INTERNATIONAL
IV NUTRITIONAL THERAPY
GLOBAL PHYSICIAN EDUCATION

Germanium, Alpha Lipoic Acid and Lipoic-Mineral Complex

(Poly MVA)

Advanced IV Therapy

by

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Germanium - “Ekasilicon”

- Metalloid
- Appears metalic
- Non metal properties
- Column Group IV A (Carbon, Silicon, Germanium, Tin, Lead)
- By product of zinc ore processing:coal
- Trace mineral

- Cystaline structure same as a diamond

inorganic

- >130 yrs ago
  - Dmitri Mendeleev. theorized its existence and properties according to the Periodic Law of Elements.
- 1886
  - discovery through German chemist Clemens Winkler in Argyrodite Ore.
- 1930’s
  - Several researchers studied the microbial, medicinal and botanical functions.
- 1948
  - Bell Laboratories used Germanium as a semiconductor

inorganic

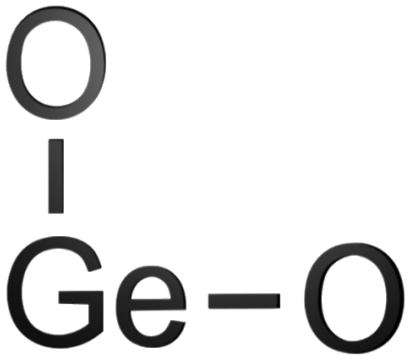
- More abundant in the Earths crust than gold, silver, mercury and cadmium
- Classified as a semi-metal (essential) with carbon, lead, silicon, and tin
- Electrical properties between metal and insulator
- Toxicity
  - Low in mammals (But, NOT the form used in IV Therapy!)
  - High in certain strains of bacteria

Inorganic

- Uses
  - Radios
  - Infrared scopes
  - Wide angle camera lenses
  - Microscope lenses
  - Silicon-germanium is becoming a very popular semiconductor faster than silicon alone
  - Solar cells

inorganic

- Germanium dioxide
  - germanium oxide
  - germania



inorganic

- Safety and Toxicity
- The ‘other’ germanium
  - Inorganic germanium is harmful in large doses
  - Typically used for topical applications
  - Germanium dioxide or germanium citrate lactate is nephrotoxic/ and pulmonary tox

inorganic

- Renal dysfunction/failure
  - Vaculor degeneration of renal tubular epithelial cells
  - Ø proteinuria,hematuria or glomerular change
- Central and peripheral nerve toxicity
- Cardiomyopathy
- Liver damage
- Bone marrow

Inorganic

- Symptoms
  - Anemia
  - Weight loss
  - Fatigue
  - Gastrointestinal dysfunction
  - Kidney dysfunction
  - Muscle weakness
    - skeletal

Organic

- **CURRENTLY NOT AVAILABLE IN USA**

Kazuhiko Asai

- Developed research and clinical use (germanium by product of coal)
  - "I have been led to believe the existence of something in germanium that cannot be fully explained in terms of science in its present stage of development, when I see that obstinate diseases for which modern medicine is powerless are successfully cured by our germanium therapy." Kazuhiko Asai

- 1967, Mironov synthesizes water-soluble organic form

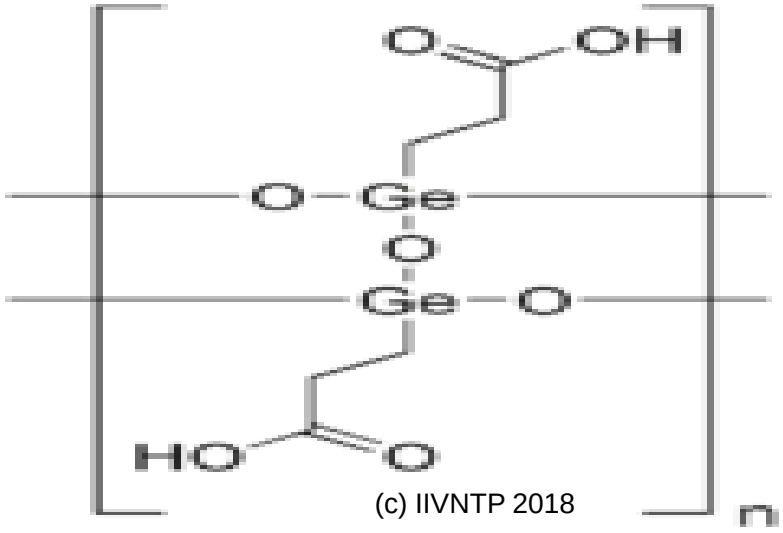
organic

- Polymorphic - can manifest as differing crystalline, particle size and weight distributions in solid form. In aqueous solution they are stable and identical.
- Ubiquitous in seawater, plants, and animal blood and tissues as an essential trace element.
- Plants with the most abundant amounts
  - Shelf fungus/Trametes Cinnabarina 800-2000 ppm
  - Garlic 754ppm
  - Ginseng 250-300ppm
  - Sanzukon/Codonopsis 257ppm
  - Sushi/Angelica pubescens 262ppm
  - Bandai Moss 255ppm
  - Waternut/Trapa japonica 239ppm
  - Comfrey 152ppm
  - Boxthorne Seed/Lycium 124ppm
  - Wisteria gall 108 ppm
  - Lithospermum officinale 88ppm
  - Aloe 77ppm
  - Chlorella 76ppm
  - Bandai Udo/Aralia cordata 72ppm
  - Pearl Barley 50ppm

  (Asai 1980)

organic

- Germanium sesquioxide
  - Bis (2-carboxyethylgermanium) sesquioxide (CEGS)
  - 2-carboxyethylgermasesquioxane
  - Propagermanium



organic

- LD 50 >6.3g/kg body wt in mice
  - 10g/kg in rats
  - 750mg/kg qd over 1 yr in rats (Asano etal, 1994)
- No acute or chronic toxicity has been associated with this form oral or IV.
- Organic Sesquioxide germanium appears safe at large doses.
  - Increases oxygen due to its affinity for Hydrogen (dehydrogenizing-detoxing)
  - Carrying oxygen to hypoxic tissues

Organic
Indications

- Cancer and Metastasis
  - Tumor necrosis
- Rheumatoid Arthritis
- Lung dz
  - Asthma, Pneumonia,
- Depressive Psychosis mental d/o
- ‘Stress’
- Eye Diseases
- Viral Diseases
- Cardiac / HTN
- Adrenal
- Epilepsy
- Prostate
- Dermal
  - Eczema,shingles,warts
- Thyroid
- G.I.
- Pain
  - external applications (Asai, 1980)

organic

- Affects enzyme activity
  - Activation
  - Inhibitory
- Elevation in SOD
- enhances NK activity
- induces IFN-g
  - inhibit tumor growth
- Increase development of T-cells
- Cytoplasmic enzyme is inhibited:
- LDH (lactate dehydrogenase)
- Inhibit viral HSV-1

- Influence on the DNA/RNA
- Enhancement of semiconductor properties regulating gene expression
- Apoptotic

organic

Contraindications/ Precautions

- Renal failure
- With nephrotoxic drugs
- Diabetes

Caution:

