Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 10, pp.40424-40432, October, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

PHARMACEUTICAL DESIGN OF NO RELEASE FROM IRON, MANGANESE AND RUTHENIUM NITROSYL COMPLEXES

***Jan Mohammad Mir, Neeta Jain and Maurya, R. C.**

Coordination, Bioinorganic & Computational Chemistry Laboratory, Department of PG Studies and Research in Chemistry and Pharmacy, RD University Jabalpur-482001

ARTICLE INFO

Article History:
Received 26th July, 2016
Received in revised form
22nd August, 2016
Accepted 20th September, 2016
Published online 30th October, 2016

Key words:

Nitrosyl, Solution, Visible light,
NO vehicles.

ABSTRACT

This manuscript is an update of some important concerns about nitrosyl complexes having the ability to act as nitric oxide releasing compounds under varied circumstances involving ligand, metal and solution properties. In current times seek for efficient and less harmful NO releasing molecules at desirable target and concentration has gained enormity in nitrosyl chemistry. Iron, ruthenium and manganese nitrosyls have been investigated to a considerable extent to disentangle their electronic transition (excitation) under visible light to act as NO donor without harming healthy cells of a target. There are many evidences supporting the NO-lability to be increased if amino acids are used as complexing ligands, design of reduction centre close to an NO grouping and development of porphyrin system based nitrosyl complexes. From the overall survey it may be concluded that desirable properties of such scaffolds need to be evaluated further to well suit with biological milieu.

Citation: Jan Mohammad Mir, Neeta Jain and Maurya, R. C. 2016. "Pharmaceutical design of No release from iron, manganese and ruthenium nitrosyl complexes", *International Journal of Current Research*, 8, (10), 40424-40432.

INTRODUCTION

During the 'Dark Ages' of nitric oxide (NO) biochemistry (1) (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 $NO^{\cdot}$). Small, simple and highly toxic pungent smelling gas as environmental pollutant found in photochemical smog (2), produced by oxidation of NH_3, incomplete combustion of gasoline in motor vehicle exhausts (3), and power stations (4), 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 (5). The discovery and elucidation of its biological functions by Louis J. Ignarro and others in the 1980s came as a surprise (6). 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 (7) culminated in 1992 with NO being declared "Molecule of the Year" by the journal *Science* (8). In addition to its role as a molecular messenger and vasodilator, endogenously (9) produced NO in living organisms (10) has been shown to be involved in a great many biological processes (11) and dysfunction (12) in NO metabolism has been associated with a number of disease state such as epilepsy, arthritis, hypertension and septic shock, tumour progression, etc. As, any aspect of biology/biological molecule that can be put to some useful application, *viz.*, drug development for human health care, is the biotechnology (12), the present work is befitting in purview of medicinal biotechnology of nitrosyl complexes in combination with chemistry from the following facts:

(i) The nitric oxide produced endogenously by nitric oxide synthase (NOS) (13), acts as a signaling molecule to regulate blood pressure, neurotransmission, inhibition of platelet aggregation, cell-mediated immune response, antimicrobial activity and cell apoptosis(14).

(ii) The biological activity of NO depends on dose and duration of exposure as well as on cellular sensitivity to NO. For example, relatively low concentration (2-300 nm) of NO produced by the constitutive NOS (nNOS and eNOS) are required for its neurological and vascular functions (15). Much larger concentration (low mM) of NO produced by activated microphages via inducible isoform of NOS (iNOS) lead to cytotoxicity (16).

(iii)NO deficiency has been implicated in the genesis and evolution of several disease states. Both medical needs and commercial opportunities have fostered attempts to

Corresponding author: Jan Mohammad Mir,
Coordination, Bioinorganic & Computational Chemistry Laboratory, Department of PG Studies and Research in Chemistry and Pharmacy, RD University Jabalpur-482001

modulate NO in the human body for therapeutic gain (17).

(iv) This prompted research in the area of development of exogenous NO carrier drugs (18) that can deliver NO at desired locales.

(v) Synthetic exogenous nitric oxide (NO) donors produce NO-related activity when applied to biological systems. So they are mainly suited to either mimic an endogenous NO-related response or substitute an endogenous NO deficiency for the treatment of various diseases (19).

1. Metal Nitrosyl Complexes

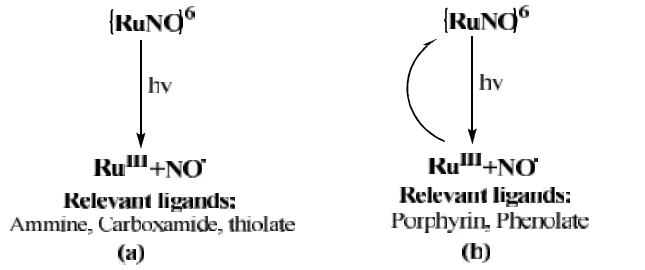
The search for new storage release systems, capable of delivering NO to desired targets, has stimulated the chemistry of metal nitrosyl complexes, which has witnessed a substantial progress since the last decade (20). The chemistry of metal nitrosyl complexes has taken on added significance (21) in recent years because of the important role involving transition metal in the biological process of NO, as well as the possibility of producing thermodynamically stable and kinetically labile species. Such strategies (21) have focused on the development of pharmacological substances capable of releasing NO at specific rates in tissues, in order to overcome NO deficiency. The great affinity of d^6 and d^5 low-spin and in low oxidation state metal complexes for NO and the versatility of NO on its own right as a ligand make the nitrosyl complexes a good alternative for such a proposal. Iron, ruthenium (22) and manganese are good candidates as a model for NO carriers. Indeed, several iron-based nitrosyls including sodium nitroprusside (SNP, $Na_2(Fe(NO)(CN)_5)$) (23) and Roussin's salts (24) were found to release NO when exposed to light. Despite its well known toxicity, SNP is largely used as a NO deliverer in clinical practices for blood pressure control in cases of acute hypertension (25). In recent years, interest in nitrosyl complexes has been renewed following the successful use of sodium nitroprusside (SNP) as a NO donor drug to control high blood pressure during hypertensive episodes (25). Interestingly, metal nitrosyls like SNP and Roussin's salts (Fe-S clusters that store multiple equivalents of NO) release NO upon illumination with light (300-500 nm) (24, 23).

However, low quantum yields, release of NO spontaneously (i.e. in the dark) and often changes in pH and temperature, and problems associated with ancillary ligands (such as cyanide in case of SNP) limit the use of such nitrosyls in PDT. Chelating ligands provide some relief from these problems. For example, the iron complex $((PaPy_3)Fe(NO))(ClO_4)_2$ was the first of many NO donors to be studied by Mascharak and co-workers (26-28). It was shown to cleanly release NO when exposed to low-intensity visible light. Unfortunately, like many other iron nitrosyls, $((PaPy3)Fe(NO))(ClO4)_2$ exhibits unpredictable stability under biological conditions. Several NO-releasing complexes of chromium (29-31) and manganese (32, 33) have also been reported, but are limited by similar effects. The only exception is the manganese nitrosyl $((PaPy_3)Mn(NO))(BF_4)$ (34-36). This photoactive NO donor has been used to deliver NO to biological targets like myoglobin, cytochrome c oxidase, and papain (37, 38). Clearly, the number of metal nitrosyls that release NO exclusively when triggered by light and exhibit stability under physiological conditions (pH ~7, presence of oxygen) is very limited.

