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Biologic Transport of Silver Ions!

FREE Information that WORKS!

Those that say silver ions complex with stomach acid to produce mostly useless compounds, have not looked at the big picture, of biologic ion transport!

Following are brief statements taken from many studies - use your "edit/find" function to jump to the links to the full report! Please note that references are to ions, not metallic atoms, cystals or salts! While body electrolytes can realease a few ions of silver from metallic silver it is far from the benefits of direct intake of billions of silver ions!

Digestion and absorption begins in the mouth!

Metallic ions, either free or disassociated from dissolved soluable salts are both absorbed sublingually and/or isolated by ligands in the saliva, usually metalloproteins. Metallothionein (MT) is a relatively small molecule that binds heavy metals including silver, cadmium, copper and zinc, and is made by most cells in our body. Your saliva has over 200 different proteins and fully one third of body proteins are metalloproteins I.E. carrying metallic ions. Thus, reactive ions (missing one or more electrons) can be transported past the stomach and thru the circulatory system without local reactions. Metal ion substitution permits even a zinc metalloprotein to take up the silver ion and release the zinc ion. The free, ionized zinc, which would be toxic if permitted to accumulate, binds to a metal regulatory element on the promoter region of the metallothionein gene and "turns on" the synthesis of more metallothionein.

Silver exporting ATPase Hydrolases: Act on acid anhydrides, Catalysing transmembrane movement of substances!

The ion pump mechanisim utilizes energy from ATP to force ions thru a cell membrane, verses the passive diffusion, in which case the protein (on the cell) that allows this transport is called an ion channel.

Proteins include:

Enzymes, Neurotransmittors and some hormones, antibodies, ion channels, receptor sites, etc.

The mammalian form of MT appears to have the principal physiological role of providing a homeostatic function for copper and zinc. They are able to distribute these metal ions when required for the synthesis of metal-dependant cellular compounds. They have been referred to as "metal transfer agents" because of their role in depositing or removing (Ed: a specific case) zinc from zinc-dependant proteins.

Metallothionein (MT) is a relatively small molecule that binds heavy metals including silver, cadmium, copper and zinc, and is made by most cells in our body. Its production can be induced in the intestinal cells where it is thought to help keep us from absorbing a lot of toxic heavy metals such as cadmium. MT is also thought to be involved in the regulation of the cellular concentration of the essential minerals copper and zinc. The lining of our blood vessels is made up of a specific cell type called endothelial cells. Whereas the intestinal cell is the first barrier to the absorption of minerals, the endothelial cells are the secondary barrier to getting minerals into our tissues and organs.

Cells are constantly pumping ions in and out through their plasma membranes. In fact, more than half the energy that our bodies consume is used by cells to drive the protein pumps in the brain that do nothing else but transport ions across plasma membranes of nerve cells. How can ions be transported across membranes that are effectively impermeable to them? Cells contain proteins that are embedded in the lipid bilayer of their plasma membranes and extend from one side of the membrane through to the other. Such transmembrane proteins can function to effect ion transport in several ways.

As to the action of silver in the body, while there may be some catalytic action, silver ions will adhere to the sulphydral groups on bacterial cell walls and thus compromise the action of enzymes and so on, silver has also been found bonded to the DNA and RNA of bacterial cells, having presumably disrupted the cell wall enough to gain entry. Interestingly, it has also been found that if one removes the silver bonded to the cell wall of bacteria, that the bacteria is able to revive.

