4).
- (c) Cisplatin interstrand cross-link (PDB 1A2E).
- (d) Oxaliplatin 1,2-d(GpG) intrastrand cross-link (PDB 1PG9).
- (e) Satraplatin 1,2-d(GpG) intrastrand cross-link (PDB 1LU5). (f) cDPCP monofunctional adduct (PDB 3CO3)





Extracellular and intracellular events that influence cisplatin activity. Attention is drawn to instances where deactivation/sequestration can occur.

Chart 1. Chemical Structures of Clinically Approved and Marketed Platinum Anticancer Drugs

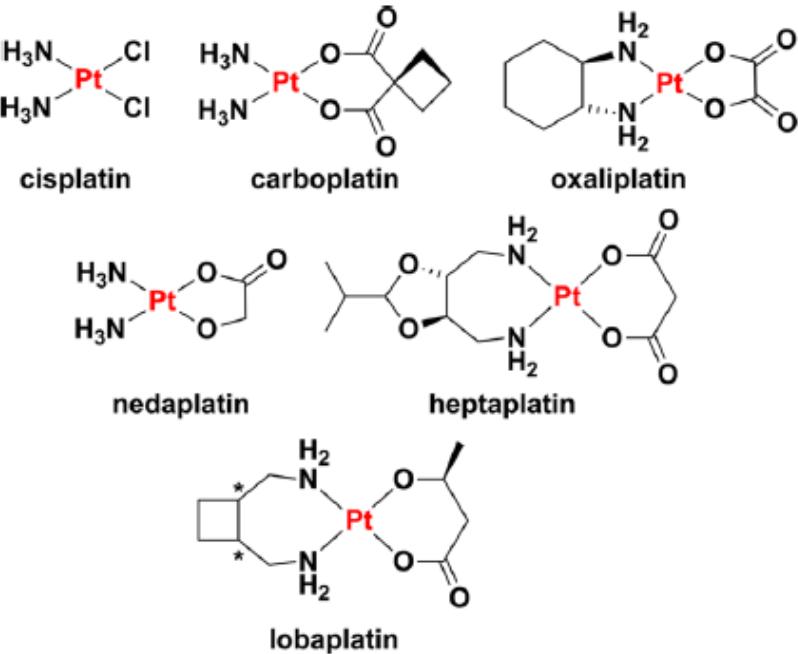
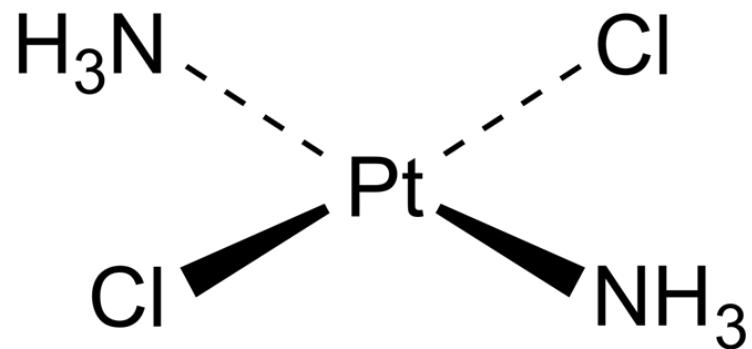
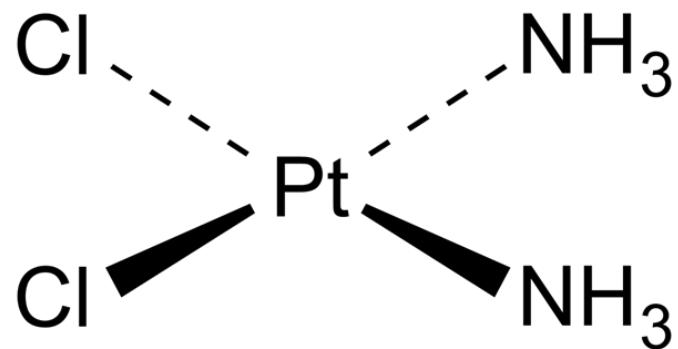


Table 1. Clinically Approved Platinum Anticancer Agents

Generic Name	Research Name	Trade Name	Approval Granted	Scope of Approval
Cisplatin	CDDP	Platinol	1978	Global
Carboplatin	JM8	Paraplatin	1989	Global
Oxaliplatin	I-OHP	Eloxatin	2002	Global
Nedaplatin	254-S	Aqupla アクプラ	1995	Japan
Heptaplatin	SKI 2053R	SunPla 선플라	1999	Korea
Lobaplatin	D-19466	洛铂	2010 ^a	China

^aSee main text for discussion.

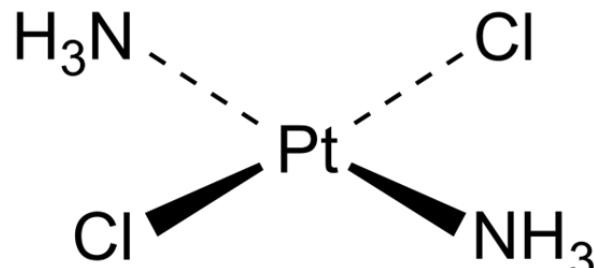
Why NOT *trans*-*Platin*?



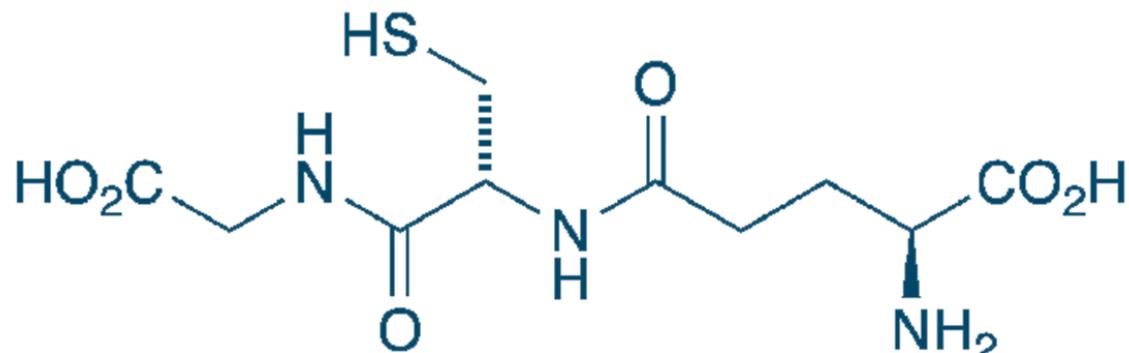
- Less reactive
- Long life
- Better efficiency

- Vigorously reactive
- Trans-effect enhances its reactivity with glutathione
- Poor efficiency

Why NOT *trans*-Platin?



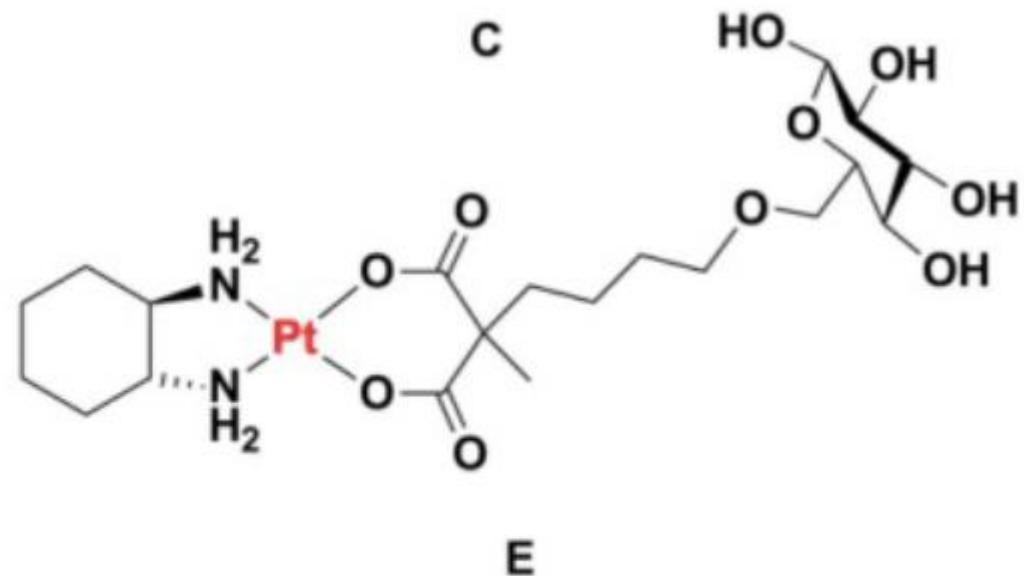
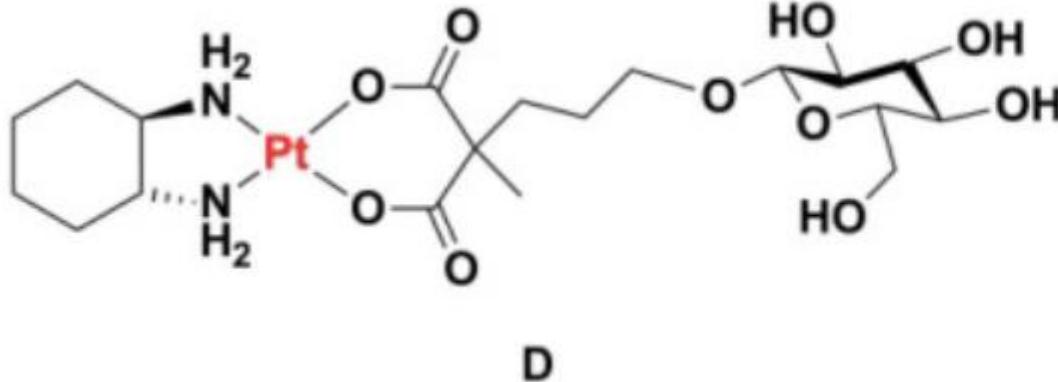
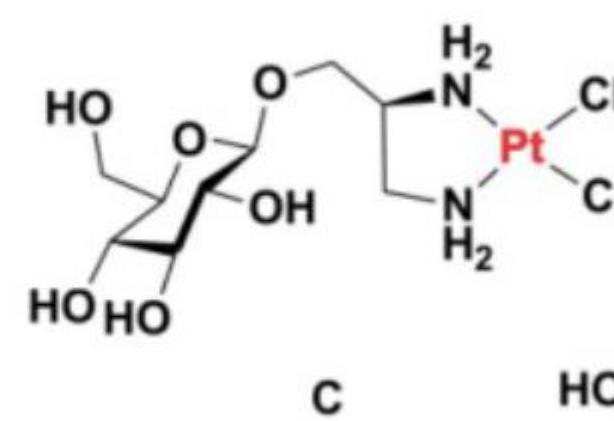
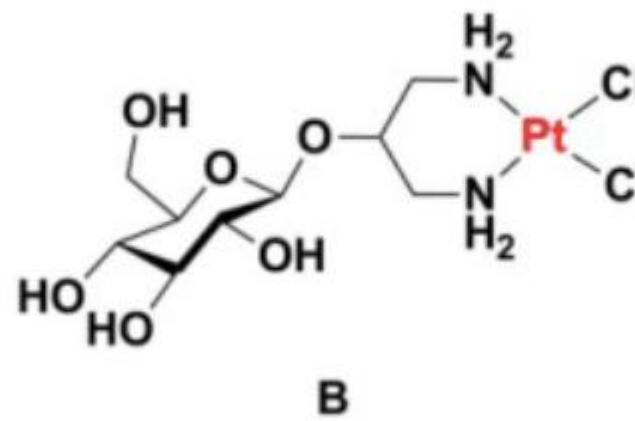
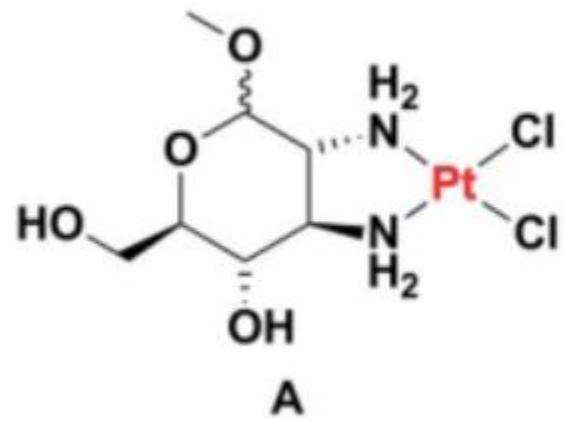
- Vigorously reactive
- Trans-effect enhances its reactivity with glutathione
- Poor efficiency