- Children
- Pregnancy
- Nursing Mothers

organic

- Side Effects with high dosing
  - Emesis (GI effects common even in IV use – Dose dependent)
  - Nausea
  - Diarrhea
  - Dermal lesions/Rashes
  - Neurological
  - Resolves with discontinued use
    - Caution to check labs if long term use

organic

- Dosages (Oral)
  - Capsules 25 mg, 150 mg
  - Subinqual Tablets 25 mg, 150 mg
  - No toxic effects with 120mg/kg/day of germanium sesquioxide over a 24 wk period
  - Prevention: 150 mg daily
  - Serious Illness: up to 2000 mg daily

  - Human studies have shown no side effects with 25, 50, and 75 mg/kg dosages.

organic

Intravenous

- 100mg/ml
  - Compounded per order
  - Typical 100mg/ml 1-5cc
- Excretion
  - 24-72 hours
  - Water soluble

Germanium: A rationale for intermittent – pulsed – IV then oral dosing in cancer patients:

Tanaka N, et. al. *Augmentation of NK activity in peripheral blood lymphocytes of cancer patients by intermittent GE-132 administration.* Gan To Kagaku Ryoho. 1984 Jun;11(6):1303-6.

Abstract

The natural killer (NK) activity of peripheral blood lymphocytes from 18 cancer patients was studied prior to and after multiple administration of organo-germanium compound (Ge-132).

In successive oral administration of Ge-132 at a dose of 1000 mg/day for 10 days, NK-activity of patients was augmented at 3 days, but by 10 days, depression of NK activity was observed in all cases. In intermittent oral administration of Ge-132, however, more than half of the patients with augmented NK activity at day 3 maintained the high activity level at day 10.

This result suggests the superiority of intermittent administration of Ge-132 for clinical use.

PMID: 6732257 [PubMed - indexed for MEDLINE]

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- Griffin, Thomas, Germanium and Cancer, 2004 May 25

GLYCYRRHIZA GLABA

- **Licorice**
- Medicinal parts:
  - Roots and dried runners

Indications and Usage:

- Liver Cancer
- Hepatitis (B)
- Anti-viral
- PMS
- Addison’s disease
- Inflammation
- Herpes simplex
- Peptic Ulcers
- Abortifacient

Indications and Usage:

- HIV and AIDS: Nine symptom free HIV positive patients received 200-800 mg glycyrrhizin IV daily for 8 weeks. The group showed increased T-helper counts, better CD4:CD8 ratios and better liver function.[2] Six AIDS patients in another study received 400-1600 mg glycyrrhizin IV daily for 30 days, after which 5 of the six exhibited reduced or negative p24 antigen which indicates active disease.[3]
- Hepatitis: Chronic hepatitis B was treated with an IV combination product containing 0.2% glycyrrhizin, 0.1% cysteine and 2.0% glycine in saline. The product improved liver function and reduced liver enzyme levels. About 40% of patients experienced complete resolution.[4]

- HOW SUPPLIED
  - Glycyrrhizic Acid, 8 mg/ml, 30 ml vial, preservative free
    - General dose: IV 16 mg – 80 mg
    - Higher doses for acute or severe chronic conditions i.e.:
    - Liver cancer, hepatitis
    - 200-1600 mg glycyrrhizin have been given safely IV for 30-60 days.

Pharmacology

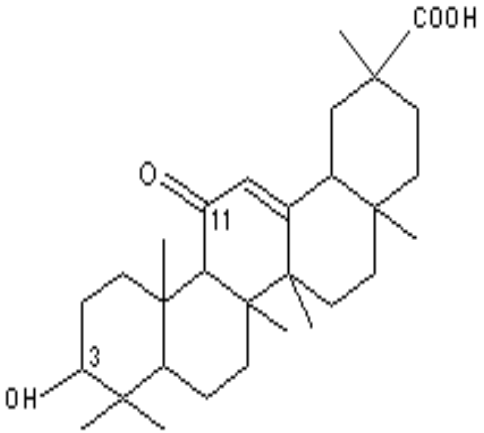
- Most of the pharmacology focuses on glycyrrhizin and glycyrrhetinic acid
  - there are may other components like flavonoids that may have pharmacological effect.
    - Estrogenic activity
    - Pseudoaldosterone activity
    - Antiallergic and anti-inflammatory
    - Antiviral and immunostimulatory
    - Antibacterial
    - Antihepatotoxic

Pharmacology

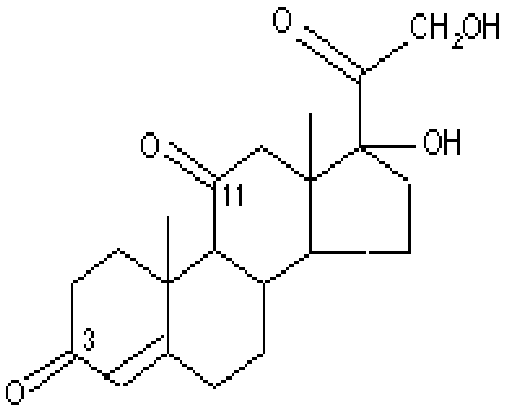
- Glycyrrhetinic acid
  - expectorant and antitussive properties (Chandler,1985)
- inhibits the enzymes (15-hydroxyprostaglandin dehydrogenase & delta 13-prostaglandin) that metabolize the prostaglandins, PGE2 and PGF2alpha to their respective 15 keto-13,14-dihydro metabolites which are inactive.
- 3-Beta-D-(monoglucuronyl)18-beta-glycyrrhetinic acid, a metabolite of glycyrrhetinic acid inhibits 11-beta-hydroxysteroid dehydrogenase which converts active cortisol to inactive cortisone in the kidneys

Pharmacology

- Chemical structure similar to cortisone
- Inhibits:
  - Inhibits renin-angiotensin aldosterone
  - DNA and RNA viruses
  - Liver cell injury due to chemical toxins



