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Review Article

Effect of resveratrol on cardio vascular system

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ABSTRACT

Resveratrol (RESV) is a polyphenolic compound found in various plants, including grapes, berries and peanuts, and its processed foods as red wine. RESV possesses a variety of bioactivities, including antioxidant, anti-inflammatory, cardioprotective, antidiabetic, anticancer, chemopreventive, neuroprotective, renal lipotoxicity preventative, and renal protective effects. The phytoantitoxin resveratrol is a plant-derived polyphenol with phytoestrogenic properties. Resveratrol protects the cardiovascular system by mechanisms that include defense against ischemic-reperfusion injury, promotion of vasorelaxation, protection and maintenance of intact endothelium, anti-atherosclerotic properties, inhibition of low-density lipoprotein oxidation, suppression of platelet aggregation, and estrogen-like actions. The purpose of this article to show the effect of resveratrol on cardiac vascular system.

Key words- Flavonoids, Resveratrol**,** Cardioprotective

INTRODUCTION

Flavonoids are an important class of natural products. They are generally known to be present in plants and plant based products. These include various fruits, vegetables, herbs and beverages such as tea and red wine. Flavonoids are associated with a broad spectrum of health promoting effects. They are an indispensable component in a variety of nutraceutical, pharmaceutical, medicinal and cosmetic applications. This is attributed to their anti-oxidative, anti inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme function [1]. Flavonols are phytochemical compounds found in high concentrations in a variety of plant-based foods and beverages.

Based on their structure, flavonols are classified as flavonoids and include the following compounds: quercitin, kaempferol, and myricetin. The specific amounts of flavonols in foods are affected by a range of factors including plant type and growth, season, light, degree of ripeness, food preparation, and processing. Despite these variables, high concentrations of flavonols can be found in apples, apricots, beans, broad beans, broccoli, cherry tomatoes, chives, cranberries, kale, leeks, pear, onions, red grapes, sweet cherries, and white currants [2].

RESVERATROL: Resveratrol is a metabolite produced in more than 70 plant species in response to environmental stress such as mechanical injury, microbial infection, and UV irradiation. Found in high concentrations in red grapes and their derivatives, whichwas first isolated in 1940.Resveratrol exists in nature in two isomeric forms (Figure 2): *trans*-resveratrol and *cis*-resveratrol .Two phenol rings are linked by a styrene double bond to generate (3,5,4'-trihydroxy-*trans*-stilbene) is a stilbenoid, a type of natural phenol, and a phytoalexin produced naturally by several plants in response to injury or when the plant is under attack by pathogens such as bacteria or fungi [3]. Food sources of resveratrol include the skin of grapes, blueberries, raspberries, and mulberries [4]. Resveratrol was first isolated from the roots of white hellebore in 1940 and later, in 1963, from the roots of Polygonum cuspidatum used in both Chinese and Japanese medicines. It was initially characterized as a phytoalexin but gained considerable attention when it was postulated to explain some of the cardioprotective effects of red wine [5]. Red wine is the most common source of resveratrol, with concentrations of up to 14 mg L-1, but its concentration varies between and within each type of grapes used. White wines generally have concentrations less than 0.1 mg L-1 [6,7]. Resveratrol is also reported to be present in peanuts, soys and other plant

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products although the amount is almost negligible compared to that in wines [6,8]. A number of resveratrol supplements have been developed, with capsules containing anywhere from 1 mg through to as much as 1g per dose. Recently Trans resveratrol has also been found in dark chocolate [9]. There are two isoforms of resveratrol: cis- and trans– resveratrol. Trans–resveratrol is biologically active isoform. The main source of resveratrol is grape skin. Also, resveratrol is present in fruits such as cranberry, lingonberry, bilberry, mulberry, deer berry, blueberry, sparkleberry, partridgeberry, jackfruit, and in a peanut orchid tree, scots pine, corn lily, white hellebore, eucalyptus, spruce etc [10,11]. Resveratrol has anti-cancer and anti-inflammatory effects and beneficial cardiovascular effects [11].

