Comparative Evaluation of Four Methods for Assay of *cis*- and *trans*-Resveratrol

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A comparative evaluation of four methods to measure the concentrations of *cis*- and *trans*-resveratrol as well as total resveratrol in commercial wines has been performed. Two of these methods utilized solid-phase extraction of resveratrol isomers prior to analysis by direct-injection gas-chromatography mass-spectrometry (GC-MS) or derivatization with *bis*-[trimethylsilyl]-trifluoroacetamide (BSTFA) prior to GC-MS analysis. Two methods utilized direct-injection high performance liquid chromatography (HPLC) in normal phase (isocratic) with absorbance detection at 306 nm, and reverse phase HPLC with gradient elution and diode array detection. In virtually all comparisons, the correlation between the values for any two methods was very satisfactory ($r > 0.900$), but some evidence of systematic bias was obtained which could not be explained by different standardization techniques. High values for *trans*-resveratrol with direct-injection GC-MS (Method 1) could be attributed, at least in part, to thermal breakdown of resveratrol glucosides to free isomers. The derivatization GC-MS technique (Method 2) showed a tendency to overestimate *cis*-resveratrol and underestimate the *trans* isomer, possibly as a consequence of *trans*- to-*cis* isomerization during the derivatization step. Somewhat lower values for *cis*-resveratrol with the normal-phase HPLC procedure (Method 3) might be a consequence of monitoring a single wavelength (306 nm) which is well above the absorption maximum of this isomer. Method 4 (reverse-phase gradient HPLC with diode array detection) has the advantage of allowing the simultaneous quantitation of many other polyphenols of biologic interest, and as of now may be considered to be the most robust method for routine application.

KEY WORDS: resveratrol, polydatin, wine, stilbenes, gas chromatography, mass spectrometry, high performance liquid chromatography, method standardization

Resveratrol (3,5,4'-trihydroxystilbene) exists as *cis* and *trans* isomers, both of which are present in red wines. It has attracted considerable interest as a phenolic constituent with biological properties potentially capable of attenuating the risk of atherosclerosis and coronary heart disease in human subjects [see Goldberg *et al.* (4) for review)] In the past several years, many papers have been published describing the concentrations of *cis*- and *trans*-resveratrol in wine (5,7,10,11,14,17,18,20,24,27). A number of investigations have been focused on the enological factors responsible for the occurrence of these stilbenes in wine, and techniques whereby their concentrations can be enriched (1,13,15,16,21,22,25,30). The methods employed have varied in their analytical principles. Organic solvent extraction (12-15,18,28), solid phase extraction (5,7,9-11,19-22,24,29,30), and direct injection techniques (6,8,17,23,26,27), have been used prior to resolution of resveratrol isomers by gas chromatography (GC) or high-performance liquid chromatography (HPLC). Most GC methods have required derivatization with bis-[trimethlsilyl]-trifluoroacetamide (BSTFA) prior to column application (3,12-14,29,30), with detection by flame ionization or mass-spectrometry (MS). Among the HPLC procedures, detection has been based upon UV absorbance (6,11,15,28), fluorescence (26), electrochemistry (23), or diode array (8,17-22,24,27).

It has been tacitly assumed that all of these methods yield similar results, although no inter-method comparisons have been performed. During the past three years, we have developed four different techniques to measure the concentrations of these stilbenes and have recently completed a comparative evaluation of these methods. The results have revealed a surprising degree of inter-method bias which can in large measure explain the differences between resveratrol concentrations of the same generic wines reported by various investigators.

Materials and Methods

Assays were performed by two methods on the same wines on the same day. A cross-check on calibration standards was carried out to eliminate standardization errors as a source of variability between methods. These were prepared from *trans*-resveratrol (Cat No R4010, Sigma Chemical Co., St. Louis, MO) irradiated to produce five different concentrations of both isomers as described by Goldberg *et al.* (5). The four methods evaluated were as follows:

Method 1: Solid phase extraction on a C-18 cartridge was followed by direct injection of the eluate on to a DB-17 HT column, temperature programmed from 150°C to 305°C over 13 minutes. *Cis*-resveratrol eluting at 4.3 minutes and *trans*-resveratrol at 5.7 minutes

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were quantitated by selective ion monitoring (SIM) at mass 228 (molecular ion) with ions at mass 227 (M-H) and 229 (C-isotope) as qualifiers (9).

Method 2: Solid phase extraction on a C-18 cartridge was followed by derivatization with BSTFA at 70°C for 60 minutes. An aliquot was injected on to a DB-5HT column, temperature programmed from 110°C to 300°C over 13 minutes. The *cis*-resveratrol derivative eluting at 8.5 minutes and the *trans*-resveratrol derivative eluting at 10.9 minutes were quantitated by SIM at mass 444 with qualifiers at masses 445 and 446 (29).

