

# **Copper Medicine**

Got Cholera?

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# Medical Uses of Copper in Antiquity Copper Applications in Health & Environment

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The first recorded medical use of copper is found in the Smith Papyrus, one of the oldest books known. The Papyrus is an Egyptian medical text, written between 2600 and 2200 B.C., which records the use of copper to sterilize chest wounds and to sterilize drinking water. Other early reports of copper's medicinal uses are found in the Ebers Papyrus, written around 1500 B.C. The Ebers Papyrus documents medicine practiced in ancient Egypt and in other cultures that flourished many centuries earlier. Copper compounds were recommended for headaches, "trembling of the limbs" (perhaps referring to epilepsy or St. Vitus' Dance), burn wounds, itching and certain growths in the neck, some of which were probably boils. Forms of copper used for the treatment of disease ranged from metallic copper splinters and shavings to various naturally occurring copper salts and oxides. A "green pigment" is spoken of which was probably the mineral, malachite, a form of copper carbonate. It could also have been chrysocolla, a copper silicate, or even copper chloride, which forms on copper exposed to seawater. In the first century A.D., Dioscorides, in his book De Materia Medica, described a method of making another green pigment known as verdigris by exposing metallic copper to the vapors of boiling vinegar. In this process, blue-green copper acetate forms on the copper surface. Verdigris and blue vitriol (copper sulfate) were used, among other things, in remedies for eye ailments such as bloodshot eyes, inflamed or "bleary" eyes, "fat in the eyes" (trachoma?), and cataracts.

In the Hippocratic Collection (named for, although not entirely written by, the Greek physician Hippocrates, 460 to 380 B.C.), copper is recommended for the treatment of leg ulcers associated with varicose veins. To prevent infection of fresh wounds, the Greeks sprinkled a dry powder composed of copper oxide and copper sulfate on the wound. Another antiseptic wound treatment at the time was a boiled mixture of honey and red copper oxide. The Greeks had easy access to copper since the metal was readily available on the island of Kypros (Cyprus) from which the Latin name for copper, cuprum, is derived.

By the time the Roman physician Aulus Cornelius Celsus began practicing medicine, during the reign of Tiberius (14 to 37 A.D.), copper and its derivatives had been firmly established as an important drug in the medical practitioner's pharmacopoeia. In Celsus' series, De Medicina, books one through six list many purposes for which copper was used together with the preparation and the form of copper most effective for each ailment. For the treatment of venereal disease, for example, Celsus prescribed a remedy consisting of pepper, myrrh, saffron, cooked antimony sulfide, and copper oxide. These were first pounded together in dry wine and when dry, once again pounded together in raisin wine and heated until dry. For a non-healing chronic ulcer, treatment consisted of copper oxide and other ingredients including enough rose oil to give a soft consistency.

Pliny (23 to 79 A.D.) described a number of remedies involving copper. Black copper oxide was given with honey to remove intestinal worms. Diluted and injected as drops into nostrils, it cleared the head and, when taken with honey or honey water, it purged the stomach. It was given for "eye roughness," "eye pain and mistiness," and ulceration of the mouth. It was blown into the ears to relieve ear problems.

In the New World the Aztecs also used copper for medical purposes. Don Francisco de Mendoza commissioned two learned Aztec Indian physicians to record the pharmacological treatments known by the Aztecs at the time of the Conquest. For the treatment of "Faucium Calor" (literally, heat of the throat, or, sore throat) they prescribed gargling with a mixture of ingredients containing copper.

Copper was also employed in ancient India and Persia to treat lung diseases. The tenth century book, Liber Fundamentorum Pharmacologiae describes the use of copper compounds for medicinal purposes in ancient Persia. Powdered malachite was sprinkled on boils, copper acetate as well as and copper oxide were used for

diseases of the eye and for the elimination of "yellow bile." Nomadic Mongolian tribes treated and healed ulcers of venereal origin with orally administered copper sulfate.

