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ARTICLE

Physicochemical Study of the Complexation of Pterostilbene by Natural and Modified Cyclodextrins

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In this paper, the interaction between pterostilbene and cyclodextrins (CDs) is described for the first time using steady-state fluorescence. It was seen that pterostilbene forms a 1:1 complex with all of the natural (α-, β-, and γ-CDs) and modified (HP-β-CD, methyl-β-CD, and ethyl-β-CD) CDs tested. Among natural CDs, the interaction of pterostilbene with β-CD was the most efficient. However, all of the modified CDs showed higher complexation constants (K_F) than β-CD. The highest K_F was found for HP-β-CD (17520 ± 981 M^{-1}), in which its value showed a strong dependence upon pH in the region where the pterostilbene begins the deprotonation of its hydroxyl group. Moreover, the values of K_F decreased as the system temperature increased. To obtain information on the mechanism of pterostilbene affinity for CD, the thermodynamic parameters of the complexation ($\Delta H°$, $\Delta S°$, and $\Delta G°$) were studied. Finally, a comparison of the K_F values obtained for three types of stilbenes revealed that both the stoichiometry and the K_F values of the complex are dependent upon the structure of the guest molecule. While the *trans*-resveratrol−HP-β-CD and pterostilbene−HP-β-CD complexes showed a 1:1 stoichiometry with a higher K_F value for the *trans*-resveratrol−HP-β-CD complexes, *trans*-stilbene showed a 1:2 stoichiometry.

KEYWORDS: Pterostilbene; cyclodextrin; fluorescence; stilbene

INTRODUCTION

Pterostilbene (*trans*-3,5-dimethoxy-4′-hydroxystilbene) (**Scheme 1**) is a naturally occurring phytoalexin, which has been identified in several plant species. It belongs to a group of phenolic compounds known as stilbenes and is found in different sources, such as the heartwood of sandalwood (*Pterocarpus santalinus*) (*1*) and *Pterocarpus marsupium* (*2*). It was also identified in the leaves of *Vitis vinifera* (*3*), in infected grape berries of varieties Chardonnay and Gamay (*4*), and in healthy and immature berries of varieties Pinot Noir and Gamay (*5*). Pterostilbene has also been found in the berries of some *Vacciunium* species (*5*), while Paul et al. (*6*) reported high levels in darakchasava, a medicinal drink made primarily from dried grape berries used to treat cardiovascular and other ailments. Finally, pterostilbene also appears to be a constituent of the bark of *Guibourtia tessmanii*, a tree found in central Africa, which is commonly used in folk medicine (*7*).

In recent years, the perceived health benefits related to pterostilbene have led to a significant increase in its consumption in a variety of food products that contain concentrations of this type of stilbene, such as blueberries and it related products and some types of grapes and wines. It has also been included in medicaments. Among its pharmacological properties are a wide range of biological activities, such as antihyperglycemic (*8*), antioxidative (*9*−*11*), anticancer (*9*−*14*), anti-inflammatory (*11*), anticholesterol (*15*, *16*), antifungus (*17*, *18*), hypolipidemic (*11*), or analgesic (*11*). Moreover, Pan et al. (*12*), using transcript profiling, recently identified the cellular pathways targeted by pterostilbene. The observed response in lipid metabolism-related genes is consistent with its known hypolipidemic properties, and the induction of mitochondrial genes is consistent with its demonstrated role in apoptosis in human cancer cell lines. Furthermore, their data show that pterostilbene has a significant effect on methionine metabolism.

However, problems concerning the physicochemical properties of pterostilbene have meant that no "*novel food*" has been fortified with this antioxidant. Indeed, pterostilbene shows very poor solubility in water (although it is more soluble in ethanol and other organic solvents), possesses low bioavailability, and is easily oxidized by several enzymes, such as laccase (*20*, *21*). For these reasons, the complexation of pterostilbene with types of molecules that can increases its bioavailability, solubility, and stability in the face of prooxidant agents is strongly desirable, as in the case of cyclodextrins (CDs).