Method 3: Twenty µL of wine was directly injected on to a Lichrospher 100 CN column. Normal phase HPLC was performed with water-acetonitrile-methanol in isocratic mode. *cis*-Resveratrol and *trans*-resveratrol eluted at 34.9 and 48.2 minutes, respectively, and were quantitated by absorbance measurement at 306 nm (6).

Method 4: Twenty µL of wine was directly injected through a C-18 guard column on to an ODS Hypersil column. Reverse-phase HPLC was performed with a gradient comprising acetic acid, methanol and water. Diode array detection at five wavelengths, combined with a software package specifying match factor and purity factor analyses, was used to quantify *trans*- and *cis*-resveratrol eluting at around 27 and 33 minutes, respectively (8).

Analytical features of the four methods: Table 1 presents the relevant information collated from the original publications (6,8,9,29).

Statistics: The data were analyzed by means of the SAS Statistical Software Package (SAS Inst. Inc., Cary, NC, USA) to generate mean and standard deviation (SD) for each data set and to determine the values for skewness and kurtosis. The significance of overall differences between two methods for each of the parameters *cis*-resveratrol, *trans*-resveratrol and total resveratrol was evaluated by performing student's t-test for paired samples. Correlation and regression analyses were carried out using the method of least-squares to provide r (the Pearson Product Moment Correlation Coefficient), and the slope (m) and intercept (c) corresponding to the equation: $y = mx + c$. Since the standard errors of m and c were also provided, we could determine by calculating the statistic "t" whether the intercepts were significantly different from zero and the slopes from unity.

Table 1. Analytical characteristics of methods[a].

	Method 1 Direct injection GC-MS	Method 2 Detiviti-zation GC-MS	Method 3 Normal phase HPLC	Method 4 Diode array HPLC
Linearity (mg/L)	0.1 - 12.5	0.1 - 33.40	0.5 - 25	0.5 - 13.2
Detection limit	10 µg/L	10 µg/L	25 µg/L	30 µg/L
Precision (CV %)	5.3 - 6.1	4.8 - 8.5	0.4 -3.9	2.0 - 3.4
Recovery (%)	92.2 - 97.5	91 - 98	100 - 105	97.5 - 105.5

[a]The following abbreviations are used: GC-MS (gas chromatography-mass spectrometry); HPLC (high performance liquid chromatography); CV (coefficient of variation).

Results

Comparison of Method 1 (Direct Injection GC-MS), with Method 2 (Derivatization GC-MS): Ninety red wines were analyzed by both methods. The