Turning to more modern times, the first observation of copper's role in the immune system was published in 1867 when it was reported that, during the cholera epidemics in Paris of 1832, 1849 and 1852, copper workers were immune to the disease. More recently copper's role in the immune system has been supported by observations that individuals suffering from Menke's disease (an inherited disease in which there is defective copper absorption and metabolism) generally die of immune system-related phenomena and other infections. Further, animals deficient in copper have been shown to have increased susceptibility to bacterial pathogens such as Salmonella and Listeria. Evidence such as this has led researchers to suggest strongly that copper compounds not only cure disease but also aid in the prevention of disease.

In 1885, the French physician, Luton, reported on using copper acetate in his practice to treat arthritic patients. For external application he made a salve of hog's lard and 30% neutral copper acetate. For internal treatment, he used pills containing 10 mg. of copper acetate. In 1895, Kobert published his review of the pharmacological actions of copper compounds. Copper arsenate had been used to treat acute and chronic diarrhea as well as dysentery and cholera. A variety of inorganic copper preparations were found to be effective in treating chronic adenitis, eczema, impetigo, scorphulosis, tubercular infections, lupus, syphilis, anemias, chorea and facial neuralgia. An organic complex of copper developed by Bayer was shown to have curative powers in the treatment of tuberculosis. Copper treatment for tuberculosis continued until the 1940s, and various physicians reported on their success in using copper preparations in intravenous injections.

In 1939, the German physician, Werner Hangarter, noticed that Finnish copper miners were unaffected by arthritis as long as they worked in the mining industry. This was particularly striking since rheumatism was a widespread disease in Finland, and workers in other industries and other towns had more rheumatic diseases than did the copper miners. This observation led Finnish medical researchers plus the Germans, Hangarter and Lübke, to begin their now classic clinical trials using an aqueous mixture of copper chloride and sodium salicylate. They successfully treated patients suffering from rheumatic fever, rheumatoid arthritis, neck and back problems, as well as sciatica.

Until recently, just as in Pliny's time, the medical profession used copper sulfate as a means to clinically induce vomiting. This is based on the fact that one of the body's natural physiological responses to prevent copper intoxication is vomiting. A Manual of Pharmacology and its Applications to Therapeutics and Toxicology, published by W. B. Saunders Company in 1957 recommends the use of 0.5 gram of copper sulfate, dissolved in a glass of water, in a single dose, or three doses of 0.25 gram fifteen minutes apart, for this purpose.

Since 1934, it has been known that individuals suffering from such diseases as scarlet fever, diphtheria, tuberculosis, arthritis, malignant tumors and lymphogranulomas exhibit an elevation of copper in their blood plasma. Since then, the list of maladies bringing about such elevation has been extended to fever, wounds, ulcers, pain, seizures, cancers, carcinogenesis, diabetes, cerebrovascular and cardiovascular diseases, and irradiation and tissue stresses, including restricted blood flow. This suggests that this redistribution of copper in the body has a general role in responding to physiological, disease, or injury stress. On the other hand, the elevation of copper in the affected organ has led some to postulate that it was this excess of copper that caused the disease. Nonetheless, this elevation of copper in diseased states is suggested to account for the natural synthesis of copper-dependent regulatory proteins and enzymes in the body required for biochemical responses to stress. It may be that these natural copper complexes expedite the relief of stress and the repair of tissues. Thus, it appears that in addition to the anti-bacterial and anti-fungal activity of inorganic copper compounds as recognized by the ancients, metallo-organic complexes of copper have medicinal capabilities that are fundamental to the healing process itself.

