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Review

Comprehensive review on the antimicrobial potency of the plant polyphenol Resveratrol

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ABSTRACT

Treatment of some infectious diseases are becoming more complicated because of increasing drug resistance rate and lack of proper antibiotics. Because of the rapid increase in drug-resistance trend, there is an urgent need for alternative microbicides to control infectious diseases. Resveratrol (RSV) is a small plant polyphenol that is naturally produced and distributed in 72 particular families of plants. The usage of natural derivatives such as RSV, have become popular among researchers for curing acute and chronic diseases. The purpose of the preset study was to comprehensively review and survey the antimicrobial potency of RSV. The present study demonstrates RSV as a natural antimicrobial agent.

1. Introduction

Infectious diseases pertain to be one of the most indispensable causes of mortality and morbidity world-wide [1]. Evidently, the treatment of some infectious diseases have become more problematic and lead to a global dilemma because of the increasing drug resistance rate and lack of proper antibiotic options. Therefore, the lack of knowledge regarding the usage of antibiotics, their excessive use in livestock and health care, alteration in some genes; such as mutation, adaptation or gene expression contributes to the emergence and expansion of drug resistance [2–4]. Antibiotics are generally indispensable for treating bacterial infections; nonetheless, side effects like nausea, diarrhea, allergic reactions, and therapeutic interactions are inevitable [5,6]. As a matter of fact, because of the rapid spread of drug-resistance, there is an urgent need for alternative microbicides to control infectious diseases [7]. Scientists are constantly trying to discover new antibiotics with high antibacterial effects and potency and the lowest side effects and complications. Natural antibiotics are one of the primary solutions for the mentioned problems [8]. Specifically among natural antibiotic, botanical antimicrobial substances have been quite useful for the treatment of gram positive and negative bacteria [9,10]. Resveratrol (RSV) (3, 5, 4′-trihydroxystilbene) is a stilbenoid compound (stilbenoids are hydroxylated stilbene derivatives) that was first isolated and characterized from the root of white hellebore, *Veratrum grandiflorum* by M. Takaoka in 1939 [11,12]. Similar to other members of stilbene family, RSV production is stimulated in response to pathogen, UV-irradiation, and exposure to ozone [13,14]. This compound is explicitly derived from various plants species, such as grape vines, pines, berries, legumes and also present with high concentrations in pomegranates, peanuts and soybeans [15–17]. Resveratrol has been recognized with a potential role in regulation of immune system and inflammation, chemoprevention, neuroprotection, cardioprotection and lipid regulation, as well as treating diseases like diabetes, Parkinson's disease and cancer. Besides, RSV has shown antibacterial, antiviral and antifungal activity [18–25]. The purpose of the present review article is to focus on the antimicrobial effects of resveratrol. As a matter of fact, there are reports regarding antibacterial and antifungal potency of RSV; nevertheless, to the best of our knowledge, this is the first comprehensive review of Resveratrol antimicrobial potency as a natural product [26].

2. Structure and derivation of RSV

RSV (3,5,4′-Trihydroxystilbene) is a small plant polyphenol with 228 g/mol molecular weight and 14-carbon skeleton. Furthermore, stilbene structure consists of precisely two aromatic rings and phenolic hydroxyl groups with double bonds that makes two *cis*- and *trans*- forms of isomers. However, the *cis*- resveratrol isomer is unstable and easily