Binding of Ag ions by Metallothioneins - http://neron.uab.es/tiol_mt/mt.htm:

As an extension of the chemistry of metal thiolates, the study on the metal-ion binding ability of recombinant MT was undertaken by this group about ten years ago. The genetic engineering approach has allowed us to express several MT of different species (mouse, drosophila, crustacean, human,...) as well as their constitutive domains separately with a high purity and yield. More recently, the metal binding abilities of these metalloproteins in the presence of several metal ions (Zn, Cd, Cu, Ag, Hg, Pb,...) has been analyzed and the influence of several factors (pH, stabilization time required, temperature, ...) considered. The quality of the recombinant proteins has provided a deeper insight on the behaviour of the proteins than that obtained from native or chemically synthetized MT. Currently, our efforts are devolved to the role of zinc as a structural element in MxZny-MT species, the possible function of MT as a radical scavenger and the genesis and differentiation of the MT proteins along the evolution of living organisms. This group is one of the two partners of the Group of Synthesis and Modeling of Transition Metal Systems, which has been awarded the qualification of Quality Research Group by the CIRIT (Generalitat de Catalunya; Identification number 1997SGR 00411). The group has a well stablished collaboration with the research groups headed by Prof. ~Agust Lleds Falc http://cc.uab.es/iqui0/frame_qft.htm (Department of Chemistry, Facultat de Ciδncies, Universitat Autnoma de Barcelona) and by Dr. Slvia Atrian i Ventura http://www.bio.ub.es/genet/memoria/mol5uk.htm (Department of Genetics, Facultat de Biologia, Universitat de Barcelona), and by Dr. William Clegg (Department of Chemistry, University of Newcastle, UK). ----------

Metalloprotein Program Project Overview http://www.scripps.edu/research/metallo/

One-third of all proteins are "metalloproteins", chemical combinations of protein atoms (carbon, nitrogen, oxygen, hydrogen, sulfur) with ions of metals such as iron, calcium, copper, and zinc. The hemoglobin, for example, that carries oxygen in the bloodstream, is an iron-containing metalloprotein. The metal ions in metalloproteins are critical to the protein's function, structure, or stability. In fact, numerous essential biological functions require metal ions, and most of these metal ion functions involve metalloproteins. Thus, metalloproteins make life on Earth possible and the ability to understand and ultimately control the binding and activity of protein metal sites is of great biological and medical importance.

complex ions, or coordinated complexes as they are also called, generally consist of a positively charged central metal atom or ion, like the zinc in tetramine zinc, surrounded by electron-donating, or basic, groups called ligands ; in the tetrammine zinc complex, the NH3 groups are the ligands. The number of bonds connecting the ligands to the central atom or ion is its coordination number, or ligancy. Transition metals (see transition elements) are especially suited for forming complex ions because they have filled or partially filled electron orbitals that can participate in bonding the ligands to the metal. The bonding holding the ligands to the central atom or ion is similar to covalent bonding between atoms but is more complex (see chemical bond). All the ligands surrounding the central ion need not be the same, and some positions can be occupied by solvent molecules. Because ligands remain in a fixed position around a central atom or ion, in many complexes different isomers , or arrangements, of the ligand groups are possible. When there are four or more ligands around a central atom, different stereoisomers, or spatial configurations, are possible (see stereochemistry). Many complex ions are colored; the specific color of a complex depends on both the central atom or ion and the ligands. For example, when cobaltous chloride is dissolved in water, a pale pink solution, sometimes called invisible ink, results because of the presence of the hydrated cobaltous ion, Co(H2O)6+2; this solution does not show up well on paper, but if the paper is heated to drive the water off, visibility improves because of the formation of a blue tetrachlorocobalt (II)-2 complex. Some of the more important complex ions are vitamin B12, chlorophyll, and the heme component of hemoglobin, in which the central metal ions are cobalt, magnesium, and iron, respectively, and the ligands are complex organic systems. Many enzymes contain a metal ion about which parts of the protein are coordinated.

Metal-Substituted Metalloproteins http://www.chem.qmw.ac.uk/iubmb/etp/etp6t11.html#p11

Scientists from several areas, dealing with spectroscopy and electron-transfer mechanisms, often use metalloproteins in which a metal at the active site has been substituted by another metal ion, like Co,Zn, Hg, Cd. Examples are zinc-substituted cytochromes and cobalt-substituted ferredoxins.

The names for such modified proteins are easily given by using indications like: 'zinc-substituted ....'. In case of multi-metal proteins, where ambiguity might arise about which metal has been substituted, one could easily add in parentheses the name of the metal that has been replaced, such as: cobalt-substituted [Fe] nitrogenase.