Copper is known to be an essential element in human metabolism. However, copper does not exist in the body in measurable amounts in ionic form. All measurable amounts of copper in the body exist in tissues as complexes with the organic compounds of proteins and enzymes. Therefore, it has been concluded that copper becomes and remains intimately involved in body processes. Some copper complexes serve to store copper, others to transport it, and yet others play important roles in key cellular and metabolic processes. Studies into the roles that these copper complexes play and the mechanisms of these roles have further confirmed that copper enters into the prevention and control of a number of disease states in the body. As will be discussed below, the key to the effective use of copper-based pharmaceuticals is not the use of inorganic compounds of copper, as used by the ancients, but rather the use of metallo-organic complexes or chelates of copper. The process of chelating metals allows them to be smuggled in the transport process across the intestinal wall and thereby enter into the mainstream of nutrient flow and usage in the body.

The first modern research on the subject of copper medicinal substances was by Professor John R. J. Sorenson,

of the University of Arkansas for Medical Sciences, College of Pharmacy, who, in 1966, demonstrated that copper complexes have therapeutic efficacy in the treatment of inflammatory diseases using doses that are nontoxic. Since then, copper metallo-organic complexes have been used to successfully treat patients with arthritic and other chronic degenerative diseases. More than 140 copper complexes of non-steroidal anti-inflammatory agents (aspirin and ibuprofen, for example) have been shown to be more active than their parent compounds. Copper aspirinate has been shown not only to be more effective in the treatment of rheumatoid arthritis than aspirin alone, but it has been shown to prevent or even cure the ulceration of the stomach often associated with aspirin therapy. Based on these experiences, the work of Professor Sorenson and other researchers around the world has progressed into the medicinal benefits of organic complexes of copper in a number of disease states. This work, thus far mainly based on animal research, has opened a whole new vista both into the understanding of copper's many-fold role in the body and in the practicality of using supplementary copper in the treatment of wound healing and inflammation-related disease states. Some of these potential indications are:

### **Ulcer and Wound-Healing Activities of Copper Complexes**

It has been demonstrated that copper complexes such as copper aspirinate and copper tryptophanate, markedly increase healing rate of ulcers and wounds. For example, copper complexes heal gastric ulcers five days sooner than other reagents. Further, it has been shown that, whereas non-steroidal anti-inflammatory drugs, such as ibuprofen and enefenamic acid suppress wound healing, copper complexes of these drugs promote normal wound healing while at the same time retaining anti-inflammatory activity.

### **Anticonvulsant Activities of Copper Complexes**

The brain contains more copper than any other organ of the body except the liver, where copper is stored for use elsewhere. This fact suggests that copper plays a role in brain functions. With reports of seizures in animals and humans following the protracted consumption of copper-deficient diets, it was reasoned that copper has a role to play in the prevention of seizures. It was subsequently discovered that organic compounds that are not themselves anti-convulsants exhibit anticonvulsant activity when complexed with copper. Further, it was found that copper complexes of all anti-epileptic drugs are more effective and less toxic than their parent drugs.

### **Anticancer Activities of Copper Complexes**

As early as 1912, patients in Germany were treated for facial epithelioma with a mixture of copper chloride and lecithin. Success of such treatment suggested that copper compounds have anticancer activity. Work at the University of Liverpool in 1913 demonstrated that subcutaneous and intravenous injections of a copper salt or colloidal copper softened and degenerated carcinomas transplanted into mice. In 1930, work in France indicated that injections of colloidal copper mobilized and expelled tumor tissue. Recent work with mice in the USA has shown that, indeed, treatment of solid tumors with non-toxic doses of various organic complexes of copper markedly decreased tumor growth and metastasis and thus increased survival rate. These copper complexes did not kill cancer cells but caused them to revert to normal cells.

#### **Anticarcinogenic Activity of Copper Complexes**

Based on work in the treatment of cancers using copper complexes, researchers have found that these same complexes may prevent or retard the development of cancers in mice under conditions where cancers are expected to be induced.