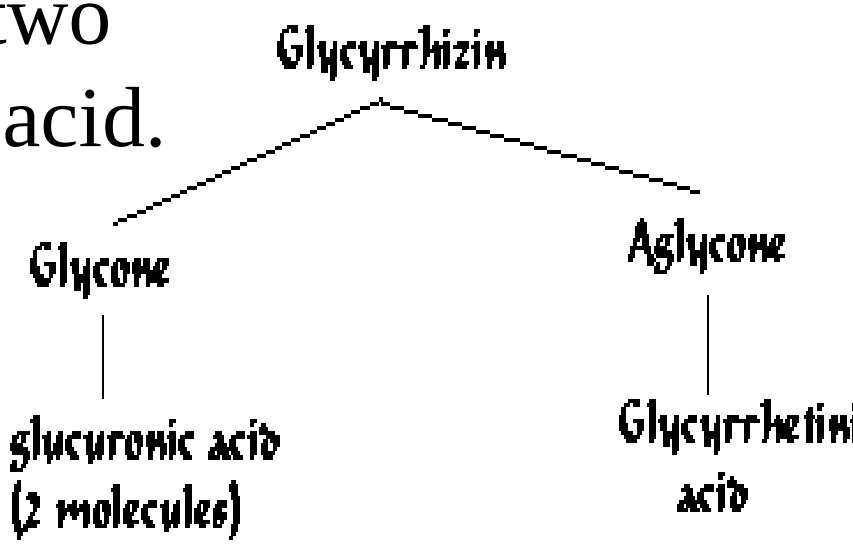
glycyrrhetinic acid



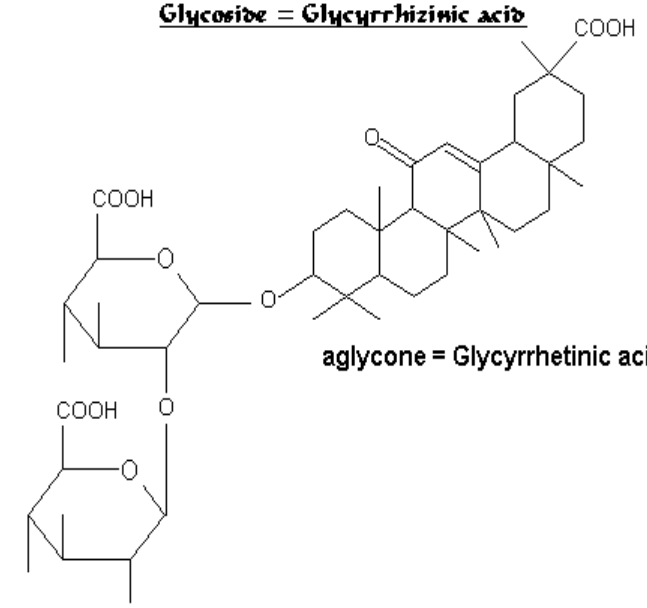
cortisone

Pharmacology

- Glychirizzhinic Acid
- With hydrolysis, the glycoside is converted to the aglycone glycyrrhetinic acid plus two molecules of glucuronic acid.

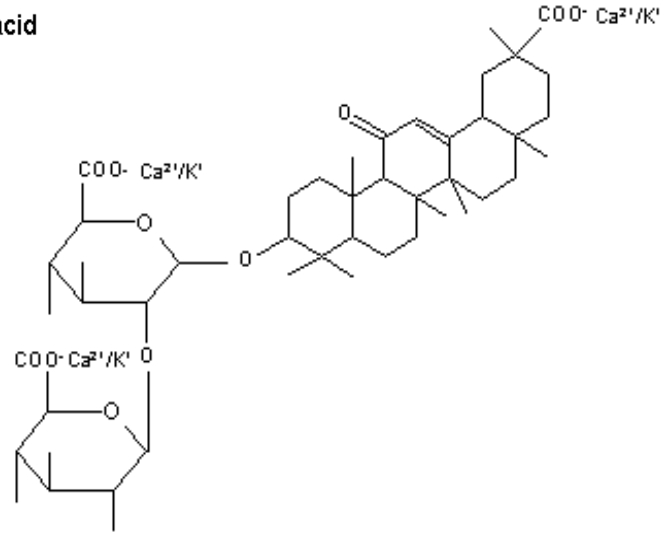


Glycoside = Glycyrrhizinic acid



aglycone = Glycyrrhetinic acid

2 molecules of glycone = glucuronic acid



Glycyrrhizin = Ca^{2-} & K^{-} salts of Glycyrrhizinic acid

- ADVERSE REACTIONS TOXICOLOGY
  - More than 3 grams per day licorice root for more than 6 weeks, or more than 100 mg per day glycyrrhizin may cause:
    - Sodium and water retention
    - Hypertension
    - Hypokalemia
    - Suppression of rennin-aldosterone system
    - Prolonged use may lead to cataracts
  - Monitoring of blood pressure and electrolytes and increasing dietary potassium intake are suggested.
- CONTRAINDICATIONS
  - Patients with history of hypertension
  - History of renal failure
  - Current use of digitalis preparations
  - Pregnancy: Not recommended due to estrogenic like action of its isoflavones
    - PGF2alpha stimulates activity of the uterus

INTRAVENOUS GLYCYRRHIZIN:

- Glycyrrhizin a.k.a. glycyrrhizic acid / glycyrrhizinic acid (GA) has great potential in the treatment of patients who have chronic viral illnesses and possibly in oncology.
- Data in humans shows it to be a safe agent [2] and helpful in Hepatitis C [1].
- Over a decade of clinical use has revealed no adverse events when used under standard dose and administration guidelines [3].

INTRAVENOUS USE GUIDELINES:

Dose: [1,2,3]

- Test dose at 40-60 mg IV on the first day
- Subsequent doses could increase to 240 mg if tolerated two times weekly

Administration:

- Intravenous dosing via either a central or peripheral line.
- Carrier solutions:
  - Dextrose 5% in Water (D5W) 100 to 1000 mL carrier solution
  - 0.9% normal saline (NS) or 0.45% (1/2NS) 100 to 1000 mL carrier solution
- Rate of administration: 60 to 180 minutes as tolerated by the patient
  - Monitor for signs of blood pressure elevation and electrolyte shifts which can be the first sign of a non-tolerated dose [3,4]
    - Dosing once to twice per week at the higher range avoids these concerns in most cases. [3,4]
  - For allergic / anaphylactic reaction treat per standard protocol.
- Other IV compatibility:
  - May be mixed with any water soluble vitamin / mineral IV solution [3]

Clinical Notes and Screening:

- Intolerance to oral GA is a caution and may exclude use in the IV setting
- Uncontrolled hypertension and sodium-potassium imbalance are cautions
- Lab studies:
  - CBC, Chemistry panel (Metabolic panel including electrolytes, bilirubin, AST/ALT/GGT, eGFR/BUN/CRE).
  - Follow blood pressure pre and post IV

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3. Anderson P, Cochran B. Personal experiences with the clinical use of intravenous substances. AMSA, BIORC and Private clinic data. Seattle Washington,2014

4. van Rossum TG, de Jong FH, Hop WC, Boomsma F, Schalm SW.'Pseudo-aldosteronism' induced by intravenous glycyrrhizin treatment of chronic hepatitis C patients. J Gastroenterol Hepatol. 2001 Jul;16(7):789-95.

