

## High Level of *Trans*-Resveratrol, a Natural Anti-Cancer Agent, Found in Korean Noul Red Wine

KIM, KWANG-SEOK<sup>1</sup>, SA-YOUL GHIM, YOUNG-BAE SEU<sup>1</sup>, AND BANG-HO SONG\*

<sup>1</sup>Department of Microbiology, Department of Biology Education, Kyungpook National University, #1370 Sankyuk-Dong, Bug-Gu, Taegu 702-701, Korea

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**Abstract** Resveratrol (*trans*-3,5,4'-trihydroxystilbene), a phenolic substance present in both grapes and wines, has been reported to have certain pharmacological effects. Using an ethylacetate-phase extraction followed by a high performance liquid chromatographic analysis, the concentration of *trans*-resveratrol was measured in 9 red wines commercially available in Korea, including the Korean red wine (Noul). Noul red wine with a 1998 vintage had a *trans*-resveratrol concentration of 3.3 mg/l, which was rather higher than the concentrations found in other wines (0.19–2.45 mg/l) with the exception of the French wine, J. P. Chenet (3.39 mg/l). In addition, the grapes of *Vitis labrusca* cv. Sheridan cultivated in the Kyungsan area showed a *trans*-resveratrol content of 6.4 mg/kg.

**Key words:** *trans*-Resveratrol, HPLC-analysis, red wine

It has been suggested that coronary heart disease and cancer can be prevented by the regular consumption of red wine in moderate amounts [13, 18, 20, 21]. Resveratrol, a stilbene derivative of natural phenol compounds, has been implicated in this beneficial action of red wine because of its ability to function as an inhibitor of platelet aggregation, an antioxidant, and an anticarcinogenic agent [17, 25]. A large number of studies demonstrated that resveratrol could act as an agonist for the estrogen receptor [9], an immunomodulating compound [6], a DNA-cleaving agent [8], and an arrestor of cell division cycle [19]. Recently, resveratrol was also shown to exhibit anti-tumor activity through apoptosis [1, 4, 12] and anti-allergic activity by inhibiting release of  $\beta$ -hexosaminidase [3].

It has been previously established that resveratrol is produced by at least 72 plant species [11, 12, 14, 15, 22] and is especially abundant in the leaf epidermis and skin of the grapes of the *Vitis* species, plus it is resistant to

pathogen invasion, UV irradiation, and ozone exposure [7, 23]. The presence of *trans*-resveratrol in white and red wines was first reported by Siemann and Creasy [24]. Resveratrol occurs in *cis* and *trans* isomeric forms (Fig. 1) as well as a 3- $\beta$ -glucoside, piceid [16], all of which are physiologically important.

Due to the lack of information on resveratrol in the commercial wines of Korea, the *trans*-resveratrol levels of these wines were determined.

The *trans*-resveratrol standard was supplied by Sigma (St. Louis, MO, U.S.A.). The 9 red wine samples, including the only Korean red wine (Noul) and 8 imported red wines, were randomly purchased from retail liquor stores. Majuang Red and Majuang Special were not included in the selection, since they are mixed red wines produced in Korea and Europe. All samples were protected from light to avoid light-induced isomerization during sample treatment. A 50 ml sample of each wine was neutralized with 1 N NaOH, adjusted to pH 7.0, and concentrated to approximately 30 ml by rotary evaporation (20°C, *in vacuo*) to remove any ethyl alcohol. The concentrate was then extracted 4 times with 30 ml of ethyl acetate, evaporated, and dissolved in 5 ml of methanol.

Ten  $\mu$ l of the methanolic extracts were injected directly into a Hitachi L-6200 HPLC system with a photodiode array UV-visible detector coupled through an Econosphere C<sub>18</sub> column (5  $\mu$ m, 4.6 $\times$ 250 mm). An HPLC analysis was performed on a reversed-phase column with elution of a

