**Model Answer of AS-2157**

**M. Sc. (Third Semester) Examination 2013**

**CHEMISTRY**

**Bio-inorganic Chemistry**

***Time Allowed: Three hours***

***Maximum Marks: 60***

*Note: Question no. 1 from section 'A' is compulsory. Solve any five questions from section 'B'.*

## Section- 'A'

**10x2= 20**

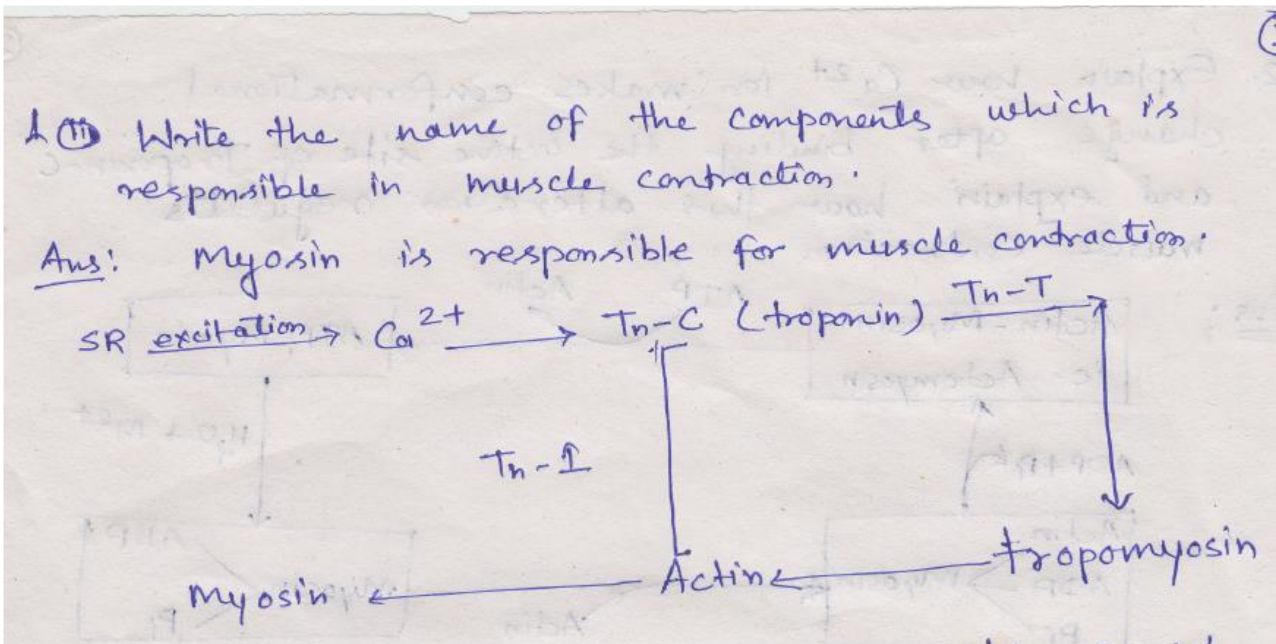
*Note: Attempt all the questions. Each question carries 2 marks.*

1. (i) How many classes of chemotherapeutic agents are present?

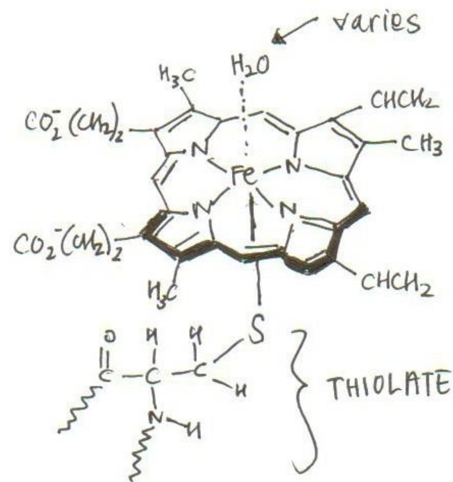
The main chemotherapeutic drugs can be divided into i) alkylating agents ii) antimetabolites iii) anthracyclines, iv) plant alkaloids v) topoisomerase inhibitors and other antitumour agents. All of these drugs affect cell division or DNA synthesis.

Alkylating agents : Alkylating agents are so named because of their ability to alkylate many nucleophilic functional groups under conditions present in cells. Cisplatin, Carboplatin, and oxaliplatin are alkylating agents. They impair cell function by forming covalent bonds with the amino, carboxyl, sulfhydryl and phosphate groups in

(ii) Write the name of the components which is responsible in muscle contraction.




(iii) Write the model complexes of the cytochrome-P450.



(iv) Write the reversible extraction of 'inorganic' components from Fe/S proteins.

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**Ans:** In Fe/S protein $Fe^{x+}$ is approximately tetrahedrally surrounded by the sulfur sites at least one of which is a cysteinyl sulfur. In the electron transport process, the $Fe^{3+}/Fe^{2+}$ couple wors and both the oxidised and reduced forms of Fe remain in high spin tetrahedral geometry. The sulfur binding site being relatively soft tends to stabilise the lower oxidation state $Fe^{2+}$ of the $Fe^{3+}/Fe^{2+}$ couple.

$$Fe^{2+} \longrightarrow e^3 t_2^3 \ (d^6)$$

$$Fe^{3+} \longrightarrow e^3 t_2^3 \ (d^5)$$

In Fe-S protein the charge transfer (LMCT) bond occurs in the range 350 – 600 nm due to $S \rightarrow Fe$ transition.

(v) Which molecule is source of oxygen during photosynthesis?

**Ans.** Water

(vi) Write active site of urease and hydrogenase.

Active site of urease is Ni(II)
Active site of hydogenage may be Fe-Fe and Fe-Ni

(vii) What are the uses of the metalloenzyme hydrogenase?

An hydrogenase is an enzyme that catalyses the reversible oxidation of molecular hydrogen.

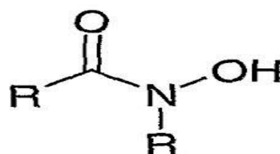
(ix) What are the main conformations of DNA?

DNA exists in many possible conformations that include A-DNA, B-DNA, and Z-DNA forms, although, only B-DNA and Z-DNA have been directly observed in functional organisms. The conformation that DNA adopts depends on the hydration level, DNA sequence, the amount and direction of supercoiling, chemical modifications of the bases, the type and concentration of metal ions, as well as the presence of polyamines in solution.

