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Review

The impact of moderate wine consumption on health

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ABSTRACT

Wine is a traditional beverage that has been associated with both healthy and harmful effects. Conceptions like the so-called "French paradox" or the beneficial impact of the Mediterranean diet suggest benefit. Wine has a complex composition, which is affected by whether it is red or white or by other variables, like the variety of grapes or others. Alcohol and phenolic compounds have been attributed a participation in the benefits ascribed to wine. The case of alcohol has been extensively studied, but the key question is whether wine offers additional benefits. Resveratrol, a non-flavonoid compound, and quercetin, a flavonol, have received particular attention. There is much experimental work confirming a beneficial balance for both substances, particularly resveratrol, in various organs and systems. The pharmacological dosages used in many of those experiments have shed doubt, however, on the clinical translation of those findings. Clinical studies are limited by their observational nature as well as for the difficulties to abstract the benefits of wine from other confounders. Notwithstanding the doubts, there is reasonable unanimity in beneficial effects of moderate wine consumption in cardiovascular disease, diabetes, osteoporosis, maybe neurological diseases, and longevity. Observations are less enthusiastic in what refers to cancer. While considering these limitations, clinicians may spread the message that the balance of moderate wine consumption seems beneficial.

Contents

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1. Introduction

The consumption of alcohol can have beneficial or harmful effects, depending on the amount consumed and the profile of the consumer. Moderate alcohol consumption is defined in the Dietary Guidelines for Americans 2010 as up to 1 drink per day for women and up to 2 drinks per day for men [1]. Some epidemiological studies have found that moderate alcohol consumption is associated with a lower risk of cardiovascular disease (CVD) and a reduced risk of all-cause mortality among middle-aged and older adults. In addition, moderate alcohol consumption may also be associated with better cognitive function.

The interest on the effects of alcohol has further grown by the data, mainly accumulated since the 1990s, which confirms that wine, especially red wine, may enclose some healthy compounds, apart from its alcohol content. This specific advantage of wine has been supported by observations like the lower cardiovascular mortality rate in France in comparison with other countries with a similar consumption of saturated fats, the so-called "French paradox" [2]. The high intake of wine by the French population has been proposed as a potential explanation. The purpose of this review is to analyze the current scientific evidence on the impact on health of moderate consumption of wine.

2. Search strategy

The Pubmed database was searched for basic and clinical articles published in the last decade. The search focused on the exposure to wine or resveratrol. These terms were paired with "mortality", "cardiovascular disease", "ischemic injuries", "risk factor", "cancer", "bone density", "osteoporosis", "cognitive decline", "neurodegeneration", "diabetes", "chronic illness", "biological markers", "sex distribution" and "Mediterranean diet". No language restrictions were imposed. The search yielded 4341 references (Fig. 1). In addition to searching the electronic database we browsed the reference list of papers (both original articles and reviews) and included 53 supplementary papers.

Relevant articles were selected using a two-phase process. Two investigators (AA and AA) reviewed all identified abstracts for eligibility. Secondly, full text articles were revised to determine their interest. Priority was given to systematic reviews and more recent original articles. We excluded studies if the information was either repetitive or of lesser relevance to our subject. Finally, 118 articles were selected for citation.

3. Bioactive compounds in wine

Understanding the potential biological responses of wine is limited by two considerations, the vast array of components and the multiple mechanisms of action of each compound. The proportion of compounds differs depending on the variety of grape, the growing region, the method of production and the aging process.

Wine is composed of water, ethanol, glycerol, polysaccharides, different types of acids and phenolic compounds. The phenolic compounds of wine can be divided into flavonoids and non-flavonoids. Flavonoids, which account for over 85% of the phenolic components in red wine, include different molecular families like flavonols (which include quercetin), flavones and anthocyanidins. Non-flavonoid compounds include hydroxycinnamic acids, hydroxybenzoic acids, stilbenes (and its derivate resveratrol) and hydrolysable tannins [3]. Red wine is known to contain 10-fold more phenolic compounds than white wine.

The biological potential of the wide range of chemical compounds in wine has been examined in extensive reviews [4,5]. In this review we will focus specifically on two, resveratrol and flavonoids.

3.1. Resveratrol

Resveratrol (3,5,4′-trihydroxystilbene), was originally isolated from the dried root *Veratrum grandiflorum* in 1940. Resveratrol passed unnoticed until the 1990s when it was related to the French paradox [2,3]. A derivative of stilbene, resveratrol has two phenolic rings joined by a styrene double bond. It exists as two structural isomers: cis- (Z) and trans- (E). Trans-resveratrol can isomerize to cis-resveratrol if exposed to ultraviolet light or heat, and is the predominant isomer found in grapes [3] (Fig. 2).

In addition to grapes, resveratrol is found in berries, peanuts, cocoa powder and medicinal plants such as *Polygonum cuspidatum* [6]. It should be noted that resveratrol concentrations in wine vary markedly, reaching concentrations in red wine from 0.1 to 14.3 mg/L [4].

Previous studies have shown that although 70% of resveratrol is rapidly absorbed after oral ingestion, only trace amounts of unchanged resveratrol could be detected in plasma. The bioavailability of resveratrol is low and is not affected by food co-consumption, including high fat meals. Once absorbed it is conjugated in the small intestine or liver, released to systemic blood circulation and finally excreted in urine. Resveratrol has a half-life of approximately 9.2 ± 0.6 hours [3,4]. Indeed, pharmacokinetic studies in humans have shown that the oral ingestion of 0.5 g resveratrol, a concentration approximately 35 times higher than that contained in one liter of a resveratrol rich wine, gives a peak blood concentration lower than 0.32 μM [7]. This consideration is important because pharmacologic studies confirm that resveratrol, when used at higher concentrations, interacts with different receptors and kinases. Among them, the silent mating type information regulation 2 homolog 1 (SIRT1), a member of the sirtuin family, which may affect different metabolic pathways possibly involved in the progression of cancer, cardiovascular or