CDs are torus-shaped oligosaccharides made up of α-(1,4)-linked glucose units. The most common CDs are α-, β-, and γ-CDs, which contain six, seven, and eight glucose units, respectively (*22*, *23*). The cavity is carpeted by hydrogen atoms and therefore has a rather hydrophobic nature, unlike the outer surface of the molecule, in which the primary and secondary hydroxyl groups are exposed to the solvent, thus making the whole molecule highly water-soluble (*22*, *23*). Poorly water-soluble

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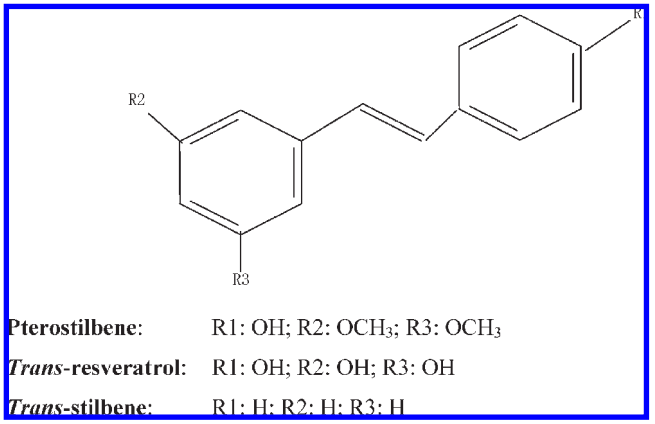
Scheme 1. Structures of Pterostilbene, *trans*-Resveratrol, and *trans*-Stilbene



compounds and hydrophobic moieties of amphiphilic molecules interact noncovalently with the CD cavity to form the so-called inclusion complexes, which are also highly water-soluble (*24*−*26*). However, the solubility of these complexes depends upon several factors, such as the type of CD used (*24*−*26*). Because CDs are able to increase the bioavailability of different compounds and to protect different molecules against the action of external agents, their use in both the pharmaceutical and food industries is increasing (*22*, *23*).

To date, although CDs have been used to complex another type of stilbene, such as *trans*-resveratrol (*27*, *28*), the effect of CDs on pterostilbene has not been published in any paper. Indeed, this is the first work where the complexation between CD and this potent antioxidant is reported. Knowledge of the stoichiometric coefficients and the complexation constants (K_F) of the CD complexes is essential if this stilbene is to be used in both the pharmaceutical and food industries.

With the above kept in mind, the main objective of this work was to analyze the complexation mechanism of pterostilbene with different types of natural (α-, *β*-, and *γ*-CDs) and modified (HP-*β*-CD, methyl-*β*-CD, and ethyl-*β*-CD) CDs under various experimental conditions of temperature and pH. The stoichiometry, K_F values, and thermodynamic parameters for the pterostilbene−CD complexes are evaluated. Finally, the effect of the structure of the stilbene on both the stoichiometry and the K_F values are discussed using other molecules of this family, such as *trans*-resveratrol and *trans*-stilbene.

To perform the study, a method that makes use of changes in fluorescence spectroscopic properties of pterostilbene in the presence of CDs was used.

MATERIALS AND METHODS

Materials. Natural (α-, *β*-, and *γ*-CDs) and modified (HP-*β*-CD, methyl-*β*-CD, and ethyl-*β*-CD) CDs, *trans*-stilbene, and *trans*-resveratrol were purchased from Sigma-Aldrich (Madrid, Spain) and used as received. Pterostilbene was from Sequoia Research Products Limited (Pangbourne, U.K.) and was used without further purification. Some stilbenes may be sensitive to the light, and irradiation of solutions containing the analyte induces the formation of other molecules, which leads to the formation of a highly fluorescent compound. Because of this, the samples were stored in darkness.