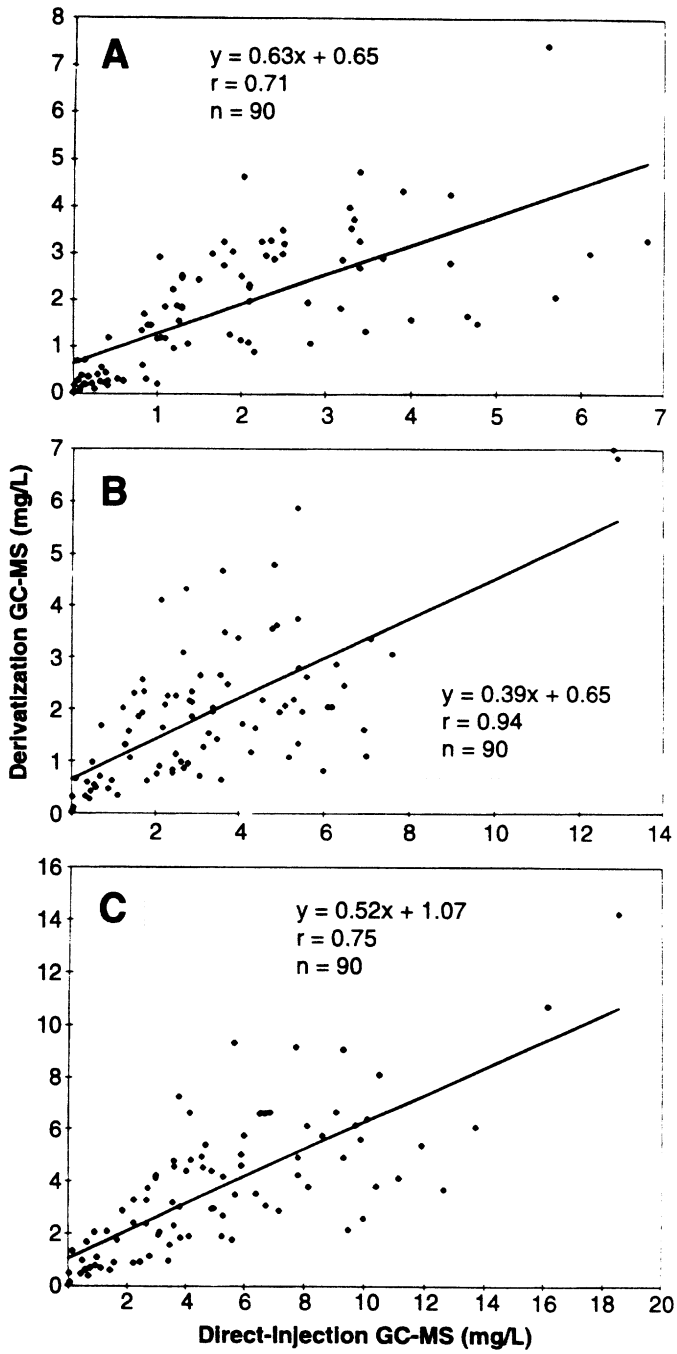

Fig. 1. Comparison of wine analysis between direct injection GC-MS (Method 1) and derivatization GC-MS (Method 2). A. *cis*-resveratrol; B. *trans*-resveratrol; C. total resveratrol. The linear regression equation and correlation coefficient (r) are shown. Ninety red wines were analyzed of which 24 were from Bordeaux, 31 from Burgundy, 26 from Italy and 9 from California.

individual data points are presented in Figure 1(A, B, C), together with the results of correlation and regression analyses. The mean (± SD) *cis*-resveratrol concentrations, 1.82 ± 1.57 mg/L for Method 1 and 1.80 ± 1.41 mg/L for Method 2 were almost identical; Method 1 gave higher values in 35 wines, Method 2 in 52 wines, and in three the values were identical. The mean *trans*-resveratrol concentrations, 3.26 ± 2.45 mg/L for Method 1 and 1.92 ± 1.40 mg/L for Method 2 were significantly different ($p < 0.005$), with Method 1 higher in 65 wines, Method 2 in 23, and identical values in 2 wines. Total resveratrol concentrations were 5.09 ± 3.82 mg/L for Method 1, 3.71 ± 2.63 mg/L for Method 2 ($p < 0.05$), Method 1 being higher in 59 wines, Method 2 in 30, and one giving identical values. The slopes of the regression lines ranged from 0.39 (*trans*) to 0.63 (*cis*), all values being significantly different from unity, but the intercepts were not significantly different from zero apart from the value of 1.07 ($p < 0.05$) for total resveratrol. This points to systematic bias between the two methods especially seen in the much higher values for *trans*-resveratrol averaging +70% with Method 1, which translated into a mean increment of 37% for total resveratrol concentrations assayed by this method.

