Medicinal Industrial & Environmental Relevance of Metal Nitrosyl Complexes: A Review

R. C. Maurya, J. M. Mir

Abstract—This review sums up the necessary research upsurges that occurred since nitric oxide (NO) was declared as the signaling molecule in the cardio-vascular system and some recent trends in its study. Metal nitrosyl complexes are the mimicking biological models that exhibit the properties of nitric-oxide-synthase. Their roles in medicine, industry and environmental equilibrium are of immense importance. Besides these, their role in plant pathogenicity is recent research tool in botany. Cancer studies also reveal the nitric oxide, the median line to cancer disease.

Index Terms— Metal nitrosyls, Nitric-oxide, Signaling molecule, Cancer, Plant pathogen, Water pollution, Air Pollution

1 Introduction

Metals play a vital role in an immense number of extensively differing biological processes. Some of these processes are quite specific in their metal ion requirements, in that only certain metal ions in specified oxidation states can accomplish the necessary catalytic structural requirement. Metal ion dependent processes are found throughout the life science and vary tremendously in their function and complexity. Respiration, nitrogen fixation, photosynthesis, nerve transmission and muscle contraction are life-critical processes requiring metal ions [1].

The role of a metal as structural component and as catalyst is broadly known. It is now appreciated that metal ions control a vast range of processes in biology. Many new and exciting developments in the field of biochemistry create interest among inorganic chemists to court in the new area called "Bioinorganic Chemistry". Due to close-lying energy bands made up of partly filled d-orbitals, transition metal ions have a rich chemistry and thus serve as unique agents in a variety of biological processes.

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In particular, this is the case for the middle and late first-row transition metal ions, with typically single occupation of at least some of their d-orbitals. For these elements, tuning the ligand field by the use of different ligands provides a useful way of influencing structure, spin state and bond-order. In essence, local structure about the metal plays an essential role for catalytic mechanisms.

One of the principal themes of bioinorganic chemistry is the synthesis of metal complexes that have the ability to mimic the functional properties of natural metalloproteins [2], [3]. Proteins, some vitamins and enzymes contain metal ions in their structure involving macromolecular ligands. The chemistry of metal complexes with multidentate ligands having delocalized π-orbitals, such as Schiff bases or porphyrins has recently gained more attention because of their use as models in biological systems. From several studies of bioinorganic systems, synthetic, structural, spectroscopic or computational, principles have emerged that tie together seemingly unrelated facts. In this article, search for such facts is the primary aim. The general interest in Molybdenum and Ruthenium nitrosyl complexes stems partly from the fact that identical or similar compounds have significant roles in biological medicine, industry and are environmentally relevant. The field of transition metal nitrosyls, referring to structural and bonding aspects, was termed a provocative subject by Enemark and Feltham [4] in their ground-breaking work from early 70ties.

Possibly less provocative today, the field is still of significant interest.

Compounds containing the NO grouping(s) are usually referred to as nitrosyl compounds [5] when addendum is inorganic in nature and as nitroso compounds when addendum is organic in nature. Recently, there has been considerable upsurge in the study of coordination compounds containing coordinated NO grouping and the reactions of the nitrosyl ligand. An impressive number of works have been published dealing with properties and applications of NO containing transition metal complexes [6-22, 57].This is due to potential applicability of these compounds to be used in biomedical science, in chemical industry as catalysts and as pollution controlling agents. Theoretical studies of metal-nitrosyl complexes has also been an immense aim of study to deal with the various energy criteria along the suitable future studies of their existence and clarification of concepts related to NO.

The initial studies of the nitric oxide (NO) molecule dates back to 1772, when Joseph Priestly called it ''nitrous air,'' and was first discovered as a colorless, toxic gas. Unfortunately, the tag of toxic gas and air pollutant continued until 1987, when it was shown to actually be produced naturally in the body. By 1987, nitric oxide's role in regulating blood pressure and relieving various heart ailments became well-established. Two years later, research revealed that nitric oxide is used by macrophages to kill tumor cells and bacteria. In 1992, nitric oxide was voted ''Molecule of the Year''. The importance of the molecule became front page news in 1998 when Louis J. Ignarro, Robert F. Furchgott and Ferid Murad were awarded the Nobel Prize for Medicine and Physiology for identifying nitric oxide as a signaling molecule. The discovery opened up newer ways of treatment for millions of patients.

Nitric oxide (NO) plays an important role in the protection against the onset and progression of cardiovascular diseases. The cardioprotective roles of NO include regulation of blood pressure and vascular tone, inhibition of platelet aggregation and leukocyte adhesion, and prevention of smooth muscle cell proliferation. Reduced bioavailability of NO is thought to be one of the central factors common to cardiovascular disease, although it is unclear whether this is a cause of, or result of, endothelial dysfunction. Any disturbance in the bioavailability of NO leads to a loss of cardio protective actions and in some cases may even increase disease progression [23].

