UNIVERSIDADE DE SÃO PAULO
FACULDADE DE FILOSOFIA, CIÊNCIAS E LETRAS DE RIBEIRÃO PRETO –
DEPARTAMENTO DE QUÍMICA

ANA PAULA SEGANTIN GASPARI GIOVANINI

**Design de complexos rutênio-nitrosilos contendo ligantes polipiridínicos:
estudos da relação estrutura-atividade e ensaios biológicos**

Tese apresentada ao Programa de Pós-graduação
em Química, da Faculdade de Filosofia, Ciências e Letras
de Ribeirão Preto, da Universidade de São Paulo, como
requisito parcial para obtenção do título de Doutor em
Ciências. Área: **Química**

Orientador: Prof. Dr. Roberto Santana da Silva

Ribeirão Preto - SP

2018

UNIVERSIDADE DE SÃO PAULO
FACULDADE DE FILOSOFIA, CIÊNCIAS E LETRAS DE RIBEIRÃO PRETO –
DEPARTAMENTO DE QUÍMICA

ANA PAULA SEGANTIN GASPARI GIOVANINI

**Desenho racional de complexos rutênio-nitrosilos contendo ligantes
polipiridínicos: estudos da relação estrutura-atividade e ensaios biológicos**

Tese apresentada ao Programa de Pós-graduação
em Química, da Faculdade de Filosofia, Ciências e Letras
de Ribeirão Preto, da Universidade de São Paulo, como
requisito parcial para obtenção do título de Doutor em
Ciências. Área: **Química**

Orientador: Prof. Dr. Roberto Santana da Silva

Ribeirão Preto - SP

2018

FICHA CATALOGRÁFICA

Gaspari Giovanini, Ana Paula Segantin

Complexos rutênio-nitrosilos contendo ligantes polipiridínicos: estudos da relação estrutura-atividade e ensaios biológicos. Ribeirão Preto, 2018.

239 p.: il. ; 30 cm

Tese de Doutorado, apresentada à Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto/USP – Área de concentração: Química.

Orientador: Silva, Roberto Santana da

1. rutênio-nitrosilos. 2. ligantes polipiridínicos. 3. câncer. 4. Atividade tripanocida.

Universidade de São Paulo

ATA DE DEFESA

Aluno: 59138 - 7537721 - 2 / Página 1 de 1

Ata de defesa pública de Tese do(a) Senhor(a) Ana Paula Segantin Gaspari Giovanini no Programa: Química, do(a) Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto da Universidade de São Paulo.

Aos 20 dias do mês de junho de 2018, no(a) Bloco 8 - sala 2 realizou-se a Defesa da Tese do(a) Senhor(a) Ana Paula Segantin Gaspari Giovanini, apresentada para a obtenção do título de Doutora intitulada:

"Design de complexos rutênio-nitrosilos contendo ligantes polipiridínicos: estudos da relação estrutura-atividade e ensaios biológicos"

Após declarada aberta a sessão, o(a) Sr(a) Presidente passa a palavra ao candidato para exposição e a seguir aos examinadores para as devidas arguições que se desenvolvem nos termos regimentais. Em seguida, a Comissão Julgadora proclama o resultado:

Nome dos Participantes da Banca	Função	Sigla da CPG	Resultado
Roberto Santana da Silva	Presidente	FCFRP - USP	<u>APROVADA</u>
Zeki Naal	Titular	FCFRP - USP	<u>APROVADA</u>
Luiz Alberto Beraldo de Moraes	Titular	FFCLRP - USP	<u>APROVADA</u>
Pedro Ivo da Silva Maia	Titular	UFTM - Externo	<u>APROVADA</u>
Adelino Vieira de Godoy Netto	Suplente	UNESP - Externo	<u>Aprovada</u>

Resultado Final: APROVADA

Parecer da Comissão Julgadora *

Eu, Cesar Pereira Brites Cesar Brites, lavrei a presente ata, que assino juntamente com os(as) Senhores(as). Ribeirão Preto, aos 20 dias do mês de junho de 2018.

Zeki Naal
Zeki Naal

Luiz Alberto Beraldo de Moraes
Luiz Alberto Beraldo de Moraes

Pedro Ivo da Silva Maia
Pedro Ivo da Silva Maia

Adelino Vieira de Godoy Netto
Adelino Vieira de Godoy Netto

Roberto Santana da Silva
Presidente da Comissão Julgadora

* Obs: Se o candidato for reprovado por algum dos membros, o preenchimento do parecer é obrigatório.

A defesa foi homologada pela Comissão de Pós-Graduação em 29.06.2018 e, portanto, o(a) aluno(a) faz jus ao título de Doutora em Ciências obtido no Programa Química.

Rosian
Presidente da Comissão de Pós-Graduação

Profa. Dra. Sonia Regina Pasian
Presidente da Comissão de Pós-Graduação

AGRADECIMENTOS

À **Deus**, por permitir a conclusão de mais uma etapa em minha vida, sempre me dando forças para seguir em frente perante as dificuldades.

Aos meus pais, Alceu e Cláudia, pelo grande apoio que deram durante todo meu percurso. Por estarem ao meu lado nos momentos felizes, mas também nos difíceis, me incentivando a lutar por aquilo que sonho.

Ao meu marido, Diego, por todo o seu amor, carinho, atenção, apoio e pelo permanente incentivo e preocupação com que sempre acompanhou meu trabalho. Não existem palavras o suficiente para expressar meu amor por você e minha alegria por ter te encontrado.

Ao meu orientador, Roberto Santana da Silva, pela confiança no meu trabalho, por me ensinar tanto nestes quatro anos, pela compreensão, pelos sábios conselhos, pelas oportunidades que me deu e por tanto contribuir em benefício do meu crescimento pessoal e profissional. Se hoje em dia me sinto preparada para esta nova etapa da minha vida, com certeza grande parte disso devo a ele.

À minha irmã, Fernanda, por ser a melhor amiga que alguém pode ter, que cresceu comigo, dividiu experiências inigualáveis, e deu a vida à pequena Ana Beatriz, que faz dos meus dias mais alegres e me mostra o quanto o amor é imensurável.

Às minhas avós Belinha (in memorian) e Maria (in memorian), que partiram deste mundo deixando imensa saudade. Obrigada por sempre acreditarem em mim e me possibilitarem ser quem eu sou.

À Família Scarati (Marlene, Maria de Lourdes e Natasha), a qual hoje em dia tenho a honra de pertencer, por me receber de braços abertos, por sempre me ouvirem com paciência, por compartilhar experiências, pelo amor e carinho e por estarem sempre ao meu lado nas dificuldades.

À Família Giovanini (Ida Adele, Paulo, Paula, Waldete) por todos os momentos felizes que passamos juntos, pelo carinho, gentileza, apoio, amor e momentos inesquecíveis.

À minha querida amiga Nelissa Pacheco Vaz, pela amizade verdadeira, pelas palavras gentis e de consolo nos momentos que mais precisei, por me ouvir com paciência mesmo estando distante, pelo compartilhamento de experiências e por ser como uma irmã para mim.

À Iara Degani e Sandra Bin, pelos preciosos conselhos, auxílio no desenvolvimento do meu trabalho, contribuição para meu crescimento pessoal e profissional.

Às queridas amigas Zumira Carneiro e Carla Lopes, por me ensinarem tudo que sei acerca de experimentos biológicos envolvendo atividade tripanocida (*in vitro* e *in vivo*), pelas discussões experimentais, por permitirem que eu me envolvesse nos trabalhos do grupo, pela consideração, confiança e carinho que tiveram ao me receber no laboratório, por me ouvirem e ajudarem com palavras gentis, sempre me dando forças para continuar. Sem vocês, com certeza o caminho seria mais tortuoso e difícil.

À Profa. Ivone Carvalho, por me receber em seu laboratório e pelas discussões sobre Química Orgânica e mecanismos sintéticos, permitindo que eu desenvolvesse um projeto totalmente novo e aprendesse inúmeros conceitos que para mim eram novos, contribuindo de forma singular para este trabalho.

Ao Prof. Sérgio de Albuquerque, pela confiança em disponibilizar seu laboratório e reagentes para que eu pudesse conduzir os experimentos relacionados à testes biológicos.

Ao Prof. Pedro Ivo, pela confiança em meu trabalho e por proporcionar que eu participasse de projetos que auxiliaram no meu crescimento profissional. Também agradeço às alunas do seu laboratório Alice Borges e Ana Resende pelo empenho e colaboração.

Ao Prof. Dr. Iouri Borissevitch por disponibilizar seu laboratório e tempo para auxiliar nos estudos fotoquímicos.

Aos professores Dr Antônio E. da Hora Machado e Dr. André L. B. Formiga, por disponibilizarem tão prontamente seu tempo e realizarem cálculos com tanto esmero e cuidado, proporcionando estudos incríveis para conhecimento dos sistemas apresentados neste trabalho.

Aos Profs. Dr. Elia Tfouni, Dra. Sofia Nikolaou, Dra Rose Naal, Dr. Zeki Naal, Dra. Joana de Jesus Andrade e Dr. Gilberto Ubida, pelos ensinamentos proporcionados desde o momento que cheguei em Ribeirão Preto até o presente momento, por acreditarem no meu trabalho e permitirem tantas oportunidades de intercâmbio de conhecimento.

Aos amigos do laboratório que estiveram comigo durante meu percurso nestes quatro anos de doutorado: Alexia Marques, Ana Cláudia Bordonal, Bruna Possato, Cassia Dias, Felipe Reis, Fernando Postalli, Jacqueline Alves, Jorge Nasser, Julia Oliveira, Juliana Uzuelly, Kelly Castro, Laena Pernomean, Laísa Negri, Leandro Máximo, Loyanne Ramos, Lilian Franco, Lucimara Ferreira, Mayara Luma, Miqueias Gomes, Mariete Moreira, Natacha Cacita, Natalia Levin, Pamela Gomes, Tassia Jói, Rafaella Rios e Renata da Silveira. Obrigada pelas discussões produtivas, companheirismo e por tornarem o ambiente de trabalho mais leve e agradável.