2. Ruthenium nitrosyl complexes: Photodynamic Therapy (PDT) and Light Activated NO Donors

PDT has been evaluated as an adjuvant therapy to other therapeutic modalities, including surgery, hyperthermia, radiotherapy, immunotherapy and chemotherapy as new approaches for the treatment of a variety of cancers and non-malignant disorders (39). In DPT two individually non-toxic components are combined to induce cellular effects in an oxygen dependent manner. The first component consists of a photosensitive molecule, a photosensitizer that preferentially localizes to a target cell and/or tissue. The second involves the administration of light of a specific wavelength that activates the sensitizer. The excited sensitizer generates highly reactive singlet oxygen and other reactive oxygen species that trigger a complex cascade of photochemical reactions and photobiological events that eventually cause injury and death of targeted cells. NO donors that release NO photochemically have generated much interest because they allow localized release of NO and could be used for photodynamic therapy of cancer cells (40). The site specificity provided by laser treatment allows for more precise targeting than systemic drugs alone. It has been demonstrated that cells subjected to PDT produce NO (41). Because NO reacts with various reactive oxygen species generated by PDT, it has been suggested that NO contributes to the effective outcome of PDT treatment (42).

Since complexes of ruthenium are in general more stable, a variety of ruthenium nitrosyls have been isolated and studied in detail in terms of their NO donating capacities (43) to biological targets on demand. In general, the nitrosyls with non-porphyrin ligands (such as amines, Schiff bases, thiolates and ligands with carboxamide groups) readily release NO upon illumination and generate Ru(III) photoproducts. In contrast, NO photorelease from ruthenium nitrosyls derived from porphyrins remains limited due to rapid recombination.



Scheme: (a) Generation of NO and Ru(III) photoproduct, (b) NO Photogeneration followed by NO recombination.

Although many ruthenium nitrosyls are known to release NO upon energy-intensive UV light irradiation (44), reports on visible light NO labilizations of ruthenium nitrosyls are rare (45). In addition, the Ru^{III} solvent complexes that result after irradiation inevitably undergo undesired side reactions in solution. One continuing challenge is, therefore, to find a Ru-NO complex that could release NO reversibly under very mild conditions without any metal-bound side reactions for biological applications. Study of photo induced NO cleavage (46-48) has shown that the NO release in Polyamidoamine functionalized with ruthenium nitrosyl compounds is made through light irradiation (λ = 355 nm) and one-electron reduction (Eu^{2+}) (49). The record of stability of phosphite coordinated to ruthenium(II) in aqueous media is also attractive work (50). NO release in some cases has been stated to be possible only if they are activated by reduction centered

on the nitrosyl ligand (50). Another important recent advancement in the nitrosyl lability is from a trinuclear ruthenium nitrosyl complex and the relevant in vitro cytotoxicity against melanoma cells (51) and certain ruthenium nitrosyl clusters have been designated a pro-drug, NO releasers. It has also been found that chronic corticosterone administration facilitates aversive memory retrieval and increases glucocorticoid receptors (GRs)/Nitric oxide synthase (NOS) immune reactivity. As retrograde messenger, NO influences the formation of long-term potentiation (LTP) and memory consolidation (52). Cell penetrating ability and cytotoxicity of nitric oxide donoring ruthenium complexes is also quite fascinating (53). Some concerns regarding the NO release with anti HIV and anti cancer activities have also been investigated. Synthesis of ruthenium nitrosyl complexes (54, 55) is thus fundamentally attentive because of the admirable facts of metal reactivity. In some cases of nitrosyl-bridged diruthenium complexes protonation of metal-metal bonds by the addition reaction of proton has been brought to light (56) and the enhanced metal basicity and spontaneous reaction with a proton (from HBF_4) in diethyl ether to afford the corresponding oxidative addition has been recorded. Some crystalline forms of the nitrosyl ruthenium complex have been worked out (57) showing volume of guest solvents, the unit cell parameters and the resulting *iso* structural arrangement with small differences in the intermolecular interactions, with caged guest solvents, that interact with the complex by hydrogen bonds.

3. Theoretical studies on certain nitrosyl complexes of ruthenium are already reported involving their geometry optimization and verification through furnished x-ray data (58) involving the complex in conformation of minimum energy and not in a transition state using Spartan programme with B3LYP hybrid density functional theory in conjunction with the 6-31G basis sets and LACVP for the Ruthenium Atom. In some cases (59) DFT geometry optimization of the complex has been carried out with the aid of GAMESS software (60) with a convergence criterion in a conjugate gradient algorithm. It is here to mention that the use of LANL2DZ (61) effective core potential for Ruthenium and the atomic 6-31G(d) basis set (62) employed for all other atoms in the complex and B3LYP hybrid functional (63) have fetched reliable results as per the reports. Molecular orbitals and the simulated electronic spectrum may also be determined by the semi-emperical ZINDO/S method (64) as implemented in the hyper chem program (65, 66). Generally Self Consistent Field Calculations are accomplished, in order to obtain RHF wave functions with reliable criterion for convergence, using the Ruthenium and Cl parameters from the literature (67). The electronic spectrum calculated on the basis of single Cl excitations in an active space and the adsorption profile can be simulated by using Gaussian functions. Computational study of (Ru(salen)(NO)Cl) species from X-ray atomic coordinates (68) has also been documented. The electronic structure calculated with ZINDO/s method and Self Consistent Reaction Field approximation in bulk solvent effects has been reported. Gaussian run UV Vis spectrum has been used in verifying the formulations for the precursor and photoproduct complexes (35), the spectra of the singlet species (Ru(Salen)(NO)Cl) represents precursor and the doublet species $(Ru(Salen)(H_2O)_2)^+$ as photoproduct. Appreciable charge transfer analysis is made through the TD-DFT programme (69). The vibrational frequency calculations are generally performed to ensure that the optimized geometries represent the local minima and there are only positive eigen values including no imaginary frequency (70). Vertical electronic excitations based on B3LYP/(U)b3LYP optimized geometries are computed for the time-dependent density functional theory (TD-DFT) formalism (71).

4. Dinitrosyl iron(II) complexes (DNICS)

Electronic structure of dinitrosyl porphyrin metal complexes has remained highly interested quest since the last decade (72) to unravel the respective stereochemistry. The class of complexes has earned much attention due to applications as nitric oxide donors as well as possessing interesting electronic structures (73). Typical Fe–NO electromerism issues are complicated by the presence of a second nitrosyl ligand.

