What I learned at UWI, Mona Campus; then applied with cobalt- and vanadium-containing compounds

Thursday, October 14, 2021

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Norfolk
VA 23529
U.S.A.

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Acknowledgements

YOU ALL!!!
THANK YOU!!

The Department of Defense

US Army Corps of Engineers®

Old Dominion University

Prof. Peter Bernath

Prof. Chris Platsoucas

Prof. John Cooper

Prof. Craig Bayse

Profs. Stephen Beebe and Floyd Beckford

Dr. Jennie Williams

Prof. Yuk-Ching Tse-Dinh

Prof. Harry B. Gray

Our logo: When we do "**GOOD**" chemistry, we do "**IRIE**" chemistry!

My motto: *Possunt quia posse videntur*, The Lodge School, Barbados

Overview

- Background and more
- Anti-cancer studies
- Notes

A Map of the Caribbean

The Inspiration Behind My Research

My Journey in Years

1985-1989, B.Sc.
1990-1994, Ph.D.
Kinetics, Co, Mo

1994-2003

THE UNIVERSITY OF TOLEDO
1872

2001-2002

Virginia Tech

2002-2003, postdoc
Ru, Pt, DNA, cells

U.W.I.

OHIO STATE

2003-2004, postdoc
ITC
carbohydrates

V
EPR
^{51}V NMR

Colorado State University

2004-2006, postdoc

THE UNIVERSITY OF SOUTHERN MISSISSIPPI

2006-2013

OLD DOMINION UNIVERSITY

2013-present

- Assistant Professor in Chemistry at The University of Southern Mississippi (USM) from August 21, 2006 until August 12, 2013
- A faculty member at the University of the West Indies (U.W.I.), Cave Hill Campus, Barbados from 1994-2003
- Postdoctoral fellow at ExxonMobil Research and Engineering Company, Virginia Tech, The Ohio State University, and Colorado State University.
- Published more than 85 articles, and several textbooks and book chapters
- Directed two postdoctoral fellows, and directed six graduate students at USM and U.W.I.
- Current research revolves around transition metal chemistry, which is (and has been) funded by the NSF, The Department of the Army, MS INBRE, ACS, ExxonMobil, the RSC, and USM
- An editorial advisory board member for the journal Recent Patents on Nanotechnology, and is on the editorial board of the E-Journal of Chemistry at Hindawi Publishing Corporation
- Co-organized the 5th International Symposium on the Chemistry and Biological Chemistry of Vanadium, 232nd Meeting of the American Chemical Society, September 10-14, 2006, San Francisco, California, U.S.A., and was a member of the National Organising Committee for the 8th International Symposium on the Chemistry, Biochemistry, and Toxicology of Vanadium, August 15-18, 2012, Washington, DC, U.S.A.
- Served as Chair (2009-2011), still a judge for the Chemical Sciences Division of the Annual Biochemical Research and Conference for Minority Students (ABRCMS)
- Awarded an NSF Career Award, entitled “CAREER: Ruthenium(II)-cobalt(II)/cobalt(III) mixed-metal complexes for photocatalytic hydrogen production from water”.

HONORS and AWARDS

06/09/2017: University of North Texas Health Science Center, Texas Center for Health Disparities Research Pilot Award, Steps Toward Academic Research (STAR) Fellowship Program.

04/26/2016: 2015-2016 College of Sciences Early Career Distinguished Research Award.

04/24/2015: A fellowship to participate in the 2015 STAR Fellowship Program on behalf of the Training and Education Core of the University of North Texas Health Science Center's Center of Excellence on Health Disparities. The year-long program commenced on July 10, 2015.

04/09/2015: The President John R. Broderick's "A Champion of Diversity" award recipient for Spring 2015 at ODU.

01/19/2015: Awarded the status of Fellow of The Royal Society of Chemistry (FRSC) from The Royal Society of Chemistry.

SELECTED RESEARCH GRANTS

07/01/2021-06/30/2022: An internal Batten College of Engineering and Technology (BCET) Multidisciplinary Research Seed Grant (MRSG). Role: Co-PI. PI: Prof. Sandeep Kumar. **$25,000**.

05/01/2021-4/30/2026: National Institutes of Health. Title: Graduate Research Training Initiative for Student Enhancement (G-RISE) at ODU. Role: Co-PI. PI: Dr. Gymama Slaughter. **$1,591,304**, with an institutional support from ODU.

06/01/2020-5/31/2021: National Institutes of Health. A supplement. Title: Maximizing Access to Research Careers (MARC) Undergraduate Student Training in Academic Research Program at ODU. Role: PI. **$84,648**.

06/01/2018-5/31/2023: National Institutes of Health. Title: Maximizing Access to Research Careers (MARC) Undergraduate Student Training in Academic Research Program at ODU. Role: PI. $1,483,525, with an institutional support from ODU.

09/01/17-08/31/21: National Science Foundation. Title: REU Site: Undergraduate Research Opportunities in Chemistry for Community College Students at Old Dominion University. Role: Co-PI. PI: Prof Craig Bayse. **$314,954**.

09/01/12-08/31/19: National Science Foundation CAREER Award. Title: CAREER: Ruthenium(II)-cobalt(II)/cobalt(III) mixed-metal complexes for photocatalytic hydrogen production from water. PI. **$530,000**. Former grant number: CHE-1151832. Present grant number: CHE-1431172.

Selected Publications (from 86)

1. Ingram, Conrad W.; Kybakaya, Geoffrey; Bacsa, John; Mathis, Stephan; Holder, Alvin A.; Rambaran, Varma H.; Dennis, Brandon; Castaneda, Esmeralda "Complex three-dimensional lanthanide metal-organic frameworks with variable coordination spheres based on pyrazine-2,3,5,6-tetracarboxylate." *CrystEngComm* 2015, 17, 5377-5388.

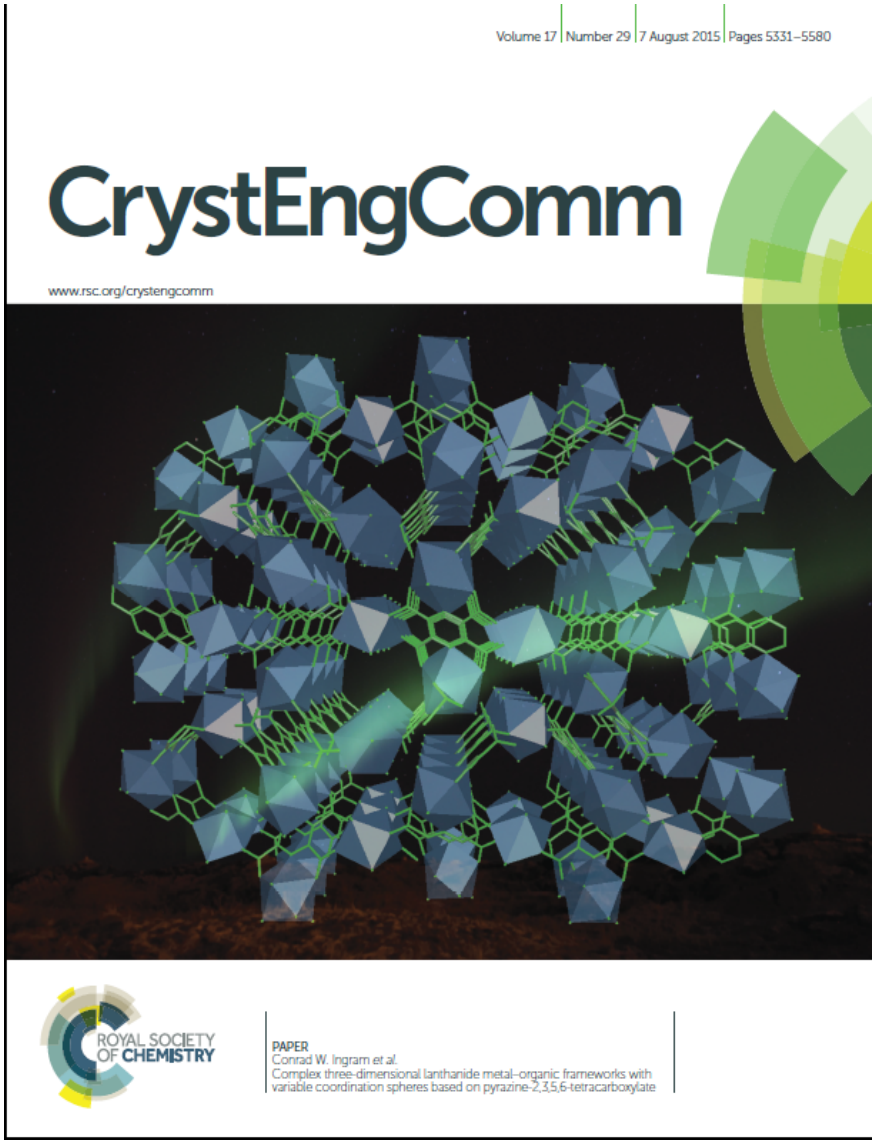
2. Lawrence, Mark A.W.; Holder, Alvin A. "Assessing the stability of the Co(I) species of two mononuclear dichlorocobalt(II) compounds bearing 2,2'-bipyridine and trans-2-(2'-quiolyl)methylene-3-quinuclidione ligands via ^{59}Co NMR spectroscopy, electrochemical, and catalyzed proton electroreduction studies." *Inorg. Chim. Acta* 2016, 441, 157-168.

3. Lawrence, Mark A.W.; Celestine, Michael J.; Artis, Edward T.; Joseph, Lorne S.; Esquivel, Deisy L.; Ledbetter, Abram J.; Cropek, Donald M.; Jarrett, William L.; Bayse, Craig A.; Brewer, Matthew I.; Holder, Alvin A. "Computational, Electrochemical, and Spectroscopic Studies of two Mononuclear Cobaloximes: The influence of an axial pyridine and solvent on the redox behaviour and evidence for pyridine coordination to cobalt(I) and cobalt(II) metal centres." *Dalton Trans.* 2016, 45, 10326-10342.

4. Smith, Chloe B.; Days, Lindsay C.; Alajroush, Duaa R.; Faye, Khadija; Khodour, Yara; Beebe, Stephen J.; Holder, Alvin A. "Photodynamic Therapy of Inorganic Complexes for the Treatment of Cancer." *Photochem. Photobiol.* **2021**, accepted for publication.

5. Holder, Alvin A. "Sustaining a legacy in STEM, the Prof. Tara Prasad Dasgupta way: The role of a mentor in our lives ." *Inorg. Chim. Acta* **2021**, 521, 120304. DOI: https://doi.org/10.1016/j.ica.2021.120304.

6. Celestine, Michael J.; Lawrence, Mark A.W.; Schott, Olivier; Picard, Vincent; Hanan, Garry S.; Marquez, Emily M.; Harold, Chekeyl G.; Kuester, Cole T.; Frenzel, Blaise A.; Hamaker, Christopher G.; Hightower, Sean E.; McMillen, Colin D.; Holder, Alvin A. "Synthesis, structure, and hydrogen evolution studies of a heteroleptic Co(III) complex." *Inorg. Chim. Acta* **2021**, 517, 120195. DOI: https://doi.org/10.1016/j.ica.2020.120195.



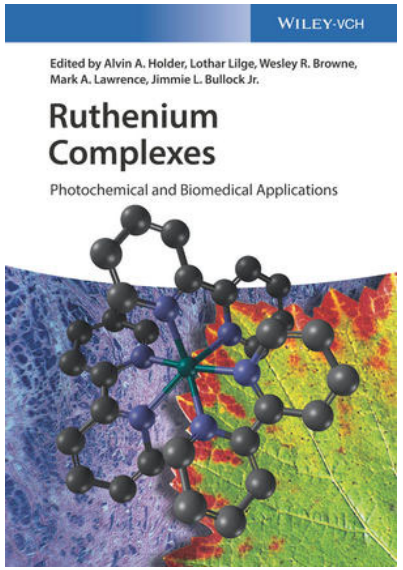
Ingram, Conrad W.; Kybakaya, Geoffrey; Bacsa, John; Mathis, Stephan; Holder, Alvin A.; Rambaran, Varma H.; Dennis, Brandon; Castaneda, Esmeralda "Complex three-dimensional lanthanide metal-organic frameworks with variable coordination spheres based on pyrazine-2,3,5,6-tetracarboxylate." *CrystEngComm* 2015, 17, 5377-5388.

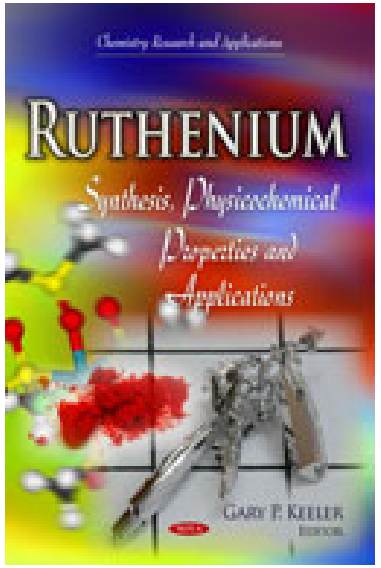
Some Chapters in Textbooks

Book title: "Ruthenium Complexes: Photochemical and Biomedical Applications." Editors: Alvin A. Holder, Wesley R. Browne, Lothar Lilge, Mark A.W. Lawrence, and Jimmie L. Bullock. Book chapter: "Coordination chemistry of ruthenium." Lawrence, Mark A.W.; Bullock, Jimmie L.; Holder, Alvin A. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA, **2018**.

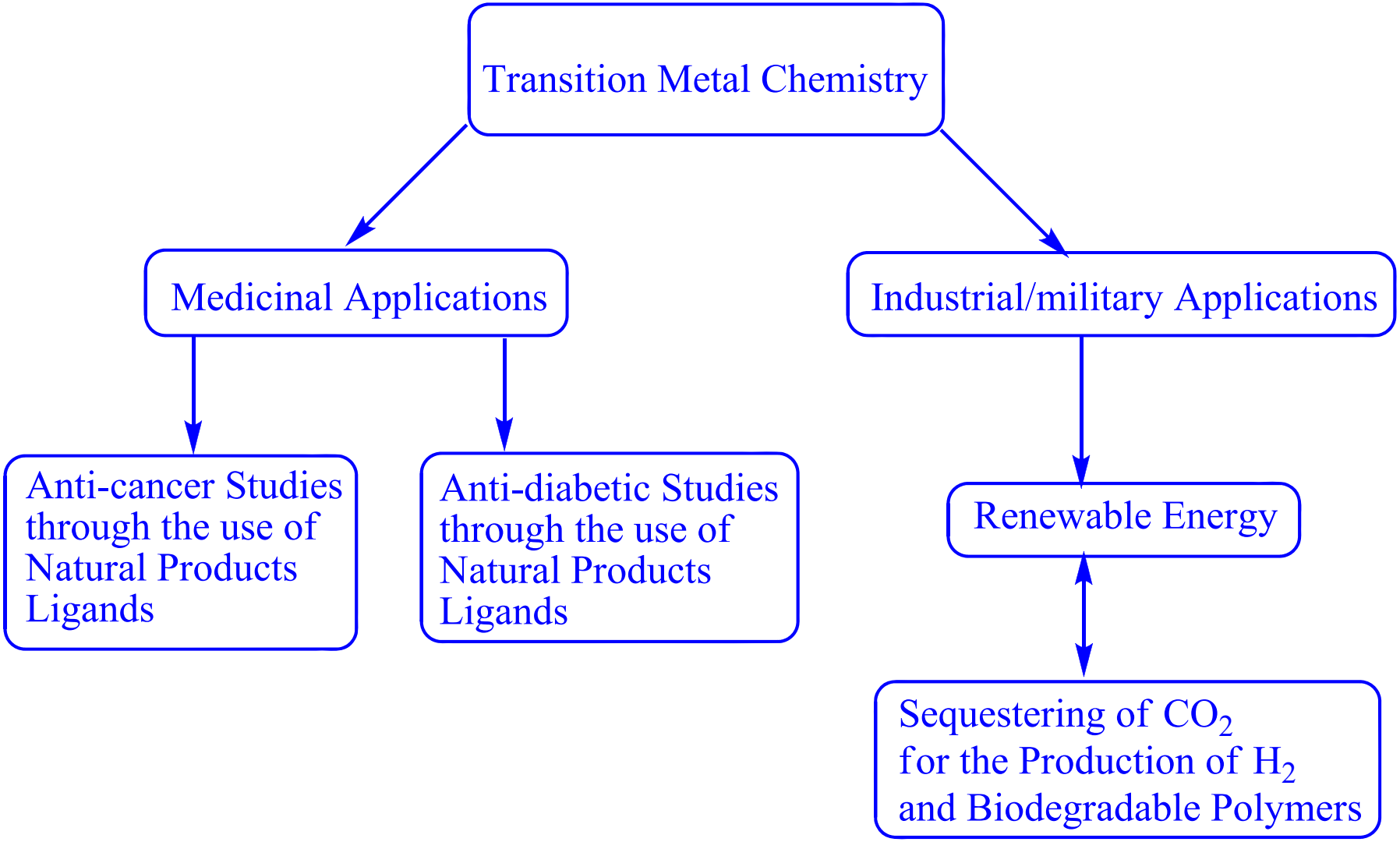
Book title: "Ruthenium Complexes; Photochemical and Biomedical Applications." Editors: Alvin A. Holder, Wesley R. Browne, Lothar Lilge, Mark A.W. Lawrence, and Jimmie L. Bullock. Book chapter: "Photodynamic therapy in medicine with mixed-metal/supramolecular complexes." Bullock, Jimmie L.; Holder, Alvin A. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA, **2018**.

Book title: "Ruthenium Complexes: Photochemical and Biomedical Applications." Editors: Alvin A. Holder, Wesley R. Browne, Lothar Lilge, Mark A.W. Lawrence, and Jimmie L. Bullock. Book chapter: "Ruthenium-containing complexes with cobalt and hydrogenases for hydrogen production." Celestine, Michael J.; Gurung, Raj K.; Bullock, Jimmie L.; Holder, Alvin A. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA, **2018**.





My Interdisciplinary Research



Previous Research at USM

- Design and develop water soluble super molecules as PDT agents
- Test each super molecule via *in vitro* studies with DNA and non-cancerous and cancer cells; *in vivo* studies shortly
- Anti-diabetic and artificial photosynthetic studies
- Training of researchers (an example with Faye)

Current and Past Graduate Students

Graduate Dissertations

Barbados and Jamaica: The University of the West Indies (UWI)

10/03: Sophia C. Marshall, Ph.D. (Inorganic Chemistry), U.W.I., Cave Hill Campus, Barbados.

11/07: Gabriel Harewood, Ph.D. (Inorganic Chemistry), U.W.I., Mona Campus, Jamaica.

12/07: Ross F.G. Brown, M.Phil. (Inorganic Chemistry), U.W.I., Mona Campus, Jamaica.

06/08: Vince C.R. Payne, Ph.D. (Inorganic Chemistry), U.W.I., Cave Hill Campus, Barbados.

U.S.A.: The University of Southern Mississippi (USM)

12/09: LaMaryet V. Moody, M.S. (Inorganic Chemistry), USM

12/11: Nerissa A. Lewis, M.S. (Inorganic Chemistry), USM

Current and Past Graduate Students

Graduate Dissertations

U.S.A.: Old Dominion University (ODU)

Click here

Click here

10/13-05/16: Mr. Jimmie Bullock (Virginia), M.S. (Inorganic Chemistry), ODU

08/13-12/20: Dr. Michael Celestine (Inorganic Chemistry) (St. Thomas, U.S. Virgin Islands)

09/14-12/20: Dr. Raj Gurung (Nepal)

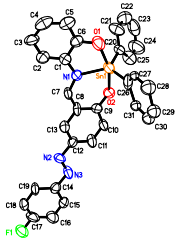
01/19-present: Ms. Elizabeth Tonsel-White (U.S.A.)

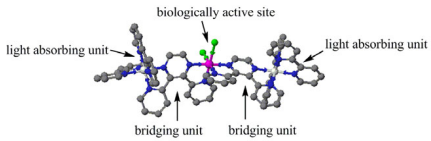
01/19-present: Ms. Criszcele Tano (U.S.A.)

01/20-present: Mrs. Duaa Alajroush (Saudi Arabia)

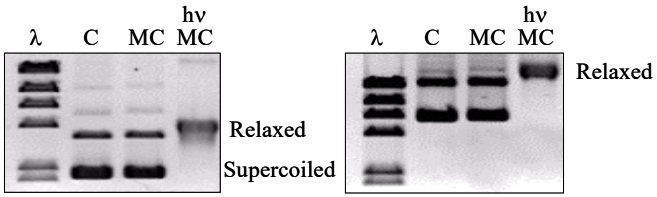
Dr. Alvin A. Holder

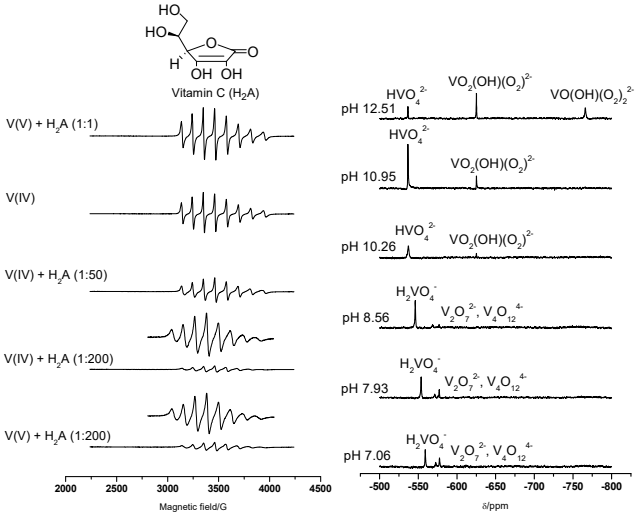
Synthesis, Characterization, and Bioinorganic Chemistry of Novel Transition Metal Complexes.





$[\{(bpy)_2Ru(dpp)\}_2RhCl_2]^{5+}$





EPR and ^{51}V NMR spectra

Insulin-like vanadium complexes: Design of novel vanadium(III/IV/V)-containing complexes. Physiological testing on STZ-induced diabetic rats.

Anti-cancer agents: Design of new transition metal complexes (Co, Cu, Mo, Os, Pd, Pt, Ru, V, Sn, and W) for DNA photocleavage and inhibition of cancer cell growth.

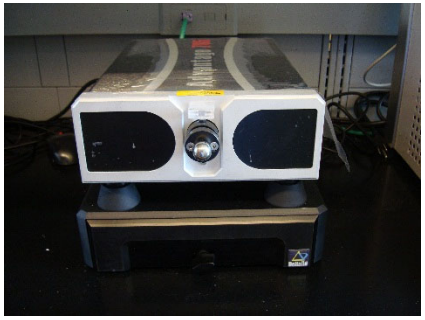
Photocatalysts: For production of H_2 from water.

Metallomesogens: Design and synthesis of metallomesogens for CO_2 sequestering and production of biodegradable polymers.

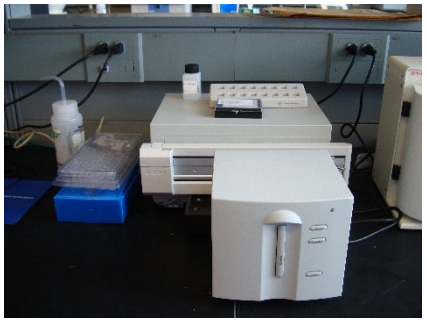
Physical characterization of various transition metal complexes: Use of X-ray crystallography, HF EPR, EPR, NMR (^{1}H, ^{11}B, ^{13}C, ^{15}N, ^{19}F, ^{31}P, ^{49}Ti ^{51}V, ^{59}Co, ^{95}Mo, ^{119}Sn, and ^{195}Pt), and fluorescence spectroscopies, and electrochemical studies.

Collaborative research in various countries: The Caribbean, Japan, South Korea, U.K., and the U.S.A.