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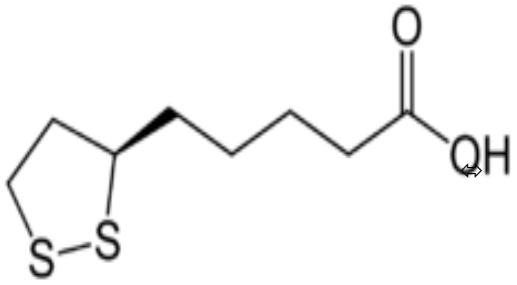
2. Mori, K. et al. The Present Status in Prophylaxis and Treatment for HIV Infected Patients with Hemophilia in Japan. Rinsho Byhori 37(11), 1200-1208, 1989.
3. Hattori T, et al. Preliminary Evidence for Inhibitory Effect of Glycyrrhizin on HIV Replication in Patients with AIDS. Antiviral Res 11(5-6), 255-261, 1989.
4. Acharya SK, et al. A preliminary Open Trial on Interferon Stimulator (SNMC) Derived from Glycyrrhiza glabra in the Treatment of Subacute Hepatic Failure. Ind J Med Res 98, 75-78, 1993.
5. Van Rossum T. G. J. et al Intravenous glycyrrhizin for the treatment of chronic hepatitis C : A double-blind, randomized, placebo-controlled phase I/II trial ,Journal of gastroenterology and hepatology **ISSN** 08159319 vol. 14, no11, pp. 1093-1099 (16 ref.) Wiley-Blackwell, Richmond, Aus. (1986) 1999
6. Georges-Louis Friedli, PgDip., MSc., PhD. http://www.sapogenin.info/index.html

Alpha Lipoic Acid

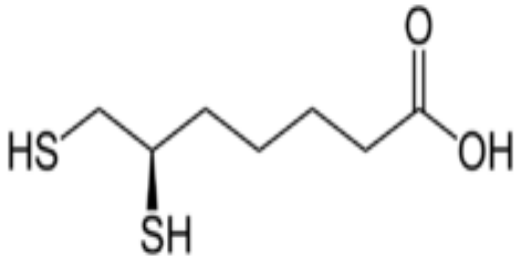
- AKA Thioctic Acid
- A naturally occurring compound that is synthesized in small amounts by living organisms - plants animals humans.

Shown it its oxidized and reduced state through its 2 thiol(sulfur) groups.

A LIPOIC ACID



DIHYDROLIPOIC ACID



ALA

- ALA is the oxidized from of dihydrolipoic acid (DHLA)
  - Scavenges hydroxyl radicals, singlet oxygen and hypochlorous acid.
  - Found in various concentrations in all muscles and internal organs
  - Potentially chelates heavy metals
  - Regenerates other antioxidants.

ALA

- Powerful Free radical scavenger
- A Fat soluble and water soluble anti-oxidant
  - creating easy oxygenation in all cells.
- A co-factor in the krebs cycle.
- A fatty acid containing two sulfur atoms.

The preventative and therapeutic role of ALA.

- Increases Glutathione levels in RBC's and lymphocytes
- Crosses the blood brain barrier
  - Through cysteine utilization
- Mobilizes (chelates) : Mercury, Arsenic, and cadmium

ALA

- Improves Peripheral neuropathy in diabetics
- PVD
- Glaucoma
- MS (myelin sheath protection)
- HIV
- Prevents radiation damage (nuclear)
- Antidote for poisonous mushrooms (amanita)

ALA

- R vs S: NO difference in intravenous metabolism and blood plasma concentrations.

- Oral: significantly increased concentrations are detected in the plasma when R form is used

ALA

- 40 to 100mg/mL

- IV infusion best in these ranges to infuse in 250cc of fluid
  - The safe dose range for ALA ranges from 40-600 mg
  - START AT LOW IV DOSE (40-80 MG) AND WORK UP SLOWLY.

- ALA has been known to have **increased adverse effects** when given as an IV push.

ALA

- 2000mg of the OLD formulation has been infused for DM peripheral neuropathy with favorable results. Newer formulations appear to be more potent so this dose may not be practical.

- Known to be metabolized in 2-4 hours

ALA - Drug/nutrient interactions

- Caution: Thiamine
  - May lead to **thiamine deficiency**
  - Note: blood sugar requires the utilization of thiamine during metabolism
- ALA causes an increase in the metabolism of glucose/blood sugar.
  - During exercise, dieting, energy requirements
  - Check blood sugar of diabetics on ALA
- Alpha-lipoic acid may lower levels of thyroid hormone – monitor thyroid function tests

ALA

- **Equipment:**
  - *** As glass is not readily available use B-Braun or like bags with low plasticizing content.**
- **Dark room or cover (ie: aluminum foil) over bottle/ tubing**
- **Precipitates with minerals**
- **Give in 0.9% Normal Saline or D5W**

ALA

- **Generally infused solo due to precipitation.**

- **Known to potentiate and regenerate**
  Vit C, glutathione, Vit E and CO-Q-10)a ‘master’ antioxidant.

ALA Research

Berkson BM, Rubin DM, Berkson AJ. Revisiting the ALA/N (alpha-lipoic acid/low-dose naltrexone) protocol for people with metastatic and nonmetastatic pancreatic cancer: a report of 3 new cases. Integr Cancer Ther. 2009 Dec;8(4):416-22.

Abstract: The authors, in a previous article, described the long-term survival of a man with pancreatic cancer and metastases to the liver, treated with intravenous alpha-lipoic acid and oral low-dose naltrexone (ALA/N) without any adverse effects. He is alive and well 78 months after initial presentation.

Three additional pancreatic cancer case studies are presented in this article. At the time of this writing, the first patient, GB, is alive and well 39 months after presenting with adenocarcinoma of the pancreas with metastases to the liver. The second patient, JK, who presented to the clinic with the same diagnosis was treated with the ALA/N protocol and after 5 months of therapy, PET scan demonstrated no evidence of disease. The third patient, RC, in addition to his pancreatic cancer with liver and retroperitoneal metastases, has a history of B-cell lymphoma and prostate adenocarcinoma. After 4 months of the ALA/N protocol his PET scan demonstrated no signs of cancer. In this article, the authors discuss the poly activity of ALA: as an agent that reduces oxidative stress, its ability to stabilize NF(k)B, its ability to stimulate pro-oxidant apoptosic activity, and its discriminative ability to discourage the proliferation of malignant cells. In addition, the ability of lowdose naltrexone to modulate an endogenous immune response is discussed. This is the second article published on the ALA/N protocol and the authors believe the protocol warrants clinical trial. **PMID: 20042414**

ALA Research

A PubMed search adds credence to an anti-tumor MOA and its use to decrease chemo side effects:

1. Ho YS, et al. Dihydrolipoic acid inhibits skin tumor promotion through anti-inflammation and anti-oxidation. Biochem Pharmacol. 2007 Jun 1;73(11):1786-95. Epub 2006 Dec 10.
2. Mythili Y, et al. Cytoprotective role of DL-alpha-lipoic acid in cyclophosphamide induced myocardial toxicity. Mol Cell Biochem. 2005 Aug;276(1-2):39-44.
3. Filatova NA, et al. Decrease in tumorigenic activity of murine hepatoma cells after treatment with antioxidants and melatonin. Tsitologiia. 2011;53(5):404-10.
4. Kennedy AR, et al. Suppression of the later stages of radiation-induced carcinogenesis by antioxidant dietary formulations. Radiat Res. 2011 Jul;176(1):62-70. Epub 2011 Apr 26.