CASSCF calculations on selected models confirm the multi configurational character of the $Fe(NO)_2$ moiety, with the largest contributor at only 44% of the total weight of the wave function. Tailoring of iron to change the nature of coordination sphere involving 4, 5 or 6 coordination numbers to release nitrosyl ligand is an important asset. Compared to the tetrahedral $\{Fe(NO)_2\}$ dinitrosyl iron complexes (74) displaying EPR signal g = 2.03, the newly synthesized six-/five-coordinate exhibit the distinct EPR signal g=2.015–2.018. It has been shown that the aspect of the geometric structure of $\{Fe(NO)_2\}$ DNICs impose electron-donating ability and conformation of the coordinated ligands regulates the Fe–NO bonding of $\{Fe(NO)_2\}$ DNICs and presumably the release of nitrosyl from DNICs. Very recently (75) a series of iron dinitrosyl complexes have been investigated and shown to undergo one-electron oxidations. Infrared spectro electrochemistry revealed that the oxidations generate the derivatives with ν_{NO}s that are ~100 cm^{-1} higher in energy indicative of $Fe(NO)_2$-centered oxidations.

5. Biological Fate of NO & its Protein Interactions

Vanin et al. (76) suggested a hypothesis that NO and its endogenous derivatives (low molecular S-nitroso thiols and dinitrosyl iron complexes (DNIC) with thiol-containing ligands) can move in the intracellular space not only by diffusion but also in an auto wave mode. This hypothesis is based on the previously reported data on auto wave distribution of DNIC with glutathione following application of a drop of a solution of Fe^{2++} glutathione onto the surface of a thin layer of S-nitroso glutathione solution. According to the report (76) of this group auto wave distribution of NO and its endogenous derivatives in the intracellular space is advantageous of over free diffusion, which might entail higher efficiency of their biological action, are discussed. Regarding nitric oxide-derived cellular adducts of their formation and biological fate (77) quantitative measurements reveal that cellular concentrations of DNIC are proportionally the largest of all NO-derived adducts (900 pmol/mg protein, or 45–90 μM). It has been established that DNIC will be formed under all cellular settings of NO production and that the contribution of DNIC to the multitude of observed effects of NO must always be considered.

6.1. DNICS in Blood Circulatory System

Cysteine based dinitrosyl-iron complexes have been found responsible for a long-lasting vasorelaxation (78). It has been found (79) that intracavernous injections of water-soluble

dinitrosyl iron complexes (DNIC) with glutathione or cysteine (0.4–6.0 μmoles/kg) to male rats induce short-term (2–3 min) penile erection along with a short-term drop of arterial pressure and appearance of protein-bound DNIC in cavernous tissue and circulating blood. The nature of a compound able to induce long-lasting relaxation of rat abdominal aorta rings after addition of rapidly (within several minutes) disappear mono- and binuclear dinitrosyl iron complexes with Cysteine. It has been reported that long-lasting vasorelaxation is not induced either by S-nitrosocysteine formed upon decomposition of DNICs or by accumulation of free nitric oxide molecules or nitrite remaining in the incubation medium. It is hypothesized that compound representing a cysteine ester of nitrosyl iron complexes, namely, a black Roussin's salt cysteine ester is responsible for long-lasting vasorelaxation. Hence, inorganic iron nitrosyl complexes will prove more beneficial in treating heart diseases and hypertension than organic nitroso forms. A comparative study of hypotensive effects of binuclear forms of dinitrosyl iron complexes (DNICs) with glutathione, S-nitrosoglutathione (GS-NO) and sodium nitrite (NaNO2) on rats in first clinical phase trial has revealed that the latter appeared to be the least efficient, viz., mean arterial pressure (MAP) decreased by 10 and 30 mm Hg at 25 and 100 lmoles/kg of $NaNO_2$ (80). In contrast, DNIC and GS-NO produced an appreciable hypotensive effect when used at much lower concentrations. It has been found that dinitrosyl iron complexes with glutathione (DNIC-GS) injected into the blood flow of rats at a dose of 0.05 μmoles/kg prior to hemorrhage significantly improve cardiac function under conditions of hemorrhagic shock manifested in increased stroke volume, left ventricular work and cardiac output to a level exceeding control values 1.5-fold (81). It has been suggested that beneficial effects of DNIC-GS on systemic circulation parameters under conditions of hemorrhagic shock are determined by their antioxidant activity and the ability to induce S-nitrosylation of proteins. It is thus, well established that nitric oxide (NO) reacts with cellular iron and thiols to form dinitrosyl iron complexes (DNIC). Among prokaryotes (*E. coli*) Iron–sulfur proteins have been designated as major source of protein-bound dinitrosyl iron complexes formed under nitric oxide stress (82). Expression of recombinant iron–sulfur proteins, but not proteins without iron–sulfur clusters, almost doubles the amount of protein-bound DNICs formed in E. coli cells after NO exposure.

Hemoproteins play central roles in the formation and utilization of nitric oxide (NO) in cellular signaling, as well as in protection against nitrosative stress (83). Key to heme–nitrosyl function and reactivity is the Fe coordination number (5 or 6). For (five-coordinate) 5c-NO complexes, the potential for NO to bind on either heme face exists, as in the microbial cytochrome c from Alcaligenes xylosoxidans (AxCYTcp), which forms a stable proximal 5c-NO complex via a distal six-coordinate NO intermediate and a putative dinitrosyl species. Strong parallels between the NO-binding kinetics of AxCYTcp, the eukaryotic NO sensor soluble guanylate cyclase, and the ferrocytochrome c/cardiolipin complex have led to the suggestion that a distal-to-proximal NO switch could contribute to the selective ligand responses in gas-sensing hemoproteins. In case of plants, exposure to nitric oxide increases the nitrosyl-iron complexes content in sorghum embryonic axes (84). Nitrosyl-Fe complexes formation has been detected in sorghum embryonic axes homogenates incubated in vitro in the presence of 1mM of NO donors: diethylenetriamine NONOate (DETA NONOate), S-nitrosoglutathione (GSNO) and sodium nitroprusside (SNP). In axes isolated from seeds incubated in vivo in the presence of 1mM SNP for 24 h, the content of NO has been found to have increased by 2-fold and the EPR spectrum from mononitrosyl-Fe complexes (MNIC) shows a concomitant increase in the fresh weight of sorghum axes. Some reports have also shown that the submicromolar NO concentration, the aerobic nitrosation of glutathione does not involve NO autoxidation but a reaction that is first order with respect to NO (85). Glutathione dinitrosyl complexes can be easily synthesized in the air at ambient temperature (86) including consecutive addition to distilled water of glutathione, which decreases the pH of the test solution to 4.0, a bivalent iron salt (e.g., ferrous sulphate) and sodium nitrite at the molar ratio of 2:1:1, with a subsequent increase in pH to neutral values. Using the electron paramagnetic resonance (EPR) and optical spectrophotometric methods, it has been established that biologically active, water-soluble dinitrosyl iron complexes (DNIC) with glutathione are predominantly represented by the diamagnetic binuclear form (B-DNIC) even in the presence of a 10-fold excess of glutathione non-incorporated into DNIC at neutral pH (87). Considering the dinitrosyl iron complexes with glutathione as NO and NO^+ donors, recently it has been reported that heating of solutions of the binuclear form of dinitrosyl iron complexes (B-DNIC) with glutathione in a degassed Thunberg apparatus (pH 1.0, 70 ˚C, 6 h) results in their decomposition with a concomitant release of four gaseous NO molecules per one B-DNIC (88). Further injection of air into the Thunberg apparatus initiates fast oxidation of NO to NO_2 and formation of two GS-NO molecules per one B-DNIC. Under similar conditions, the decomposition of B-DNIC solutions in the Thunberg apparatus in the presence of air is complete within 30–40 min and is accompanied by formation of four GS-NO molecules per one B-DNIC. It has been suggested that the latter events are determined by oxidation of B-DNIC iron and concomitant release of four nitrosonium ions (NO^+) from each complex. Binding of NO^+ to thiol groups of glutathione provokes GS-NO synthesis. At neutral pH, decomposition of B-DNIC is initiated by strong iron chelators, viz., o-phenanthroline and N-methyl-D-glucamine dithiocarbamate (MGD). In the former case, the reaction occurs under anaerobic conditions (degassed Thunberg apparatus) and is accompanied by a release of four NO molecules from B-DNIC. Under identical conditions, MGD-induced decomposition of B-DNIC gives two EPR-active mononuclear mononitrosyl iron complexes with MGD (MNIC–MGD) able to incorporate two iron molecules and two NO molecules from each B-DNIC. The other two NO molecules released from B-DNIC (most probably, in the form of nitrosonium ions) bind to thiol groups of MGD to give corresponding S-nitrosothiols. Acidification of test solutions to pH 1.0 initiates hydrolysis of MGD and, as a consequence, decomposition of MNIC–MGD and the S-nitrosated form of MGD; the gaseous phase contains four NO molecules (as calculated per each B-DNIC). The data obtained testify to the ability of B-DNIC with glutathione (and, probably, of B-DNIC with other thiol containing ligands) to release both NO molecules and nitrosonium ions upon their decomposition. As far as nitrosyl iron complexes with non-thiol-containing ligands predominantly represented by the mononuclear mononitrosyl iron form (MNIC) are concerned, their decomposition yields exclusively NO molecules.