Equipment in my laboratory



A Raman spectrometer



Agilent spectrophotometer

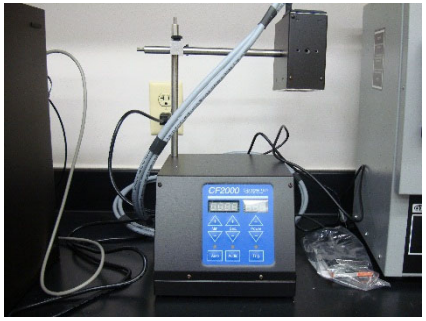
Electrochemical Apparatus

A GC

A Paar hydrogenator

An ITC

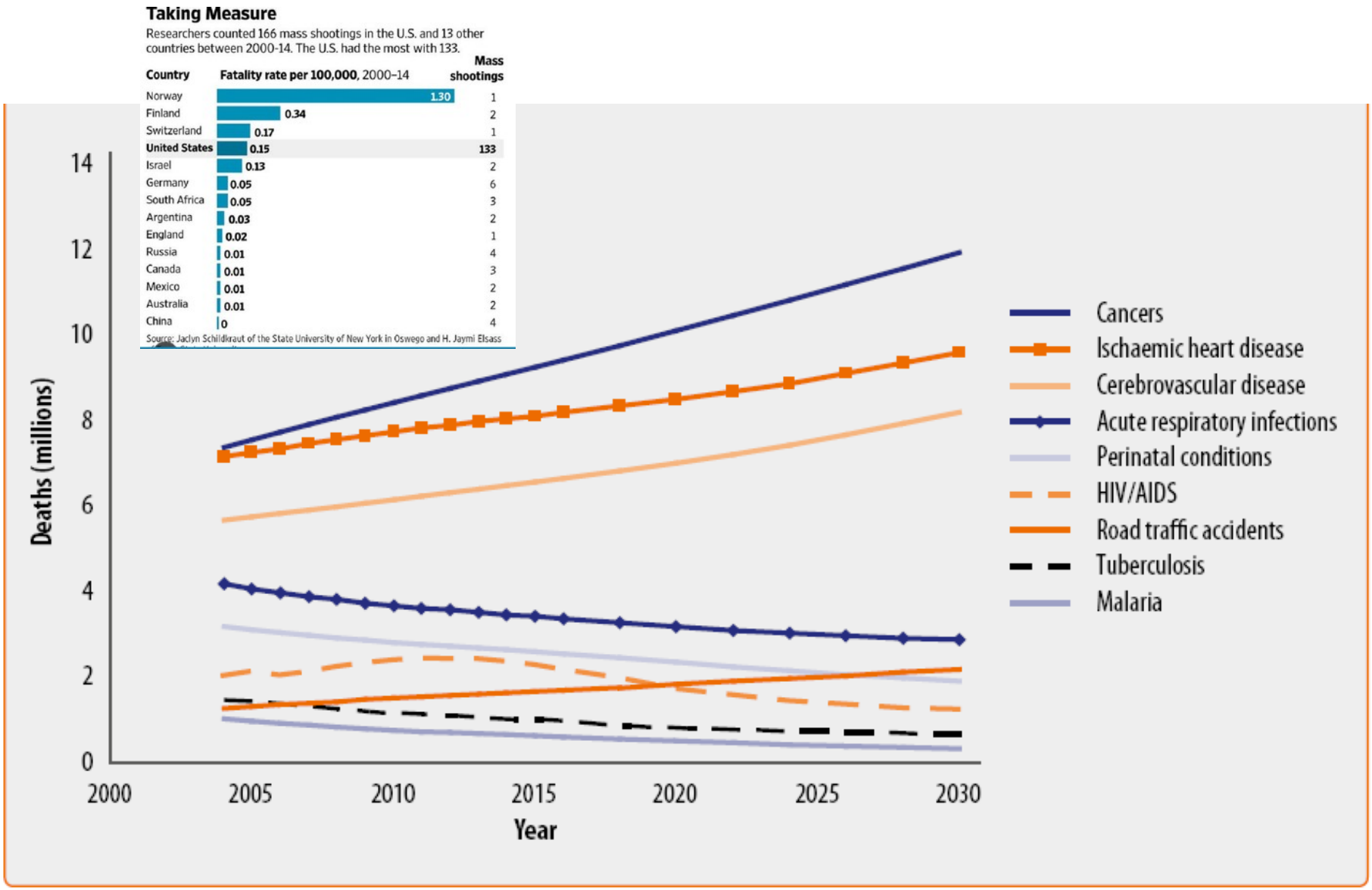
A glove box



A 740 nm irradiation system

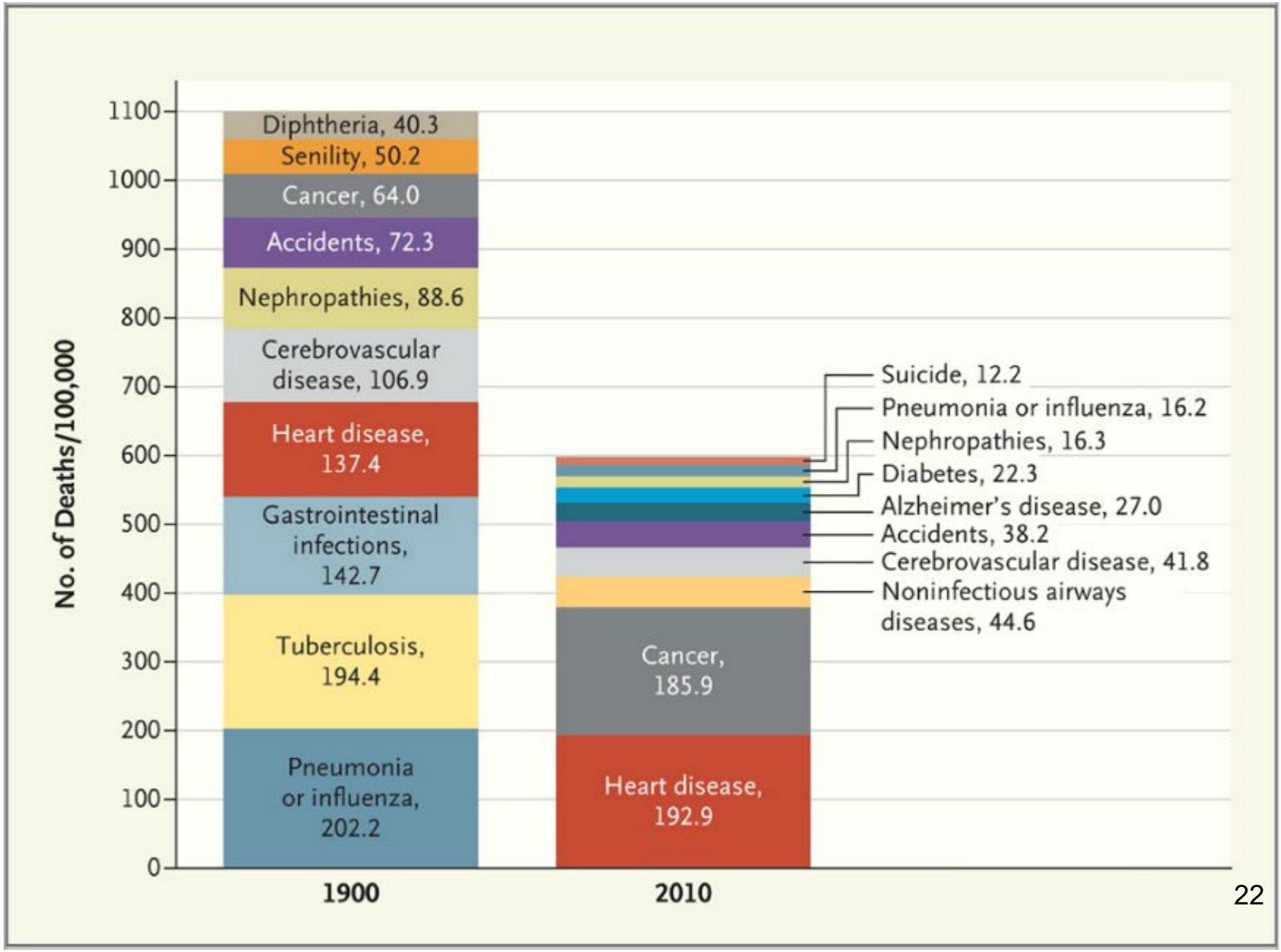
A stopped-flow spectrophotometer

Projected Global Deaths for Selected Causes, 2004-2030

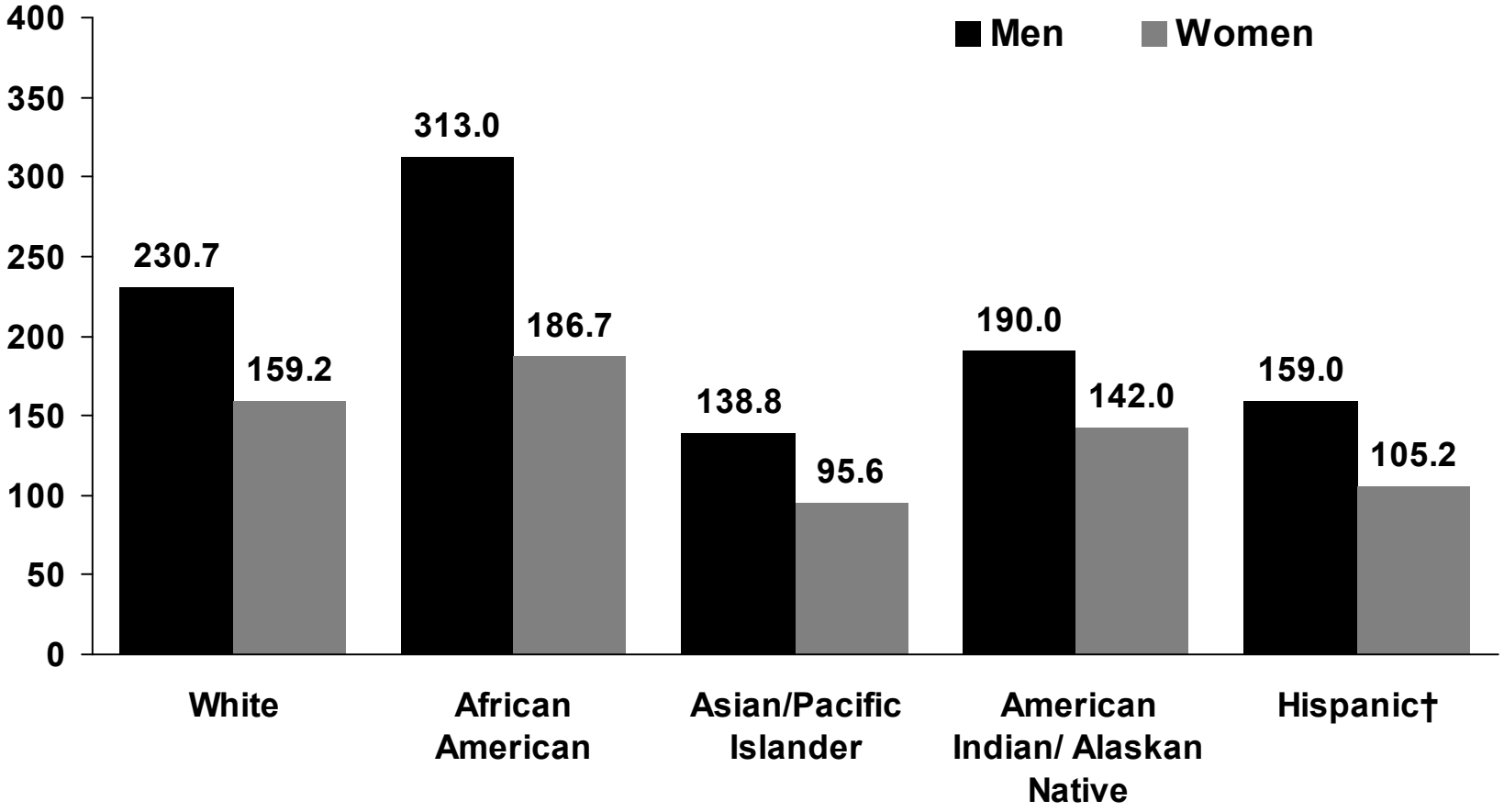


The global burden of disease. 2004 Update. WHO (World health Organization)
http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf

Top 10 Causes of Diseases



Cancer Death Rates* by Race and Ethnicity, US, 2001-2005



*Per 100,000, age-adjusted to the 2000 US standard population.

† Persons of Hispanic origin may be of any race.

Source: Surveillance, Epidemiology, and End Results Program, 1975-2005, Division of Cancer Control and Population Sciences, National Cancer Institute, 2008.

Cancer in Barbados

There were 1,144 new cancer cases diagnosed in Barbados in 2015, with prostate, breast, colorectal, corpus uteri, and stomach being the most common types. It is predicted that in the year 2035, there will be 1,657 new cancer cases and 858 cancer-related deaths.

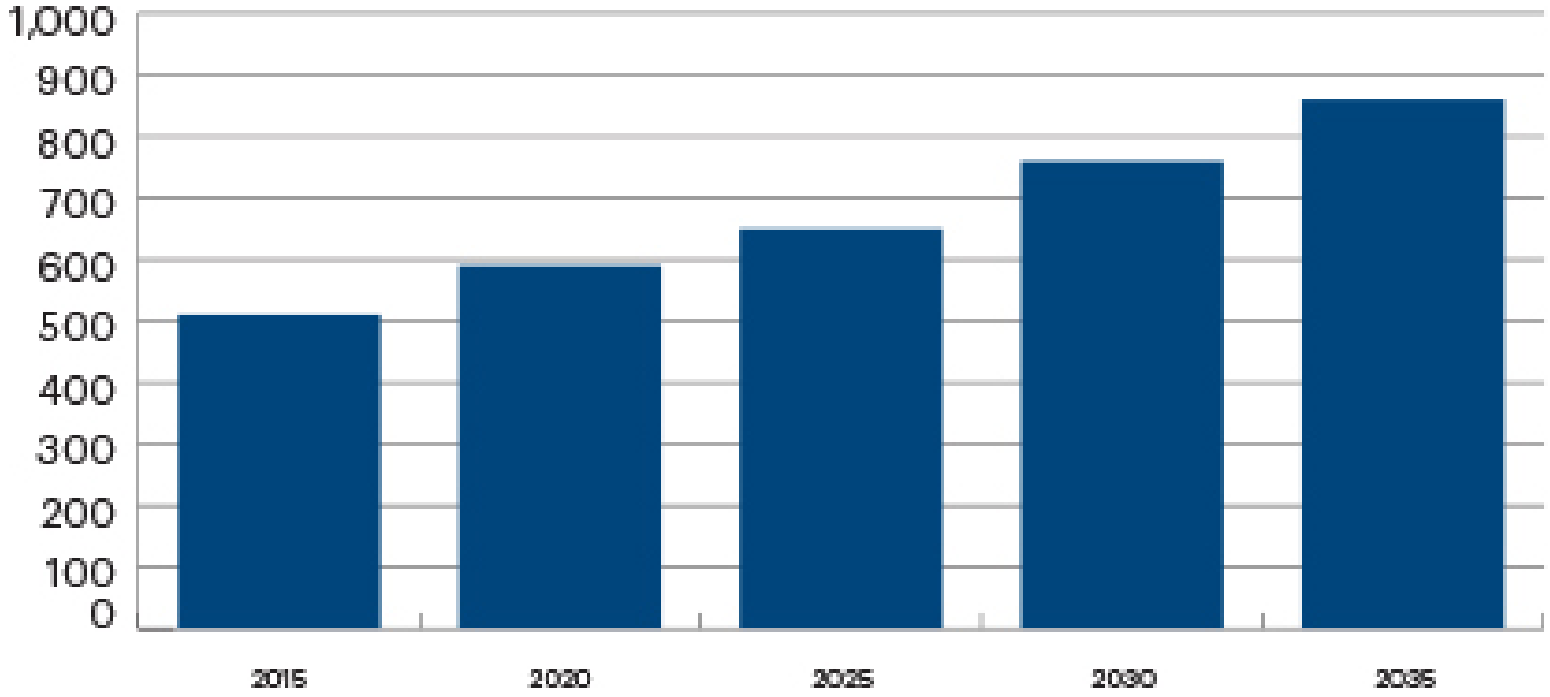
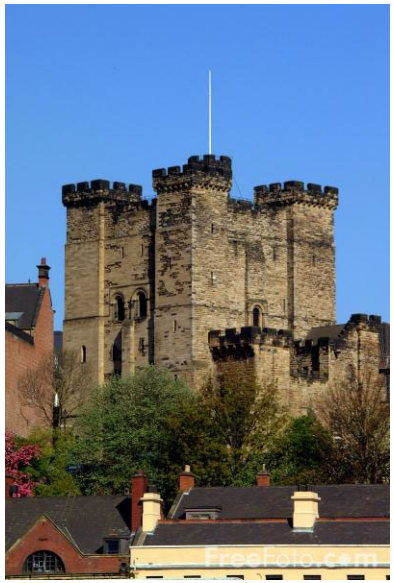


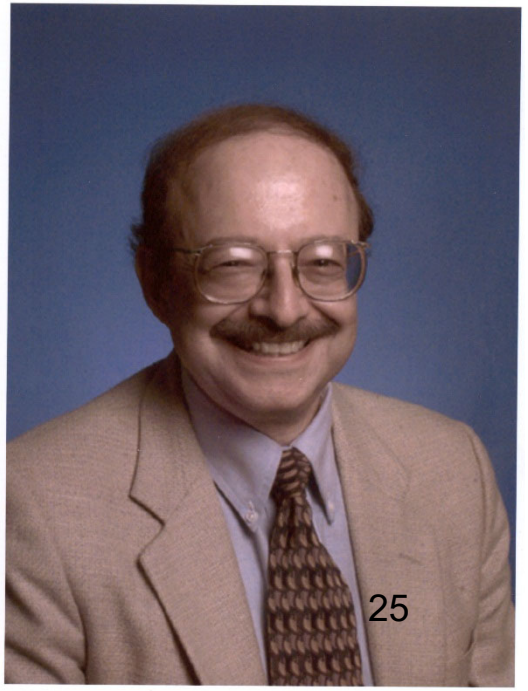
Figure 1.Trends in cancer-related mortality in Barbados: 2015-2035.

https://www.ascopost.com/issues/september-10-2018/cancer-on-the-global-stage-barbados/

UNIVERSITY OF
NEWCASTLE UPON TYNE

EXXON
Mobil





My Chemistry Teacher, Friends, and Prime Minister

Possunt quia posse videntur, The Lodge School, Barbados

The Latin quote by the Roman poet Virgil is the school's motto chosen by Mr. Emtage, is also the school motto for Christ College, Brecon, Wales (founded by Royal Charter in 1541 by King Henry VIII) as well as for The Harvard-Westlake School in Los Angeles California.

- Mr. Cornelius O'Shea, February 2006
- **Dr. Edward I. Stiefel September 04, 2006**
- Prof. A. Geoffrey Sykes, July 10, 2007
- Mr. Errol Barrow
- Mr. George Jones, 2010 diagnosis
- Mr. David Thompson, MP, Saturday, October 23, 2010 at about 2:10 a.m., age 48
- Prof. Malcolm Chisholm, Friday, November 13, 2015

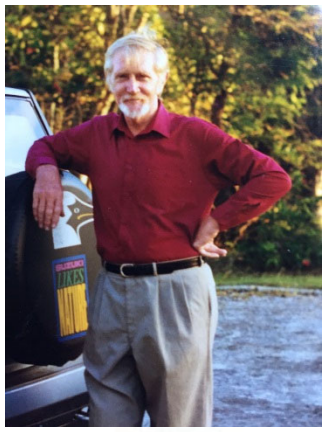
http://cropoverbarbados.com/george-back-brink-and-making-difference-0

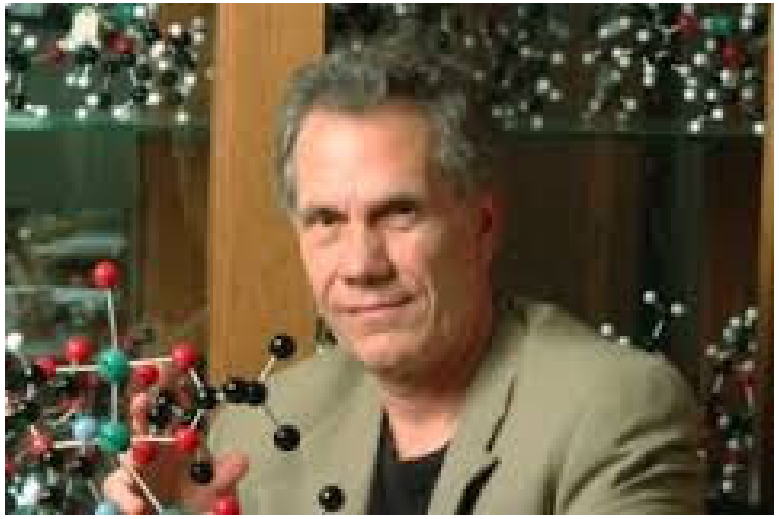
https://www.princeton.edu/morel/publications/pdfs/morelSCIENCE2006.pdf

http://www.redorbit.com/news/science/1073974/professor_geoff_sykes_pioneer_of_bioinorganic_chemistry/

https://barbadosfreepress.wordpress.com/2010/10/23/barbados-prime-minister-david-thompson-dead-of-cancer-at-48/

My Friends, Mentors, and Former Prime Minister





Chadwick Boseman

- Chadwick Boseman, Marvel's Black Panther, dies after **cancer battle** at age 43 (Friday, August 28, 2020).

- Calling him “a true fighter,” Boseman’s family revealed the actor was diagnosed with colon cancer four years ago. He never made his diagnosis public, even after photos of the gaunt-looking actor appeared on social media.

- https://www.yahoo.com/entertainment/chadwick-boseman-marvel-black-panther-dies-colon-cancer-024040826.html

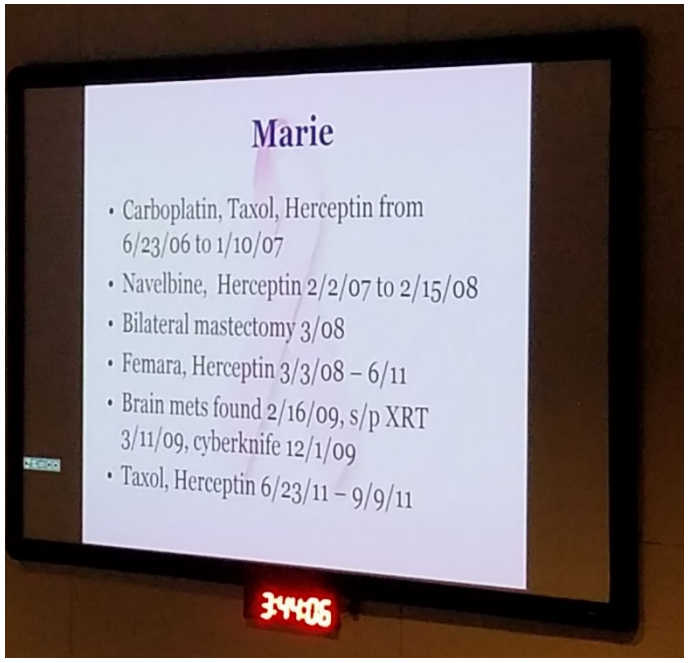
12th Annual Conference on Health Disparities, Evidence-Based Approaches to Reducing Cancer Health Disparities: Discover, Develop, Deliver, & Disseminate, June 8-9, 2017, University of North Texas Health Science Center, Fort Worth, Texas

Some photos from the presentation entitled “Clinical perspectives in breast cancer” by Robyn R. Young, M.D., Center for Cancer and Blood disorders, Fort Worth, Texas

https://thecentertx.com/physician/robyn-r-young/

You may find the following slide to be very gross, but this is a health disparity among African American women, viz., triple negative breast cancer (TNBC)

A Case Study


Marie
• Carboplatin, Taxol, Herceptin from 6/23/06 to 1/10/07
• Navelbine, Herceptin 2/2/07 to 2/15/08
• Bilateral mastectomy 3/08
• Femara, Herceptin 3/3/08 – 6/11
• Brain mets found 2/16/09, s/p XRT 3/11/09, cyberknife 12/1/09
• Taxol, Herceptin 6/23/11 – 9/9/11

With Jo (Administrative Assistant, Chemistry Department, University of York, U.K.), a Breast Cancer Survivor (Monday, July 10, 2017)

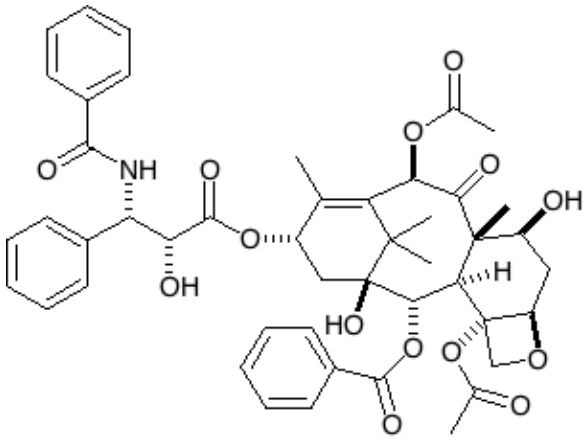
What I Tell My Friends

https://www.instagram.com/p/CEhq9hsA5Gi/?igshid=kryzho4otu8e

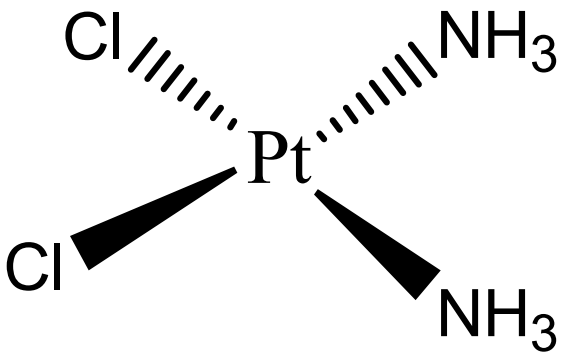
Treatment of Cancer

1. Chemotherapy
2. Radiation therapy
3. Surgery
4. Other methods: hormonal therapy, herbal supplements, aromatherapy, exercise routines, and massage

Aromatherapy



Taxol



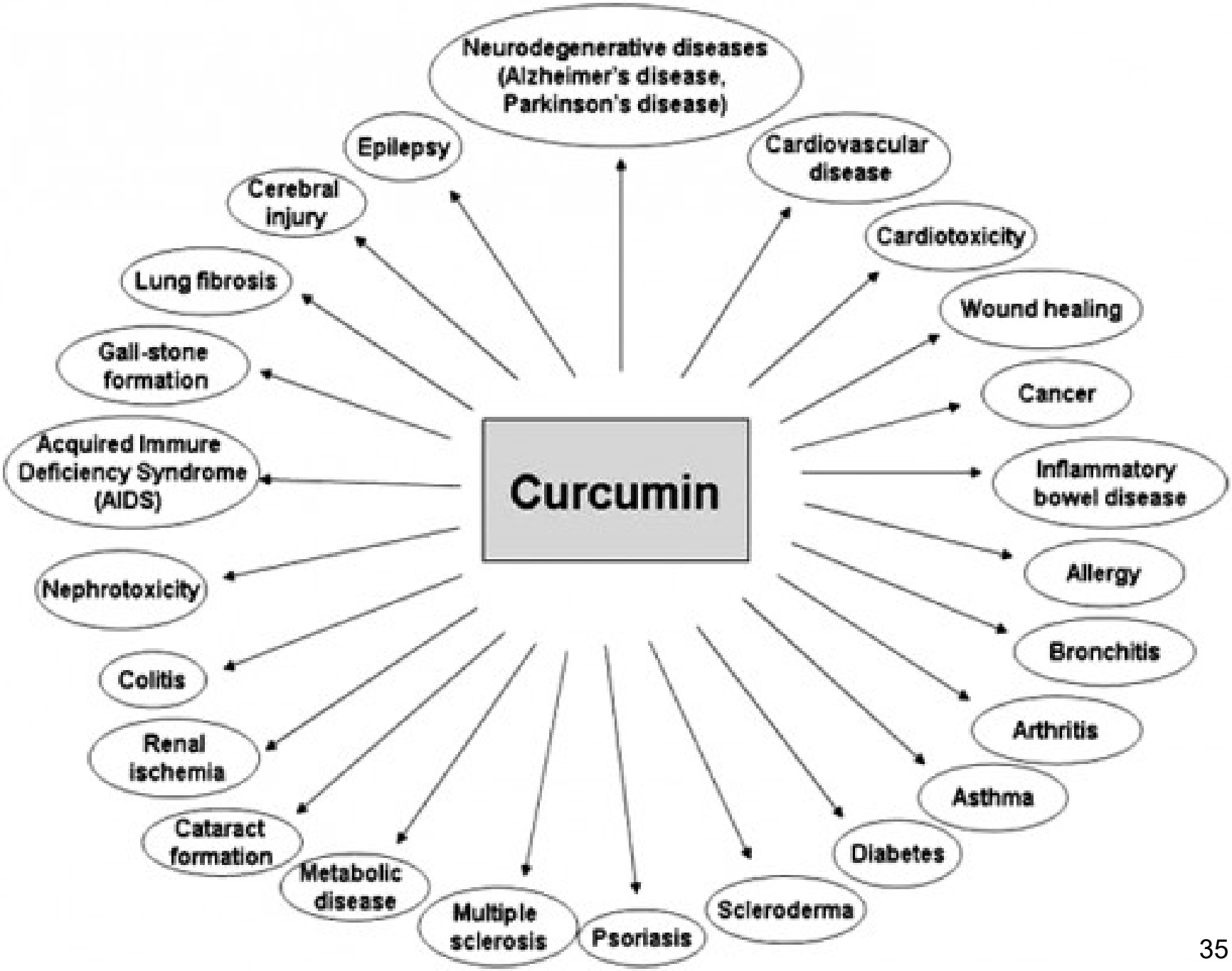
Cisplatin

http://www.knowcancer.com/cancer-treatment/

Tumeric and Its Benefits

Benefits of Turmeric

- Natural antiinflammatory
- Natural antibiotic
- Natural antiseptic
- Natural analgesic
- Speeds up wound healing
- Improves digestion
- Blood purifier
- Helps prevent gas/bloating
- Lowers cholesterol
- Heals stomach ulcers
- Improves skin conditions (psoriasis, eczema, etc)
- Helps prevent cancer (breast, prostate, skin, colon, lymphoma, leukemia)


Curcumin
Neurodegenerative diseases (Alzheimer's disease, Parkinson's disease)
Epilepsy
Cerebral injury
Lung fibrosis
Gall-stone formation
Acquired Immure Deficiency Syndrome (AIDS)
Nephrotoxicity
Colitis
Renal ischemia
Cataract formation
Metabolic disease
Multiple sclerosis
Psoriasis
Scleroderma
Diabetes
Asthma
Arthritis
Bronchitis
Allergy
Inflammatory bowel disease
Cancer
Wound healing
Cardiotoxicity
Cardiovascular disease

Useful Elements

Bioinorganic Chemistry: Inorganic Elements in the Chemistry of Life: An Introduction and Guide
by Wolfgang Kaim, Brigitte Schwederski, and Axel Klein

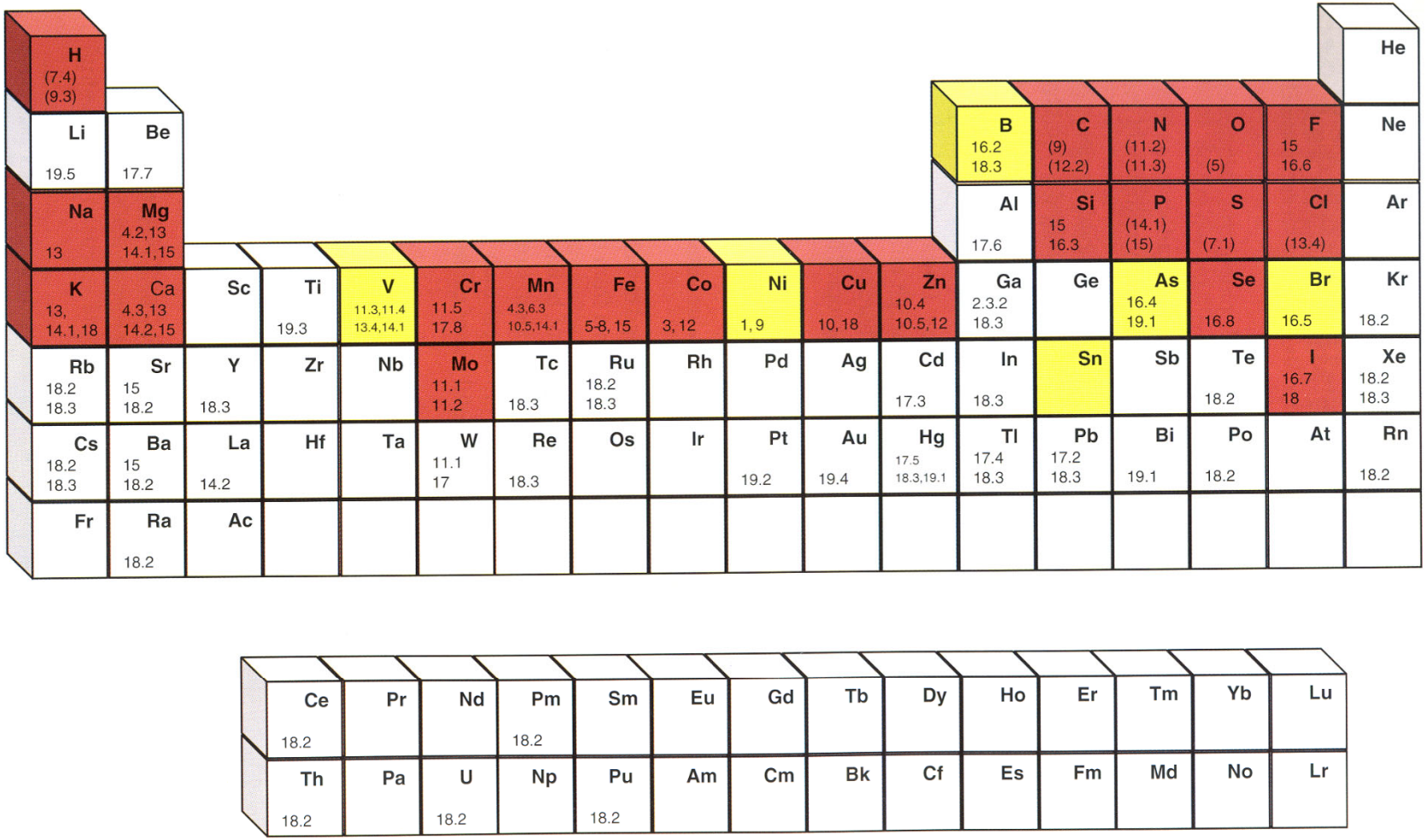


Figure 1.4

Periodic table of the elements. Indicated are the chapters and sections in which each element is discussed in this book. essential element; presumably essential element for human beings.