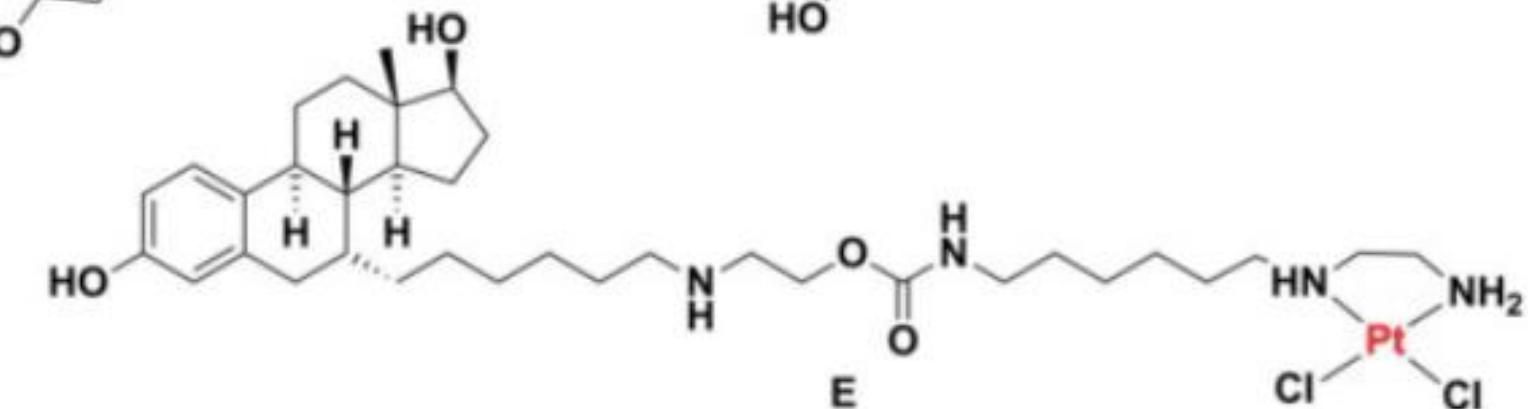
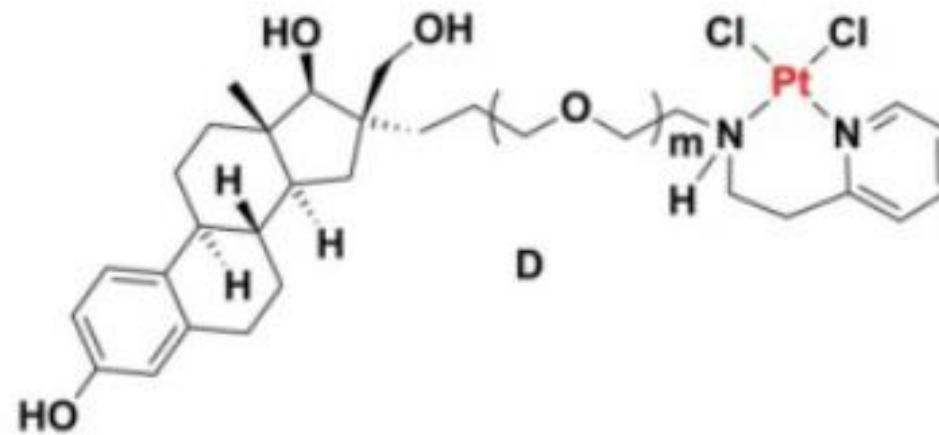
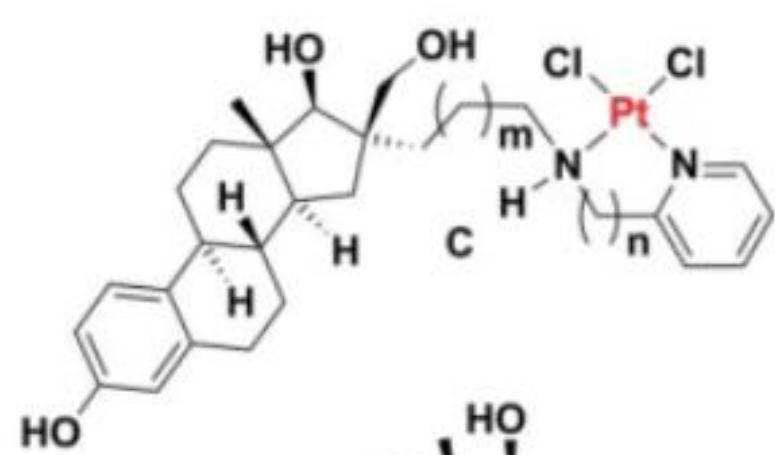
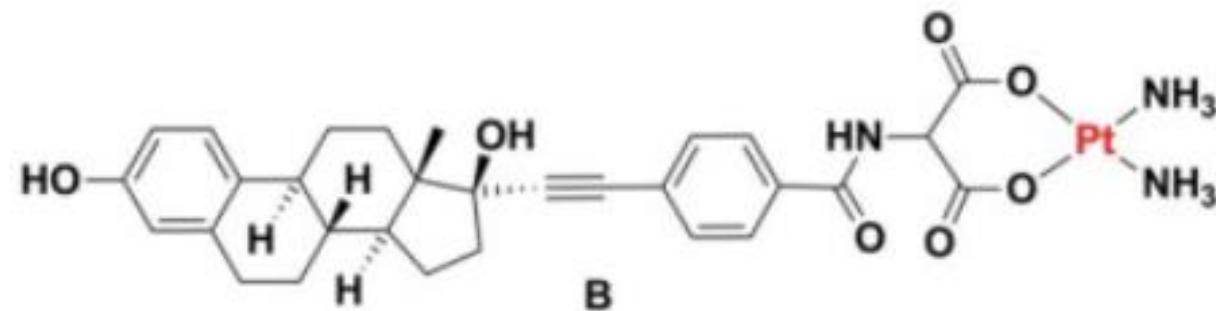
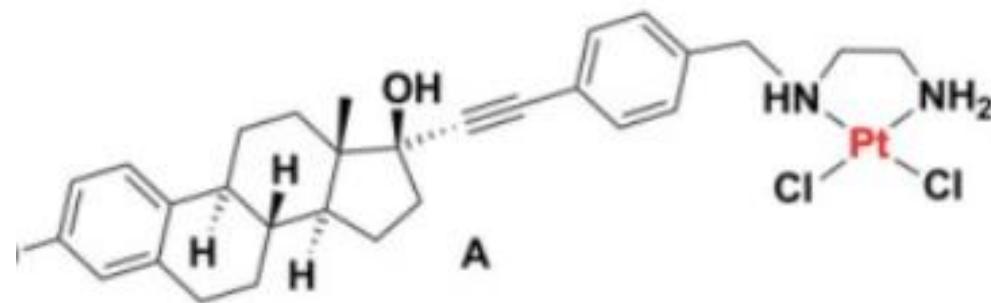
Glutathione plays a crucial role in antioxidant defense, detoxification processes, and maintaining cellular health