6.2. Application of DNICS as Antitumor Agents

Comparative antitumor effect of curcumin and dinitrosyl iron complexes against melanoma cells has indicated a synergistic

cytotoxic effect on mouse melanoma B16-F10 cells *in vitro* (89). In vitro DNA cleavage assay showed that the DNICs could cause plasmid DNA damage through releasing NO under UV irradiation. The cytotoxicity assay demonstrated these DNICs were toxic to B16-F10 cells in vitro, and the estimated values of LD50 (24 h of incubation) of NC01 and NC02 were 1 μM, while the values of LD50 of NC03 was 200 μM. No synergistic cytotoxicity effect was noted in the treatments of the combinations of curcumin and DNICs. DNIC with thiosulfate have been reported to manifest pro-apoptotic activity during incubation of HeLa cells in Versene's solution supplemented with ethylene diamine tetraacetate (EDTA) known to induce the decomposition of these DNIC (90). The water-soluble o-phenanthroline derivative bathophenanthroline disulfonate (BPDS) had shown similar effect on DNIC with glutathione during incubation of HeLa cells in Eagle's medium. It has been assumed that EDTA or BPDS induced pro-apoptotic effect of DNIC with thiosulfate or glutathione coupled with the ability of decomposing DNIC to initiate S-nitrosylation of proteins localized on the surface of HeLa cells. Intraperitoneal injection of dinitrosyl glutathione iron complexes has been reported to suppress endometrioid tumours (91). To gain insight into the possible genotoxic effects of DNIC, the interaction of histidinyl dinitrosyl iron complexes (HIS-DNIC) with DNA by means of circular dichroism and the formation of DNIC monitored by EPR, FTIR spectroscopy and vibrational bands indicate that HIS-DNIC changes the conformation of the DNA in a dose-dependent manner in 10 mM phosphate buffer (pH 6). Increase of the buffer pH or ionic strength decreased the effect. Comparison of HIS-DNIC DNA interaction with the effect of hydrated Fe^{2+} ion revealed many similarities (92). The importance of iron ions in HIS-DNIC induced genotoxicity has been confirmed by plasmid nicking assay and imply that there is no direct interrelationship between iron–NO coordination and their mutual toxicity modulation (92).

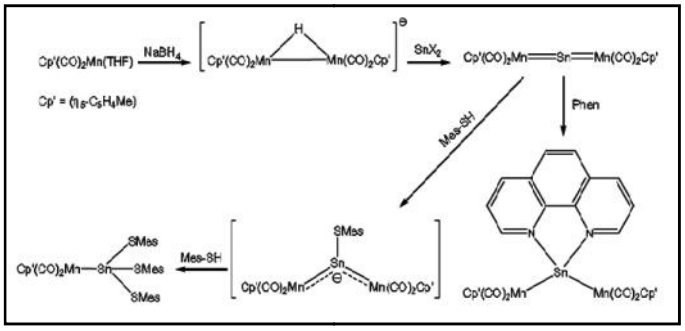
7.Manganese(II) nitrosyl complexes

Based on NO reduction of some manganese nitrosyl complexes and their studies based on IR spectral data reveal non-bridging structure (93). However, the sequential reaction of certain dimanganese complexes with NO (5% in N_2) at room temperature and NO_2, present a nitrite ligand bridging the dimetal centre through the N and O atoms (94). Non-innocent ("suspect") behaviour of redox active, $NO^+/NO^{\bullet}/NO^-$ either substrates or supporting components is now even discussable in biochemical context interacting with manganese (95).

7.1. Manganese Nitrosyl Complexes

EPR based studies on manganese (II) nitrosyl complexes shown effects of site-specific chemical modification of the distal histidine on ligand-binding structures (96). The surface chemistry of NO with respect to manganese metal surface has also attained a good research momentum. Adsorption of nitric oxide (NO) and carbon monoxide (CO) and the co-adsorption of (NOCCO) and (COCNO) over the manganese (II)-exchanged studied by infrared spectroscopy has shown to be effected by pressure, temperature and evacuation on these NO/CO species have been studied (97). Investigations on the influence of pre-sorbed CO molecule on the adsorption of NO molecules over the catalysts indicated that the pre-adsorption of CO molecules strongly affects the NO adsorption. The concentration of NO/CO species varies with the NO/CO pressure, reaction temperature and evacuation. Spectroscopy, microscopy and theoretical study of NO adsorption on MoS_2 and Co–Mo–S hydrotreating catalysts (98) via infrared (IR) spectroscopy using NO as a probe molecule has been one of the important methods for characterizing hydrotreating catalysts, since this technique provides information on the nature and quantity of active edge sites of these catalysts. Thus, it is possible to use NO as a probe molecule to obtain detailed atomic-scale information on hydrotreating catalysts and the origins of activity differences.