1.1 NO Reactivity inside a Living System

NO is composed of an atom each of nitrogen and oxygen such that seven electrons from nitrogen and eight electrons from oxygen are involved to form an uncharged molecule (N:O). The high reactivity of NO is not due to the fact that it contains an unpaired electron having a half life of 2–30 s. If this were the case, how would tissues survive in presence of molecular oxygen with two unpaired electrons at a concentration of 20–200 l M [24]. Nitric oxide only reacts with those biological molecules that have unpaired orbital electrons e.g., other free radicals or transition metal ions. Since most of the biological molecules have completely filled orbitals, it renders nitric oxide non-reactive towards them [25]. The reactivity of NO depends upon its physical properties, such as its small size, high diffusion rate, and lipophilicity. Moreover, the reaction products of nitric oxide, i.e. the related species, also react with biological molecules and may have toxic effect as well [26]. At low levels, NO can protect cells; however, at higher levels, it is a known cytotoxin, having been implicated in tumor angiogenesis and progression [27].

1.2 NO in Electron Transport System

Mitochondrial diseases arise as a result of dysfunction of the respiratory chain, leading to inadequate ATP production required to meet the energy needs of various organs. On the other hand, nitric oxide (NO) deficiency can occur in mitochondrial diseases and potentially play major roles in the

pathogenesis of several complications including stroke-like episodes, myopathy, diabetes, and lactic acidosis. NO deficiency in mitochondrial disorders can result from multiple factors including decreased NO production due to endothelial dysfunction, NO sequestration by cytochrome c oxidase, NO shunting into reactive nitrogen species formation, and decreased availability of the NO precursors arginine and citrulline (Fig. 1 and 2).

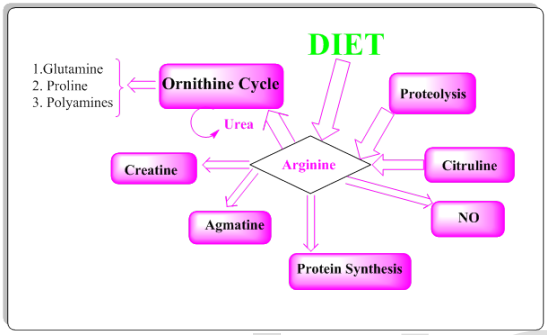


Fig.1. *Schematic Presentation of Ornithine cycle and Nitric Oxide: NO*

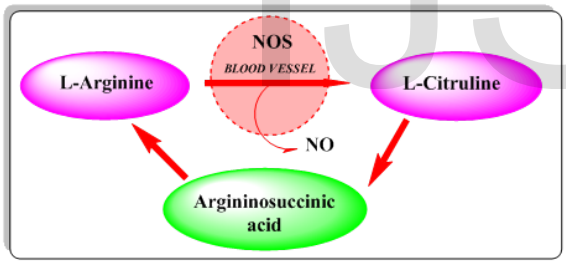


Fig.2. L-Citruline Efficiency of NO

Arginine and citrulline supplementation can result in increased NO production and hence potentially have therapeutic effects on NO deficiency-related manifestations of mitochondrial diseases. Citrulline is a more efficient NO donor than arginine as it results in a greater increase in de novo arginine synthesis, which plays a major role in driving NO production [28], [29]. This concept is supported by the observation that the three enzymes responsible for recycling citrulline to NO (argininosuccinate synthase and lyase, and nitric oxide synthase) function as a complex that can result in compartmentalizing NO synthesis and channeling citrulline efficiently to NO synthesis. Clinical research evaluating the effect of arginine and citrulline in mitochondrial diseases is limited to uncontrolled open label studies demonstrating that arginine administration to subjects with MELAS (Mitochondrial Encephalopathy, Lactic acidosis, and Stroke-like episodes) syndrome results in improvement in the clinical symptoms associated with stroke-like episodes and a decrease in the frequency and severity of these episodes. Therefore, controlled clinical studies of the effects of arginine or citrulline supplementation on different aspects of mitochondrial diseases are needed to explore the potential therapeutic effects of these NO donors [30], [31], [32].

1.3 Promotion and Demotion of Cell Growth

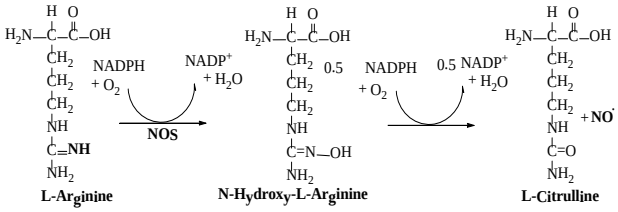
Thus Nitric oxide (NO), a free radical having both cytoprotective as well as tumor promoting agent is formed from L-arginine by converting it to L-citrulline via nitric oxide synthase enzymes. The reaction product of nitric oxide with superoxide generates potent oxidizing agent, peroxynitrite which is the main mediator of tissue and cellular injury [33]. Peroxynitrite is reactive towards many biomolecules which includes amino acids, nucleic acid bases; metal containing compounds, etc. NO metabolites may play a key role in mediating many of the genotoxic/ carcinogenic effects as DNA damage, protein or lipid modification, etc. The basic reactions of nitric oxide can be divided as direct effect of the radical where it alone plays a role in either damaging or protecting the cell milieu and an indirect effect in which the by-products of nitric oxide formed by convergence of two independent radical generating pathways play the role in biological reactions which mainly involve oxidative and nitrosative stress [34]. Nitric oxide is also capable of directly interacting with mitochondria through inhibition of respiration or by permeability transition. Reaction of nitric oxide with metal ions includes its direct interaction with the metals or with

oxo-complexes thereby reducing them to lower valent state. Excessive production of nitric oxide can be studied by inhibiting the synthetic pathway of nitric oxide using both selective or specific nitric oxide synthase inhibitor and nonselective nitric oxide synthase inhibitor with respect to isoforms of nitric oxide [35].