### Radiation Protection and Radiation Recovery of Copper Complexes

Ionizing radiation, such as that used in the treatment of cancer, has been shown to induce massive systemic inflammation. Ideally, such radiation-induced injury might be prevented or ameliorated by chemical repair mechanisms in the body. Thus, pharmacological approaches to the repair of radiation-damaged tissue are needed. As early as 1984, copper metallo-organic complexes have been shown to have radiation protection and radiation recovery activities. They are capable of causing rapid recovery of immunocompetence and recovery from radiation induced tissue changes. The mechanism of this activity appears to be tied to the ability of certain copper complexes to deactivate the superoxide, or "free," radicals liberated by ionizing radiation. In addition, since radiation has the capability of breaking the bonds of natural copper enzymes in the body, supplementing these with non-toxic doses of pharmaceutical copper complexes restores the lost tissue-repair capability. Since these complexes may also have anticarcinogenic activity, it is suggested that there would be merit in using copper complexes in the treatment of cancer and in particular, treating patients undergoing ionizing radiation therapy for their cancer, accidental exposure to radiation, and astronauts undertaking space travel.

# **Heart Disease and Copper Complexes**

Numerous studies have drawn attention to the relationship between copper deficiency and heart disease. First observed in rats in 1936, this effect has now been traced to both a deficiency in copper and an imbalance in the copper-to-zinc ratio in the body. Work by Dr. L.M. Klevay at the U.S. Department of Agriculture, Human Nutrition Research Center in 1973 has led to the postulation that copper has a direct effect on the control of cholesterol. In continuing work published in 1975, he theorized that a metabolic imbalance between zinc and copper - with more emphasis on copper deficiency than zinc excess - is a major contributing factor to the etiology of coronary heart disease. Subsequent work by other investigators has shown that copper complexes also can have a valuable role in the minimization of damage to the aorta and heart muscle as oxygenated blood reperfuses into tissues following myocardial infarction. This action is based on the anti-inflammatory action of copper complexes. These and other studies suggest the use of copper dietary supplements as a means of preventing and controlling such diseases as atherosclerosis (a form of arteriosclerosis), coronary heart disease, aortic aneurysms and myocardial infarction. It has been speculated that the reason that the heart attack rate in France is lower than in the rest of Europe is because of the French practice of drinking red wine. Red wine has a higher copper content than white wine because it is prepared with the skin of the grape intact. The copper originates in the wine from the copper fungicides used on the grapes in the field.

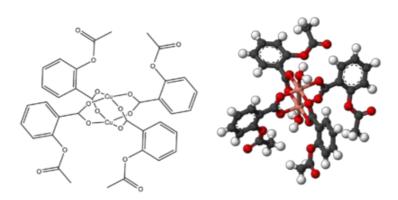
Based on an abundance of historical data such as the foregoing, many researchers anticipate that copper will become an increasingly important component of tomorrow's medical treatments.

#### References

The historical part of this paper is based on H.H.A. Dollwet and J.R.J. Sorenson, Historic uses of copper compounds in medicine, Trace Elements in Medicine, Vol. 2, No. 2, 1985, pp 80 - 87.

http://en.wikipedia.org/w/index.php?title=Copper\_aspirinate&oldid=465679308

# **Copper Aspirinate**



IUPAC name -- dicopper 2-acetyloxybenzoate

Other names --

tetrakis-µ-acetylsalicylato-dicopper(II), copper(II) aspirinate, cupric acetylsalicylate, cupric aspirinate, cupric aspirinate,

Identifiers

CAS number -- 23642-01-5 YesY

PubChem -- 92244

## **Properties**

Copper(II) aspirinate is an aspirin chelate of copper(II) cations (Cu2+). It is used to treat rheumatoid arthritis.

Molecular formula C36H28Cu2O16

Molar mass 843.69g/mol

Appearance Bright blue crystalline solid. Melting point 248-255 °C (decomp.)

Related compounds -- Aspirin; Other cations -- Zinc aspirinate, Aluminium aspirinate

Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)

## Preparation

Copper aspirinate can be prepared by several methods. In one route of preparation, an excess of acetylsalicylic acid is dissolved in aqueous sodium carbonate. Sodium hydroxide is not suitable for this purpose, because it will hydrolyse acetylsalicylic acid (ASA) into salicylic acid and sodium acetate.