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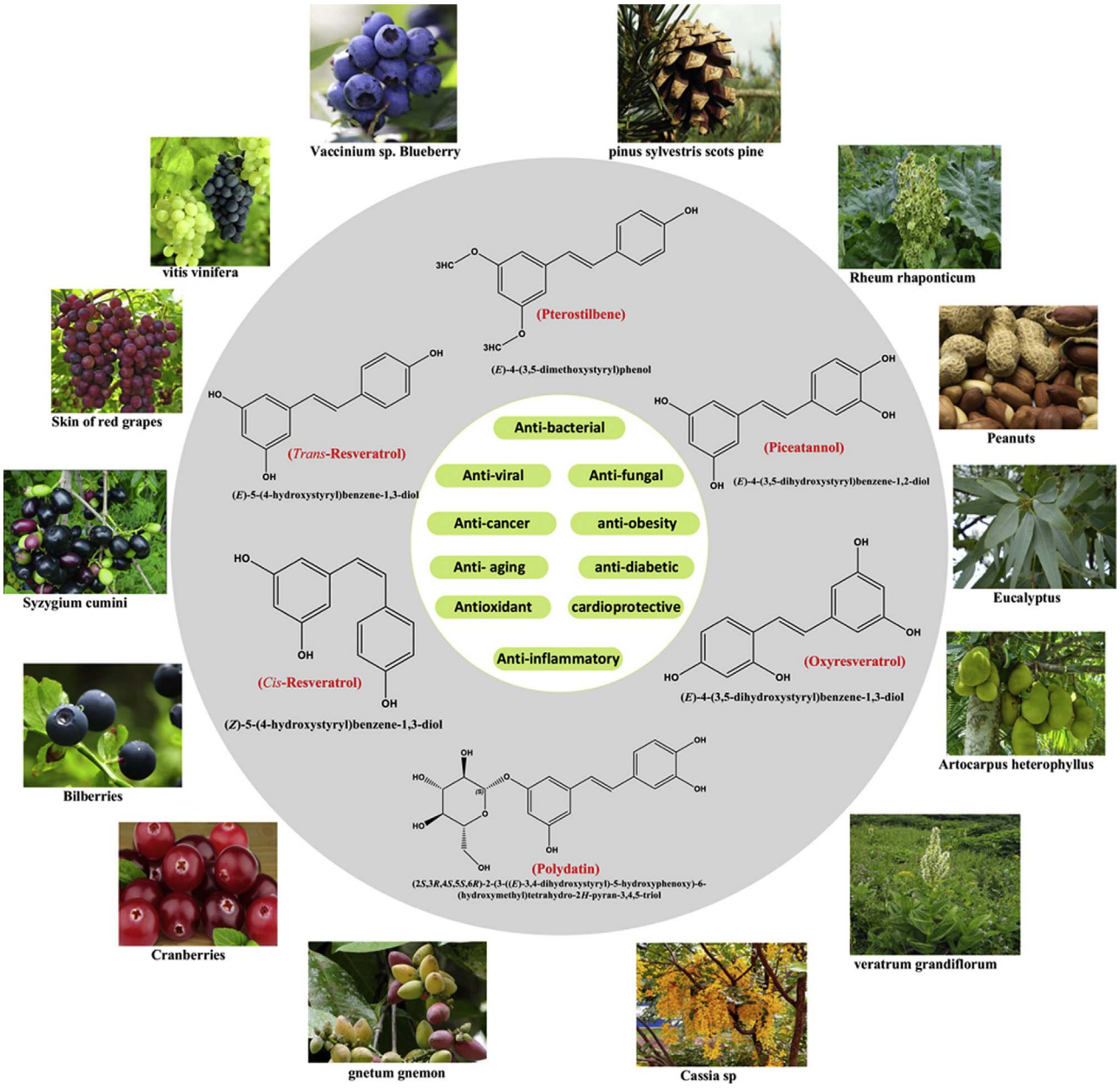

Fig. 1. Sources of resveratrol, derivatives and their therapeutic effects.

transforms into the *trans*-form when a reaction occurs with the light [27] (Fig. 1). Categorically, RSV is soluble in polar solvents such as ethanol and dimethyl sulfoxide; in contrast, it has poor water solubility [17,28,29]. RSV is considered as a phytoalexin (antimicrobial and often antioxidative substances that are synthesized by plants) and has been utilized in some drug preparations such as darakchasava or manakka [26]. RSV is naturally produced and distributed in 72 particular families of plants including Japanese knotweed, peanuts, grapevines, pines, different kinds of berries, legumes and grasses, pinus sylvestris scots, pine, Eucalyptus, *Rheom rhaponticum*, artocarpus heterophyllus, syzygium cumini, veratrum grandiflorum, and cassia [30–35].

3. Different analogs, sources and biological effects of RSV

Apart from natural *cis* and *trans* isomers, several other natural and synthetic analogs exist. For instance, piceatannol (trans-3,4,3′,5′-tetrahydroxystilbene) which is found in skins of grapes can inhibit tyrosine kinase activity in lymphoid malignancies. Therefore, in comparison to RSV, piceatannol exhibits higher bioactivities as an inhibitor of cyclooxygenase 2 and the CSN-associated kinase because of better solubility of piceatannol in H_2O. Moreover, it inhibits the activation of p40 and p56 protein tyrosine kinases and NF-kappa B [15,36,37].

Pterostilbene (trans-3, 5-dimethoxy-4-hydroxystilbene) activates caspases 3/7 and has antioxidant, anti-inflammatory and anticarcinogenic activities. Oral administration of this compound to diabetic rats resulted in attenuated vascular disease and ameliorated diabetes [38,39]. Another derivative polydatin (resveratrol-3-*O*-β-mono-D-glucoside) has been shown to exert several biological activities including anti-inflammatory, antioxidant, modulation of β-defensin 2, IL-6 and IL-8, increasing the gene expression levels of tumor necrosis factor-alpha, increasing the heat shock protein (Hsp)70B′ gene expression and decreasing IL-17 production. This derivative additionally demonstrated numerous protective benefits against myocarditis through dilating blood vessel, antagonizing platelet aggregation and thrombosis [40]. The oxyresveratrol (trans-2,30,4,50-tetrahydroxystilbene) inhibits nitric oxide (NO), activates NF-κB in macrophages and then reduces