6.3 Phenolic compounds with practical uses

6.31Phenolic compounds used as antiseptics

a)Ortho-phenylphenol is used on skin of citrus fruit and nuts to prevent mold growth.

b)Hexyl resorcinol is found in throat lozenges such as Strepsils Extra (most popular sore throat lozenge in England) and some mouthwashes; it produces a local anesthetic effect. It's questionable whether the concentration of hexyl resorcinol released into the saliva is enough to have any clinical effect on bacterial growth(Wilson and Gisvold's Medicinal Chemistry)

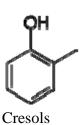
e)Hexachlorophene(active ingredient of pHisohex) is a chlorinated phenolic disinfectant that has been commonly used for scrubbing hands before surgery in hospitals to kill gram positive bacteria (particularly Staph. aureus) on the skin. It is gradually absorbed into the skin and repeated or prolonged scrubbing is needed to build up bacteriocidal activity. Unfortunately it is not active against gram negative bacteria. It used to be used for bathing babies, but in 1972 evidence that it is absorbed through babies' skins was published and that it might cause brain damage. It was taken off the OTC market and is now available only by prescription.

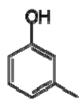
f)Triclosan is still another chlorinated bacteriostatic phenolic compound that is being used in hand soaps, body washes, detergents, dish washing liquids and anti-microbial creams, and lotions. There is evidence that bacteria are becoming resistant to these chlorinated phenolic bacteriocides.

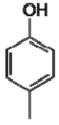


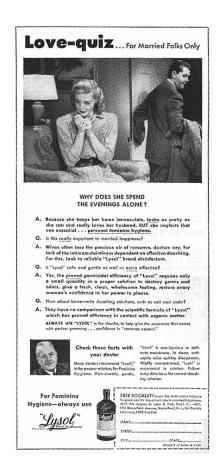
Creative Commons: http://www.flickr.com/photos/14936293@N03/2389378576/ Jack Black's Stunt Double

g) The original formulation of Lysol contained a mixture of cresols (ortho, meta and para forms of methylphenol) and was used as a feminine hygiene product until the AMA argued against its use, concerned that it could kill off natural flora and leave the vagina more susceptible to pathogenic bacteria. It was heavily market from ~1920 to 1960.











mum.org

Other non-phenolic antiseptics and bacteriocides.

Benzoyl peroxide is used in the treatment of acne. It causes sluffing of the top layer of skins cells, stimulating growth of lower epithelial cells.

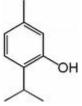
Hydrogen peroxide (H_2O_2 as a 3% solution) is used as a common wound disinfectant. It decomposes to form O_2 which is toxic to anaerobic bacteria that can cause serious infections in wounds.

Chlorhexidine.

Chlorhexidine is chlorinated imine that is a common ingredient in mouthwash designed to reduce gingivitis. It is also used in some scrubbing soaps.

6.32 Phenolics used as flavoring agents

a) Thymol is a naturally occurring phenolic compound isolated from the herb thyme and the resin myrrh that was used in biblical times.



It is used as a (minor) ingredient in Listerine and some brands of cigarettes.
thyme myrrh myrrh tree



Creative commons: Thyme - by Marie Richie.jpg



Creative commons: <u>Somali_man_Myrrh_tree.jpg</u>
Somalia Ministry of Information and National Guidance



Living clean.com



Pagandreams.co.uk

b)Eugenol is a phenolic compound found in cloves as well as nutmeg and cinnamon. It is sometimes added to "natural toothpastes" or mouthwashes. It contributes a clove flavor to the product and also has some antiseptic and local anesthetic effect. It is used in root canal packings.

Clove cigarettes(kretek) are a mixture of ground clove and tobacco (typically about a 40:60 mix) that were first created in Indonesia in the 1880's and became very popular fad in the US in the 1980's. Besides the pleasant clove smell, the eugenol would provide some anesthetic effect. Unfortunately the eugenol also probably reduces smooth muscle motility, making it more difficult for the lungs to remove some of the tar that has been inhaled. Clove cigarettes typically provide nicotine and tar at twice the levels of typical American brand of cigarettes. They received bad publicity when several smokers of clove cigarettes came down with severe pulmonary problems and their popularity has dropped since their peak in the 1980's. Several states have made the sale of clove cigarettes illegal, and similar bills have been introduced in the US senate in 2004, presumably with the blessing of the US tobacco manufacturers. In 2005 Phillip Morris

bought control of one Indonesian clove cigarette company. (If you can't beat them, buy them out!)



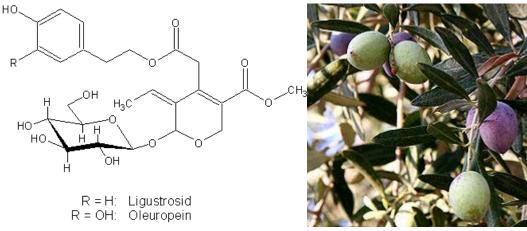


Wikipedia: clove cigarettes

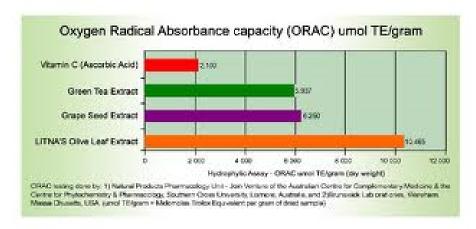
Eugenol

c) Oleuropein

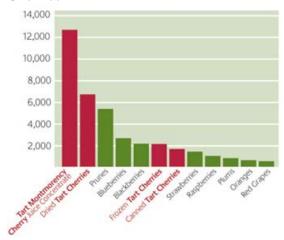
Oleuropein is a phenolic compound in olives that has a very bitter taste. Small amounts invirgin olive oil give a slight bitterness. It is removed from olives by long soaking in an alkaline brine. The alkali converts the phenolic groups into phenolate ions which increases the water solubility of the oleuropein and increases the amount that leaches out of the olives.