Aos técnicos de laboratório Juliana, Júnior, Cristiana, Jorge e Marcelo, que sempre estiveram dispostos a ajudar no que precisasse para os objetivos serem alcançados.

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), pela bolsa concedida.

À Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) e Conselho Nacional de Desenvolvimento Científico e Tecnológico pelo suporte financeiro.

A todos que participaram e contribuíram de alguma forma para a execução deste trabalho, que me incentivaram e torceram pela vitória, meus sinceros agradecimentos.

*“Não há ensino sem pesquisa e pesquisa sem ensino. Esses que-
fazeres se encontram um no corpo do outro. Enquanto ensino,
continuo buscando, reprocuro. Ensino porque busco, porque
indaguei, porque indago e me indago. Pesquiso para constatar,
constatando intervenho, intervindo educo e me educo. Pesquiso para
conhecer o que ainda não conheço e comunicar ou anunciar a
novidade”.*

(Paulo Freire)

RESUMO

Gaspari Giovanini, Ana P. S. **Desenho racional de complexos rutênio-nitrosilos contendo ligantes polipiridínicos: estudos da relação estrutura-atividade e ensaios biológicos.** 2018, 239 f. Tese (Doutorado em Ciências. Área: Química) – Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto/SP.

O comportamento do óxido nítrico (NO) em sistemas biológicos vem sendo explorado desde a descoberta de sua importância em processos regulatórios, fisiológicos e em patologias. Atualmente há o grande interesse no desenvolvimento de compostos que possam liberar o NO de forma controlada em locais específicos nas células. Neste contexto, os complexos rutênio-nitrosilos têm se mostrado bastante promissores, visto que podem liberar NO no interior celular por processos redutimétricos, viabilizando sua utilização como agentes antitumorais e/ou tripanocida. Este estudo se baseia na premissa de que a liberação de NO pode ser direcionada para o interior celular através da modulação dos ligantes de forma a obter complexos biocompatíveis. Assim, o presente trabalho visou o delineamento de complexos rutênio-nitrosilos inéditos contendo ligantes polipiridínicos e/ou derivados de aminoácidos e, condução de experimentos a nível biológico. Os novos complexos rutênio-nitrosilos contendo os ligantes 3-etilpiridina (3-ety), derivado triazol de lisina e derivado imínico de triptofano foram sintetizados e purificados com êxito. Os ligantes foram caracterizados por RMN de ^1H e ^{13}C RMN, HSQC e ^1H - ^1H COSY, espectrometria de massas e espectroscopia no infravermelho. Os complexos foram caracterizados por espectroscopia na região do UV-visível e FTIR, análise elementar, voltametria cíclica e espectrometria de massas. Os complexos foram testados frente a linhagens celulares B16-F10, MCF-7, MDA-MB231 e comparados com os testes em células de mama sadia MCF-10A. Além disso, os complexos foram aplicados a formas amastigotas de *Trypanosoma cruzi*. Os resultados de viabilidade celular mostraram que os complexos contendo derivado triazol de lisina ocasionam citotoxicidade às células MCF-7, MB-231 e B16-F10. O complexo *cis*-[Ru(NO)(bpy)₂(3-ety)](PF₆)₃.2H₂O (onde bpy = 2,2'-bipiridina) apresentou excelente resultado nos testes *in vitro* e *in vivo* frente a cepa Tulahuén LacZ e modelo murino, quando da sua associação ao benzonidazol. Os resultados obtidos sugerem possíveis relações existentes entre estrutura-atividade, abrindo novos caminhos para a pesquisa na busca pelo entendimento deste sistema, assim como o desenvolvimento de uma nova classe de compostos.

Palavras-chave: rutênio-nitrosilos, ligantes polipiridínicos, aminoácidos, câncer, *Trypanosoma cruzi*

ABSTRACT

Gaspari Giovanini, Ana P. S. **Design of ruthenium-nitrosyl complexes containing polypyridines: studies of the *structure-activity relationship* and biological assays.** 2018, 239 f. Thesis (Doctorate in Sciences. Area: Chemistry – at Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto/SP. 2018.

The behavior of nitric oxide (NO) in biological systems has been explored since the discovery of its importance in regulatory, physiological, and pathological processes. Currently, there is a great interest in the development of compounds that can release NO at specific sites inside cells in a controlled manner. In this context, the ruthenium-nitrosyl complexes have shown to be very promising, since they can release NO inside cells by reduction processes, turning possible its applications as antitumor and/or trypanocides agents. This study is based on the premise that the release of NO can be directed to inside cells by modulating the ligands in order to obtain biocompatible complexes. In this way, the present work aimed at the design of new ruthenium-nitrosyl complexes containing polypyridine ligands and/or amino acid derivatives, and tests of biological activity. The new ruthenium-nitrosyl complexes containing 3-ethynylpyridine, triazole lysine derivative, and tryptophan imino derivative were synthesized and purified successfully. Ligands were characterized by ^1H and ^{13}C NMR, HSQC, and COSY, mass spectrometry and infrared spectroscopy. The complexes were characterized by spectroscopy in the UV-visible region and FTIR, elemental analysis, cyclic voltammetry, and mass spectrometry. The complexes were tested against cell lines B16-F10, MCF-7, MDA-MB231 and the normal breast cell model MCF-10A. In addition, the complexes were tested against amastigote forms of *Trypanosoma cruzi*. Cell viability results showed that triazole derivative-lysine complexes cause cytotoxicity to MCF-7, MB-231, and B16-F10 cells. The *cis*-[Ru(NO)(bpy)₂(3-etpy)](PF₆)₃.2H₂O (where bpy = 2,2'-bipyridine) complex presented excellent results *in vitro* and *in vivo* tests against the Tulahuén LacZ strain and the murine model, respectively, when it was associated with benzonidazole. The results suggest possible relationships between structure and activity, opening new prospectives in the search for understanding this system, as well as the development of a new class of compounds.

Keywords: ruthenium-nitrosyls, polypyridines, amino acids, *Trypanosoma cruzi*

REFERÊNCIAS BIBLIOGRÁFICAS

ABBASPOUR, N.; HURRELL, R.; KELISHADI, R. Review on Iron and Its Importance for Human Health. **Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences**, v. 19, n. 2, p. 164–174, fev. 2014.

ABID, M.; SHAMSI, F.; AZAM, A. Ruthenium Complexes: An Emerging Ground to the Development of Metallopharmaceuticals for Cancer Therapy. **Mini-Reviews in Medicinal Chemistry**, v. 16, n. 10, p. 772–786, 2016. Disponível em: <<http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1389-5575&volume=16&issue=10&spage=772>>.

ABU-DIEF, A. M.; MOHAMED, I. M. A. A Review on Versatile Applications of Transition Metal Complexes Incorporating Schiff Bases. **Beni-Suef University Journal of Basic and Applied Sciences**, v. 4, n. 2, p. 119–133, jun. 2015.

AEBI, S et al. Loss of DNA Mismatch Repair in Acquired Resistance to Cisplatin. **Cancer Research**, v. 56, n. 13, p. 3087–3090, 1996. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/8674066>>.

AL ZOUBI, W. et al. Synthesis, Characterization, and Biological Activity of Schiff Bases Metal Complexes. **Journal of Physical Organic Chemistry**, v. 31, n. 2, p. e3752, 2018. Disponível em: <<http://doi.wiley.com/10.1002/poc.3752>>.

ALEXANDER, J W. History of the Medical Use of Silver. **Surgical Infections**, v. 10, n. 3, p. 289–292, 2009. Disponível em: <<http://www.liebertonline.com/doi/abs/10.1089/sur.2008.9941>>.

AMPTOULACH, S.; TSAVARIS, N.. Neurotoxicity Caused by the Treatment with Platinum Analogues. **Chemotherapy Research and Practice**, v. 2011, p. 1–5, 2011. Disponível em: <<https://www.hindawi.com/archive/2011/843019/>>.

ANANIEVA, E. Targeting Amino Acid Metabolism in Cancer Growth and Anti-Tumor Immune Response. **World Journal of Biological Chemistry**, v. 6, n. 4, p. 281, 2015.

ANDREWS, P A; HOWELL, S B. Cellular Pharmacology of Cisplatin: Perspectives on Mechanisms of Acquired Resistance. **Cancer Cells (Cold Spring Harbor, N.Y.: 1989)**, v. 2, n. 2, p. 35–43, 1990. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/2204382>>.

ANTHONY SAMY, A. et al. Synthesis, Characterization and Electrochemistry of 4'-

Functionalized 2,2':6',2''-Terpyridine Ruthenium(II) Complexes and Their Biological Activity. **Dalton Transactions**, v. 0, n. 16, p. 2136–2143, 2008. Disponível em: <<http://pubs.rsc.org/en/content/articlelanding/2008/dt/b716011a>>.

ANTONY, A. et al. Amino Acid Based Schiff Bases and Its Zn (II) Complexes. **Research & Reviews: Journal of Chemistry**, v. 5, p. 37–44, jul. 2016.

ARAÚJO, P. F. et al. Sexual transmission of American trypanosomiasis in humans: a new potential pandemic route for Chagas parasites. **Memórias do Instituto Oswaldo Cruz**, v. 112, n. 6, p. 437–446, jun. 2017.

ARNELLE, D R; STAMLER, J S. NO⁺, NO, and NO⁻ Donation by S-Nitrosothiols: Implications for Regulation of Physiological Functions by S-Nitrosylation and Acceleration of Disulfide Formation. **Archives of Biochemistry and Biophysics**, v. 318, n. 2, p. 279–285, 1995. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/7733655>>.

ARNOLD, W P; LONGNECKER, D E; EPSTEIN, R M. Photodegradation of Sodium Nitroprusside: Biologic Activity and Cyanide Release. **Anesthesiology**, v. 61, n. 3, p. 254–260, 1984. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/6089613>>.

