Do heavy metals counter the potential health benefits of wine?

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Introduction

The possibility that wine, consumed in modest amounts, can have health benefits has been highlighted frequently in the public and scientific press and was recently briefly reviewed in the South African medical literature.[1] Much of the benefit is attributed to the antioxidant activity of wine. In contrast, concern was recently expressed about exposure to heavy metal ions in wines[2] even at intakes of 250 mL/day, partly because they may promote oxidative stress. A brief review of heavy metals, their content in wine as well as in food, and their possible adverse effects on health is thus opportune.

Cardiovascular disease is prevalent in the developed world and is rising in the developing world.[3] Preventive measures that involve lifestyle are appropriate, with the possible inclusion of the consumption of wine. Trends and potential hazards of some heavy metals were updated recently,[4] with a warning that intakes may still be on the increase, especially in the developing world. If the heavy metal content of wine is significant, the beneficial effect of wine to lessen cardiovascular risk may be outweighed by other adverse effects in the very long term.

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Heavy metals with an impact on health

Strictly speaking, heavy metals were defined as those with a higher density than 5 g/mL[4] but the collective term now includes arsenic (As), cadmium (Cd), chromium (Cr), copper (Cu), iron (Fe), lead (Pb), manganese (Mn), mercury (Hg), molybdenum (Mo), nickel (Ni), vanadium (V) and zinc (Zn). Some interest also exists in aluminium, cobalt, strontium and other rarer metals. Potassium, calcium and magnesium are expected in wine because of their high intracellular content. Physiologic roles are known for Fe (haem moeities of haemoglobin and cytochromes), Cu (amine oxidases, caeruloplasmin, dopamine hydrolase and collagen synthesis), Mn (superoxide dismutase), Zn (protein synthesis, stabilisation of DNA and RNA) with low requirements of Cr (glucose homeostasis). Other heavy metals ions are not believed to be essential to health, even in trace amounts.

Heavy metal metabolism

Heavy metals may be complexed to phenolic compounds in food and wine, but free ions are available for absorption and this is favoured by the low gastric pH. Red wines may have a health advantage over white wines because Pb may be less available for absorption[5] as a result of binding to proanthocyanidins. Even though some of the heavy metals are essential for health, their uptake is limited and they are generally bound to proteins in the body as well as in cells. Heavy metals may enter cells through various mechanisms. Divalent cations may utilise transporter proteins to enter the cell. Cd seems to enter through calcium channels owing to the similarity in ionic radii.[6] Anionic transporters could import compounds such as chromates. Insoluble forms of heavy metals could enter cells by phagocytosis.

The toxicity of heavy metals could be by the displacement of physiologically appropriate metals: Cd can replace Cu and Fe in cytoplasmic and membrane proteins. Especially in divalent form, the free heavy metal ions can promote the generation of superoxide and hydroxyl radicals which, in turn, can lead to oxidative damage of lipids, nucleic acids and proteins. Although not directly producing superoxide, at least some of the promotion of apoptosis by Cd is through the generation of hydrogen peroxide and this effect could be antagonised by the antioxidant, glutathione.[7] At low concentrations Cd also promotes lipid peroxidation and nucleic acid damage in a glioma cell culture model.[7] Divalent ions can bind to proteins and disrupt their function. Divalent ions could also have adverse effects on DNA, particularly at CpG nucleotide sequences where methylation of cytosine requires the nucleotides to be intact. Guanosine undergoes oxidative damage which is reversible by excision repair by oxoguanosine DNA glycosylase. The oxoguanosine and the oxidation of 5-methylcytosine to 5-hydroxymethylcytosine may alter methylation and this can lead to epigenetic phenomena with adverse effects on the cell. These effects were postulated to explain how Pb could have an adverse influence on Alzheimer disease risk.[8]

Despite the potential for harm through these mechanisms, evidence was recently reviewed in support of a neuroprotective effect for wine.[9] Cd incorporation into chromatin could have similar effects to Pb as well as additional effects to harm the reproductive system and embryonal development.[5] Many metals have been linked to an higher risk for cancer and it is postulated that the mechanism may be through oxidative stress.[10] Cd has been linked to skeletal damage.[4] Natural defense against divalent cations does exist. The expression of metallothionein in the liver results in the binding and transport of metals to the kidney for excretion. Ferritin[11] can bind Cd, Cu and Zn in addition to Fe.