2 Biomedical application of Nitrosyl compounds

During the 'Dark Ages' of nitric oxide (NO) biochemistry [36] (**pre-1980**), very little was known about the biological role of NO. However, the chemical roles of NO have been known and studied by chemists for a long time. Chemically, NO is a diatomic radical species (often denoted as NO·). Small, simple and highly toxic pungent smelling gas as environmental pollutant found in photochemical smog [37], produced by oxidation of NH_3, incomplete combustion of gasoline in motor vehicle exhausts [38], and power stations [39], it was long known for its reactivity as an oxidant, reductant, radical initiator and a strong ligand to transition metal centers to form metal nitrosyls [40]. **The discovery and elucidation of its biological functions by Louis J. Ignore and others in the 1980s came as a surprise** [41-45] Well known as being responsible for the physiological actions of endothelial relaxing factor (EDRF), its early implication in a diverse number of medically important processes [46] culminated in 1992 with NO being declared **"Molecule of the Year"** by the journal ***Science*** **[47]**.

Within mammalian cells the biosynthesis of NO is reported to be catalyzed by a family of nitric oxide synthase (NOS) [48]. The enzyme NOS converts L-arginine (an amino acid available in living organism) to citrulline and NO. The Co-substrates for the reaction include NADPH and O_2 (Scheme 1).



Scheme1. *The reaction catalyzed by nitric oxide synthase (NOS)*

2.1. Free radical entry in medicine.

In 1980 **nitric oxide (NO·)** was discovered to be one of the most important physiological regulator, including cardiovascular control (blood pressure regulation), neuronal signaling, platelet activation, immune response, and as agents for defense mechanisms against microorganisms and tumors. **Robert F. Furchgolt, Louis J. Ignore and Ferid Murad won the 1998 Nobel Prize in Physiology and Medicine on their work on NO as a signaling molecule in cardiovascular system leading to cardiovascular control.**

Smooth muscle in cardiovascular system is often the target of NO action, leading to vasodilatation in blood vessels and thus regulating the blood pressure [49]. In the central nervous system, this free radical gas acts as a diffusible intercellular signalling molecule. NO is synthesized from L-arginine, in a NADPH-dependent reaction, by NO synthase. Neuronal and endothelial NO synthases appear to be constitutive calcium- dependent enzymes, whereas other NO synthase isozymes, i.e., those found in smooth muscle and macrophages, are expressed as a result of activation by various cytokines and are calcium-independent. The localization of a brain-specific isozyme of NO synthase suggests that NO has widespread action in the central nervous system.

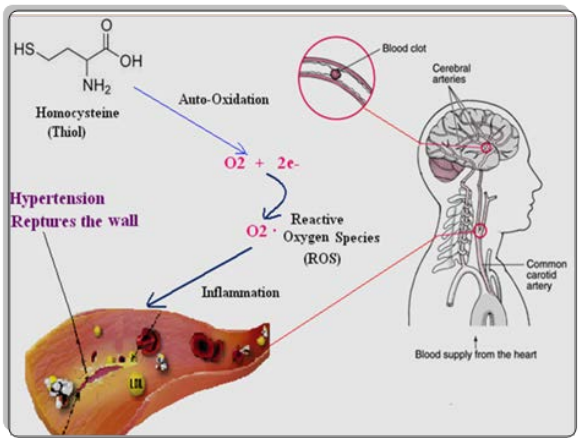


Fig.3 Relation of Reactive oxygen Species and Hypertension

2.2 Optimum production of NO, a necessity

There are some diseases that result from quantitative or functional NO deficiency. NO insufficiency may be characterized by a net tissue NO deficit, enhanced NO inactivation, impaired NO availability, or altered NOS catalysis [50]. In all these states, a NO deficiency would limit NO-dependent signal transduction pathways to the detriment of normal cellular function. For example, dysfunction of the normally protective endothelium is found in several cardiovascular diseases, including atherosclerosis, hypertension, heart failure (HF), coronary heart disease (CHD), arterial thrombotic disorders, and stroke [51-53]. Endothelial dysfunction leads to NO deficiency, which has been implicated in the underlying pathobiology of many of these disorders. In the case of the gastrointestinal tract, NO is a critical mediator of mucosal defense and repair [54].

2.3 NO in Nerve and Memory study

Nitric oxide (NO) is widely used in neural circuits giving rise to learning and memory [55, 56]. NO is an unusual neurotransmitter in its modes of release and action. Is its association with learning and memory related to its unusual properties? Reviewing the literature might allow the formulation of a general principle on how NO and memory are related. However, other than confirming that there is indeed a strong association between NO and memory, no simple rules emerge on the role of NO in learning and memory (Fig. 4).