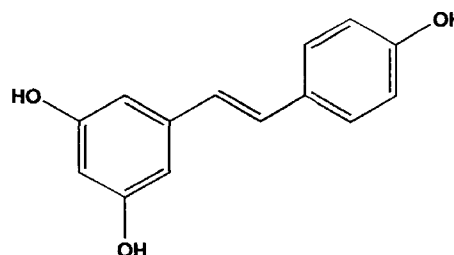
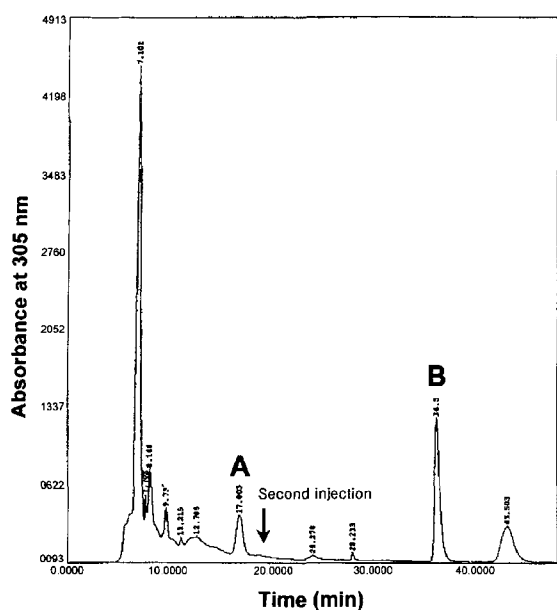


Fig. 1. Chemical structure of *trans*-resveratrol in red wine.

\*Corresponding author

Phone: 82-53-950-5913; Fax: 82-53-955-0820;

E-mail: bhsong@kyungpook.ac.kr



**Fig. 2.** HPLC chromatogram of red wine and *trans*-resveratrol standard at 305 nm.

The arrow indicates the second injection point, and the retention time for the *trans*-resveratrol was about 17 min. Peak A represents *trans*-resveratrol in the red wine extract; and peak B does the *trans*-resveratrol standard.

22% acetonitrile-78% water mixture at a flow rate of 0.4 ml/min. The typical HPLC profile of a red wine is shown in Fig. 2. Peaks were identified at 305 nm by comparing the retention time and peak areas to those of known amounts of the authentic standard.

Table 1 summarizes the results obtained from the analysis of *trans*-resveratrol in the 9 different red wines with various appellations and vintages. The levels of *trans*-resveratrol in these wines were similar to those described in a global survey [10]: 2.88–4.39 mg/l for French wines and 1.06–1.64 mg/l for other wines. The J. P. Chenet (3.39 mg/l) French wine showed the highest levels of *trans*-resveratrol among the all wines analyzed in the present

**Table 1.** Concentration of *trans*-resveratrol in red wines.

Variety <sup>a</sup>	Vintage	Country	Resveratrol (mg/l) <sup>b</sup>
Noul	1998	Korea	3.3
Delicato	1994	USA	0.52
Sutter Home	1995	USA	0.79
Riunite	1996	Italy	0.33
Beaujolais	1996	France	2.45
Beaujolais-Village	1996	France	1.10
J. P. Chenet	1997	France	3.39
Medoc	1996	France	0.19
Merlot	1996	France	2.09

<sup>a</sup>10 bottles were analyzed for each wine.

<sup>b</sup>Results of HPLC analysis are expressed in milligrams per liter of *trans*-resveratrol equivalents based on the absorbance of the *trans*-resveratrol standard at 305 nm.

experiment. The Korean Noul red wine contained a considerably high level of *trans*-resveratrol, averaging 3.3 mg/l compared to 0.19–2.45 mg/l for the rest. This is the first report on the presence of *trans*-resveratrol in a Korean red wine made from grapes cultivated in Korea. As for the content of *trans*-resveratrol, the J. P. Chenet and Noul red wines compare favorably with other wines analyzed.

Red wines usually contain much larger amounts of *trans*-resveratrol than white or rose wines. It is already known that the grape cultivar, area of cultivation, climate, agronomic techniques, state of health of the grapes, and wine-processing conditions all influence the *trans*-resveratrol content in wines [2]. Accordingly, the content of *trans*-resveratrol was determined for grapes from *Vitis labrusca* cv. Sheridan collected in the Kyungsan area, which were used for manufacturing Noul red wine. Extraction and analysis of their berries and skins were followed by the method described for wine. The *trans*-resveratrol concentration of the Sheridan grapes was 6.4 mg/kg, which is significantly higher than the level reported for 5 UV-untreated cultivars grown in New York (less than 1 mg · cm<sup>-2</sup>) [5]. Further research on other cultivars grown in Korea is needed to improve the amounts of *trans*-resveratrol in red wines.

In conclusion, these experimental results indicate that Noul red wine exhibits a higher level of *trans*-resveratrol than any of the other commercially available red wines in Korea thus far analyzed, with the exception of the French wine J. P. Chenet.

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