Medicinal Inorganic Chemistry

3000 BC : Egyptians used **Cu** to sterilize water

2500 BC : Chinese empire uses **Au** in a variety of medicine

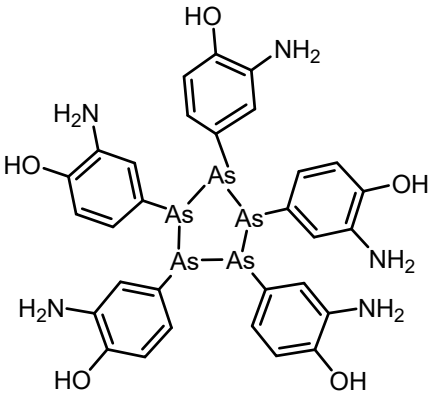
400 BC : Hippocrates used **Hg**

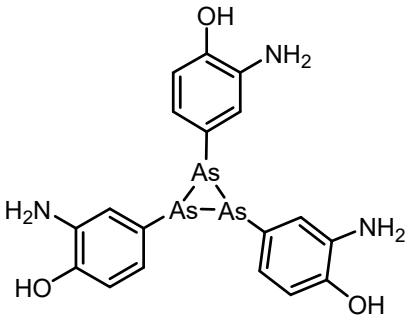
1600s : Paracelsus pioneered the use of minerals in medicine using **Sb, As,** and **Mg** salts

Early 1900s: Metals started making an impact on modern medicine

$K[Au(CN)_2]$ used for tuberculosis

Salvarsan for the treatment of syphilis (Henry VIII comes to mind)

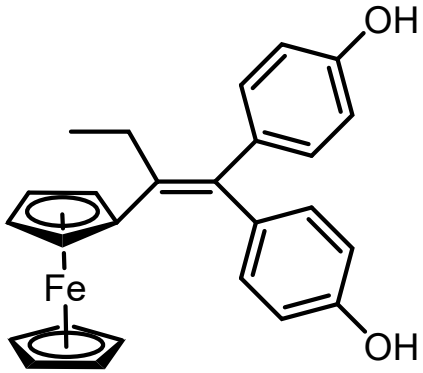


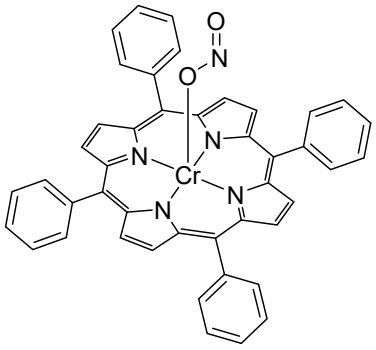


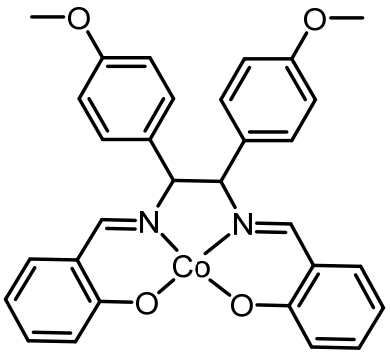
Jaouen, G. *Bioorganometallics*, **2006,** 1st ed., pp. 1-32

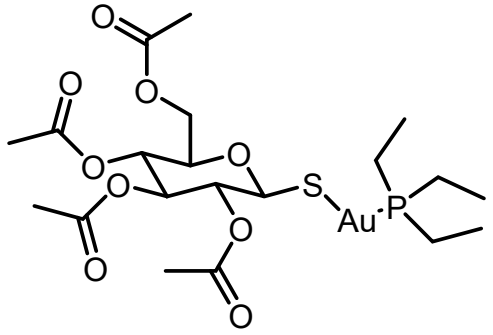
Orvig, C.; Abrams, M.J. *Chem. Rev.* **1999**, *99*, 2201

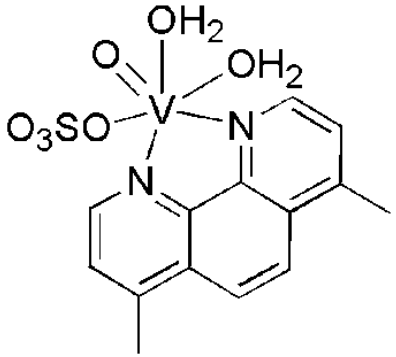
Alternatives to Platinum-based Complexes

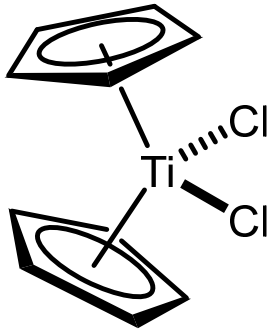


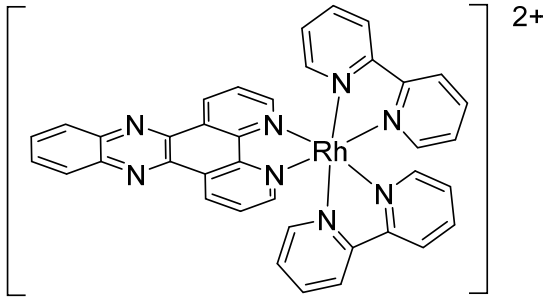


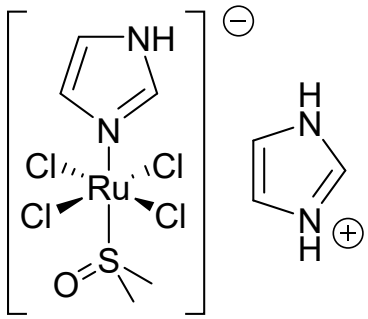




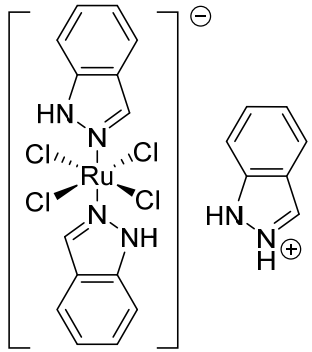






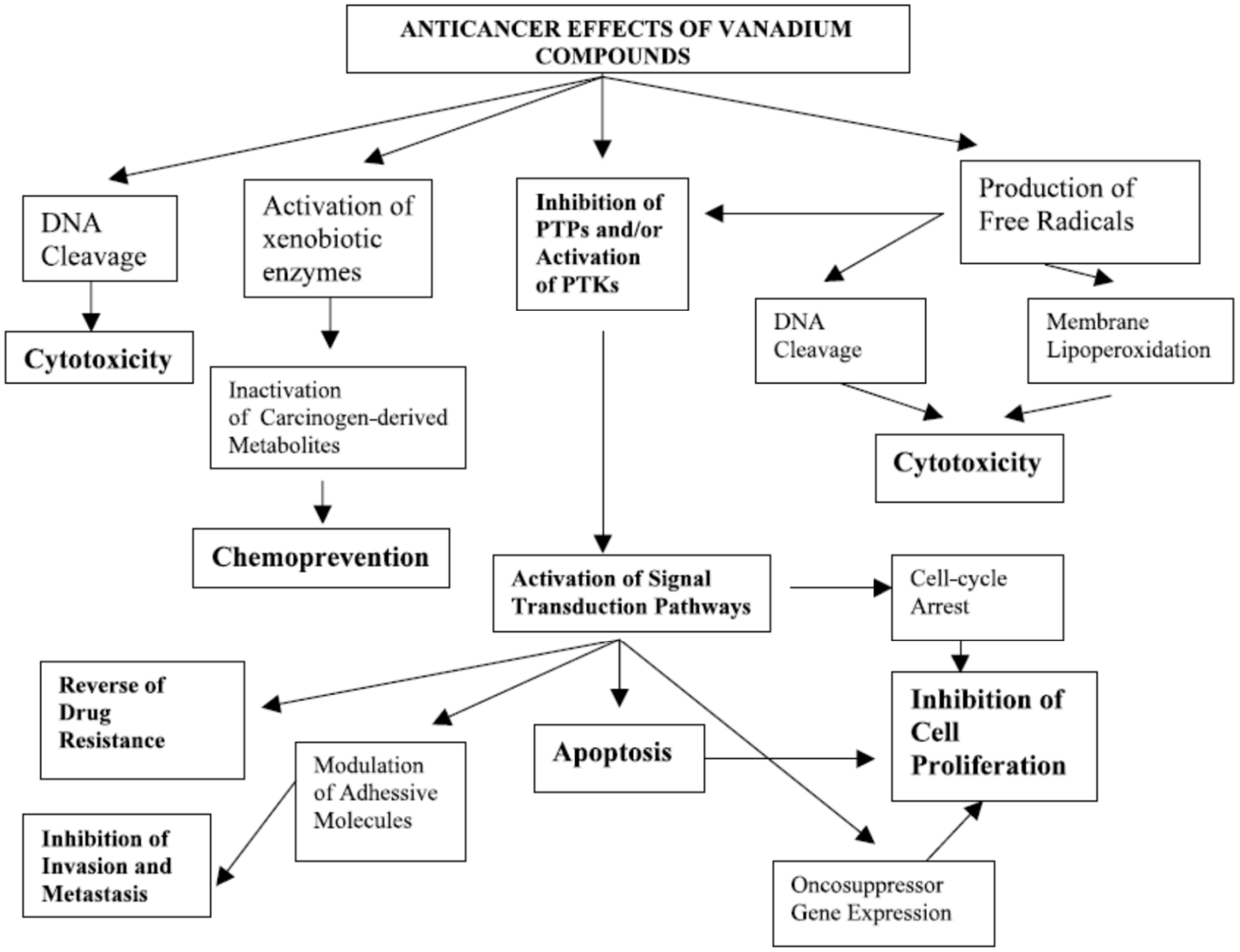


NAMI A



KP1019

Vanadium to Kill Cancer



Evangelou Angelos, M. *Crit. Rev. Oncol. Hematol.* **2002**, *42*, 249.

Vanadium History

“Vanadis”, the old Norse name for the Scandinavian Goddess, Freyja.

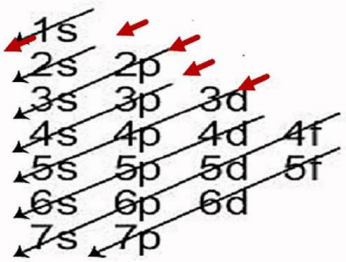
www.candlesandwicksmydeities.blogspot.com
Click here for the best reference

Vanadium

Electron Configuration Chart

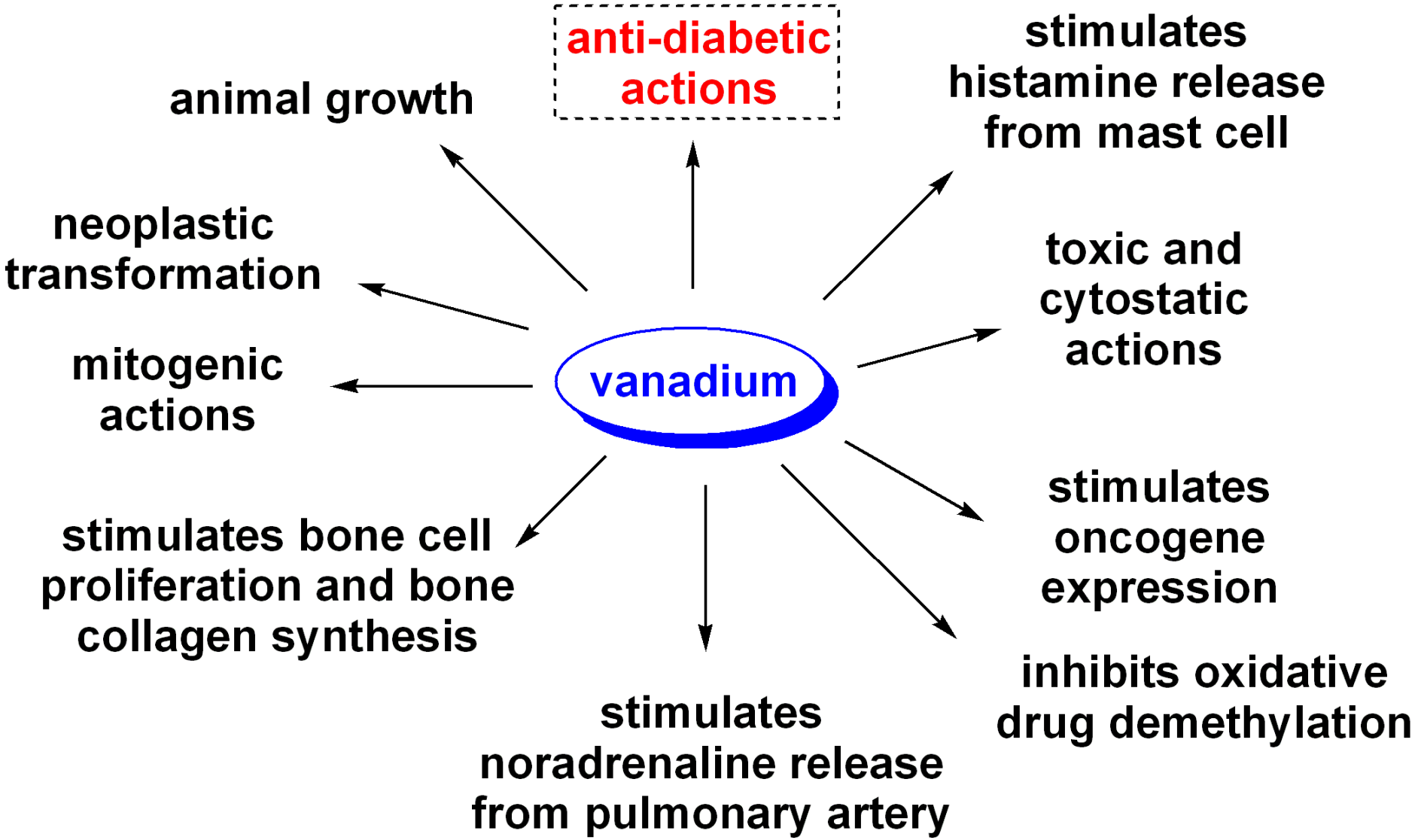
s holds up to **2** **p** holds up to **6** **d** holds up to **10**

23
V
Vanadium
50.94



$1s^2$

Physiological Roles of Vanadium



Lyonnet, B.M.; Martz-Martin, E. *La Presse Medicale* **1899**, *7*, 191

Barbados on Diabetes High

by George Alleyne

- With the alarming statistics that one in every five Barbadians is living with diabetes, this island holds the unwanted distinction of having a percentage of the affected population that is double the world's affliction rate.
- The pervasive nature of this non-communicable disease in Barbados is the state of affairs with which the country greeted **World Diabetes Day**, today.
- What is worse is that the rate at which people contract diabetes in Barbados has been on an upward trend over the years with no end in sight.

https://barbadostoday.bb/2018/11/16/barbados-on-diabetes-high/

https://www.loopnewsbarbados.com/content/men-talking-get-amputation-capital-dropped-barbados-profile

Chem. Rev. **1999,** *99,* 2561–2571

Vanadium Compounds as Insulin Mimics

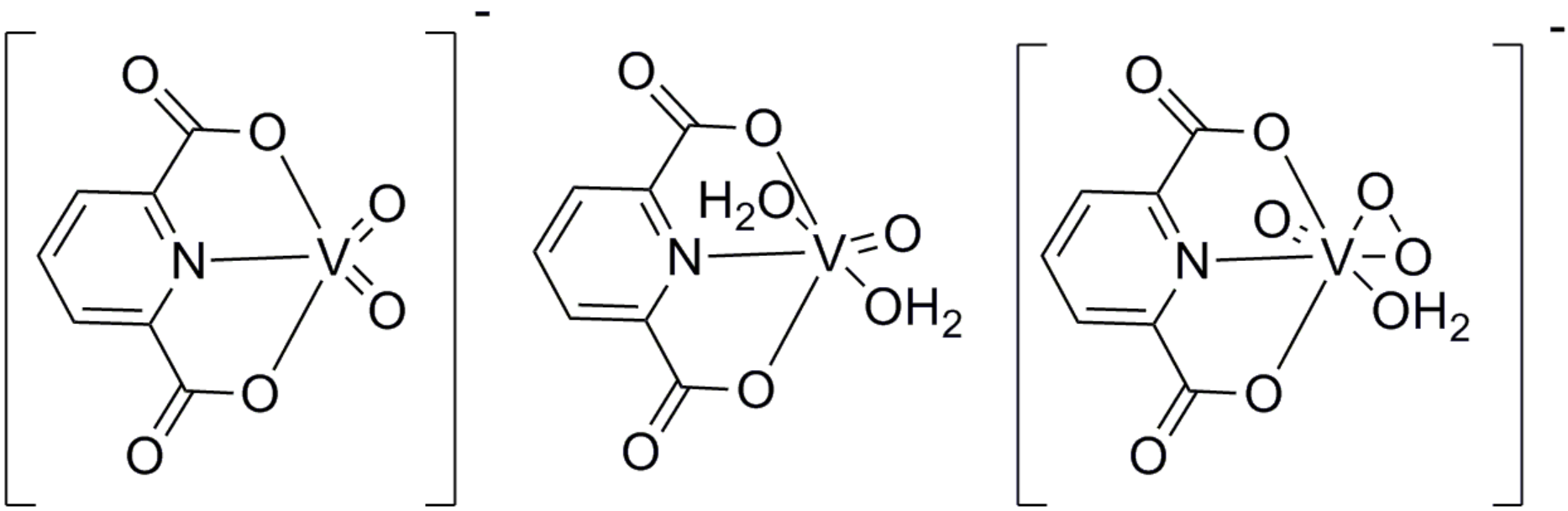
Katherine H. Thompson, John H. McNeill, and Chris Orvig*

Medicinal Inorganic Chemistry Group, Chemistry Department, and Faculty of Pharmaceutical Sciences, The University of British Columbia, Vancouver, British Columbia, Canada V6T 1Z1

- In the late 19th and early 20th centuries, before the 1922 discovery of insulin, French physicians found administering sodium metavanadate ($NaVO_3$) improved the health of patients with diabetes mellitus
- Vanadium, as vanadyl sulfate, is believed to regulate fasting blood sugar levels and improve receptor sensitivity to insulin.
- Based on available research, vanadyl sulfate appears to be a useful intervention for type 2 diabetic individuals with insulin resistance.
- Vanadyl sulfate has been reported to be 6-10 times less toxic than sodium metavanadate.

Lyonnet B, Martz X, Martin E. Therapeutic use of the derivatives of vanadium *La Presse Med.* **1899**,1, 191. [Article in French]

Anti-diabetic (Insulin-like) Complexes and Protein Phosphatases Inhibitors



V(V)
Insulin-like as well

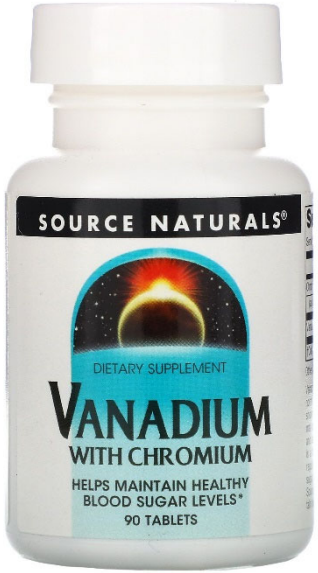
V(IV)
Insulin-like as well

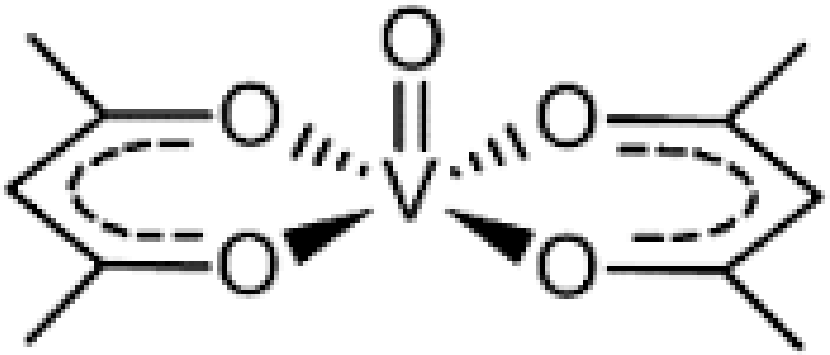
V(V)

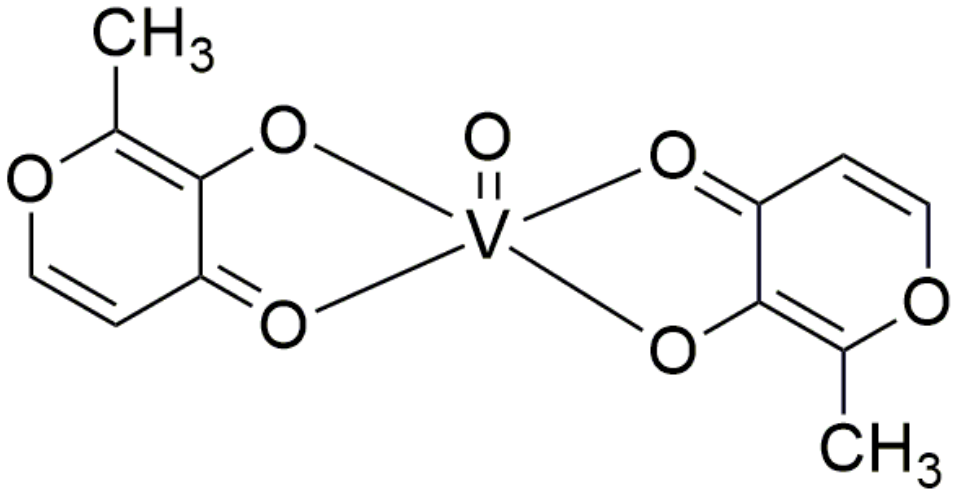
The Chemistry and Biochemistry of Vanadium and the Biological Activities Exerted by Vanadium Compounds

Crans, D.C.; Smee, J.J.; Gaidamauskas, E.; Yang, L. *Chem. Rev.* **2004**, 104, 2, 849-902.

Some Vanadium(IV) Insulin-like Species







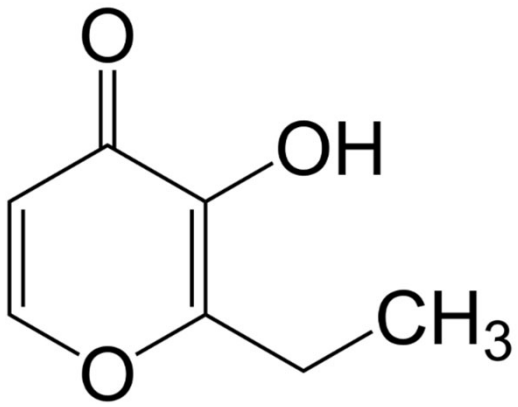
BMOV, $[VO(mal)_2]$

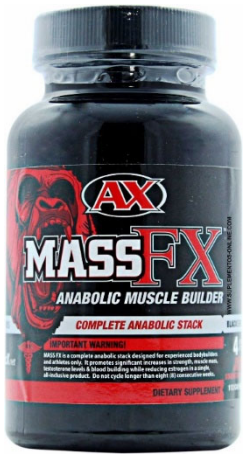
Crans, D.C.; Smee, J.J.; Gaidamauskas, E.; Yang, L. *Chem. Rev.* **2004**, 104, 2, 849-902.

Ethyl Maltol and BMOV

- Ethyl maltol is an ideal food additive with the characterics of safe and non-toxic, versatile, good effects, and rarely dosage.
- It is a good flavor and sweet synergist for food, beverages, meat products, flavors, and fruit wine.
- It has anti-bacterial, anti-corrosion performances to extend the food storage period.

- It is a white solid with a sweet smell that can be described as caramelized sugar and cooked fruit.





