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A review of the content of the putative chemopreventive phytoalexin resveratrol in red wine

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Abstract

Resveratrol, a naturally occurring compound of various fruits such as grapes, is thought to possess chemopreventive properties. The levels of resveratrol in grapes and grape products including wine, varies from region to region and from one year to another. This paper reviews the resveratrol content in red wine based on relevant published data. Red wine contains an average of 1.9 ± 1.7 mg *trans*-resveratrol/l (8.2 ± 7.5 μM), ranging from non-detectable levels to 14.3 mg/l (62.7 μM) *trans*-resveratrol. In general, wines made from grapes of the Pinot Noir and St. Laurent varieties showed the highest level of *trans*-resveratrol. No region can be said to produce wines with significantly higher level of *trans*-resveratrol than all other regions. Levels of *cis*-resveratrol follow the same trend as *trans*-resveratrol. The average level of *trans*-resveratrol-glucoside (*trans*-piceid) in a red wine may be as much as 29.2 mg/l (128.1 μM), i.e., three times that of *trans*-resveratrol.

Keywords: Resveratrol levels; Piceid; Red wine; Grape varieties; Pooled analysis

1. Introduction

Resveratrol (3,5,4′-trihydroxystilbene) is a polyphenol present in a variety of plant species, used for human consumption, e.g., peanuts, berries and grapes. The highest levels of naturally occurring resveratrol is found in the roots of Japanese Knotweed (*Polygonum cuspidatum*), which has been used in traditional Asian herb medicine for hundreds of years to treat inflammation (Aggarwal et al., 2004). Grapes are probably the most important source of resveratrol for humans, since the compound is also found in one of the end products of grapes, i.e., wine (Siemann & Creasy, 1992). Resveratrol is found in white, rose and red wines, but as the highest amount of resveratrol are found in red wines (Pervaiz, 2003), the present review focus on these wines.

The interest of the scientific community in the phytoalexin resveratrol has increased over the last years. The interest was originally sparked by epidemiological studies, indicating an inverse relationship between moderate wine consumption and risk of coronary heart disease, the so called “French Paradox” (Goldberg et al., 1995, review) and by the fact that cancer preventive properties of resveratrol was observed in vitro and in vivo (Jang et al., 1997). However, the health promoting properties of red wine over other alcoholic beverages is not yet consolidated, as was recently discussed by Grønbæk (2004) and Li and Mukamal (2004).

Although several reviews on resveratrol have been published (Aggarwal et al., 2004, and references therein) none has yet compared the reported levels of resveratrol in red wine. Therefore, the exact intake of resveratrol in the published epidemiological studies is very uncertain. The purpose of this review is to fill that gap, by comparing the levels of resveratrol in different red wines from a

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single grape variety (mono-varietal red wines), and by comparing the resveratrol content of red wines from different regions.

1.1. Biosynthesis of resveratrol

In grapes, resveratrol is synthesized almost entirely in the skin and the synthesis peaks just before the grapes reach maturity. The terminal enzyme in the biosynthesis of resveratrol is stilbene synthase, which is activated in response to exogenous stress factors, such as injury, ultra violet irradiation and chemical signals from pathogen fungi. The levels of resveratrol peak approximately 24 h after stress exposure, and decline after 42–72 h as result of activation of stilbene oxidase (Pervaiz, 2003; Soleas, Diamandis, & Goldberg, 1997). The degree of increase in resveratrol levels in grapes depend on the variety and stress exposure (Adrian et al., 2000; Douillet-Breuil, Jeandet, Adrian, & Bessis, 1999).

Because resveratrol is produced in response to exogenous stress factors the levels in red wine are expected to vary between regions and vintages, as previously noted (Goldberg et al., 1995; Goldberg, GarovicKocic, Diamandis, & PaceAsciak, 1996; Martinez-Ortega, Carcia-Parrilla, & Troncoso, 2000). Furthermore, various factors during the wine making process also affects the levels of *trans*-resveratrol in the final red wines; increased temperature, higher levels of SO_2 and/or decreased pH results in higher resveratrol levels (Gambuti, Strollo, Ugliano, Lecce, & Moio, 2004; Mattivi & Nicolini, 1993; Netzel et al., 2003; Trela & Waterhouse, 1996).