Equipment and Experimental Procedure. *Fluorescence Studies*. Fluorescence intensity was measured in a Kontron SFM-25 spectrofluorimeter equipped (Zurich, Switzerland) with thermostatically controlled cells and with a xenon lamp source and quartz cell, which were used to perform all fluorescence measurements. Excitation and emission bandwidths were both set at 2 nm. The excitation wavelengths for pterolstilbene, *trans*-resveratrol, and *trans*-stilbene were 330, 334, and 250 nm, respectively. The emission wavelengths for pterostilbene, *trans*-resveratrol, and *trans*-stilbene were 374, 385, and 374 nm, respectively. The relative fluorescence intensity values were recorded at 25 °C. To avoid inner filter effects, 2 mm quartz cells were used.

Temperature Studies. The K_F values were determined at the following temperatures: 15, 25, 30, and 37 °C, using a Thermomixer Comfort (Eppendorf Ibérica, Madrid, Spain) to control the temperature. The thermodynamic parameters $\Delta H°$, $\Delta S°$, and $\Delta G°$ can be calculated using the following thermodynamic relationship equation:

$$\ln K_F = \frac{-\Delta H°}{RT} + \frac{\Delta S°}{R} \quad (1)$$

where K_F is the complexation constant of the inclusion complex, T is the temperature, R is the gas constant, and $\Delta H°$ and $\Delta S°$ are standard enthalpy and entropy changes of complex formation in the mobile phase. For a linear plot of ln K_F versus $1/T$, the slope and intercept are $-\Delta H°/R$ and $\Delta S°/R$, respectively. The Gibbs free energy change for the interactions that take place during the inclusion process may be found by the following equation:

$$\Delta G° = \Delta H° - T\Delta S° \quad (2)$$

RESULTS AND DISCUSSION

Study of the Complexation of Pterostilbene by Cyclodextrins: Stoichiometry of the Complexes and Determination of the Complexation Constants. To date, no paper has reported the possible interaction between pterostilbene and any type of CD. For this reason, we have selected *β*-CD, the most widely used natural CD, to evaluate the hypothetical interaction between this potent antioxidant and CDs. To quantify the interaction between pterostilbene and *β*-CD, the K_F was determined using, as an analysis technique, the steady-state fluorescence, which takes into account the changes in the physicochemical state of this antioxidant with the concentration and following the Benesi−Hildebrand method (*29*).

Assuming that the composition of the complex was 1:1, the following expression can be written as

$$\text{pterostilbene} + \beta - \text{CD} \rightleftarrows \beta - \text{CD} - \text{pterostilbene}$$

The complexation constant, K_F, is given by

$$K_F = \frac{[\beta - \text{CD/pterostilbene}]}{[\text{pterostilbene}][\beta - \text{CD}]} \quad (3)$$

where [*β*-CD], [pterostilbene], and [*β*-CD/pterolstilbene] are equilibrium concentrations.

From the experimental data of **Figure 1**, the difference in the intensity of the emission fluorescence of pterostilbene in the absence and presence of different amounts of *β*-CD was plotted versus the *β*-CD concentration (inset of **Figure 1**). A representative plot of the variation in fluorescence intensity at the wavelength band used as a function of the *β*-CD concentration was analyzed by the Benesi−Hildebrand method.

The K_F value for the inclusion complex can be determined by typical double-reciprocal (or Benesi−Hildebrand) plots:

$$\frac{1}{F - F_0} = \frac{1}{(F_\alpha - F_0)K_F[\beta - \text{CD}]} + \frac{1}{F_\alpha - F_0} \quad (4)$$

where [*β*-CD] denotes the *β*-CD concentration, F_0 is the fluorescence intensity of pterostilbene in the absence of *β*-CD, F_∞ is the fluorescence intensity when all of the pterostilbene molecules are essentially complexed with *β*-CD, and F is the observed fluorescence intensity at each *β*-CD concentration tested.