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gain entry. Interestingly, it has also been found that if one removes the silver bonded to the cell wall of bacteria, that the bacteria is able to revive.

Some links to papers discussing the role of metallothioneins :

http://bssv01.lancs.ac.uk/StuWork/BIOS316/Bios31698/Mthion/MET.HTM

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Metallothionein Structure

The protein is composed of a polypeptide chain of 61 amino acid residues of which there are 20 cysteine residues and many lysineês and arginines. The amino acid structure of MTs has been highly conserved throughout evolution and changes have been conservative with regard to chemical and space-filling properties. It should also be noted that there are no aromatic amino acids and very few bulky aliphatic ones. All the cysteines occur in the reduced forms and the metal ions are co-ordinated to them through mercaptide bonds.

http://www.nal.usda.gov/ttic/tektran/data/000009/46/0000094696.html Metallothionein (MT) is a relatively small molecule that binds heavy metals including silver, cadmium, copper and zinc, and is made by most cells in our body. Its production can be induced in the intestinal cells where it is thought to help keep us from absorbing a lot of toxic heavy metals such as cadmium. MT is also thought to be involved in the regulation of the cellular concentration of the essential minerals copper and zinc. The lining of our blood vessels is made up of a specific cell type called endothelial cells. Whereas the intestinal cell is the first barrier to the absorption of minerals, the endothelial cells are the secondary barrier to getting minerals into our tissues and organs.

http://lowdose.org/pubs/ehp/members/klaassenfull.html Metallothionein (MT) is a low-molecular-weight protein ubiquitous in the animal kingdom (1). MT has an unusual amino acid composition in that it has no aromatic amino acids and one-third of its residues are cysteines. These cysteine residues bind and store metal ions (2). The MT multigene family is composed of at least four isoforms. MT-I and -II exist in all tissues, are regulated in a coordinate fashion, and appear functionally equivalent (1-3). Other members of the MT gene family, however, show different patterns of expression: MT-III is found mainly in brain (4) and MT-IV in stratified squamous epithelium (5). MT-III and -IV are regulated very differently than MT-I and -II and their significance is not yet understood. Evidence also suggests a role for MT in protection aginst oxidative stress. MT can serve as a sacrificial scavenger for hydroxyl radicals in vitro (35) and protect against free radical-induced DNA damage (36-38). MT can also assume the function of superoxide dismutase in yeast (39) and protect against lipid peroxidation in erythrocyte ghosts produced by xanthine oxidase-derived superoxide anion and hydrogen peroxide (40). Hepatocytes from MT-null mice are more sensitive than control cells to oxidative damage produced by t-butylhydroperoxide and paraquat (41,42). MT is induced by oxidative stress-producing chemicals (43) and thus may protect against oxidative damage (7) and the toxicity of alkylating anticancer drugs (8).

http://bssv01.lancs.ac.uk/StuWork/BIOS316/Bios31699/AgMet/AgMet.html The proteins of the metallothionein superfamily are resposible for primary metal storage, transport and detoxification of the cell. Most are found within the cytosol but a few are found in the nucleus, especially in mammalian metallothioneins in the ACE1 complex which is concerned with gene expression. Ag-metallothionein has only been found in Saccharomyces Crevisiae to date.

Ag-Metallothionein

The chain wraps around the silver ions so that they are enclosed by two parallel loops leaving a cup like cleft where the Ag cluster resides. Fig.2 shows the arrangement of the ligand binding residues from infront of(fig.2a) and behind(fig.2b) the protein as well as looking at the open cleft(fig.2c). In Fig.3a the two parallel loops can be seen at the left and right hand sides of the diagram with the open end of the cup facing. Fig.3b shows a spacefill representation of the metallothionein in the same orientation. It can be seen from this that the open face of the cup leaves the metal cluster slightly exposed. (see pictures there)

http://www3.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&dopt=r&uid=96159028