Resveratrol exists in two isoforms, *cis*- and *trans*-resveratrol, the latter being most widely studied, although *cis*-resveratrol may also possess health promoting properties (Bertelli et al., 1996). In red wine, resveratrol may also be found as resveratrol-glucoside (piceid). These conjugates may inhibit tumor metastasis (Kimura & Okuda, 2000), though the exact biological activity is unclear (Chun, Ryu, Jeong, & Kim, 2001; Ito et al., 2003). Here, we report the levels of *trans*- and *cis*-resveratrol and their glucosides based on 31 papers. In total, 21 grape varieties from 18 regions are included in the analysis. The levels are reported as the units of mg/l and μM to comply with the concentrations used in in vitro studies. Where applicable, data are presented as the range as well as mean ± standard deviation.

2. Resveratrol content in red wine

2.1. Levels of trans-resveratrol in different mono-varietal wines

The levels of *trans*-resveratrol in mono-varietal red wine varied greatly between varieties (Table 1). The highest average level of *trans*-resveratrol was found in wines made from Pinot Noir grown in France while wines made from Spanish and Italian Pinot Noir had the second highest level of *trans*-resveratrol. The lowest average level of *trans*-resveratrol was found in wines made from the Zinfandel variety grown in the USA. Although some variety-region combinations were found to be significantly different from other variety-region combinations, such as, e.g., Brazilian Merlot compared to Japanese Merlot, no variety-region combination significantly differed from all other combinations ($p \leqslant 0.05$, Student's t-test, data not shown).

The five highest levels of *trans*-resveratrol on average, disregarding region, was found in wines made from Pinot Noir, St. Laurent, Marzemino, Merlot, and Blaufränkisch with levels of 3.6 ± 2.9 mg/l (15.9 ± 12.5 μM), 3.2 ± 1.8 mg/l (14.0 ± 8.1 μM), 3.0 ± 2.1 mg/l (13.1 ± 9.2 μM), 2.8 ± 2.6 mg/l (12.5 ± 11.5 μM), 2.6 ± 1.3 mg/l (11.3 ± 5.5 μM), respectively (Table 1). Wines of the Agiorgitiko variety, predominantly grown in Greece, contained the lowest level on average (0.6 ± 0.2 mg/l (2.6 ± 0.9 μM)). Although some varieties were found to be significantly different with respect to average levels of *trans*-resveratrol, no variety was found to be different from all other varieties (Table 1).

When comparing wines made from the thin skinned grapes with wines made from the thick skinned grapes (Table 2), no trend suggest that the thickness of the grape skin correlates to the content of *trans*-resveratrol in the red wine.

2.2. Levels of trans-resveratrol in wines from different regions

The average levels of *trans*-resveratrol in red wine vary greatly from one region to another (Table 3). Although significant differences were found between regions, no specific region was significantly different from all other. The average red wine was estimated to contain 1.9 ± 1.7 mg/l (8.2 ± 7.5 μM) *trans*-resveratrol, ranging from not detectable in wines from China (Gao, Chu, & Ye, 2002), Greece (Sakkiadi, Stavrakakis, & Haroutounian, 2001), Portugal (de Lima et al., 1999), Spain (Lopez, Martinez, Del Valle, Orte, & Miro, 2001; Martinez-Ortega et al., 2000; Moreno-Labanda et al., 2004), and USA (Lamuela-Raventos & Waterhouse, 1993) to 11.9 mg/l (52.1 μM) in a 1997 Swiss wine made from the Pinot Noir grape (Adrian et al., 2000), and 14.3 mg/l (62.7 μM) in a Hungarian, 2002 Merlot (Mark, Nikfardjam, Avar, & Ohmacht, 2005).

Canada produced red wines with the highest average level of *trans*-resveratrol of 3.2 ± 1.5 mg/l (14.2 ± 6.6 μM) (Table 3) with Greece and Japan at the other end with 1.0 ± 0.5 mg/l (4.4 ± 2.2 μM) and 1.0 ± 0.6 mg/l (4.4 ± 2.6 μM), respectively. When comparing average *trans*-resveratrol content with the latitude of the producing region, it appears that the higher north on the northern hemisphere, the higher average level of *trans*-resveratrol (data not shown). The trend for the southern hemisphere is that the closer to equator the higher average level of *trans*-resveratrol.