The first published reports of A-DNA X-ray diffraction patterns—and also B-DNA—used analyses based on Patterson transforms that provided only a limited amount of structural information for oriented fibers of DNA. An alternate analysis was then proposed by Wilkins *et al.*, in 1953, for the *in vivo* B-DNA X-ray diffraction/scattering patterns of highly hydrated DNA fibers in terms of squares of Bessel functions. In the same journal, James Watson and Francis Crick presented their molecular modeling analysis of the DNA X-ray diffraction patterns to suggest that the structure was a double-helix.

(x) Write the names of the functional group desferrioxamine B and enterobactin.

Hydroxamic acid group

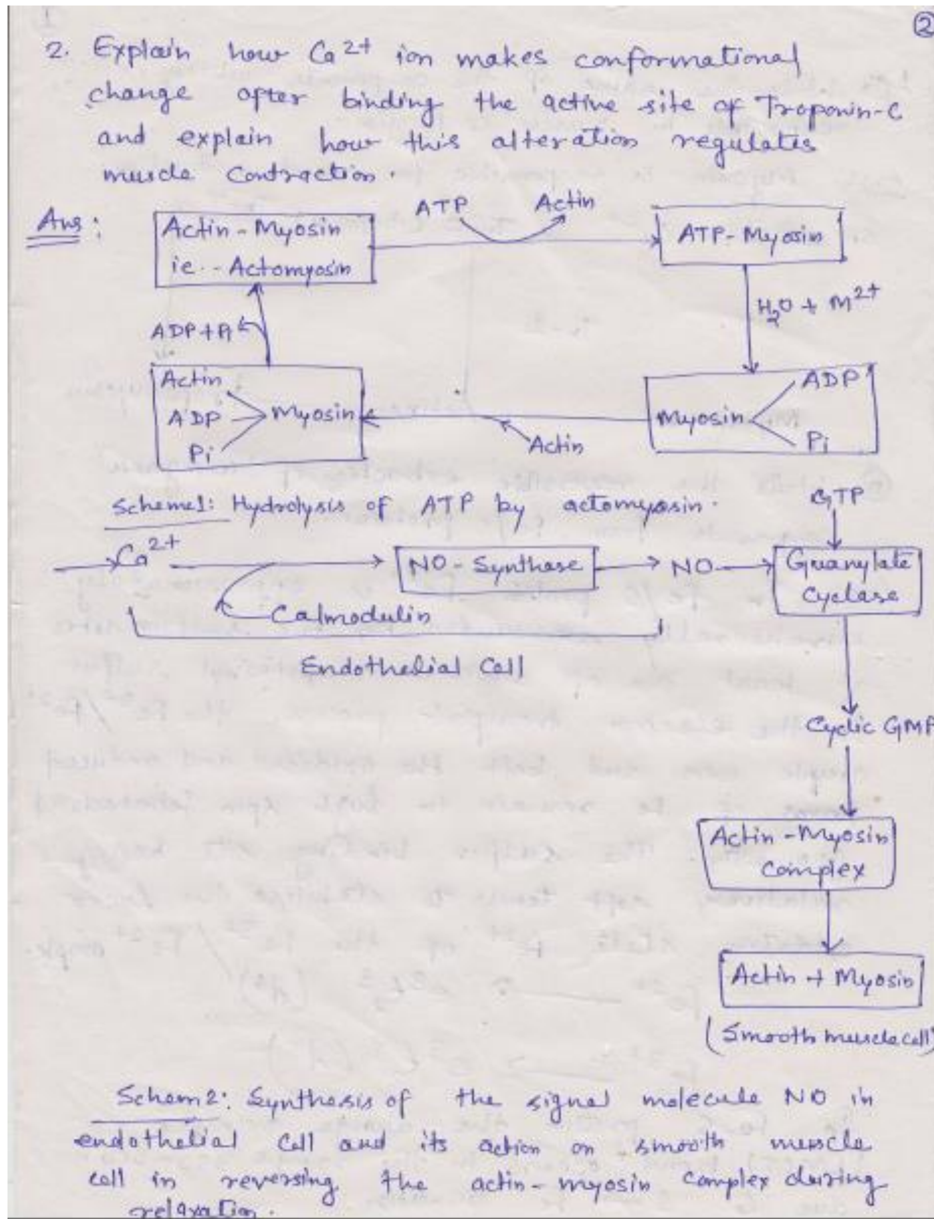



**Section- 'B'**

## (Long Answer Type Questions) 5x8= 40

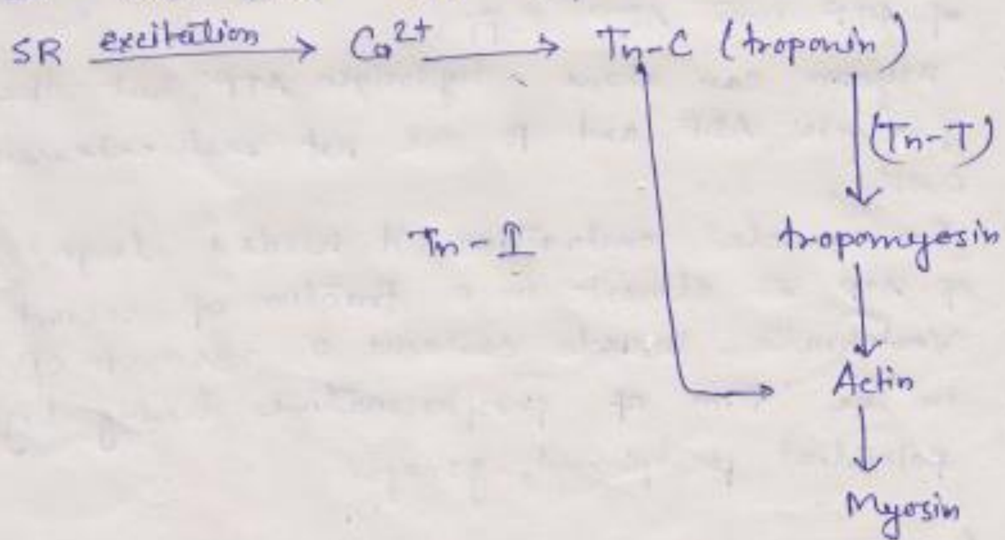
*Note: Attempt any five questions. Each question carries 8 marks.*

2. Explain how $Ca^{2+}$ ion makes conformational change after binding the active site of Troponin-C and explain how this alteration regulates muscle contraction.



The interaction between actin and myocin is mediated by tropomyosin and troponin complex. Tropomyosin, troponin and actin constitute a thin filament in muscle tissue where tropomyosin and troponin block the active sites of actin which can interact with the myosin through these sites.