In our study, a plot of $1/F - F_0$ versus $1/[\beta\text{-CD}]$ gave a straight line with a linear correlation higher than 0.99, indicating that the

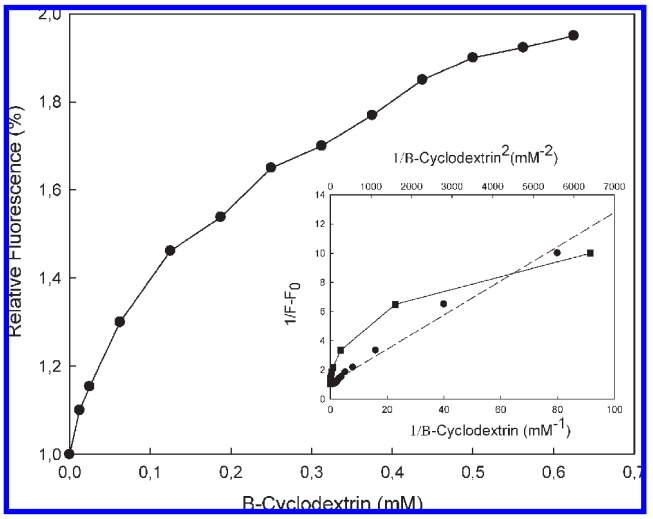


Figure 1. Dependence of emission fluorescence intensities of pterostilbene (30 μM) on β-CD concentrations. (Inset) Double-reciprocal plot of pterostilbene complexed to β-CD for determining the stoichiometry of β-CD/pterostilbene complexes: $1/(F - F_0)$ versus $1/[\beta\text{-CD}]$ (assumption of a 1:1 complex) (●) and $1/(F - F_0)$ versus $1/[\beta\text{-CD}]^2$ (hypothesis of a 1:2 complex) (■).

presumed stoichiometry of the β-CD/pterostilbene complexes formed was 1:1 (filled circles in the inset of **Figure 1**).

The plot of $1/(F - F_0)$ as a function of $1/[\beta\text{-CD}]^2$ was also analyzed because it was thought that it might provide information about the presence of higher order complexes, especially at higher β-CD concentrations. Assuming the stoichiometry of the inclusion complex to be 1:2, the following expression is obtained (*30*):

$$\frac{1}{F - F_0} = \frac{1}{(F_\alpha - F_0)K_{F12}([\beta - \text{CD}])^2} + \frac{1}{F_\alpha - F_0} \qquad (5)$$

However, none of the experimental data provided a good linear fit in these plots, ruling out this possibility. When $1/(F - F_0)$ was plotted against $1/([\beta\text{-CD}])^2$, a nonlinear relationship was obtained (linear correlation of 0.86) (filled squares in the inset of **Figure 1**), which indicates that the stoichiometry of the inclusion complex is not 1:2.

When the data obtained was fitted to eq 4, the K_F value for this physiological pH was calculated as $8120 \pm 440\ M^{-1}$, demonstrating for first time the interaction between pterostilbene and CD. These results are in good agreement with those previously obtained for the 1:1 complexes between β-CD and several compounds with structures similar to pterostilbene (*27*, *28*).

Effect of the Cyclodextrin Structure on Complexation Constants. The K_F values between pterostilbene and CDs were determined with different types of CDs in an attempt to characterize the interaction between pterostilbene and the host CD at a molecular level. Three types of natural CDs with GRAS status and approved recently as additives in the European Union (α-, β-, and γ-CDs) were used to this end. Indeed, recently, the three natural cyclodextrins have been included in the European list of additives approved for alimentary use, and the correspondent E numbers have been assigned for α-, β-, and γ-CDs (E-457, E-458, and E-459 correspondingly). Fitting the values of relative intensity to the equations previously described provides the corresponding K_F. With regard to the different species, α-, β-, and γ-CDs, it can be observed that the highest K_F value ($K_F = 8120 \pm 440\ M^{-1}$) was found for β-CD, followed by α-CD ($K_F = 4920 \pm 340\ M^{-1}$) and, finally, γ-CD ($K_F = 361 \pm 25\ M^{-1}$). These results are in good agreement with those published for the most of the papers that compare the complexation of several compounds and natural CDs (*22*, *23*). In our study, the inner diameter of the CD formed by seven units of glucose (β-CD, 6.0−6.4 Å) fitted pterostilbene better than the inner diameter of six units (α-CD, 4.7−5.2 Å) or eight units (γ-CD, 7.5−8.3 Å) of glucose. For this reason, β-CD was considered the most suitable CD to continue the present investigation.