Table 1
Average *trans*-resveratrol levels in mono-varietal red wine

Variety	*trans*-Resveratrol (mg/l)[A]			Number of samples[B]	References
Region	Lowest	Highest	Mean		
Pinot Noir					
Brazil	1.1	4.2	2.9 ± 1.6	3	(Souto et al., 2001)
Czech Republic	1.3	10.5	3.4 ± 3.0	10	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
France	3.8	7.4	5.4 ± 1.2	8	(Adrian et al., 2000)
Hungary	2.8	3.7	3.2 ± 0.5	4	(Mark et al., 2005)
Italy	3.2	6.0	4.8 ± 1.4	3	(Mattivi, 1993)
Japan	0.4	2.3	1.3 ± 1.3	2	(Sato et al., 1997)
Spain	2.3	8.0	5.1 ± 4.0	2	(Lamuela-Raventos et al., 1995)
Switzerland	–	–	11.9	1	(Adrian et al., 2000)
USA	0.2	5.8	2.3 ± 2.3	10	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999)
All samples[C]	0.2	11.9	3.6 ± 2.9^{a}	43	
St. Laurent					
Czech Republic	1.0	5.6	$3.2 \pm 1.8^{a,b}$	14	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
Marzemino					
Italy	1.2	5.3	$3.0 \pm 2.1^{a,b,c}$	3	(Mattivi, 1993)
Merlot					
Australia	–	–	1.0	1	(Shao et al., 2003)
Brazil	3.1	5.1	4.0 ± 1.0	3	(Souto et al., 2001)
Czech Republic	–	–	1.3	1	(Melzoch et al., 2001)
Hungary	1.3	14.3	3.9 ± 4.0	10	(Mark et al., 2005)
Italy	0.5	6.0	3.4 ± 2.3	4	(Goldberg & Ng, 1996; Mattivi, 1993)
Japan	0.6	2.1	1.5 ± 0.6	5	(Sato et al., 1997)
Spain	1.0	7.7	4.0 ± 2.9	4	(Lamuela-Raventos et al., 1995)
USA	0.4	2.7	1.5 ± 1.0	4	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Gu et al., 1999)
All samples	0.3	14.3	$2.8 \pm 2.6^{a,b,c}$	32	
Blaufränkisch					
Czech Republic	1.4	4.8	2.5 ± 1.1	12	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
Hungary	1.1	5.6	2.8 ± 1.7	6	(Mark et al., 2005)
All samples	1.1	5.6	$2.6 \pm 1.3^{a,b,c}$	18	
Portugieser					
Czech Republic	2.0	6.2	4.1 ± 3.0	2	(Melzoch et al., 2001)
Hungary	0.3	2.0	1.3 ± 0.7	7	(Mark et al., 2005)
All samples	0.3	6.2	$1.9 \pm 1.7^{b,c}$	9	
Grenache					
Spain	0.8	2.8	$1.9 \pm 0.8^{b,c}$	5	(Abril et al., 2005; Lamuela-Raventos et al., 1995)
Zweigelt					
Czech Republic	0.9	2.1	1.3 ± 0.6	6	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
Hungary	0.6	4.7	2.7 ± 1.7	4	(Mark et al., 2005)
Japan	–	–	2.0	1	(Sato et al., 1997)
All samples	0.6	4.7	1.9 ± 1.2^{c}	11	
Negroamaro					
Italy	1.5	2.0	1.8 ± 0.2^{c}	3	(Wang et al., 2002)
Shiraz					
Australia	0.2	3.2	1.9 ± 0.9	8	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Shao et al., 2003)
Greece	–	–	2.0	1	(Sakkiadi et al., 2001)
Hungary	1.2	1.8	1.5 ± 0.4	2	(Mark et al., 2005)
All samples	0.2	3.2	1.8 ± 0.9^{c}	11	
Cabernet Sauvignon					
Australia	0.2	1.5	0.9 ± 0.6	4	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Gu et al., 1999; Shao et al., 2003)
Brazil	1.3	2.3	1.8 ± 0.5	4	(Souto et al., 2001)
Czech Republic	–	–	3.7	1	(Melzoch et al., 2001)
Greece	–	–	1.0	1	(Dourtoglou et al., 2005)
Hungary	1.2	9.3	2.9 ± 2.5	9	(Mark et al., 2005)
Italy	1.3	7.2	4.0 ± 3.1	4	(Goldberg & Ng, 1996; Mattivi, 1993)

(*continued on next page*)

Table 1 (*continued*)