2 HC9H7O4 + Na2CO3 ? 2 NaC9H7O4 + CO2? + H2O

The resulting solution is then filtered to remove any undissolved acetylsalicylic acid and is mixed with a solution containing Cu2+ cations (copper(II) sulfate is suitable), precipitating bright blue crystals of copper aspirinate immediately. The crystals can then be filtered from solution, washed, and dried. An excess of acetylsalicylic acid is used in the first step, because it eliminates the possibility of unreacted carbonate anions precipitating the copper in this step.

4 NaC9H7O4 + 2 CuSO4 ? C36H28Cu2O16? + 2 Na2SO4

#### **Medicinal Use**

Copper aspirinate has been proven effective as a treatment for **rheumatoid arthritis**.[1] The studies on animal models suggest that copper aspirinate is very promising in treating against **thrombotic diseases** and it has all the prospects of success in becoming an antithrombotic drug that prevents and treats thrombotic diseases in humans. [2]

#### Other uses

The use of copper aspirinate as a pigment in PVC and Polystyrene has also been investigated.[3]

#### **Footnotes**

- 1. ^ "Rheumatoid Arthritis (RA)". Copper Development Association. June 2000. http://www.copper.org/innovations/2000/06/medicine-chest.html.
- 2. ^ Weiping Liu,corresponding author1 Huizhou Xiong, Yikun Yang Ling Li, Zhiqiang Shen, and Zhihe Chen (1998). "Potential Application of Copper Aspirinate in Preventing and Treating Thromboembolic Diseases". Met Based Drugs. (Hindawi Publishing Corporation) 5 (3): 123–126. doi:10.1155/MBD.1998.123. PMC 2365110. PMID 18475833. http://www.copper.org/innovations/2000/06/medicine-chest.html.
- 3. ^ Allan, J R; A Renton, W E Smith, D L Gerrard, J Birnie (1991). "A Study of the Performance of Bis(acetylsalicylate) Copper(II) and the Cobalt(II), Nickel(II) and Copper(II) Complexes of Pyridine-3,4-dicarboxylic Acid as Colouring Materials for Poly(vinyl chloride) and Polystyrene". Eur. Polym. J. 27 (7): 669–672. doi:10.1016/0014-3057(91)90155-H.

### **Salicylates**

Salicylic acid
Aspirin
Aloxiprin
Methyl salicylate
Magnesium salicylate
Ethyl salicylate
Bismuth subsalicylate
Sodium salicylate
Sodium salicylate
Salicylamide
Salicin
Benorilate
Salsalate

Ethenzamide

Diflunisal

Trolamine salicylate

Homosalate
Salicylmethylecgonine
Octyl salicylate
Aluminon
Benzyl salicylate
Copper aspirinate
Potassium salicylate

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# **Copper Aspirinate Synthesis**

by

#### **Brian Fraser**

10-4-03b



Disclaimer: The following is a summary of the procedure I used to make copper aspirinate. I offer it here for informational purposes to show that copper aspirinate can be made with commonly available materials and equipment. A similar procedure is typically done by second-year college chemistry students as a laboratory exercise in a setting supervised by a professional instructor. I do NOT recommend that people do this at home. Some aspects of these procedures are hazardous, and the typical home kitchen simply has too many distractions and interruptions for a student to carry out these procedures safely. Your wife ( or mom) will also be furious if you get copper sulfate stains on her kitchen counter!

Copper Aspirinate synthesis (kitchen method)

Equipment and Materials required

- 1. Saturated copper acetate solution. See procedure below.
- 2. Pure aspirin crystals. See procedure below.
- 3. Ethanol (95%; liquor store ethanol like Everclear (190 proof, UPC 088352100036) is what was used here.
- 4. Vacuum filtration facilities (Büchner funnel, coarse and medium porosity filter paper, aspirator, filter flask, seals, tubing, clamps, stand, etc. These common lab tools are not absolutely necessary, but can speed things up considerably.)
- 5. Containers for liquid such as Rubbermaid 24 fl. oz. servin' saver tm (used here as a "beaker").