Effect of the Chemical Modification of β-CD on the Complexation Constants of the Pterostilbene/CD Complexes. Because β-CDs were the most effective for complexing pterostilbene, different types of modified β-CDs were studied, adding different functional groups to the macrocyclic ring. Qualitatively different results were obtained when HP-β-CD, methyl-β-CD, and ethyl-β-CD were used instead of β-CD, with the K_F values being higher for all of the modified CDs than the natural CD. In **Figure 2A**, we can see the relative fluorescence values for all of the modified CDs tested and β-CD. As is shown, the addition of increasing concentrations of modified CDs leads to greater increases in the relative intensity fluorescence values than when β-CD was used. As can be seen in **Figure 2B**, HP-β-CD showed the highest K_F value followed by ethyl-β-CD, methyl-β-CD, and finally, the natural CDs. As can be seen, the K_F for the complexation of pterostilbene by different modified CDs is dependent upon the length of the aliphatic chain of the β-CD substituent; the greater the number of carbon atoms in the substituent, the higher the K_F value for the resulting complex. Modification of β-CD occurs principally at position 2 of the sugar residues situated on one side of the torus at the edge and orientated inward (*32*), thus increasing the hydrophobicity of the channel. The higher K_F observed for the pterostilbene/modified CD complexes could be due to the hydrophobic interactions with one side of the CD molecule (that bearing the methyl, ethyl, or hydroxypropyl groups). Moreover, the dramatic changes occurring in the hydrophobicity of the CD torus provoked by the substitution of the internal −OH groups would also explain the behavior of K_F. Moreover, our results are in good agreement with others that regard the use of HP-β-CD as the most effective type of CD for complexing other stilbene compounds. For this reason, HP-β-CD was chosen as a host CD for the following sections of the paper.

Effect of the Temperature on the Complexation of Pterostilbene by HP-β-CD. One of the most important physicochemical factors to be take into account when a compound is used as a fortifier or nutraceutical in the food industry is the temperature. For this reason, we have studied in this paper the effect of the temperature in the K_F values of the pterostilbene/HP-β-CD complexes.

Although inclusion complexes usually dissociate when the temperature is increased (*23*, *32*), a previous paper published by our group showed that the K_F values between CDs and different polyunsaturated fatty acids increased with temperature (*31*). For this reason, the next step in our investigation was to study the effect of the temperature on the K_F values for the pterostilbene−HP-β-CD complex interactions at four different temperatures: 15, 25, 30, and 37 °C. To prevent the results from being affected by changes in the buffer pH with temperature, the pH of the buffer was adjusted at the indicated temperature. The values of K_F for 15, 25, 30, and 37 °C were $23\,800 \pm 1120$, $17\,520 \pm 981$, $14\,300 \pm 720$, and $872 \pm 32\ M^{-1}$ (**Figure 3**), respectively. These results might be interpreted as a lower degree of interaction at higher temperatures possibly because of the fact that hydrogen bonds are usually weakened by heating. Our results are in good agreement with those reported in recent years concerning the complexation of another type of stilbene, *trans*-resveratrol, with different types of CDs (*27*, *28*).

Thermodynamic Parameters for the Pterostilbene−HP-β-CD Complexes. The thermodynamic parameters of the complexation

