Examples of ionophores with the ions upon which they act.
Valinomycin (K⁺)
Salinomycin (K⁺)
Gramicidin A (H⁺, Na⁺, K⁺) ---- It is a transmembrane channel forming ionophore.
Nonactin (NH₄⁺)
Ionomycin (Ca²⁺)
2,4-Dinitrophenol (H⁺)
Monensin (H⁺, Na⁺) ---- used in cattle feed

* Crown ethers are the laboratory analogues of ionophores.

41.12) Why Gadolinium salts are used as MRI agents?
* A good MRI agent should have following characteristics:
  1) High magnetic moment;
  2) Long electron-spin relaxation time;
  3). Low toxicity;
* Gd³⁺ salts like [Gd(dtpa)(H₂O)]²⁻ (gadopentetate dimeglumine) and [Gd(dota)(H₂O)]⁻ (gadoterate meglumine) fit this for the purpose.

Practice questions
1) Identify one significant role in biological processes for the elements Fe, Mo, Mn and Cu.

2) In biological systems, the metal ion involved in the dioxygen transport besides Fe is
   a) Co       b) Zn       c) Mg       d) Cu

3) In photosynthesis, the predominant metal involved in the reaction centre of photosystem II is
   (a) Zn       (b) Mn       (c) Fe       (d) Cu

4) Zn in carbonic anhydrase is coordinated by three histidine and one water molecule. The reaction of CO₂ with this enzyme is an example of
   (a) electrophilic addition       (b) electron transfer
   (c) nucleophilic addition       (d) electrophilic substitution.

5) The metals involved in nitrogenase are
   (a) Fe and Mg       (b) Mo and K       (c) Mo and Fe       (d) Fe and K

6) The transition metal present in vitamin B₁₂ is_______

7) The trivalent ion of lanthanoid element which is used as NMR contrasting agent is
   1) Gadolinium  2) Technetium  3) Cerium  4) Lutetium

8) Match the following
   1) Li⁺       A) Ulcer treatment
   2) Bi³⁺      B) Eczema
   3) Sb³⁺      C) Anemia
   4) Fe²⁺      D) Depression

9) The enzyme which removes C-terminal amino acid from a peptide is
   1) Carbonic anhydrase  2) Carboxy peptidase  3) Zymase  4) All
Hint: The stability constant of complex formed by valinomycin with $K^+$ is $10^6$, whereas that with $Na^+$ is 10.

42) Non-heme iron-sulfur proteins are involved in:
1. Electron transfer.
2. Proton transfer.
3. Both electron and proton transfer
4. Oxygen transfer.

**Explanation**
* Iron-sulfur proteins are proteins characterized by the presence of iron-sulfur clusters containing sulfide-linked di-, tri-, and tetrariron centers in variable oxidation states.
E.g., Ferredoxins, as well as NADH dehydrogenase, hydrogenases, nitrogenase etc.,
* Iron-sulfur clusters are best known for their role in the oxidation-reduction reactions of mitochondrial electron transport.
* Additionally some Fe-S proteins regulate gene expression.
* Fe-S proteins are vulnerable to attack by biogenic nitric oxide.

In most iron-sulfur proteins, the clusters function as electron-transfer groups.

**Additional information:**
1) **Ferredoxins:** are small proteins containing iron and sulfur atoms organized as iron-sulfur clusters. These biological "capacitors" can accept or discharge electrons, the effect being change in the oxidation states (+2 or +3) of the iron atoms. Thus ferredoxin acts as electron transfer agents in biological redox reactions.

The following diagram illustrates the redox scheme between low-potential and high-potential (HiPIP) ferredoxins containing Fe$_4$S$_4$ clusters. The formal oxidation numbers of the iron ions can be [2Fe$^{3+}$, 2Fe$^{2+}$] or [1Fe$^{3+}$, 3Fe$^{2+}$] in low-potential ferredoxins. The oxidation numbers of the iron ions in high-potential ferredoxins can be [3Fe$^{3+}$, 1Fe$^{2+}$] or [2Fe$^{3+}$, 2Fe$^{2+}$].