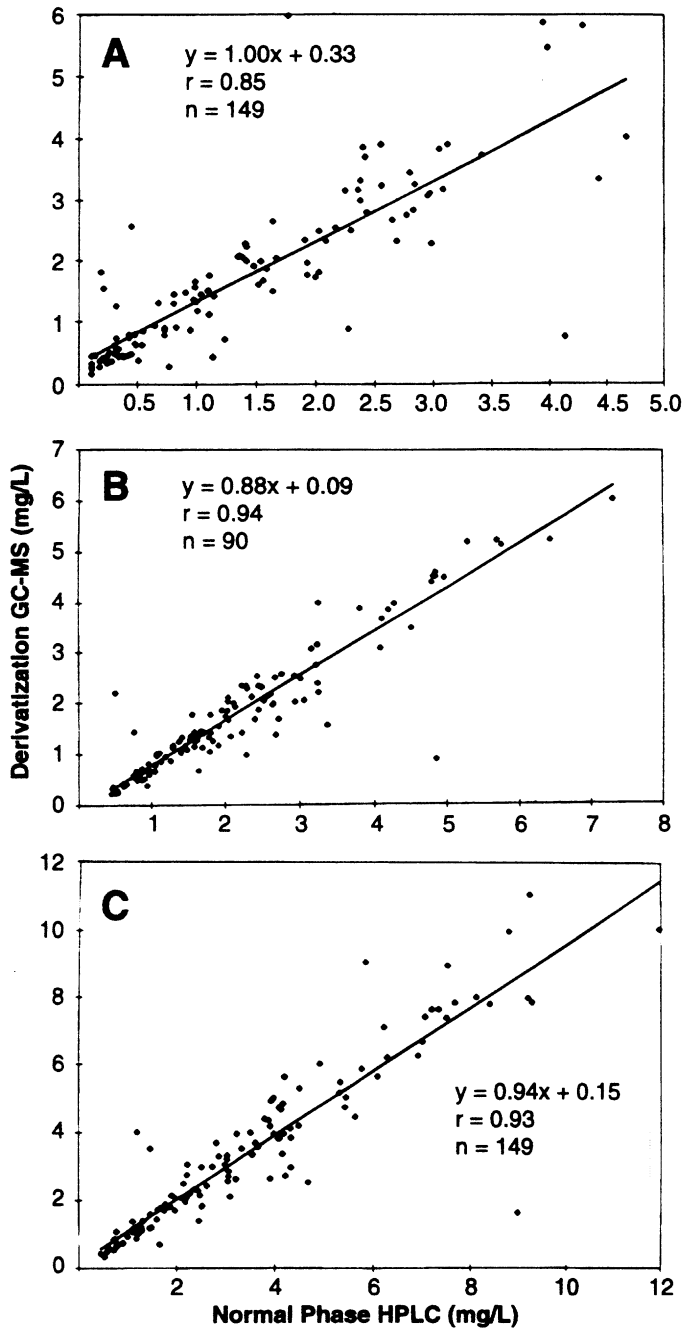

Fig. 2. Comparison of wine analysis between normal phase HPLC (Method 3) and derivatization GC-MS (Method 2). A. *cis*-resveratrol; B. *trans*-resveratrol; C. total resveratrol. The linear regression equation and correlation coefficient (r) are shown. One hundred forty-nine wines were analyzed of which 28 were from Bordeaux, 30 from Burgundy, 49 from Italy, 22 from California, and 20 were from miscellaneous regions.

Comparison of Method 3 (Normal Phase HPLC) with Method 2 (Derivatization GC-MS): One hundred forty-nine red wines were analyzed by both methods. The individual data, correlation and regression analyses are presented in Figure 2 (A, B, C). The mean *cis*-resveratrol concentrations for Method 2 (1.58 ± 1.31 mg/L) and for Method 3 (1.37 ± 1.12 mg/L) were significantly different ($p < 0.01$) because Method 2 gave higher results in 131 wines, Method 3 in 14, with identical results in two wines. For *trans*-resveratrol, Method 3 gave a mean of 2.13 ± 1.45 mg/L and Method 2 a mean of 1.77 ± 1.35 mg/L, with Method 3 giving higher values in 140 wines, Method 2 in 7 wines and equal values in two ($p < 0.005$). The total resveratrol concentrations (mean of 3.35 ± 2.47 mg/L for Method 2 and 3.40 ± 2.44 mg/L for Method 3) were not significantly different. The intercepts were not significantly different from zero for any of the equations listed in Figure 2, but the slope of 0.88 ($p < 0.01$) for the comparison of *trans*-resveratrol with the two methods (Fig. 2B) pointed to a systematic bias towards lower values with Method 2.

Comparison of Method 3 (Normal Phase HPLC) and Method 4 (Reverse Phase HPLC with Diode Array): Of the 170 red wines utilized for this comparison, 169 had valid results for *trans*-resveratrol and 147 for *cis*-resveratrol based on match factor and purity checks provided by the diode array detector. The mean values for the latter (Method 3 given first) were 1.41 ± 1.27 mg/L and 1.64 ± 1.26 mg/L ($p < 0.05$) and for the former 1.67 ± 1.12 mg/L and 1.53 ± 1.11 mg/L (not significant). For *cis*-resveratrol, Method 4 gave higher results with 114 wines, Method 3 with 29, and both were identical in four. In the case of *trans*-resveratrol, Method 3 gave higher values in 113 wines, Method 2 in 52, with four yielding identical values. The mean total resveratrol concentrations of 3.24 ± 2.17 mg/L (Method 3) and 3.33 ± 2.13 mg/L (Method 4) were not significantly different. As shown in Figure 3, correlation was excellent; the slopes of the regression equations for both isomers and total resveratrol were not significantly different from unity and the intercepts did not differ significantly from zero.

Comparison of Method 2 (Derivatization GC-MS) with Method 4 (Reverse Phase HPLC

with Diode Array): Ninety-six red wines, in all of which both isomers of resveratrol were measurable, were analyzed by both methods. The mean concentrations of *cis*-resveratrol measured by Method 2 (1.70 ± 1.47 mg/L) and Method 4 (1.38 ± 1.19 mg/L) were significantly different ($p < 0.001$), with Method 2 generating higher results in 82 wines and Method 4 in 16. For *trans*-resveratrol, the mean concentrations measured by Method 2 (2.07 ± 1.80 mg/L) and Method 4 (2.10 ± 1.69 mg/L) were in good agreement, Method 4 giving higher results in 56 wines and Method 2 in 40. The mean total resveratrol concentrations measured by Method 2 (3.78 ± 3.09 mg/L) and Method 4 (3.48 ± 2.74 mg/L) were significantly different ($p < 0.01$), with the latter higher in 35 and the former in 61 of the 96 wines