Supplement Facts

Serving Size: **1 Capsule** Servings Per Container: **112**

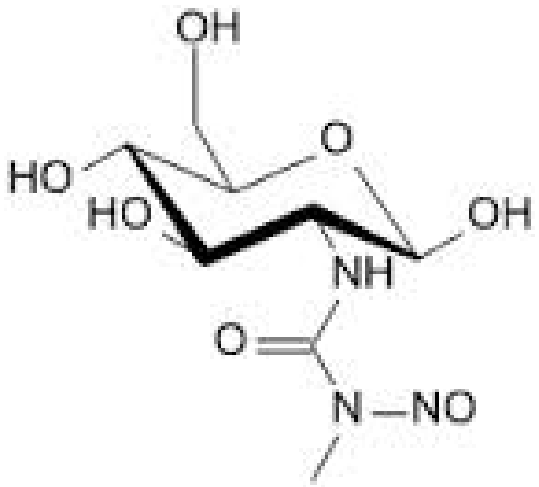
Ingredients	Amount Per Serving:	% DV*
Optimize Endocrine Function		
Zinc (as Zinc Amino Acid Chelate)	**12.5mg**	114%
Vitamin D3 (Cholecalciferol)	**1250iu**	208%
Boron (as Boron Glycinate)	**2.5mg**	**
Elevate Free Testosterone		
UDAX™ (Urtica SHGB Lignan Complex)	**500mg**	**
Control Estrogen		
7-MF (7-Methoxyflavone)	**37.5mg**	**
Increase Total Testosterone		
Methyl EAA™ (N-Methyl-aspartic acid)	**22.5mg**	**
Regulate Insulin and Blood Glucose		
Vanadium (as BMOV Bis-(Maltolato)oxovanadium[IV])	**2.5mg**	**
EPO Blood Building		
Cobalt (as Cobalt Amino Acid Chelate)	**3.75mg**	**
cAMP Inactivation Inhibitor		
Theobromine (Increases vasodilation and oxygen/nutrient flow to muscles)	**50mg**	**

*% Daily Value based on a 2,000 calorie diet. ** Percent of Daily Value Not Established

ATHLETIC XTREME MASS FX BLACK: To build big muscle - bigger than testosterone can build alone - you need to intensify the insulin response. That's why Mass FX contains BMOV. BMOV mimics insulin, improves insulin sensitivity, and intensifies the insulin response. And this helps load your muscles with the aminos and glycogen they need to grow as big as your testosterone is telling them to.

Streptozotocin

- A naturally occurring chemical that is particularly toxic to the insulin-producing beta cells of the pancreas in mammals.
- It is used for treating certain cancers of the Islets of Langerhans and used in medical research to produce an animal model for Type 1 diabetes in large dose as well as Type 2 diabetes with multiple low doses.



BMOV, bis(maltolato)oxovanadium(IV), Insulin-like in Nature

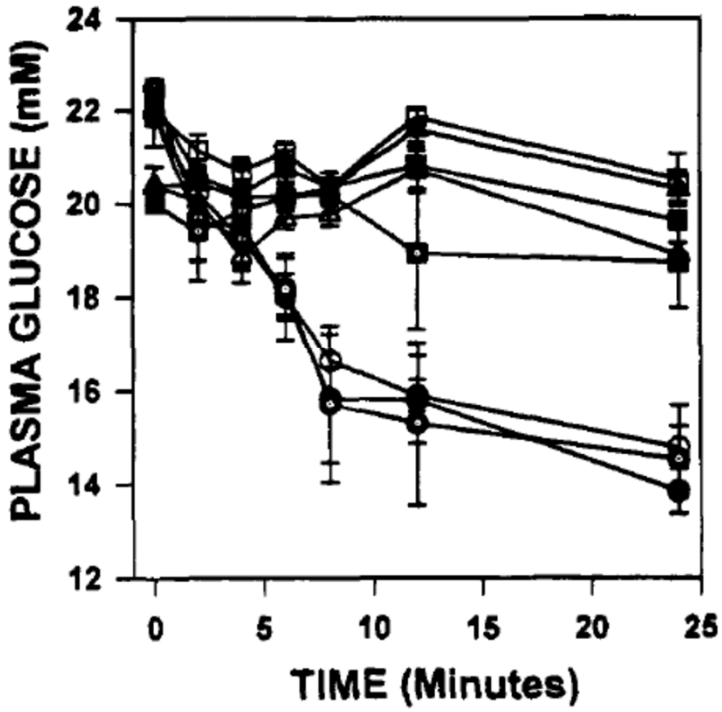


Figure 3. Plasma glucose values over time following the oral gavage administration of a single dose. A 10-fold excess of Hma was administered either preceeding or following treatment with vanadium-(IV) as vanadyl sulfate (VS) or $VO(ma)_2$. The doses of the compounds administered were $VO(ma)_2$ 0.4 mmol kg^{-1}, VS 0.4 mmol kg^{-1}, Hma 4 mmol kg^{-1}, or 3% gum arabic. The eight experimental groups were $VO(ma)_2$ (●, $n = 6$), Hma preceeding $VO(ma)_2$ (O, $n = 6$), $VO(ma)_2$ preceeding Hma (⊙), $n = 6$), VS (■, $n = 6$), Hma preceeding VS (□, $n = 6$), VS preceeding Hma (⊡, $n = 6$), Hma (▲, $n = 6$), and 3% gum arabic (△, $n = 6$). * Significantly different $p < 0.05$.

Orvig, C.; Caravan, P.; Gelmini, L.; Glover, N.; Herring, F. G.; Li, H.; McNeill, J. H.; Rettig, S. J.; Setyawati, I. A., Reaction chemistry of BMOV, bis(maltolato)oxovanadium(IV), a potent insulin mimetic agent. *J. Am. Chem. Soc.* **1995,** *117* (51), 12759-12770.

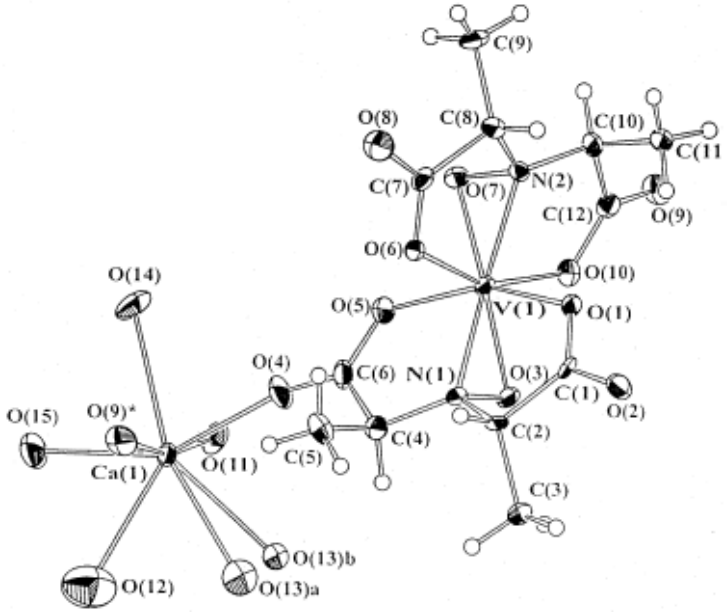
Vanadium in Nature

An *Ascidian nigra* tunicate

Crude oil

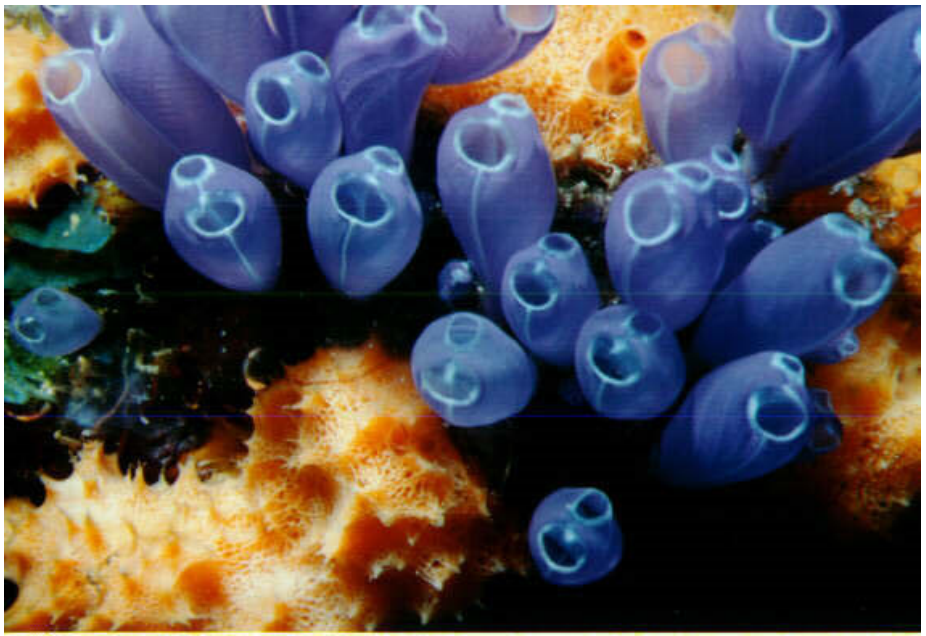
Vanadite [$Pb(VO_4)_3Cl$]

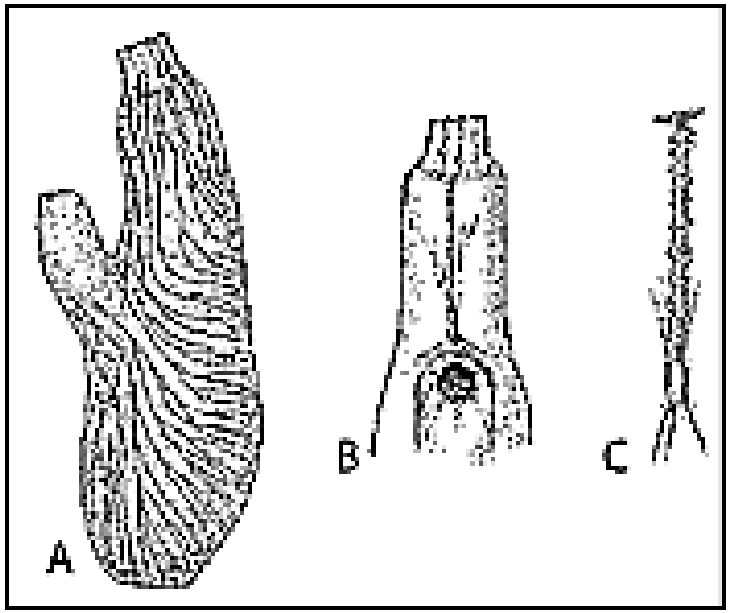
The *Amanita muscaris* mushroom



The crystal structure of Amavadin

Tunicates





Phallusia nigra. (A) With tunic removed. (B) Dorsal view of siphon region. (C) Neural duct. (from Abbott et al. 1997)

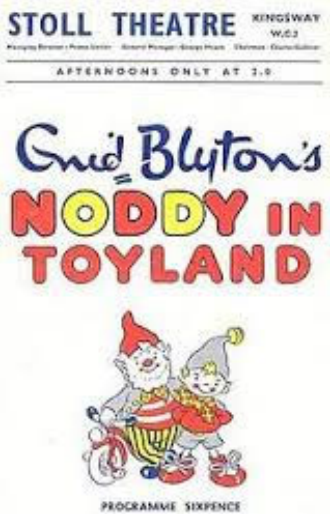
Ascidia nigra tunicates

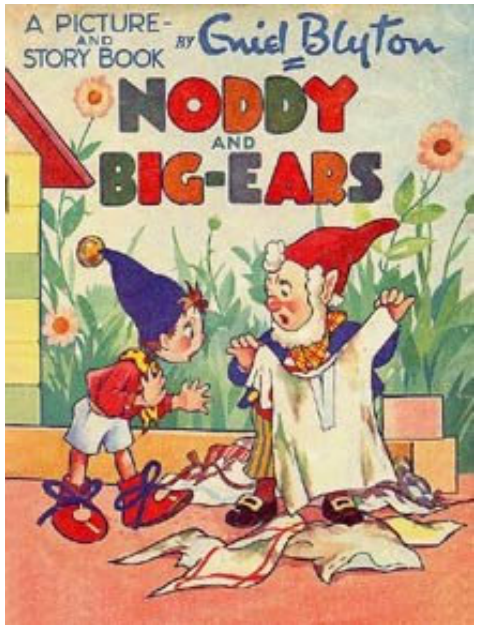
http://www.springerlink.com/content/h22746v80461mp51/

Vanadium biochemistry: The unknown role of vanadium-containing cells in ascidians (sea squirts)

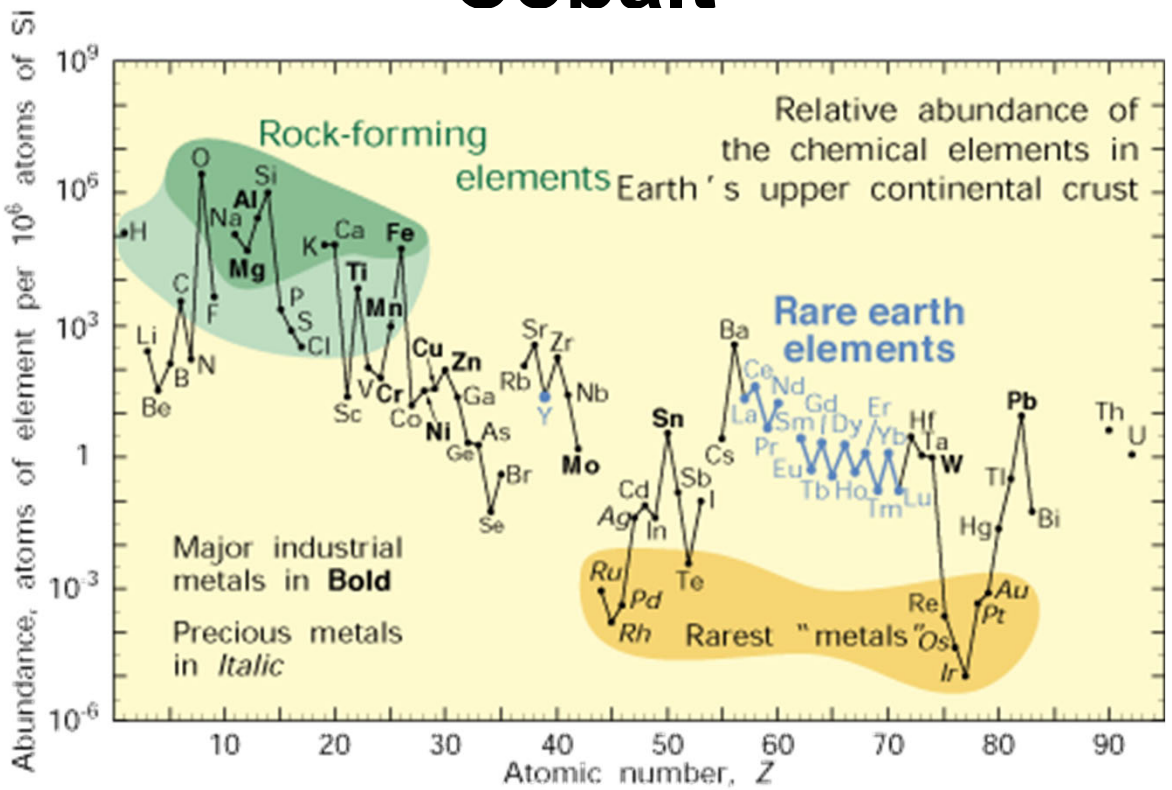
Ascidia nigra tunicates from Port St. Charles, Barbados and Port Royal, Jamaica

Where Noddy and Big Ears reside: You know the mushroom!!





Cobalt



Discovery date: 1739
Discovered by Georg Brandt
The origin of its name: The name is derived from the German word 'kobald', meaning goblin.
Cobalt's abundance in the Earth's Crust: 0.003%

http://periodictable.com/Properties/A/CrustAbundance.an.html
http://www.rsc.org/periodic-table/element/27/cobalt
http://education.jlab.org/itselemental/ele027.html
http://www.smithsonianmag.com/science-nature/what-is-rarer-than-gold-45073180/

Introductory Examples in Bioinorganic Chemistry

Especially with Vitamin B_{12} and the coenzyme:

- Therapeutic benefits of cobalamin
- Early use of

    (i) chromatography

    (ii) purification methods

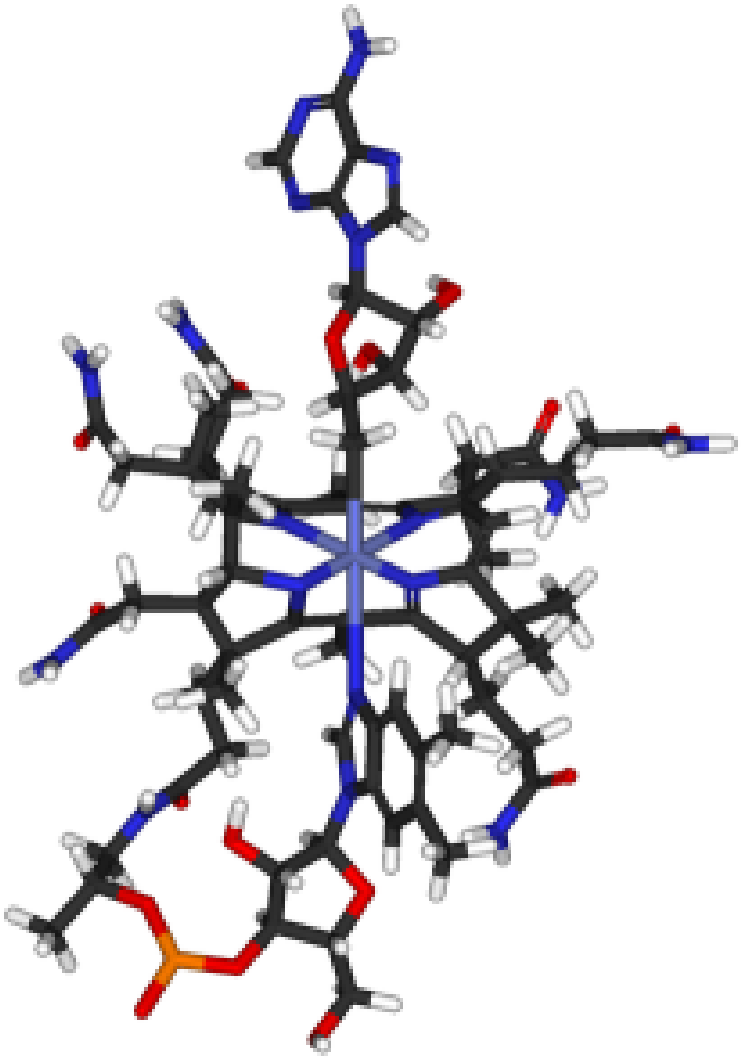
    (iii) structural elucidation by X-ray crystallography

Note, modern natural product synthesis and both bioorganic and organometallic chemistry have profited from studies of the B_{12} system, all thanks to Prof. Dorothy Crowfoot Hodgkin (1964 Nobel Prize in Chemistry)

Nobel Lecture, The X-Ray Analysis Of Complicated Molecules, by Dorothy Crowfoot Hodgkin, British Chemist/Nobel Laureate, December 11, 1964 at Stockholm Concert Hall, Stockholm, Sweden

I became captivated by the edifices chemists had raised through experiment and imagination -- but still I had a lurking question. Would it not be better if one could really 'see' whether molecules as complicated as the sterols, or strychnine were just as experiment suggested? Prof. Dorothy Crowfot Hodgkin

The Structure of Vitamin B_{12}



- **A monoanion corrin**
- **A Co(III) metal centre**

http://neutronsforbreakfast.wordpress.com/2010/05/21/dorothy-hodgkin-britains-greatest-scientist/
neutrons for breakfast, Dorothy Hodgkin- Britain's greatest scientist. May 21, 2010 by Ross.

Average Chemical Composition of a Human

70 kg

Element	Mass/g	Element	Mass/g	Element	Mass/g
O	43,000	Cl	95	B[b]	0.018
C	16,000	Mg	25	Ni	0.015
H	7,000	F	5.0 (var.)	I	0.015
N	1,800	Fe	4.0	Se	0.014
Ca	1,200	Zn	2.3	Mn	0.012
P	780	Si	1.0 (var.)	Li	0.007
S	140	Ti[a]	0.70	Mo	0.005
K	125	Br	0.26	Cr	0.002 (var.)
Na		Cu	0.07	Co	0.002

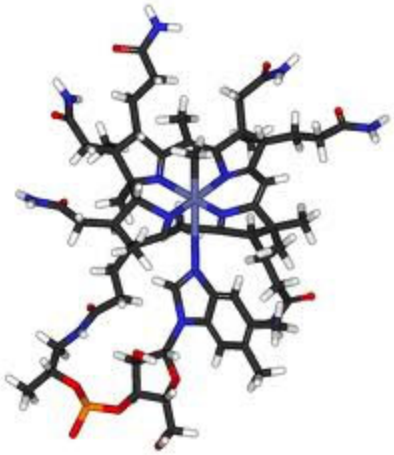
[a] Not rated essential

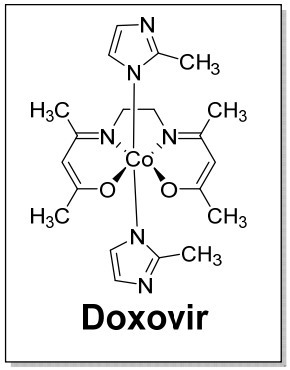
[b] Essential character not unambiguous

Nota Bien

- The Co-CH_2R moiety in alkylcobalamins is resitant to hydrolysis in neutral aqueous solution in the presence of O_2
- The Co-C bond has a special reactivity:- the enzymatically controlled formation of reactive primary alkyl radicals
- Pernicious anemia
- The contributions of Prof. Dorothy Crowfoot Hodgkin

The CH_3 group in methylcobalamin (see below) can be substituted by the ligands, H_2O, OH^-, or CN^-, to produce aqua-, hydroxo-, or cyanocobalamin (vitamin B_{12})



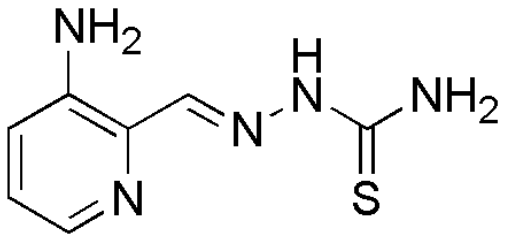


Cobalt's Medicinal Application

- A substantial amount of literature on bioactive cobalt compounds has been published in the last decade, demonstrating its rich potential in medicinal applications.
- The rationale behind the design and mechanisms of many of these compounds has not been clearly elucidated
- To date, the only cobalt-based therapeutic that has reached clinical trials is Doxovir, a Co(III) Schiff base complex effective against drug-resistant herpes simplex virus 1.

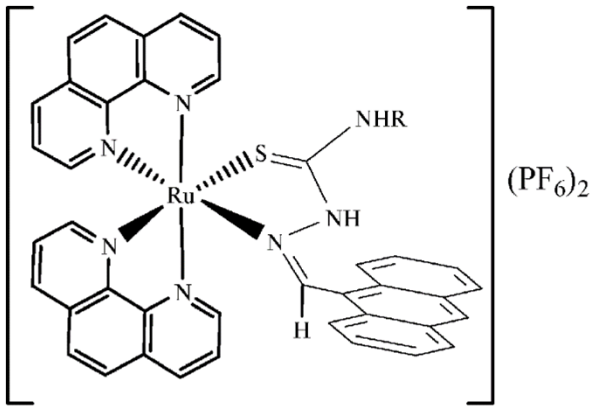
1. Hall, M. D.; Failes, T. W.; Yamamoto, N.; Hambley, T. W. *Dalton Trans.* **2007**, (36), 3983-3990.
2. Heffern, M. C.; Yamamoto, N.; Holbrook, R. J.; Eckermann, A. L.; Meade, T. J. *Curr. Opin. Chem. Biol.* **2013,** 17, (2), 189-196.
3. Munteanu, C. R.; Suntharalingam, K. *Dalton Trans.* **2015,** 44, (31), 13796-13808.
4. Schwartz, J. A.; Lium, E. K.; Silverstein, S. J. *J. Virol.* **2001,** 75, (9), 4117-4128.
5. Chang, E. L.; Simmers, C.; Knight, D. A. *Pharmaceuticals* **2010,** 3, 1711-1728.

Thiosemicarbazones and Complexes used in Cancer Treatment

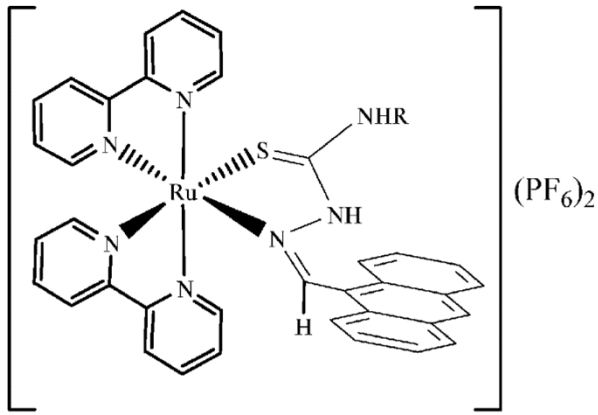


3-aminopyridine-2-carboxaldehyde thiosemicarbazone (3-AP) (triapine)

- First reported thiosemicarbazone to enter phase II clinical trials as an anti-cancer agent



1 R = H
3 R = CH_3
5 R = C_2H_5



2 R = H
4 R = CH_3
6 R = C_2H_5

1. Li, J.; Luo, X.; Wang, Q.; Zheng, L.-M.; King, I.; Doyle, T. W.; Chen, S. H. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3159.
2. Beckford, F, A; Shaloski, M, Jr.; Leblanc, G; Thessing, G; Lewis-Alleyne, L, C; Holder, A, A; Li, L; Seeram, L. *Dalton Trans.* **2009**, 10757-10764.

Fighting TNBC: Mechanistic Investigations With a Novel Co(III) Complex

- Thiosemicarbazones and their corresponding complexes are a very promising class of compound for the treatment of many diseases

- Manikandan *et al.* previously reported on the anti-tumor activity of Co(III)-thiosemicarbazone complexes

- Based on this work we investigated the mechanism of action of this class of complexes in **triple negative breast cancer (TNBC)** cells

- It was proposed that transition metal chemotherapeutics would act synergistically with nanosecond pulsed electric fields (nsPEFs) to kill cancer cell

Bullock, J. L., Jr. Synthesis and Mechanistic Investigations of Transition Metal Complexes and Ligands for Chemotherapeutic Applications. M.S. Thesis, Old Dominion University, 2016.

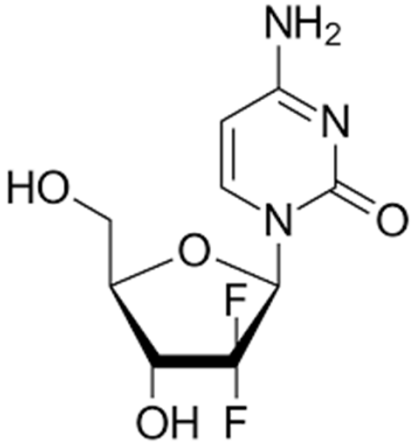
Manikandan, R.; Viswanathamurthi, P.; Velmurugan, K.; Nandhakumar, R.; Hashimoto, T.; Endo, A. *J. Photochem. Photobiol. B: Biol.* **2014**, **130**, 205-216.