Feature	Cisplatin	Transplatin
Geometry	Cis (amine groups adjacent)	Trans (amine groups opposite)
Major DNA adducts	1,2-intrastrand crosslinks	Interstrand and monofunctional
DNA distortion	Marked, persistent kinks and shrinkage	Mild, transient—diminishes with time
DNA binding strength	High affinity, persistent	Low affinity, less stable
Biological effect	Efficiently blocks replication, apoptosis	Weak block, little cytotoxicity
Antitumor efficacy	Very high	Ineffective

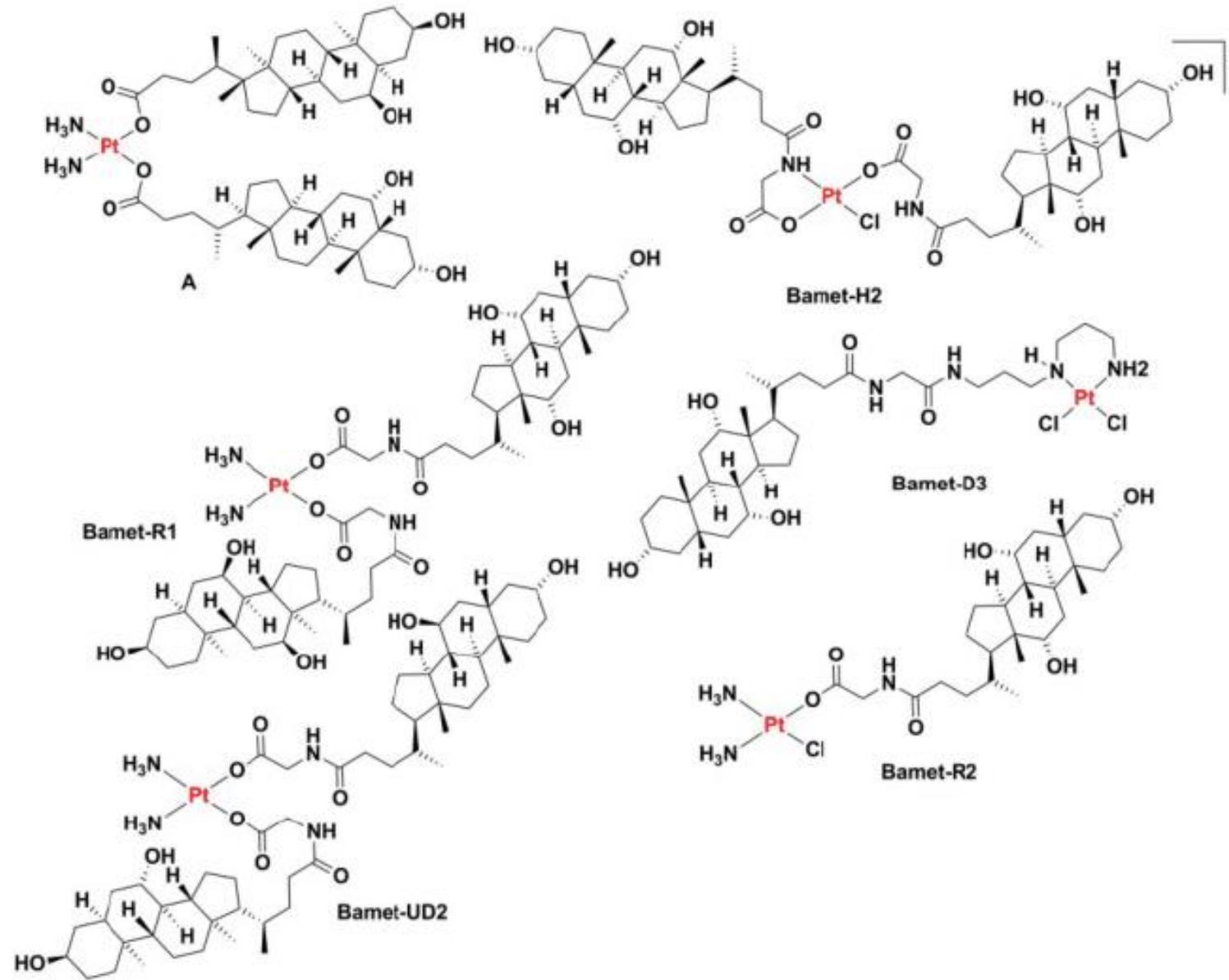
Chemical structures of sugar-conjugated platinum(II) complexes



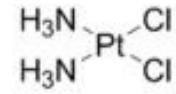
Chemical structures of estrogen receptor ligands tethered to Pt(II) complexes



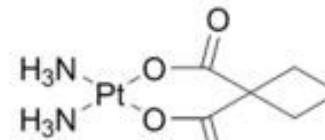
Chemical structures of bile-acid tethered Pt(II) agents



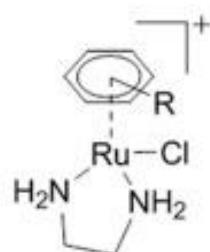
Intracellular Catalysis with Selected Metal Complexes and Metallic Nanoparticles: Advances toward the Development of Catalytic Metallocdrugs



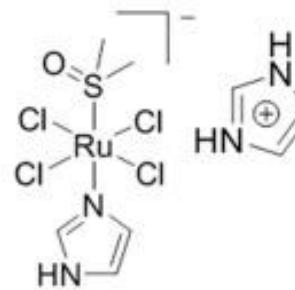
Cisplatin



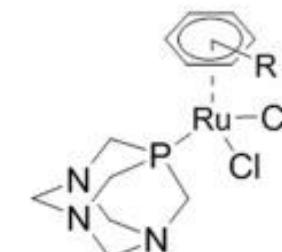
Carboplatin



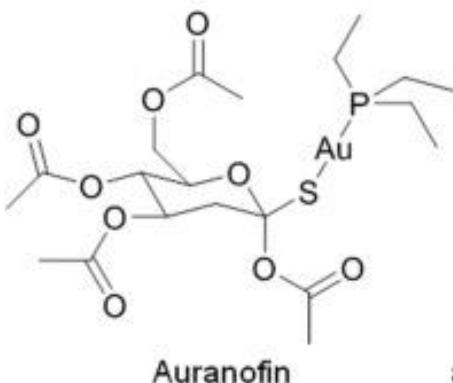
$[\text{areneRu}(\text{en})\text{Cl}]$



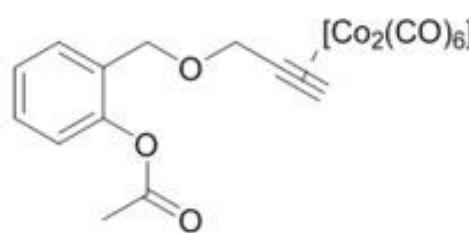
NAMI-A



Rapta-C



Auranofin



aspirin–hexacarbonyldicobalt conjugate

Chem. Rev. 2019, 119, 2, 829

Chemical structures of metal-based drugs and drug candidates which react only one time with their targets

Catalytic metallodrugs

First, metal compounds designed to perform reactions usually performed by natural enzymes (enzyme mimics). Of particular medicinal interest in this category are mimics of superoxide dismutase, but proteases (an enzyme that breaks down protein) and nucleases (a class of enzymes that degrade nucleic acids, *i.e.*, DNA and RNA) have also been studied for medicinal applications.

Second, metal complexes capable of generating reactive oxygen species (ROS), sometimes with a known mechanism and sometimes with unknown mechanisms. Also in this category are metal complexes that are capable of generating singlet oxygen inside cells upon irradiation with light (photodynamic therapy, PDT), which is a large field with metal compounds close to clinical application already.

Catalytic metallodrugs

Third, metal complexes are capable of degrading proteins, peptides, DNA, or RNA. In this category are compounds such as Ni^{II} and Cu^{II} compounds containing the ATCUN moiety (an amino terminal peptide with His in position 3) which have been shown to cleave proteins and RNA. Also in this category are [Co^{II}(cyclen)] derivatives, Cu^{II}-EDTA-biotin or Cu^{II}-1,10-phenanthroline-arenesulphonamide derivatives, which can cleave peptide deformylase, amyloids, streptavidin, carbonic anhydrase, and other proteins depending on their ligand design.

A fourth group of catalytic metallodrug candidates, which has moved into the focus recently. These compounds are capable of performing reactions well-known in the organic synthesis repertoire, such as C–C cross-coupling reactions, cycloadditions, hydrogenation, and transfer hydrogenation reactions, thiol oxidation, or functional group deprotection reactions, inside living cells. It is also worth noticing that some of those catalytic reactions have been used for the *in situ* labelling of proteins, thus allowing the study of such proteins or their functionalization.