Heavy metal intake in general

Though most of the intake of heavy metals is from food, other sources may contribute significantly. The concern is that wine may contribute heavy metals to the point where toxicity may emerge. Information was meticulously gathered for heavy metal intake from beverages in Denmark[12] where the average total daily intakes of Pb, Cd, Ni, Cr and As and Hg were 37, 20, 170, 43, 114 and 6.5 µg respectively. Per litre, wine contained an average of 66, 45 and 32 µg respectively for Pb, Ni and Cr. Previously, decanters and glass could leach significant amounts of Pb into alcoholic beverages, leading to saturnine gout.

Pollution of air may cause significant exposure to Pb but tetraethyl lead has been removed from petrol to diminish such exposure. A careful analysis[12] revealed that wine poured over the rim of the bottle had a three times higher concentration of Pb when the stopper was covered by lead foil. The final concentration of lead can thus exceed the limit of 200 µg/L recommended by the Organisation Internationale de la Vigne et du Vin. Abandonment of lead foil has thus had merit! It appears that the Pb content of wine has decreased over recent decades and this was attributed to the waning use of brass.[13] In the Danish study[12] wine was also found to be a significant source of Ni and Cr but the full range of metals was not analysed. Cigarette smoking provides significant intake of Cd.

Instant coffee also contains significant amounts of Cd. Cocoa has very variable and often high amounts of Cd. Vegetable and tomato juice may contain significant amounts of Ni. Since industrial pollution could render local produce toxic, studies examined exposure in Germany[14] and China.[15,16] At least in the region studied, German children consuming home-grown food did not have higher intakes of As, Cd, Pb and Hg compared with rural peers. Similarly, in China, no individual heavy metal intake was a specific concern for adults or children as intakes were below the recommended intake for life. However, Cd seemed more of a concern for adults and mercury more of a concern in children owing to their relative contributions to the total intake. Water may provide significant quantities of As. A study in Chile[17] revealed that fish and shellfish contributed much to the intake of As, Cd and Hg whilst the sugar-containing foodstuffs provided the highest content of Pb. A study in Catalonia[18] confirmed the trend for As from fish and shellfish and noted that fish also supplied Hg. Mercury assimilates in lipid stores as methylmercury.

Heavy metals in wine

The heavy metal content in wine can be related to factors operating before the grape berry is harvested and to factors affecting it through the processing, sale and consumption. The factors influencing the content in the grape relate not only to the natural soil content but also the addition from fertilisers and pesticides (e.g. blue vitriol), as well as pollution. An analysis[19] found the chief source of Cu in wines to be the soil. This study also found that red grapes contained more Cu, Fe, Mn and Zn than white grapes and that wines contained less heavy metals than the grapes. Some metal ions may be lost in the processing but exposure to precipitants and containers may also contribute to heavy metals in some wines. Analyses of wines have revealed very different concentrations of heavy metals, depending on their origins. An investigation into the heavy metal contents in soil, grapes and wines in Croatia[19] revealed that, despite enrichment of the soil, wines still conformed to permissible levels. In white and red wines the masses, in decreasing order of mass, were Cu, Mn, Cr, Fe, Zn, Pb, Ni and As. Given that the metal content can vary due to so many factors, extensive and regular surveillance would be required for foods and beverages to ensure their safety. Although there are variations in contents of heavy metals in wines from the same country, comparisons of heavy metals in wines could even be used to verify authenticity.[20] The concentrations of heavy metals in South African wines are not known. In the interest of health, it would be important to establish the heavy metal content of locally produced foods and wines.