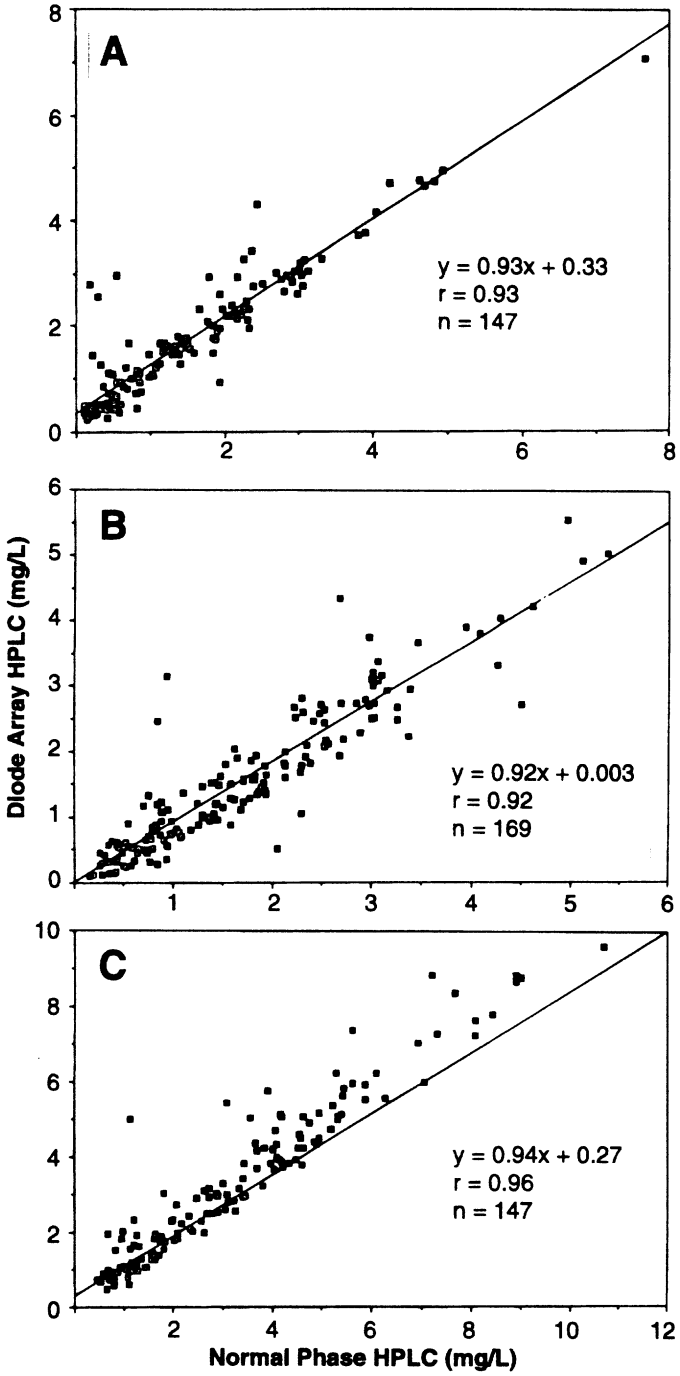

Fig. 3. Comparison of wine analysis between normal phase HPLC (Method 3) and diode array HPLC (Method 4). A. *cis*-resveratrol; B. *trans*-resveratrol; C. total resveratrol. The linear regression equation and correlation coefficient (r) are shown. Of the 169 wines analyzed, 30 were from Bordeaux, 28 from Burgundy, 34 from Italy, 29 from California, 18 from the Rhone Valley, 16 from Australia, and 14 were from miscellaneous regions.