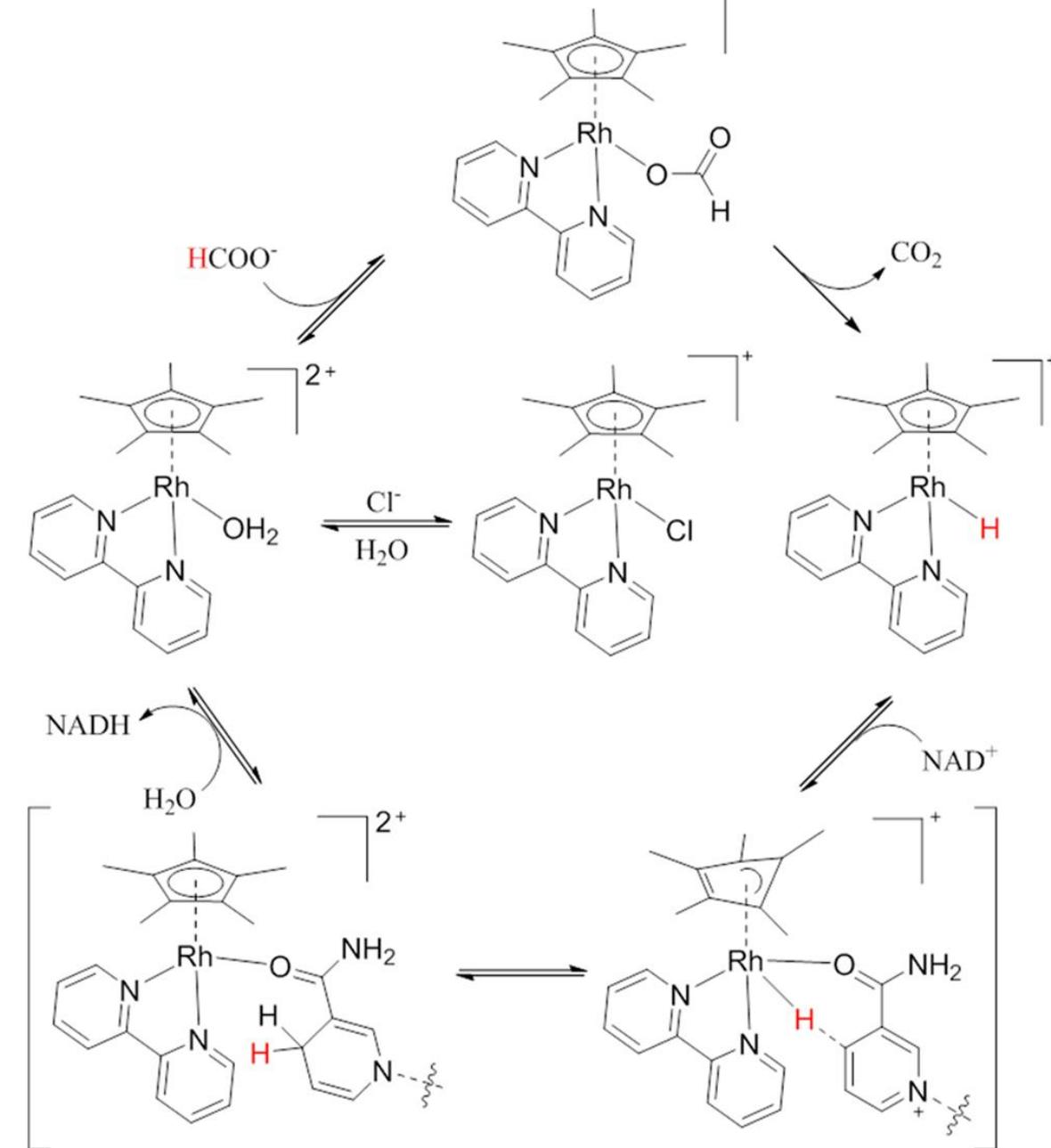
Advances toward the Development of Catalytic Metallocdrugs

NADH (nicotinamide adenine dinucleotide in its reduced form) plays a vital role in cellular metabolism, particularly in energy production through the mitochondrial electron transport chain, where it donates electrons for ATP synthesis.

Example of biomolecule transformation:

Reduced Nicotinamide Adenine Dinucleotide (NADH) Regeneration and Reduction of Pyruvate.

In 1991, Steckhan et al. developed the first series of TH catalysts that were capable of regenerating NADH in aqueous media, pH 7 and 37 °C (i.e., under biologically relevant conditions), using high concentrations of formate as hydride source. Organometallic Rh^{III} bipyridine (bpy) complexes were shown to reduce NAD⁺ efficiently with high turnover frequencies. **The most active compound presented was [Cp*Rh^{III}(bpy)Cl]⁺ with a TOF of 77.5 h⁻¹**



Metals Used in Various Diagnosis and Treatments!

X-ray Imaging Contrast Agent

Single Photon CT Scan

MRI
Contrast
Agent

MRI Contrast Agent

Cu⁶⁴ in Positron Emission Tomography (PET) imaging

X-ray
Imaging
Contrast
Agent

X-ray Imaging Contrast Agent

MRI
Contrast
Agent

SERS Assisted Imaging

Paramagnetic Metal Ions As MRI Contrast Agents!



Chemistry of MRI Contrast Agents: Current Challenges and New Frontiers

MRI contrast agents help by enhancing the visibility of internal tissues and abnormalities, primarily by altering the relaxation times (T1 and/or T2) of nearby water protons. This manipulation increases the difference in signal intensity between normal and abnormal tissues, making certain structures stand out more clearly on MRI scans.

- **T1 Shortening (Positive Contrast Agents):**

- Most clinically used contrast agents, such as gadolinium-based compounds, are paramagnetic and shorten the T1 relaxation time of nearby protons.
- This makes those areas appear **brighter** on T1-weighted images, improving the detection of lesions, tumors, blood vessels, and areas of abnormal breakdown in the blood-brain barrier.

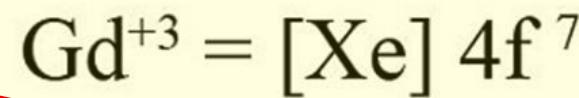
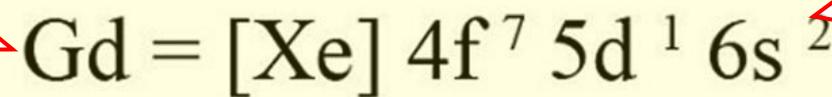
- **T2 Shortening (Negative Contrast Agents):**

- Some agents, especially superparamagnetic iron oxide particles, shorten the T2 or T2* relaxation time.
- This makes affected tissues appear **darker** on T2-weighted images, which is helpful for certain organ targeting and cell tracking applications.

Metal Ions (Gd^{3+} , Fe^{3+} , Mn^{2+}) as MRI Contrast Agents!



The Best!!



Not in use anymore

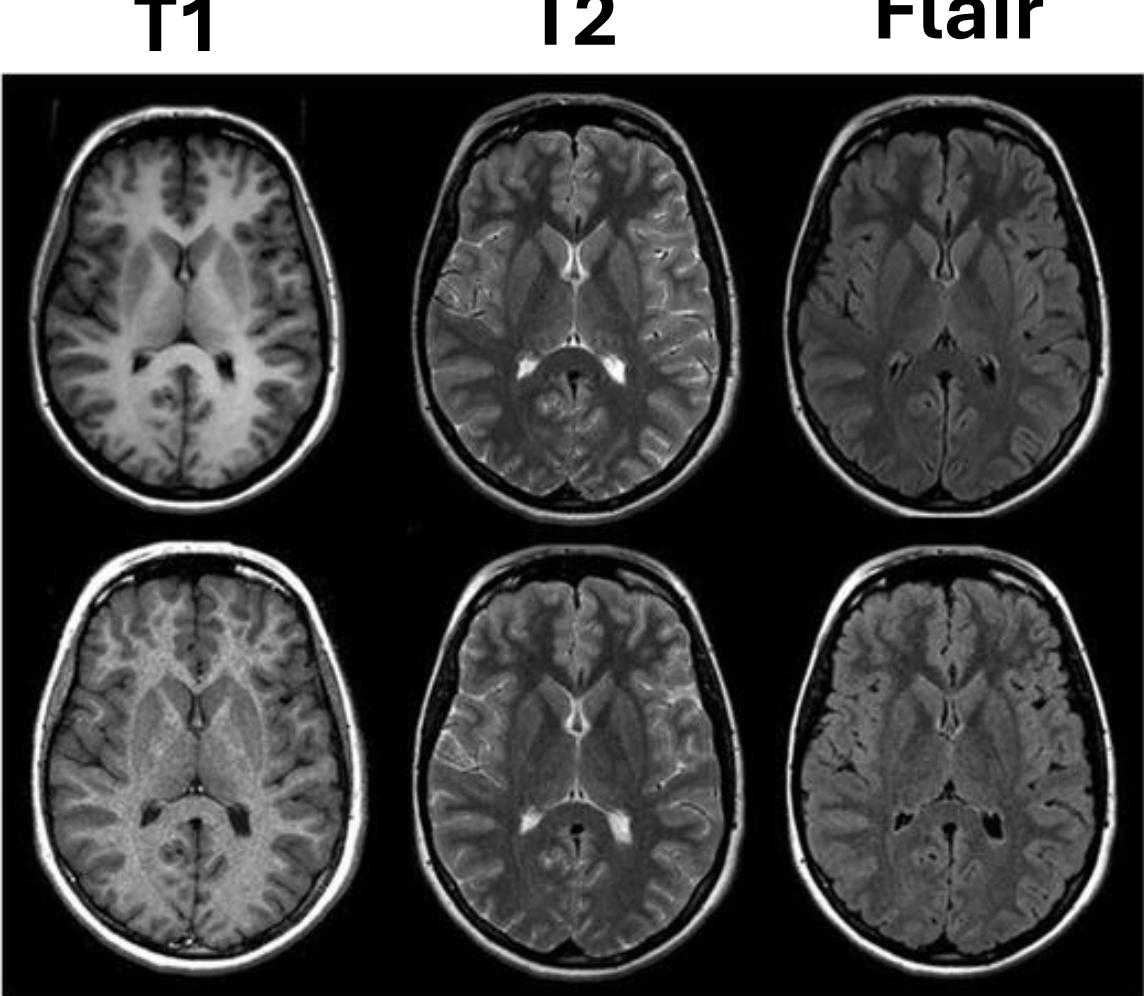
MRIs with Different Relaxations!

👉 **Shorter T₁ (like in fat)** → Spins recover quickly, appearing **bright** on T₁-weighted images.

👉 **Longer T₁ (like in water)** → Spins recover slowly, appearing **dark** on T₁-weighted images.

👉 **Shorter T₂ (like in muscle)** → Loses sync fast, appearing **dark** on T₂-weighted images.

