Salicylic Acid in Wine as a Therapeutic Agent in Cardiovascular Disease

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Abstract

Introduction Epidemiological evidence consistently links moderate wine consumption with reduced mortality, mostly due to reduced incidence of cardiovascular disease. Recent scientific reports indicating that a diet rich in fruit and vegetables, together with moderate amounts of alcohol, but more specific red wine in moderation, is protective against various degenerative diseases, created a renewed interest in the consumption of grapes and wine as part of a healthy diet and lifestyle.

Aims The aims of this investigation were to determine from the available information whether there are grounds for these claims. The cardioprotective effects of wine may be due to the presence of pharmacological active ingredients such as acetyl-salicylic acid (aspirin) or salicylic acid.

Methods In this study twelve different South African wines were analyzed according to standardized pharmacological methods for the presence of salicylic acid and acetyl-salicylic acid.

Results Our results indicate that although all the red and white wine samples contain varying amounts of salicylic acid, it is noteworthy that no acetyl-salicylic acid could be detected in any wine sample.

Conclusions There is significant epidemiological and laboratory evidence to promote the consumption of grapes and wine as part of a balanced diet and lifestyle for certain individuals to prevent cardiovascular disease. The presence of salicylic acid and other phenolic compounds may provide protection against platelet aggregation by altering eicosanoid metabolism in favour of increased prostacycline and decreased thromboxane A_2 synthesis. Alcohol consumption guidelines should emphasize that it is inappropriate to indiscriminately advise non-drinkers, and for those people who should not drink at all to take up alcohol for health reasons.

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Introduction

Research consistently show that regular moderate consumption of alcohol *per sé*, whether in the form of wine, beer or spirits, exerts a protective effect against coronary heart disease.[1-3] Although heavy alcohol intake increases overall mortality[1, 4] and mortality due to cardiovascular diseases,[5-6] moderate intake appears to have a protective effect against coronary heart disease, as compared to drinking no alcohol.[7-9]

Evidence based on studies of diverse populations suggests that wine consumers have a lower risk for coronary heart disease and death from all causes. While red wine has been considered healthier than white wine, both red and white wine users were shown to have a lesser risk of dying from coronary artery disease than beer or liquor drinkers.[10] More recently a new set of data from the Copenhagen heart study revealed that wine drinkers were the least likely to die during the 12-year study period.[11] In this study, intake of spirits implies increased risk, while beer drinking did not affect mortality. Light and moderate drinking is associated with a dose dependant decrease in mortality attributable to cardiovascular and cerebrovascular disease as well as from other causes. Moderate consumption of wine is considered to be one to two glasses (125 – 250 ml) per day for men, and one glass per day for women, corresponding to 10 – 30 g ethanol per day.

The French lifestyle includes risk factors for coronary heart disease (high fat consumption, high frequency of smoking, lower exercise consciousness)

more than in North Americans, yet they have a lower incidence of this disease. This has appropriately been called the "French Paradox".[12,13] It has been postulated that the French are protected against coronary heart disease mortality by the large amount of wine they drink, particularly red wine.[14] Red wines, which have undergone extended grape skin contact and oak maturation, contain phenolic antioxidants, which inhibit lipid peroxidation, and could prevent atheromatous plaque formation. White wines have much lower concentrations of these antioxidants than red wines[14-17] which would support the view that red wine is more protective against atherosclerosis and coronary heart disease than white wine.

Wine may have benefits due to the presence of factors such as ethanol or other non-alcoholic components, and even other associated lifestyle factors associated with wine consumption. Epidemiological studies are not capable of determining the specific causes for the observed effects, and it is therefore important to establish whether or not there are identifiable molecular mechanisms whereby wine nutrients could affect cardiovascular disease.

Aims

Our interest is directed towards the role of phytochemicals in plant foods and wine in reducing platelet aggregation and thrombosis. Platelet aggregation is largely mediated by thromboxane A_2, a compound formed by enzymatic conversion of arachidonic acid via cyclo-oxygenase to PGH_2 and then to thromboxane A_2, a potent pro-aggregatory agent.[18,19] The synthesis of these compounds by cyclo-oxygenase is enhanced by lipid hydroperoxides.[20] These hydroperoxides are readily generated in response to tissue injury and during inflammatory reactions, in the presence of activated macrophages and platelets.[21,22]

Acetyl-salicylic acid (aspirin) inhibits cyclo-oxygenase and reduces the thrombotic tendency of platelets.[23-26] In vivo, aspirin is quickly de-acetylated to salicylate. Both the salicylate and the acetate ions into which aspirin is converted, contributes to the overall activity of aspirin. Furthermore, in a high dose, salicylate completely inhibits aspirin's (ASA) effect on platelet cyclooxygenase activity.[27] According to these authors, platelet and/or vascular cyclooxygenase might be spared acetylation by acetyl salicylic acid if the plasma levels of salicylate is carefully balanced with the plasma level of acetyl salicylate. The salicylate moiety may also interfere with the platelet and/or leukocyte lipo-oxygenase pathway of arachidonic acid metabolism, preventing hydroperoxide formation.