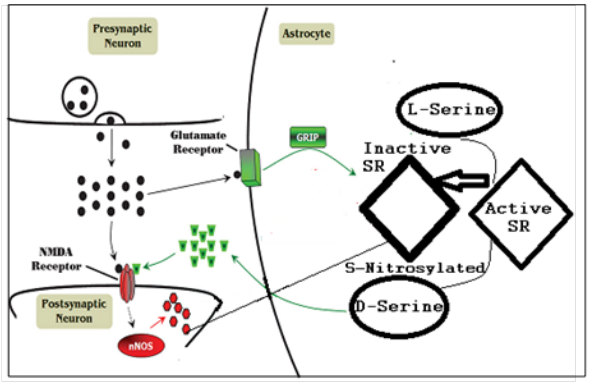


Fig.4. *Learning and Memory Nerve circuit Intervened by NO.*

The effects of NO are not associated with a particular stage or form of memory and are highly dependent on species, strain, and behavior or training paradigm. Nonetheless, a review does provide hints on why NO is associated with learning and memory. Unlike transmitters acting via receptors expressed only in neurons designed to respond to the transmitter, NO is a promiscuous signal that can affect a wide variety of neurons, via many molecular mechanisms. In circuits giving rise to learning and memory, it may be useful to signal some events via a promiscuous messenger having widespread effects. However, each circuit will use the promiscuous signal in a different way, to achieve different ends [56].

2.4 Nitrosyls, Nitroso & Cyano-nitrosyls

Design and characterization of inorganic nitrosyls is an essence for the issue to replace organic nitroso forms. Our lab has been outputting a great number of nitrosyl complexes since 1988 [57], but due to cyano poisoning it is necessary to replace cyano-nitrosyl complexes with new ones devoid of CN^- as a ligand. As the pathways of NO-metabolism is an immense mesh in tracing through the human body, so is a sensi-

tive issue to be seen keenly.

3 Cancer and Nitric oxide, a special role

An involvement of nitric oxide, a diatomic radical, has been described for numerous areas from environmental pollution to cardiovascular disease, carcinogenesis, tumor progression, genotoxicity, and angiogenesis. Previously, it has been demonstrated that NO may perform different functions dependent on NO levels achieved in a particular microenvironment. Furthermore, researchers also have discovered and identified the various sources of NO, which can elicit different biological responses of NO. In order to better understand the biological consequences of NO responses, one must first understand the chemical biology of NO. Since the first discussions during the early 1990s, it became widely accepted that NO chemical biology can be classified into two classes: direct interaction and indirect interaction. These two classes provided us with the means to understand the basic chemical toxicological effects of NO and its resulting reactive nitrogen species (RNS). NO has been reported to be involved in several steps of carcinogenesis, including interactions with p53 at both the genetic and the protein level and through regulation of the apoptotic pathways and DNA repair mechanisms. Recently, NO has also been linked to various immune and inflammation responses, especially in cancer development and wound healing process (Fig. 3). Tumors are known to alter the immune response and tissue vascularization which involves NO. Therefore, a better understanding of the roles of NO in immune response modulation and wound healing would allow us to design a better treatment plan and improve NO drug efficacy.

3.1 Genetic control and NO

The P1 isoform of the phase II detoxification enzyme glutathione-*S*-transferase (GST-P1) is often expressed at higher levels in certain tumor cells [58]. GST binds glutathione (GSH) catalyzing its reaction with aromatic substrates such as 1-chloro-2, 4-dinitrobenzene (CDNB), forming a stable product that inhibits the enzyme [59]. The nucleofugality of a diazeniumdiolate is comparable to the chloride of CDNB [60] and this has been exploited for drug design. By installing an aryl group similar to CDNB as the R1 substituent, the O^2-arylated diazeniumdiolate JS-K becomes an excellent substrate for GST, releasing the NONOate group, and thereby NO, upon activation [61]. While this may be one of the pathways by which JS-K is cytotoxic, results from in vitro studies [62] that have been conducted on the anti-tumor effects of JS-K point to the existence of multiple modes of action [63] including GST inhibition and GSH depletion. Despite the lack of clear-cut evidence about its mode of action, JS-K is a worthy lead in anti-cancer drug discovery [64].

3.2 NO-NSAIDs

Colorectal cancer (CRC) is the second largest type of cancer prevalent in the United States. In the 1970s [65], [66] some research groups reported that PG E2 was found in higher concentration in colorectal tumor tissue, which led to the hypothesis that NSAIDs could be employed in its treatment. Extensive studies demonstrated that COX-2 inhibitors produced a marked inhibition of carcinogenesis in rodents. NO-NSAIDs are comparable to regular NSAIDs in their ability to inhibit PG synthesis [67]. Three NONSAIDs, NO-ASA, NO-sulindac, and NO-ibuprofen were shown to reduce the growth of cultured HT-29 colon adenocarcinoma cells much more effectively than the corresponding NSAIDs [68]. The metabolic steps by which NO-NSAIDs produce NO have not been established [69] yet. However, since the "linker" between the NSAID and NO-release warhead was assumed to be inert, the superior pharmacological properties of NO-NSAIDs, compared to the parent NSAID, were ascribed to NO [70].