Following is Fe$_2$S$_2$ type of ferredoxin.

Note: High potential iron-sulfur proteins (HiPIPs) form a unique family of Fe$_4$S$_4$ ferredoxins that function in anaerobic electron transport chains.

* Aconitase hydratase contains Fe$_3$S$_4$ cluster in active form and Fe$_5$S$_4$ cluster in inactive form.
* Rubredoxin is considered as another iron-sulfur protein which does not contain inorganic sulfide. It is also an electron transport agent.
* Hb coordinated to dioxygen is called oxy-hemoglobin. It is also referred to as R-state (relaxed). In oxy-hemoglobin the sixth coordinated position of iron is occupied by dioxygen in ‘end on bent’ geometry.
* In deoxy-Hb, the porphyring ring is dome shaped. Fe(II) is in high spin state and is paramagnetic. It is bigger in size (0.78 Å) and situated above the plane of the porphyring ring.
* In oxy-Hb, the iron is in low spin state and diamagnetic. It is smaller in size (0.61 Å) and can fit into the cavity of porphyrin ring (which now becomes planar). Now Fe(II) can move into the cavity of porphyrin ring and drags the proximal histidine which inturn triggers the confirmational changes in other globin subunits and opening of other heme sites. As a result, enhances the binding capacity of other heme irons (cooperativity through allostery).

* There are two theories to explain the nature of Fe in oxy-Hb or oxy-Mb.
**Pauling model:** Suggests presence of low spin Fe(II) and singlet O₂. Both are diamagnetic.
**Weiss model:** Suggests presence of Fe(III) and superoxide radical anion (O₂⁻). Both are paramagnetic. But strong paramagnetic coupling results in diamagnetic nature. The O-O...
42.12) What is the active site in Hemerythrin? Mention its role in marine invertebrates?
Ans:- Hemerythrin is a iron containing NON HEME oligomeric protein which transports \( \text{O}_2 \) in marine invertebrates. It is a respiratory protein.

The monomer of hemerythrin is myohemerythrin, which is present in the muscles of marine invertebrates and stores dioxygen. (hemerythrin contains 8 subunits)

Deoxy forms are colorless, whereas oxy forms are violet pink in color.

**Active site:** The oxygen binding site is a binuclear iron centre. Deoxyhemerythrin contains two high-spin ferrous ions bridged by hydroxyl group

The iron ions are coordinated to the protein through the carboxylate side chains of *one glutamate, one aspartate, and five histidine* amino acid residues. *One iron is hexacoordinate and another is pentacoordinate.*

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\begin{align*}
\text{His} & \quad \text{His} \\
\text{Asp} & \quad \text{Asp} \\
\text{His} & \quad \text{His} \\
\end{align*}
\]
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The pentacoordinated Fe(II) binds a triplet dioxygen(\( \text{O}_3 \)) and oxidized to Fe(III). Then the hydrogen on hydroxy group is transferred onto peroxide group. Now the second Fe(II) is also oxidized to Fe(III). In this process, an oxo bridge is formed between iron ions.

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\[
\begin{align*}
\text{Fe}^{2+} & \quad \text{O} \quad \text{O} \\
\text{Fe}^{2+} & \quad \text{O} \quad \text{O} \\
\text{Fe}^{2+} & \quad \text{O} \quad \text{O} \\
\text{Asp} & \quad \text{Asp} \\
\text{His} & \quad \text{His} \\
\text{His} & \quad \text{His} \\
\end{align*}
\]
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Unlike in hemoglobin, there is no cooperative effect observed in case of hemerythrin. Its affinity towards CO is less than with \( \text{O}_2 \).

42.12) What is the active site in Hemocyanin? Mention its role?
Ans:- Hemocyanin is respiratory protein containing two copper centres at the active site. It is a dioxygen carrier suspended in the hemolymph (blood) of most molluscs and arthropods. It contains NO HEME.

The deoxy form contains Cu(I) ions and is colorless, whereas the oxy form contains Cu(II) and is blue in color.