3D solution structure of copper and silver-substituted yeast metallothioneins. For the first 40 residues in both structures, the polypeptide backbone wraps around the metal cluster in two large parallel loops separated by a deep

cleft containing the metal cluster. Minor differences between the two structures include differences in hydrogen bonds and the orientation of the N-terminus with the overall protein volume conserved to within 6.5%.

p://www.thorne.com/altmedrev/fulltext/tox3-4.html

A second adaptive and protective response to toxic metal exposure is induction of metallothionein synthesis. Metallothioneins are a fascinating group of low molecular weight, intracellular proteins that serve as a storage depot for copper and zinc, and "scavenge" sulfhydryl-reactive metals that enter the cell. Metallothioneins across species are rich in cysteine (~30%) and have higher affinities for Hg and Cd than for zinc.25 Therefore as Hg and Cd bind to metallothionein, and are restricted from entering the mitochondria, zinc is released. The free, ionized zinc, which would be toxic if permitted to accumulate, binds to a metal regulatory element on the promoter region of the metallothionein gene and "turns on" the synthesis of metallothionein.25 Such induction of metallothionein provides increased binding capacity for both toxic metals (protective) and zinc (functional).

http://link.springer.de/search for Volume 74, Issue 4/5, pp 190-195 in Archives of Toxicology Total uptake of Ag (subcutaneously with ($AgNO_3$)) into the liver was not stimulated, but its uptake into the MT fraction increased significantly in the LEC rats.

l Elemental Composition

Cells are 90% water. Of the remaining molecules present, the dry weight is approximately:

50% protein

15% carbohydrate

15% nucleic acid

10% lipid

10% miscellaneous

Total approximate composition by element:

60% H

25% O

12% C

5% N

Note that these four elements make up almost the entire composition of all living organisms. The only other notable elements that are significant constituents of biological molecules are P, phosphorus, and S, sulphur. In addition, living things use traces of sodium, magnesium, chlorine, potassium, calcium, and iron, and even less of certain other metals (see Purves page 20). Organelles are small structures within cells that perform dedicated functions. As the name implies, you can think of organelles as small organs. There are a dozen different types of organelles commonly found in eukaryotic cells.

Nucleus

This is where the DNA is kept and RNA is transcribed. RNA is transported out of the nucleus through the nuclear pores. Proteins needed inside the nucleus are transported in through the nuclear pores. The nucleolus is usually visible as a dark spot in the nucleus (note the dark nucleolus in this electron microscope photo of a nucleus), and is the site of ribosome formation.

Ribosomes

Ribosomes are the sites of protein synthesis , where RNA is translated into protein. Protein synthesis is extremely important to cells, and so large numbers of ribosomes are found throughout cells (often numbering in the hundreds or thousands). Ribosomes exist floating freely in the cytoplasm, and also bound to the endoplasmic

reticulum (ER). ER bound to ribosomes is called rough ER because the ribosomes appear as black dots on the ER in electron microscope photos, giving the ER a rough texture. These organelles are quite small, made up of 50 proteins and several long RNAs intricately bound together. Ribosomes have no membrane. Ribosomes disassemble into two subunits when not actively synthesizing protein.

Mitochondria

Mitochondria (singular: mitochondrion) are the sites of aerobic respiration, and generally are the major energy production center in eukaryotes. Mitochondria have two membranes, an inner and an outer, clearly visible in this electron microscope photo of a mitochondrion. Note the reticulations, or many infoldings, of the inner membrane, This serves to increase the surface area of membrane on which membrane-bound reactions can take place. The existence of this double membrane has led many biologists to theorize that mitochondria are the descendants of some bacteria that was endocytosed by a larger cell billions of years ago, but not digested. This fascinating theory of symbiosis, which might lend an explanation to the development of eukaryotic cells, has additional supporting evidence. Mitochondria have their own DNA and their own ribosomes; and those ribosomes are more similar to bacterial ribosomes than to eukaryotic ribosomes.