It has been demonstrated, mostly in preclinical models that, NO donor molecules are selective and efficacious agents alone and in combination with cytotoxic therapy in a

variety of solid tumor malignancies. Recent data [71] indicate that NO levels can be altered by activation of iNOS which in turn activate multiple targets such as EGFR, COX-2, HIF-1α, and VEGF. These molecules that inhibit iNOS could have the potential for wide and selective alteration of multiple targets associated with tumor growth, metastasis, and resistance. Quintero and his colleagues demonstrated that "nitric oxide is a factor in stabilization of HIF-1α in cancer by mechanisms dependent on free radical" [72]. Collectively, these effects [73] contribute significantly to the therapeutic synergy with anticancer drugs.

3.3 Challenges in the case

A major challenge for designing novel antineoplastic drugs is the generation of compounds with improved efficacy, lower side effects, and potential synergism with currently available antitumor agents. In spite of extensive research to develop new pharmacotherapeutic approaches to prevent or cure the disease, successful anticancer therapy is still not found. The major problem in this field arises from the intrinsic (before therapy) and acquired (caused by therapy) drug resistance. In light of this, the discovery of a compound with the potential to adapt its mode of action to cellular specificity and be "bright enough" to overcome the eventual barriers, such as nonfunctional apoptotic mediators or over functional protective signals, is one of the most desirable events. Different from the most cytostatic drugs, the intracellular response to GIT-27NO treatment is dictated by cell specificity, but not by the drug alone. Independently from this, the compound nonselectively down regulated the growth of a large spectrum of different types of tumors, apoptotic sensitive or resistant, p53 deficient or wild-type counterpart, and even in caspase-inhibited conditions promoted by itself. These data warrant further studies to evaluate the possible translation of these findings to the clinical settings.

4 Plants also join the NO party

Nitric oxide first came to prominence within the context of regulating plant defence during plant–pathogen interactions [74]. Nitric oxide has been implicated in defence against Pseudomonas syringae pathogens [75], [76] in barley infected with powdery mildew and downy mildew on pearl millet [77], [78] or Botrytis cinerea-challenged Arabidopsis [79]. With mammalian systems, bacterial LPS, a contributor to pathogen-associated molecular patterns triggered immunity (PTI), proved to be a highly effective initiator of NO [80]. Given these plant responses, it is unsurprising that many pathogens have evolved genes that could suppress NO-associated event(s).

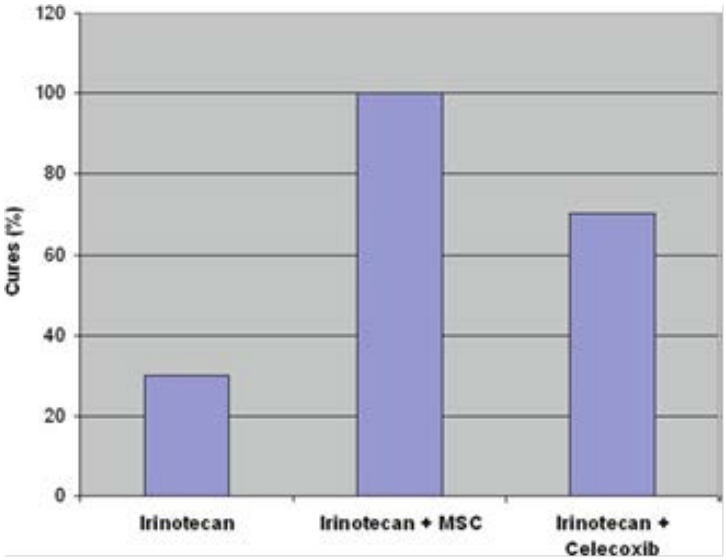


Fig. 5 *Inhibition of COX-2 leads to enhanced antitumor activity of irinotecan against FaDu Xenografts*

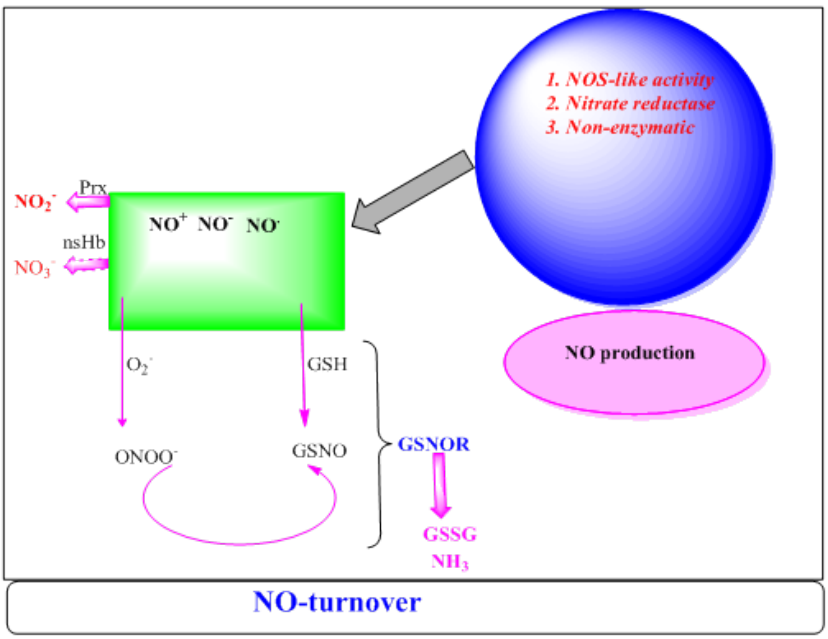


Fig.6 *NO-Production Pathways in Plants*

For example, Erwinia chrysanthemi expresses the flavohaemoglobin (fHb) HmpX, which oxidizes NO to NO_3^- [81]. In other cases, the pathogen may actively elicit host NO to aid in the infection process. For example, the virulence factor cryptogein produced by the oomycete Phytophthora cryptogea aids pathogenesis by promoting host cell death via NO generation [82], [83]. In addition, pathogen-generated NO can promote the formation of key fungal infection structures [84], [85]. Thus, depending on the pathogenic lifestyle, NO can act as either as a pathogen virulence or a host defense factor [86].