Nanosecond Pulse Electric Fields (nsPEFs)

- Extremely short pulse durations, high voltage, but low energy, and non-thermal effects

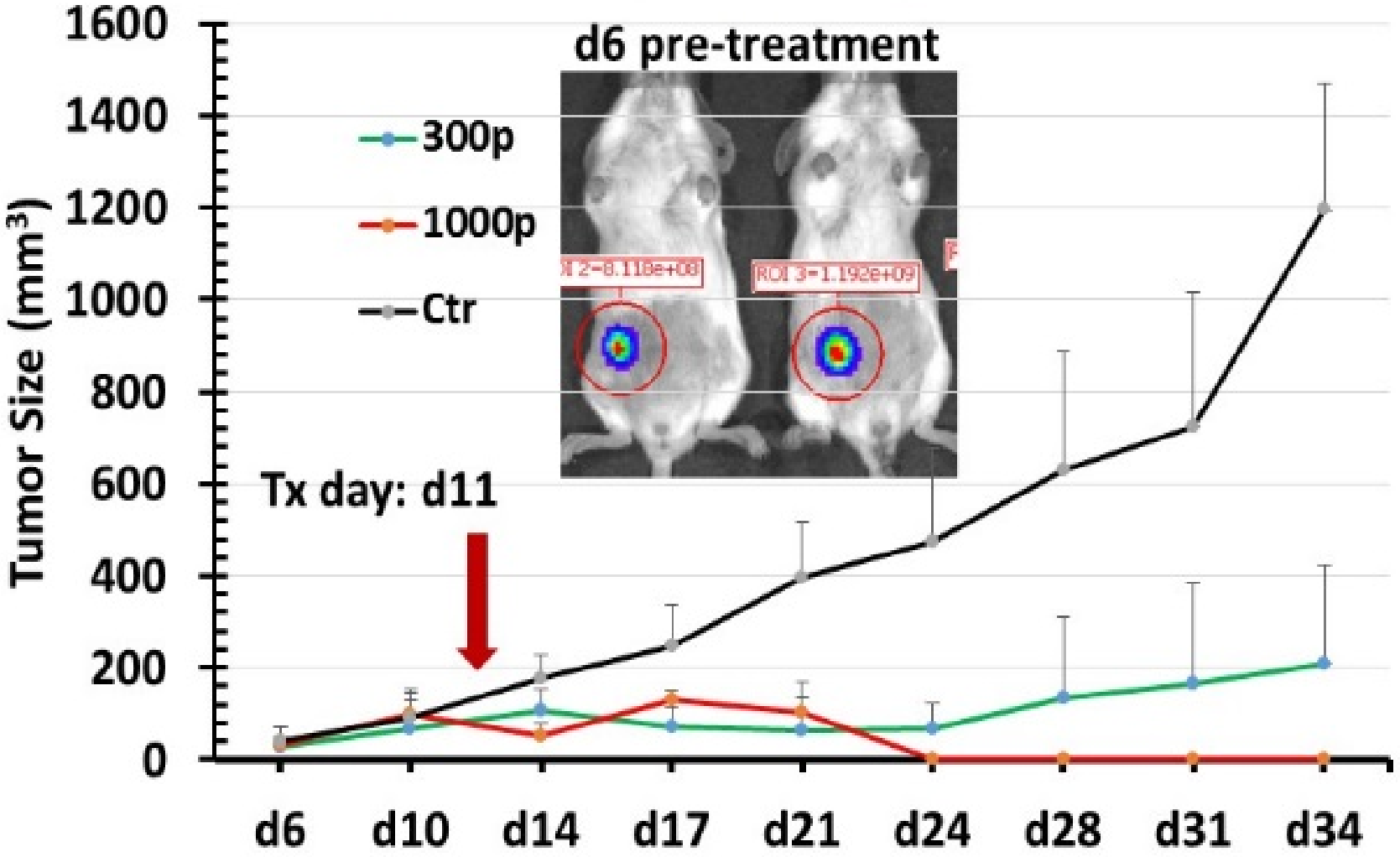
- Has been shown that nsPEF sensitize oral squamous cells to the chemotherapeutic agent, gemcitabine

- To investigate whether a synergism exists between chemotherapeutic transition metal complexes and nsPEF technology



Beebe, S. J.; Sain, N. M.; Ren, W. *Cells* **2013**, *2*, 136.
Wang, J.; Guo, J.; Wu, S.; Feng, H.; Sun, S.; Pan, J.; Zhang, J.; Beebe, S.J. *Plos One* **2012**, *7*, e43213.
Ren, W.; Sain, N.M.; Beebe, S.J. *Biochem. Biophys. Res. Commun.* **2012**, *421*, 808.

Effect of nsPEFs on 4T1-Luc mammary tumors



Courtesy of Dr. Beebe: Effects of nsPEFs on sham control tumor size (control (Ctr), black; 0 kV/cm) and size of tumors treated with 300 (green) and 1000 (red) pulses at 1 Hz, 100 ns, and 42-46 kV/cm (1 week after injection, ~0.5 x 0.5 cm) at various times after tumor cell injection (n = 8). The inset shows appearance of two tumors on day 6 prior to treatment.

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journal homepage: www.elsevier.com/locate/jinorgbio

Synthesis, characterization, DNA binding, topoisomerase inhibition, and apoptosis induction studies of a novel cobalt(III) complex with a thiosemicarbazone ligand

Stephen J. Beebe[a], Michael J. Celestine[b], Jimmie L. Bullock[b], Shayna Sandhaus[c], Jessa Faye Arca[d], Donald M. Cropek[e], Tekettay A. Ludvig[b], Sydney R. Foster[b], Jasmine S. Clark[b], Floyd A. Beckford[f], Criszcele M. Tano[b], Elizabeth A. Tonsel-White[b], Raj K. Gurung[b], Courtney E. Stankavich[b], Yuk-Ching Tse-Dinh[c], William L. Jarrett[g], Alvin A. Holder[b,*]

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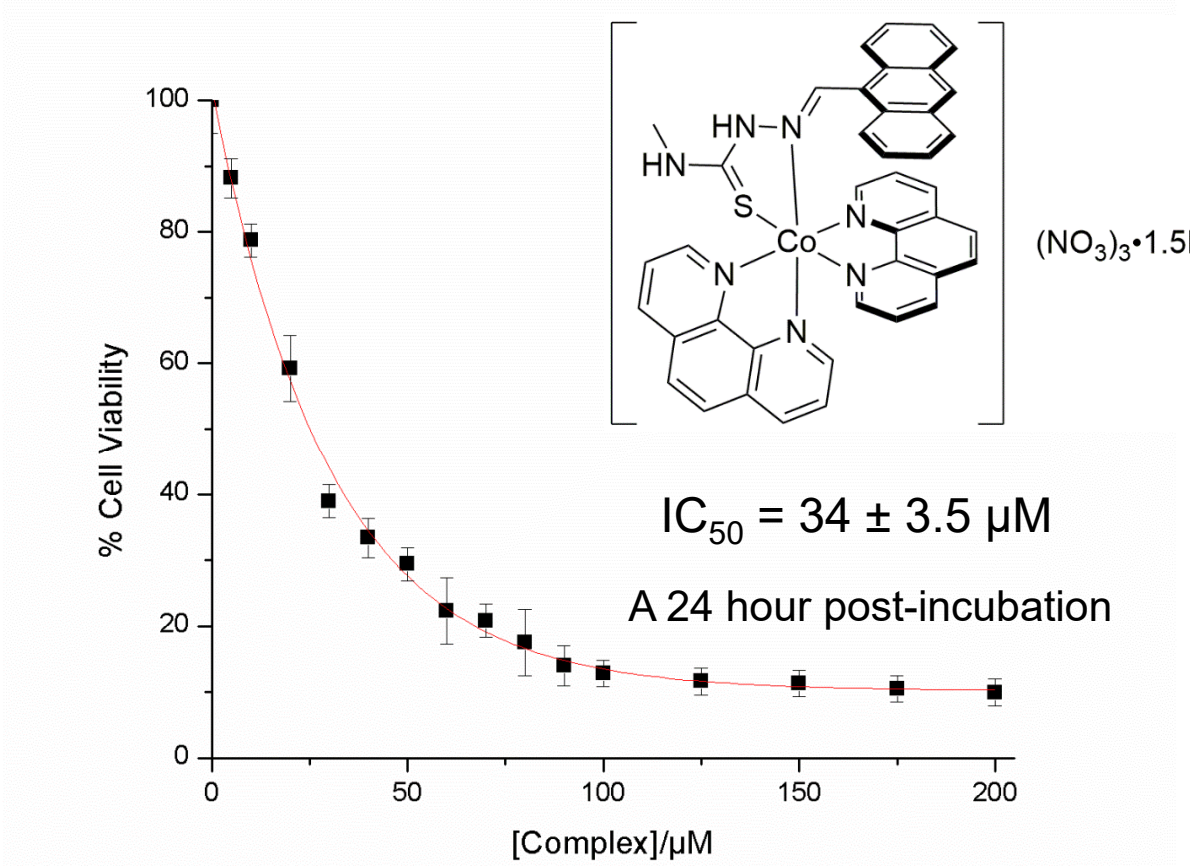
[b] Department of Chemistry and Biochemistry, Old Dominion University, 4541 Hampton Boulevard, Norfolk, VA 23529, USA
[c] Department of Chemistry and Biochemistry, Biomolecular Sciences Institute, Florida International University, 11200 SW 8th St., Miami, FL 33199, USA
[d] Department of Chemistry and Biochemistry, The University of Southern Mississippi, 118 College Drive, Hattiesburg, MS 39406, USA
[e] U.S. Army Corps of Engineers, Construction Engineering Research Laboratory, Champaign, IL 61822, USA
[f] The University of Virginia's College at Wise, 1 College Avenue, Wise, VA 24293, USA
[g] School of Polymers and High-Performance Materials, The University of Southern Mississippi, 118 College Drive, #5050, Hattiesburg, MS 39406, USA

Ms. Jasmine Clark, ODU's MARC Trainee (2020)

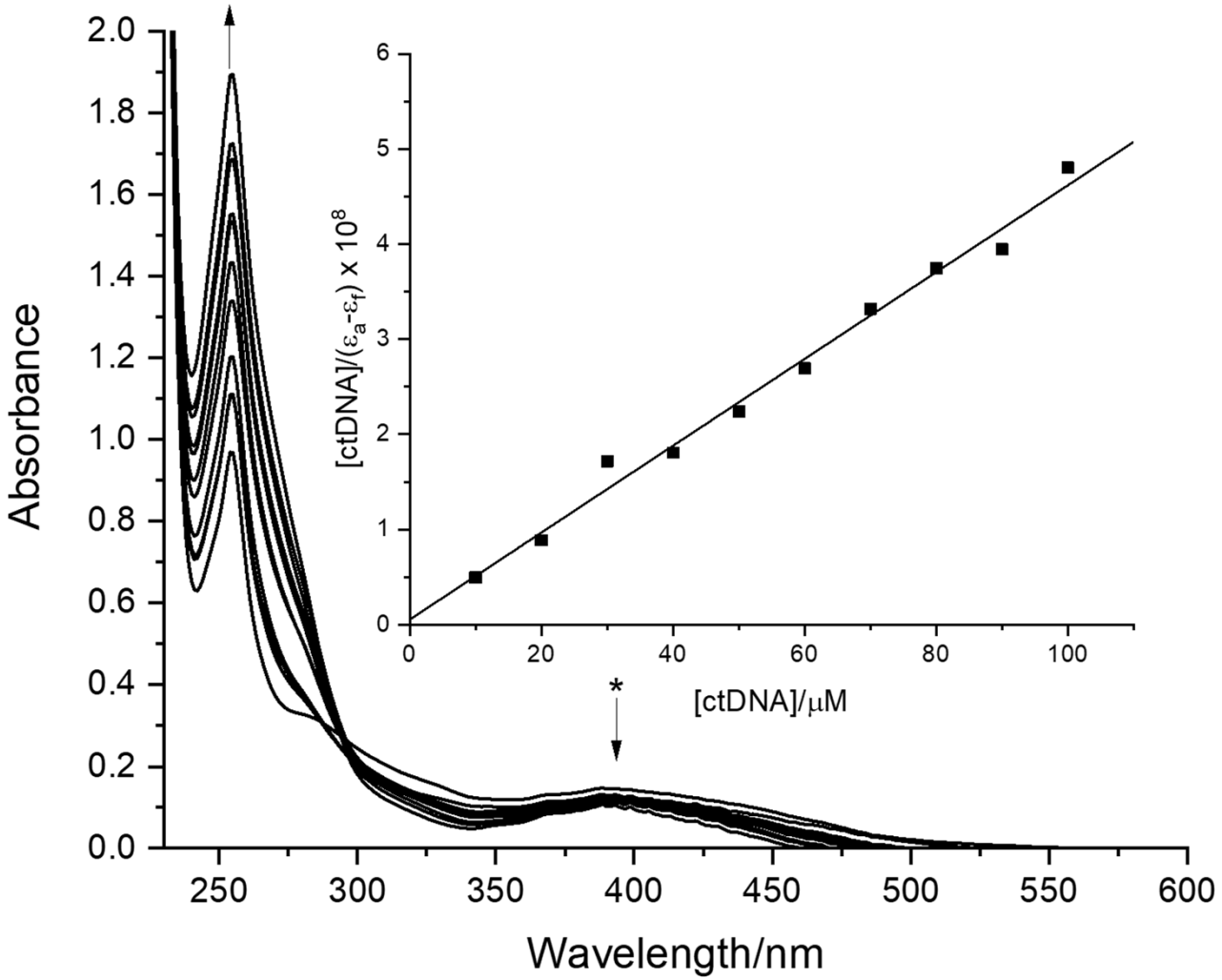
Growth Inhibition in 4T1-luc Cells: An MTS Assay

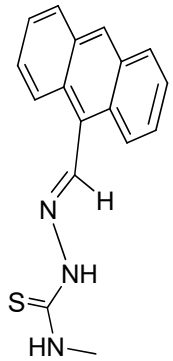


Controls: 9-anthraldehyde-*N*(4)-methylthiosemicarbazone (MeATSC), IC_{50} = 50 μM, $[Co(phen)_2(H_2O)_2](NO_3)_3$, IC_{50} >100 μM, and for cisplatin, IC_{50} = 3.75 ± 1.08 μM.

The **4T1** metastatic breast cancer model is a syngeneic xenograft model based on **4T1**-luc12B, a luciferase-expressing clone of the well characterized **4T1** mouse mammary tumor cell line.

Spectrophotometric Titration of MeATSC with Calf Thymus DNA (ctDNA)

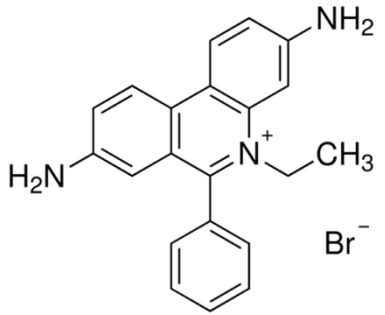




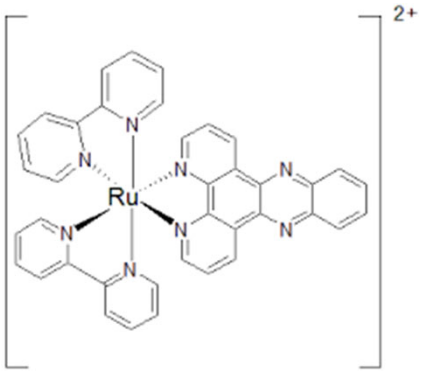
MeATSC

Inset: A plot of [ctDNA]/(ε_a-ε_f) versus [ctDNA]. [MeATSC] = 20 μM, pH = 7.68 ± 0.02, and Tris-HCl buffer ([Tris] = 5 mM, [HCl] = 3.55 mM, and [NaCl] = 25 mM).

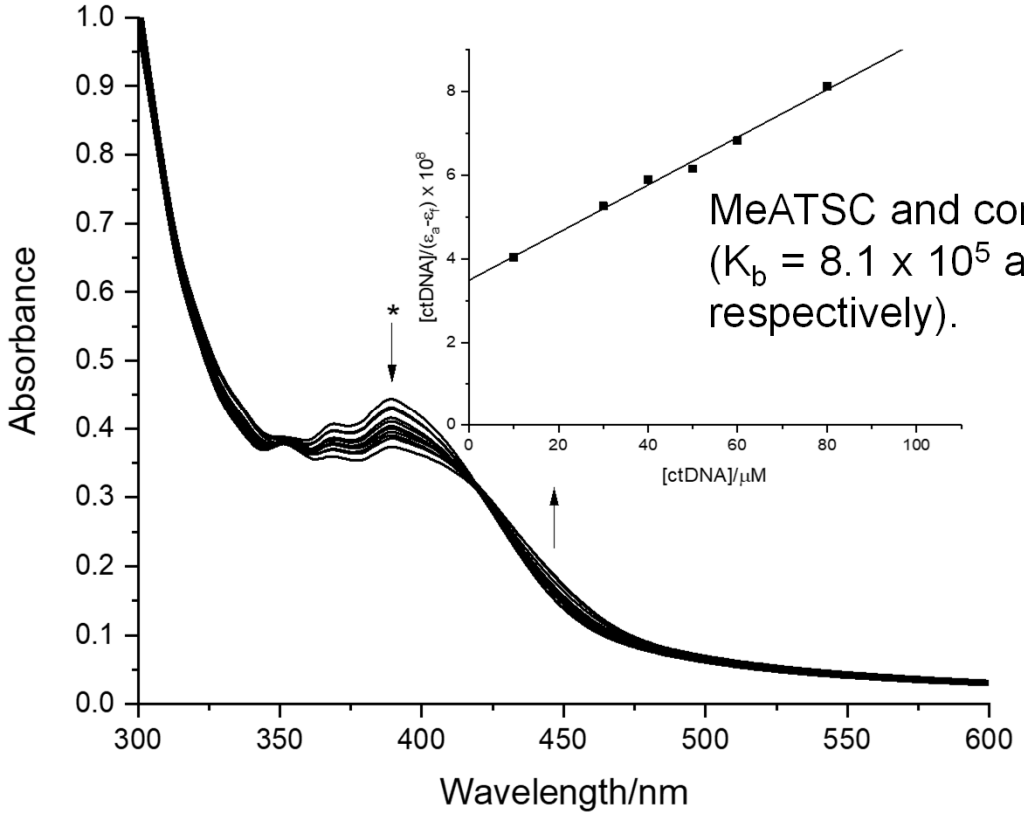
DNA Interaction Studies with CtDNA



ethidium bromide



$[Ru(bpy)_2(dppz)]^{2+}$



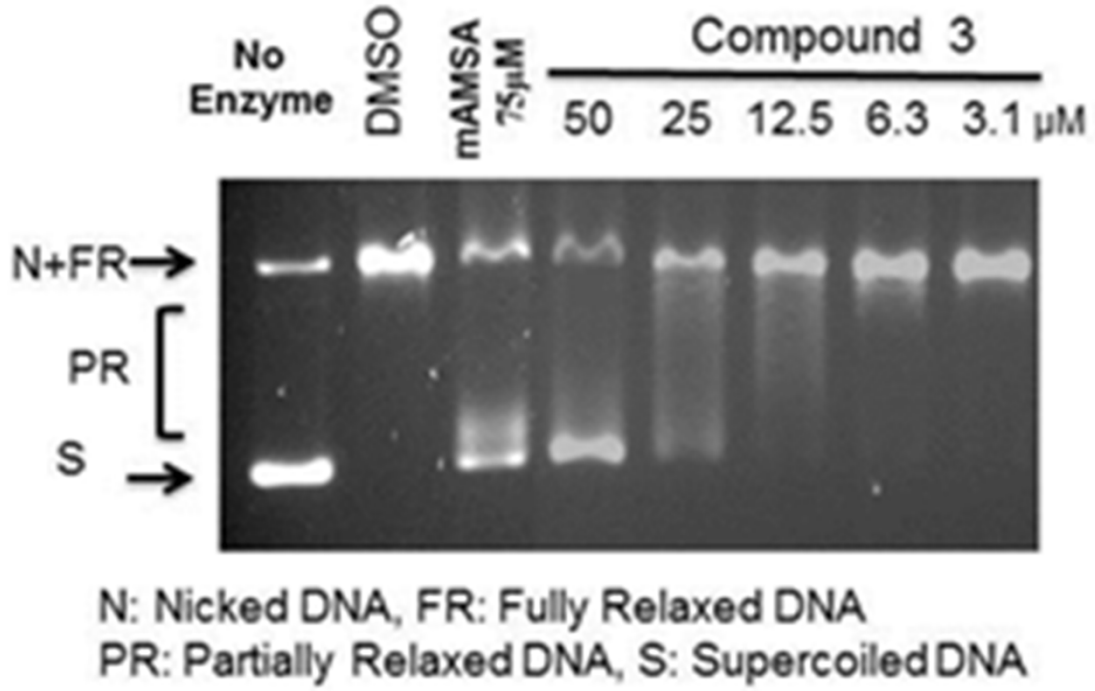
MeATSC and complex **3** (K_b = 8.1 x 10^5 and 1.6 × 10^4 M^{-1}, respectively).

[complex] = 50 μM; pH = 7.72 ± 0.03 (Tris-HCl buffer).

The complex binds weakly with CTDNA, albeit with less efficiency than ethidium bromide (K_b = 1.4 x 10^6 M^{-1})[1] and metallointercallators such as $[Ru(bpy)_2(dppz)]^{2+}$ (where dppz = dipyrido[3,2-*a*:2′,3′-*c*]phenazine, K_b >10^6 M^{-1}).[2,3]

1. Lepecq, J.B.; Paoletti, C. *J. Mol. Biol.* **1967**, 27, 87.
2. Friedman, A.E.; Chambron, J.C.; Sauvage, J.P.; Turro, N.J.; Barton, J.K. *J. Am. Chem. Soc.* **1990**, 112, 4960.
3. Erkkila, K.E.; Odom, D.T.; Barton, J.K. *Chem. Rev.* **1999**, 99, 2777.

Inhibition of Human Topoisomerases

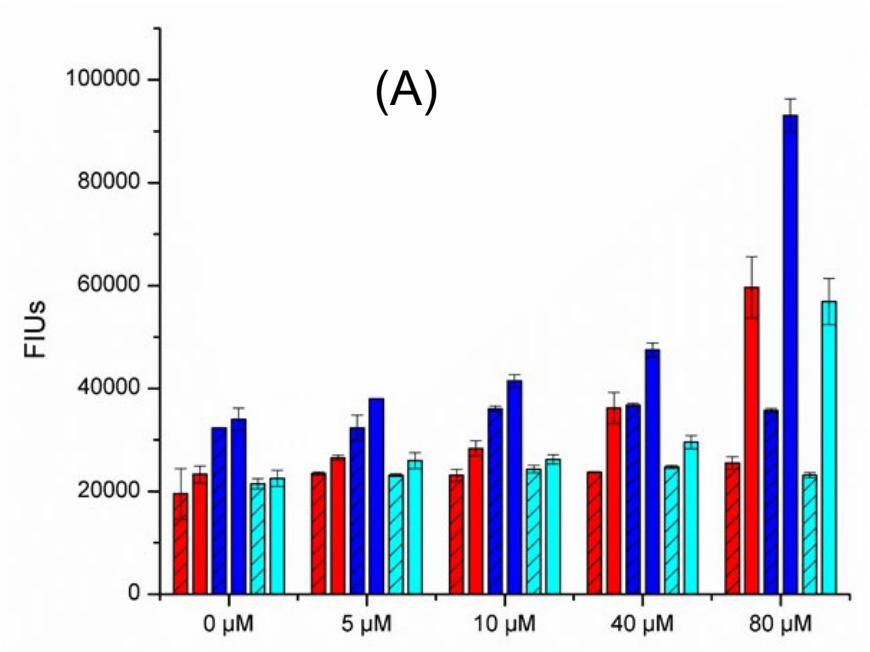


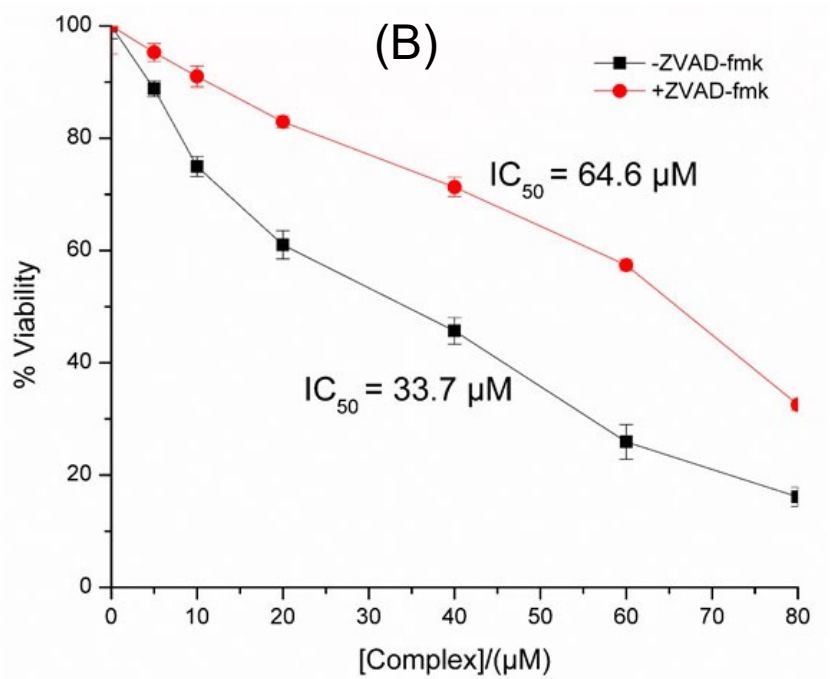
From the Tse-Dinh laboratory at Florida International University

Relaxation of supercoiled DNA by human topoisomerase II (of hTOP2α) is inhibited by the complex (compound **3**). A typical experiment is shown for the effect of compound **3** as determined by relaxation activity using supercoiled plasmid DNA as substrate. Relaxation of supercoiled DNA was inhibited by compound **3** with an IC_{50} value of ~25 μM. Relaxation activity of hTOP1 was found to be inhibited by compound **3**, with an IC_{50} value of ~6.3 μM.

Role of Caspase Cleavage on Cell Death

(A) The complex induces increases in caspase 3/7 catalytic activity in 4T1-luc cells in a concentration- and time-dependent manner. 4T1-luc cells were preincubated in the presence (stripped bars) or absence (open bars) of 10 μM pan caspase inhibitor z-VAD-fmk for four hours followed by exposure to the complex for various time: 1 h (red), 3 h (blue), 5 h (cyan).