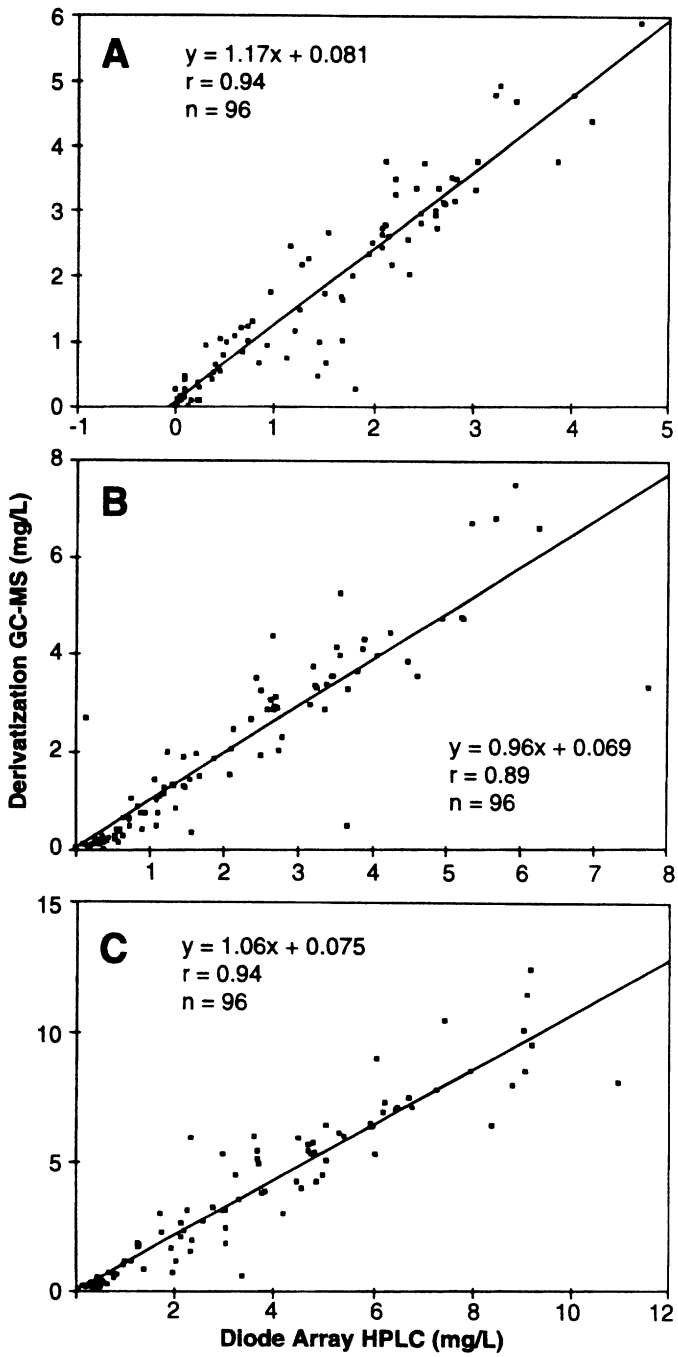

Fig. 4. Comparison of wine analysis between diode array HPLC (Method 4) and derivatization GC-MS (Method 2). A. *cis*-resveratrol; B. *trans*-resveratrol; C. total resveratrol. The linear regression equation and correlation coefficient (r) are shown. Of the 96 wines analyzed, 15 were from Bordeaux, 14 from Burgundy, 20 from Italy, 19 from California, 10 from the Rhone Valley, 12 from Australia and 10 from other regions.

compared. From Figure 4, it is clear that the correlation coefficients were very satisfactory, values ranging between 0.89 and 0.94 and the intercepts were all not significantly different from zero. However, the regression slopes for *cis* and total resveratrol were consistent with a 17% and 6% bias in favor of Method 2 ($p < 0.01$ for both comparisons).

Discussion

Sources of variability in four methods evaluated: Methods 1 and 2 involve a single-step solid-phase extraction prior to GC-MS analysis, whereas Methods 3 and 4 utilize direct sample injection on to a HPLC column. Since the total resveratrol concentrations measured by Method 2 were not lower than those of Methods 3 and 4, solid-phase extraction does not seem to be associated with loss of resveratrol. This stands in sharp contrast to organic solvent extraction (*vide infra*) which, based on a survey of the published literature on the resveratrol concentrations of commercial wines, consistently leads to lower estimates. It is not clear why Method 2 gave significantly higher values for total resveratrol than Method 4, since comparison between Methods 2 and 3 and between Methods 3 and 4 demonstrated almost identical mean values for this parameter. The difference between Methods 2 and 4 approximated only 8% and was entirely due to the higher values of *cis*-resveratrol provided by the former.

The mean value for *cis*-resveratrol was higher with Method 2 than with Method 3, and Method 2 yielded a significantly lower mean value for *trans*-resveratrol. It is conceivable that some isomerization of *trans*- to *cis*-resveratrol occurs during the derivatization step despite the exclusion of light and oxygen. This is consistent with the fact that in this particular set of experiments, the two opposing trends almost neutralized each other to the extent that the mean total resveratrol concentrations for Methods 2 and 3 were in quite good agreement. The same is true for mean total resveratrol concentrations provided by Methods 3 and 4. The only significant difference in the comparison of these two methods was an increase of approximately 15% in the mean *cis*-resveratrol concentrations provided by Method 4. This suggests that, since all reported peaks with Method 4 are subjected to purity and spectral identity analyses, Method 3 is not prone to overlapping contaminants that would give rise to falsely elevated values. The lower *cis*-resveratrol concentrations with Method 3 may reflect the fact that absorbance was measured only at 306 nm, the maximum wavelength for *trans*-resveratrol, whereas that for the *cis* isomer occurs at 280 nm.

By far the biggest discrepancy occurred in comparing the two GC-MS methods. Whereas near-identical mean values were provided for the *cis* isomer, *trans*-resveratrol was 67% higher with Method 1. Since introducing this method, we and others have recognized the relatively high concentrations of the resveratrol ß-3-glucosides *cis* and *trans*-polydatin in commercial red wines (6,14,17,22,27,31). Further, using *trans*-polydatin extracted from the dried roots of *Polygonum cuspidatum* and partly converted to the *cis* isomer by photo-isomerization, we found that these glucosides when directly injected in ethyl acetate solution into the GC-MS apparatus yielded significant but unpredictable amounts of free isomer generating the characteristic mass ion spectra at the appropriate retention times for *cis*- and *trans*-resveratrol. It is therefore apparent that Method 1 overestimates the resveratrol free isomer content of wine as a consequence of thermal hydrolysis of resveratrol glucosides, notably the *trans*-isomer, although this will surely vary with the relative concentrations of all four compounds in a given wine. For this reason, we did not carry out further comparative evaluations with this method. The data revealed by comparing Methods 1 and 2 can best be interpreted as follows: both isomers are higher than their true concentrations in Method 1; the *trans*- to-*cis* isomerization that may occur during derivatization with Method 2 compensates for the increment in the former when results with the two methods are compared.