Variety / Region	*trans*-Resveratrol (mg/l)[A] Lowest	Highest	Mean	Number of samples[B]	References
Japan	–	–	0.9	1	(Sato et al., 1997)
Spain	0.7	1.9	1.2 ± 0.4	8	(Abril et al., 2005; Goldberg & Ng, 1996; Lamuela-Raventos et al., 1995)
USA	n.d.[D]	2.2	0.5 ± 0.6	11	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Lamuela-Raventos & Waterhouse, 1993)
All samples	n.d.	9.3	1.7 ± 1.7[c]	43	
Nero d'Avola					
Italy	0.6	2.9	1.6 ± 1.1[c]	5	(Careri et al., 2003)
Teroldego					
Italy	1.3	1.6	1.5 ± 0.2[c]	3	(Mattivi, 1993)
Tempranillo					
Spain	0.2	2.5	1.3 ± 0.7[c]	12	(Abril et al., 2005; Lamuela-Raventos et al., 1995; Martinez-Ortega et al., 2000)
Cabernet Franc					
Brazil	1.1	2.1	1.6 ± 0.5	3	(Souto et al., 2001)
Hungary	0.7	1.2	1.0 ± 0.2	5	(Mark et al., 2005)
All samples	0.7	2.1	1.2 ± 0.5[c]	8	
Liatiko					
Greece	0.8	1.4	1.0 ± 0.3[c]	4	(Kallithraka et al., 2001; Sakkiadi et al., 2001)
Xinomauro					
Greece	0.4	2.1	1.0 ± 0.5[c]	10	(Dourtoglou et al., 2005; Kallithraka et al., 2001; Sakkiadi et al., 2001)
Muscat Bailey A					
Japan	0.2	1.5	0.8 ± 0.5[c]	5	(Sato et al., 1997)
Zinfandel					
Italy	–	–	9.6	1	(Wang et al., 2002)
USA	n.d.	1.3	0.4 ± 0.5	5	(Goldberg, Ng et al., 1996; Gu et al., 1999; Lamuela-Raventos & Waterhouse, 1993)
All samples	n.d.	2.2	0.7 ± 0.9[c]	6	
Agiorgitiko					
Greece	0.3	0.9	0.6 ± 0.2[c]	9	(Dourtoglou et al., 2005; Kallithraka et al., 2001; Sakkiadi et al., 2001)

[A] The average values were calculated on basis of levels of *trans*-resveratrol given by the cited references. Data are presented as mean ± standard deviation. Varieties sharing the same letter are not significantly different ($p \leqslant 0.05$) according to Student's *t*-test based on all available samples.
[B] The number of samples included in each mean.
[C] The mean data of varieties stemming from two or more regions are summarised.
[D] Below the level of detection.

2.3. Levels of *cis*-resveratrol in mono-varietal and blended wines

Levels of *cis*-resveratrol in red wines (mono-varietal and blended) followed the same trend as seen for *trans*-resveratrol. The highest average level of *cis*-resveratrol was found in wines from Canada, while the lowest levels were found in wines from Spain and Chile (Table 4). No wines from one region were significantly different than wines from any other region. The five highest level of *cis*-resveratrol on average, disregarding region, was found in wines made from Negroamaro, Pinot Noir, Blaufränkisch, Shiraz, Zweigelt with levels of 2.7 ± 0.8 mg/l (11.8 ± 3.7 μM), 1.9 ± 1.3 mg/l (8.5 ± 5.9 μM), 1.6 ± 1.0 mg/l (7.1 ± 4.4 μM), 1.6 ± 0.9 mg/l (6.9 ± 3.9 μM), 1.2 ± 0.2 mg/l (5.4 ± 0.8 μM), respectively (data not shown). Wines of the Tempranillo variety, predominantly grown in Spain, contained the lowest level on average 0.4 ± 0.3 mg/l (2.0 ± 1.4 μM), data not shown. No variety was found to be significantly different from all other varieties ($p \leqslant 0.05$, Student's *t*-test, data not shown).