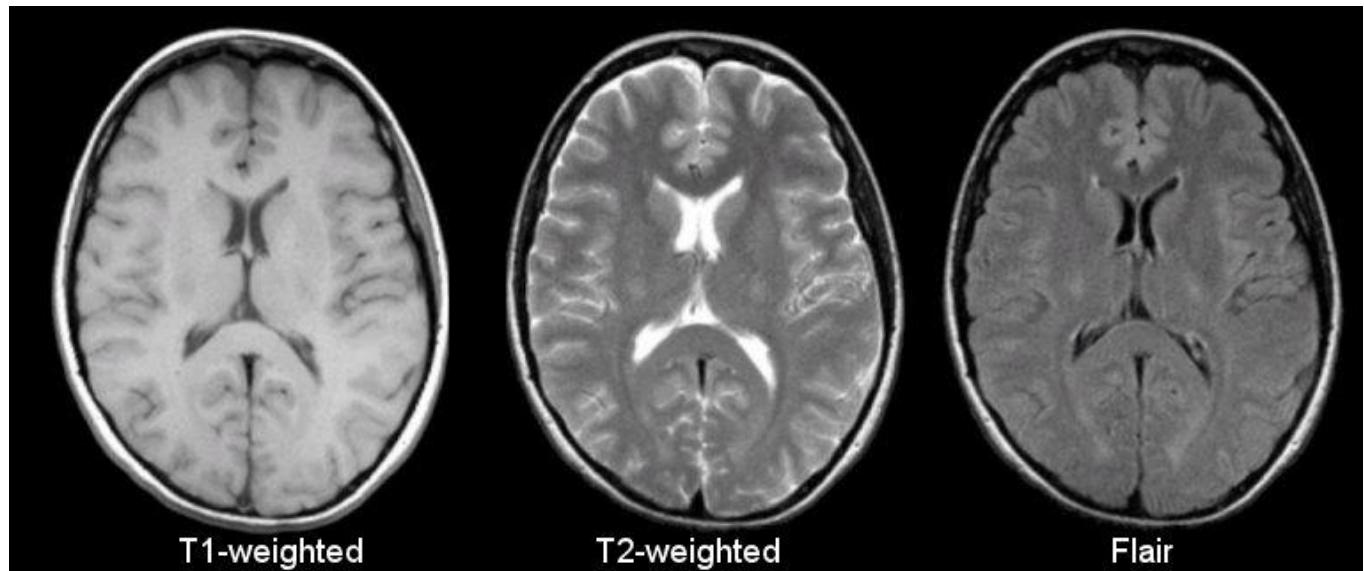
👉 **Longer T₂ (like in water)** → Stays in sync longer, appearing **bright** on T₂-weighted images.



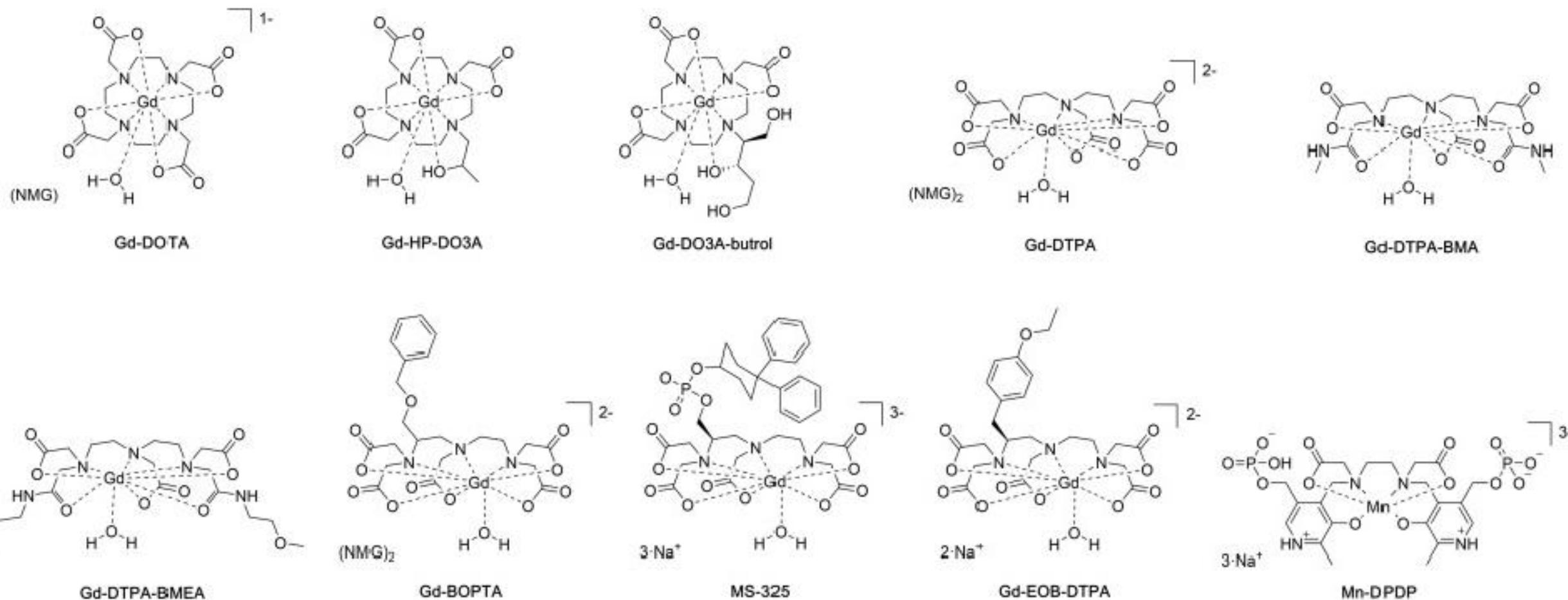
A FLAIR image in MRI refers to a specialized sequence called Fluid-Attenuated Inversion Recovery, which is primarily used to suppress the signal from cerebrospinal fluid (CSF) while retaining strong T2-weighted contrast—this makes lesions and abnormalities in the brain more visible, especially those near the ventricles or cortical surface.

How the Contrasting Agents Improve T1 and T2 Relaxations?

- They speed up the T1 relaxation and delay the T2 relaxation because of the large number of unpaired (paramagnetic) electrons in them.
- These unpaired electrons exert a strong magnetic field in tissues being mapped!