ALA Research

Abstract
Lipoic acid is a disulfhydryl-containing compound used in clinical medicine and in experimental models as an antioxidant. We developed a stable isotope dilution capillary gas chromatography/mass spectrometry assay for lipoic acid. We assayed a panel of the metabolites of transmethylation and transsulfuration 30 min after injecting 100 mg/kg lipoic acid in a rat model. Lipoic acid values rose 1000-fold in serum and 10-fold in liver. A methylated metabolite of lipoic acid was also detected but not quantitated. Lipoic acid injection caused a massive increase in serum S-adenosylhomocysteine and marked depletion of liver S-adenosylmethionine. Serum total cysteine was depleted but liver cysteine and glutathione were maintained. Serum total homocysteine doubled, with increases also in cystathionine, N,N-dimethylglycine, and alpha-aminobutyric acid. In contrast, after injection of 2-mercaptoethane sulfonic acid, serum total cysteine and homocysteine were markedly depleted and there were no effects on serum S-adenosylmethionine or S-adenosylhomocysteine. We conclude that large doses of lipoic acid displace sulfhydryls from binding sites, resulting in depletion of serum cysteine, but also pose a methylation burden with severe depletion of liver S-adenosylmethionine and massive release of S-adenosylhomocysteine. These changes may have previously unrecognized deleterious effects that should be investigated in both human disease and experimental models.
Ref: Free Radic Biol Med. 2009 Oct 15;47(8):1147-53. Epub 2009 Jul 17.

ALA Research

Discussion

The research was performed using a rat model and may not transfer directly to humans. The full-text article reveals the equivalent human dose was about 5 grams for a 50 kg person; the normal maxiumum dosing for i.v. treatments is about 1/3 of this. Cysteine is normally the rate limiting substrate for GSH synthesis, but research shows that liver GSH levels increase after ALA administration. Doubling of the rat's homocysteine levels should have increased blood viscosity significantly, but this was not measured.

ALA Research

Discussion

Could it be that some of the adverse events seen with i.v. pushes or too high doses of ALA are related to the phenomena observed in this paper? Perhaps in patients who undergo repeated infusions of ALA it would be prudent to make sure that:

1. Thiamine is supplied
2. Cysteine is replete. This could be administered p.o. in the days prior to the i.v. or could be included in a nutrient i.v. prior to the ALA
3. Methyl donors are available. Methylcobalamin is safe and is an effective methyl donor. Trimethylglycine (TMG, Betaine) is another good donor.
4. The chemical structure of biotin is similar to that of LA, and there is some evidence that high concentrations of LA can compete with biotin for transport across cell membranes

ALA

Abstract: The authors describe the long-term survival of a patient with pancreatic cancer without any toxic adverse effects.

The treatment regimen includes the intravenous alpha-lipoic acid and low-dose naltrexone (ALA-N) protocol and a healthy lifestyle program. The patient was told by a reputable university oncology center in October 2002 that there was little hope for his survival. Today, January 2006, however, he is back at work, free from symptoms, and without appreciable progression of his malignancy. The integrative protocol described in this article may have the possibility of extending the life of a patient who would be customarily considered to be terminal.

The authors believe that life scientists will one day develop a cure for metastatic pancreatic cancer, perhaps via gene therapy or another biological platform. But until such protocols come to market, the ALA-N protocol should be studied and considered, given its lack of toxicity at levels reported. Several other patients are on this treatment protocol and appear to be doing well at this time.

Berkson BM, Rubin DM, Berkson AJ. The long-term survival of a patient with pancreatic cancer with metastases to the liver after treatment with the intravenous alpha-lipoic acid/low-dose naltrexone protocol. Integr Cancer Ther. 2006 Mar;5(1):83-9. PMID: 16484716

ALA

Abstract:

We report here that alpha-lipoic acid (a-LA), a naturally-occurring antioxidant, scavenges reactive oxygen species (ROS) followed by an increase in apoptosis of human hepatoma cells.

Apoptosis induced by a-LA was dependent upon the activation of the caspase cascade and the mitochondrial death pathway. a-LA induced increases in caspase-9 and caspase-3 but had no significant effect on caspase-8 activity.

Apoptosis induced by a-LA was found to be mediated through the tensin homologue deleted on chromosome 10 (PTEN)/Akt pathway. Prior to cell apoptosis, PTEN was activated and its downstream target Akt was inhibited. Our findings indicate that increasing ROS scavenging could be a therapeutic strategy to treat cancer.

Shi D, et.al. Alpha-lipoic acid induces apoptosis in hepatoma cells via the PTEN/Akt pathway. FEBS Letters 582 (2008) 1667–1671

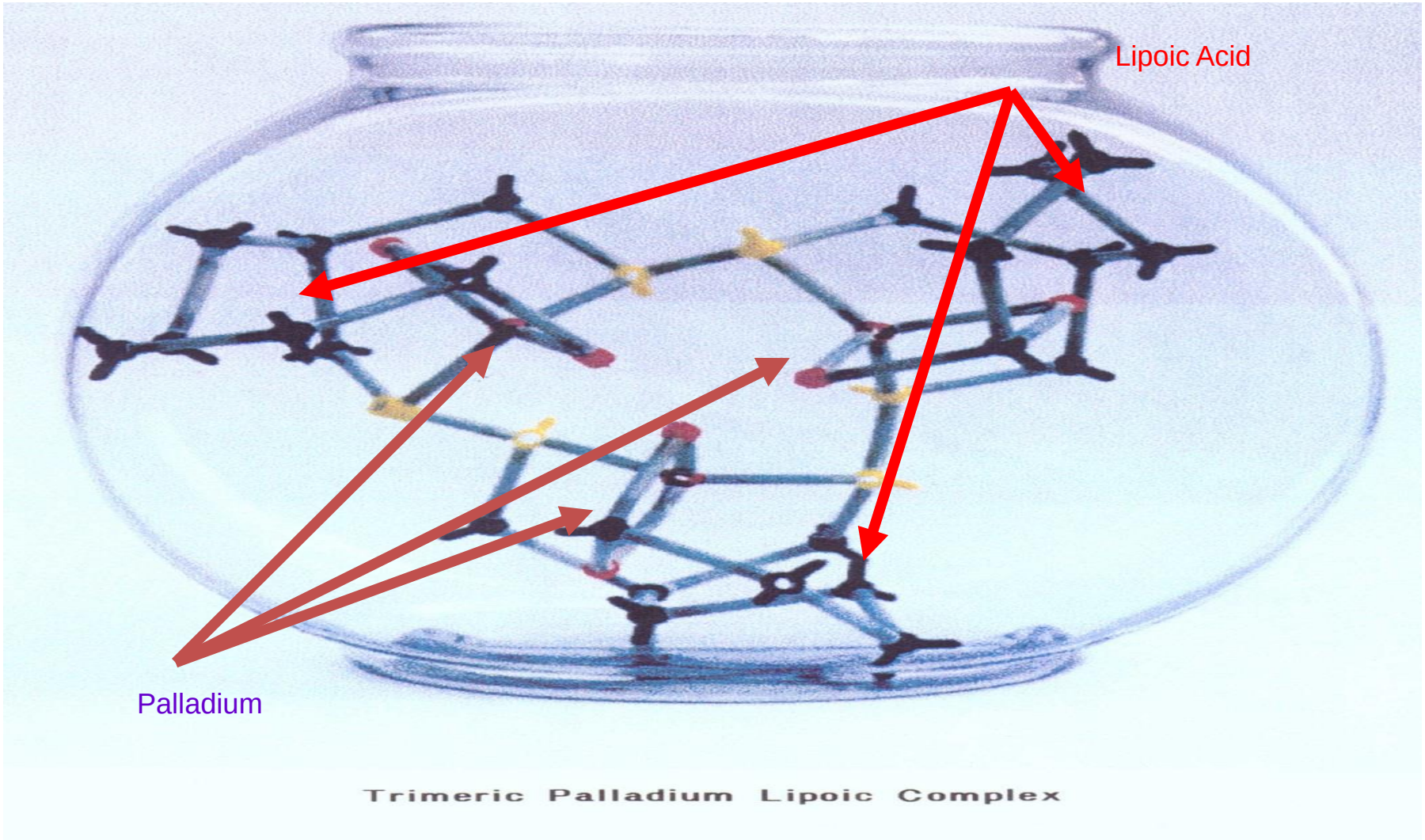
Poly MVA

Poly – MVA

Composition of POLY-MVA*.