2.4. Levels of resveratrol-glucoside (piceid)

The levels of *trans*-resveratrol-glucoside (*trans*-piceid) varied greatly between regions (Table 5) with Hungary having the highest level (7.1 ± 2.4 mg/l (31.0 ± 10.7 μM)) and USA having the lowest level (0.3 ± 0.3 mg/l (1.4 ± 1.4 μM)). The highest reported level of *trans*-resveratrol-glucoside (*trans*-piceid) was 29.2 mg/l (128.1 μM)

Table 2
Average levels of *trans*-resveratrol in wines from thin and thick skinned grapes

Variety	Skin thickness	*trans*-Resveratrol (mg/l)[A]			Number of samples[B]	References
		Lowest	Highest	Mean		
Pinot Noir	Thin	0.21	11.9	3.6 ± 2.9^{a}	40	(Adrian et al., 2000; Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Kolouchova-Hanzlikova et al., 2004; Lamuela-Raventos et al., 1995; Lamuela-Raventos & Waterhouse, 1993; Mark et al., 2005; Mattivi, 1993; Melzoch et al., 2001; Sato et al., 1997; Souto et al., 2001)
St. Laurent	Thick	1.02	5.57	$3.2 \pm 1.8^{a,b}$	14	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
Merlot	Thick	0.29	14.32	$2.8 \pm 2.6^{a,b}$	37	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Gu et al., 1999; Lamuela-Raventos et al., 1995; Mark et al., 2005; Mattivi, 1993; Melzoch et al., 2001; Sato et al., 1997; Shao et al., 2003; Souto et al., 2001)
Grenache	Thin	0.83	2.83	$1.9 \pm 0.8^{b,c}$	5	(Abril et al., 2005; Lamuela-Raventos et al., 1995)
Shiraz	Thick	0.18	3.17	1.8 ± 0.9^{c}	11	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Mark et al., 2005; Sakkiadi et al., 2001; Shao et al., 2003)
Cabernet Sauvignon	Thick	n.d.[C]	9.34	1.7 ± 1.7^{c}	57	(Abril et al., 2005; Dourtoglou et al., 2005; Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Lamuela-Raventos et al., 1995; Lamuela-Raventos & Waterhouse, 1993; Mark et al., 2005; Mattivi, 1993; Melzoch et al., 2001; Sato et al., 1997; Shao et al., 2003; Souto et al., 2001)
Tempranillo	Thick	0.16	2.46	1.3 ± 0.7^{c}	12	(Abril et al., 2005; Lamuela-Raventos et al., 1995; Martinez-Ortega et al., 2000)
Cabernet Franc	Thin	0.66	2.1	1.2 ± 0.5^{c}	8	(Mark et al., 2005; Souto et al., 2001)

[A] The average values were calculated on basis of levels of *trans*-resveratrol given by the cited references. Data are presented as mean ± standard deviation. Varieties sharing the same letter are not significantly different ($p \leqslant 0.05$) according to Student's *t*-test.
[B] The number of samples included in each mean. The lower limit for inclusion into this analysis was three or more samples.
[C] Below the level of detection.

found in a 2002 Spanish red wine of unknown variety (Moreno-Labanda et al., 2004). There was no significant difference in the levels of *cis*-resveratrol-glucoside (*cis*-piceid) between regions (Table 5).

3. Discussion

In the present report, the levels of isomers of resveratrol and resveratrol-glucoside (piceid) in red wines have been compared. The variation of average levels of resveratrol was very unambiguous, why no specific variety or region was found to be outstanding in relation to the level of *trans*- or *cis*-resveratrol. Furthermore, no clear trend was found to suggest different levels in thick skinned grapes, compared to their thin skinned counterparts. Levels of *trans*-resveratrol-glucoside (*trans*-piceid) differ between most regions used in this comparison, while levels of *cis*-resveratrol-glucoside (*cis*-piceid) are the same across all regions included.

An average red wine was estimated to contain 1.9 ± 1.7 mg/l (8.2 ± 7.5 μM) *trans*-resveratrol, based on 511 samples from 18 regions. However, given the large variation between regions and varieties, and the fact that the *trans*-resveratrol content may be anything between below the detection level and 14.3 mg/l (62.7 μM), the notion of average resveratrol content is quite dubious.

There is a great variance in the levels of resveratrol across variety (Table 1) and regions (Table 3). This variance may be explained by the fact that resveratrol is produced by the grape in response to exogenous stress factors, and thus is pruned to depend on variations in the local climate. The logic being that a dry year would be less favourable to fungi than a more moist year, thus less resveratrol would be synthesized by the grape. Another factor behind the variance between resveratrol content in red wines is the wine making technique, as double maceration is concomitant with high levels of resveratrol (Alonso, Dominguez, Guillen, & Barroso, 2002). The variations in local climate may also explain the observed trend that average level of *trans*-resveratrol on the southern hemisphere is higher the closer the region of origin is to equator.