Chloroplasts

These organelles are the site of photosynthesis in plants and other photosynthesizing organisms. They also have a double membrane. There is a more complete description of the chloroplast here, in the chapter on photosynthesis. Endoplasmic Reticulum (ER) The ER is the transport network for molecules targeted for certain modifications and specific final destinations, as opposed to molecules that are destined to float freely in the cytoplasm. There are two types of ER, rough and smooth. Rough ER has ribosomes attached to it, and smooth ER does not. Golgi apparatus This organelle modifies molecules and packages them into small membrane bound sacs called vesicles. These sacs can be targetted at various locations in the cell and even to its exterior. Lysosome This organelle digests waste materials and food within the cell, breaking down molecules into their base components with strong digestive enzymes . Here we can see an advantage of the compartmentalization of the eukaryotic cell: the cell could not support such destructive enzymes if they were not contained in a membrane-bound lysosome . http://esg-www.mit.edu:8001/esgbio/cb/membranes/transport.html The big picture..... In practice, given the structure of known membrane proteins , these holes are only large enough to allow the passage of small molecules through the plasma membrane, almost always simple ions like hydrogen, potassium or sodium. The ions may pass through the hole or orifice by passive diffusion, in which case the protein that allows this transport is called an ion channel. Alternatively, the transmembrane protein may invest energy, usually derived from ATP, to actively force ions from one side of the plasma membrane to the other, in which case it will be an ion pump

http://esg-www.mit.edu:8001/esgbio/cb/membranes/proteins.html

Cells are constantly pumping ions in and out through their plasma membranes. In fact, more than half the energy that are bodies consume is used by cells to drive the protein pumps in the brain that do nothing else but transport ions across plasma membranes of nerve cells. How can ions be transported across membranes that are effectively impermeable to them? Cells contain proteins that are embedded in the lipid bilayer of their plasma membranes and extend from one side of the membrane through to the other. Such transmembrane proteins can function to effect ion transport in several ways. But how can they cope with the energetically highly unfavorable situation in which an ion must pass through the hydrophobic inner layers of the plasma membrane?

Domains

If we examine the detailed structures of many transmembrane proteins, we see that they often have three different domains, two hydrophilic and one hydrophobic . A hydrophilic domain (consisting of hydrophilic amino acids) at the N-terminus is poking out in the extracellular medium, a hydrophobic domain in the middle of the amino acid chain, often only 20-30 amino acids long, is threaded through the plasma membrane, and a hydrophilic domain at the C-terminus protrudes into the cytoplasm. The transmembrane domain, because it is made of amino acids having hydrophobic side chains, exists comfortably in the hydrophobic inner layers of the plasma membrane. Because these transmembrane domains anchor many proteins in the lipid bilayer,these proteins are not free-floating and cannot be isolated and purified biochemically without first dissolving away the lipid bilayer with detergents. (Indeed, much of the washing we do in our lives is necessitated by the need to solubilize proteins that are embedded in lipid membranes using detergents!)

Cells have ion gates, valve like proteins that permit specific ions to enter!

Some examples of proteins

Antibodies: they recognise molecules of invading organisms.

Receptors: part of the cell membrane, they recognise other proteins, or chemicals, and inform the cell... 'The Door Bell'.

Enzymes: assemble or digest.

Neurotransmittors and some hormones: Trigger the receptors... (the finger on the door bell...)

Channels,and pores: holes in the cell membrane (with or without a gate). Usually, filter the flow...

http://www.iacr.bbsrc.ac.uk/notebook/courses/guide/prot.htm for a review of protein structure and diversity!

Huge source list of data on proteins: http://www.iacr.bbsrc.ac.uk/notebook/links/protein.htm ----------
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[LinkDB] Silver exporting ATPase

ENTRY EC 3.6.3.53

NAME Ag+-exporting ATPase

CLASS Hydrolases

Acting on acid anhydrides Catalysing transmembrane movement of substances

SYSNAME ATP phosphohydrolase (Ag+-exporting)

REACTION ATP + H2O + Ag+(in) = ADP + Orthophosphate + Ag+(out)

SUBSTRATE ATP H2O Ag+

PRODUCT ADP Orthophosphate

COMMENT A P-type ATPase that exports Ag+ ions from pathogenic microorganisms as well as from some animal tissues.