Palladium α-lipoic acid complex (1:1)	3.72×10^{-2} mmol/L
Thiamine	2.17×10^{-3} mmol/L
N-acetyl cysteine	1.13×10^{-3} mmol/L
Riboflavin	4.62×10^{-4} mmol/L
N-formyl methionine	1.46×10^{-4} mmol/L
Cyanocobalamin (Vitamin B12)	1.37×10^{-4} mmol/L
Rhodium	1.34×10^{-4} mmol/L
Molybdenum	4.63×10^{-4} mmol/L
Ruthenium	1.42×10^{-5} mmol/L
Sodium chloride	2.64×10^{-1} mmol/L

* Data supplied by manufacturer of POLY-MVA, El-Gen LLC, 7 Shirley Street, Bohemia, NY 11716-1735, USA.



Trimeric Palladium Lipoic Complex

LAMC

- Notice no free palladium and no free alpha lipoic acid. This enhances solubility in fat and water.
- Palladium bound is non toxic and a novel way of using a transition mineral to serve as a very efficient catalyst in aerobic respiration.
- More efficient redox since it is a polymer, rather than a single molecule.
- LAMC provides cellular energy by facilitating aerobic metabolism

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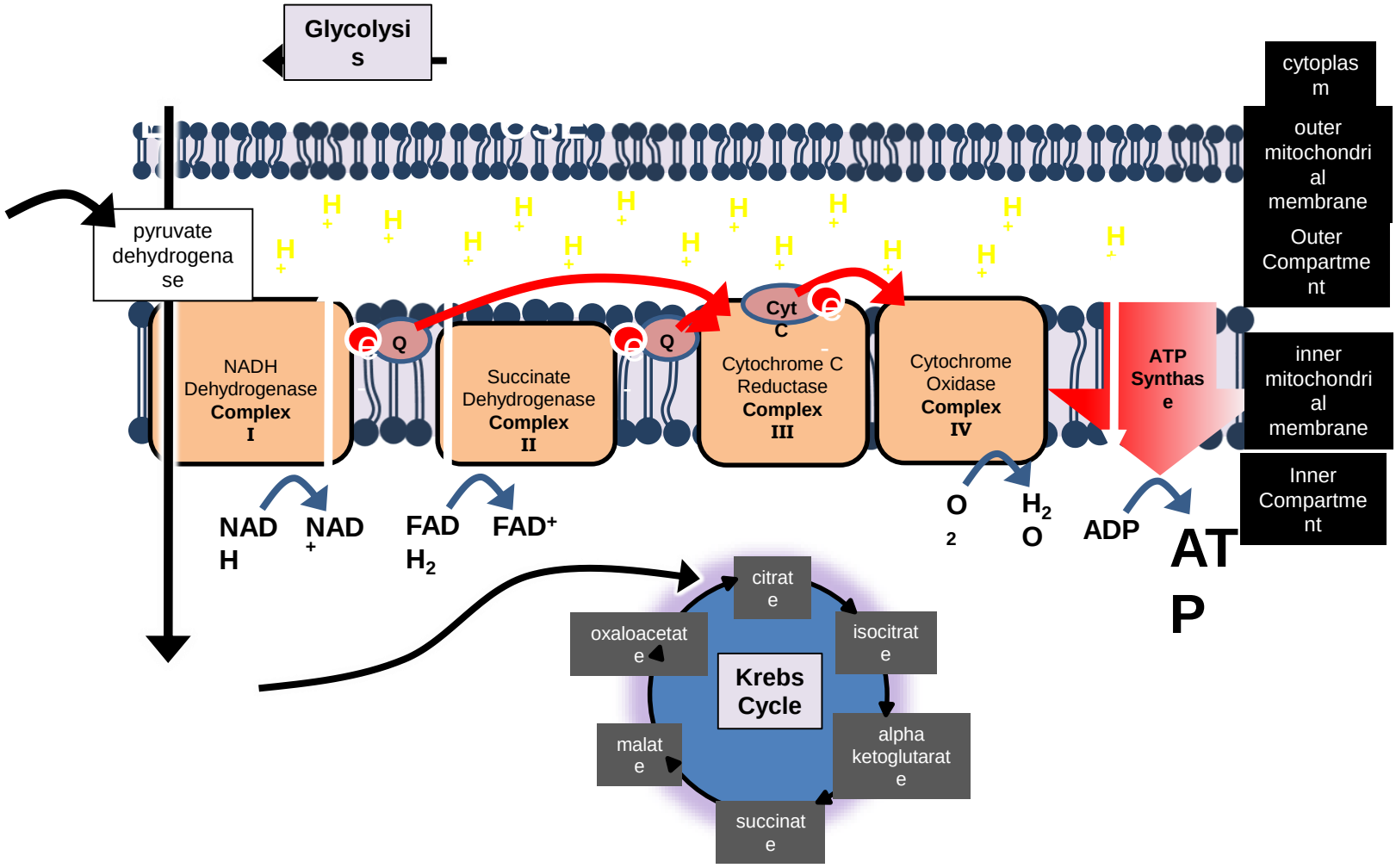
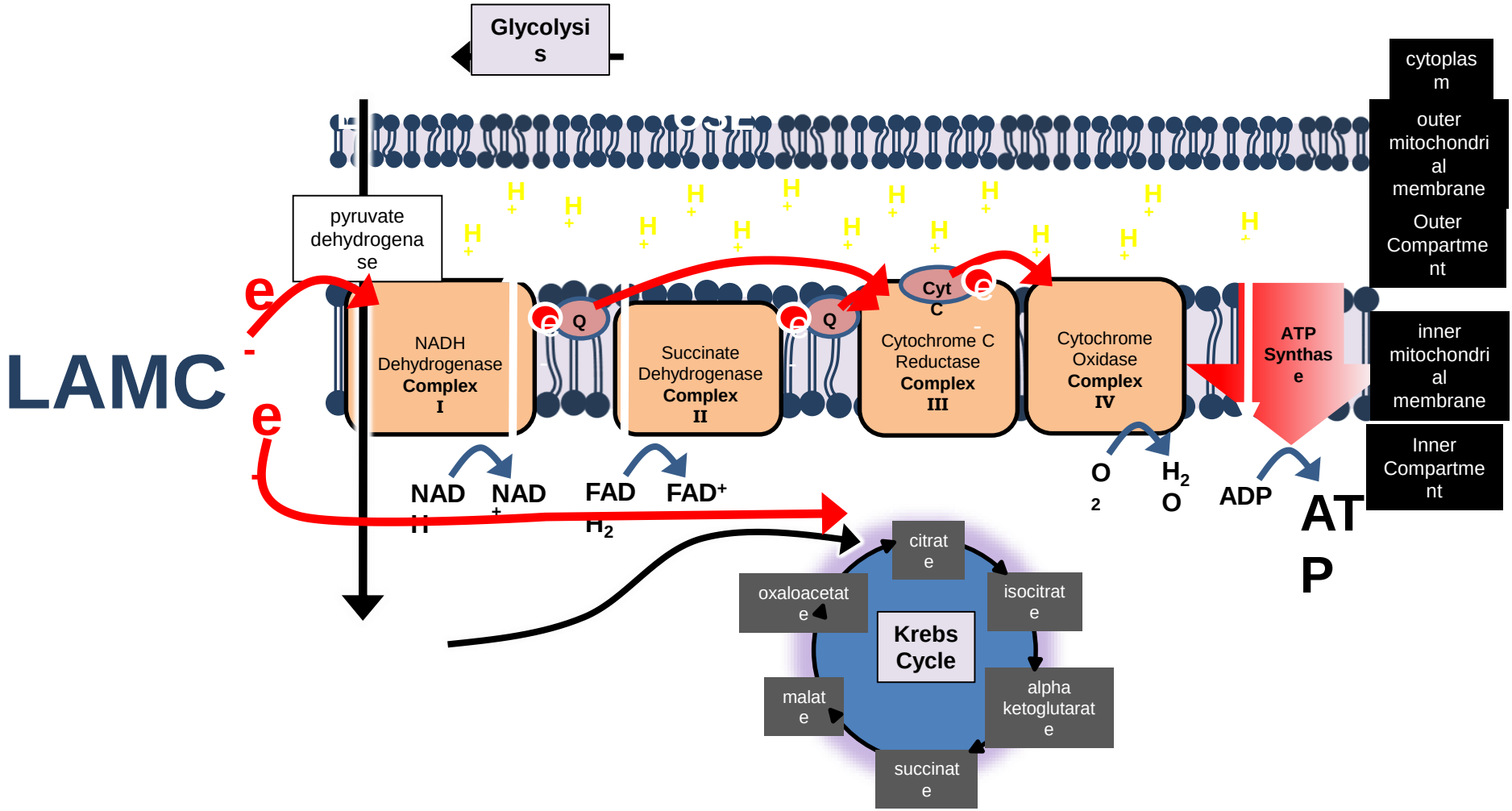
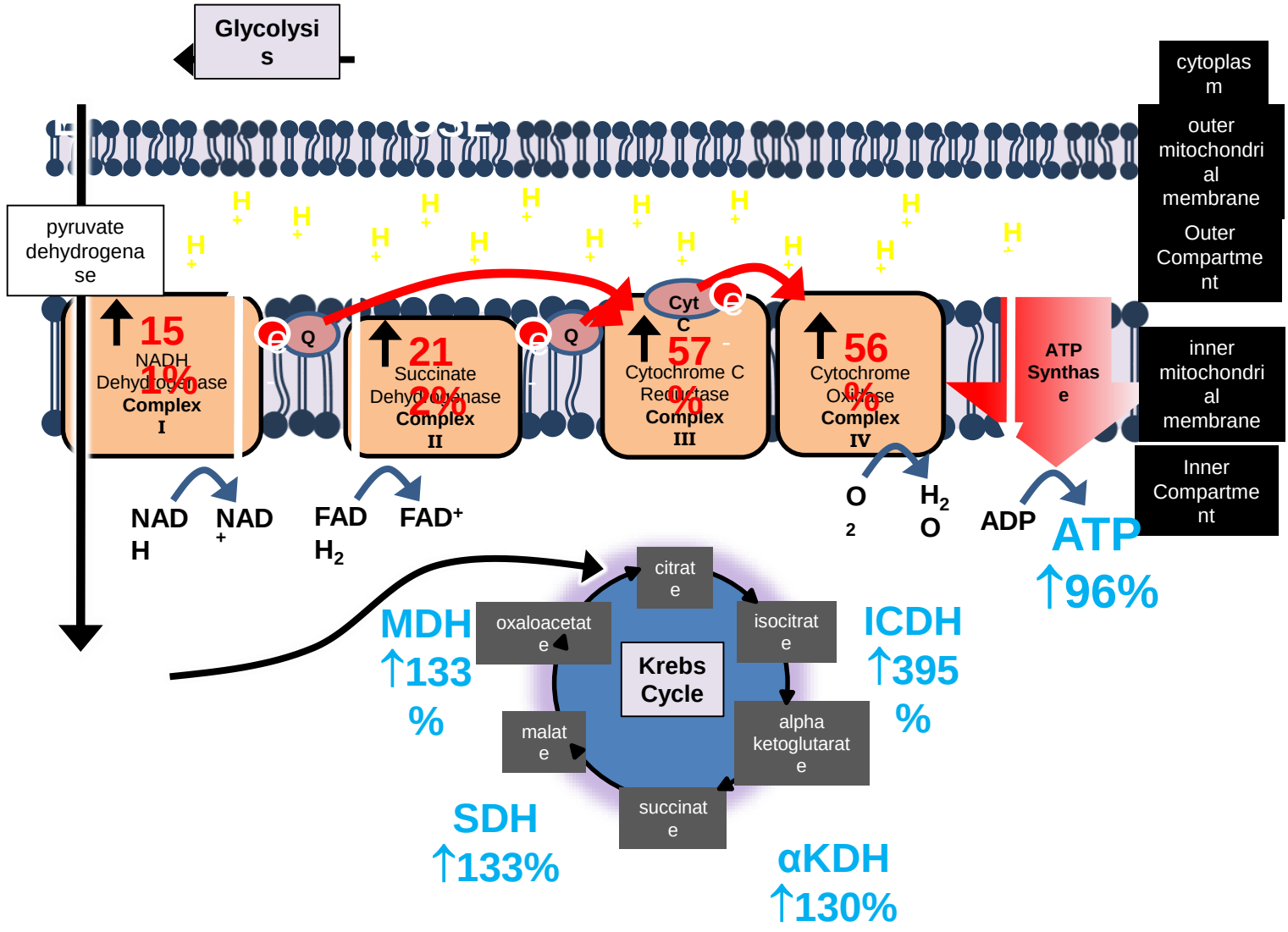

Glycolysis
cytoplasm
outer mitochondrial membrane
Outer Compartment
inner mitochondrial membrane
Inner Compartment
pyruvate dehydrogenase
NADH Dehydrogenase Complex I
Succinate Dehydrogenase Complex II
Cyt C
Cytochrome C Reductase Complex III
Cytochrome Oxidase Complex IV
ATP Synthase
Q
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
citrate
isocitrate
alpha ketoglutarate
succinate
malate
oxaloacetate
Krebs Cycle