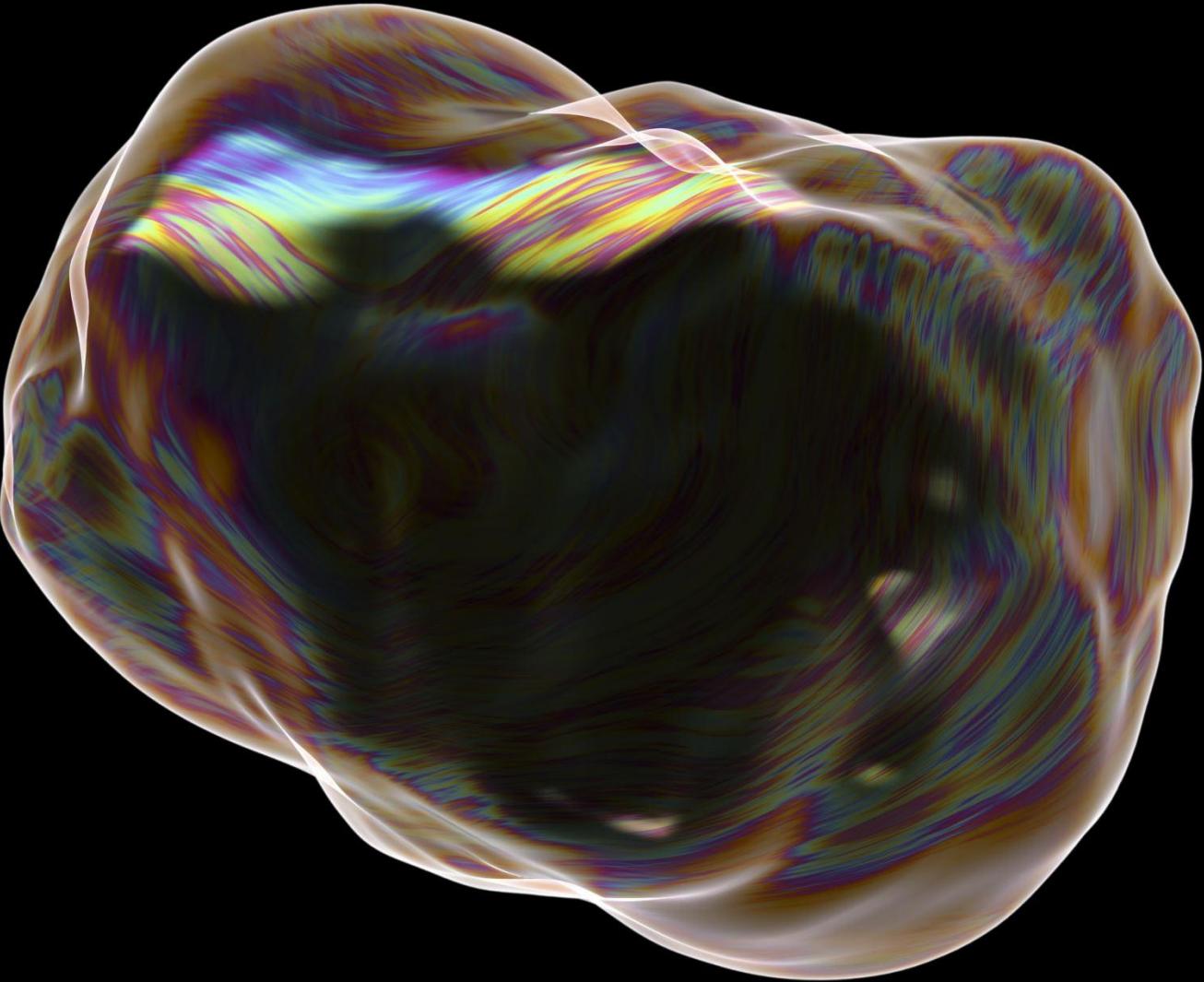


Chemistry of MRI Contrast Agents: Current Challenges and New Frontiers

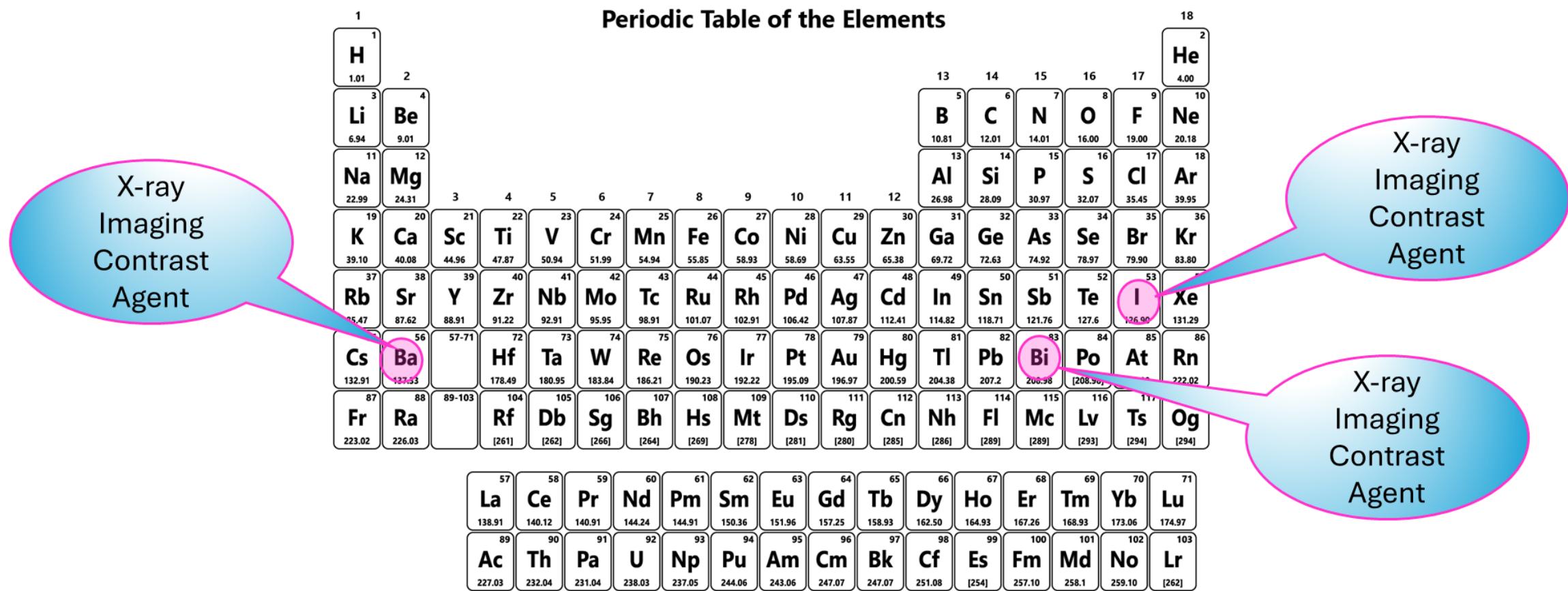


MRI contrast agents shorten the relaxation times of nuclei within body tissues following oral or intravenous administration. According to biodistribution and applications, MRI contrast agents may be categorised into three types: extracellular fluid, blood pool and target/organ-specific agents

Metal Ions as
X-ray Imaging
Contrast
Agents!



The Choice of X-Ray Contrast Agents!





Why only These?

- Not so toxic
- They have high atomic number
- Radiopaque in nature
- Easily secreted out by your kidneys

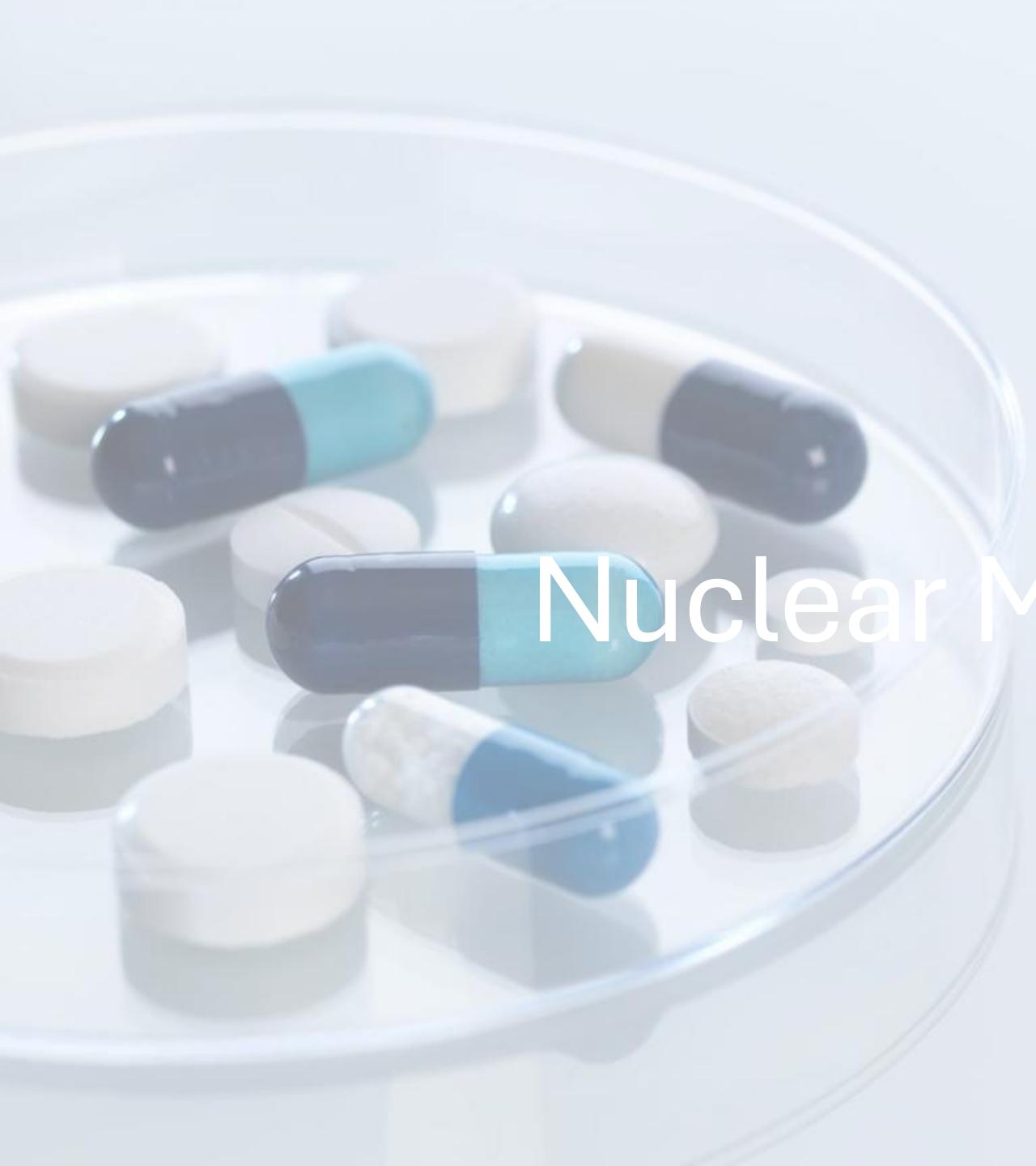


With BaSO_4 Ingestion

How do they work?

- High atomic number is the reason
- So, they can absorb more X-ray photons
- When the X-ray film detects the photons passing through other soft tissues, the part ingested with contrast agents would appear brighter





Nuclear Medicines!

What are they and how they are different?

- These are metals and their compounds with radioactivity.
- Their chemistry interest the least, but their radioactivity delivers the desires in treatment and diagnosis
- These are mainly used as/in
 - Radiopharmaceuticals in Therapeutic Applications
 - Imaging Techniques



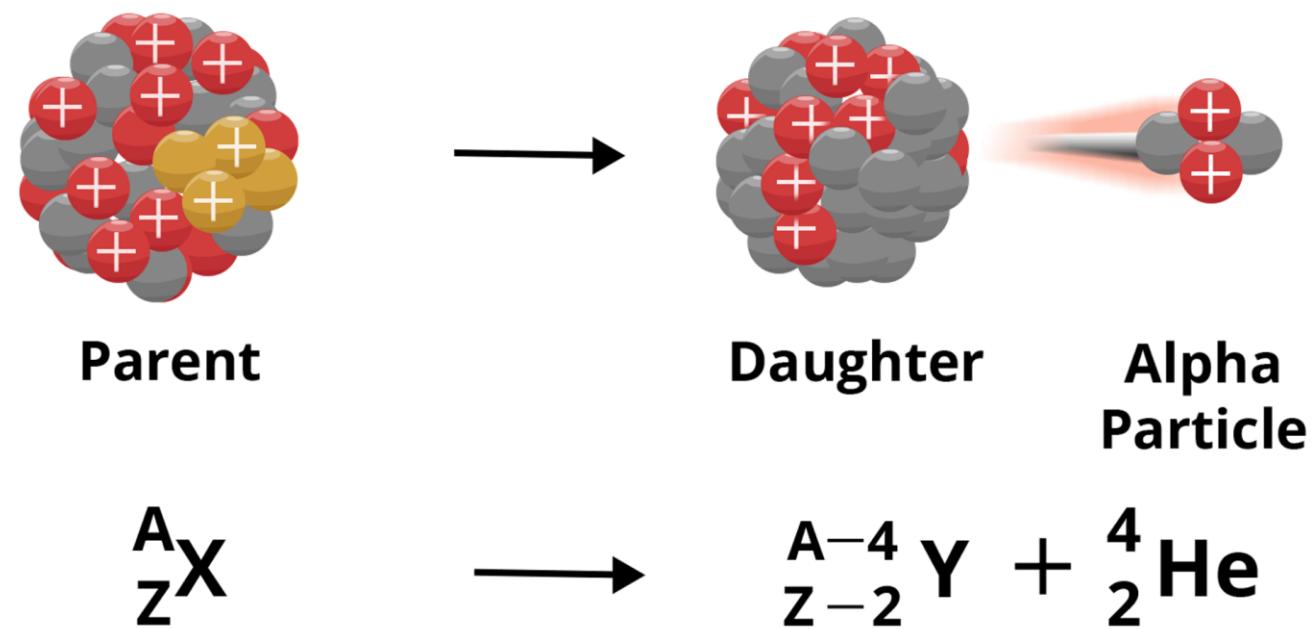
Basics of Radioactivity: Radioactive Decay!