Not only is the content of heavy metals in the wine of importance for health reasons, but also their intake from other sources and the duration of the exposure. Furthernore, individual susceptibility may vary, depending on environmental and genetic factors. Information for humans is largely observational and is thus imperfect. Intakes of heavy metals can be assessed in various ways[21]: acceptable daily intakes, no observed effect levels, or no observed adverse effect levels. A provisional tolerable weekly intake (PTWI) has been used to serve as a guide for exposure to individual heavy metals. Another method has been proposed to evaluate lifelong exposure to heavy metals: the target health quotient (THQ).[22] This formulation has the ideal value of less than unity. $THQ = f.t^{e}.m.c/1000.R.w.t^{n}$ where f is the frequency of exposure in days/year, te is the time of exposure in years, m is the mass of beverage consumed in g/day, c is the concentration of the metal in the beverage in µg/g, R is the oral reference intake dose in mg/kg/day, w is the body mass and tn is the time averaging for noncarcinogens in days. For the consumption of wine, the time is generally taken from 18 years of age to the average life expectancy and the average masses for males and females are applied in the calculation. The sum of THQ values of different metals could be taken as a crude global exposure.

In conclusion

With better control of infectious and cardiovascular disease, there is the expectation of a longer duration of life. Moreover, the quality of life towards the end of the lifespan requires increasing consideration. In this context it becomes important to pay attention to avoidable risk factors that could unfavourably affect later life. Much research needs

to be done on the impact of dietary heavy metals on health in all phases of life, susceptibility to these metals and ways of preventing or treating such effects. Clearly, this topic is not only important in the wine industry but is also important for all foodstuffs. There is a rising expectation by consumers that their foods should conform to recommendations and should declare all the contents that impact on health. However, modern equipment for the accurate measurement of these metals may not generally be available and standardisation is required for uniformity and comparability. A recent study instigated by the Australian government[23] indicated that reported concentrations varied when identical samples were distributed for analysis. Better and more detailed surveillance and study of foodstuffs and beverages will ensure that heavy metal intake will not become (more) harmful. Once heavy metal content is accurately known for foodstuffs and wines, more individualised advice can be provided where risk of toxicity may be especially high in individuals or regions. Wines selected from Italy, Brazil and Argentina were generally low in heavy metals.[2] This is in contrast to potentially hazardous content of V in wines from Hungary and Slovakia. Mn, Ni and Zn were more prominent in Czech, Spanish and Serbian wines.

The impact of the heavy metals on oxidative stress to lipids, proteins and nucleic acids would be relatively easy to assess in vitro and ex vivo and could provide mechanistic insight into potential harm. In vivo studies for harmful effects would be difficult and, at least in the short term, may not reveal (cumulative) damage. Large long-term population studies with reliable and detailed information about dietary and beverage intakes, possibly involving genetic and metabonomic substudies as well, are required to be able to properly evaluate the impact of heavy metals on health. Although the heavy metals play a role in the organoleptic characteristics and ageing of wine,[24] research is required to fully understand their requirements in the wine-making process and the impact that methods to remove the individual or collective heavy metals have on the storage and appreciation of wine.

Wine can thus be viewed as a source of heavy metals needed for nutritional reasons, but it may also expose the consumer to undesirable doses or kinds of heavy metals. Even if not toxic in the short to medium term, the heavy metals may pose a cumulative risk especially when the individual has a high exposure to these metals from other sources. The medical profession and the public should be aware of the potential deleterious effects of heavy metal intake. There are currently, however, no clear recommendations for heavy metal content in and intake from wine but there are some recommendations for nutritional intake. The balance of epidemiologic studies suggests a favourable effect of wine on cardiovascular risk[1] despite the variable and possibly disadvantageous intake of heavy metals. A healthy lifestyle with moderate consumption of wine may thus continue without undue concern, provided that wines are screened for undesirably high heavy metal concentrations and dietary intake is within acceptable limits.

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