- In resting condition thus the interaction between actin actin and myosin is prevented by tropomyosin and troponin.
- Tropomyosin (70 KDa) is a double helix protein. Troponin consists of three polypeptide chains. troponin-C (Tn-C) troponin-I and troponin-T. Tn-C is the Calcium binding site. Tn-I binds with actin and Tn-T bind with actin tropomyosin.
- Nerve excitation triggers the released $Ca^{2+}$ ions bind with from sacroplasmic reticulum (SR) to the surrounding muscle fibres. These released $Ca^{2+}$ ions bind with troponin.



(4)

- This change pulls Tn-I away from the actin and consequently it uncovers the myosin binding sites on actin. The structural change in Tn-C is also transmitted to tropomyosin through Tn-T.
- Due to this conformational change in tropomyosin the blocking of the active site in actin by tropomyosin is removed.
- Then myosin can interact with the active site of actin of filament. It generates the contractile force.
- Again the $Ca^{2+}$ - pump (ATP-driven) transports the $Ca^{2+}$ ions into SR and consequently the interaction between actin and myosin is stopped at the resting condition.
- In reality actomyosin catalyses the hydrolysis of ATP into ADP & $P_i$.
- Myosin can alone hydrolyse ATP, but the products ADP and $P_i$ are not released easily.
- For muscle contraction, it needs a large amounts of ATP almost in a fraction of second. Vertebrate muscle contains a reservoir of ATP in the form of phosphocreatine having high potential phosphoryl group.

3. Explain the structure of cytochrome P-450 and its catalytic cycle of cytochrome P-450 in the oxygenation reaction.

Description of the following catalytic cycle along with structure:

(6.7)

**Figure 6.5**
Correlation diagram of d orbitals for the tetragonal distortion (compression and elongation) of an originally octahedral $d^4$ metal complex

4. Describe the nitrogen fixation catalyzed by nitrogenase and also discuss the thermodynamic and kinetic aspects of nitrogen fixation.

***Description of the following graph and mechanism:***

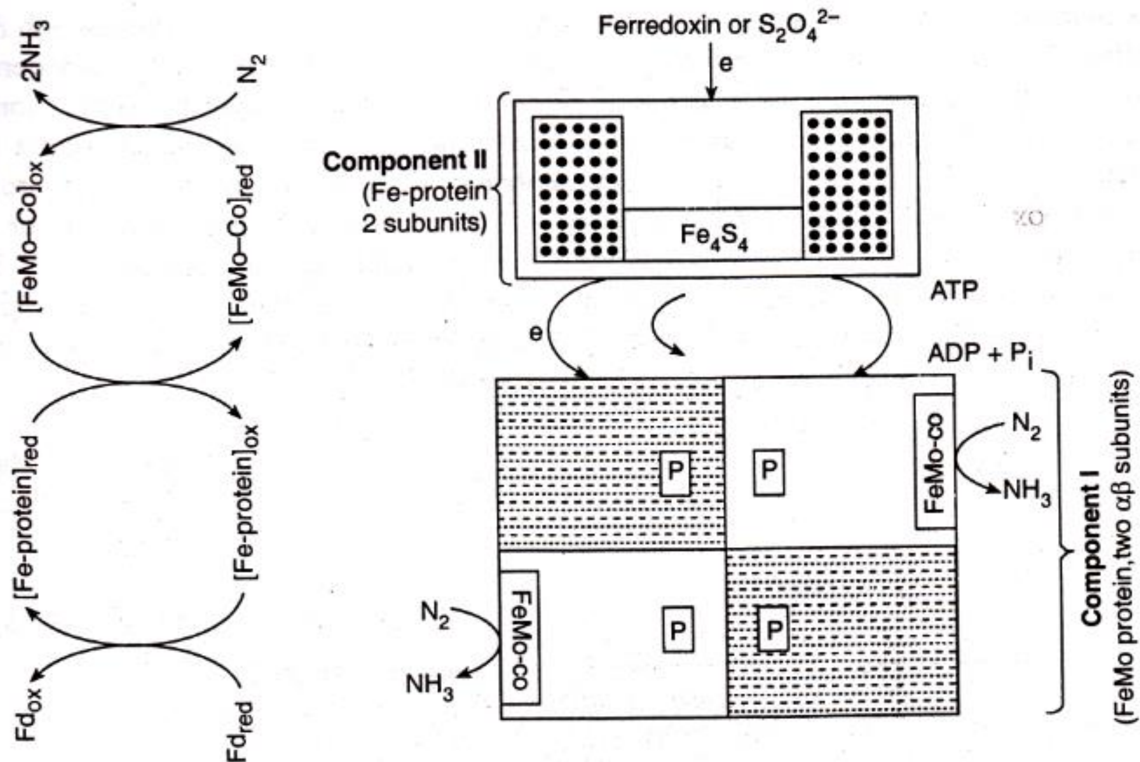



*Figure 8.3.2.1 : Schematic representation of different components of nitrogenase enzyme.*