Table 3
Average levels of *trans*-resveratrol in red wine of different regions

Region	*trans*-Resveratrol (mg/l)[A]			Number of samples[B]	References
	Lowest	Highest	Mean		
Canada	1.2	5.8	3.2 ± 1.4^{a}	7	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg et al., 1995)
Czech Republic	0.7	10.5	$2.8 \pm 1.9^{a,b}$	52	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
France	0.3	7.6	$2.8 \pm 1.6^{a,b}$	27	(Adrian et al., 2000; de Lima et al., 1999; Goldberg et al., 1995; Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999)
Brazil	1.1	5.8	$2.7 \pm 1.5^{a,b}$	18	(Souto et al., 2001)
Hungary	0.1	14.3	$2.4 \pm 2.1^{a,b,c}$	67	(Mark et al., 2005)
Australia	0.2	10.6	$2.0 \pm 2.6^{a,b,c}$	14	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999; Shao et al., 2003)
Italy	0.3	7.2	$2.0 \pm 1.5^{a,c}$	67	(Careri et al., 2003; Gambuti et al., 2004; Goldberg & Ng, 1996; Gu et al., 1999; Mattivi, 1993; Mozzon et al., 1996; Wang et al., 2002)
China	n.d.[C]	3.2	$1.8 \pm 1.3^{a,b,c,d}$	5	(Gao et al., 2002)
South America	0.8	2.2	$1.6 \pm 0.6^{c,d}$	5	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996)
Portugal	n.d.	5.2	$1.5 \pm 1.1^{c,d,}$	22	(Baptista et al., 2001; de Lima et al., 1999; Gu et al., 1999; Ratola et al., 2004)
Spain	n.d.	8.0	1.4 ± 1.4^{d}	103	(Abril et al., 2005; Goldberg & Ng, 1996; Goldberg et al., 1995; Gu et al., 1999; Lamuela-Raventos et al., 1995; Lopez et al., 2001; Martinez-Ortega et al., 2000; Moreno-Labanda et al., 2004; Rodriguez-Delgado et al., 2002)
USA	n.d.	5.8	1.3 ± 1.6^{d}	37	(Goldberg & Ng, 1996; Goldberg, Ng et al., 1996; Goldberg et al., 1995; Goldberg, Tsang et al., 1996; Gu et al., 1999; Lamuela-Raventos & Waterhouse, 1993)
Chile	0.8	1.6	1.2 ± 0.4^{d}	4	(Goldberg et al., 1995; Gu et al., 1999)
Greece	n.d.	2.5	1.0 ± 0.5^{d}	57	(Dourtoglou et al., 2005; Kallithraka et al., 2001; Sakkiadi et al., 2001)
Japan	0.1	2.3	1.0 ± 0.6^{d}	22	(Sato et al., 1997)
All regions	n.d.	14.3	1.9 ± 1.7	511	

[A] The average values were calculated on basis of levels of *trans*-resveratrol given by the cited references. Data are presented as mean ± standard deviation. Regions sharing the same letter are not significantly different ($p \leqslant 0.05$) according to Student's *t*-test.
[B] The number of samples included in each mean. The lower limit for inclusion into this analysis was three or more samples.
[C] Below the level of detection.

Wines made from the Pinot Noir variety have previously been perceived to contain high amounts of *trans*-resveratrol. This report shows that wines of the Pinot Noir variety do indeed contain the highest average levels of *trans*-resveratrol. Surprisingly, wines made from the St. Laurent variety, grown for instance in Slovakia, the Czech Republic, and Austria, contained the second highest average levels of *trans*-resveratrol, and were not significantly different from Pinot Noir.

Although the average levels of *cis*-resveratrol are lower than *trans*-resveratrol, this isoform may be important. The levels of *cis*-resveratrol in wine is a product of vinification (Jeandet et al., 1995; Mattivi, Reniero, & Korhammer, 1995) and isomerisation from the *cis* to the *trans* isoform is facilitated by low pH (Trela & Waterhouse, 1996), thus the total level of available resveratrol after consumption may be the sum of *trans*- and *cis*-resveratrol. Also *trans*-resveratrol-glucoside (*trans*-piceid) may prove important as the average level of that conjugate may by as much as 29.2 mg/l (128.1 μM), i.e., three times that of trans-resveratrol (Moreno-Labanda et al., 2004).

