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A quantum chemical study on the antioxidant activity of bioactive polyphenols from peanut (*Arachis hypogaea)* and the major metabolites of *trans*-resveratrol

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ABSTRACT

Trans-resveratrol, a polyphenolic compound, which is found in grape and red wine, exhibits inhibiting effect against tumour growth and shows strong antioxidant activity. In the human liver cells and intestinal epithelial ones this compound is converted to the following bioavailable metabolites: O-sulphates, O-disulphates, O-trisulphate and O-glucuronide conjugates. To explain the equilibrium structure–antioxidant radical scavenging capacity relationships of these metabolites and the major peanut polyphenols (arachidin-1, arachidin-2, arachidin-3 and *trans*-isopentadienylresveratrol), the accurate quantum-chemical calculations in the gas phase and water medium with the use of density functional theory have been performed for the first time. The hydrogen atom transfer mechanism for free radicals scavenging is found more preferable than the single-electron transfer mechanism in the media studied. The importance of 4′-OH group as a hydrogen atom donor is indicated. The metabolites and peanut polyphenols are found to be more active donors of hydrogen atoms in the gas phase than in water medium, in which the compounds studied are more susceptible to electron donation than in the gas phase. The calculations have shown that the O-sulphates, O-disulphates and O-trisulphate studied are more efficient hydrogen donors than *trans*-resveratrol. According to the phenolic O–H bond dissociation enthalpies of the peanut stilbenoids were found to be efficient antioxidants. It was found that arachidin-1 is the most effective antioxidant among the compounds studied. The metabolites of *trans*-resveratrol are shown to have a similar ability to scavenge free radicals as the parent compound and can synergistically reduce oxidative stress in human cells. This study provides rational approach for investigation of the antioxidant activity of other bioactive *trans*-resveratrol derivatives.

1. Introduction

Trans-resveratrol (*trans*-3,5,4′-trihydoxystilbene, TR, Fig. 1) is a natural polyphenolic compound with a variety of bioactivities associated with health promotion. This stilbenoid shows wide spectrum of antioxidant, anticancer and anti-inflammatory activities [1–3]. Moreover, the positive cardiovascular effects are associated with consumption of red wine, which contains little amounts of TR. The most accepted mechanism of cardioprotection by this compound is the inhibition of platelet aggregation [4]. The cardioprotective activity of TR may be due to its vasorelaxation properties [5]. TR contains three active hydroxyl groups that have been shown to posses high potency to scavenge the harmful radicals in human cells. Soares et al. [6] have demonstrated that antioxidant potency of TR is higher than that of vitamin C and E. Hence, TR prevents oxidative stress-induced cellular damage. King et al. [7] have shown that this phytoalexin inhibits oxidative-induced apoptosis in human retinal pigment epithelium. It should be stressed that the antioxidant activity of TR can be explained by its ability to protect against the progression of atherosclerosis. For example TR has been found to inhibit copper-initiated oxidation of porcine LDL [8].

To get information on absorption, metabolism, and the bioavailability, TR has been investigated by different approaches including *in vitro*, *ex vivo*, and *in vivo* models. Recently Wenzel and Somoza [9] have shown that the oral bioavailability of TR is almost equal to zero. This is a consequence of its rapid and extensive metabolism and the consequent formation of various metabolites such as TR O-glucuronides and TR O-sulphates. Yu et al. [10] investigated the metabolites of TR formed after dietary intake. Additionally, TR-3-sulphate, TR-3,4′-disulphate, TR-3,5-disulphate, TR-3-glucuronide and TR-4′-O-glucuronide have been identified as main metabolites of TR.

Recently, many authors have reported that antioxidant stilbenoids, such as arachidin-1, arachidin-2 and arachidin-3, demonstrate beneficial effects on human health. Abbott et al. [11] have investigated the antioxidant activity of these compounds isolated from *Arachis hypogaea* hairy root cultures. Their results show that lipid oxidation was inhibited at a 14, 7, and 14 μM doses of purified

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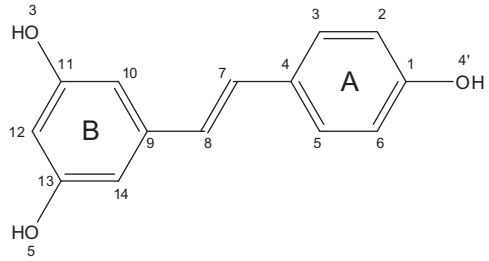

Fig. 1. Molecular structure of *trans*-resveratrol.

resveratrol, arachidin-1, and arachidin-3, respectively. Glucuronidation process of peanut polyphenols was studied by Radominska-Pandya et al. [12]. It has been demonstrated that that lung-expressed UGT1A7 and intestinal UGT1A10 UDP-glucuronosyltransferases can participate in metabolism of these polyphenols. The antioxidant potency of TR, *trans*-arachidin-1, *trans*-arachidin-3, and *trans*-isopentadienylresveratrol has been studied by Ju-Chun et al. [13]. They have demonstrated that the stilbenoides considered exhibit potent antioxidant and anti-inflammatory activities and that this potency which is mainly determined by number of hydroxyl groups, isopentenyl and isopentadienyl moiety. Theoretical study by Mikulski and Molski [14] has demonstrated that 3-O-glucuronide conjugate of TR can have therapeutic potential to scavenge free radicals.