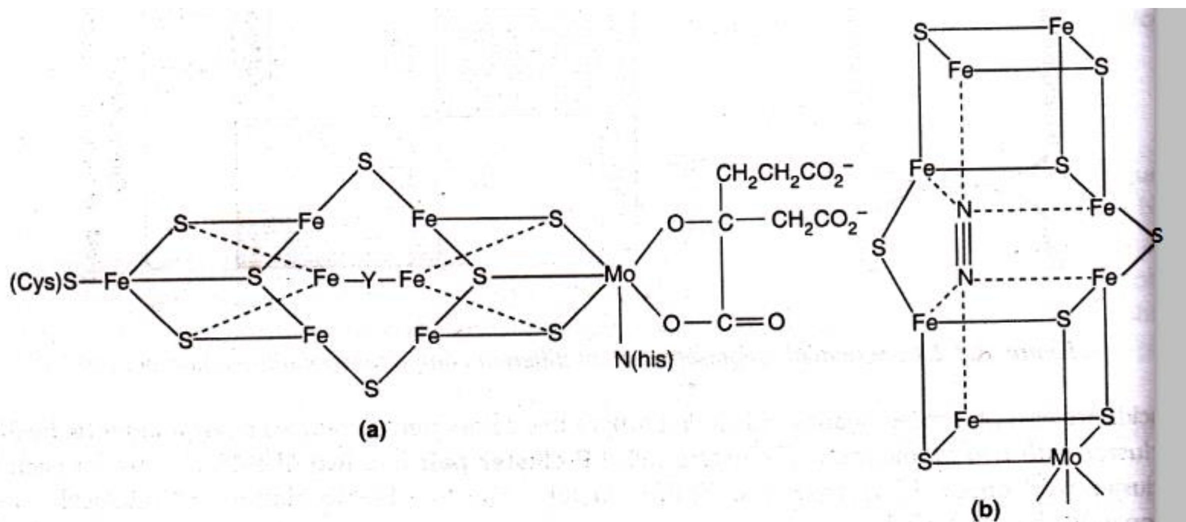
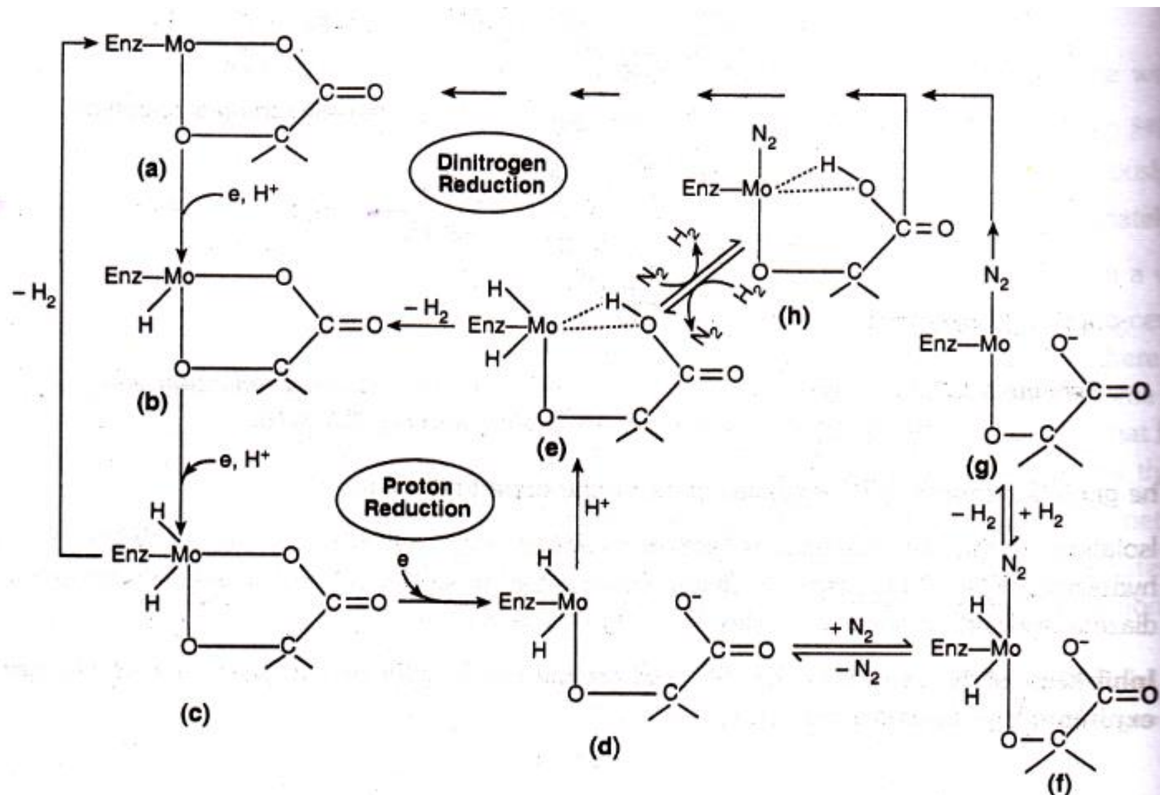
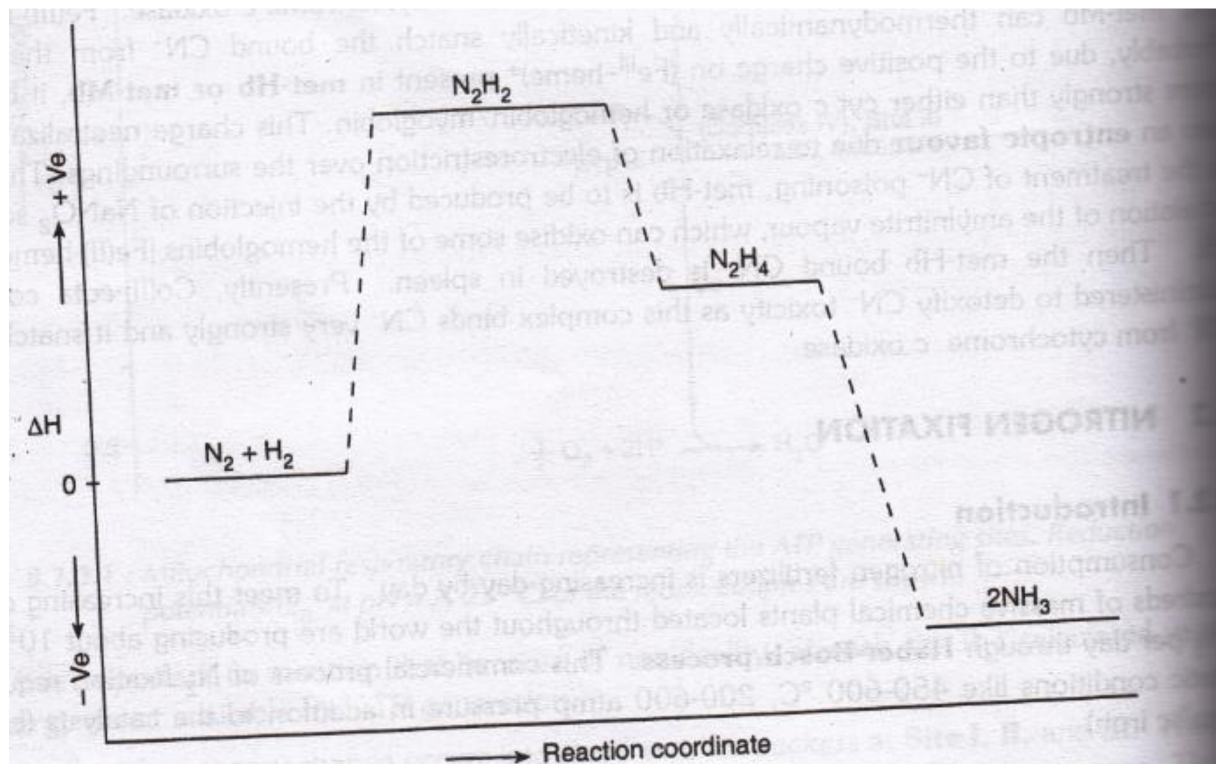