Selective catalytic reduction (SCR) of nitrogen oxides (NO_x) with ammonia is one of the processes for cleaning the flue gas and by using diffuse reflectance infrared Fourier transform spectroscopy (DRIFT) of Fe–Mn/TiO_2 revealed that surface OH species are consumed during NO adsorption, indicating that O_2 could promote the dehydration reaction of the manganese oxides to produce active oxygen and greatly enhance the amount of NO complexes on the catalyst (99). The role in metathesis by the application of Cyclopentadienyl-$Mn(CO)(NO)SnCl_3$ pronounces the industrial relevance of manganese(II) nitrosyl complexes (100) as shown in the scheme below



Scheme 1

7.2. NO-delivery from manganese nitrosyls at the biological target

Chemical mechanisms relevant to roles played by nitrogen monoxide species in mammalian bio-regulation and immunology have proved very useful in probing these mechanisms (101). Keen interests are developed to build strategies to deliver NO to biological targets upon demand for such goals as the sensitization of radiation damage in hypoxic tissue. One such strategy would be to employ a precursor that displays relatively low thermal reactivity but is photo chemically active to release NO. This proposition has led us to investigate the flash and continuous photolysis kinetics of a number of different nitrosyl complexes. Manganese nitrosyls have found potential application in inhibiting papain by the S-nitrosylation inhibiting the hydrolytic ability triggered by light-induction (102). Mn porphyrins allow us to design optical and electrochemical selective HNO sensors (103). Mn(II) substituted myoglobins has been found applicable in nitrite reduction Towards understanding necessary components of Mb nitrite reductase activity to nitric oxide drawing increasing attention as a protective mechanism to hypoxic injury in mammalian physiology (104).

Conclusion

In the conspicuous trials as discussed above all the three photo labile class of metal nitrosyls represent interesting quests to

emerge out the appropriate coordination milieu around the central metal atom to depict the efficient NO release at the desirable target and in desirable concentration. The further studies of redox potential variation and animating the appropriate solution pH should be dealt. The solution impact upon the solubility of the complexes should be unfurled further to arrive at the most feasible NO releaser at the cost of universal solvent *i.e.*, water. Besides experimental set ups theoretical/computational invokes should also be used to pave the ways for competing the NO releasing phenomenon among various model complexes.

Acknowledgements

Dr J. M. Mir acknowledges Miss Tabssum for her encouragement to embody the present work. Authors feel thankful to HOD Chemistry and Pharmacy RD University, Jabalpur for interesting and useful discussions to empower the present work with authentic ideas.

REFERENCES

1. M. J. Rose and P. K. Mascharak, Fiat Lux: selective delivery of high flux of nitric oxide (NO) to biological targets using photoactive metal nitrosyls, *Curr. Opin. Chem. Biol*., 12 (2008) 238.
2. G. F. Caramori and G. Frenking, The effects of N-Heterocyclic ligands on the nature of the Ru–(NO) bond in Ruthenium tetraammine nitrosyl Complexes, *Croat. Chem. Acta*, 82 (2009) 219.
3. J. A. McCleverty, Chemistry of nitric oxide relevant to biology, *Chem. Rev.*, 104 (2004) 403.
4. M. Delledonne, NO news is good news for plants, Curr. *Opin. Plant Biol*., 8 (2005) 390.
5. R. C. Maurya, "Synthesis and Characterization of Some Novel Nitrosyl Compounds" Pioneer Publications, *Jabalpur*, 2000.
6. J. L. Ignarro, Endothelium-derived nitric oxide: pharmacology and relationship to the actions of organic nitrate esters, *Pharmacol Res*., 6 (1989) 651.
7. X. Zhang and M. Broderick, Amperometric detection of nitric oxide, *Mod. Asp. Immunobiol*., 1 (2000) 160.
8. E. Culotta and D. E. Koshland Jr, "NO News is Good News (nitric oxide; includes information about other significant advances & discoveries of 1992) (Molecule of the Year)", *Science*, 258 (1992) 1862.
9. A. A. Eroy-Reveles, C. G. Hoffman,-Luca and P. K. Mascharak, Formation of a triply bridged μ-oxo diiron(III) core stabilized by two deprotonated carboxamide groups upon photorelease of NO from a $\{Fe–NO\}^6$iron nitrosyl, *Dalton Trans*., (2007) 5268.
10. C. Y. Chiang, M. Y. Darensbourg, Iron nitrosyl complexes as models for biological nitric oxide transfer reagents, *J. Biol. Inorg. Chem*., 11, (2006) 359.
11. G. M. Halpenny and P. K. Mascharak, Accelerated photorelease of NO from {Ru-NO} 6 nitrosyls containing carboxamido-N and carboxylato-O donors: syntheses, structures, and photochemistry, *Inorg. Chem*., 48 (2009) 1490, and references therein.
12. H. K. Das, Textbook of Biotechnology, 3rd edition, Wiley India (P) Ltd., p-xiii, 2007.
13. S. Pfeiffer, B. Mayer and B. Hemmens, Nitric oxide: chemical puzzles posed by a biological messenger, *Angew. Chem. Int. Ed*., 38, (1999) 1714.
14. L. J. Ignarro, Nitric Oxide: Biology and Pathobiology, Academic Press, San Diego, CA, 2000.
15. T. Li, T. L. Poulos, Structure-function studies on nitric oxide synthases, *J. Inorg. Biochem*., 99 (2005) 293.
16. B. Brune, Nitric oxide: NO apoptosis or turning it ON? Cell Death Diff., 10 (2003) 864.
17. C. Napoli and L. J. Ignarro, Nitric oxide-releasing drugs, *Ann. Rev. Pharmaco. Toxicol*., 43 (2003) 97.
18. H. H. Al-Sa'doni and A. Ferro, Current status and future possibilities of nitric oxide-donor drugs: focus on S-nitrosothiols, *Rev. Med. Chem*., 5, (2005) 247.
19. L. J. Ignarro, G. Cirino, A. Casini, C. Napoli, Nitric oxide as a signaling molecule in the vascular system: an overview, *J Cardiovasc Pharmacol*., 34 (1999) 879.
20. E. Tfouni, M. Krieger, B. R. McGarvey, and D. W. Franco, Structure, chemical and photochemical reactivity and biological activity of some ruthenium amine nitrosyl complexes, *Coord. Chem. Rev.*, 236 (2003) 57.
21. C. N. Lunardi, R.S. da Silva1 and L.M. Bendhack, New nitric oxide donors based on ruthenium complexes**,** Brazil. *J. Med. Biol. Res*., 42 (2009) 87.
22. J. C. Toledo, H. A. S. Silva, M. Scarpellini, V. Mori, A. J. Camargo, M. Bertotti, and D. W. Franco, Ruthenium tetraammines as a model of nitric oxide donor compounds, *Eur. J. Inorg. Chem*., (2004) 1879.
23. S. Kudo, J. L. Bourassa, S. E. Boggs, Y. Sato, P. C. Ford, In situ nitric oxide (NO) measurement by modified electrodes: NO labilized by photolysis of metal nitrosyl complexes, *Anal. Biochem*., 247 (1997) 193.
24. A. R. Butler, I. L. Megson, Non-heme iron nitrosyls in biology, *Chem. Rev*., 102 (2002) 1155.
25. A. S. Torsoni, B. F. de Barros, J. C. Toledo Jr., M. Haun, M. H. Kriger, E. Tfouni, and D W. Franco, Hypotensive properties and acute toxicity of trans-[Ru (NH 3) 4 P (OEt) 3 (NO)](PF 6) 3, a new nitric oxide donor, Nitric oxide; *Biology and Chemistry*, 6 (2002) 247.
26. A. K. Patra, R. K. Afshar, M. M. Olmstead, P. K. Mascharak, The first non-heme iron (III) complex with a ligated carboxamido group that exhibits photolability of a bound NO ligand, Angew. *Chem. Int. Ed*., 41 (2002) 2512.
27. A. K. Patra, J. M. Rowland, D. S. Marlin, E. Bill, M. M. Olmstead, P. K. Mascharak, Iron nitrosyls of a pentadentate ligand containing a single carboxamide group: syntheses, structures, electronic properties, and photolability of NO, Inorg. *Chem*., 42 (2003) 6812.
28. R. K. Afshar, A. K. Patra, M. M. Olmstead, P. K. Mascharak, Syntheses, Structures, and Reactivities of $\{Fe−NO\}^6$ nitrosyls derived from polypyridine-carboxamide ligands: Photoactive NO-donors and reagents for S-Nitrosylation of alkyl thiols, *Inorg. Chem*., 43 (2004) 5736.
29. F. DeRosa, X. Bu and P. C. Ford, Chromium(III) Complexes for Photochemical Nitric Oxide Generation from Coordinated Nitrite: Synthesis and Photochemistry of Macrocyclic Complexes with Pendant Chromophores, *trans*-$[Cr(L)(ONO)_2]BF_4$, *Inorg. Chem*., 44 (2005) 4157.
30. M. A. De Leo, P. C. Ford, .Photoreactions of coordinated nitrite ion. Reversible nitric oxide labilization from the chromium (III) complex [trans-Cr (cyclam)$(ONO)_2]^+$**,** *Coord. Chem. Rev*., 208 (2000) 47.
31. M. Fischer, F. Warneck, Photodecomposition of nitrite and undissociated nitrous acid in aqueous solution, *J. Phys. Chem*., 100 (1996) 18750.