BARON, A. et al. Click Chemistry on a Ruthenium Polypyridine Complex. An Efficient and Versatile Synthetic Route for the Synthesis of Photoactive Modular Assemblies. **Inorganic Chemistry**, v. 51, n. 11, p. 5985–5987, 4 jun. 2012. Disponível em: <<http://pubs.acs.org/doi/10.1021/ic300227j>>.

BELANI, K. et al. Sodium Nitroprusside in 2014: A Clinical Concepts Review. **Journal of Anaesthesiology Clinical Pharmacology**, v. 30, n. 4, p. 462, 2014.

BERALDO, H. Tendências atuais e as perspectivas futuras da química inorgânica. **Ciência e Cultura**, 1. v. 63, p. 29–32, 2011.

BERTINI, I. (Org.). **Biological inorganic chemistry: structure and reactivity**. Sausalito, Calif: University Science Books, 2007.

BHASKAR, G. et al. Matrix-Assisted Laser Desorption/Ionization Studies on Transition Metal Complexes of Benzimidazole Thiosemicarbazones. **European Journal of Mass Spectrometry**, v. 13, n. 2, p. 135–145, abr. 2007.

BHUTIA, Y. D. et al. Amino Acid Transporters in Cancer and Their Relevance to “Glutamine Addiction”: Novel Targets for the Design of a New Class of Anticancer Drugs. **Cancer**

Research, v. 75, n. 9, p. 1782–1788, maio 2015.

BHUTIA, Y. D. et al. The amino acid transporter SLC6A14 in cancer and its potential use in chemotherapy. **Asian Journal of Pharmaceutical Sciences**, v. 9, n. 6, p. 293–303, 2014. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S1818087614000221>>.

BIERSACK, B.; SCHOBERT, R. Current State of Metal-Based Drugs for the Efficient Therapy of Lung Cancers and Lung Metastases. In: AHMAD, Aamir; GADGEEL, Shirish (Org.). . **Lung Cancer Pers. Med.** Cham: Springer International Publishing, 2016. v. 893. p. 211–224.

BIJELIC, A. et al. X-Ray Structure Analysis of Indazolium Trans- [Tetrachlorobis(1 H - Indazole)Ruthenate(III)] (KP1019) Bound to Human Serum Albumin Reveals Two Ruthenium Binding Sites and Provides Insights into the Drug Binding Mechanism. **Journal of Medicinal Chemistry**, v. 59, n. 12, p. 5894–5903, 2016. Disponível em: <<http://pubs.acs.org/doi/10.1021/acs.jmedchem.6b00600>>.

BLATTER, L A; WIER, W G. Nitric Oxide Decreases $[Ca^{2+}]_i$ in Vascular Smooth Muscle by Inhibition of the Calcium Current. **Cell Calcium**, v. 15, n. 2, p. 122–131, 1994. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/8149412>>.

BOGDAN, C. Nitric Oxide and the Immune Response. **Nature Immunology**, v. 2, n. 10, p. 907–916, 2001. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/11577346>>.

BORGES, S. S. et al. Ruthenium Nitrosyl Complexes with N-Heterocyclic Ligands. **Inorganic Chemistry**, v. 37, n. 11, p. 2670–2677, 1998. Disponível em: <<https://doi.org/10.1021/ic951563s>>.

BOS, C.; TOMÉ, D. Lysine Requirement through the Human Life Cycle. **The Journal of Nutrition**, v. 137 (6), p. 599S–1601S, jun. 2007.

BOTTOMLEY, F. Nitrosyl Complexes of Ruthenium. **Coordination Chemistry Reviews**, v. 26, n. 1, p. 7–32, 1978. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S0010854500820639>>.

BREMER, V. et al. Role of Nitric Oxide in Rat Nephrotoxic Nephritis: Comparison between Inducible and Constitutive Nitric Oxide Synthase. **Journal of the American Society of Nephrology: JASN**, v. 8, n. 11, p. 1712–1721, nov. 1997.

CALLAHAN, R W; MEYER, T J. Reversible electron transfer in ruthenium nitrosyl complexes. **Inorganic Chemistry**, v. 16, n. 3, p. 574–581, 1977. Disponível em:

<<https://doi.org/10.1021/ic50169a015>>.

CAO, X.; FISCHER, G. Infrared Spectral, Structural, and Conformational Studies of Zwitterionic L-Tryptophan. **The Journal of Physical Chemistry A**, v. 103, n. 48, p. 9995–10003, dez. 1999.

CARLIN, R. L. Inorganic electronic spectroscopy (Lever, A. B. P.). **Journal of Chemical Education**, v. 46, n. 9, p. A628, set. 1969. Disponível em: <<http://pubs.acs.org/doi/abs/10.1021/ed046pA628.1>>. Acesso em: 20 ago. 2018.

CARNEIRO, Z. A. et al. Photocytotoxic Activity of a Nitrosyl Phthalocyanine Ruthenium Complex — A System Capable of Producing Nitric Oxide and Singlet Oxygen. **Journal of Inorganic Biochemistry**, v. 105, n. 8, p. 1035–1043, ago. 2011.

CARVALHO, I. et al. “Click Chemistry” Synthesis of a Library of 1,2,3-Triazole-Substituted Galactose Derivatives and Their Evaluation against Trypanosoma Cruzi and Its Cell Surface Trans-Sialidase. **Bioorganic & Medicinal Chemistry**, v. 18, n. 7, p. 2412–2427, 2010. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/20335038>>.

CAVALCANTI JUNIOR, G. B.; KLUMB, Claudete Esteves; MAIA, Raquel C. p53 e as hemopatias malignas. **Revista Brasileira de Cancerologia**, v. 48 (3), p. 419–427, 2002.

CERSOSIMO, R. J. Hepatotoxicity Associated with Cisplatin Chemotherapy. **Annals of Pharmacotherapy**, v. 27, n. 4, p. 438–441, abr. 1993.

CHEN, J C et al. Electronic structures and SARs of the isomeric complexes α -, β -, γ -[Ru(mazpy)₂Cl₂] with different antitumor activities. **Journal of Molecular Structure: THEOCHEM**, v. 728, n. 1, p. 93–101, 2005. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0166128005004331>>.

CICILLINI, S. A. et al. Nitric oxide and singlet oxygen photo-generation by light irradiation in the phototherapeutic window of a nitrosyl ruthenium conjugated with a phthalocyanine rare earth complex. **Polyhedron**, v. 28, n. 13, p. 2766–2770, 2009. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0277538709003349>>.

CLARKE, Michael J. Ruthenium metallopharmaceuticals. **Coordination Chemistry Reviews**, v. 232, n. 1, p. 69–93, 2002. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0010854502000255>>.

COHEN, R. A. Role of Nitric Oxide in Diabetic Complications. **American Journal of**

Therapeutics, v. 12, n. 6, p. 499–502, 2005. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/16280643>>.

CORTE-RODRÍGUEZ, M. et al. Quantitative Evaluation of Cellular Uptake, DNA Incorporation and Adduct Formation in Cisplatin Sensitive and Resistant Cell Lines: Comparison of Different Pt-Containing Drugs. **Biochemical Pharmacology**, v. 98, n. 1, p. 69–77, 2015. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/26352094>>.

COULTER, J. A. et al. Nitric Oxide—A Novel Therapeutic for Cancer. **Nitric Oxide**, v. 19, n. 2, p. 192–198, set. 2008.

COZZI, P. G. Metal–Salen Schiff Base Complexes in Catalysis: Practical Aspects. **Chemical Society Reviews**, v. 33, n. 7, p. 410–421, set. 2004.

CULLINANE, C. et al. Synthesis and Antiproliferative Activity of a Series of New Platinum and Palladium Diphosphane Complexes. **Dalton Transactions**, v. 47, n. 6, p. 1918–1932, 2018. Disponível em: <<http://pubs.rsc.org/en/content/articlelanding/2018/dt/c7dt04615d>>.

DA SILVA, R. S.; DE LIMA, R. G.; DE PAULA MACHADO, Sérgio. Design, Reactivity, and Biological Activity of Ruthenium Nitrosyl Complexes. **Adv. Inorg. Chem.** [S.l.]: Elsevier, 2015. v. 67. p. 265–294. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S0898883814000099>>.

DASARI, S.; BERNARD TCHOUNWOU, P. Cisplatin in Cancer Therapy: Molecular Mechanisms of Action. **European Journal of Pharmacology**, v. 740, p. 364–378, out. 2014.

DE BIASI, A. R.; VILLENA-VARGAS, J.; ADUSUMILLI, P. S. Cisplatin-Induced Antitumor Immunomodulation: A Review of Preclinical and Clinical Evidence. **Clinical Cancer Research**, v. 20, n. 21, p. 5384–5391, nov. 2014.

DE LA CRUZ, C.; SHEPPARD, N.. A Structure-Based Analysis of the Vibrational Spectra of Nitrosyl Ligands in Transition-Metal Coordination Complexes and Clusters. **Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy**, v. 78, n. 1, p. 7–28, 2011. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S1386142510003781>>.

DE LIMA, R. G. et al. Influence of ancillary ligand L in the nitric oxide photorelease by the [Ru(L)(tpy)NO]³⁺ complex and its vasodilator activity based on visible light irradiation. **Inorganica Chimica Acta**, v. 359, n. 8, p. 2543–2549, 2006. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0020169306001277>>.

DÉRIEN, S.; MONNIER, F.; DIXNEUF, P. H. Ruthenium-Catalyzed C–C Bond Formation. In: BRUNEAU, Christian; DIXNEUF, Pierre H. (Org.). . **Ruthenium Catal. Fine Chem.** Berlin, Heidelberg: Springer Berlin Heidelberg, 2004. v. 11. p. 1–44.