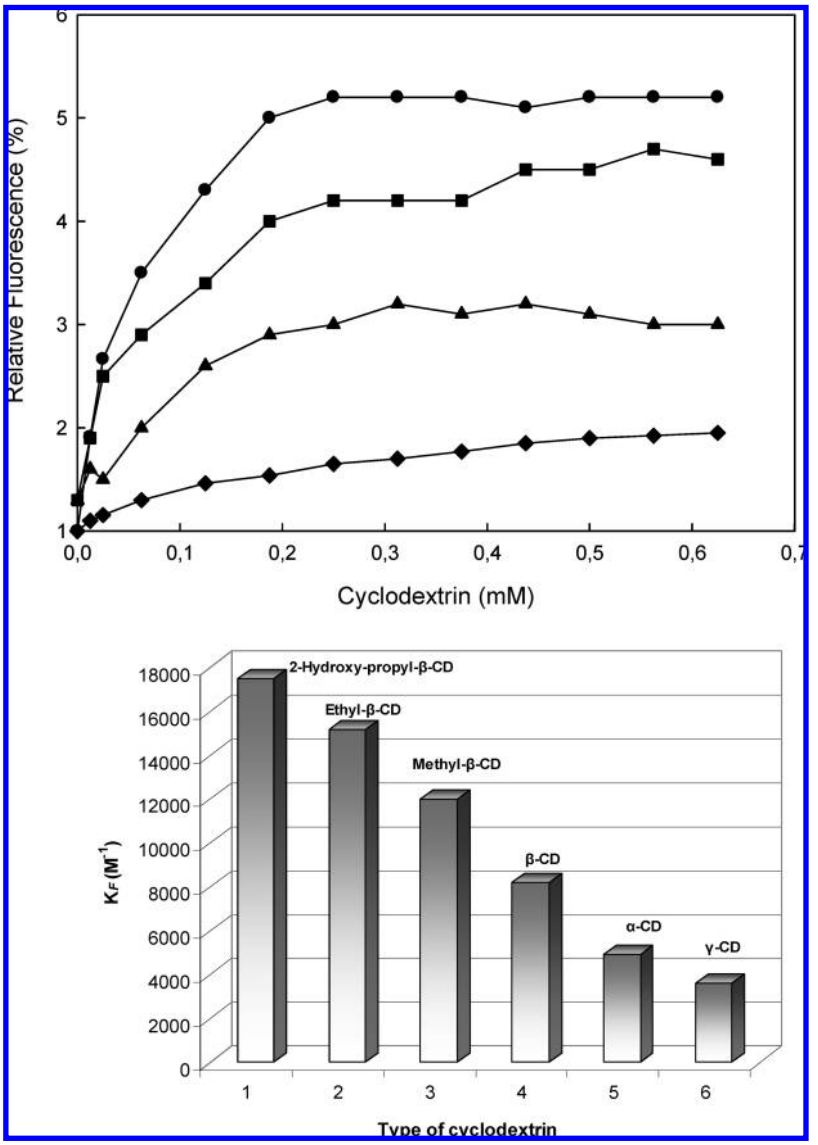


Figure 2. (A) Dependence of emission fluorescence intensities of pterostilbene (30 μM) on modified β-CD concentrations. (B) Effect of the structure of modified and natural CDs on the complexation constant (K_F) of pterostilbene−CD complexes at 25 °C in 0.1 M sodium phosphate buffer at pH 7.0.

of pterostilbene by HP-β-CD ($\Delta H°$, $\Delta S°$, and $\Delta G°$ at 25 °C) were obtained from a van't Hoff plot (eq 1) to gain information about mechanistic aspects of pterostilbene affinity for this type of CD. The ln K_F versus $1/T$ plot was obtained for HP-β-CD complexes, and the van't Hoff plot was linear, with a correlation coefficient higher than 0.99 (inset of **Figure 3**).

The exothermic nature of the interaction processes of pterostilbene with HP-β-CD is demonstrated by the negative values obtained for enthalpy changes. The enthalpy change is -29.20 kJ mol^{-1}, which is typical of hydrophobic interactions, because of the displacement of water molecules from the cavity of HP-β-CD, increased van der Waals interactions between the molecules, and the formation of hydrogen bonds and other interactions (*33*). The changes of entropy are also negative in these processes (-17.64 J mol^{-1} K^{-1}). The fact that complexation decreases the translational and rotational degrees of freedom of the complexed pterostilbene compared to the free ones, leading to a more ordered system, may justify this negative entropy value. Finally, our data show that the inclusion process is spontaneous because of the negative value obtained for the Gibbs free energy change (eq 2) for the interactions that take place during the inclusion process at 25 °C (-23.94 kJ mol^{-1}).