*Figure 8.3.3.1 : (a) Structural representation of $MoFe_7S_8$ cluster of nitrogenase. (b) Speculated structure of $MoFe_7S_8$ binding $N_2$ (at the site of Y) as a central bridge between the thiocubane fragments.*




*Scheme 8.3.7.5* : *Proposed scheme of binding of $N_2$ at the Mo-centre after reduction of the enzyme and the reaction sequence according to* ***Thorneley -- Lowe mechanism.***

## Thermodynamic and kinetic aspects of nitrogen fixation




*ure 8.2.2.1* : *Qualitative representation of energetics of conversion of $N_2 \rightarrow 2NH_3$ through the possible intermediates $N_2H_2$ and $N_2H_4$.*

5. Write notes on PS-I and PS-II of photosynthetic system.

***Description of the following mechanism:***

**Table 4.1** Active components in photosystems I and II of plants

| | |
|---|---|
| **photosystem I** (including cytochrome b/f complex) | |
| about 200 | antenna chlorophylls |
| about 50 | carotenoids |
| 1 | reaction center $P_{700}$ |
| 1 | chlorophyll *a* (primary acceptor $A_0$) |
| 1 | vitamin $K_1$ (secondary acceptor $A_1$) |
| 3 | Fe/S-clusters (FeS) |
| 1 | bound ferredoxin (Fd) |
| 1 | soluble ferredoxin (Fp) |
| 1 | plastocyanin (PC, primary donor) |
| 1 | RIESKE Fe/S center |
| 1 | cytochrome *f* (cyt *f*) |
| 2 | cytochromes $b_6$ (cyt $b_6$) |
| **photosystem II** (including OEC) | |
| about 200 | antenna chlorophylls |
| about 50 | carotenoids |
| 1 | reaction center $P_{680}$ |
| 2 | chlorophylls |
| 2 | pheophytins (primary acceptor)[b] |
| 2 | plastoquinones (PQ) |
| 2 | tyrosine residues (primary donor)[a] |
| 4 | manganese centers |
| 1 | calcium ion $Ca^{2+}$ |
| several | chloride ions $Cl^-$ |
| 1 | cytochrome $b_{559}$ |