To our knowledge, this review is the first to produce a pooled analysis of the reported resveratrol content in red wine. This study focused foremost on variety and region because this is how the average wine customer can be expected to think of wine. This approach does however result in potential statistical weaknesses in that some varieties have only been studied by one laboratory and from a single vintage. To obtain a more exact picture of the resveratrol content in red wine, a more systematical analysis of mono-varietal with emphasis on the ruling variety of each region or country is needed. Studies of poly-varietal wines

Table 4
Average levels of *cis*-resveratrol in red wine of different regions

Region	*cis*-Resveratrol (mg/l)[A]			Number of samples[B]	References
	Lowest	Highest	Mean		
Canada	0.7	3.4	1.9 ± 1.1[a]	4	(Goldberg, Ng et al., 1996; Goldberg et al., 1995)
Czech Republic	0.6	5.1	1.6 ± 1.0[a]	52	(Kolouchova-Hanzlikova et al., 2004; Melzoch et al., 2001)
France	0.3	4.0	1.5 ± 1.0[a]	24	(Adrian et al., 2000; de Lima et al., 1999; Goldberg, Ng et al., 1996; Goldberg et al., 1995; Goldberg, Tsang et al., 1996; Gu et al., 1999)
Australia	0.3	2.6	1.2 ± 0.9[a]	6	(Goldberg, Ng et al., 1996; Goldberg, Tsang et al., 1996; Gu et al., 1999)
South America	0.5	1.7	1.2 ± 0.6[a]	3	(Goldberg, Ng et al., 1996)
Italy	n.d.[C]	3.6	1.2 ± 0.7[a]	44	(Goldberg, Tsang et al., 1996; Gu et al., 1999; Mozzon et al., 1996; Wang et al., 2002)
Japan	n.d.	2.7	0.8 ± 0.7[a]	22	(Sato et al., 1997)
USA	n.d.	3.0	0.8 ± 0.9[a]	22	(Goldberg, Ng et al., 1996; Goldberg et al., 1995; Goldberg, Tsang et al., 1996; Gu et al., 1999)
Portugal	0.2	2.6	0.7 ± 0.8[a]	15	(Baptista et al., 2001; de Lima et al., 1999; Gu et al., 1999)
Spain	n.d.	2.5	0.5 ± 0.6[a]	51	(Abril et al., 2005; Goldberg et al., 1995; Gu et al., 1999; Lamuela-Raventos et al., 1995; Martinez-Ortega et al., 2000)
Chile	0.0	0.9	0.4 ± 0.4[a]	4	(Goldberg et al., 1995; Gu et al., 1999)
All regions	n.d.	5.1	1.0 ± 0.9	250	

[A] The average values were calculated on basis of levels of *cis*-resveratrol given by the cited references. Data are presented as mean ± standard deviation. Regions sharing the same letter are not significantly different ($p \leqslant 0.05$) according to Student's *t*-test.
[B] The number of samples included in each mean. The lower limit for inclusion into this analysis was three or more samples.
[C] Below the level of detection.

Table 5
Average levels of *trans*- and *cis*-resveratrol-glucoside (*trans*- and *cis*-piceid) in red wine of different regions

Region	Lowest	Highest	Mean	Number of samples[B]	References
trans-Resveratrol-glucoside (mg/l)[A]					
Hungary	n.d.[C]	16.4	7.1 ± 2.4[a]	67	(Mark et al., 2005)
Spain	n.d.	29.24	6.1 ± 6.1[a]	79	(Goldberg et al., 1995; Lamuela-Raventos et al., 1995; Martinez-Ortega et al., 2000; Moreno-Labanda et al., 2004)
France	0.16	13	4.1 ± 5.4[a,b]	8	(Adrian et al., 2000; de Lima et al., 1999; Goldberg et al., 1995)
Portugal	0.19	11.8	3.5 ± 3.0[b]	14	(Baptista et al., 2001; de Lima et al., 1999)
Japan	0.17	3.54	0.8 ± 0.8[b]	22	(Sato et al., 1997)
USA	n.d.	0.59	0.3 ± 0.3[b]	4	(Goldberg et al., 1995)
All regions	n.d.	29.24	5.4 ± 4.8	194	
cis-Resveratrol-glucoside (mg/l)					
France	0.4	4.5	1.8 ± 1.4[a]	8	(Adrian et al., 2000; de Lima et al., 1999; Goldberg et al., 1995)
Japan	0.0	6.6	1.7 ± 1.8[a]	22	(Sato et al., 1997)
Spain	0.1	5	1.4 ± 2.8[a]	79	(Goldberg et al., 1995; Lamuela-Raventos et al., 1995; Martinez-Ortega et al., 2000; Moreno-Labanda et al., 2004)
USA	n.d.	14.8	1.4 ± 1.2[a]	4	(Goldberg et al., 1995)
Portugal	0.2	2.8	0.8 ± 1.5[a]	14	(Baptista et al., 2001; de Lima et al., 1999)
All regions	n.d.	14.8	1.4 ± 2.4	127	