DBLINKS ExPASy - ENZYME nomenclature database: 3.6.3.53

WIT (What Is There) Metabolic Reconstruction: 3.6.3.53

http://www.sph.umich.edu/eih/heavymetals/Manuscripts/HerrinR.htm (full text)

Summary:

Results of competing ligand equilibration experiments indicate that the majority of Ag(I) in the filtered phase of river water and sewage treatment plant effluent is strongly complexed to ligands present in those systems. Furthermore, appreciable fractions of these Ag(I) complexes adsorb to Teflon surfaces in unacidified samples. These complexes do not, however, adsorb to glass surfaces. Oxidation of river water and effluent reduce the fraction of Teflon-adsorbed Ag to undetectable levels. These observations indicate that Ag(I) in river waters and effluents is present in the form of strong complexes that are hydrophobic in nature. Organic matter containing thiol functionalities is likely to cause this behavior. Formation of hydrophobic complexes may enhance the bioavailability of Ag(I).

http://www.sph.umich.edu/eih/heavymetals/Manuscripts/FortinC.htm (full text)

Summary:

Short-term (< 1 h) silver uptake by the green alga Chlamydomonas reinhardtii was measured in the laboratory in defined inorganic media in the presence or absence of ligands (chloride and thiosulfate). In contradiction to the

Free-Ion Model of metal uptake, silver accumulation by the alga proved to be sensitive to the choice of ligand used to buffer the free silver concentration. For a low fixed free Ag+ concentration of 10 nM, silver uptake in the presence of thiosulfate (0.11 μM) was 2X greater than in the presence of chloride (4 mM). When sulfate was removed from the exposure medium, silver uptake in the presence of thiosulfate was even more markedly enhanced (more than 4X greater than in the presence of chloride). Varying the sulfate concentration in the exposure medium only affected silver uptake if thiosulfate was present. We conclude that silver-thiosulfate complexes are transported across the plasma membrane via sulfate / thiosulfate transport systems, and that sulfate acts as a competitive inhibitor of this uptake mechanism.

http://www.envsci.rutgers.edu/~reinfldr/ reinfelder@envsci.rutgers.edu request source for: Reinfelder, J.R. and S.I. Chang. (1999) Speciation and microalgal bioavailability of inorganic silver. Environ. Sci. Technol. 33:1860-1863

http://www.orgchm.bas.bg/~kaneti/base.html

Silver ion chromatography has been and still is the core method of lipid analysis. The method is based on the distinctive property of unsaturated organic compounds to form weak charge transfer complexes with silver ion [1]. Thus, lipid molecules are separated into groups according to the overall number of the double bonds in the fatty acid residues.

http://www.google.com/search?q=cache:www.scar.utoronto.ca/~96wongal/new/silver.pdf+ligand+silver

Analysis of Silver in Freshwater and Freshwater Sedimentation Introduction

Silver (Ag), in its ionic form, is one of the most toxic heavy metals, surpassed only by mercury. When presented as silver nitrate in laboratory water, Ag is highly toxic to freshwater fish, with median lethal concentration (LC50) values between 5 - 60 μg Ag/L.1 However, Ag complexed with inorganic cations such as thiosulfate and sulfide have been shown to be less toxic by orders of magnitude for both fathead minnows (Pimephales promelas) and rainbow trout (Oncorhynchus mykiss).2 It is clear that water chemistry plays a crucial role in the toxicity of Ag in freshwater species.As a type-B metal cation, Ag+ tends to coordinate and complex soft bases such as sulfur, and the high stability constants for organosulfurs complexed with silver are indicative of this fact. Elevated concentrations of silver are usually associated with industrial processes such as mining and photographic processing and Silver found in photographic effluents is predominantly discharged as a soluble, undissociated silver thiosulfate complex. During secondary waste treatment, the thiosulfate complexes are converted to chemically inert silver sulfide (Ag2S), which is highly insoluble in water (solubility coefficient = 310-10 mg/L for natural waters).3 As a result, the majority of the silver which is treated is incorporated into sludge, which is later shipped away from the treatment plant as solid waste. Hence, silver which is discharged to the environment exists in a colloidal or particulate phase and is very quickly scavenged by suspended sediments. Background aqueous Ag(I) concentrations in freshwater samples are generally very low (in units of picomols/L) because of the strong binding of silver with sulfur. 4