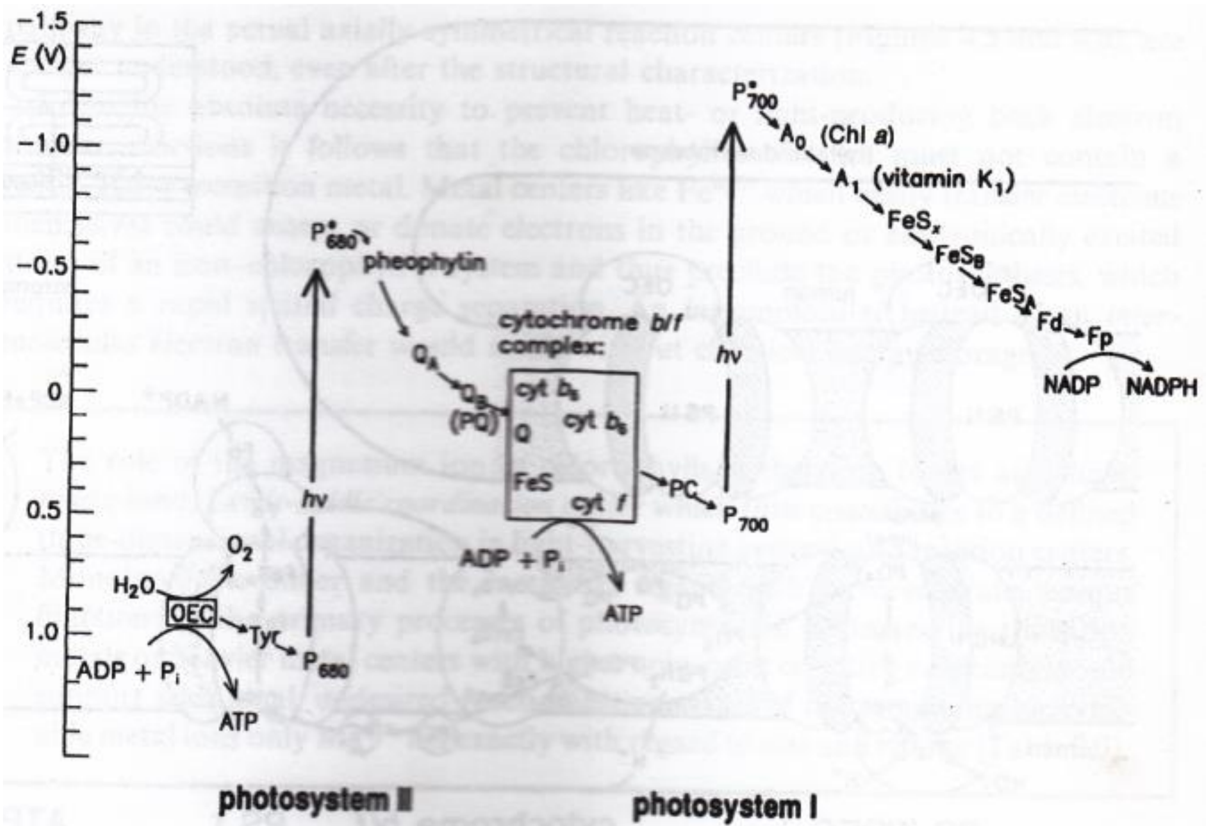



**Figure**
**Z scheme of electron transfer in plant photosynthesis**

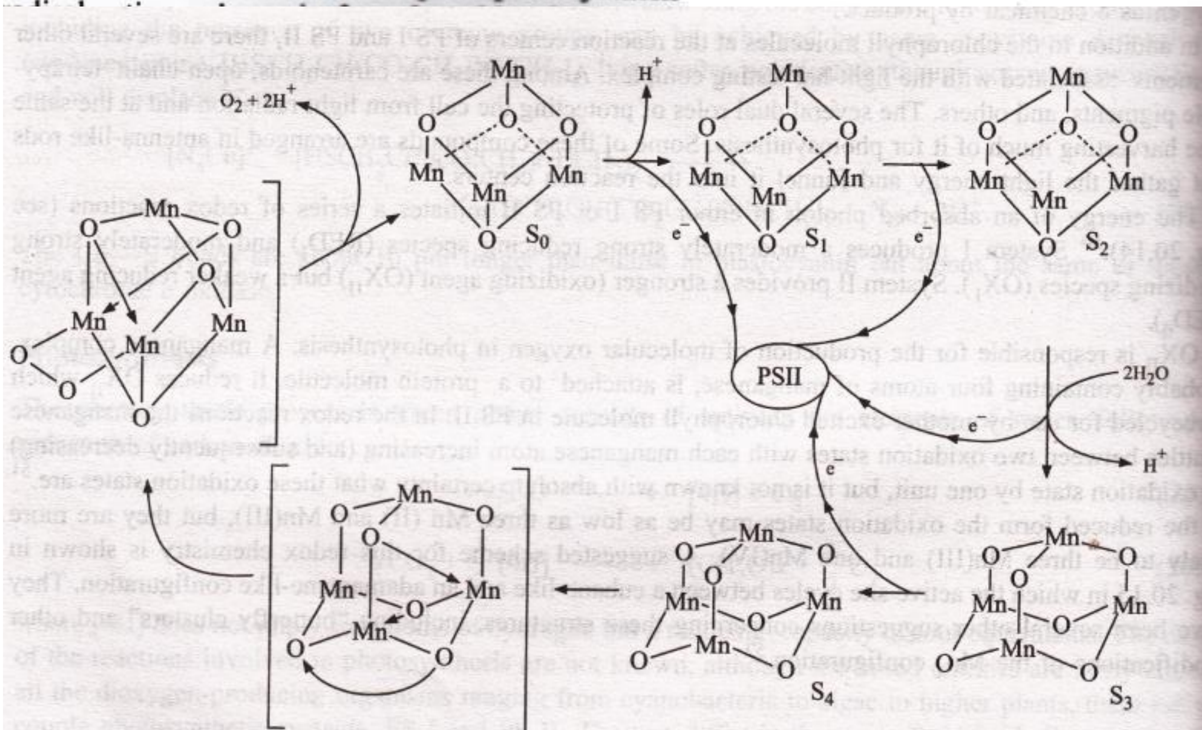
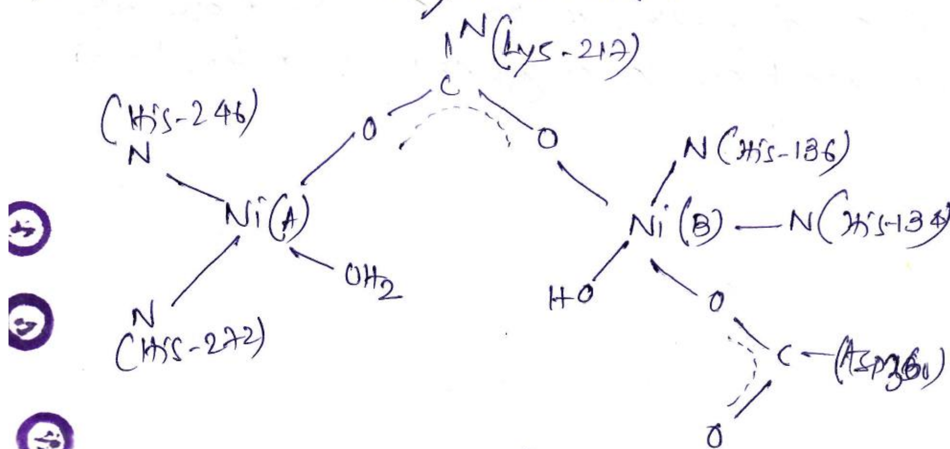



**Fig.** One proposal for the involvement of Mn centers in the photoevolution of dioxygen. [Modified from Brudivg, G. W. Crabtree, R. H. *Natl. Acad. Sci. U.S.A.* **1987**, *83*, 4586. Reproduced with permission.]

6. Give brief account on the following
   (a) Urease (b) Hydrogenase

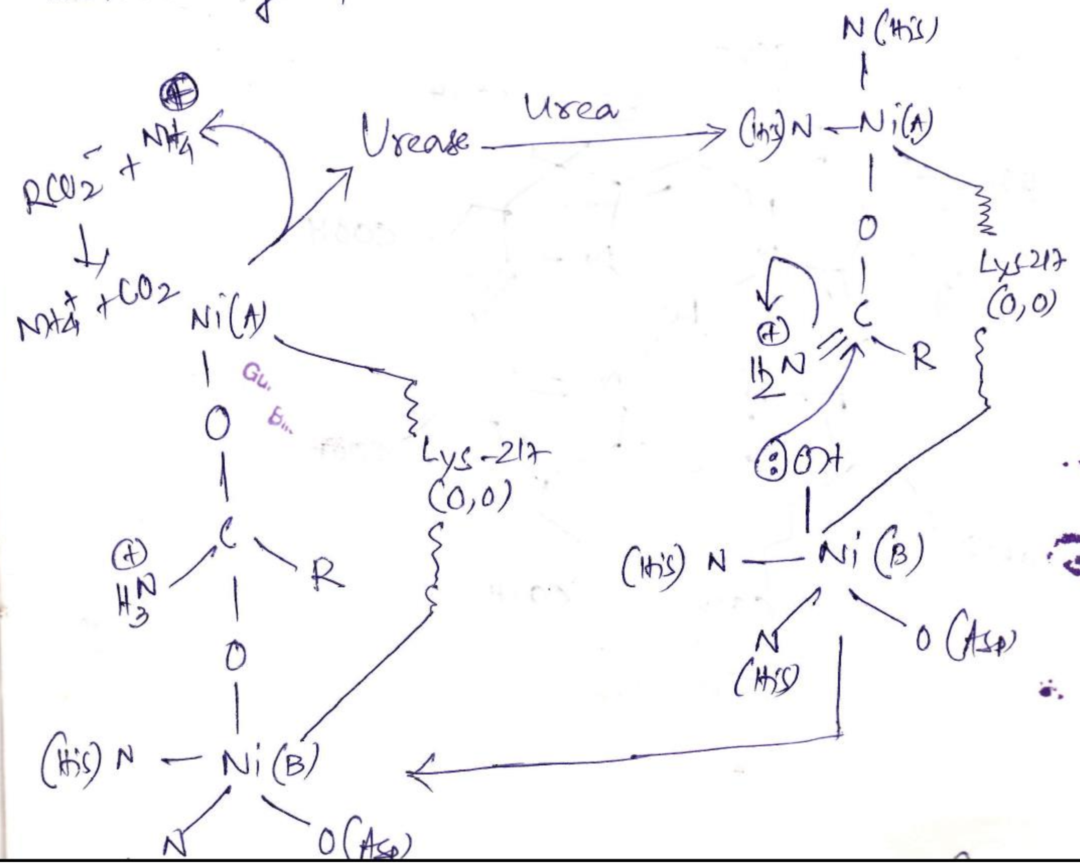
<u>Urease</u>: Ni(II) is relatively less important compared to many other transition metal ions of the first series. Recently Ni(II) has been found in hydrogenase, CO-dehydrogenase, S-methyl coenzyme-M reductase (required in methane formation in the methogen bacteria). All the Ni(II) proteins known till date are plants and bacteria. In higher animals, no Ni-protein is yet reported.