An unstable atomic nuclei lose energy by emitting radiation, transforming into more stable nuclei

- This process changes the original atom into a different element or a different isotope of the same element.

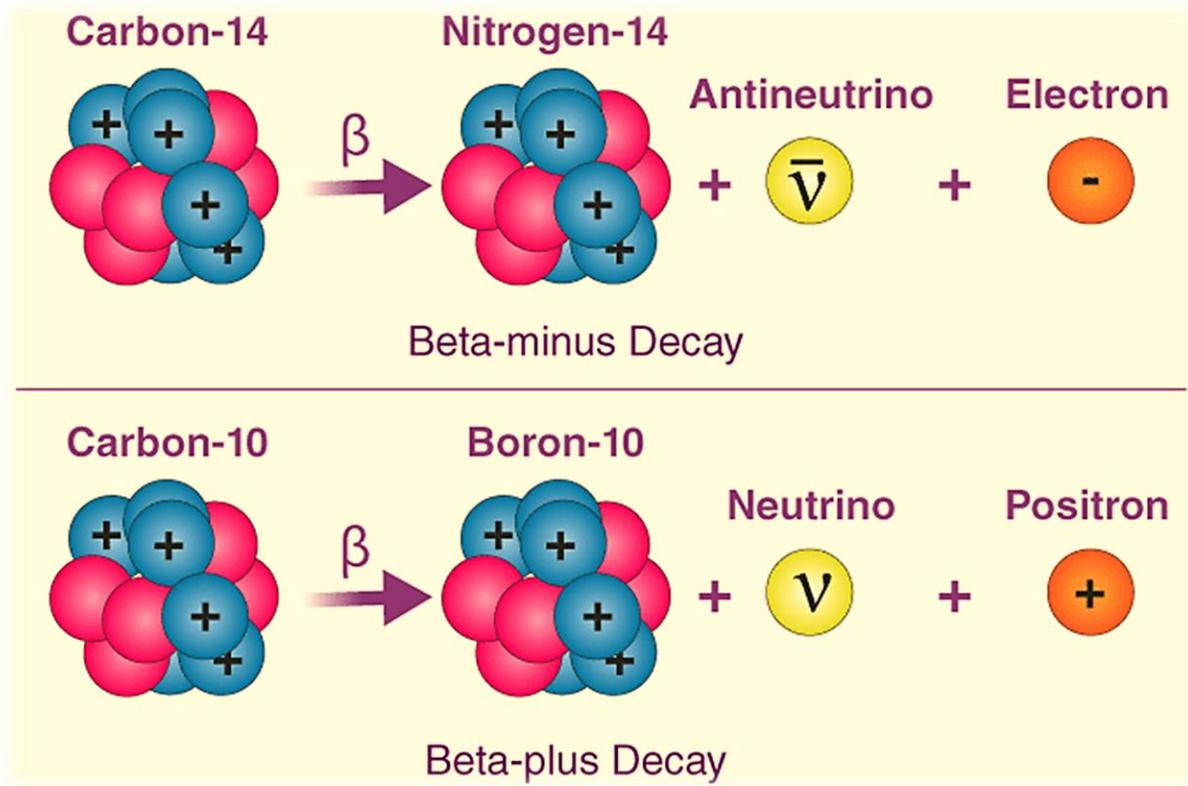
Alpha Decay (α -decay)

- An α particle consists of 2 protons and 2 neutrons (equivalent to a He nucleus/ or He^{2+} ion).
- This decreases the atomic number by 2 and the atomic mass by 4.
- Example: U^{238} decays to Th^{234} by emitting an α particle.



Beta Decay (β -decay)

- A neutron is transformed into a proton, or vice versa
- Resulting in the emission of a beta particle (either an electron or a positron).
- **Beta-minus (β^-) decay:** A neutron converts into a proton and emits an electron and an antineutrino. The atomic number increases by 1, but the mass remains unchanged.
- **Beta-plus (β^+) decay:** A proton converts into a neutron, emitting a positron and a neutrino. The atomic number decreases by 1.



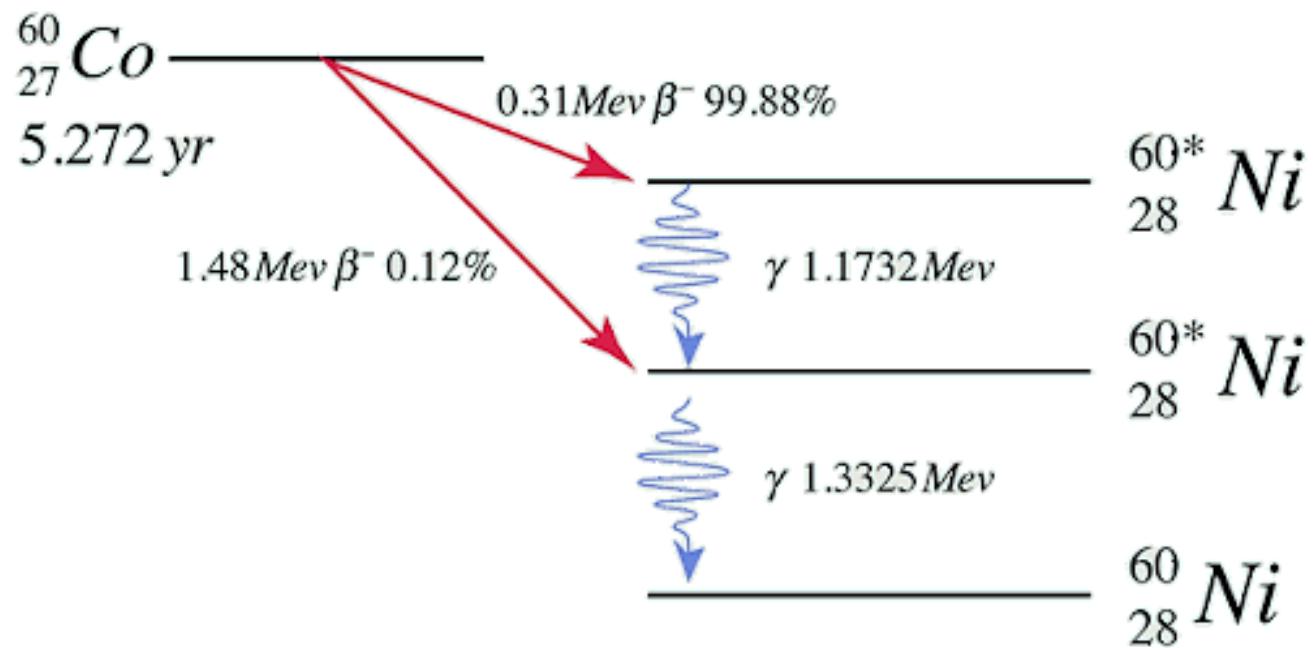
Neutron: A heavier particle made of other smaller particles found in atomic nucleus

Neutrino: A tiny fundamental particle with very low mass

P.S. **Neutrino** and **Antineutrino** have the same mass and are chargeless but have different spin.

Gamma Decay (γ -decay)

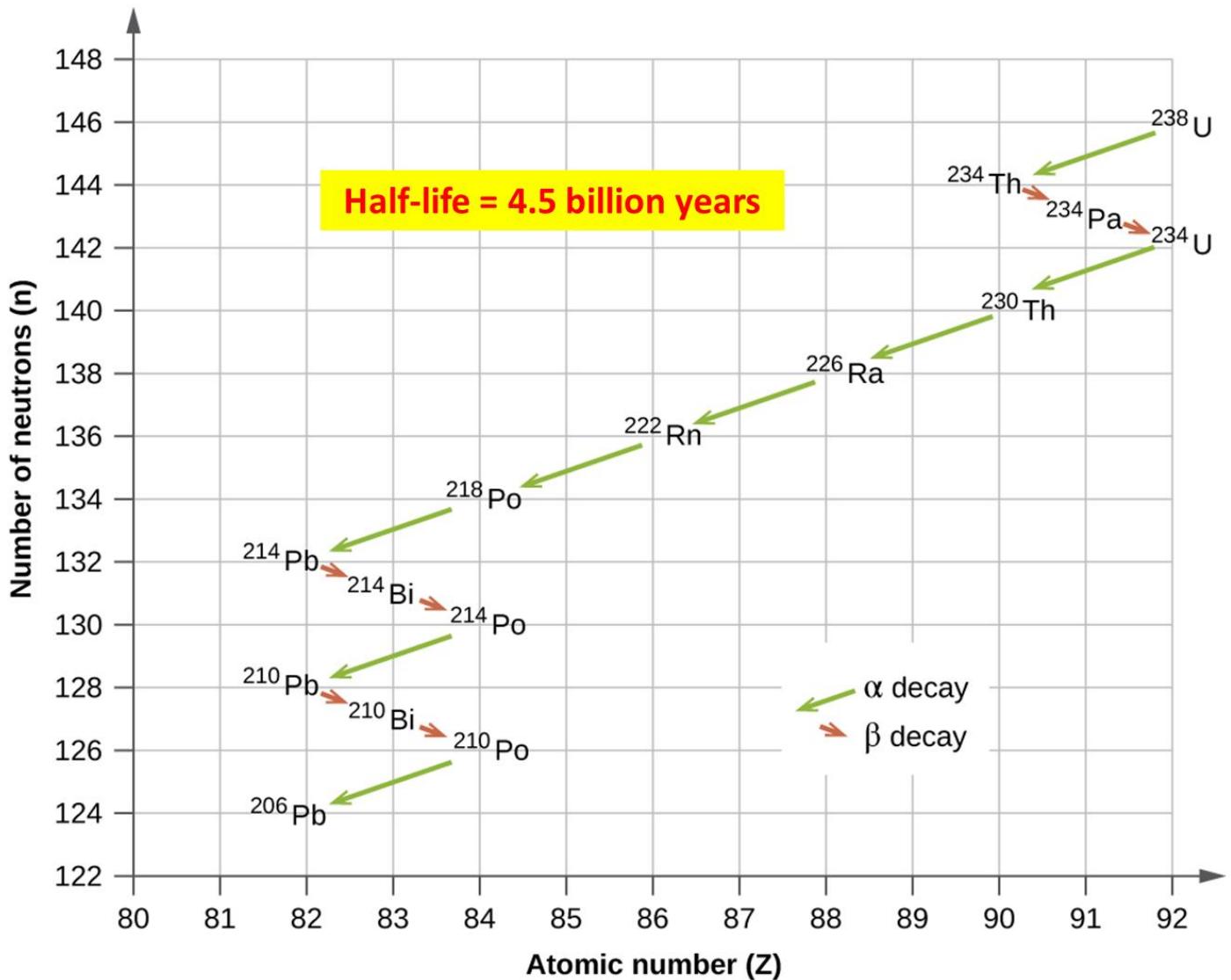
- In γ decay, an excited nucleus releases excess energy by emitting a gamma photon (a high-energy photon).
- Gamma decay does not change the atomic number or mass,
- It involves only the release of energy without changing the number of protons or neutrons.
- Cobalt-60 undergoes gamma decay after beta decay to release excess energy.