32. K. J. Franz, S. J. Lippard, Nitrosyl transfer from manganese to iron in tropocoronand complexes**,** Inorg. *Chem*., 39 (2000) 3722.
33. K. S. Suslick, R. A. Watson, Photochemical reduction of nitrate and nitrite by manganese and iron porphyrins**,** Inorg. *Chem*., 30 (1991) 912.
34. A. A. Eroy-Reveles, Y. Leung, P. K. Mascharak, Release of nitric oxide from a sol-gel hybrid material containing a photoactive manganese nitrosyl upon illumination with visible light, *J. Am. Chem. Soc*., 128 (2006) 7166.
35. K. Ghosh, A. A. Eroy-Reveles, M. M. Olmstead, P. K. Mascharak, Reductive nitrosylation and proton-assisted bridge splitting of a (μ-Oxo)dimanganese(III) complex derived from a polypyridine ligand with one carboxamide group, Inorg. *Chem*., 44 (2005) 8469.
36. K. Ghosh, A. A. Eroy-Reveles, B. Avila, T. R. Holman, M. M. Olmstead, P. K. Mascharak, Reactions of NO with Mn(II) and Mn(III) centers coordinated to carboxamido nitrogen: Synthesis of a Manganese nitrosyl with photolabile NO, Inorg. *Chem*., 43 (2004) 2988.
37. I. Szundi, M. J. Rose, I. Sen, A. A. Eroy-Reveles, P. K. Mascharak, O´. Einarsd´ottir, A new approach for studying fast biological reactions involving nitric oxide: generation of NO using photolabile ruthenium and manganese NO donors**,** *Photochem. Photobiol*., 82 (2006) 1377.
38. R. K. Afshar, A. K. Patra, P. K. Mascharak, Light-induced inhibition of papain by a $\{Mn–NO\}^6$ nitrosyl: Identification of papain–SNO adduct by mass spectrometry**,** *J. Inorg. Biochem*., 99 (2005) 1458.
39. J. Bradley, M. Ju and G. Robinson, Combination therapy for the treatment of ocular neovascularization, *Angiogenesis*, 10 (2007) 141.
40. C. M. Pavlos, H. Xu, and J. P.Toscano, Photosensitive precursors to nitric oxide, *Curr. Top. Med. Chem*., 5 (2005) 637.
41. S. M. Ali and M. Olivo, Nitric oxide mediated photo-induced cell death in human malignant cells**,** *Int. J. Oncol*., 22 (2003) 751.
42. F. Yamamoto, Y. Ohgari, , N. Yamaki, S. Kitajima, O. Shimokawa, H. Matsui and S. Taketani, The role of nitric oxide in δ-aminolevulinic acid (ALA)-induced photosensitivity of cancerous cells, *Biochem. Biophys. Res. Commun*., 353 (2007) 541.
43. M. J. Rose, P. K. Mascharak, Photoactive ruthenium nitrosyls: effects of light and potential application as NO donors**,** Coord. Chem. Rev. 252 (2008) 2093, and references therein.
44. R.C. Maurya and J.M. Mir, Medicinal industrial & environmental relevance of metal nitrosyl complexes: A review, *Int. J. Sci. Eng. Res*., 5 (2014) 305.
45. M.G. Sauaia, R.S. da Silva, The reactivity of nitrosyl ruthenium complexes containing polypyridyl ligands, *Trans. Met. Chem*., 28 (2003) 254–
46. T. Yonemura, J. Nakata, M. Kadoda, M. Hasegawa, K. Okamoto, T. Ama, H. Kawaguchi, T. Yasui, Photoinduced denitrosyl dinuclearizing reaction of dinitrosyl-molybdenum $[Mo(didentate\text{-}N,S)_2(NO)_2]$ complexes, Inorg. *Chem. Commun*., 4 (2001) 661.
47. T. Yonemura, T. Hashimoto, M. Hasegawa, T. Ikenoue, T. Ama, H. Kawaguchi, A novel mixed valence tetranuclear nitrosyl complex bridged by tetraoxomolybdate**,** Inorg. *Chem. Commun*., 9 (2006) 183.
48. T. Yonemura, Nitrosyltris (pyridine-2-thiolato-κ2N, S) molybdenum(II) dihydrate**,** *Acta Cryst*., 65 (2009) 1463.
49. A. C. Roveda Jr., T. B. Ruiz Papa, E. E. Castellano, D. W. Franco, PAMAM dendrimers functionalized with ruthenium nitrosyl as nitric oxide carriers, Inorganic. *Chim. Acta*, 409 (2014) 147.
50. Daniela R. Truzzi, Douglas W. Franco, Stability of phosphite coordinated to ruthenium(II) in aqueous media**,** Polyhedron, 81 (2014) 238.
51. Z. A. Carneiro, J. C. Biazzotto, A. D. P. Alexiou, S. Nikolaou, Nitric oxide photorelease from a trinuclear ruthenium nitrosyl complex and its in vitro cytotoxicity against melanoma cells**,** *J Inorg. Biochem*., 134 (2014) 36.
52. T. B. Santos, I. C. Cespedes, M. B. Viana, Chronic corticosterone administration facilitates aversive memory retrieval and increases GR/NOS immunoreactivity, *Behav. Brain Res*., 267 (2014) 46.
53. E. Tfouni, L. E. Figueiredo, E. M. Cilli, R. A. S. Molina, E. M. Espreafico, Synthesis and cytotoxicity of a ruthenium nitrosyl nitric oxide donor with isonicotinic acid and a cell penetrating peptide, Inorg. *Chem. Commun*., 28 (2013) 60.
54. Maxim A. Il'in, A. N. Makhinya, I. A. Baidina, S. V. Tkachev, Synthesis, crystal structure and acidic properties in aqueous solution of phosphate ammine complexes of ruthenium nitrosyl, Inorg. *Chim. Acta*, 413, (2014) 90.
55. D. R. Truzzi, D. W. Franco, trans-$[Ru(NO)(NH_3)P(O^-)(OEt)_2]^{2+}$: A new and robust NO/HNO-donor in aqueous media**,** *Inorg. Chim. Acta*, 421 (2014) 74.
56. T. Mayer, H. C. Bottcher, Protonation of metal–metal bonds in nitrosyl-bridged diruthenium complexes, Polyhedron, 69 (2014) 240.
57. R. S. Correa, J. P. Barolli, M. I. F. Barbosa, J. Ellena, A. A. Batista, The effect of guest molecules on the conformation and molecular assembly of the fac-$[RuCl_3(NO)(dppb)]$ complex**,** *J. Mol. Struc*.,1048 (2013) 11.
58. J. M. Mir and R. C. Maurya, Metal Complexes of Medicinal Relevance, *LAP Lambert Academic Press Publishing*, 1, 2016.
59. Z. A. Carneiro et al. Photocytotoxic activity of a nitrosyl phthalocyanine ruthenium complex—A system capable of producing nitric oxide and singlet oxygen, *J. Inorg. Biochem*., 105 (2011) 1035.
60. M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M.S. Gordan, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, J. A. Montgomery, General atomic and molecular electronic structure system, *J. Computational Chem*., 14 (1993) 1347.
61. P. J. Hay, W. R. Wadt, Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals**,** *J. Chem. Phys*., 82 (1985) 270.
62. M. M. Francl, W. J. Pietro, W. J Hehre, J.S. Binkley, D. J. De Frees, J. A. Pople, M. S. Gordon, Self-consistent molecular orbital methods. XXIII. A polarization-type basis set for second-row elements, *J. chem. Phys*., 77 (1982) 3654.
63. A. D. Becke, Density-functional thermochemistry. III. The role of exact exchange *J. Chem. Phys*., 98 (1993) 5684.
64. M. C. Zerner, G.H. Loew, R. F. Kirchner, U. T. Mueller-Westerhoff, An intermediate neglect of differential overlap technique for spectroscopy of transition-metal complexes. Ferrocene, *J. Am. Soc*., 102 (1980) 589.
65. Hyperchem for Windows, Release 7.01. Hypercube Inc., 115 NW 4th street, Gainesville, FL 32601, USA.
66. A. L. B. Formiga, A.F. Nogueira, K. Araki, H.E. Toma, Contrasting photoelectrochemical behaviour of two isomeric supramolecular dyes based on meso-tetra(pyridyl)