DEROSA, F.; BU, X.; FORD, P. C. 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]₂BF₄. **Inorganic Chemistry**, v. 44, n. 12, p. 4157–4165, 2005. Disponível em: <<http://pubs.acs.org/doi/abs/10.1021/ic048311o>>.

DI PASQUA, A. J; GOODISMAN, J.; DABROWIAK, J. C. Understanding how the platinum anticancer drug carboplatin works: From the bottle to the cell. **Inorganica Chimica Acta**, v. 389, p. 29–35, 2012. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0020169312000291>>.

DONATO, E. M. et al. Espectrofotometria derivada: uma contribuição prática para o desenvolvimento de métodos. **Revista de Ciências Farmacêuticas Básica e Aplicada**, v. 31, n. 2, p. 125–130, jun. 2010.

DONNICI, C. L.; ARAUJO, M. H.; STOIANOFF, M. A. R. Ruthenium Complexes as Antifungal Agents. In: BROWNE, Wesley R et al. (Org.). . **Ruthenium Complexes.** Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA, 2017. p. 293–318.

DOS SANTOS, E. R et al. Cytotoxic Activity and Structural Features of Ru(II)/Phosphine/Amino Acid Complexes. **Journal of Inorganic Biochemistry**, v. 182, p. 48–60, 2018. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S016201341730510X>>.

DUAN, L. et al. Highly Efficient and Robust Molecular Ruthenium Catalysts for Water Oxidation. **Proceedings of the National Academy of Sciences**, v. 109, n. 39, p. 15584–15588, set. 2012.

EGBEWANDE, F. A. et al. Synthesis, Characterization and Cytotoxicity of (η^6 -*p*-Cymene)Ruthenium(II) Complexes of α -Amino Acids: (η^6 -*p*-Cymene)Ruthenium(II) Complexes of α -Amino Acids. **European Journal of Inorganic Chemistry**, v. 2014, n. 7, p. 1174–1184, mar. 2014.

ELLAHIOUI, Y.; PRASHAR, S.; GÓMEZ-RUIZ, S.. Anticancer Applications and Recent Investigations of Metallodrugs Based on Gallium, Tin and Titanium. **Inorganics**, v. 5, n. 1, p. 4, 2017. Disponível em: <<http://www.mdpi.com/2304-6740/5/1/4>>.

ENRIQUEZ-CABRERA, A. et al. Replacing Two Chlorido Ligands by a Bipyridine Ligand in Ruthenium Nitrosyl Complexes with NO-Release Capabilities: A Comparative Study: Replacing Two Chlorido Ligands by a Bipyridine Ligand in Ruthenium Nitrosyl Complexes with NO-Release Capabilities: A . **European Journal of Inorganic Chemistry**, v. 2017, n. 11, p. 1446–1456, mar. 2017.

ERDTMAN, E. et al. Computational Studies on Schiff-Base Formation: Implications for the Catalytic Mechanism of Porphobilinogen Synthase. **Computational and Theoretical Chemistry**, v. 963, n. 2–3, p. 479–489, fev. 2011.

ERKKILA, K. E.; ODOM, D. T.; BARTON, J. K. Recognition and Reaction of Metallointercalators with DNA. **Chemical Reviews**, v. 99, n. 9, p. 2777–2796, set. 1999.

ESMADI, F. T et al. Synthesis, Characterization and Biological Activity of Some Unsymmetrical Schiff Base Transition Metal Complexes. **Drug and Chemical Toxicology**, v. 39, n. 1, p. 41–47, 2016. Disponível em: <<http://www.tandfonline.com/doi/full/10.3109/01480545.2015.1017882>>.

ESTEBAN-FERNÁNDEZ, D. et al. Analytical Methodologies for Metallomics Studies of Antitumor Pt-Containing Drugs. **Metallomics: Integrated Biometal Science**, v. 2, n. 1, p. 19–38, 2010. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/21072372>>.

FARRELL, N. Biomedical uses and applications of inorganic chemistry. An overview. **Coordination Chemistry Reviews**, v. 232, n. 1, p. 1–4, 2002. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0010854502001005>>.

FEDOROV, R. et al. Structures of Nitric Oxide Synthase Isoforms Complexed with the Inhibitor AR-R17477 Suggest a Rational Basis for Specificity and Inhibitor Design. **Proceedings of the National Academy of Sciences**, v. 101, n. 16, p. 5892–5897, abr. 2004.

FEELISCH, M. et al. Tissue Processing of Nitrite in Hypoxia: An Intricate Interplay of Nitric Oxide-Generating and -Scavenging Systems. **The Journal of Biological Chemistry**, v. 283, n. 49, p. 33927–33934, 2008. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/18835812>>.

FONTES, A. P. S.; ALMEIDA, S. G. de; NADER, L. de A. Compostos de platina em quimioterapia do câncer. **Química Nova**, v. 20, n. 4, p. 398–406, 1997. Disponível em: <http://www.scielo.br/scielo.php?script=sci_abstract&pid=S0100-0421997000400010&lng=en&nrm=iso&tlng=pt>.

FORNARO, A.; COICHEV, N. Ácido L-Ascórbico: Reações de Complexação e de Óxido-Redução Com Alguns Íons Metálicos de Transição. **Química Nova**, v. 21, n. 5, p. 642–650, 1998. Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40421998000500017&lng=pt&nrm=iso&tlng=pt>.

FORTNEY, C. F. **Ligands Designed for Ruthenium Nitrosyl Transport**. 2007. University of Pittsburgh, 2007.

FRANK, S. et al. Nitric Oxide Drives Skin Repair: Novel Functions of an Established Mediator. **Kidney International**, v. 61, n. 3, p. 882–888, 2002. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/11849442>>.

FREI, E. Albumin binding ligands and albumin conjugate uptake by cancer cells. **Diabetology & Metabolic Syndrome**, v. 3, p. 11, 2011. Disponível em: <<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3133998/>>.

FREITAS, L. B. O. et al. A Reação “Click” Na Síntese de 1,2,3-Triazóis: Aspectos Químicos e Aplicações. **Química Nova**, v. 34, n. 10, p. 1791–1804, 2011. Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422011001000012&lng=pt&nrm=iso&tlng=en>.

FRIEDERICH, J A; BUTTERWORTH, J F. Sodium Nitroprusside: Twenty Years and Counting. **Anesthesia and Analgesia**, v. 81, n. 1, p. 152–162, 1995. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/7598246>>.

GASCON, J.; BERN, C.; PINAZO, M. Chagas Disease in Spain, the United States and Other Non-Endemic Countries. **Acta Tropica**, v. 115, n. 1–2, p. 22–27, jul. 2010.

GASPARI, A. P. S. **Considerações sobre a liberação fotoquímica de óxido nítrico, sensibilizada por corantes**. 2013. Dissertação de Mestrado – Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto. Universidade de São Paulo., Ribeirão Preto/SP, 2013.

GORELSKY, S I; LEVER, A B P. Electronic Structure and Spectra of Ruthenium Diimine Complexes by Density Functional Theory and INDO/S. Comparison of the Two Methods. **Journal of Organometallic Chemistry**, v. 635, n. 1–2, p. 187–196, 2001. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S0022328X01010798>>.

GROESSL, M. et al. Structure–Activity Relationships for NAMI-A-Type Complexes (HL)[Trans -RuCl₄L(S -Dmso)Ruthenate(III)] (L = Imidazole, Indazole, 1,2,4-Triazole, 4-Amino-

1,2,4-Triazole, and 1-Methyl-1,2,4-Triazole): Aquation, Redox Properties, Protein Binding, and Anti. **Journal of Medicinal Chemistry**, v. 50, n. 9, p. 2185–2193, 2007. Disponível em: <<http://pubs.acs.org/doi/abs/10.1021/jm061081y>>.

GU, L. et al. Antimetastatic Activity of Novel Ruthenium (III) Pyridine Complexes. **Cancer Medicine**, v. 5, n. 10, p. 2850–2860, 2016. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/27605356>>.

HANNIBAL, L. Nitric Oxide Homeostasis in Neurodegenerative Diseases. **Current Alzheimer Research**, v. 13, n. 2, p. 135–149, 2016. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/26391043>>.

HEIN, J. E; FOKIN, V. V. Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC) and beyond: New Reactivity of Copper(I) Acetylides. **Chemical Society Reviews**, v. 39, n. 4, p. 1302–1315, 2010. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/20309487>>.

HEINRICH, T. A. et al. Biological Nitric Oxide Signalling: Chemistry and Terminology: NO Chemical Biology and Terminology. **British Journal of Pharmacology**, v. 169, n. 7, p. 1417–1429, ago. 2013.

HENRY, Y.; GUISSANI, A. Interactions of Nitric Oxide with Hemoproteins: Roles of Nitric Oxide in Mitochondria. **Cellular and Molecular Life Sciences: CMLS**, v. 55, n. 8–9, p. 1003–1014, jul. 1999.

HESEK, D. et al. Preparation and Structural Elucidation of Novel Cis Ruthenium(II) Bis(Bipyridine) Sulfoxide Complexes†. **Journal of the Chemical Society, Dalton Transactions**, v. 0, n. 21, p. 3701–3709, jan. 1999.

HEUDI, O.; CAILLEUX, A.; ALLAIN, P. Interactions between Cisplatin Derivatives and Mobile Phase during Chromatographic Separation. **Chromatographia**, v. 44, n. 1–2, p. 19–24, jan. 1997.

HOLDER, A. A et al. **Ruthenium Complexes**. [S.l.]: Wiley VCH, 2018. Disponível em: <<https://www.amazon.co.uk/Ruthenium-Complexes-Photochemical-Biomedical-Applications/dp/3527339574>>.

HOPP, T.; FISCHER-GÖDDE, M.; KLEINE, T. Ruthenium Stable Isotope Measurements by Double Spike MC-ICPMS. **Journal of Analytical Atomic Spectrometry**, v. 31, n. 7, p. 1515–1526, jun. 2016.