Urease consists of six sub units. Each subunit contains two Ni(II) centres. Ni(II) centres are present at the prosthetic group. In each subunit two Ni(II) centres are about 3.5 A° apart. The Ni(II) sites are bridged by carbamylated Lys-217. One Ni(II) centre (denoted by NiB) is 5 coordinate with His-134, His-136, Asp-360, bridging O-site of Lys-217 and a ~~water molecule~~ hydroxide as ligands in a distorted trigonal bipyramidal geometry. The other Ni(II) centre (denoted by Ni(A) is 3-coordinate with His 246, His-272 and bridging O-site of Lys-217. However the fourth site of Ni(A) may be occupied by a water molecule which is replaced by the substrate in the enzyme activity.

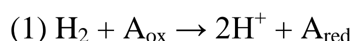



The Structural features of the dinickel centre in urease.

may critically participate in the protonation - deprotonation process. The carbonyl O of the substrate first coordinates to the active site of one Ni(II) centre ie (Ni A). The Lewis acidity of the Ni(II) centre facilitates the nucleophilic attack at the carbonyl C by -OH group or $H_2O$ molecule bound to the second nickel site (Ni B). It leads to the formation of a binuclear bridged complex where the Lewis acidity of the two Ni(II) centres jointly act to make the C- centre of the carbonyl group of the substrate sufficiently electron deficient to receive a nucleophilic attack by $H_2O$. Here the protonated $NH_2$ group ($-\overset{+}{N}H_3$) acts as a better leaving group in the interchange process and at the same time it also enhances the carbonium character of the C-centre to facilitate the nucleophilic attack at the C-centre. This nucleophilic attack at the last step produces $NH_4^+$ and carbamate through the interchange process.



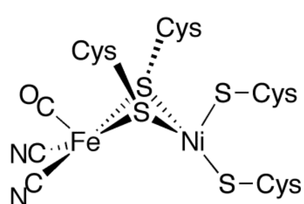
A **hydrogenase** is an enzyme that catalyses the reversible oxidation of molecular hydrogen ($H_2$), as shown in below:



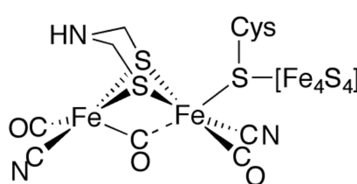
$$(1)\ H_2 + A_{ox} \rightarrow 2H^+ + A_{red}$$

$$(2)\ 2H^+ + D_{red} \rightarrow H_2 + D_{ox}$$

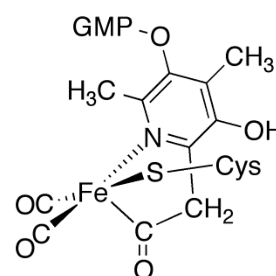
Hydrogen uptake (1) is coupled to the reduction of electron acceptors such as oxygen, nitrate, sulfate, carbon dioxide, and fumarate. On the other hand, proton reduction (2) is coupled to the oxidation of electron donors such as ferredoxin (FNR), and serves to dispose excess electrons in cells (essential in pyruvate fermentation). Both low-molecular weight compounds and proteins such as FNRs, cytochrome $c_3$, and cytochrome $c_6$ can act as physiological electron donors or acceptors for hydrogenases.




[NiFe]$H_2$ase




[FeFe]$H_2$ase




[Fe]$H_2$ase

The [NiFe] hydrogenases are heterodimeric proteins consisting of small (S) and large (L) subunits. The small subunit contains three iron-sulfur clusterswhile the large subunit contains the active site, a nickel-iron centre which is connected to the solvent by a molecular tunnel. In some [NiFe] hydrogenases, one of the Ni-bound cysteine residues is replaced by selenocysteine. On the basis of sequence similarity, however, the [NiFe] and [NiFeSe] hydrogenases should be considered a single superfamily. To date, periplasmic, cytoplasmic, and cytoplasmic membrane-bound hydrogenases have been found. The [NiFe] hydrogenases, when isolated, are found to catalyse both $H_2$ evolution and uptake, with low-potential multihaem cytochromes such as cytochrome $c_3$ acting as either electron donors or acceptors, depending on their oxidation state. Generally speaking, however, [NiFe] hydrogenases are more active in oxidizing $H_2$..

Like [FeFe] hydrogenases, [NiFe] hydrogenases are known to be deactivated by molecular oxygen ($O_2$). Recently, a novel hydrogenase from *Ralstonia eutropha* have been found to be oxygen-tolerant. This finding increased hope that hydrogenases can be used in photosynthetic production of molecular hydrogen via splitting water.

7. What is DNA probe. Discuss its details biological applications using schematic presentation.

DNA Probe : A lebelled segment of DNA used to find specific sequence of nucleotides in a DNA molecule.

Probes may be synthesized in the laboratory with a seqnence complementary to the target DNA - sequence.

Individvals, how are we made? Through a single cell that penetrates into another cell is the manner we are made of. From our parent cells, genes are synthesising and creating a brand new individual. The DNA is the mere reason of how we look like, what traits we possess with and whenever we possess an inherited disease, this is the main reason we carry it. What most concerns us is the disease we carry along with us as we grow and mature. In breeding, we are created and we inherit the traits of our parents, including their diseases. DNA is the basic unit of a cell. It is the most basic structure of us. that we can't accessibly take a look on it. The DNA may be invisible in bare eyes but it plays a great role in our system, especially our health. We can trace why we suffer a specific medical condition through observing our DNA.

With the help of medical technology, we are able to identify medical conditions that an individual may have possessed. This is made possible with the use of a DNA probe. A DNA probe is a

radioactive or chemiluminescent DNA or RNA sequence. DNA probes are used to detect and identify the presence of any infectitions disease in our body. DNA probe is an agent inserted into a medium to be abled to get information about the structure of the medium. With DNA probe we may visualize the structure of our DNA, can find out any abnormalities within it. DNA probes have been very helpful to the medical field. DNA probe has been used to identify the presence of abnormal DNA sequence or change of DNA structures brought about by infectitian agents.