4.1 Routes of NO yield in Plants

Three routes to yield NO have been described in plants: non-enzymatic conversion of nitrite to NO in the apoplast, nitrate reductase (NR)-dependent NO formation and NO synthase (NOS)-like activity, that is arginine dependent NO formation [87].

Plant biologists have been lucky that NIA1 has proven to be a major source of NO despite some functional redundancy with NIA2. Thus, the nia1 mutant exhibits reduced NO production even when NIA2 is still functional [88]. However, for other NO generation mechanisms, problems with lethality, functional redundancy or their activation only under precise conditions (for example, normoxia and hypoxia) may be the reason that no generation mutants have been isolated. Thus, it may be that the plant ROS field offers a salutary lesson, as here generation mechanisms have often been characterized via biochemical means. This also highlights another theme of our review, the necessity to develop a better means of measuring NO, both to assay NO generation and the site of its generation.

4.2 Challenges to the NO news of plants

Currently, no technique fully meets all these requirements but we have noted ongoing developments in fluorescent dyes that could ultimately provide NO scientists with a key resource. Moving to consider NO signalling, currently a major focus is on S-nitrosylation and nitration events. We hope that our review suggesting that NO acts with cGMP will serve to inspire a revisiting of this possibility and may, incidentally, reveal a signalling pathway that is similar to that found in animals. Our last theme is one that is, understandably, often not

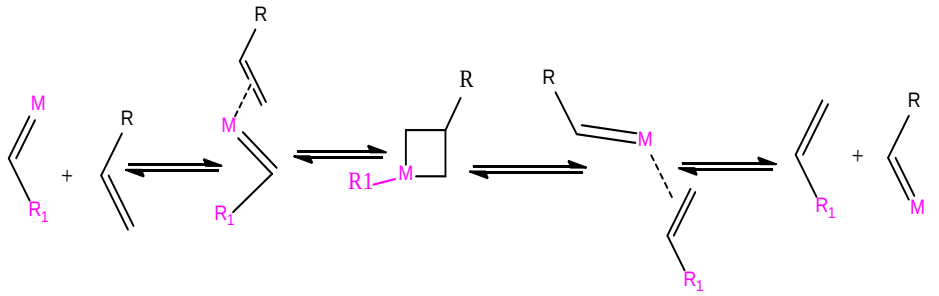
considered by laboratory-based plant scientists, namely how do plant signalling pathways function in an open environment. This is particularly apposite for NO as plants are being exposed to this signal from many exogenous sources. We therefore suggest that NO scavenging, e.g. by endogenous Hb, should be considered to be as important as NO generation in understanding in plants NO signalling. Finally, as plants are exposed to NO from a number of external sources, investigations into the control of NO scavenging by such as non-symbiotic haemoglobins and other sinks for NO should feature more highly. Thus need of producing best suited scavenging models by an inorganic chemist is one o the most important responsibility to upsurge the related research field of nitrosyl chemistry.

5 Industrial applications of Nitrosyl Compounds

New olefins are produced with the transition-metal-catalyzed olefin metathesis allowing the transformation of exchange of the olefinic carbene units [Scheme 2] [90].This reaction was discovered in the late 1950s by Herbert S. Eleuterio, at DuPont's petrochemicals department, in Delaware, USA, on investigations with propene over heterogeneous molybdenum catalysts and initiated widespread studies of this field in industry as well as in academic institutions [91], [92]. In fact, there is earlier evidence for the discovery of the metathesis reaction in polymer chemistry (ROMP) [93].The large majority of these catalysts contained molybdenum or tungsten centers in high oxidation states. Low-valent nitrosyl derivatives of molybdenum have also been successfully used [94]. For the propagation cycle, principally three parallel olefin metathesis routes have been envisaged to drive the ROMP metathesis cycle. They are denoted as the "ylid", the "*C*-nitroso", and the "iminate" routes.

5.1 Metathesis in polymer chemistry via NO-complexes

The formed ylid function attacks a nitrosyl ligand, which leads in a Wittig-type reaction to elimination of phosphine oxide as a key step providing a thermodynamic driving force for the initial reaction course. The initial "ylid route" thus merges into the "iminate route" along which carbene species are assumed to be provided to drive the ROMP propagation and the total polymerization process by alternating rhenacyclobutane formations and cycloreversions according to Scheme 2