HOTZE, A. C. G. et al. Structure-Dependent in Vitro Cytotoxicity of the Isomeric Complexes [Ru(L)2Cl2] (L=o-Tolylazopyridine and 4-Methyl-2-Phenylazopyridine) in Comparison to [Ru(Azpy)2Cl2]. **JBIC Journal of Biological Inorganic Chemistry**, v. 9, n. 3, p. 354–364, abr. 2004.

HOUSTON, M.; HAYS, L. Acute Effects of an Oral Nitric Oxide Supplement on Blood Pressure, Endothelial Function, and Vascular Compliance in Hypertensive Patients. **The Journal of Clinical Hypertension**, p. n/a-n/a, jun. 2014.

HU, W. et al. A Study on Platinum(IV) Species Containing an Estrogen Receptor Modulator to Reverse Tamoxifen Resistance of Breast Cancer. **Metallomics**, v. 10, n. 2, p. 346–359, 2018.

HUISGEN, R. Kinetics and Mechanism of 1,3-Dipolar Cycloadditions. **Angewandte Chemie International Edition in English**, v. 2, n. 11, p. 633–645, nov. 1963.

HURD, C. D. The Chemistry of Alkenes. Saul Patai, Ed. Interscience (Wiley), New York, 1964. x + 1315 Pp. Illus. \$37. **Science**, v. 148, n. 3673, p. 1079–1079, maio 1965.

IALENTI, A.; MONCADA, S.; ROSA, M. Modulation of Adjuvant Arthritis by Endogenous Nitric Oxide. **British Journal of Pharmacology**, v. 110, n. 2, p. 701–706, out. 1993.

IBRAHIM, O. B.; MOHAMED, M. A.; REFAT, M. S. Nano Sized Schiff Base Complexes with Mn(II), Co(II), Cu(II), Ni(II) and Zn(II) Metals : Synthesis, Spectroscopic and Medicinal Studies. **Canadian Chemical Transactions**, p. 108–121, abr. 2014.

IGNARRO, L J. Physiology and Pathophysiology of Nitric Oxide. **Kidney International. Supplement**, v. 55, p. S2-5, 1996. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/8743501>>.

ISENBERG, J. S. et al. Nitric Oxide in Wound-Healing. **Microsurgery**, v. 25, n. 5, p. 442–451, 2005.

JUNG, Y.; LIPPARD, S. J. Direct Cellular Responses to Platinum-Induced DNA Damage. **Chemical Reviews**, v. 107, n. 5, p. 1387–1407, maio 2007.

JURIS, A. et al. Ru(II) polypyridine complexes: photophysics, photochemistry, eletrochemistry, and chemiluminescence. **Coordination Chemistry Reviews**, v. 84, p. 85–277, 1988. Disponível em: <<http://www.sciencedirect.com/science/article/pii/0010854588800328>>.

KAJAL, A. et al. Schiff Bases: A Versatile Pharmacophore. **Journal of Catalysts**, v. 2013, p.

1–14, 2013. Disponível em: <<https://www.hindawi.com/archive/2013/893512/>>.

KASPARKOVA, J. et al. DNA Interstrand Cross-Links of the Novel Antitumor Trinuclear Platinum Complex BBR3464: CONFORMATION, RECOGNITION BY HIGH MOBILITY GROUP DOMAIN PROTEINS, AND NUCLEOTIDE EXCISION REPAIR. **Journal of Biological Chemistry**, v. 277, n. 50, p. 48076–48086, dez. 2002.

KEEFER, L. K. et al. Chemistry of the Diazeniumdiolates I. Structural and Spectral Characteristics of the [N(O)NO]– Functional Group. **Nitric Oxide**, v. 5, n. 4, p. 377–394, ago. 2001.

KESZTHELYI, D.; TROOST, F. J.; MASCLÉE, A. M. Understanding the Role of Tryptophan and Serotonin Metabolism in Gastrointestinal Function. **Neurogastroenterology & Motility**, v. 21, n. 12, p. 1239–1249, dez. 2009.

KINGWELL, B. A. et al. Nitric Oxide Synthase Inhibition Reduces Glucose Uptake During Exercise in Individuals With Type 2 Diabetes More Than in Control Subjects. **Diabetes**, v. 51, n. 8, p. 2572–2580, ago. 2002.

KNOTT, A. B.; BOSSY-WETZEL, E. Nitric Oxide in Health and Disease of the Nervous System. **Antioxidants & Redox Signaling**, v. 11, n. 3, p. 541–553, mar. 2009.

KOLB, H. C; SHARPLESS, K. B. The growing impact of click chemistry on drug discovery. **Drug Discovery Today**, v. 8, n. 24, p. 1128–1137, dez. 2003.

KOSTIN, G. A. et al. Reaction of $[\text{RuNO}(\text{NO}_2)_4\text{OH}]^{2-}$ with Sulfamic Acid as a Pathway to Mixed Nitro Pyridine Ruthenium Nitrosyl Complexes: Reaction of $[\text{RuNO}(\text{NO}_2)_4\text{OH}]^{2-}$ with Sulfamic Acid as a Pathway To . **European Journal of Inorganic Chemistry**, v. 2016, n. 25, p. 4045–4053, set. 2016.

KOSTOVA, I.; SASO, L. Advances in Research of Schiff-Base Metal Complexes as Potent Antioxidants. **Current Medicinal Chemistry**, v. 20, n. 36, p. 4609–4632, nov. 2013.

KRAUSE, R. A.; KRAUSE, K. Chemistry of Bipyridyl-like Ligands. Isomeric Complexes of Ruthenium(II) with 2-(Phenylazo)Pyridine. **Inorganic Chemistry**, v. 19, n. 9, p. 2600–2603, set. 1980.

KROENER, R.; HEEG, M. J.; DEUTSCH, E. Synthesis and Characterization of Polypyridine Ruthenium(II) Complexes Containing S-Bonded Thioether Ligands. X-Ray Crystal Structures of Cis- and Trans-Bis(2,2'-Bipyridine)Bis(Phenothiazine-S)Ruthenium(II)

Hexafluorophosphates. **Inorganic Chemistry**, v. 27, n. 3, p. 558–566, fev. 1988.

KUHN, H. J.; BRASLAVSKY, S. E.; SCHMIDT, R. Chemical Actinometry (IUPAC Technical Report). **Pure and Applied Chemistry**, v. 76, n. 12, p. 2105–2146, 2004.

KUMAR, S. V. et al. Antimicrobial Properties of Tris(Homoleptic) Ruthenium(II) 2-Pyridyl-1,2,3-Triazole “Click” Complexes against Pathogenic Bacteria, Including Methicillin-Resistant *Staphylococcus Aureus* (MRSA). **Inorganic Chemistry**, v. 55, n. 19, p. 9767–9777, out. 2016.

KURIYAMA, K.; OHKUMA, S. Role of Nitric Oxide in Central Synaptic Transmission: Effects on Neurotransmitter Release. **Japanese Journal of Pharmacology**, v. 69, n. 1, p. 1–8, set. 1995.

LEIJEN, S. et al. Phase I/II Study with Ruthenium Compound NAMI-A and Gemcitabine in Patients with Non-Small Cell Lung Cancer after First Line Therapy. **Investigational New Drugs**, v. 33, n. 1, p. 201–214, fev. 2015.

LENTZ, F. et al. Pharmacokinetics of a Novel Anticancer Ruthenium Complex (KP1019, FFC14A) in a Phase I Dose-Escalation Study. **Anti-Cancer Drugs**, v. 20, n. 2, p. 97–103, fev. 2009.

LEVER, A B P. **Inorganic electronic spectroscopy**. [S.l.]: Elsevier, 1984. Disponível em: <<https://books.google.com.br/books?id=bvfvAAAAMAAJ>>. (Studies in physical and theoretical chemistry).

LEVIN, N. et al. Structural, Spectroscopic, and Photochemical Investigation of an Octahedral NO-Releasing {RuNO}⁷ Species. **Inorganic Chemistry**, v. 55, n. 16, p. 7808–7810, ago. 2016.

LEVINA, A.; MITRA, A.; LAY, P. A. Recent Developments in Ruthenium Anticancer Drugs. **Metallomics**, v. 1, n. 6, p. 458, 2009.

LI, C. et al. Click Chemistry to Fluorescent Amino Esters: Synthesis and Spectroscopic Studies. **European Journal of Organic Chemistry**, v. 2010, n. 12, p. 2395–2405, 2010. Disponível em: <<http://doi.wiley.com/10.1002/ejoc.201000042>>.

LI, F.; COLLINS, J. G.; KEENE, F. R. **Ruthenium Complexes as Antimicrobial Agents**. **Chemical Society Reviews**. [S.l.: s.n.], 2015

LIANG, L.; ASTRUC, D. The Copper(I)-Catalyzed Alkyne-Azide Cycloaddition (CuAAC) “Click” Reaction and Its Applications. An Overview. **Coordination Chemistry Reviews**, v.

255, n. 23–24, p. 2933–2945, dez. 2011.

LIM, S. et al. Lysine-Specific Demethylase 1 (LSD1) Is Highly Expressed in ER-Negative Breast Cancers and a Biomarker Predicting Aggressive Biology. **Carcinogenesis**, v. 31, n. 3, p. 512–520, 2010. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/20042638>>.

LIMA, A. P. et al. Cytotoxicity and Apoptotic Mechanism of Ruthenium(II) Amino Acid Complexes in Sarcoma-180 Tumor Cells. **PLoS ONE**, v. 9, n. 10, p. e105865, 2014. Disponível em: <<http://dx.plos.org/10.1371/journal.pone.0105865>>.

LIMA, R. G; de. **Reatividade química e fotoquímica de complexos nitrosilos de rutênio do tipo [Ru(terpy)(L)NO]ⁿ⁺**. 2006. 289 f. Tese de Doutorado – Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto. Universidade de São Paulo., Ribeirão Preto/SP, 2006.