Due to the fact that the quantum-chemical studies of TR metabolites and peanut polyphenolic constituents have still not been performed, in this paper attention is paid to quantum-chemical interpretation of free radical scavenging activity of the compounds under consideration. Since the free radical-scavenging action

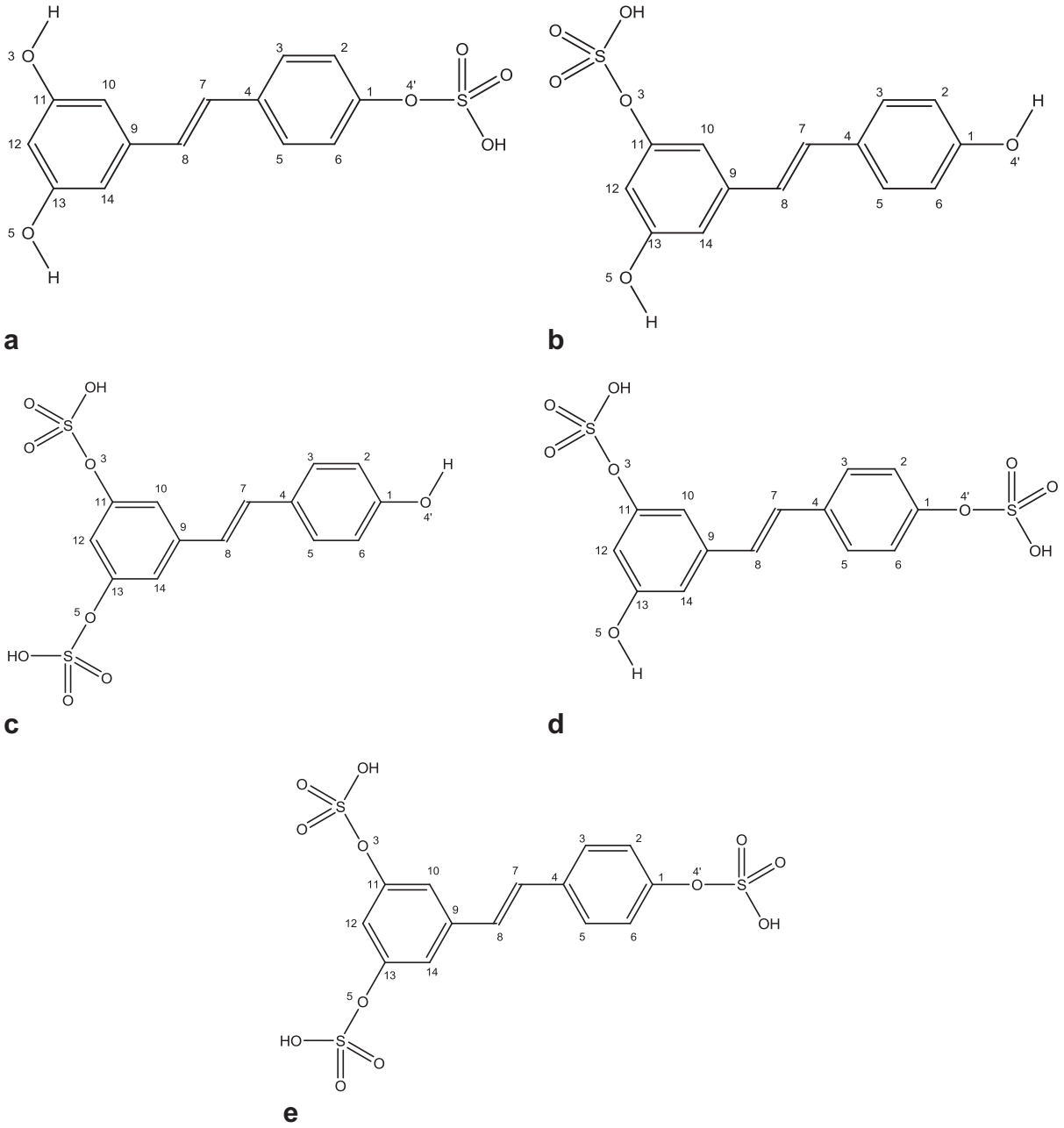

Fig. 2. Structures of TR O-sulphates: 4′-O-sulphate (a), 3-O-sulphate (b), 3,5-O-disulphate (c), 4′,3-O-disulphate (d), 4′,3,5-O-trisulphate (e).