[A] The average values are calculated on basis of levels of *trans*- and *cis*-resveratrol-glucoside (*trans*- and *cis*-piceid) given by the cited references. Data are presented as mean ± standard deviation. Regions sharing the same letter are not significantly different ($p \leqslant 0.05$) according to Student's *t*-test.
[B] The number of samples included in each mean. The lower limit for inclusion into this analysis was three or more samples.
[C] Below the level of detection.

are also needed, though the level of resveratrol in these wines can be expected to vary more than for the mono-varietal wines, as the contribution from the used varieties to make a certain wine usually vary from vintage to vintage.

It will be of great importance to the scientific community if this first comparison is followed by further comparisons based on many additional investigations. In the process of making the present analysis on pooled data, we encountered different levels of information accompanying the measurements of resveratrol. We therefore propose that any future measurements of resveratrol content be made publicly available on-line and at least contain the following information: (1) type of wine (red, white, or rose); (2) description of the wine being mono-varietal or blended. In case of the wine being mono-varietal, the grape variety should be stated; (3) vintage and when possible also appellation; (4) local region or at least country; (5) levels of at least clearly stated *trans*- and *cis*-resveratrol. As *trans*- and *cis*-resveratrol-glucoside (*trans*- and *cis*-piceid) may prove to be interesting the levels of these conjugates should also be reported. In order to take the wine-making process into consideration in later combined analyses, authors should also include knowledge about specific methods used to make the wines. Lastly, authors should strive to avoid using only regional names for a given variety.

3.1. Conclusion

Based on the nature of variations in *trans*-resveratrol content it is not possible to accentuate a single wine producing region or variety. An average red wine can be expected to contain 1.9 ± 1.7 mg/l (8.2 ± 7.5 μM) *trans*-resveratrol, with non-detectable levels as the lower limit. The highest levels of *trans*-resveratrol measured are 14.3 mg/l (62.7 μM). Levels of *cis*-resveratrol follow the same pattern as *trans*-resveratrol; no region or variety can be emphasized as producing red wines with significantly different levels of *cis*-resveratrol. Levels of *trans*-resveratrol-glucoside (*trans*-piceid) varied significantly between regions studied while no significant difference in levels of *cis*-resveratrol-glucoside (*cis*-piceid) between regions could be found. The average level of *trans*-resveratrol-glucoside (*trans*-piceid) may be as much as three times that of *trans*-resveratrol, ranging from not detectable to 29.2 mg/l (128.1 μM).

4. Methods

4.1. Data collection

All data used in this review were collected from tables of resveratrol content in red wines published between 1993 and 2005. In the case of data in a reference was presented as mean with standard deviation, the mean value was treated as a single measurement. When there were doubts whether data in a reference stemmed from red wine, the data was not collected.

In some publications, where the local synonym for a grape variety was used, the more common name was found by referencing oenological encyclopedia and on-line queries. In the latter case, the common name was accepted if two or more web-sites in different languages produced the same relationship between a local synonym and the common name of the grape variety. The linguistic requirement was imposed to avoid cross referencing two automated copies of the same original document. In case of any doubt, the local name was used.

Comparison between different grape varieties was done by grouping data by variety using only data from reports where the wine was known to stem from a single grape variety. Comparison between regions was done by grouping data into regions, ignoring whether the wine stemmed from a single or several grape varieties. In both cases, only groups containing three or more measurements were considered for comparison.

4.2. Statistical analysis

Grouped data was assumed to be normal distributed. Homogeneity of variance between each group of data was tested with the *F*-test. Comparison between grouped data was performed using Student's two-tailed *t*-test assuming non-homogeneous variance between the compared sets.

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