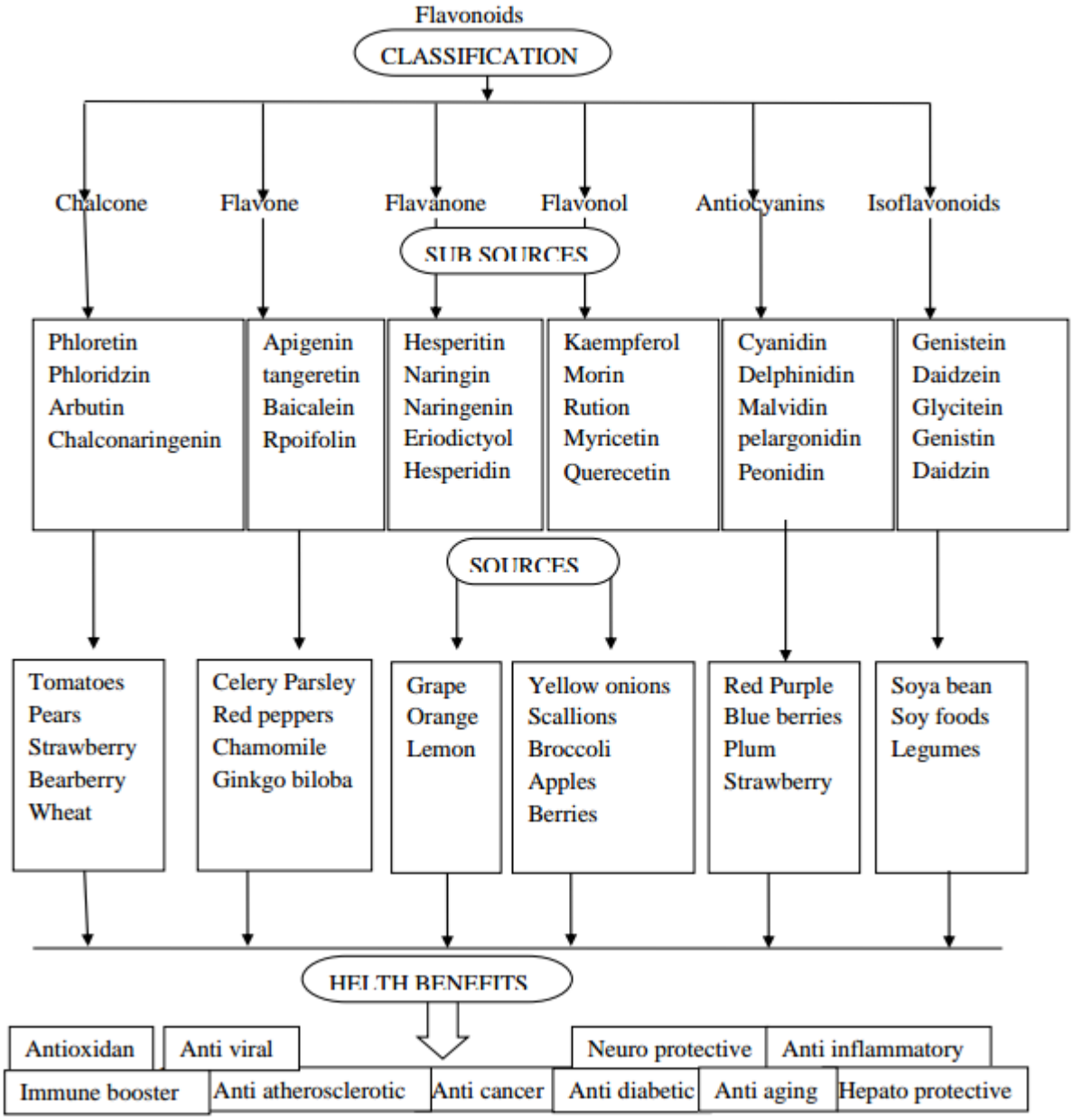

Figure1: Classification of flavonoids, sub sources, sources of flavonoids and benefits