Wikipedia: olive

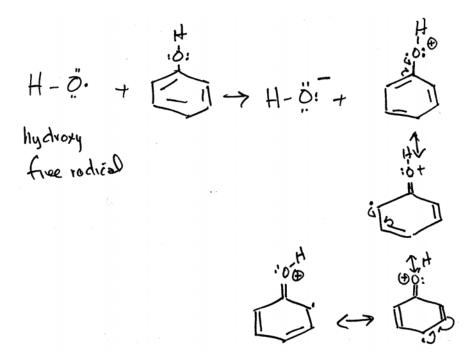


Cherries



6.33 Phenol compounds with electron transfer and antioxidant roles

A variety of naturally occurring molecules with multiple phenol groups (**polyphenols or polyphenolics**) have been promoted as antioxidants in the popular press. The term antioxidant is not clearly defined. The name implies that antioxidants prevent oxidation reactions. Many antioxidants react with free radicals that are formed during oxidation reactions and reduce the damage that may occur to other molecules. In the process, they often become a free radical. However the unpaired electron can be delocalized over the whole benzene ring, in a manner analogous the pi electrons of benzene, and this stabilizes the unpaired electron and frequently allows the further metabolism of the phenol free radical in a less destructive manner.



A variety of phenolic plant molecules called **flavonoids** contribute to the color of many fruits (red grapes, apples, colored vegetables) and have been found to be antioxidants in test tube (in vitro) studies. Epidemiological data suggests that people who eat large amounts of fruits and vegetables are at lower risk of cancer and cardiovascular disease and the result has been that many dietary supplements containing these compounds have been promoted as antioxidants which would reduce the risk of cancer and cardiovascular disease. It needs to be pointed out (and the dietary supplement marketers don't do this) that there is virtually no direct data showing that taking these supplements actually improves health in a carefully done randomized controlled study.

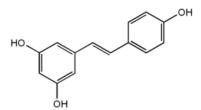
Flavonoids are found in fruits and leafy green vegetables. They are usually found covalently bonded with sugars which are hydrolyzed off in the process of absorption and metabolism. Absorption of flavonoids from the GI tract into the bloodstream is typically less than 5% and metabolism in the liver appears to be rapid with excretion in the urine. This makes it difficult to argue that their presence in the blood stream is high enough and long enough for them to be physiologically important antioxidants. Recent research suggests that some other factor besides the antioxidant activity of the flavonoids themselves may be responsible for the improved health of individuals eating lots of fruits and vegetables.

a)Quercetin. Quercetin is one of the most studied flavonoids. It is found in tea, onions, and a variety of fruits combined with a sugar to produce a quercitin glycoside called rutin.

(upside down)

b)Resveratrol is a polyphenolic that is found in the skins of red grape, red wine, and other fruits. It appears to inhibit the growth of fungi and molds. It received a lot of media attention in 2003 when Harvard Professor David Sinclair published a paper showing that feeding yeast high concentrations of resveratrol extended their lives. His research has worked its way up the family tree, showing similar results in nematodes (a microscopic worm), fruit flies, fish and most recently on mice fed a high fat diet. It was heralded as the molecule responsible for the "French paradox" (the relatively long life span of the French whose traditional diet has been high in saturated fats). However, the amount of resveratrol needed to produce these results far exceeds the amount found in grapes and other fruits (by a factor of ~ 1000) and would require supplements to attain the same blood levels in humans. There is no data yet available in humans to show that resveratrol reduces disease or increases life span of humans, but this has not prevented resveratrol from becoming a very popular dietary supplement.



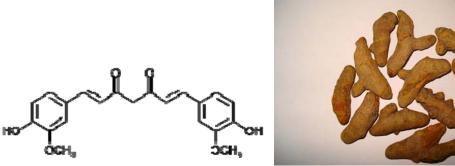


Resveratrol

Wikimedia Commons: <u>San Diego Bay Wine & Food Festival</u> Chocolate (particularly dark chocolate) contains a variety of phenolic flavonols.

(What type of geometric isomer is the C=C between the two benzene rings?)

c) Curcumin is a primary ingredient in turmeric spice which is often a component of curry. A large variety of claims have been made for it (anti-inflammatory, anticancer, treatment of psoriasis) based on limited data. It does have two phenolic rings which may provide some anti-oxidation properties.



Creative commons: haldi phalli: miansari66



Creative commons: Chicken curry: Quadeli

d)Vitamin E (tocopherol) is a naturally occurring antioxidant which slows down the oxidation of oils and membranes inside the cell.

e)Hydroquinone is a common structure found in larger biological molecules which undergoes oxidation and reduction. A hydroquinone is the active center of the coenzyme Q10; it helps transfer H atoms from the metabolism of sugar and fats in a multi-step process to the final H acceptor, molecular oxygen, O₂. In the process it is converted into quinone.

Hydroquinone



http://www.flickr.com/photos/superskinlightener/4927625326/sizes/l/in/photostream/



Wikipedia: Michael Jackson

Hydroquinone/quinone structures are also found in vitamin K. Hydroquinone is used as an OTC and prescription skin whitener.

f) **Butylated hydroxytoluene** (**BHT**) is an antioxidant added to food and food packaging material to scavenge oxygen free radicals and to slow down the rate at which food goes rancid. There are numerous contradictory claims in the literature about its health effects.