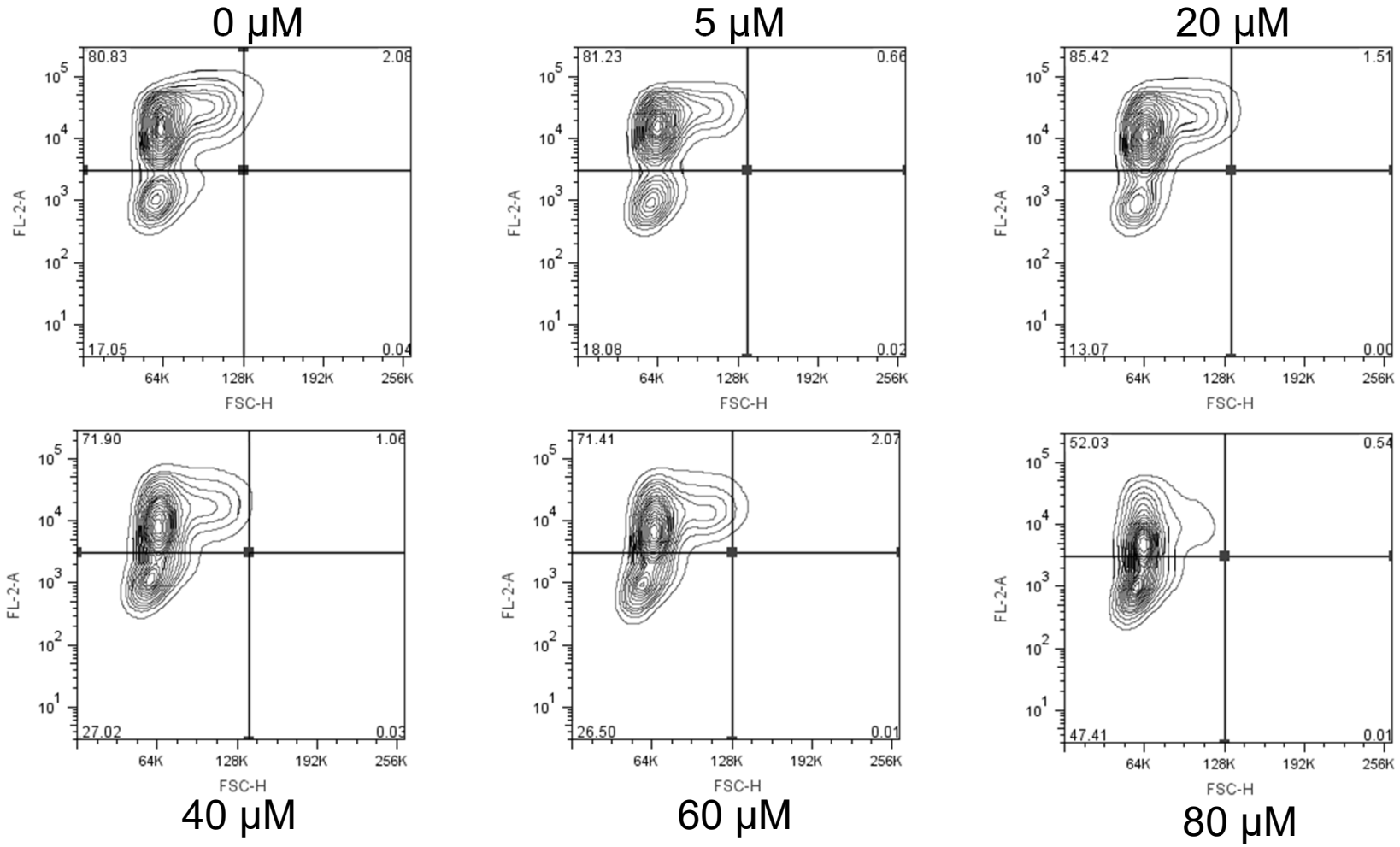
[ZVAD-fmk] = 10 μM

(B) Cellular viability following exposure to the complex drastically increased when caspase 3 activity inhibited via z-VAD-fmk

A Cell-Permeant Pan Caspase Inhibitor of Apoptosis.

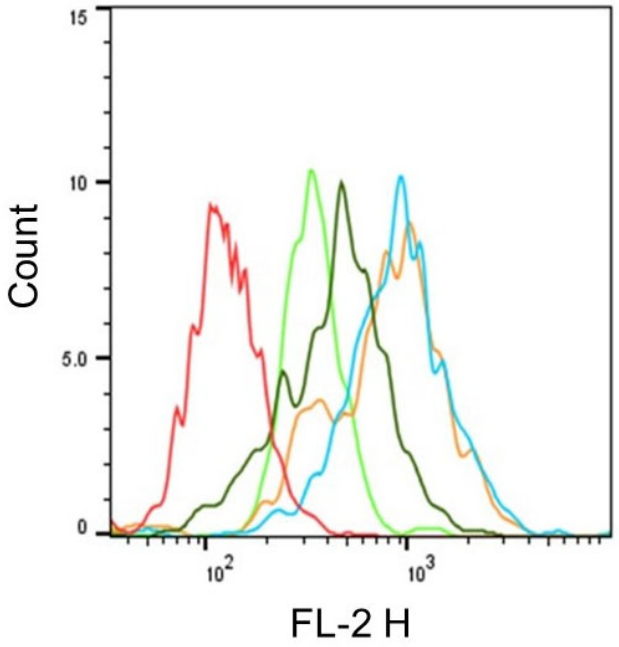
Z-VAD-fmk (carbobenzoxy-valyl-alanyl-aspartyl-[O-methyl]-fluoromethylketone) is a cell-permeant pan caspase inhibitor that irreversibly binds to the catalytic site of caspase proteases and can inhibit induction of apoptosis.

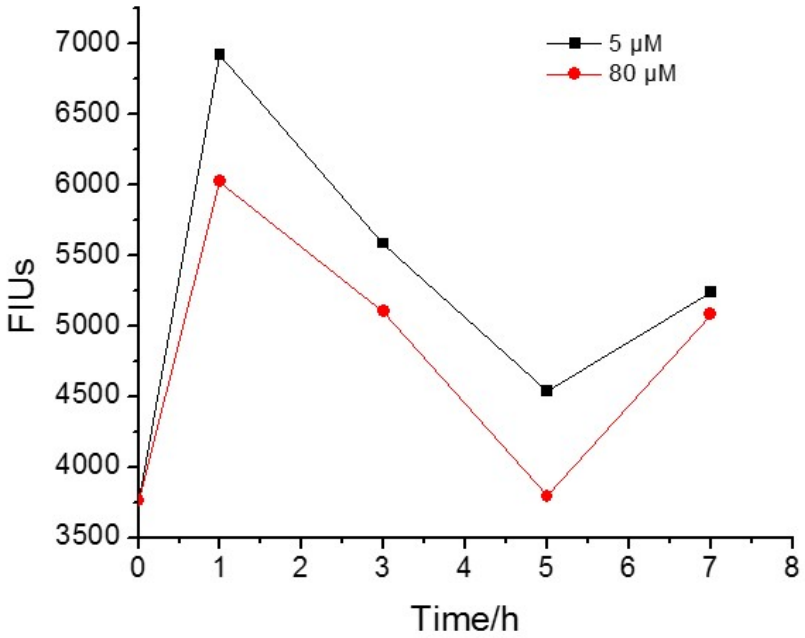
Modulation of Mitochondrial Membrane Potential ($\Delta\Psi_m$) (2 h)



The complex causes mitochondria membrane potential ($\Delta\Psi_m$) dissipation in 4T1-luc cells. The $\Delta\Psi_m$ was determined in 4T1 cells 2 h after incubation with various concentrations of the complex. Complex **3** decreases the mitochondria membrane potential.

Induction of Autophagy



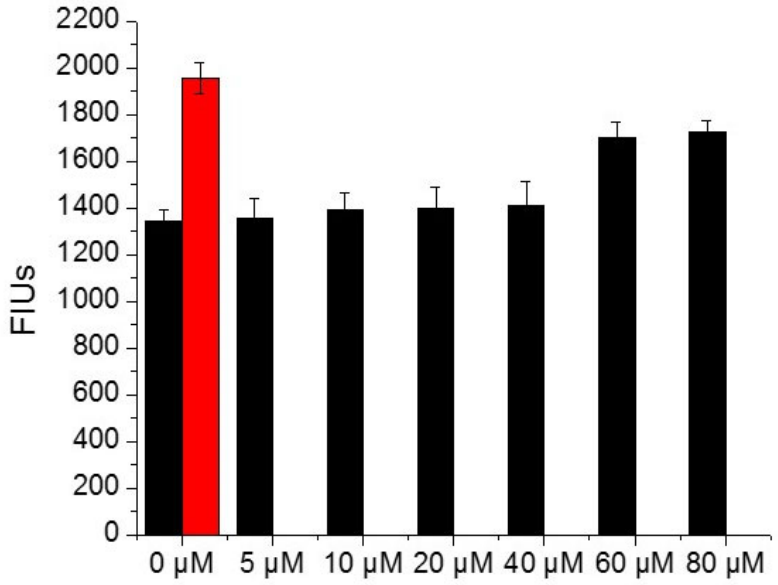


Red: unstained cells; dark green: 0 μM; cyan: 5 μM; yellow: 10 μM; and lime green: 80 μM.

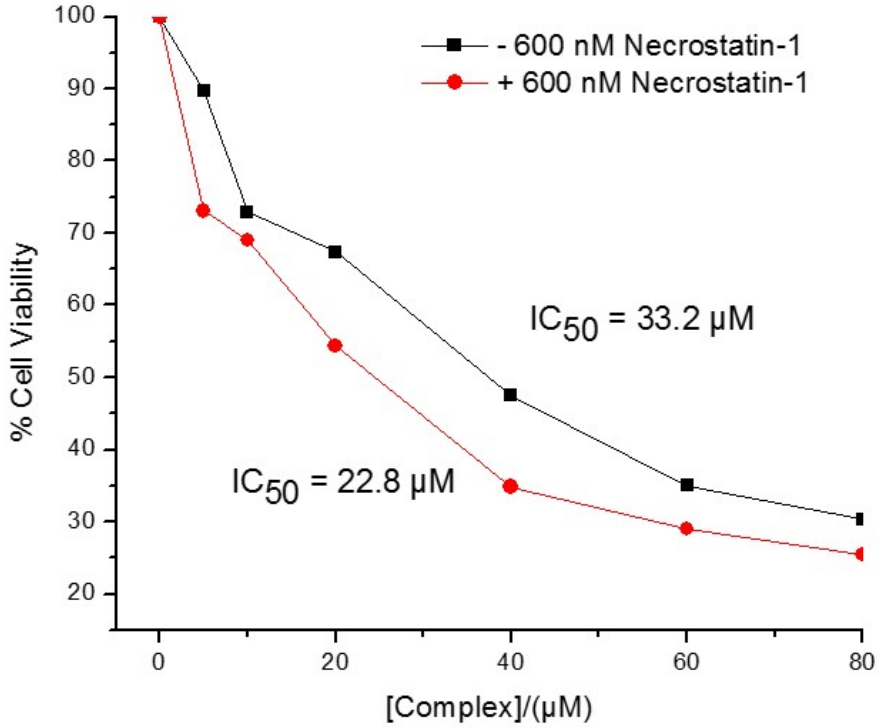
Time-dependent effects of low and high concentrations of complex on autophagic flux – 4T1-luc cells were treated with 5 μM (black) and 80 μM (red) complex **3** and autophagic flux was determined at the indicated times by fluorescence intensity on flow cytometry.

Inhibition of Autophagy with Necrostatin-1

Autophagy provides some protection against the complex

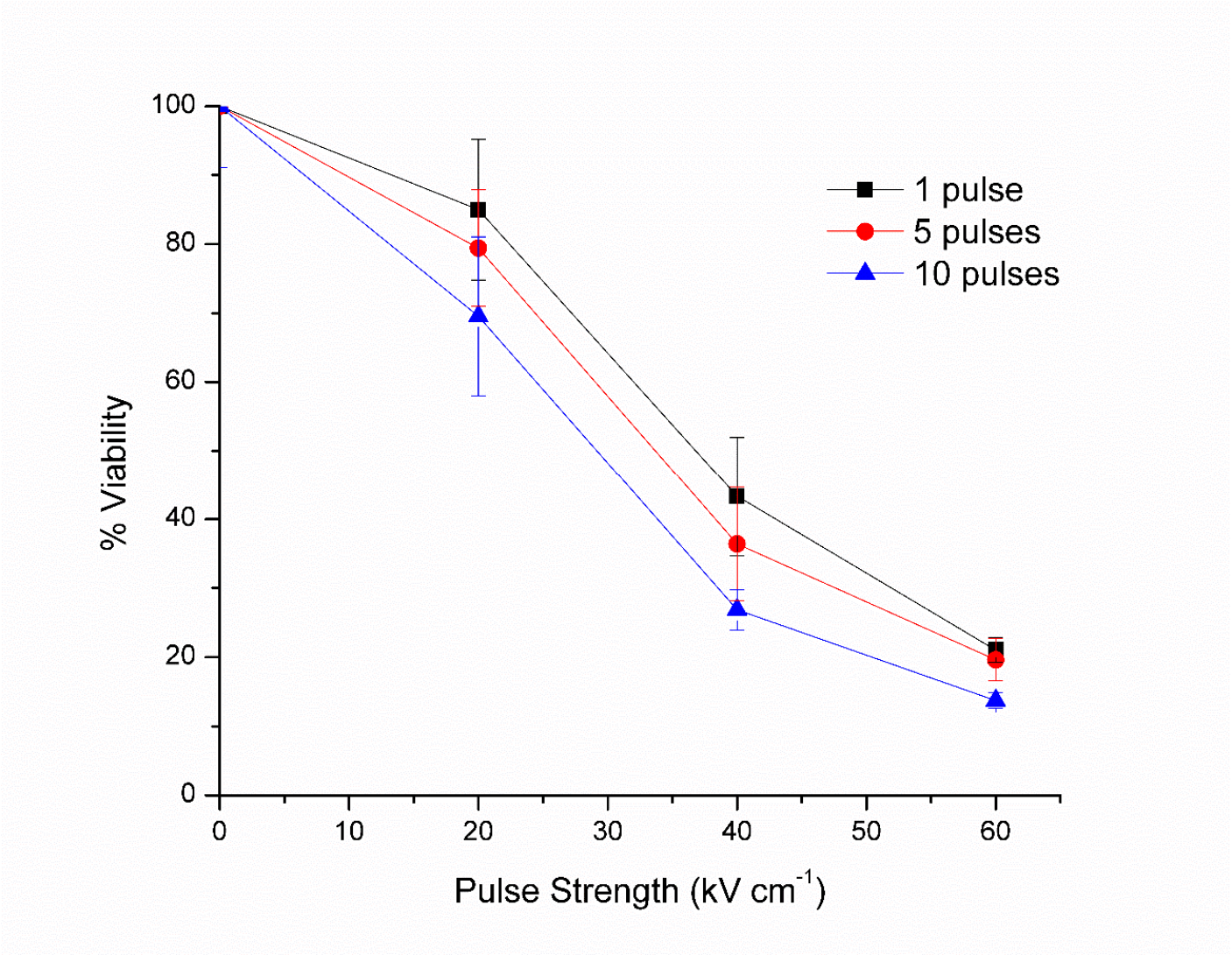


[Necrostatin-1] = 600 nM

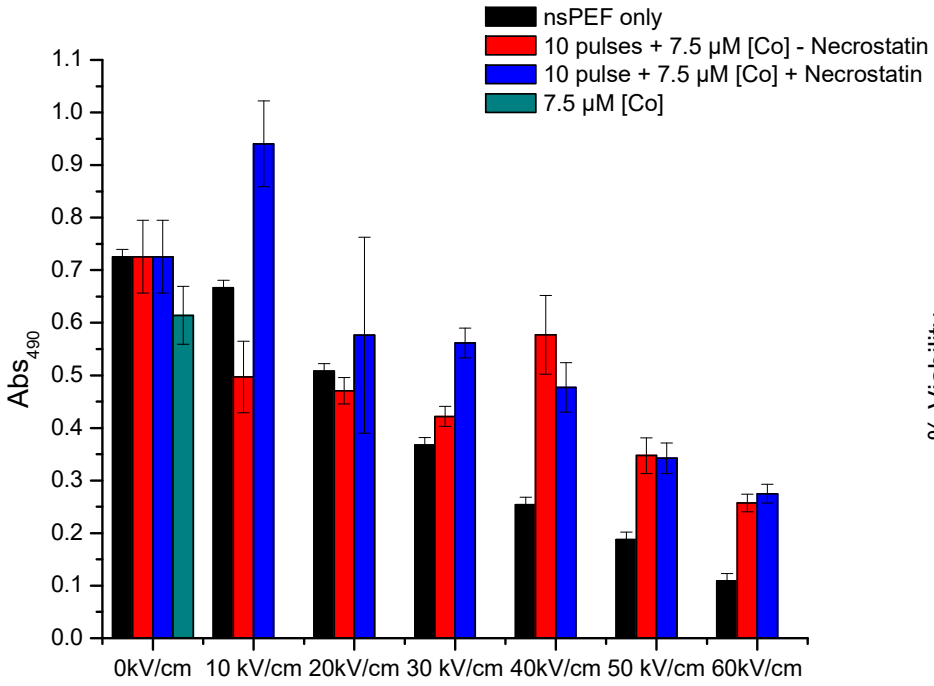


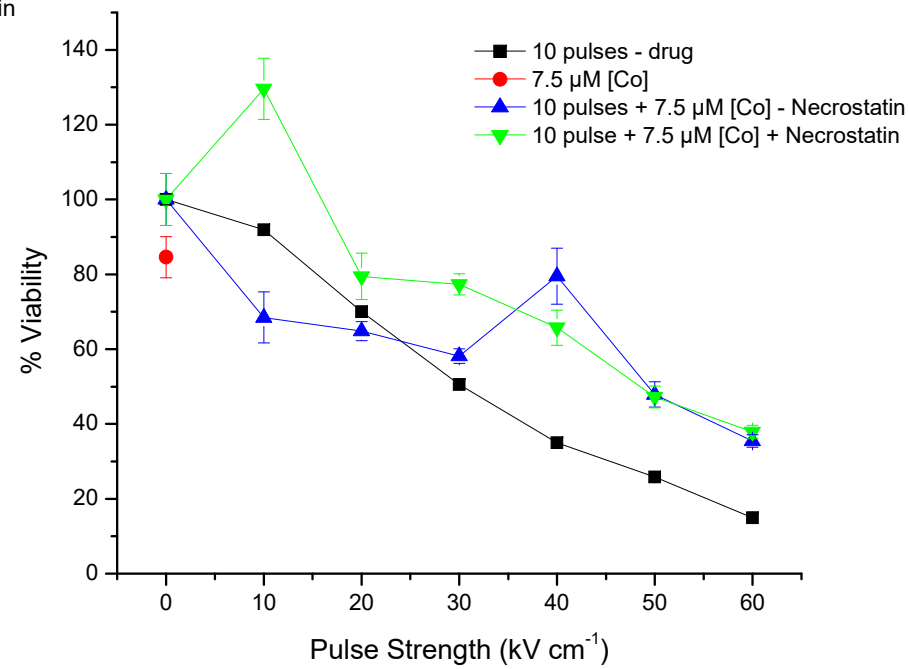
Effect of complex on autophagy in the presence of necrostatin-1 inhibition of autophagy. **4T1-luc cells were preincubated with 600 nM necrostatin-1 for 4 h. Cells were then washed and incubated with the indicated concentrations of complex for 24 h; then analyzed for autophagy by flow cytometry.** Taking this inhibitor for its effects on regulated cell death (RCD), the cobalt(III) complex does not have a great impact on necroptosis.

Growth Inhibition of 4T1-luc Cells with nsPEFs



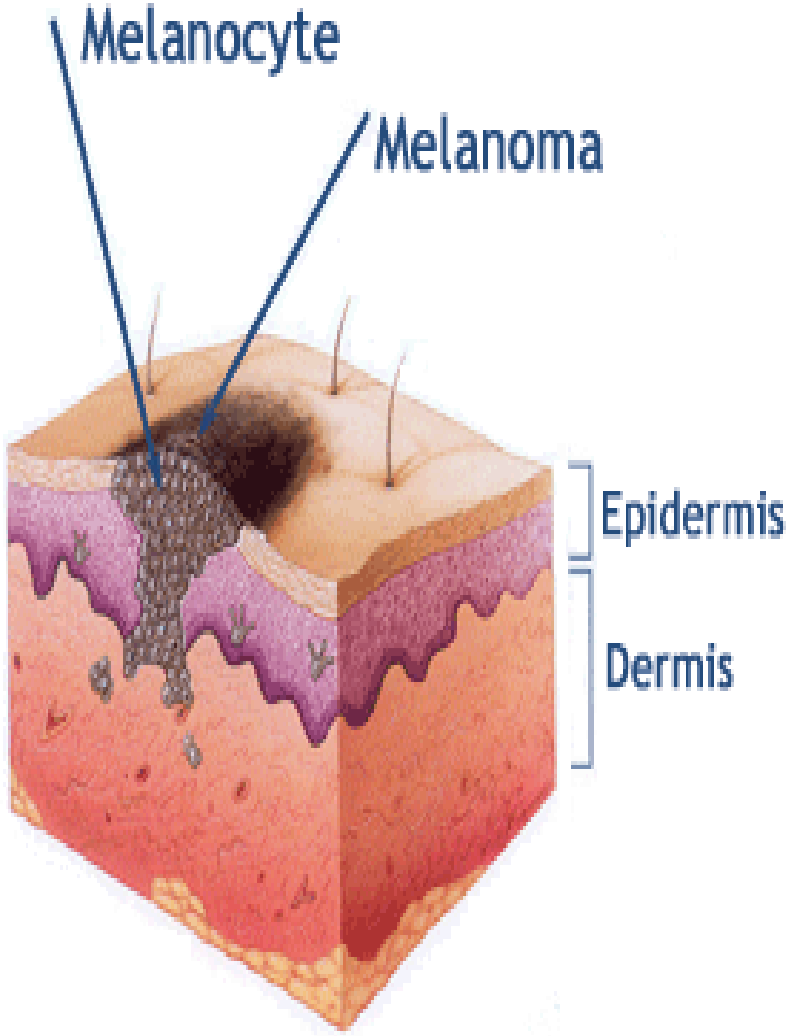
Dual Treatment Therapy With the Complex and nsPEFs





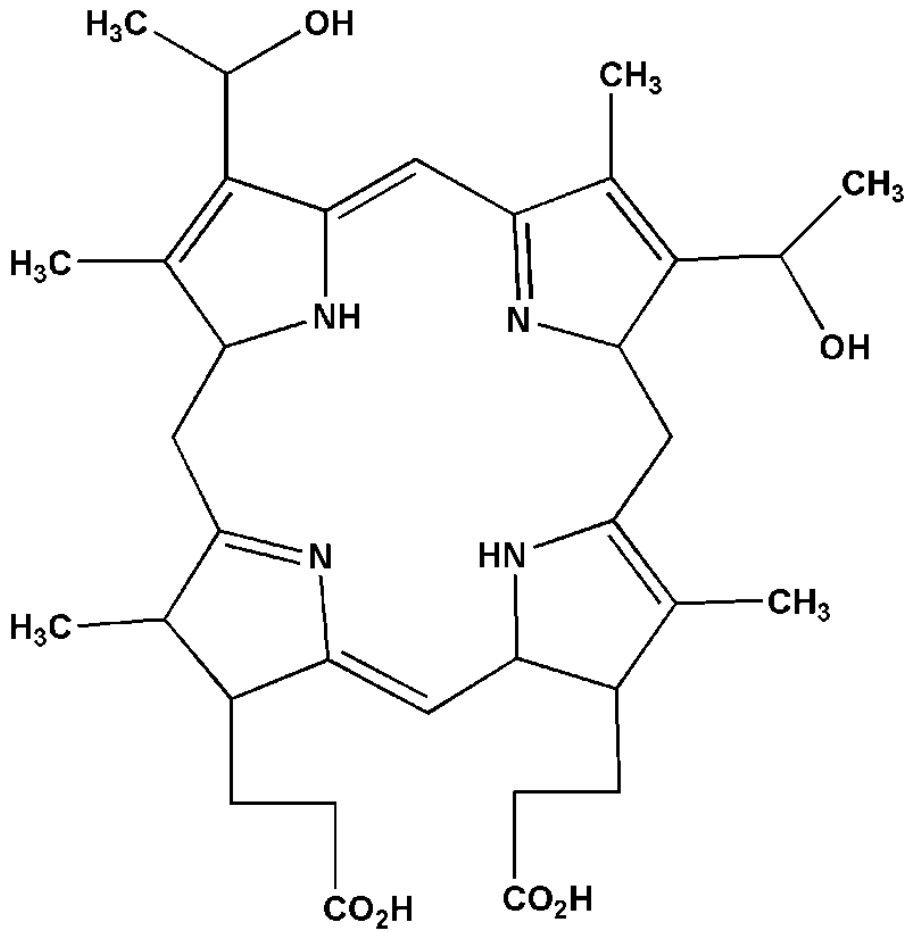
[necrostatin-1] = 600 nM

Melanoma



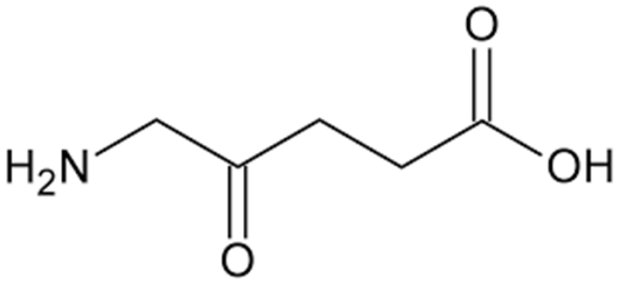
Photodynamic Therapy (PDT)

PDT: destroys cancer cells by using light to activate a drug at the tumor site.