LIU, X. et al. Multidentate unsymmetrically-substituted Schiff bases and their metal complexes: Synthesis, functional materials properties, and applications to catalysis. **Coordination Chemistry Reviews**, v. 357, p. 144–172, fev. 2018.

LLOYD, N. C. et al. The Composition of Ehrlich's Salvarsan: Resolution of a Century-Old Debate. **Angewandte Chemie (International Ed. in English)**, v. 44, n. 6, p. 941–944, jan. 2005.

LOCKWOOD, A. et al. **Sodium Nitroprusside-Associated Cyanide Toxicity in Adult Patients – Fact or Fiction? A Critical Review of the Evidence and Clinical Relevance.**

LUO, X. et al. Synthesis and Evaluation of Novel O₂-Derived Diazeniumdiolates as Photochemical and Real-Time Monitoring Nitric Oxide Delivery Agents. **Organic Chemistry Frontiers**, v. 4, n. 12, p. 2445–2449, nov. 2017.

MALAKYAN, M. et al. Synthesis, Characterization and Toxicity Studies of Pyridinecarboxaldehydes and L-Tryptophan Derived Schiff Bases and Corresponding Copper (II) Complexes. **F1000Research**, v. 5, p. 1921, ago. 2016.

MALINA, J. et al. Biophysical Analysis of Natural, Double-Helical DNA Modified by Anticancer Heterocyclic Complexes of Ruthenium(III) in Cell-Free Media. **Journal of Biological Inorganic Chemistry: JBIC: A Publication of the Society of Biological Inorganic Chemistry**, v. 6, n. 4, p. 435–445, 2001. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/11372202>>.

MANZOTTI, C. et al. BBR 3464: A Novel Triplatinum Complex, Exhibiting a Preclinical Profile of Antitumor Efficacy Different from Cisplatin. **Clinical Cancer Research: An Official Journal of the American Association for Cancer Research**, v. 6, n. 7, p. 2626–2634, jul. 2000.

MARCONDES, F. G et al. In vivo effects of the controlled NO donor/scavenger ruthenium cyclam complexes on blood pressure. **Life Sciences**, v. 70, n. 23, p. 2735–2752, 2002. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S002432050201528X>>.

MATIJEVIĆ, E. (Org.). **Fine particles in medicine and pharmacy**. New York: Springer, 2012.

MATTHYS, K. E.; BULT, H. Nitric Oxide Function in Atherosclerosis. **Mediators of Inflammation**, v. 6, n. 1, p. 3–21, 1997.

MCCARTNEY-FRANCIS, N. Suppression of Arthritis by an Inhibitor of Nitric Oxide Synthase. **Journal of Experimental Medicine**, v. 178, n. 2, p. 749–754, ago. 1993.

MCCLEVERTY, J. A. Chemistry of Nitric Oxide Relevant to Biology. **Chemical Reviews**, v. 104, n. 2, p. 403–418, 2004. Disponível em: <<https://doi.org/10.1021/cr020623q>>.

METZKER, G.; CARDOSO, D. R.; FRANCO, D. W. Reaction of ruthenium nitrosyl complexes with superoxide. **Polyhedron**, v. 50, n. 1, p. 328–332, 2013. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0277538712008509>>.

MICHAEL, D.; MINGOS, P.; SHERMAN, D. J. Transition Metal Nitrosyl Complexes. In: SYKES, A G (Org.). . **Adv. Inorg. Chem.** [S.l.]: Academic Press, 1989. v. 34. p. 293–377. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S0898883808600197>>.

MJOS, K. D.; ORVIG, C. Metallodrugs in Medicinal Inorganic Chemistry. **Chemical Reviews**, v. 114, n. 8, p. 4540–4563, abr. 2014.

MOCELLIN, S.; BRONTE, V.; NITTI, D. Nitric Oxide, a Double Edged Sword in Cancer Biology: Searching for Therapeutic Opportunities. **Medicinal Research Reviews**, v. 27, n. 3, p. 317–352, 2007. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/16991100>>.

MONCADA, S.; PALMER, R. M.; HIGGS, E. A. Nitric Oxide: Physiology, Pathophysiology, and Pharmacology. **Pharmacological Reviews**, v. 43, n. 2, p. 109–142, jun. 1991.

MONCADA, S; HIGGS, E A. Endogenous Nitric Oxide: Physiology, Pathology and Clinical

Relevance. **European Journal of Clinical Investigation**, v. 21, n. 4, p. 361–374, 1991.
Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/1718757>>.

MONTALTI, M.; MUROV, S. L. (Org.). **Handbook of photochemistry**. 3rd ed ed. Boca Raton: CRC/Taylor & Francis, 2006.

MOREIRA, M. M. **Complexos Trinucleares de Rutênio com ponte μ -oxo contendo ligantes N-heterocíclicos e Monóxido de Carbono: Síntese, Caracterização e Estudo de Interação com Biomoléculas**". 2016. 134 f. Universidade de São Paulo, Ribeirão Preto, 2016.

MOSMANN, T. Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays. **Journal of Immunological Methods**, v. 65, n. 1–2, p. 55–63, dez. 1983.

MOTSWAINYANA, W. M.; AJIBADE, P. A. Anticancer Activities of Mononuclear Ruthenium(II) Coordination Complexes. **Advances in Chemistry**, v. 2015, p. 1–21, 2015.

NAGAO, H. et al. **Synthesis, Properties, and Molecular Structure Of** . Disponível em: <<https://pubs.acs.org/doi/abs/10.1021/ic00320a006>>.

NAPOLI, C.; IGNARRO, L. J. Nitric Oxide and Atherosclerosis. **Nitric Oxide**, v. 5, n. 2, p. 88–97, abr. 2001.

NATHAN, C; XIE, Q W. Nitric Oxide Synthases: Roles, Tolls, and Controls. **Cell**, v. 78, n. 6, p. 915–918, 1994. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/7522969>>.

NAVARRO, M. et al. Metal-Based Drugs for Malaria, Trypanosomiasis and Leishmaniasis: Recent Achievements and Perspectives. **Drug Discovery Today**, v. 15, n. 23–24, p. 1070–1078, dez. 2010.

NEVES, A. P.; VARGAS, M. D. Platinum(II) Complexes in Cancer Therapy. **Revista Virtual de Química**, v. 3, n. 3, 2011.

NICHOLSON, R. S.; SHAIN, I.. Theory of Stationary Electrode Polarography for a Chemical Reaction Coupled between Two Charge Transfers. **Analytical Chemistry**, v. 37, n. 2, p. 178–190, fev. 1965.

NOVAKOVA, O. et al. Correlation between Cytotoxicity and DNA Binding of Polypyridyl Ruthenium Complexes. **Biochemistry**, v. 34, n. 38, p. 12369–12378, set. 1995.

NYFFELER, P. T. et al. The Chemistry of Amine-Azide Interconversion: Catalytic

Diazotransfer and Regioselective Azide Reduction. **Journal of the American Chemical Society**, v. 124, n. 36, p. 10773–10778, set. 2002.

OHNO, K. et al. Matrix-isolation infrared spectra of 2-, 3- and 4-pyridinecarboxaldehyde before and after UV irradiation. **Journal of Molecular Structure**, v. 825, n. 1, p. 143–150, dez. 2006.

OMAE, I. Intramolecular Five-Membered Ring Compounds and Their Applications. **Coordination Chemistry Reviews**, v. 248, n. 11–12, p. 995–1023, jun. 2004.

ONODERA, S.; IKEGAMI, Y. Far-Infrared Spectra of Ammonium, Potassium, Rubidium, and Cesium Metavanadates. **Inorganic Chemistry**, v. 18, n. 2, p. 466–468, fev. 1979.

PACOR, S. Intratumoral NAMI-A Treatment Triggers Metastasis Reduction, Which Correlates to CD44 Regulation and Tumor Infiltrating Lymphocyte Recruitment. **Journal of Pharmacology and Experimental Therapeutics**, v. 310, n. 2, p. 737–744, abr. 2004.

PAKEN, J. et al. Cisplatin-Associated Ototoxicity: A Review for the Health Professional. **Journal of Toxicology**, v. 2016, p. 1–13, 2016.

PAREKH, H. M.; MEHTA, S. R.; PATEL, M. N. Synthesis, Structural Characterization, and Antifungal Activity of Schiff Bases and Their Transition Metal Mixed-Ligand Complexes. **Russian Journal of Inorganic Chemistry**, v. 51, n. 1, p. 67–72, jan. 2006.

PARKER, R J et al. Acquired Cisplatin Resistance in Human Ovarian Cancer Cells Is Associated with Enhanced Repair of Cisplatin-DNA Lesions and Reduced Drug Accumulation. **Journal of Clinical Investigation**, v. 87, n. 3, p. 772–777, mar. 1991.

PASETTO, L. M. et al. The Development of Platinum Compounds and Their Possible Combination. **Critical Reviews in Oncology/Hematology**, v. 60, n. 1, p. 59–75, out. 2006.

PAVIA, D. L et al. **Introdução à espectroscopia**. [S.l: s.n.], 2010.

PETHERICK, A. Chagas disease in the Chaco. **Nature**, v. 465, n. n7301_supp, p. S18–S20, jun. 2010.

PINATO, O.; MUSETTI, C.; SISSI, C. Pt-Based Drugs: The Spotlight Will Be on Proteins. **Metallomics**, v. 6, n. 3, p. 380–395, 2014.

PIZARRO, A. M.; SADLER, P. J. Unusual DNA Binding Modes for Metal Anticancer Complexes. **Biochimie**, v. 91, n. 10, p. 1198–1211, out. 2009.

PLATTEN, M; WICK, W; VAN DEN EYNDE, B J. Tryptophan Catabolism in Cancer:

Beyond IDO and Tryptophan Depletion. **Cancer Research**, v. 72, n. 21, p. 5435–5440, 2012.
Disponível em: <<http://cancerres.aacrjournals.org/cgi/doi/10.1158/0008-5472.CAN-12-0569>>.