http://www.google.com/search?q=cache:www.epa.gov/sab/epec0006.pdf+ligand+silver

Background

The Biotic Ligand Model (BLM) is a model that incorporates metal speciation and the protective effects of competing cations to predict metal binding at the fish gill or other site of action of acute metal toxicity in aquatic organisms (i.e., the "biotic ligand") (Figure 1). The Agency has proposed that the BLM be included in an integrated approach to metals management, including establishment of metals water quality criteria. National ambient water quality criteria (WQC) consist of 3 components: the concentration of the pollutant that will protect 95% of aquatic species; a time period over which exposure is to be averaged; and the allowable frequency for exceeding the criteria. The allowable concentrations of the pollutant generally are based on laboratory toxicity tests using a specified array of test species, and are expressed in terms of a criterion maximum concentration (CMC) to protect against acute (short-term) effects and a criterion continuous concentration (CCC) to protect against chronic (long-term) effects. At the request of the EPA Office of Water, the Ecological Processes and Effects Committee (EPEC) of the Science Advisory Board (SAB) met on April 6-7, 1999 to review the Biotic Ligand Model (BLM) for predicting the acute toxicity of metals to aquatic organisms. The BLM has been developed to improve the estimation of the bioavailable fraction of dissolved metals, such as copper and silver, that may pose a risk to aquatic organisms in surface waters. The Agency proposes to incorporate the BLM in its approach to establishing water quality criteria that will be protective of aquatic organisms. The distinguishing feature of the model, in contrast to approaches based only upon estimation of free metal ions as the toxic species, is its capability to predict the competition of the free metal ion with other cations (e.g., Ca, H) and other ligands

(DOC) for binding with the "biotic ligand" (the site of membrane transport and route of direct uptake of freely dissolved metals). The presence of these cations and ligands in solution can mitigate toxicity in a predictable fashion based on their relative concentrations and strengths of binding. The model allows changes in toxicity under equilibrium conditions to be estimated across ranges of key water quality parameters (pH, alkalinity, hardness, and DOC). Furthermore, through the model's ability to integrate the binding site density of the biotic ligand, conditional stability constants for the metal-ligand complex and competing cations, and measured or postulated water quality conditions, the acute toxicological effects of a metal in a broad range of waters can be normalized to a common metric (e.g., gill-metal LC50). This unifying feature offers a powerful and consistent approach to comparing potential effects of metals among effects of metals among differing surface waters and changing conditions within a single water body.

http://www.hei.org/htm/gold.htm

Preparation of Colloidal Gold Conjugates.

Colloidal gold has been used for centuries in the preparation of stained glass for windows and fine glassware. In recent years, colloidal gold particles have become a useful tool for microscopists. Colloidal gold particles are especially useful for biological electron microscopy. Some of the reasons why are listed below. Homogeneous preparations of particles varying in size from 3 nm to 20 nm can be easily prepared. Colloidal gold suspensions are inexpensive to prepare. Most proteins can be easily coupled to colloidal gold particles. Proteins coupled to gold particles do not appear to lose their biological activity. The colloidal gold particles can be easily seen in the electron microscope. Colloidal gold probes can be used for light microscopy. The larger gold particles can be directly observed by the light microscope. Smaller particles are detected by silver enhancement or epipolarized illumination. The same probes can be used for both LM and TEM immunocytochemistry.