Effect of pH on the Complexation of Pterostilbene by HP-β-CD. Another important factor to be considered when a CD complex is used in the food industry is its behavior at different protonation states. To evaluate the effect of the pH medium on pterostilbene−HP-β-CD complexation, the K_F values for this type of complex were determined in the pH range of 5.5−10.0. **Figure 4** shows the significant dependence of K_F upon pH, passing from a stable value of around 17 520 ± 981 M^{-1} (when the medium pH is between 5.5 and 7.5) to about 10 050 ± 740 M^{-1} (when the medium pH is between 7.5 and 10.0), as happens during the titration of a weak ionizable group. This behavior is similar to that reported by our group for the effect of pH on the K_F values of resveratrol−HP-β-CD complexes and other substances, such as *trans*-resveratrol or polyunsaturated fatty acids (*28*, *32*). As shown in **Figure 4**, the strong decrease in the K_F value coincides with the region where the stilbenoids begin the deprotonation of their hydroxyl groups. A possible cause for this dependence of K_F on pH is the hypothetical formation of a hydrogen bond between the hydroxyl group of the pterostilbene and the hydrophilic groups of CD at pH values below the pK_a value, because hydrogen bonding is one of the most important types of interaction in the stabilization of inclusion complexes

(*22*, *23*). The fact that the complexes between HP-β-CD and the protonated form of pterostilbene were more stable than the interaction with the deprotonated forms of this lipophilic antioxidant is of great interest for the food industry, because the protonated form of pterostilbene presents several beneficial biological effects on human health, as indicated above.

Effect of the Structure of Different Stilbenes on the Complexation Constants of the Pterostilbene/HP-β-CD Complexes. Finally, to obtain information on the mechanism involved in the complexation of different compounds of the stilbenoid family by HP-β-CD, both the K_F values and the stoichiometry for the complexation of three molecules (differing in the number of the hydroxyl groups and in the type of substituents of the aromatic ring) were determined. In **Scheme 1**, the three types of stilbenoids studied (pterostilbene, *trans*-resveratrol, and *trans*-stilbene) are presented.

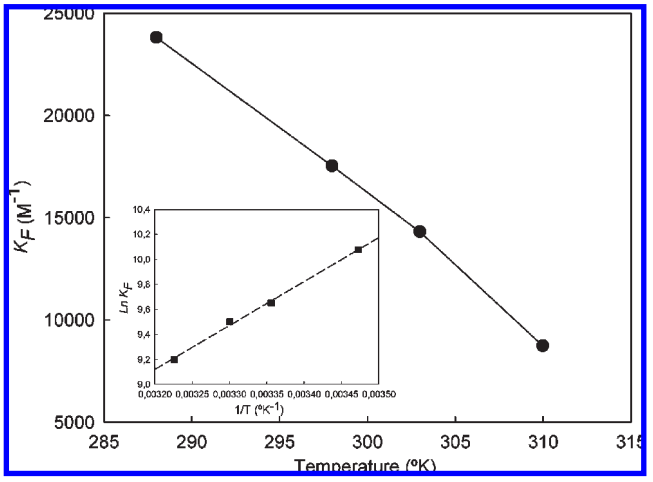


Figure 3. Effect of the temperature on the complexation constant (K_F) of pterostilbene−HP-β-CD complexes at pH 7.0. (Inset) van't Hoff plot (ln K_F versus 1/*T*) for pterostilbene−HP-β-CD complexes in 0.1 M sodium phosphate buffer at pH 7.0.