Scheme 2 *Mechanism of cycloreversion Reaction Catalyzed by Metal Nitrosyls*

Catalytic applications of transition metal nitrosyl complexes are of current interest to organometallic and organic chemists. The dinitrosyl compounds of molybdenum have gained considerable interest due to their applicability as homogeneous catalysts. Some dinitrosyl molybdenum (0) complexes were reported to be used as catalysts in isomerization reactions of alkenes. $[Re(NO)_2(phosphine)_2]^+$ Cations for use in metathesis catalysis were first of all triggered by the lack of investigations on homogeneous rhenium-based systems in low oxidation states. Furthermore, the high activity of the isoelectronic dinitrosyl molybdenum and tungsten complexes [95], [96], [97], [98] for which, however, the actual catalytically ac-

tive species is not yet reliably established, The dinitrosyl compounds of molybdenum have gained considerable interest due to their applicability as homogeneous catalysts [99]. Certain dinitrosyl complexes [100] of transition metals were found to catalyze the conversion of CO and NO to the less harmful gases CO_2 and N_2O, which is of intrinsic interest because of their environmental relevance. It has been reported by Keller and Matusiak [101] that [Mo $(NO)_2(OCR)_2$ – Lewis acid] catalysts (Lewis acid = $TiCl_4$, $SnCl_4$, $EtAlCl_2$; R = phenyl, methylvaleric, ethylhexanoic) induce monosubstituted acetylenes (phenylacetylene, tert-butylacetylene) to polymerize. The catalytic ability of these catalysts strongly depends on the Lewis acid and solvent. A low-valent rhenium dinitrosyl bisphosphine complexes in catalytic ROMP activity of the cationic species has been observed.The unexpected reactivity as none of their ligands can be envisaged to be converted into a carbene unit. It could be shown that the formation of a carbene ligand is accomplished in situ from the initially formed rhenium complexes with highly strained, non-functionalized cyclic olefins, like norbornene. It was found that the carbene formation as the initiation step does not take place using functionalized cyclic olefins like bicycle [2.2.1]-5-heptene-2,3-dicarboxylate or 5-norbornene-2-carbonitrile. The mechanism supported by experimental and theoretical studies involving the cleavage of the strained olefinic bond by phosphine migration, forming ylid carbene complexes has been reported. The formed ylid function attacks a nitrosyl ligand, which leads in a Wittig-type reaction to elimination of phosphine oxide as a key step providing a thermodynamic driving force for the initial reaction course. The initial "ylid route" thus merges into the "iminate route" along which carbene species are assumed to be provided to drive the ROMP propagation and the total polymerization process by alternating rhenacyclobutane formations and cycloreversions according to Scheme 2.

5.2 Other Industrial Applications of NO-complexes

For over a century a famous nitrosyl compound sodiumnitroprusside SNP has been used as an analytical reagent for the qualitative and quantitative analysis of organic and inorganic compounds illustrated by the following examples. It is used as an indicator in the volumetric determination of halides, cyanides and the estimation of mercuric acetate in non-aqueous solvents. Its use as an indicator is proposed in the mercumetric estimation of chloride formed on the hydrolysis of chlorobutanol, and it is used in conjunction with certain dyes as an indicator in the estimation of reducing sugars. The intense yellow color given by SNP and caustic alkalis or alkaline-earth hydroxides serves to indicate the presence of these compounds. In general the use of SNP for the qualitative and quantitative analysis of cations is based on the formation of insoluble nitroprussides. All sulphur bearing anions give colorations with SNP. For example SNP has been used in the determination of the sulphite anion where it forms a red complex whose color is intensified in the presence of alkali metal ions [102], [103], [104]. Further, it is used to detect and estimate hydrosulphide derivatives, amino acids, polypeptides and proteins containing sulphur. It is also used for microbiological tests, blood and urine analysis [105].

5.3 NO in Food Industry

Nitrosyl complexes are available in market in the form of nitric-oxide boosters usually in organic form and there is an immense use of such products in body building and to eradicate the endothelial dysfunction problems among common masses. Some of the commonly available NO-boosters available in market are shown below (Fig. 7).

Fig. 7 *Commonly Used NO-boosters available in Market.*

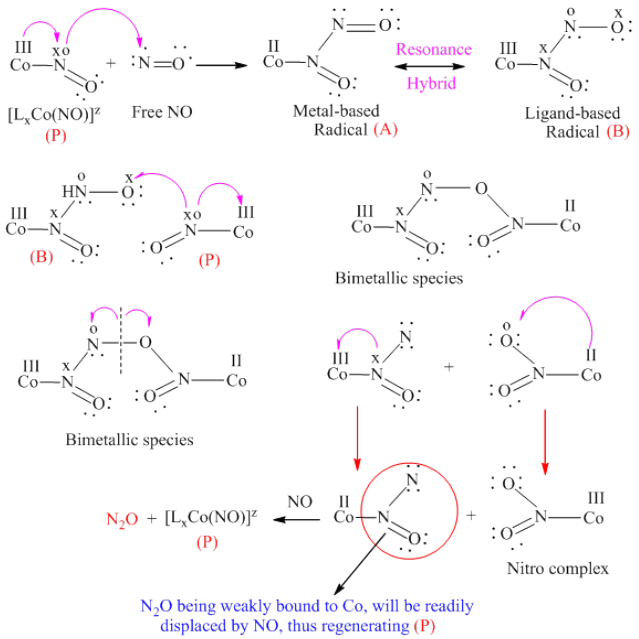


Fig. 8 *Catalytic Mechanism of NO to NO_2 Conversion by Cobalt nitrosyl*

5.4 Develop an Interest in Inorganic-NO Complex

One of the main drawbacks in consuming these products is that a large portion may remain undigested in the body and may result in stone formation , this is due to the fact of covalent bond in organic forms, so inorganic nitrosyl complexes should replace these products to be human-friendly and easily digestible.