Decay Chain!

Decay Energy and Radiation Emission

- Radioactive decay releases energy, typically in the form of kinetic energy of emitted particles and gamma radiation.
- This energy can ionize atoms and molecules, which is the basis for both the biological effects of radiation and its detection in nuclear medicine.



Radiotherapy!

Drugs combined with radioactive isotopes for specific targeting within the body

1. External Beam Radiotherapy (EBRT)
2. Internal Radiotherapy (Brachytherapy)
3. Systemic Radiotherapy



External Beam Radiotherapy (EBRT) vs Internal Radiotherapy (Brachytherapy)

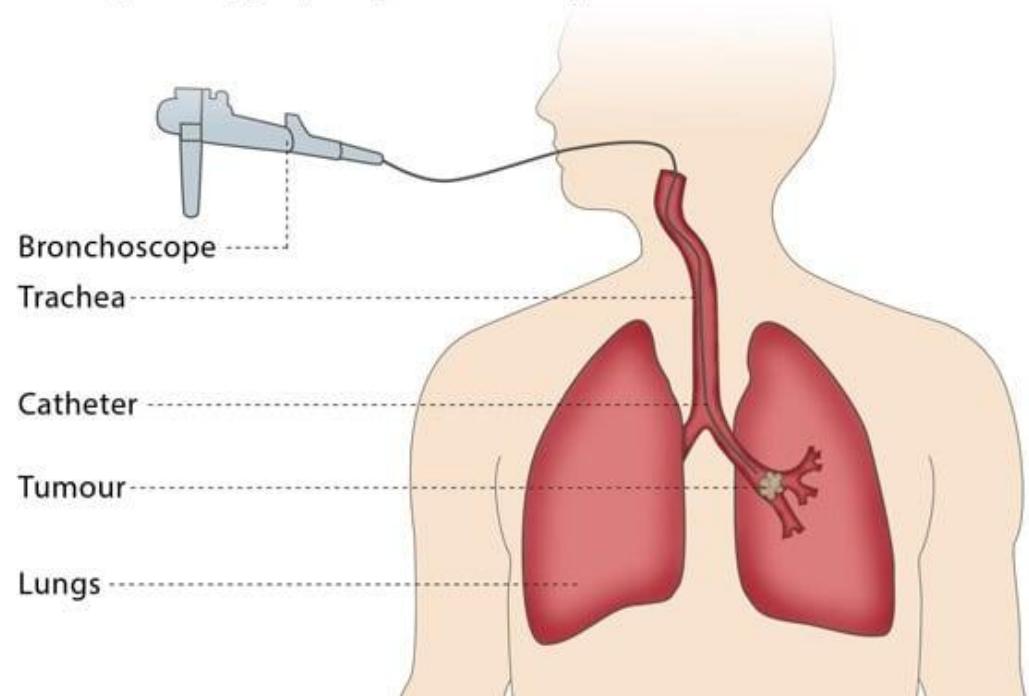
EBRT uses machines like linear accelerators to deliver high-energy radiation beams

- e.g., gamma rays or X-rays from outside the body, targeting the tumour.
- Co^{60} , a radioactive isotope, is often used as a gamma-ray source in EBRT.

In brachytherapy, a radioactive source is placed inside or near the tumour.

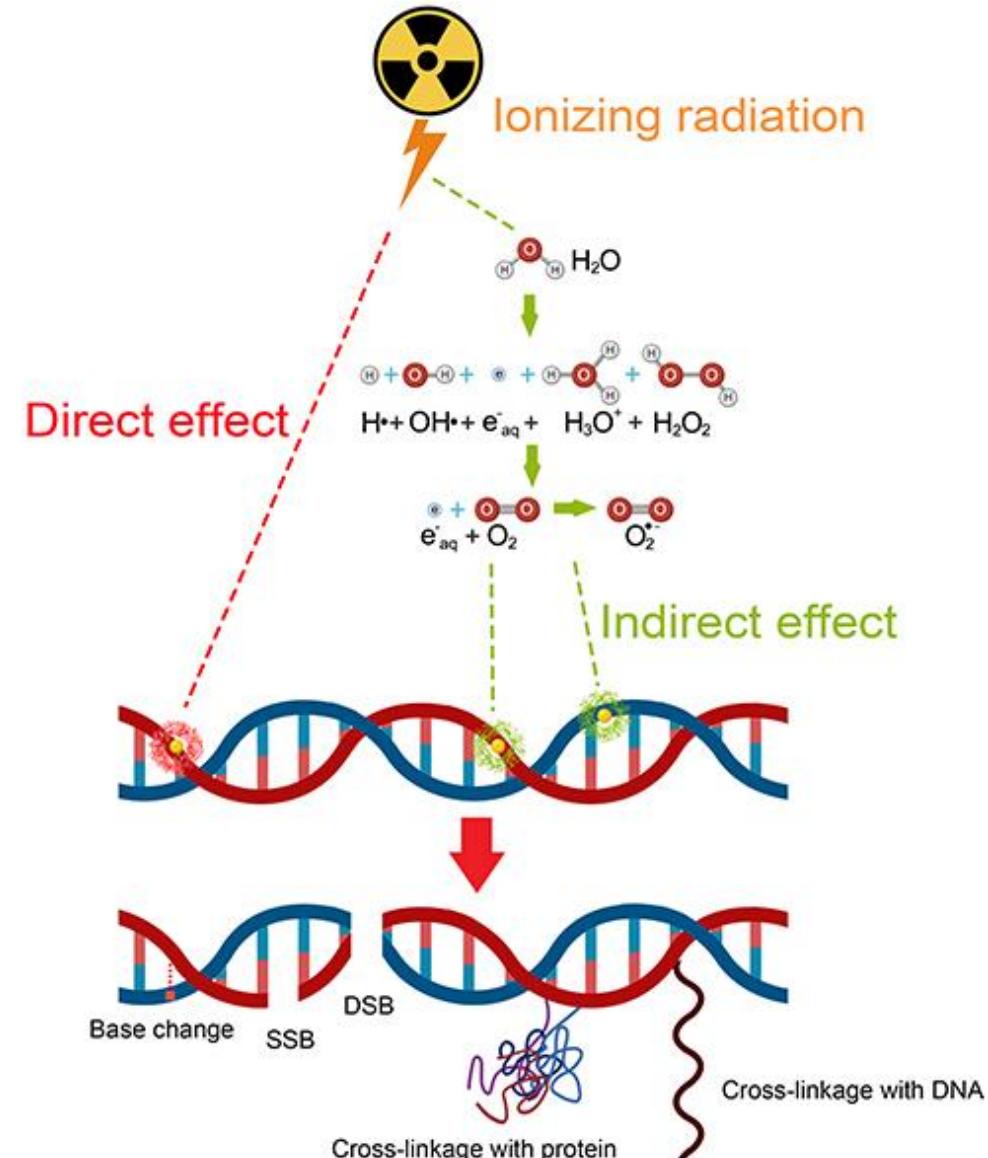
- Commonly used for cancers of the prostate, cervix, breast, and head and neck.
- I^{125} , Ir^{192} , and Cs^{131} are commonly used

Brachytherapy (example in the lung)



Mechanism of Action!

- The radiation emitted by radioactive isotopes causes ionization, which damages the DNA in cancer cells.
- This DNA damage prevents the cells from dividing and growing, leading to cell death.
- Cancer cells are generally more sensitive to radiation than normal cells due to their rapid growth rate.



Systemic Radiotherapy!

Injecting or swallowing radioactive isotopes, which travel through the bloodstream and target cancerous cells

- **Iodine-131** is commonly used to treat thyroid cancer because the thyroid gland naturally absorbs iodine, allowing precise targeting.
- **Radium-223** is used to treat bone metastases in prostate cancer
- **Lutetium-177** and **Yttrium-90** are used in peptide receptor radionuclide therapy (PRRT), targeting neuroendocrine tumors.
 - Both Lu-177 and Y-90 are **linked to somatostatin analogs**