porphyrin incorporating four (μ_3-oxo)- triruthenium(III) clusters, *New J. Chem.*, 32 (2008) 1167.
67. J. J. P. Stewart, Optimization of parameters for semiempirical methods I. *Method, J. Comput. Chem*., 10 (1989) 209.
68. Bordini et al. Nitric oxide photorelease from ruthenium salen complexes in aqueous and organic solutions**,** Inorg. *Chem*., 41 (2002) 5410.
69. Lapes et al. Reactivity of *trans*-$[Ru(NH_3)_4P(OEt)_3NO]X_3$ $(X = PF_6^-, CF_3COO^-)$ modulation of the release of NO by the trans-effect, Inorg. *Chem. Acta*, 358, (2005) 2883.
70. M. Cossi, V. Borane, Time-dependent density functional theory for molecules in liquid solutions**,** *J. Chem. Phys*., 115 (2001) 4708.
71. M. Cossi, N. Rega, G. Scalmani, V. Borane, Energies, structures, and electronic properties of molecules in solution with the C-PCM solvation model, *J. Comput. Chem*., 24, (2003) 669.
72. E. Tangen, A. Ghosh, Electronic structure of cis-Mo (P)$(NO)_2$, where P is a porphyrin: An organometallic perspective of metalloporphyrin–NO complexes, *J. Inorg. Biochem*., 99 (2005) 959.
73. JMMPKV R.C. Maurya, Some Aspects of Physiologically Relevant Signaling by Gasotransmitters, NO, CO and H2S: A Review, Journal of Ravishankar University, Raipur – Part-B [Science] 28 (2015) 1.
74. W. C. Shih, T. Te Lu, L. B. Yang, F. T. Tsai, M. H. Chiang, J. F. Lee, Y. W. Chiang, W. F. Liaw, New members of a class of dinitrosyliron complexes (DNICs): The characteristic EPR signal of the six-coordinate and five-coordinate {Fe (NO) 2} 9 DNICs, *J. Inorg. Biochem*., 113 (2012) 83.
75. M. W. Jones, D. R. Powell, G. B. Richter-Addo, Synthesis, characterization, and fiber-optic infrared reflectance spectroelectrochemical studies of some dinitrosyl iron diphosphine complexes $Fe(NO)_2L_2$ ($L = P(C_6H_4X)_3$), *J. Organomet. Chem*., 754 (2014) 63.
76. A. F. Vanin, V. D. Mikoyan, N. M. Rubtsov, L. N. Kubrina, Autowave distribution of nitric oxide and its endogenous derivatives in biosystems strongly enhances their biological effects: A working hypothesis**,** *Nitric Oxide*, 23 (2010) 175.
77. J. R. Hickok, S. Sahni, H. Shen, A. Arvind, C. Antoniou, L. W. M. Fung, D. D. Thomas, Dinitrosyliron complexes are the most abundant nitric oxide-derived cellular adduct: biological parameters of assembly and disappearance, *Free Rad. Bio. & Med*., 51 (2011) 1558.
78. V. P. Mokh, A. P. Poltorakov, V. A. Serezhenkov, A. F. Vanin, On the nature of a compound formed from dinitrosyl-iron complexes with cysteine and responsible for a long-lasting vasorelaxation, *Nitric Oxide*, 22 (2010) 266.
79. A. A. A. Andriyevsky, V. D. Mikoyan, V. A. Serezhenkov, A. F. Vanin, Penile erectile activity of dinitrosyl iron complexes with thiol-containing ligands, *Nitric Oxide*, 24 (2011) 217.
80. E. I. Chazov, O. V. Rodnenkov, A. V. Zorin, V. L. Lakomkin, V. V. Gramovich, O. N. Vyborov, A. G. Dragnev, A. A. Timoshin, L. I. Buryachkovskaya, A. A. Abramov, V. P. Massenko, E. V. Arzamastsev, V. I. Kapelko, A. F. Vanin, Hypotensive effect of Oxacom containing a dinitrosyl iron complex with glutathione: Animal studies and clinical trials on healthy volunteers, *Nitric Oxide*, 26 (2012) 148.
81. M. I. Remizova, N. I. Kochetygov, K. A. Gerbout, V. L. Lakomkin, A. A. Timoshin, E. N. Burgova, A. F. Vanin, Effect of dinitrosyl iron complexes with glutathione on hemorrhagic shock followed by saline treatment, *Eu. J. Pharm*., 662 (2011) 40.
82. A. P. Landry, X. Duan, H. Huang, H. Ding, Iron–sulfur proteins are the major source of protein-bound dinitrosyl iron complexes formed in Escherichia coli cells under nitric oxide stress, *Free Radical Bio. & Med*., 50 (2011) 1582.
83. M. A. Hough, S. V. Antonyuk, S. Barbieri, N. Rustage, A. L. McKay, A. E. Servid, R. R. Eady, C. R. Andrew , S. Samar Hasnain, Distal-to-proximal NO conversion in hemoproteins: the role of the proximal pocket**,** *J. Mol. Biol*., 405 (2011) 395.
84. M. Simontacchi, A. Buet, L. Lamattina, S. Puntarulo, Exposure to nitric oxide increases the nitrosyl-iron complexes content in sorghum embryonic axes**,** *Plant Science*, 183 (2012) 159.
85. B. Kolesnik, K. Palten, A. Schrammel, H. Stessel, K. Schmidt, B. Mayer, A. C. F. Gorren, Efficient nitrosation of glutathione by nitric oxide, *Free Radical Bio. & Med*., 63 (2013) 51.
86. R. R. Borodulin, L. N. Kubrina, V. O. Shvydkiy, V. L. Lakomkin, A. F. Vanin, A simple protocol for the synthesis of dinitrosyl iron complexes with glutathione: EPR, optical, chromatographic and biological characterization of reaction products, Nitric Oxide, 35 (2013) 110.
87. R. R. Borodulin, L. N. Kubrina, V. A. Serezhenkov, D. S. Burbaev, V. D. Mikoyan, A. F. Vanin, Redox conversions of dinitrosyl iron complexes with natural thiol-containing ligands, *Nitric Oxide*, 35 (2013) 35.
88. A.F. Vanin, Anti-fibrotic Effects of Reserpine on Lung Fibrosis: Stem Cells in the Pathogenesis of Pneumofibrosis, "*Open Conference Proc*.," *J* 4 (2013): 31.
89. Y. D. Wena, Y. L. Ho, R. J. Shiau, J. K. Yeh, J. Y. Wua, W. L. Wanga, S. J. Chiou, Synergistic antitumor effect of curcumin and dinitrosyl iron complexes for against melanoma cells**,** *J. Organomet. Chem*., 695 (2010) 352.
90. N. Y. Giliano, L. V. Konevega, L. A. Noskin, V. A. Serezhenkov, A. P. Poltorakov, A. F. Vanin, Dinitrosyl iron complexes with thiol-containing ligands and apoptosis: studies with HeLa cell cultures**,** *Nitric Oxide*, 24 (2011) 151.
91. A. F. Vanin, V. D. Mikoyan, L. N. Kubrina, R. R. Borodulin, E. N. Burgova, Mono- and binuclear dinitrosyl iron complexes with thiol-containing ligands in various biosystems, *Biophysic*., 60 (2015) 603.
92. H. Lewandowska, T. M. Stepkowski, J. Sadlo, G. P. Wojciuk, K. E. Wojciuk, A. Rodger, M. Kruszewski, Coordination of iron ions in the form of histidinyl dinitrosyl complexes does not prevent their genotoxicity, *Bioorg. & Med. Chem*., 20 (2012) 6732.
93. Y. S. Chen, J. E. Ellis, Highly reduced organometallics 52. Synthesis and chemistry of tricarbonylnitrosylmanganate (2−), $[Mn(CO)_3(NO)]^{2-}$, *Inorg. Chim. Acta*, 300 (2000) 675.
94. M. E. Garcia, S. Melon, M. A. Ruiz, L. Marchio, A. Tiripicchio, Nitrosyl derivatives of the unsaturated dihydrides [Mn2(μ-H) 2(CO)6(μ-L2)] (L2 = Ph 2PCH2PPh2, (EtO)2POP(OEt) 2), *J. Organomet. Chem*., 696 (2011) 559.
95. W. Kaim, B. Schwederski, Non-innocent ligands in bioinorganic chemistry—An overview, *Coord. Chem. Rev.*, 254 (2010) 1580.