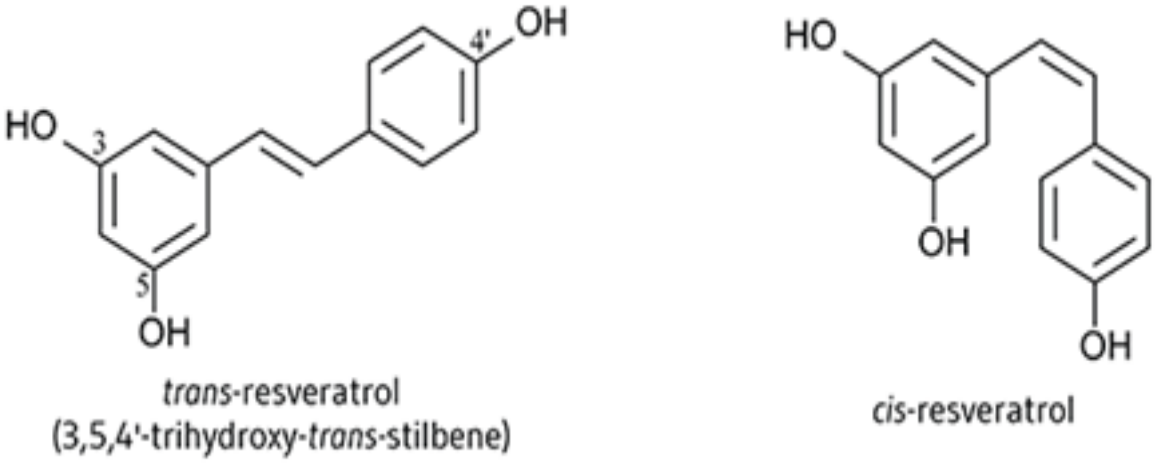

Figure 2: Trans-resveratol, Cis- resveratol

Bioavailability of resveratrol: After oral administration, resveratrol absorbs rapidly (75%) by transepithelial diffusion. It is detected in a 15-min post-administration and reaches peak concentrations after 30 min. Values returned to baseline within 4 h [12]. Previously, we showed that different bile acids micellar solutions improved resveratrol solubilization [13]. The metabolism of resveratrol is extensive in the intestine and liver. Because of intense metabolism, an oral bioavailability of resveratrol is less than 1%. The major active metabolites of resveratrol are glucuronides (trans-resveratrol-3-O-glucuronide) and sulfates (transresveratrol-3-sulfate). Also, colonic bacterial metabolism plays an important role in resveratrol metabolism [14].

Resveratrol used as Cardioprotective

It has long been known that moderate drinking of red wine reduces the risk of heart disease [15]. Studies suggest that resveratrol in red wine may play an important role in this phenomenon [16].

It achieves the effects by the following functions [17].

1. Inhibition of vascular cell adhesion molecule expression;
2. Inhibition of vascular smooth muscle cell proliferation;
3. Stimulation of endolethelial nitric oxide synthase (eNOS) Activity;
4. Inhibition of platelet aggregation;
5. Inhibition of LDL peroxidation; The cardioprotective effects of resveratrol are also theorized to be a form of preconditioning—the best method of cardioprotection, rather than direct therapy.

Table 1: Some Proposed Mechanisms of Action of Resveratrol in rats that May Decrease Cardiovascular Disease in Humans

Cardiovascular disease	Mechanism of action of resveratrol
Coronary heart disease and myocardial infarction	Cardiac preconditioning including reducing reactive oxygen species, improving vasorelaxation and angiogenesis, activation of adenosine A1 and A3 receptors, which then transmit survival signals via PI3-kinase-Akt-Bcl-2, increasing heme oxygenase-1 expression, activation of sirtuins, preventing inflammation and apoptosis, preventing platelet aggregation, inhibition of cardiac fibroblast proliferation and differentiation, delaying atherosclerosis as well as decreasing cardiovascular remodeling [18,19,20,21,22,23].
Cardiac arrhythmias	Reduction of the duration of arrhythmia and incidence of ventricular tachycardia, along with enhanced action potential duration (APD) [24,25].
Hypertension	Activation of sirtuins, increased production of NO and decreased superoxide concentrations, reduced Ca2+ uptake into vascular smooth muscle cells [26,27,28].
Atherosclerosis	Delay at multiple levels such as cellular signalling, enzymatic pathways, apoptosis and gene expression [29].

Cardiac Preconditioning with Resveratrol: Preconditioning describes the development of resistance to injure to the heart caused by extended ischaemia and reperfusion [30]. Physiological mechanisms include short periods of ischaemia followed by reperfusion but the therapeutic potential lies in the possibility that pharmacological agents will selectively induce preconditioning. Resveratrol may imitate this process of preconditioning, providing a pharmacological stimulus to reduce heart damage from ischaemia [31, 32,33].

Vascular Remodelling as a Target for Resveratrol: As in the heart, activation of SIRT1 may initiate the vascular actions of resveratrol. SIRT1 is important as a key regulator of vascular endothelial homeostasis controlling angiogenesis, vascular tone and endothelial dysfunction [34,35].

Cardiac Remodelling as a Target for Resveratrol: The heart responds with remodeling during chronic cardiovascular disease such as hypertension, heart failure or myocardial infarction. The remodeling process involves hypertrophy of myocytes, hyperplasia of fibroblasts and vascular smooth muscle cells, excessive collagen deposition and conduction abnormalities [36,33].

CONCLUSION

The therapeutic use of a dietary component such as resveratrol in humans requires evidence of clinical effectiveness. This requires an assessment of an effective dose of the active drug at the target tissue to identify suitable nutritional or therapeutic doses without toxicity. Continuing studies on the mechanisms of action of resveratrol at a molecular level are necessary to define therapeutic potential. Rodent models of human cardiovascular disease have shown that resveratrol improves cardiovascular structure and function within the context of a wide range of cardiovascular conditions.

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