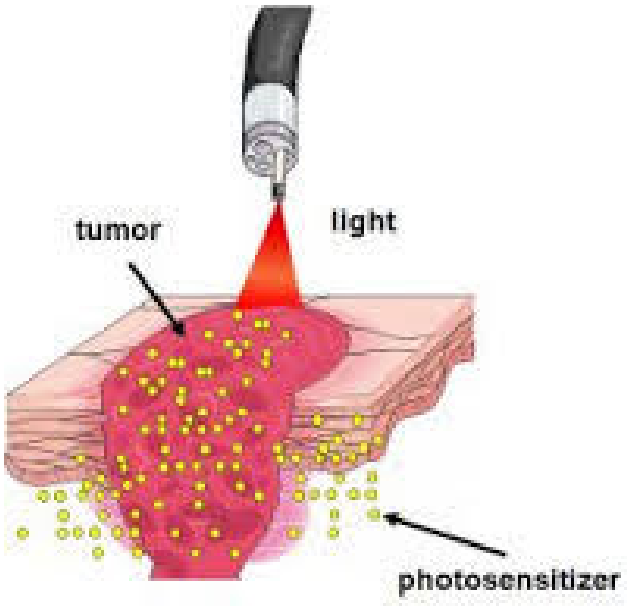


Hematoporphyrin

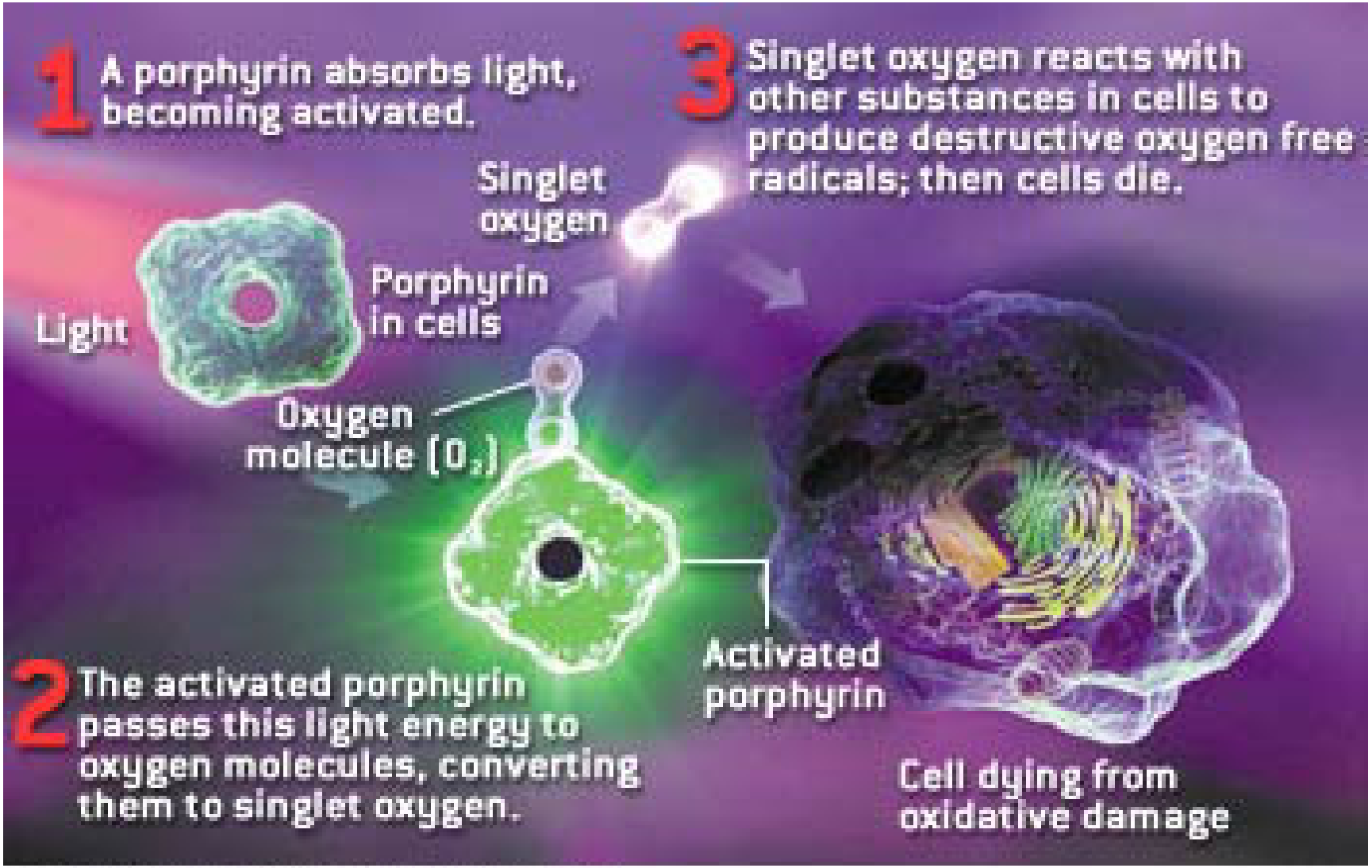
A PDT Precursor



5-aminolevulinic acid



The Mechanism Behind PDT

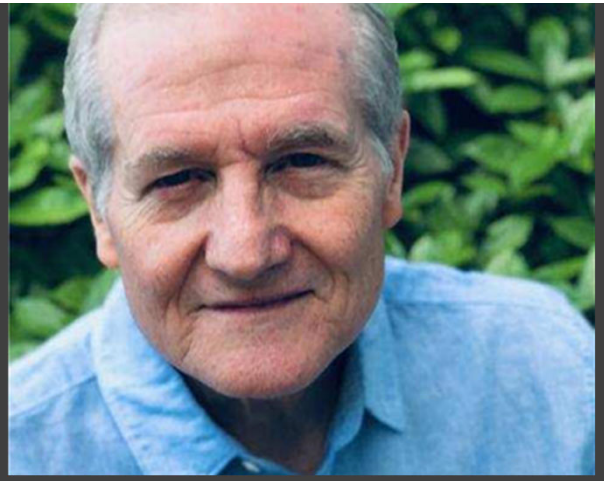


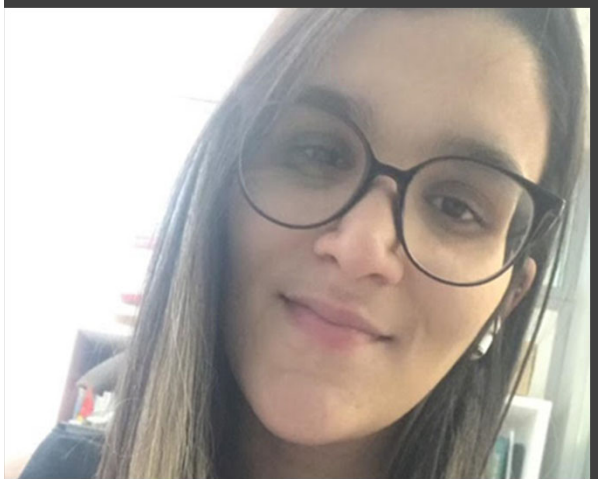
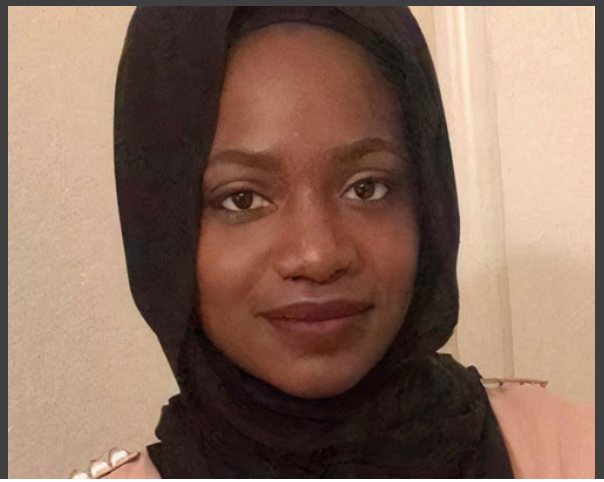
N. Lane, “New Light on Medicine”, *Scientific American*, January **2003**.

PDT Applications: Success Stories

- Esophageal cancer
- ENT Squamous cell carcinoma
- Age-related macular degeneration
- Head and neck cancer
- Cancer of the bladder

"The History of Photodetection and Photodynamic Therapy", Ackroyd, R.; Kelty, C.; Brown, N.; Reed, R. *Photochem. Photobiol.* **2001**, 74, 656-669.

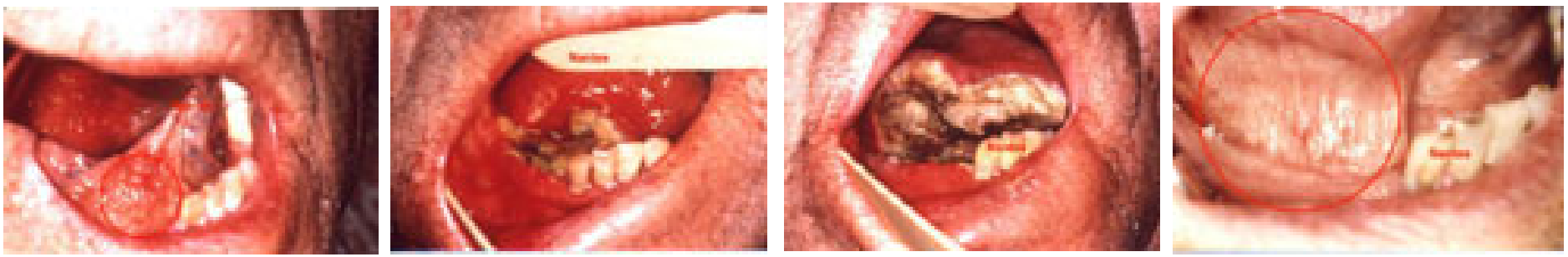



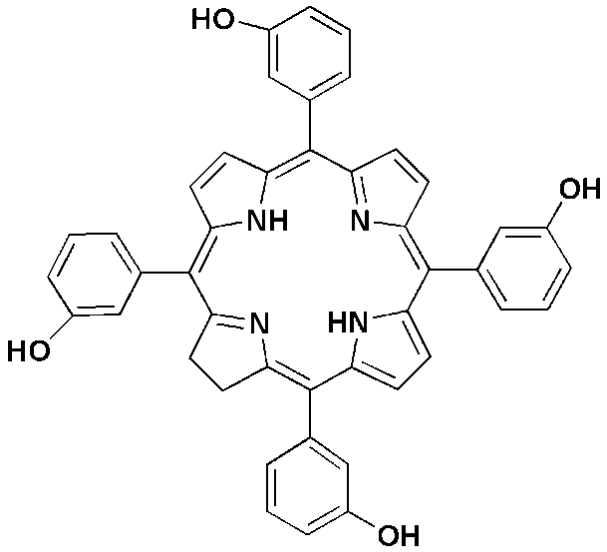
Chloe and Lindsay (A special issue: An invited review in honour of Prof. Karen J. Brewer of Virginia Tech, R.I.P.):

Smith, Chloe B.; Days, Lindsay C.; Alajroush, Duaa R.; Faye, Khadija; Khodour, Yara; Beebe, Stephen J.; Holder, Alvin A. "Photodynamic Therapy of Inorganic Complexes for the Treatment of Cancer." *Photochem. Photobiol.* **2021**, accepted for publication.
DOI: https://doi.org/10.1111/php.13467

ENT Squamous Cell Carcinoma Treated with *Meta*-tetrahydroxyphenylchlorin (*m*-THPC) PDT



Before | 24 hours | 7 days | 4 months

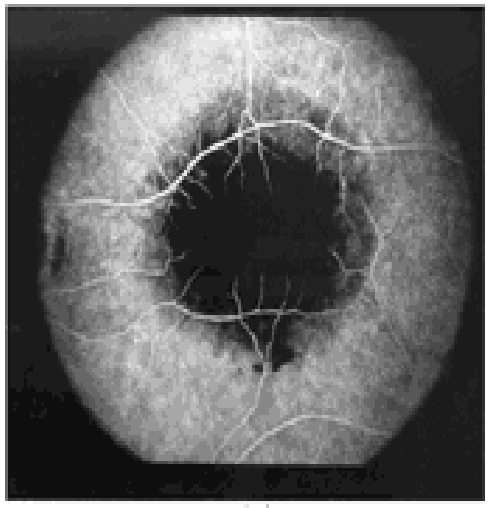


m-THPC

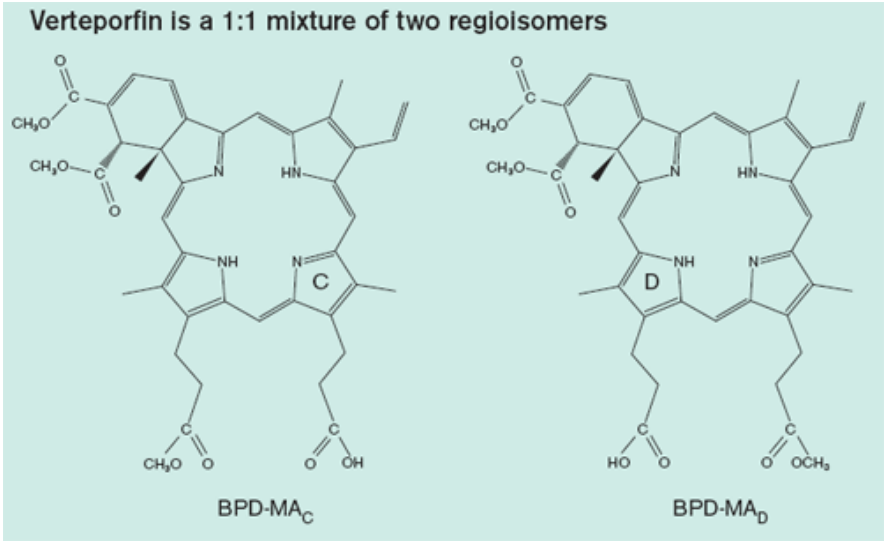
http://www.sante.univ-nantes.fr/med/laser/an/pdteffects.html

Age-Related Macular Degeneration Before and After Treatment with Verteporfin

(a)



(b)



Photos provided by QLT Phototherapeutics and Jason Slakter, MD.

Therapeutic Advantages of PDT

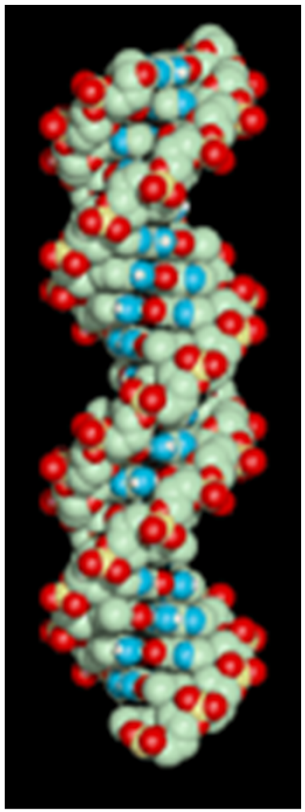
- PDT is less invasive than surgery
- PDT can be targeted very precisely
- Unlike radiation, PDT can be repeated several times at the same site if necessary
- PDT may result in less scarring

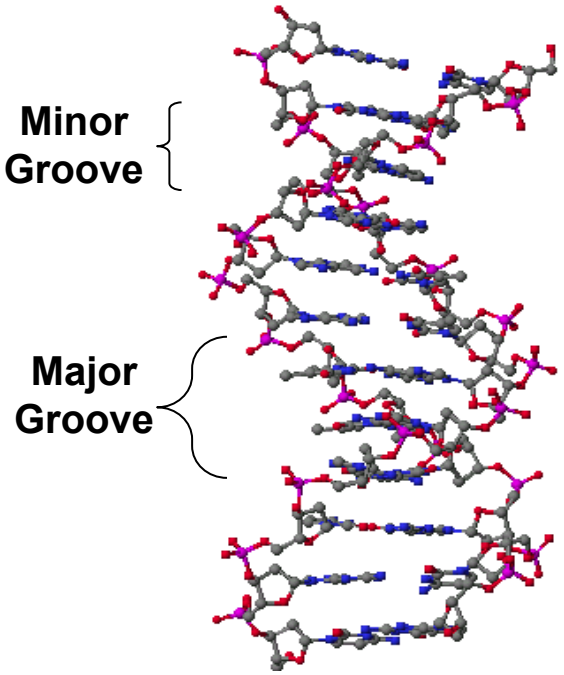
Influence of Vanadium and Other Metals on DNA

- Cytotoxic activity results from interaction with DNA.

- **Modes of interactions of metal complexes with DNA:**
  - **Ion-pairing**
  - **Non-covalent**
  - **Covalent**

- e.g., Ru, Pt, Cu, Ni, Au, Sn, Fe, Ga, and V.





Double-stranded DNA
(the β-form)

Kowol, C. R.; Eichinger, R.; Jakupec, M. A.; Galanski, M.; Arion, V. B.; Keppler, B. K. *J. Inorg. Biochem.* **2007**, *101*, 1946.

Abbreviations of Terminal and Bridging Ligands

pbt = 2-(2'-pyridyl)benzothiazole

tpphz = tetrapyrido[3,2-*a*:2′,3′-*c*:3″,2″-*h*:2‴,3‴-*j*]phenazine

$phen_2DTT$ = 1,4-bis(1,10-phenanthrolin-5-ylsulfanyl)butane-2,3-diol

MeATSC = 9-anthraldehyde-*N*(4)-methylthiosemicarbazone

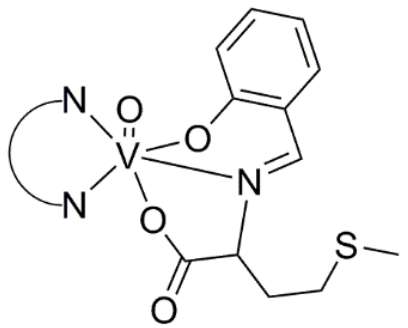
N-ethhymethohcarbthio = (*E*)-*N*-ethyl-2-(4-hydroxy-3-methoxybenzy-lidene)hydrazinecarbothioamide

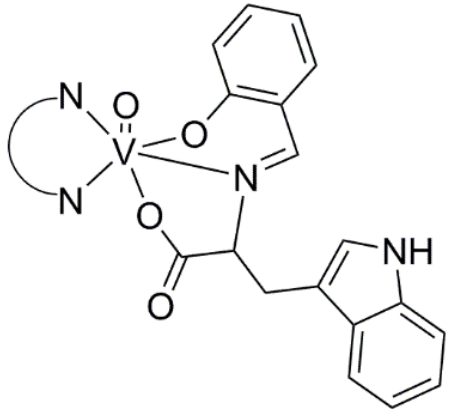
acetylethTSC = (*E*)-*N*-ethyl-2-(1-(thiazol-2-yl)ethylidene)hydrazine-carbothioamide

sal-*L*-tryp = *N*-salicylidene-*L*-tryptophanate

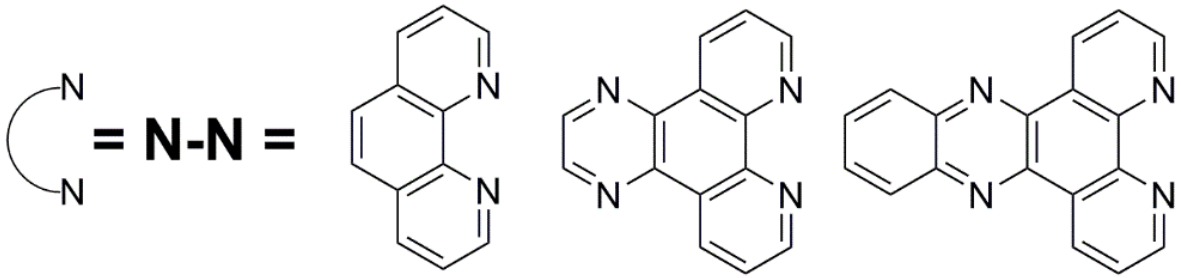
Holder, A.A.; Taylor, P.; Magnusen, A.R.; Moffett, E.T.; Meyer, K.; Hong, Y.; Ramsdale, S.E.; Gordon, M.; Stubbs, J.; Seymour, L.A.; Acharya, D.; Weber, R.T.; Smith, P.F.; Dismukes, G. C.; Ji, P.; Menocal, L.; Bai, F.; Williams, J.L.; Cropek, D.M.; Jarrett W.L. *Dalton Trans.* **2013**, 42, 11881–11899.

Vanadium(IV) PDT Agents





[VO(sal-*L*-met)(N-N)] **[VO(sal-*L*-tryp)(N-N)]**

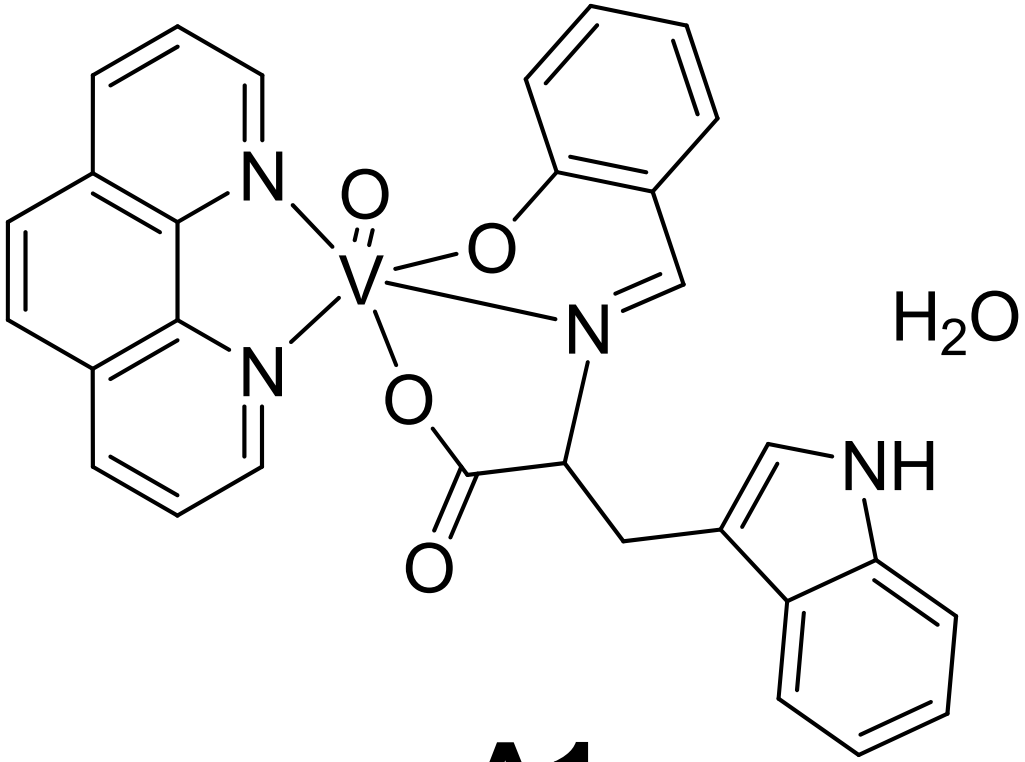


phen **dpq** **dppz**

dpq = dipyrido[3,2-d:2',3'-f]quinoxaline and dpphz = dipyrido[3,2-a:2',3'-c]phenazine

Sasmal, P.K.; Patra, A.K.; Nethaji, N.; Chakravarty, A.R. *Inorg. Chem.* **2007**, 46, 11112.

Structure of [VO(sal-*L*-tryp)(phen)]•H_2O



A1

Sasmal, P.K.; Patra, A.K.; Nethaji, N.; Chakravarty, A.R. *Inorg. Chem.* **2007**, 46, 11112.

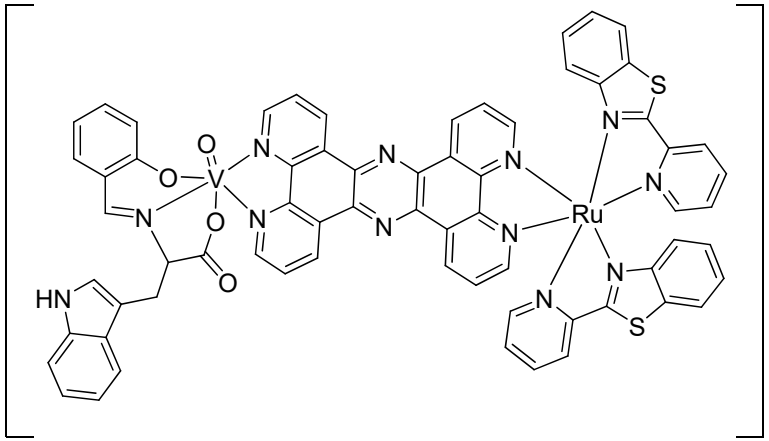
In Vitro Studies With Complexes 3 and 4 At 740 nm

They were used as chloride salts on the following:

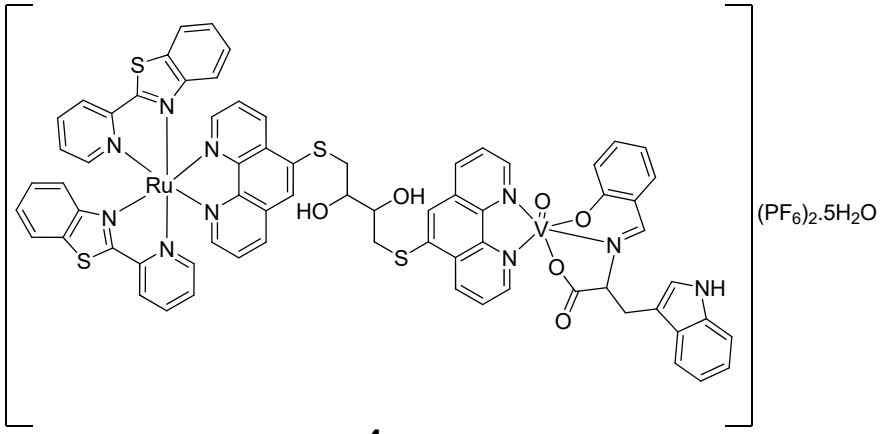
Melanoma cancer cells

Human fibroblast cells (non-cancerous)

Why use a wavelength of 740 nm!!