Both red and white wines are excellent sources of salicylic acid and its metabolites 2,3 dihydrobenzoic acid and 2,5 dihydrobenzoic acid,[28] all of which have vasodilator and anti-inflammatory activities. Many plants other than grapes produce salicylic acid. Salicylic acid is postulated to be a plant hormone.[29]

South Africa has one of the highest incidences of myocardial infarction in the world. Serious consideration should be given to prevent this epidemic of disabling disease that affects the young economically active sector of our country. Since South Africa produces good wines, we have decided to analyse various South African wine cultivars for the presence of salicylic acid and acetyl-salicylic acid (aspirin).

A thorough literature search to identify any applicable data and other information concerning the presence of salicylic acid (SA) and acetyl-salicylic acid (ASA) or aspirin in wine and their possible role in the prevention and management of coronary heart disease was carried out.

Available international data may differ from South African conditions; therefore comparative studies are necessary. Our aim was therefore to detect anti-platelet factors such as SA and ASA in twelve South African wine cultivars.

Materials and Methods

We decided to analyse 12 different high quality wine samples from the Stellenbosch region. The sample included 5 red wines, and 7 white wines with high concentrations of phenolic acids and antioxidants according to previous analysis.[17]

An assay for quantitating SA and ASA to determine the values in wine samples was developed. A minor modification of a method was previously developed for quantification of SA and ASA in human plasma. A known quantity of wine was diluted with concentrated perchloric acid, and injected onto the HPLC column. To determine the retention times of ASA and SA, and to calculate the concentration of ASA and SA in the wine, the same volume of perchloric treated wine samples were spiked with a known quantity of ASA and SA. To obtain a solution of ASA equivalent to 206 ng/ml in the wine and SA equivalent to 826 ng/ml (the standard addition method).

Thereafter the samples were analysed again. The retention times were 10.1 minutes for salicylic acid and 11.6 minutes for acetyl-salicylic acid. The lower limit of quantification for the assay during the study was set at the lowest acceptable calibration standard used consistently during the assay of the study samples: 33.1 ng/ml for acetyl-salicylic acid and 133 ng/ml for salicylic acid.

Results

The results of the acetylsalicylic acid and the salicylic acid determinations are presented in Table I.

The analysis of the South African wines for salicylic acid (SA) and acetyl-salicylic acid (ASA) revealed interesting results. None of the wine samples analysed contained ASA, whilst SA was present in all the samples in concentrations ranging from 126 to 383 ng/ml (Table I). These values differ significantly from concentrations in several Californian wines [28] where concentrations of SA values of 11 100-21 000 ng/ml were found, which are two orders of magnitude higher than the levels detected in the South African wines. This discrepancy is not explicable. However, researchers from Pennsylvania, reported an average value of 660 ng/ml in seven Vidal blanc wines [30] which is more comparable to our results.

Table I: Acetylsalicylic and Salicylic Acid content of a selection of South African wines.

Wine (ng/ml)	Acetylsalicylic acid (mg/ml)	Salicylic acid (ng/ml)
Sauvignon Blanc '96	none	318
Merlot '93	none	277
Chardonnay '95	none	126
Pinotage '93	none	277
Cabernet Sauvignon '92	none	232
Tassenberg Red	none	348
Rosé	none	234
Rhine Riesling '96	none	154
Sauvignon/Chardonnay '95	none	175
Special Late Harvest '96	none	207
Noble Late Harvest '90	none	383
Chardonnay '93	none	132

Discussion

Our results indicate that the concentration of SA is on average 300ug/L which equates to 100x less than the proposed 30 mg aspirin per day for protective effect.[31] Therefore wine does not have sufficient anti-platelet effect to protect against cardiovascular disease. We suggest that because wine is usually taken with a balanced meal, the additive effect of the wine- and the food salicylates may provide the necessary protection. The intake of salicylates in foods may have contributed to the decline in cardiovascular mortality in the United States .[32]

The amounts of salicylates in a variety of diets are evidently low; in an analysis of red wine, 0,7 mg salicylic acid per litre but also no acetyl-salicylic acid was found.[33] This is probably insufficient to affect disease risk.[34] In wine, however, salicylic acid and other antioxidants co-exist with ethanol and the synergistic effects between these substances may have a beneficial role in cardiovascular well being.

Salicylic acid and its metabolites, 2,3-dihydrobenzoic acid, and 2,5-dihydrobenzoic acid have vasodilatory and anti-inflammatory activities. Their combined effect in wine is not equivalent to the effect of the recommended daily dose of 30 mg acetyl-salicylic acid to maintain cardiovascular well being as a platelet inhibitor .[31]

The presence of salicylic acid in wine may, in part, explain the cardioprotective effect of wine. In wine, salicylic acid co-exists with ethanol that may have a synergistic effect for cardiovascular well being. Although a tablet of aspirin a day may be beneficially associated with a regular daily use of a couple of glasses of red wine, the possibility of an increased haemorrhagic risk of concomitant consumption of aspirin and wine should be considered.

There is significant evidence to promote the use of grapes and wine in moderation as part of a balanced diet. If salicylates and antioxidants play a role in the prevention and management of cardiovascular disease, it is possible that grapes and wine can make a positive contribution in this regard. Further investigations should be done to clarify the situation with regard to the protective effects of wine on the heart.

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