POPOLIN, C. P. et al. Cytotoxicity and Anti-Tumor Effects of New Ruthenium Complexes on Triple Negative Breast Cancer Cells. **PLOS ONE**, v. 12, n. 9, p. e0183275, set. 2017.

QIN, W. et al. **Schiff Bases: A Short Survey on an Evergreen Chemistry Tool**. **Molecules**. [S.l: s.n.], out. 2013

QIN, Y.; PENG, Q. **Ruthenium Sensitizers and Their Applications in Dye-Sensitized Solar Cells**. **International Journal of Photoenergy**. [S.l: s.n.], 2012

RAJA, W. et al. Cisplatin Induced Paroxysmal Supraventricular Tachycardia. **Indian Journal of Medical and Paediatric Oncology**, v. 34, n. 4, p. 330, 2013.

RAMESH, R.; SIVAGAMASUNDARI, M. Synthesis, Spectral and Antifungal Activity of Ru(II) Mixed-Ligand Complexes. **Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry**, v. 33, n. 5, p. 899–910, jan. 2003.

RATHGEB, A. et al. Ruthenium-Nitrosyl Complexes with Glycine, L -Alanine, L -Valine, L -Proline, . **Inorganic Chemistry**, v. 53, n. 5, p. 2718–2729, mar. 2014.

REES, D.; BEN-ISHAY, D.; MONCADA, S. Nitric Oxide and the Regulation of Blood Pressure in the Hypertension-Prone and Hypertension-Resistant Sabra Rat. **Hypertension**, v. 28, n. 3, p. 367–371, set. 1996.

REN, J. et al. Acquired Cisplatin Resistance in Human Lung Adenocarcinoma Cells Is Associated with Enhanced Autophagy. **Cancer Biotherapy & Radiopharmaceuticals**, v. 25, n. 1, p. 75–80, fev. 2010. Disponível em: <<http://www.liebertonline.com/doi/abs/10.1089/cbr.2009.0701>>.

RHO, J. K. et al. The Effect of Acquired Cisplatin Resistance on Sensitivity to EGFR Tyrosine Kinase Inhibitors in EGFR Mutant Lung Cancer Cells. **Oncology Research**, v. 19, n. 10–11, p. 471–478, 2011.

RICHARD, D. M. et al. L-Tryptophan: Basic Metabolic Functions, Behavioral Research and Therapeutic Indications. **International Journal of Tryptophan Research : IJTR**, v. 2, p. 45–60, mar. 2009.

RIDDELL, D. R.; OWEN, J. S. Nitric Oxide and Platelet Aggregation. **Vitamins and Hormones**, v. 57, p. 25–48, 1999.

RIDNOUR, L. A. et al. The Biphasic Nature of Nitric Oxide Responses in Tumor Biology. **Antioxidants & Redox Signaling**, v. 8, n. 7–8, p. 1329–1337, 2006. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/16910780>>.

RODRIGUES, F. P. et al. Incorporation of a ruthenium nitrosyl complex into liposomes, the nitric oxide released from these liposomes and HepG2 cell death mechanism. **Coordination Chemistry Reviews**, A Volume in Honor of Peter Ford. v. 306, p. 701–707, jan. 2016.

RODRIGUES, G. J. et al. Pharmacological Characterization of the Vasodilating Effect Induced by the Ruthenium Complex Cis-[Ru(NO)(NO₂)(Bpy)₂](PF₆)₂. **Journal of Cardiovascular Pharmacology**, v. 65, n. 2, p. 168–175, nov. 2015.

ROSA, V. et al. Imine Ligands Based on Ferrocene: Synthesis, Structural and Mössbauer Characterization and Evaluation as Chromogenic and Electrochemical Sensors for Hg⁺². **New Journal of Chemistry**, 2018.

ROSENBERG, B.; VANCAMP, L. The Successful Regression of Large Solid Sarcoma 180 Tumors by Platinum Compounds. **Cancer Research**, v. 30, n. 6, p. 1799–1802, jun. 1970.

ROSENBERG, B. et al. Platinum Compounds: A New Class of Potent Antitumour Agents. **Nature**, v. 222, n. 5191, p. 385–386, 1969. Disponível em: <<https://www.nature.com/articles/222385a0>>.

ROSENBERG, B.; VAN CAMP, L.; KRIGAS, T. Inhibition of Cell Division in Escherichia Coli by Electrolysis Products from a Platinum Electrode. **Nature**, v. 205, n. 4972, p. 698–699, 1965. Disponível em: <<https://www.nature.com/articles/205698a0>>.

ROSTOVTSEV, V. V. et al. A Stepwise Huisgen Cycloaddition Process: Copper(I)-Catalyzed Regioselective “Ligation” of Azides and Terminal Alkynes. **Angewandte Chemie (International Ed. in English)**, v. 41, n. 14, p. 2596–2599, 2002. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/12203546>>.

SATO, T.; MORINAGA, T.; ISHIZUK, T. Preparation, Physicochemical Properties and Battery Applications of a Novel Poly(Ionic Liquid). In: KADOKAWA, Jun-ichi (Org.). **Ion. Liq. - New Asp. Futur.** [S.l.]: InTech, 2013. .

SAUAIA, M. G et al. Photoinduced NO Release by Visible Light Irradiation from Pyrazine-

Bridged Nitrosyl Ruthenium Complexes. **Journal of the American Chemical Society**, v. 125, n. 48, p. 14718–14719, 2003. Disponível em: <<https://doi.org/10.1021/ja0376801>>.

SAUAIA, M. G.; SILVA, Roberto Santana da. The Reactivity of Nitrosyl Ruthenium Complexes Containing Polypyridyl Ligands. **Transition Metal Chemistry**, v. 28, n. 3, p. 254–259, 2003. Disponível em: <<https://link.springer.com/article/10.1023/A:1022964510682>>.

SAUAIA, M. G. et al. Syntheses, Characterization and Photochemical Properties of New NO–ruthenium(II) Complexes. **Inorganic Chemistry Communications**, v. 8, n. 4, p. 347–349, 2005. Disponível em: <<http://linkinghub.elsevier.com/retrieve/pii/S1387700305000201>>.

SCHMUNIS, G. A.; YADON, Z. E. Chagas Disease: A Latin American Health Problem Becoming a World Health Problem. **Acta Tropica**, v. 115, n. 1–2, p. 14–21, jul. 2010.

SCHULZ, J. B.; MATTHEWS, R. T.; BEAL, M. F. Role of Nitric Oxide in Neurodegenerative Diseases. **Current Opinion in Neurology**, v. 8, n. 6, p. 480–486, dez. 1995.

SCORSATO, A. P.; TELLES, J. E. Q. Fatores Que Interferem Na Qualidade Do DNA Extraído de Amostras Biológicas Armazenadas Em Blocos de Parafina. **Jornal Brasileiro de Patologia e Medicina Laboratorial**, v. 47, n. 5, p. 541–548, 2011. Disponível em: <http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1676-24442011000500008&lng=pt&nrm=iso&tlng=en>.

SEABRA, A. B. et al. Antibacterial Nitric Oxide-Releasing Polyester for the Coating of Blood-Contacting Artificial Materials. **Artificial Organs**, v. 34, n. 7, p. E204-214, jul. 2010.

SEDDON, E. A.; SEDDON, K. R.; CLARK, R. J. H. **The Chemistry of Ruthenium**. [S.l.]: Elsevier Science, 2013.

SERLI, B. et al. Synthesis and Structural, Spectroscopic, and Electrochemical Characterization of New Ruthenium Dimethyl Sulfoxide Nitrosyls. **Inorganic Chemistry**, v. 41, n. 15, p. 4033–4043, jul. 2002.

SHAHROOSVAND, H.; ESKANDARI, M. Ultrafast Interfacial Charge Transfer from the LUMO+1 in Ruthenium(II) Polypyridyl Quinoxaline-Sensitized Solar Cells. **Dalton Transactions**, v. 47, n. 2, p. 561–576, 2018.

SHARMA, J. N.; AL-OMRAN, A.; PARVATHY, S. S. Role of Nitric Oxide in Inflammatory Diseases. **Inflammopharmacology**, v. 15, n. 6, p. 252–259, dez. 2007.

SHEN, D.-W. et al. Cisplatin Resistance: A Cellular Self-Defense Mechanism Resulting from Multiple Epigenetic and Genetic Changes. **Pharmacological Reviews**, v. 64, n. 3, p. 706–721, jul. 2012.

SHRIVER, D F; ATKINS, P W. **Química inorgânica**. Porto Alegre (RS): Bookman, 2008.

SILVA, R. S. et al. Synthesis, Spectral and Redox Properties of Tetraammine Dioxolene Ruthenium Complexes. **Journal of the Chemical Society, Dalton Transactions**, v. 0, n. 22, p. 4078–4088, jan. 2000.

SIZOVA, O. V. et al. Chemistry of Ruthenium Polypyridine Complexes: VIII. Electronic Structure and Reactivity of Cis-[Ru(2,2'-Bpy)₂(L)Cl]⁺ Complexes in Excited States. **Russian Journal of General Chemistry**, v. 73, n. 12, p. 1846–1856, dez. 2003.

SOCRATES, G. Infrared Characteristic Group Frequencies: Tables and Charts. **Journal of Chemical Education**, v. 72, n. 4, p. A93, 1995. Disponível em: <<http://pubs.acs.org/doi/abs/10.1021/ed072pA93.5>>.

SOUSA, G. F. de; WLODARCZYK, S. R.; MONTEIRO, G. Carboplatin: molecular mechanisms of action associated with chemoresistance. **Brazilian Journal of Pharmaceutical Sciences**, v. 50, n. 4, p. 693–701, dez. 2014.

STEFANOVIC-RACIC, M.; STADLER, J.; EVANS, C. H. Nitric Oxide and Arthritis. **Arthritis & Rheumatism**, v. 36, n. 8, p. 1036–1044, set. 1993.