Trough ~~DNA~~ the DNA probes we are able to identify different kind of medical conditions that involves DNA pattern. A DNA probe is much of help if we try to identify any underlying inherited genes of medical condition such as cancer, hyperthyroidism, cretinism and any other debilitating disease. Some psychological abnormalities may also be genetically inherited to offspring. Some parents would want to have genetic counselling before they are engaged in breeding. The [illegible] genetic abnormal

8. Describe the mode of coordination of iron in transferrins and explain transferring, recognition and demetallation process.

**Description of the following Structure:**

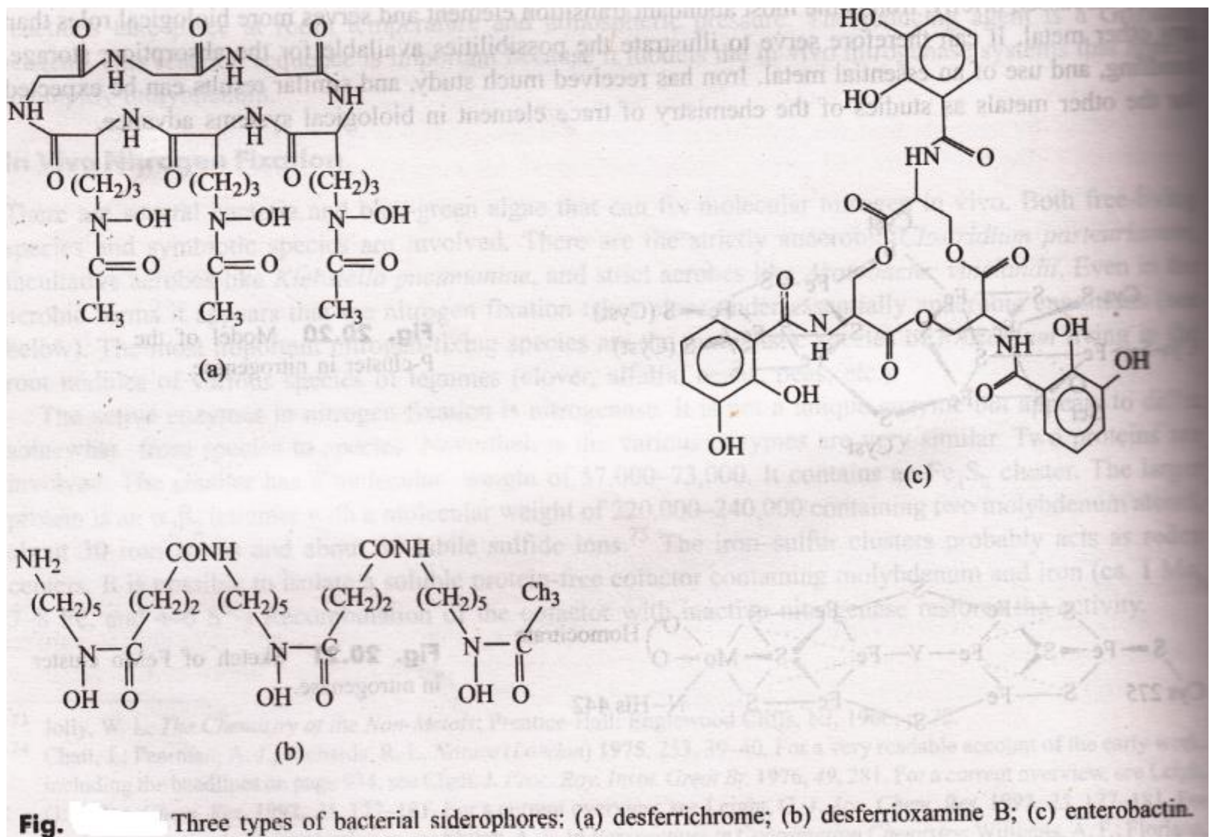



Fig. Three types of bacterial siderophores: (a) desferrichrome; (b) desferrioxamine B; (c) enterobactin.

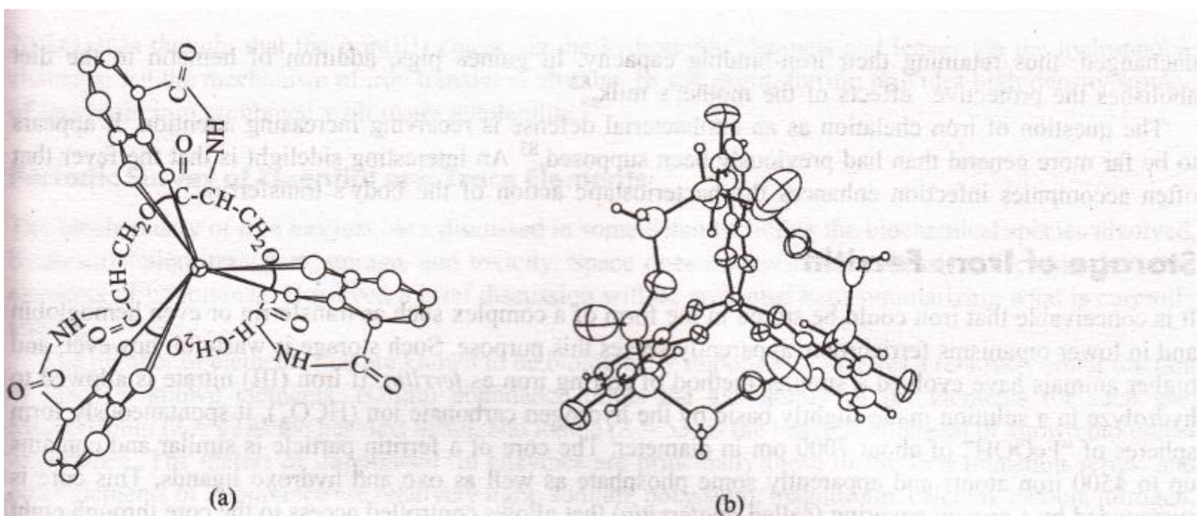



**Fig.** The Δ-cis isomers of metal enterobactins. The metal lies at the center of a distorted octahedron of the six oxygen atoms of the three catechol ligands with approximate $C_3$ symmetry. (a) The structure of iron(III) enterobactin as determined by CD spectra. (b) ORTEP plot of the structure of V(IV) enterobactin as determined crystallographically. Note that although both structures are viewed down the approximate threefold axis and the atoms (except Fe/V) are the same in (b) as in (a), the views are 180° apart. S. S.; Kuo, G.; Raymond, K. N. *J. Am. Chem. Soc.* **1976,** *98, 1763*; Karpishin, T. B.; Raymond, K. N. *Angew. Chem. Int. Ed. Engl.* **1992,** *31,* 466–468.