96. F. Masuya, H. Hori, EPR studies on the photoproducts of manganese(II) protoporphyrin-IX substituted myoglobin nitrosyl complexes trapped at low temperature: effects of site-specific chemical modification of the distal histidine on ligand-binding structures, *Biochim. et Biophy. Acta*., 1203 (1993) 99.
97. D. B. Akolekar, S. K. Bhargava, NO and CO adsorption studies on transition metal-exchanged silico-aluminophosphate of type 34 catalysts, Appl. Catalysis A: *Gen*., 207 (2001) 355.
98. N. Y. Topsoe, A. Tuxen, B. Hinnemann, J. V. Lauritsen, K. G. Knudsen, F. Besenbacher, H. Topsoe, Spectroscopy, microscopy and theoretical study of NO adsorption on MoS_2 and Co–Mo–S hydrotreating catalysts, *J. Catalysis*, 279 (2011) 337.
99. I. A. Rodionov and I. A. Zvereva, Photocatalytic activity of layered perovskite-like oxides in practically valuable chemical reactions, *Russian Chem. Rev*., 85 (2016).
100. A. Blokhin, A. Pasynskii, M. Scheer, A. Virovets, Y. Torubaev, Synthesis and molecular structure of mixed-metal stannylene derivatives of cyclopentadienyl (nitrosyl) (carbonyl) manganese, *J. Organomet. Chem*., 724 (2013) 75.
101. P. C. Ford, S. Wecksler, Photochemical reactions leading to NO and NO_x generation, *Coord. Chem. Rev*., 249 (2005) 1382.
102. R. K. Afshar, A. K. Patra, P. K. Mascharak, Light-induced inhibition of papain by a $\{Mn\text{-}NO\}^6$ nitrosyl: identification of papain-SNO adduct by mass spectrometry, *J. Inorg. Biochem*., 99 (2005) 1458.
103. F. Doctorovich, D. Bikiel, J. Pellegrino, S. A. Suareza, A. Larsen, M. A. Marti, Nitroxyl (azanone) trapping by metalloporphyrins, *Coord. Chem. Rev*., 255, (2011) 2764.
104. J. L. Heinecke, J. Yi, J. C. M. Pereira, G. B. R. Addo, P. C. Ford, Nitrite reduction by Co(II) and Mn(II) substituted myoglobins: towards understanding necessary components of Mb nitrite reductase activity. *J. Inorg. Biochem*., 107(2012) 47.

****