### Procedure

- 1. Add 1 fl. oz. of saturated copper acetate solution to a beaker.
- 2. Dissolve 1 tsp (teaspoon) pure aspirin crystals in about 1 fl. oz. of ethanol (95%) in another beaker
- 3. Pour the aspirin solution into the copper acetate solution. Stir occasionally.
- 4. Dark blue crystals will gradually form on the sides and bottom of the beaker. The initial layer will form immediately if the beaker has been freshly cleaned and scoured. The layer will gradually thicken and become bluer and darker. This process may take several hours. The endpoint is reached when the liquid has turned a

light blue and no more blue crystals are forming on the walls of the beaker. (You can verify the endpoint by siphoning the clear liquid, evaporating it in a separate container, and checking the residue. The residue should be mostly aspirin crystals.)

This procedure requires no heating. If you heat the liquid to increase the reaction rate, be aware that aspirin can hydrolyze into acetic and salicylic acids in a moist or liquid environment. If that happens, the liquid will turn dark green, and the yield of copper aspirinate will be greatly reduced.

- 5. Cool the mixture in a refrigerator.
- 6. Scrape the crystals off the sides and bottom of the beaker. Then vacuum filter the whole mixture. (Save the first filtrate in a separate container if you do ethanol solvent recycling.)
- 7. Wash the blue powder on the filter with cold distilled water.
- 8. Dry the powder and filter paper in an oven at about 120F. Store the dry powder in a small dark bottle with a label identifying the contents and the date of creation.

#### Alternative Procedure

Substitute isopropanol (99%) for the ethanol in step #2 and use 1/2 teaspoon, instead of 1 teaspoon, of aspirin crystals and 1/2 fl. oz. isopropanol instead of 1 fl. oz of ethanol. After several hours of initial crystallization, add 1/2 fl. oz. of distilled water and place the beaker in the refrigerator and wait a few more hours for more crystals. This variation gives about the same results as the ethanol procedure. Its advantages are that it uses less excess aspirin and a less expensive alcohol.

Aspirin purification (kitchen method)

### Equipment and Materials required

- 1. One bottle of 1000 commercial aspirin tablets (preferably the uncoated kind).
- 2. A pint or two of isopropyl alcohol (99%). This is usually available from a hardware store. Sometimes it can be found in a drugstore (UPC: 341226909730) Isopropanol is extremely flammable, so be very careful not to expose vapors to hidden or unexpected ignition sources.
- 3. A couple of gallons of deionized or distilled water.
- 4. Three, 24 fl. oz. wide-mouthed polypropylene containers with covers, such as Rubbermaid servin' saver tm.
- 5. Oven thermometer (easily read dial type is best)
- 6. Modified turkey baster (see construction procedure below)
- 7. One kitchen (with sink, refrigerator, oven, etc)

#### Procedure:

- 1. Dump a few hundred aspirin tablets into a wide-mouthed container.
- 2. Add distilled water to the container and stir. This will break up the aspirin tablets and dissolve the hydroxypropyl methycelluose coating that is usually used to coat aspirin tablets. Let the mixture settle for an hour or so in the refrigerator.
- 3. Siphon most of the water out with a modified turkey baster.
- 4. Repeat steps #2 and #3 a total of three to five times. This will largely get rid of the methycellulose coating, which tends to clog filters. You might not need to repeat these steps if you use uncoated aspirin.
- 5. Vacuum filter the mixture from #4 and dry the powder in air. (Caution: aspirin tends to decompose when heated in a moist environment).
- 6. Add the powder to a quart container. Add about a half-cup of isopropyl alcohol (99%). Stir. This will dissolve

part, but not all, of the aspirin. Let the mixture settle.