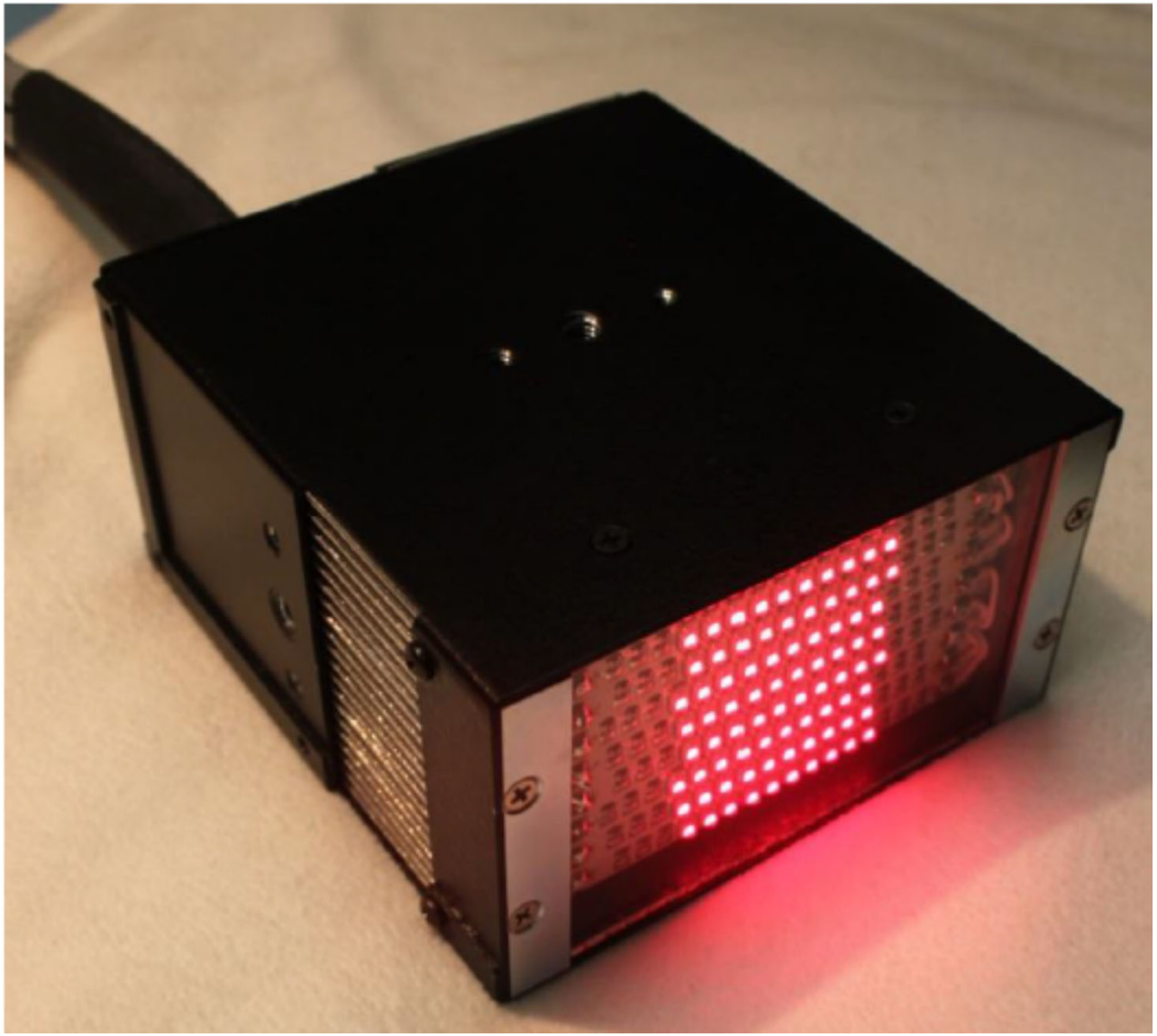


3

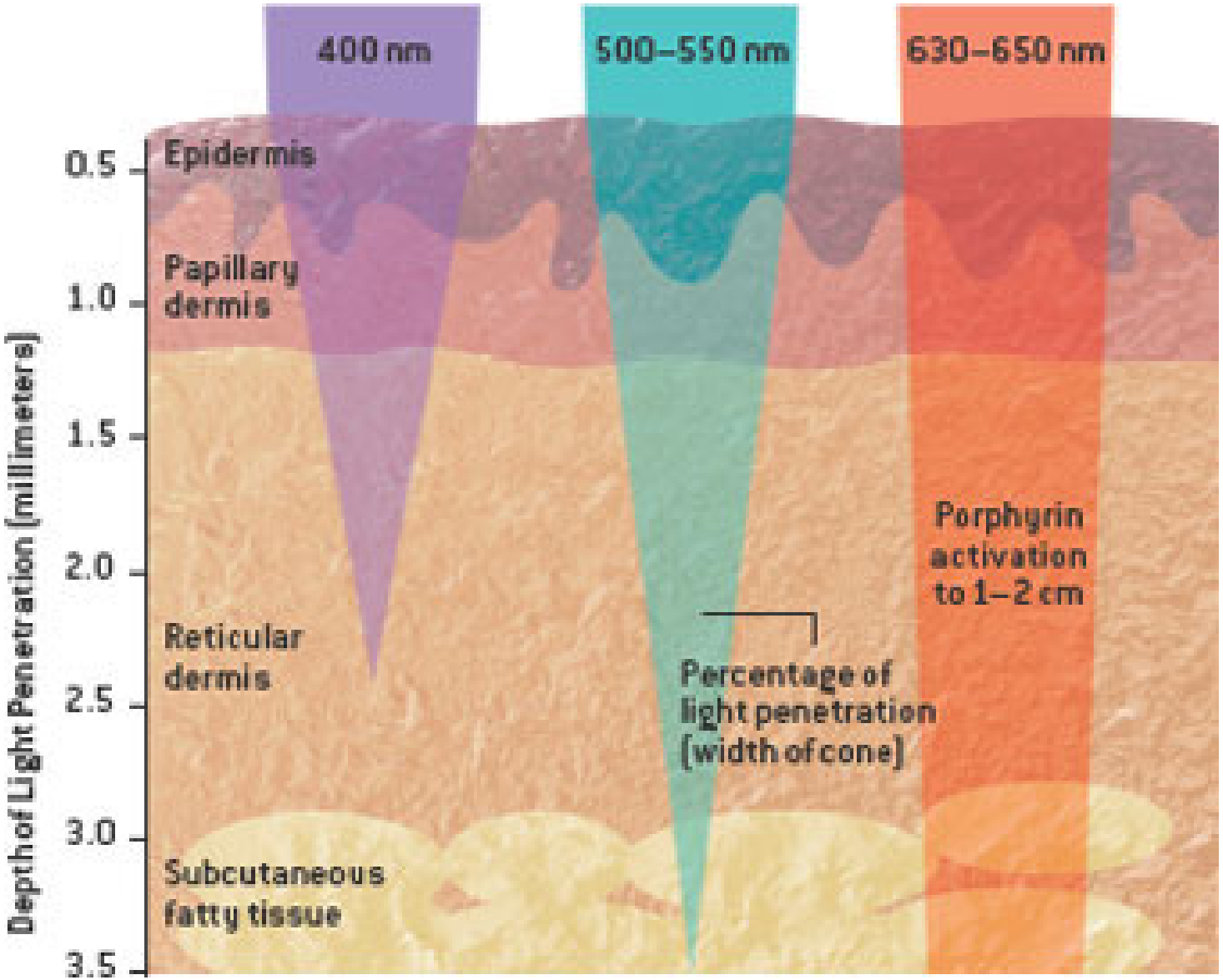


4

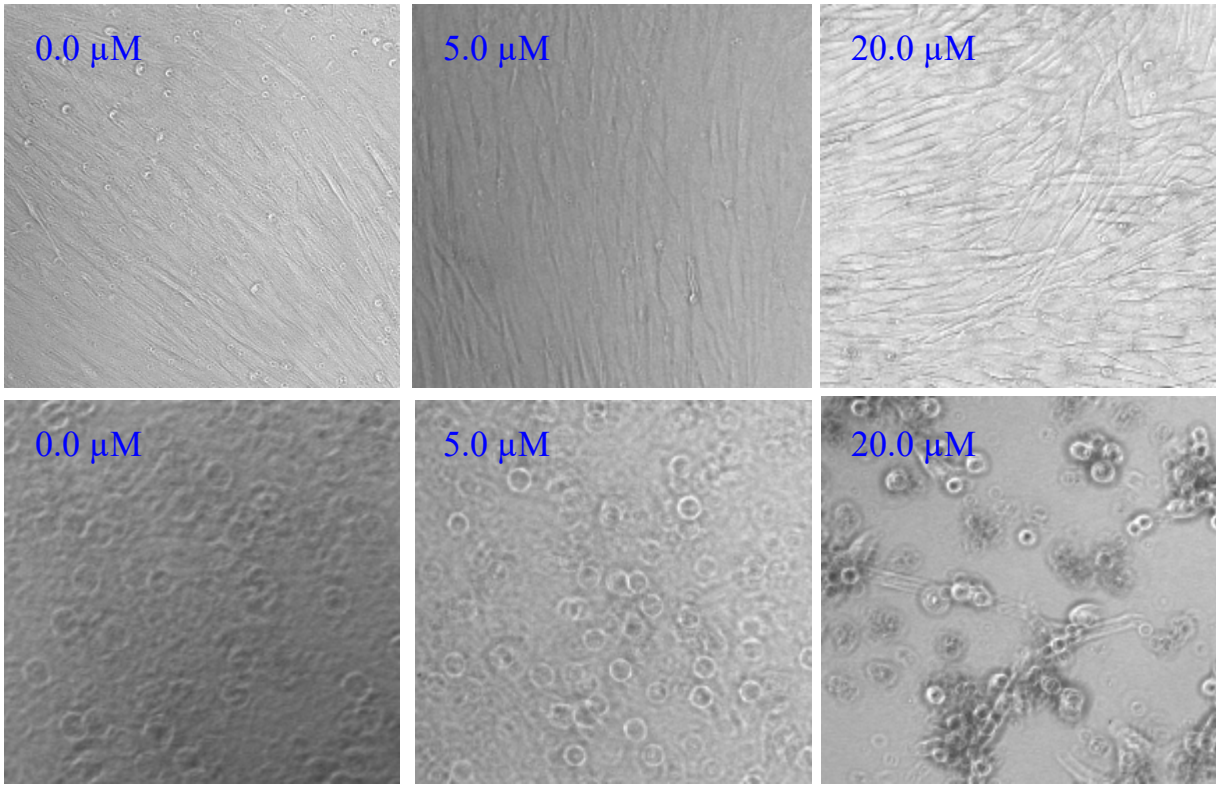
A Photo of the 740 nm LEDs



Depth of Light Penetration

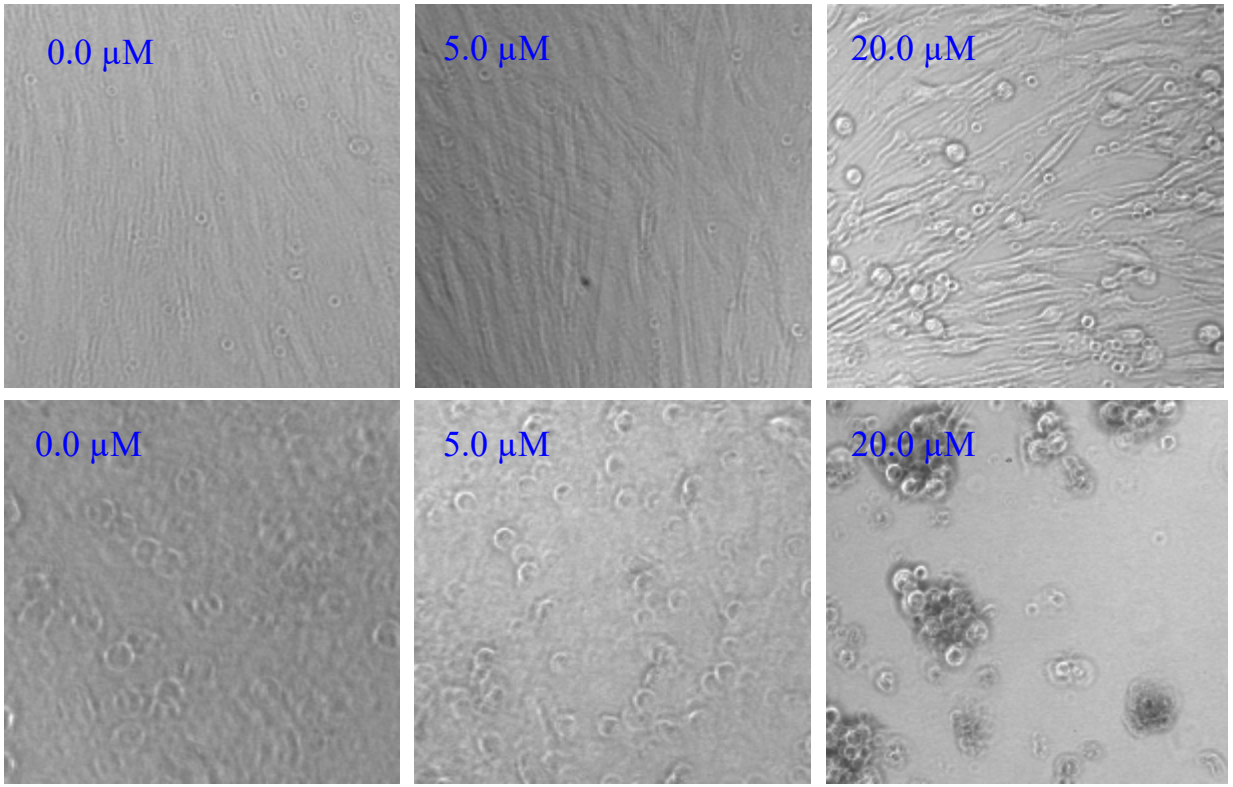


Light Toxicity with Complex 3 As a Chloride Salt



Upper panel = HFF, Lower panel = A431

Light Toxicity with Complex 4 As a Chloride Salt

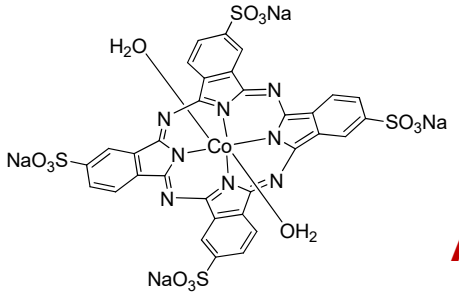


Upper panel = HFF, Lower panel = A431

IC_{50} Values from the MTT Assay (Dark Toxicity)

Complex	A431 $IC_{50}/\mu M$	HFF $IC_{50}/\mu M$
AH2	$1000 \leq IC_{50} \leq 2000$	>2000
[VO(sal-*L*-tryp)(phen)]•H_2O	41.62 ± 5.8	63.13 ± 28.27
3	41.25 ± 7.6	100.7 ± 17.7
4	48.6 ± 13.1	204.37 ± 45.1
cisplatin	40.08 ± 11.52	81.97 ± 8.92

A431 = human epidermoid carcinoma cells
HFF = human skin fibroblast



AH2

sodium diaqua-4,4',4",4'"tetrasulfophthalocyaninecobaltate(II)

Conclusions

- Our PDT agents with Ru(II) and V(IV) metal centres are selective against melanoma and not toxic to HFF.

- Using spectroscopic techniques the DNA has been identified as a target of $[Co(phen)_2(MeATSC)](NO_3)_3 \cdot 1.5H_2O \cdot C_2H_5OH$ with a moderate binding strength

- Screening of the chemotherapeutic potential of this drug gave a calculated IC_{50} = 34 μM, showing moderate anti-cancer activity in a highly metastatic TNBC cell line

- Studies indicate the caspase cleavage is necessary to facilitate cell death. Taken with the spectroscopic and mitochondrial data, it is suggested that the intrinsic apoptotic signaling pathways is the predominate cell death mechanism

- As an alternative regulated cell death (RCD) mechanism, the autophagic signaling pathway is also activated following exposure to the compound

- We were unable to detect any synergism with nsPEFs under the employed conditions

My Advice For All of Us

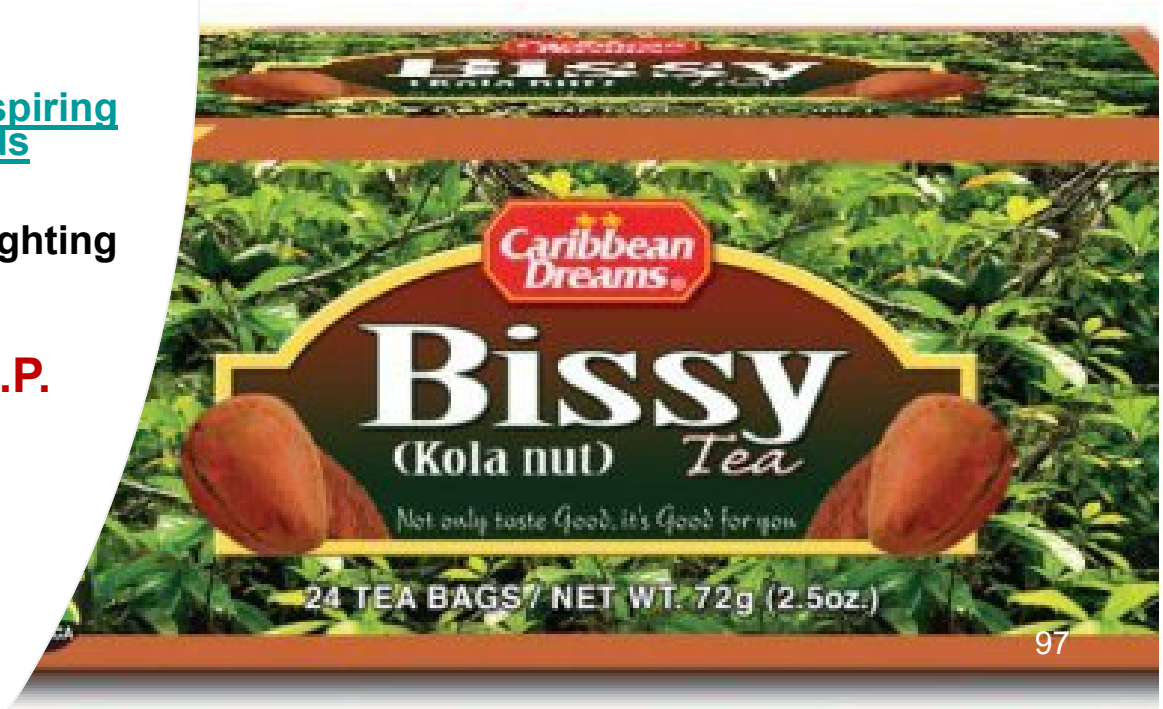
- Mammograms
- PSA tests and digital rectal examination
- Colonoscopy
- Other cancer detection techniques
- Diet and exercise
- Processed meats, WHO October 26, 2015 statement
- No stress
- Clean water, workforce safety, and the environment
- Follow the rules and use commonsense against COVID-19

Notes

- We can use some of our complexes to fight breast cancer and melanoma
- More research is yet to be carried out, but guess what my high school friend used to fight COVID-19?

Inspirations For You to Fight

- Dr. Sonia Peter's **Biocultural Education and Research Programme**
- Alvin Holder under the breadfruit tree
- A British brush with coronavirus in Barbados Today
- **Watch: George Jones' inspiring acceptance speech at CNCF Awards**
- **What my cousin went through fighting COVID-19 with herbs**
- **My advisor/father/mentor, R.I.P.**
- **Click here**



In His Honour, R.I.P.

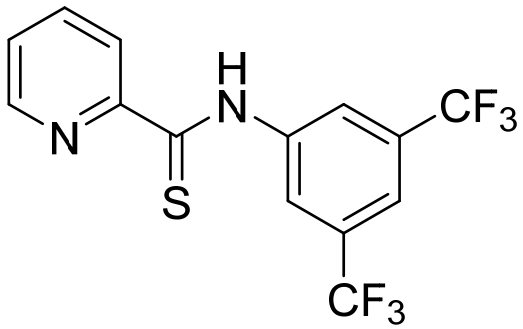
- Holder, Alvin A. “Sustaining a legacy in STEM, the Prof. Tara Prasad Dasgupta way: The role of a mentor in our lives .” *Inorg. Chim. Acta* **2021**, 521, 120304.

DOI: https://doi.org/10.1016/j.ica.2021.120304

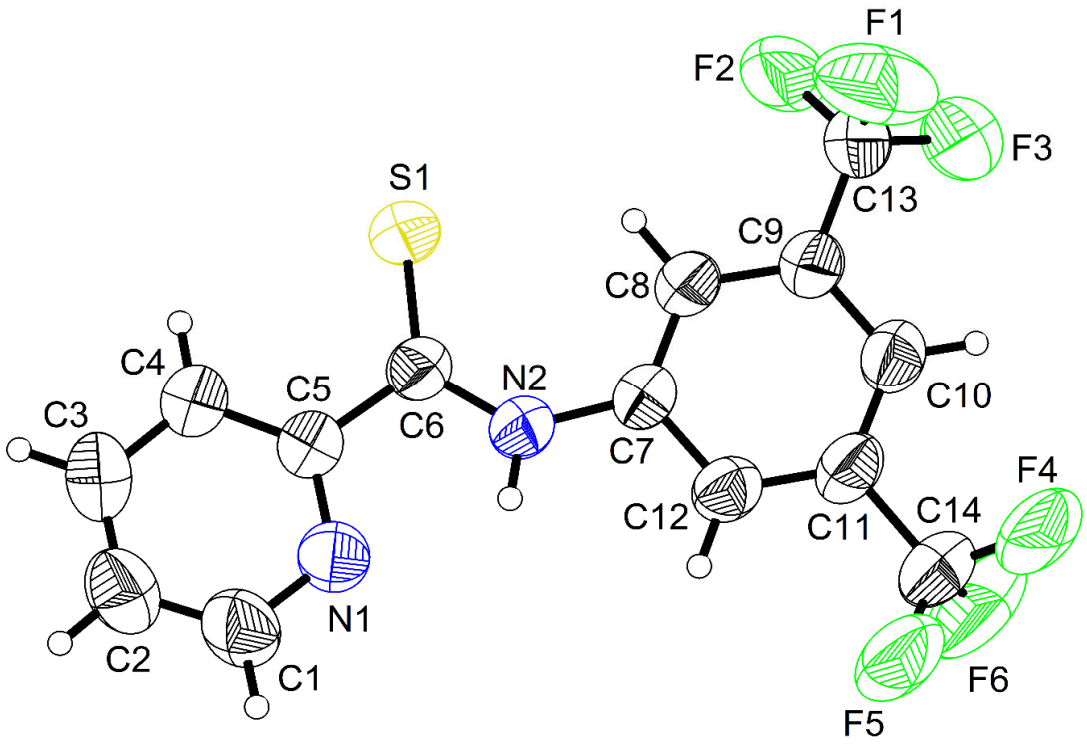
Thanks UNTHSC, Harlan, and Dr. Basha

Thank You!!!

An ORTEP Diagram of A Novel PCA



PCA-$(CF_3)_2$



A *N*-substituted-pyridine-2-thiocarboxamide (PCA)

Bullock, J. L., Jr. Synthesis and Mechanistic Investigations of Transition Metal Complexes and Ligands for Chemotherapeutic Applications. M.S. Thesis, Old Dominion University, 2016.

Mentoring

Raj and Michael are the PILLARS of my research group

What are students' perspectives of effective:

- *My current advisor is very down to earth and places everything into perspective. Be it research, classes or professional growth. He doesn't force his opinion of these things on me, but allows me to make my own priorities and live with the consequences*

- *I value my advisor's devotion to his graduate students--he wants us to succeed, learn to do research well, reach lofty goals, and graduate in a reasonable amount of time. ...I value the faculty's commitment to graduate students' work and quality of life*

Excerpts taken from a document entitled "*How to Mentor Graduate Students: A Guide for Faculty*".

Dr. Carol Fierke, Dean of the Rackham Graduate School, Vice Provost for Academic Affairs

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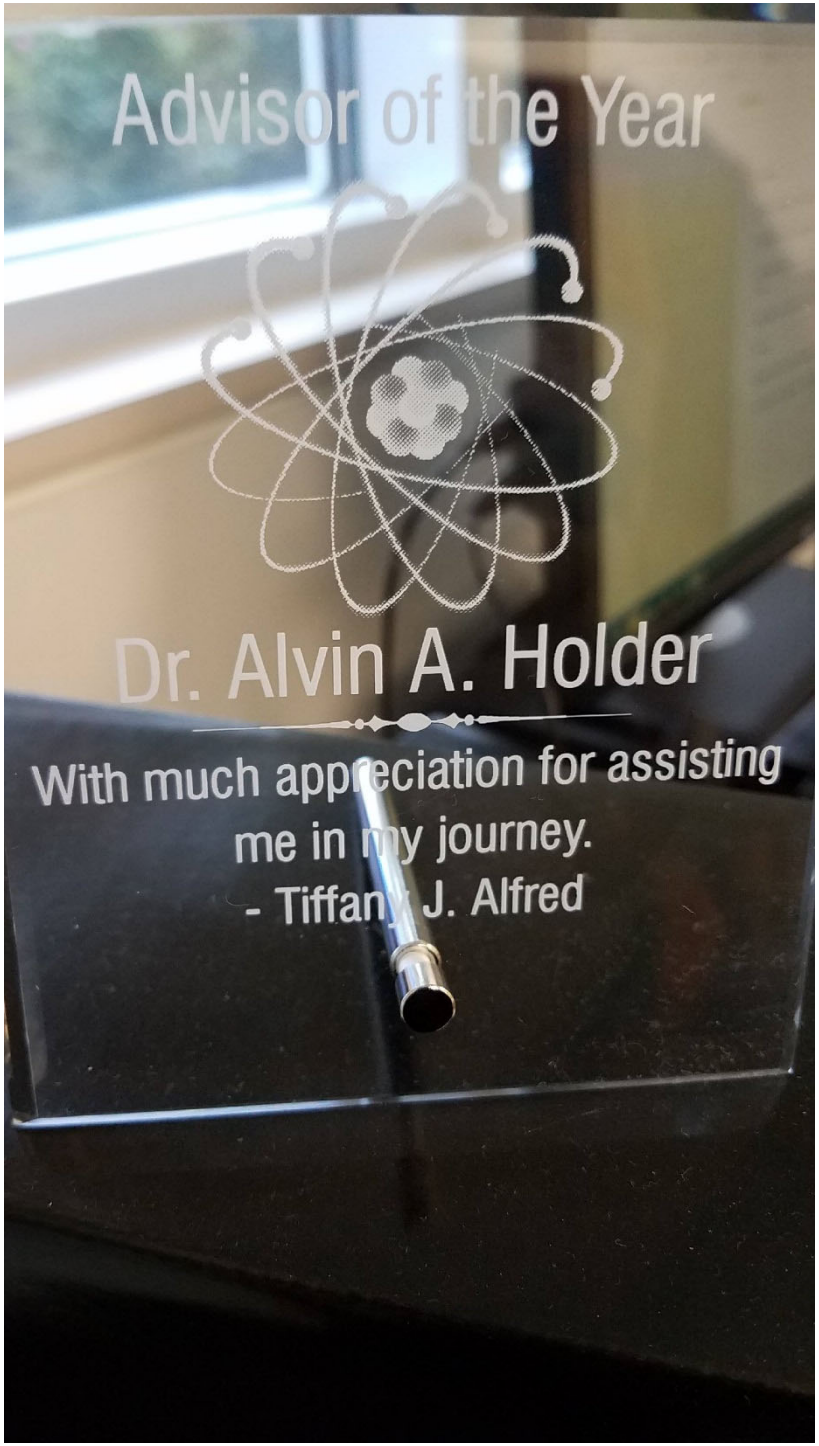
What Makes Us Proud

Tiffany J. Edwards, a former student of NSU:

- Half Guyanese
- Half Jamaica
- Half Indian descent
- Half African descent
- Worked with Raj in summer 2016
- 09/27/16: A partial Annual Biomedical Research Conference for Minority Students (ABRCMS) Student Travel Award to attend the Annual Biomedical Research Conference for Minority Students, Tampa, Florida, November 9-12, 2016
- Now a Pharm.D. student at Hampton University




WHAT
a
gift
YOU
are.

Too often

life just rolls along

and we don't take the time

to tell those

who have touched our lives

in some special way

how much they mean…

You have such a good heart.

And I want to be sure you know

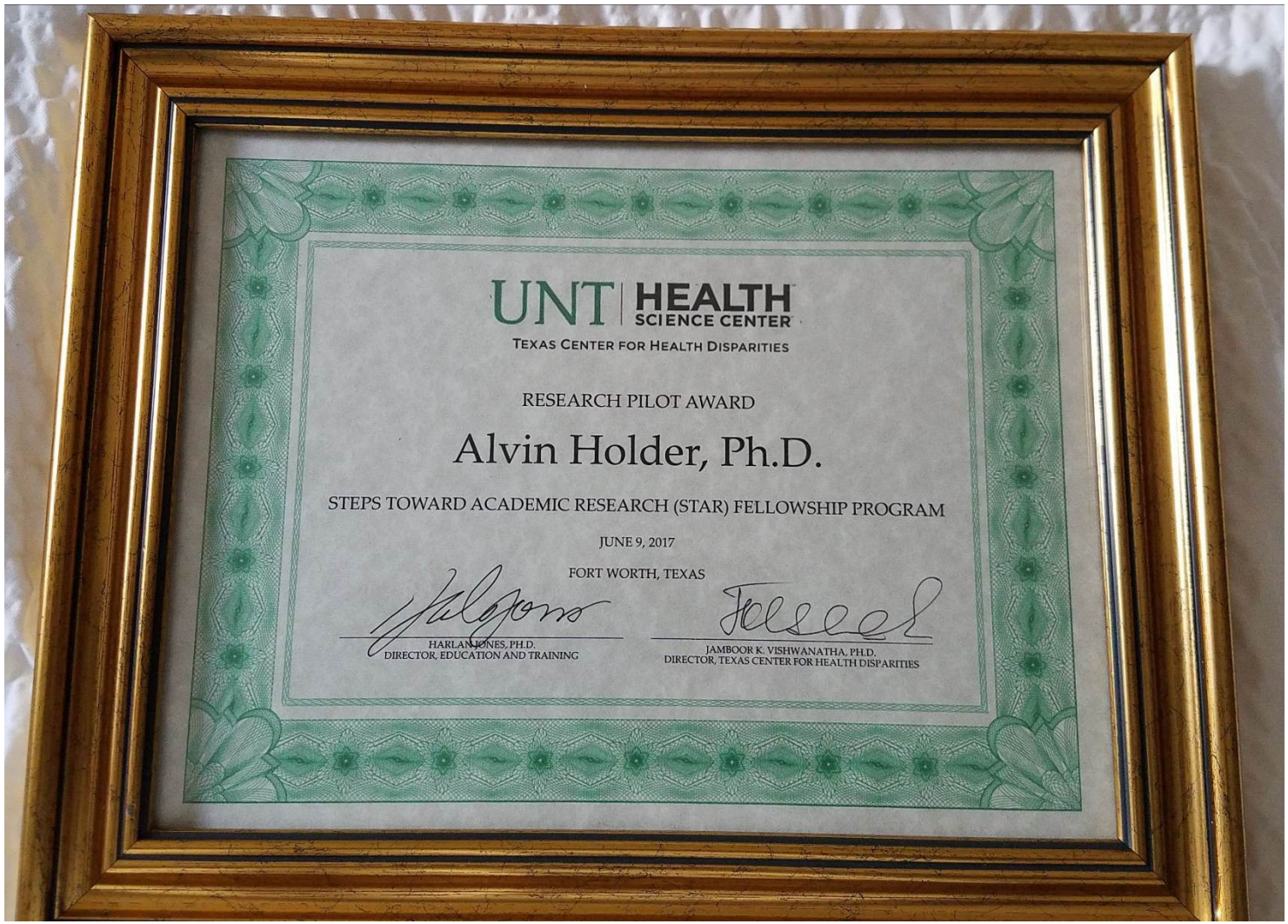
how much you are appreciated

and what a gift you truly are.

Dr Holder,
This is just a little token of my appreciation for all the help and advice you've given me. I really enjoyed the research group and learned a lot. I wish there were more caring people like you, the world would be a much better place. I don't know what the future holds for me, but I must say that this is a great start. Have a wonderful Summer.

Kristen Burley

12th Annual Conference on Health Disparities, Evidence-Based Approaches to Reducing Cancer Health Disparities: Discover, Develop, Deliver, & Disseminate, June 8-9, 2017, University of North Texas Health Science Center, Fort Worth, Texas



A Potluck Among Themselves In Summer 2016


northern
rock

Past Group Members