STEVENS, S. K. et al. The Anticancer Ruthenium Complex KP1019 Induces DNA Damage, Leading to Cell Cycle Delay and Cell Death in *Saccharomyces Cerevisiae*. **Molecular Pharmacology**, v. 83, n. 1, p. 225–234, jan. 2013. Disponível em: <<http://molpharm.aspetjournals.org/cgi/doi/10.1124/mol.112.079657>>.

STEVERDING, D. The history of Chagas disease. **Parasites & Vectors**, v. 7, p. 317, jul. 2014.

TFOUNI, E. et al. Tailoring NO Donors Metallopharmaceuticals: Ruthenium Nitrosyl Amines and Aliphatic Tetraazamacrocycles. **Current Medicinal Chemistry**, v. 17, n. 31, p. 3643–3657, 2010. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/20846113>>.

TFOUNI, E. et al. Structure, Chemical and Photochemical Reactivity and Biological Activity of Some Ruthenium Amine Nitrosyl Complexes. **Coordination Chemistry Reviews**, v. 236, n. 1–2, p. 57–69, jan. 2003.

THATCHER, G. R. J. et al. Nitrates and NO Release: Contemporary Aspects in Biological and Medicinal Chemistry. **Free Radical Biology and Medicine**, v. 37, n. 8, p. 1122–1143, out. 2004.

THOMAS, D. D. Breathing New Life into Nitric Oxide Signaling: A Brief Overview of the Interplay between Oxygen and Nitric Oxide. **Redox Biology**, v. 5, p. 225–233, 2015. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/26056766>>.

TODD, R. C.; LIPPARD, Stephen J. Inhibition of Transcription by Platinum Antitumor Compounds. **Metallomics**, v. 1, n. 4, p. 280, 2009.

TOGNILOLO, V.; SANTANA DA SILVA, R.; TEDESCO, A. C. Photo-induced nitric oxide release from chlorobis(2,2'-bipyridine)nitrosylruthenium(II) in aqueous solution. **Inorganica Chimica Acta**, v. 316, n. 1, p. 7–12, 2001. Disponível em: <<http://www.sciencedirect.com/science/article/pii/S002016930100370X>>.

TOLEDO, J. C. et al. Ruthenium Tetraammines as a Model of Nitric Oxide Donor Compounds. **European Journal of Inorganic Chemistry**, v. 2004, n. 9, p. 1879–1885, maio 2004.

TOLEDO, J. C.; AUGUSTO, O. **Connecting the Chemical and Biological Properties of Nitric Oxide**. **Chemical Research in Toxicology**. [S.l: s.n.], maio 2012

TORIGOE, T. et al. Cisplatin Resistance and Transcription Factors. **Current Medicinal Chemistry. Anti-Cancer Agents**, v. 5, n. 1, p. 15–27, jan. 2005.

TRACHTMAN, H. Nitric Oxide and Glomerulonephritis. **Seminars in Nephrology**, v. 24, n. 4, p. 324–332, jul. 2004.

TRONDL, R. et al. NKP-1339, the First Ruthenium-Based Anticancer Drug on the Edge to Clinical Application. **Chem. Sci.**, v. 5, n. 8, p. 2925–2932, abr. 2014.

TURNBULL, C. M. et al. Mechanism of Action of Novel NO-Releasing Furoxan Derivatives of Aspirin in Human Platelets. **British Journal of Pharmacology**, v. 148, n. 4, p. 517–526, 2006. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/16702997>>.

TYLKOWSKI, B.; JASTRZĄB, R.; ODANI, A. Developments in platinum anticancer drugs. **Physical Sciences Reviews**, v. 3, n. 1, jan. 2018.

VAN RIJT, S. H.; SADLER, P. J. Current Applications and Future Potential for Bioinorganic Chemistry in the Development of Anticancer Drugs. **Drug Discovery Today**, v. 14, n. 23–24,

p. 1089–1097, dez. 2009.

VARGIU, A. V. et al. The Hydrolysis Mechanism of the Anticancer Ruthenium Drugs NAMI-A and ICR Investigated by DFT–PCM Calculations. **The Journal of Physical Chemistry B**, v. 112, n. 14, p. 4401–4409, abr. 2008.

VELDERS, A. H. et al. Dichlorobis(2-Phenylazopyridine)Ruthenium(II) Complexes: Characterisation, Spectroscopic and Structural Properties of Four Isomers. **Dalton Trans.**, n. 3, p. 448–455, 2004.

VINCENT, S. R. Nitric Oxide Neurons and Neurotransmission. **Progress in Neurobiology**, v. 90, n. 2, p. 246–255, fev. 2010.

VIRARKAR, M. et al. L-Arginine and Nitric Oxide in CNS Function and Neurodegenerative Diseases. **Critical Reviews in Food Science and Nutrition**, v. 53, n. 11, p. 1157–1167, jan. 2013.

VIZI, E.S. Nitric Oxide in Neurotransmission. **Trends in Pharmacological Sciences**, v. 22, n. 11, p. 595, nov. 2001.

WALLACE, J. L. Nitric oxide as a regulator of inflammatory processes. **Memórias do Instituto Oswaldo Cruz**, v. 100, n. suppl 1, p. 5–9, mar. 2005.

WANG, P. G.; CAI, T. B.; TANIGUCHI, N. **Nitric Oxide Donors: For Pharmaceutical and Biological Applications**. [S.l.]: John Wiley & Sons, 2005.

WANG, T. et al. Nitric Oxide-Releasing Polymeric Furoxan Conjugates. **Polymer Chemistry**, v. 6, n. 44, p. 7737–7748, 2015. Disponível em: <<https://pubs.rsc.org/en/content/articlelanding/2015/py/c5py01335f>>.

WANSTALL, J. C. et al. Vascular Smooth Muscle Relaxation Mediated by Nitric Oxide Donors: A Comparison with Acetylcholine, Nitric Oxide Andnitroxyl Ion. **British Journal of Pharmacology**, v. 134, n. 3, p. 463–472, out. 2001.

WEI, X. et al. Altered Immune Responses in Mice Lacking Inducible Nitric Oxide Synthase. **Nature**, v. 375, n. 6530, p. 408–411, jun. 1995. Disponível em: <<http://www.nature.com/doifinder/10.1038/375408a0>>.

WHEATE, N. J. et al. The Status of Platinum Anticancer Drugs in the Clinic and in Clinical Trials. **Dalton Transactions**, v. 39, n. 35, p. 8113, 2010.

WILLIAMS, K. R; BRAVO, R. Micelles in the Physical Chemistry Laboratory: Diffusion Coefficients and Half-Wave Potentials of Ferrocene. **Journal of Chemical Education**, v. 77, n. 3, p. 392, 1 mar. 2000. Disponível em: <<https://doi.org/10.1021/ed077p392>>.

WINK, D A; MITCHELL, J B. Chemical Biology of Nitric Oxide: Insights into Regulatory, Cytotoxic, and Cytoprotective Mechanisms of Nitric Oxide. **Free Radical Biology & Medicine**, v. 25, n. 4–5, p. 434–456, 1998. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/9741580>>.

WITTE, M. B; BARBUL, A. Role of Nitric Oxide in Wound Repair. **American Journal of Surgery**, v. 183, n. 4, p. 406–412, 2002. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/11975928>>.

WLODARCZYK, M. T. et al. Platinum(II) Complex-Nuclear Localization Sequence Peptide Hybrid for Overcoming Platinum Resistance in Cancer Therapy. **ACS Biomaterials Science & Engineering**, v. 4, n. 2, p. 463–467, fev. 2018.

WOZNIAK, K.; CZECHOWSKA, A.; BLASIAK, J. Cisplatin-evoked DNA fragmentation in normal and cancer cells and its modulation by free radical scavengers and the tyrosine kinase inhibitor STI571. **Chemico-Biological Interactions**, v. 147, n. 3, p. 309–318, abr. 2004.

XAVIER, A; SRIVIDHYA, N. Synthesis and Study of Schiff base Ligands. **IOSR Journal of Applied Chemistry**, v. 7, n. 11, p. 06-15, 2014.

YANG, M.; LI, J.; CHEN, P. R. Transition Metal-Mediated Bioorthogonal Protein Chemistry in Living Cells. **Chemical Society Reviews**, v. 43, n. 18, p. 6511–6526, 2014. Disponível em: <<http://www.ncbi.nlm.nih.gov/pubmed/24867400>>.

YEON, L. S. et al. A novel liposomal nanomedicine for nitric oxide delivery and breast cancer treatment. **Bio-Medical Materials and Engineering**, n. 1, p. 61–67, 2014.

YOO, J.; FUKUTO, J. M. Oxidation of N-Hydroxyguanidine by Nitric Oxide and the Possible Generation of Vasoactive Species. **Biochemical Pharmacology**, v. 50, n. 12, p. 1995–2000, dez. 1995.

YOUSIF, E. et al. Metal Complexes of Schiff Base: Preparation, Characterization and Antibacterial Activity. **Arabian Journal of Chemistry**, v. 10, p. S1639–S1644, maio 2017.

ZACHARIA, I. G.; DEEN, W. M. Diffusivity and Solubility of Nitric Oxide in Water and Saline. **Annals of Biomedical Engineering**, v. 33, n. 2, p. 214–222, fev. 2005.

ZANICHELLI, P.G. et al. The Effects of Ruthenium Tetraammine Compounds on Vascular Smooth Muscle. **Nitric Oxide**, v. 16, n. 2, p. 189–196, mar. 2007.

ZENG, L. et al. The Development of Anticancer Ruthenium(II) Complexes: From Single Molecule Compounds to Nanomaterials. **Chemical Society Reviews**, v. 46, n. 19, p. 5771–5804, 2017.

ZOUBI, W. A. Biological Activities of Schiff Bases and Their Complexes: A Review of Recent Works. **International Journal of Organic Chemistry**, v. 03, n. 03, p. 73–95, 2013.