- 7. Vacuum filter the above mixture using medium porosity filter paper. Pour the filtrate into a clear glass container for inspection. If the filtrate is not clear, re-establish vacuum on the filter, and filter it again. (Sometimes simply letting the mixture settle and then siphoning the clear liquid with a turkey baster is more effective than filtration; the latter, however, may be faster.)
- 8. Pour the clear filtrate containing the dissolved aspirin into the second container, cover it, and place it in the freezer (about 5 F or so). After an hour or so the aspirin will crystallize out of solution. Return the powder on the filter to its original quart container.
- 9. After the aspirin crystals have formed, remove the container from the freezer. Carefully decant the liquid back into the first container that contains the impure aspirin powder. Then scrape out the pure aspirin crystals into a third container.
- 10. Cover this first container (impure aspirin powder and recovered isopropanol) and let it warm to room temperature. Agitate it occasionally so that more aspirin will again dissolve.
- 11. Repeat steps 7 through 10 until you have recovered all the aspirin, and the filter paper has only a thin layer of the excipients (typically calcium phosphate, starch, talc, etc. These impurities are added to the tablets to help them break up in water). Discard the filter paper. Dump the isopropanol down the drain, and wash it down with some tap water.
- 12. Using new filter paper (medium porosity), filter any remaining isopropanol from the recovered aspirin crystals (third container). Rinse the third container with distilled water and wipe it dry. Dump the filtered crystals back into the third container and cover them with cold distilled water. Re-establish vacuum on the filter and filter the crystals again. This will rinse off any remaining isopropanol. Discard the liquid. (Repeat the procedure if you can still smell isopropanol on the crystals).
- 13. Finally, gently dry the aspirin crystals. (I dried mine in an oven at 120 F. If you do this, BE SURE you have rinsed the crystals well enough so that there are no isopropanol vapors present. Isopropanol forms explosive vapors with air, and allowing these to accumulate in a confined space is a recipe for serious trouble. Also, aspirin tends to decompose when heated, especially in hot water, so I use only a warm temperature setting.)

Copper acetate synthesis (kitchen method)

Equipment and Materials required

- 1. Copper sulfate pentahydrate 99%. This is usually available from a hardware store in the form of a product used to kill tree roots in sewers and septic tanks, such as Roebic K-77.
- 2. Arm and Hammer Baking soda (sodium bicarbonate).
- 3. A couple of quarts of distilled vinegar (5% acetic acid).
- 4. A Pyrex casserole dish (22 x 11 x 6 cm or similar)
- 5. Vacuum filtration facilities.
- 6. Various clean, quart containers.

Procedure

Preparation of filtered copper sulfate solution

- 1. Dissolve 3/4 cupful of copper sulfate crystals in about a quart of warm distilled water.
- 2. Vacuum filter the solution through coarse porosity filter paper. This will filter out suspended solids (metal flecks, "dirt", etc.). Pour the filtrate off into a clear inspection container. Vacuum filter the solution again with medium porosity paper until it is clear blue. Note that the filtrate may still contain significant impurities (lead, arsenic, cadmium, etc.) at this point. Remember that this product is normally used in sewers.
- 3. Save the clear blue solution for later use.

(4. If you want higher purity copper sulfate, you can re-crystallize it at this point.)

Preparation of sodium carbonate solution

- 1. Pour a cup full of sodium bicarbonate into a Pyrex casserole dish. Add distilled water sufficient to dissolve it.
- 2. Heat the solution in an oven to about 200F. This will cause the bicarbonate to decompose into the carbonate with the evolution of carbon dioxide. The end result will be a solution of sodium carbonate.
- 3. Let the solution cool to room temperature. Carbonates are somewhat less soluble than bicarbonates; add more distilled water if necessary to keep the material in solution.