Since Method 4 allows the simultaneous determination of a wide range of biologically active phenols in red wine and has sophisticated software features to prevent false elevation by contaminating constituents eluting at or near the retention times of *cis*- and *trans*-resveratrol, it is the most flexible and robust of the current methods to quantitate these hydroxystilbenes in wine.

Variability in published values for wine resveratrol concentrations: Serious interest in resveratrol as a constituent of wine followed the landmark paper of Siemann and Creasy in 1992 (28), dominated by *trans*-resveratrol which was the first isomer of this stilbene to be identified in wine. Most reports, until recently, were based upon anecdotal analyses of a Cabernet Sauvignon here and a Pinot noir there, with little attempt to develop a solid statistical description of the resveratrol profile of wines in distinct and definable categories according to cultivar and region of production. Some publications did, in fact, focus upon one region, but rarely have as many as 50 red wines been analyzed in these investigations. In several papers (5,7,10), we have described the resveratrol concentrations of large collections of wines from all the major red-wine producing regions of the world assayed by solid phase extraction and direct-injection GC-MS, and it is both opportune and timely that we should now compare our data with other reports to point out areas of agreement and inconsistency, and to hazard a guess at methodological problems possibly accounting for the latter.

As we originally pointed out (10) , our values for *trans*-resveratrol concentrations are almost an order of magnitude greater than those of Siemann and Creasy (28) where direct comparisons are possible: *e.g.,* California and Bordeaux. An even greater set of discrepancies exist between our data for California wines and those put forward by Lamuela-Raventos and

Waterhouse (18). Their highest value for a wine from Cabernet Sauvignon was given as 0.09 mg/L, the three other wines from this cultivar having apparently yielded 0.05 mg/L. Three wines from Pinot noir had *trans*-resveratrol concentrations ranging from 0.21 to 0.68 mg/L. In contrast, we have consistently found *trans*-resveratrol concentrations in California Cabernet Sauvignon and Pinot noir wines more than one order of magnitude higher and averaging 0.67 and 5.30 mg/L, respectively (7,10). We have attributed these differences to the multiple solvent extraction steps required by these methods with the possibility of large losses prior to HPLC [55% in the method of Lamuela-Raventos and Waterhouse (18)] as well as incomplete resolution of *trans*-resveratrol from interfering compounds (18).

Two years later, the same group published an excellent and comprehensive report in the course of which they presented data for a large array of polyphenols in Californian wines, including the sum of *cis*- and *trans*-resveratrol (3). The latter was measured by BSTFA derivatization followed by GC-MS, analogous to our Method 2, except that liquid-liquid extraction was performed. A recovery of 96% and CV of 4% were obtained. Only one Pinot noir wine was analyzed (total resveratrol = 0.98 mg/L), but five wines from Cabernet Sauvignon had concentrations of 2.25, 1.93, 1.16, 1.75, and 1.46 mg/L. The former is well below the mean concentration of 9.18 mg/L that we found for total resveratrol in Californian Pinot noir wines, whereas the latter are in the same range but above the mean of 1.07 that we obtained for 30 Californian wines from this cultivar. It is disappointing that Frankel *et al.* (3) do not grapple with the inconsistencies between these data and their 1993 report, but simply state that "the resveratrol levels ..... followed the same patterns as in other studies."

Of special relevance is the fact that McMurtrie *et al.* (23) who used direct injection HPLC with electrochemical detection reported *trans*-resveratrol values for Californian Cabernet Sauvignon, Zinfandel, and Pinot noir, as well as a Cabernet-Merlot blend from Chile (one example only of each wine) and two Beaujolais, all of which were in excellent agreement and close to the means for these wines which we had obtained with our direct-injection GC-MS procedure (Method 1). On the other hand, Jeandet *et al.* (14), using a six-step solvent extraction, followed by BSTFA derivatization and GC analysis with flame ionization detection, reported total resveratrol concentrations < 2 mg/L in 16 Burgundy red wines vinted from Pinot noir; *trans*-resveratrol never exceeded 50% of the total, and in all but two, represented < 40%. Using our Method 1, we obtained a mean total resveratrol concentration of 7.77 mg/L among 68 red Burgundy wines with a mean *cis*:*trans* ratio of 0.87 (7). The discrepancy between these findings is consistent with overall reduced recovery during solvent extraction allied with *trans*- to-*cis* isomerization during derivatization. Jeandet *et al.* (13,15) have more recently followed their original solvent extraction with separation by HPLC and quantitation by UV absorbance. The second of these papers (15) presented data for the total resveratrol concentrations of wines of three vineyards over a 13-year period; these values ranged from approximately 0.8 to 3.2 mg/L, in good agreement with their 1993 report, but they did not indicate the relative proportions of the two isomers. In the first (15), using their original GC procedure, they reported on the resveratrol isomer concentrations of wines subjected to different treatments during vinification. Under all circumstances, the *trans* isomer was more than twice as high as the *cis* isomer, but they did not comment on this contradiction with their previous results (14).