6 Potentiality of nitrosyl complexes in pollution control

Another stimulus to investigating NO reactivity of metal nitrosyl complexes, has been the developments in pollution control [107], largely stemming from attempts to remove, or at least diminish the concentration of NO in exhaust gases emitted by the internal combustion engine. Certain dinitrosyl complexes of transition metals were found to catalyze the conversion of CO and NO to the less harmful gases CO_2 and N_2O, [5] which is of intrinsic interest because of their environmental relevance (Fig. 8).

Not only in air-pollution there is the role of nitrosyl-complexes but to detect pollutants of water both qualitatively as well as quantitatively the use of sodium nitroprusside has also been reported.

6.1 Water Pollution and NO

Comparison of nitroprusside-cyanide spectrophotometric method to iodometric method for the determination of S^{2-} in stagnant wastewater from Mitchell Hall of residence, Makerere University [106] using Nitroprusside as a tool to study the case (Table 1). Thus nitric-oxide complexes may be seen as future tool to treat pollutants of water as well. Moreover due to their anti-microbial action might result in development of powerful disinfectant tools.

The combustion of fossil fuels generates SO_2 and NO_X pollutants which cause acid rain and urban smog, these harmful gases may be adsorbed and converrted to less harming or useful compounds [108].

Table 1 *Comparison of Nitroprusside-cyanide Spectrophotometric Method to Iodometric Method for the Determination of S^{2-}*

S.N.	Nitroprusside method, $S^{2-}/\mu g\ mL^{-1}$	Iodimetric method, $S^{2-}/\mu g\ mL^{-1}$
1	12±0.2	14± 0.3
2	10±0.2	13± 0.3
3	08±0.2	12± 0.3
4	07±0.2	12± 0.3
5	11±0.2	14± 0.3
6	07±0.2	12± 0.3
7	09±0.2	13± 0.3

The current technique for post combustion control of nitrogen oxide emissions, ammonia-based selective catalytic reduction, suffers from various problems [109], [110], including poisoning of the catalysts by fly ash rich in arsenic or alkali, disposal of spent toxic catalysts and the effects of ammonia by-products on plant components downstream from the reactor. To circumvent the need for separate schemes to control SO_2 and NO_x, an iron (II) thiochelate complex that enhances the solubility of NO in aqueous solution by rapidly and efficiently absorbing NO to form iron nitrosyl complexes has been reported. The bound NO is then converted to ammonia by electrochemical reduction, regenerating the active iron (II) catalyst for continued NO capture, suggesting that this process can be readily integrated into existing wet limestone scrubbers for the simultaneous removal of SO_2 and NO_x [111]. Flue-gas desulphurization scrubbers involve wet limestone processes which are efficient for controlling SO_2 emissions but are incapable of removing water-insoluble nitric oxide. So needs more intervention of scientific approaches.

In view of above, this overview, therefore, primarily focuses our recent work related to the synthesis, characterization and 3D-moleclar modeling of some mixed nitrosyl complexes of $\{Mo(NO)_2\}$, $\{MnNO\}$ and $\{Mn(NO)_2\}$ electron configurations in different organic donor environments [57]. The role in the theoretical field is a novel step to solve the various altitudes and longitudes of various redox potential concepts and bonding parameters. The disadvantage of feeding organic NO boosters should be substituted by inorganic photolabile nitrosyl complexes of more advantages. The mystery of memory power would be more explored if nitrosyl complexes are studied deeply. The role of nitrosyl complexes in plants is yet at door steps and needs preference to provide botanists scavenging and donoring models of nitrosyl complexes. World is at the verge of deadly pollution problems and various methods are being employed to eradicate the contamination of various components of biosphere and lithosphere. Nitrosyl complexes are also the prominent delegates of the issue. Various polymerization reactions may use nitrosyl complexes as a catalyst to enhance reactivity. Their use as anticancer drugs and antihypertensive medicine is a gift to the medicinal research.

A major challenge for designing novel antineoplastic drugs is the generation of compounds with improved efficacy, lower side effects, and potential synergism with currently available antitumor agents. In spite of extensive research to develop new pharmacotherapeutic approaches to prevent or cure the disease, successful anticancer therapy is still not found. The major problem in this field arises from the intrinsic (before therapy) and acquired (caused by therapy) drug resistance. In light of this, the discovery of a compound with the potential to adapt its mode of action to cellular specificity and be "bright enough" to overcome the eventual barriers, such as nonfunctional apoptotic mediators or over functional protec-

tive signals, is one of the most desirable events. Different from the most cytostatic drugs, the intracellular response to GIT-27NO treatment is dictated by cell specificity, but not by the drug alone. Independently from this, the compound nonselectively down regulated the growth of a large spectrum of different types of tumors, apoptotic sensitive or resistant, p53 deficient or wild-type counterpart, and even in caspase-inhibited conditions promoted by itself. These data warrant further studies to evaluate the possible translation of these findings to the clinical settings.

7 References

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