Glycolysis
cytoplasm
outer mitochondrial membrane
Outer Compartment
inner mitochondrial membrane
Inner Compartment
pyruvate dehydrogenase
LAMC
e-
e-
NADH Dehydrogenase Complex I
Q
Succinate Dehydrogenase Complex II
Q
Cyt C
Cytochrome C Reductase Complex III
Cytochrome Oxidase Complex IV
ATP Synthase
H+
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
citrate
isocitrate
alpha ketoglutarate
succinate
malate
oxaloacetate
Krebs Cycle

LAMC


Glycolysis
cytoplasm
outer mitochondrial membrane
Outer Compartment
inner mitochondrial membrane
Inner Compartment
pyruvate dehydrogenase
15
NADH Dehydrogenase Complex I
1%
21
Succinate Dehydrogénase Complex II
2%
Cyt C
57
Cytochrome C Reductase Complex III
%
56
Cytochrome Oxidase Complex IV
%
ATP Synthase
NADH
NAD+
FADH2
FAD+
O2
H2O
ADP
ATP
↑96%
citrate
isocitrate
alpha ketoglutarate
succinate
malate
oxaloacetate
Krebs Cycle
MDH
↑133 %
ICDH
↑395 %
SDH
↑133%
αKDH
↑130%

Poly – MVA
(Internal AMARC Document)

Benefits of Lipoic Acid Palladium Complexes include:

- **Discourages abnormal cell growth**
- **Supports normal metabolism**
- **Slows the aging process from cellular breakdown**
- **Supports cellular function and raises energy levels**
- **Supports appetite**
- **Protects cellular DNA**
- **Converts free radicals into an energy source**
- **Has many mineral, vitamin, and antioxidant functions**

*These statements have not been evaluated by the Food and Drug Administration.
This product is not intended to diagnose, treat, cure or prevent any disease.

Poly – MVA / MOA

Is POLY-MVA's proposed mechanism of action directly related to its structural formulation?

POLY-MVA's unique electronic and redox properties appear to be the key to its physiological effectiveness. When glucose enters a cell, it is broken down under anaerobic conditions (absence of oxygen) into pyruvate. Pyruvate subsequently enters the mitochondria, via complex I, and is quickly oxidized, in the presence of alpha-lipoic acid, to acetyl-CoA. In aerobic respiration, acetyl-CoA is then channeled into the Krebs/Citric Acid Cycle to create the reduced forms of nicotinamide adenine dinucleotide (NADH) and flavin adenine dinucleotide (FADH2). NADH and FADH2 donate their electrons to the electron transport chain to make the high energy molecule ATP.

Recent studies in India (Sudheesh et al., 2009) have demonstrated Palladium Lipoic Acid Complex's ability to facilitate aerobic metabolism, which is responsible for ATP production in healthy cells. The energy needs of the body are supplied by splitting ATP into adenosine diphosphate (ADP) and a free phosphate (Griffin et al. 2006).

Poly – MVA / MOA

Studies have demonstrated that POLY-MVA provides electrons to DNA, via the mitochondria. Electrons are lost in normal cells as a result of oxidative damage from radiation and chemotherapy (Garnett and Garnett 1996).

POLY-MVA electron transfer provides an additional energy source to normal cells. However, cancer cells are metabolically challenged, and function in a hypoxic environment. Since there is less oxygen and more free electrons in the cancer cell, generation of free radicals occurs at the tumor mitochondrial membrane (Antonawich et al. 2004).

This activates apoptosis by facilitating the release of cytochrome C from the inner mitochondrial membrane, allowing the formation of an apoptotic complex in the cytoplasm. This complex, results in the subsequent activation of the caspase cascade of enzymes that destroy the malignant cells.

Poly – MVA / MOA

At significantly higher concentrations of POLY-MVA necrosis becomes apparent in the malignant cell. Given that normal cells are richly oxygenated, POLYMVA is nontoxic to them and they actually benefit from the energy boost (Antonawich et. al 2006).

Additional findings have examined the role of PdLA complex and a malignant cell's ability to physiologically adapt to a hypoxic environment. These physiological changes appear to be mediated by a molecule called HIF -1 (hypoxia inducible factor-1), which increases in hypoxic conditions to promote an increase in (Brown et al. 2006; Paul et al. 2004): Vascular Endothelial Growth Factor (VEGF) - a promoter of angiogenesis; Glucose Transport 1 (GLUT1) and glycolytic enzymes – critical components in anaerobic respiration; and Erythropoietin (EPO) – responsible for the differentiation of red blood cells) (Bacon et al 2004; Weinmann et al. 2004).

Poly – MVA / MOA

POLY-MVA appears to decrease the production of HIF - 1 thus restricting the ability of the cells to adapt to its environment and subsequently making it more vulnerable to the apoptotic cell death discussed above.

In summary, the POLY-MVA appears to be a selective metabolic modulator. Since it is a potent redox molecule, it has the ability to provide an alternative energy source to cells. While this is certainly of benefit to both normal and ischemic cells, based on their metabolic dysfunction it is detrimental to malignant cells.

Poly – MVA: Research Areas

- Chronic Neurological Disease
  - Mitochondrial support
  - Cell support
- Fatigue States
  - Mitochondrial energy / repair support
- Adjunctive Cancer Care
  - Quality of life
  - Potential for antimetabolic supporrt

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

Effect of POLY-MVA, a palladium α-lipoic acid complex formulation against declined mitochondrial antioxidant status in the myocardium of aged rats

N.P. Sudheesh [a], T.A. Ajith [b], K.K. Janardhanan [a], C.V. Krishnan [c,d,*]

Results of this study reveal that palladium α-lipoic acid formulation is an effective agent to protect the age-linked decline of myocardial mitochondrial antioxidant status and thus is capable to enhance the energy production of normal cell mitochondria.

Poly – MVA

- Oral form available
- Given without other additives
- Generally added to a small normal saline (NS) bag
  - (See protocol section)

LAMC

- Oral form available
  - Orally given 2-4 tsp/day often for fatigue, neurological, mitochondrial issues.
  - Up to 8 tsp per day in oncology support

- Intravenous form available
  - Given without other additives
  - Generally added to a small normal saline (NS) bag

  (See protocol section)

Poly-MVA

Poly-MVA for IV Use:

1 – No oxidative therapies / HDIVC within 12 hours of Poly-MVA IV

2 – Infuse Poly-MVA per protocol over 30-90 minutes

3- Infusion Frequency: Two IV's weekly for six weeks then re-evaluate

Poly-MVA Research Areas:

- Corduneanu O1, Chiorcea-Paquim AM, Garnett M, Oliveira-Brett AM. Lipoic acid-palladium complex interaction with DNA, voltammetric and AFM characterization. Talanta. 2009 Mar 15;77(5):1843-53. doi: 10.1016/j.talanta.2008.10.046. Epub 2008 Nov 6. PMID: 19159808
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- Sudheesh NP1, Ajith TA, Janardhanan KK, Krishnan CV. Effect of POLY-MVA, a palladium alpha-lipoic acid complex formulation against declined mitochondrial antioxidant status in the myocardium of aged rats. Food Chem Toxicol. 2010 Jul;48(7):1858-62. doi: 10.1016/j.fct.2010.04.022. Epub 2010 Apr 20. PMID: 20412826
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