Three reports have focused on Italian red wines. In the first (19), solid phase extraction was followed by HPLC analysis. Fifteen wines from five cultivars (three of each) produced in the Trentino region had *trans*-resveratrol concentrations between 1.20 and 7.17 mg/L. In a companion paper (20), 101 mono-varietal wines from the same region yielded *trans*-resveratrol concentrations of 0.70 to 4.59 mg/L. It is, therefore, a little surprising that as many as six of the 15 wines in the first report exceeded this upper limit. Thirty-two Tuscan red wines (all but 4 of them Chianti) analyzed by the same methodology had total resveratrol concentrations ranging from 0.9 to 3.9 mg/L; in 25, the *trans* isomer was higher, in five the *cis* isomer predominated, and in two both isomers were present in equal concentrations (24). We obtained a mean total resveratrol concentration of 1.98 mg/L in 34 Tuscan red wines, with the *trans* isomer higher in most. Although we have not specifically analyzed wines from Trentino, the concentration of *trans*-resveratrol averaged 0.83 mg/L in wines from Veneto (n = 25), 1.36 mg/L in wines from Piedmont (n = 25), and 1.18 mg/L in wines from other regions of Italy (n = 23). Our results are, therefore, consistent with the data of Mozzon *et al.* (24), but not with those of Mattivi (19,20).

Two sets of authors have published data for Spanish red wines. Gonzalo *et al.* (11) obtained mean values of 1.78 (range 0.34 - 6.70) and 1.33 (range 0.05 - 4.78) for *trans*- and *cis*-resveratrol (mg/L), respectively, when analyzing 34 wines from the province of Catalonia, using solid phase extraction followed by HPLC (gradient elution) and quantitation by UV absorbance. Lamuela-Raventos *et al.* (17) assayed 18 red wines (all but 3 from Catalonia) and recorded mean values of 2.48 mg/L and 0.56 mg/L for *trans*- and *cis*-resveratrol, respectively. Their method (the third to be developed in association with the UC, Davis group) utilized direct injection of wine sample onto a HPLC column followed by gradient elution and monitoring the absorbance at 306 nm and 285 nm. It is intriguing that both sets of investigators reported near identical concentrations for total resveratrol of 3.11 (11) and 3.04 (17) although there was a more than three-fold difference in their isomer ratios (1.34 and 4.43, respectively). Our own analyses on 35 red wines from all Spanish viticultural regions (Rioja being predominant) gave a mean total

resveratrol concentration of 2.76 mg/L and an isomer ratio of 2.07.

Roggero and Archier (27) reported values for *trans*-resveratrol concentrations in eight red wines from the Rhone Valley, Provence and Midi appellations of France ranging from 0.3 - 4.8 mg/L (27). These, as well as single values for one example each of red wines from Burgundy. Beaujolais and Bordeaux, were in good agreement with our values for these respective wines. Finally, our mean of 4.78 mg/L for the *trans*-resveratrol content of 10 Swiss red wines (7) is consistent with the data of Pezet *et al.* (26) for the red wines of this country.

Need for international standardization: From this survey of the literature and a comparison with our own data, it is apparent that not only have widely divergent data for resveratrol isomer concentrations been reported by different authors using a variety of methods, but sequential reports by the same authors employing similar or different methods have revealed inconsistencies which have often been unacknowledged or unrecognized, and rarely explained. The last several years have witnessed a fascination with the health-promoting properties of wine and the extent to which the polyphenols, relatively enriched in red wines, can complement the beneficial effects which have been established for moderate consumption of ethanol. Resveratrol has been a particular focus of attention, but many others, including quercetin — now established as an anticancer agent worthy of clinical trial (2) — and antioxidants such as gallic acid, catechin and myricetin (3), are beginning to capture the interest of medical scientists. It is not too difficult to imagine a future in which the concentrations of certain key constituents will be announced on the labels of wine bottles much as is the case for most other items of dietary importance. Developments along these lines can do nothing but good for the wine industry in raising public consciousness to its potential health benefits. To render this concept feasible, it will be essential to utilize standardized analytical methods that are intrinsically accurate and reproducible between laboratories. This is a task that national and international bodies (including the American Society for Enology and Viticulture) should address sooner rather than later, in preparation for a tide of public and political opinion that seems about to turn from a hostile to a more affirmative posture.

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