## Preparation of copper carbonate

- 1. In a large container, gradually combine the copper sulfate solution with the sodium carbonate solution. A blue-green precipitate will immediately form along with the vigorous release of carbon dioxide. Let the precipitate settle out.
- 2. At this point the liquid portion will have either an excess of sodium carbonate or of copper sulfate. If you add a drop of sodium carbonate and see some precipitate form, then the bulk mixture needs more sodium carbonate solution added. Likewise, if you add a drop of copper sulfate and see a precipitate, then the bulk mixture needs more copper sulfate solution added. Make these adjustments as necessary until there is no longer an unambiguous formation of the blue-green precipitate.
- 3. Vacuum filter the mixture with a coarse porosity paper filter. Discard the liquid. Wash with cold distilled water and then refilter. This will wash out any excess sodium carbonate or copper sulfate.

### Preparation of copper acetate solution

- 4. To a quart container, add the still moist copper carbonate powder from the previous step. Then slowly pour vinegar into the container. Carbon dioxide will evolve and copper acetate will form. The solution will gradually become a deep blue color. A blue-green precipitate may also settle to the bottom of the container.
- 5. Let the solution settle out. If there is a substantial amount of blue-green precipitate at the bottom of the container, add more vinegar. Try to dissolve most, but not all, of this precipitate. An excess of vinegar is harder to remove than a little of the precipitate.
- 6. Using coarse paper, vacuum filter the resulting copper acetate solution. Repeat until clear. Discard the paper. Save the blue filtrate.
- 7. Slowly evaporate the blue filtrate in a Pyrex casserole dish in an oven (150F) for several hours. Periodically scrape down the sides of the dish to prevent a build up of crystals. Continue the evaporation until some blueblack crystals of copper acetate begin to form (and do not redissolve). The mixture may also have some bluegreen "pond scum" in it too.
- 8. Cool and filter the dark blue solution. Store it in a clear glass container for observation (a one quart vinegar bottle works fine). This is the saturated copper acetate solution that will be used to make copper aspirinate.
- 9. If you want to make copper acetate crystals, continue the evaporation process until blue-black crystals form. This will require evaporating most, but not all, of the solution. Impurities (and excess vinegar) tend to remain in solution instead of crystallizing out. Hence, it is necessary to discard a small portion of the original solution. Collect the crystals on the vacuum filter and discard the leftover liquid. Wash the blue-black crystals with a little bit of cold distilled water. Then dry and store them in a labeled container.

# Conversion of Aspirin to Salicylic acid (kitchen method)

- 1. Put about 4 tsp of pure aspirin crystals (see above) and 1/2 cup distilled water into a small, clean jar (such as one used for canning pickles or olives).
- 2. Place jar on a hot pad in a shallow pan in an oven set to about 225F. Let the aspirin hydrolyze into acetic and salicylic acids for an hour or two. (Add a little more water if all the crystals have not dissolved in the hot liquid.)

- 3. Cool the liquid in the refrigerator. You should see needle-like crystals.
- 4. Vacuum filter and wash the crystals with cold distilled water. This will remove acetic acid residue.
- 5. Dump the crystals out of the filter and air dry them. (they usually come out as a mat of fine needles). Store in a properly labeled bottle.

Conversion of Salicylic acid to Phenol

Phenol (carbolic acid) is an important disinfectant and germicide, as well as an important organic reagent.

According to the Merck Index (10th ed.), salicylic acid sublimes at 76 C, melts at 159 C, and will decompose into phenol and carbon dioxide when rapidly heated at atmospheric pressure.

Copper Salicylate Synthesis (kitchen method)

- 1. In a small custard dish, dissolve 1/4 tsp of sodium bicarbonate (baking soda) in a few of teaspoons of distilled water.
- 2. Add about 1/2 tsp of the salicylic acid crystals recovered from the conversion described above. Mixture will fizz a little. Stir until all the crystals dissolve.
- 3. Test the pH. Add more salicylic acid or bicarbonate to get pH of about 6 (slightly acid). This is now a solution of sodium salicylate.
- 4. Add copper sulfate solution drop by drop. An ugly green precipitate (copper salicylate) will form.