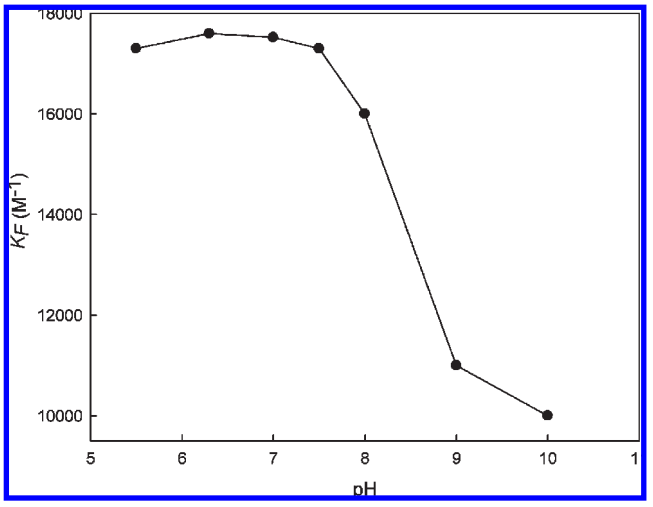


Figure 4. Effect of pH on the complexation constant (K_F) of pterostilbene−HP-β-CD complexes at 25 °C.

As is shown in **Table 1**, the complexes formed between both pterostilbene and *trans*-resveratrol with HP-β-CD presented a 1:1 stoichiometry. Moreover, a comparison of the K_F values (**Table 1**) showed that the interaction was more effective for the *trans*-resveratrol−HP-β-CD complexes than for the pterostilbene−HP-β-CD complexes. Among causes of this behavior may be the hydrophobicity or the resonance structure of the guest molecules. Indeed, *trans*-resveratrol has three hydroxyl groups in its structure, while pterostilbene has only one. Moreover, *trans*-resveratrol does not contain any methyl groups in its structure, while pterostilbene has two methyl groups, which may diminish the efficiency of the complexation by CDs. On the other hand, the resonance structure of *trans*-resveratrol produces a high stability in this type of stilbene, which is not shown by pterostilbene, and may influence its complexation with CDs.

However, the results obtained for the complexation of *trans*-stilbene by HP-β-CD showed important differences with respect to that shown by the pterostilbene and *trans*-resveratrol complexes. In the first place, determination of the stoichiometry of the complexes provided different results from those obtained for the other stilbenoids. When a plot of $1/(F - F_0)$ versus 1/[HP-β-CD] was constructed (filled circles in **Figure 5**), no straight line was obtained (and a linear correlation lower than 0.90), indicating that the presumed stoichiometry of the HP-β-CD/trans-stilbene complex formed was not 1:1 (**Table 1**). However, a plot of $1/(F - F_0)$ against $1/([\text{HP-}\beta\text{-CD}])^2$ (filled squares in **Figure 5**) pointed to a linear relationship (linear correlation higher

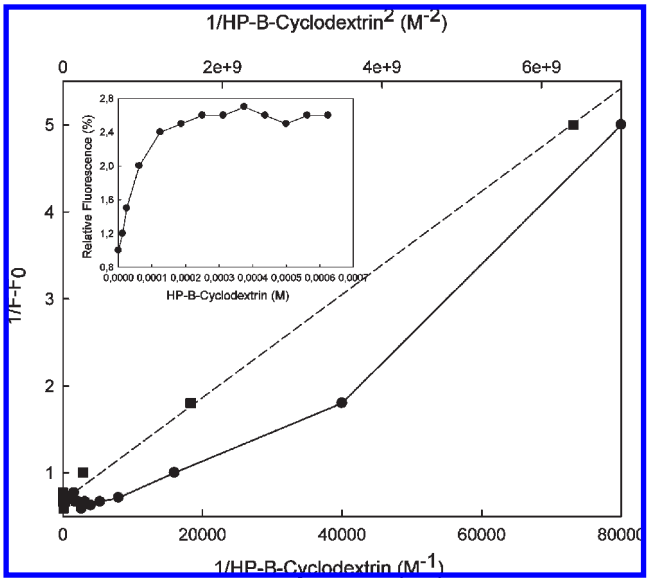


Figure 5. Double-reciprocal plot of *trans*-stilbene complexed to HP-β-CD for determining the stoichiometry of HP-β-CD/*trans*-stilbene complexes: $1/(F - F_0)$ versus 1/[HP-β-CD] (assumption of a 1:1 complex) (●) and $1/(F - F_0)$ versus $1/[\text{HP-}\beta\text{-CD}]^2$ (assumption of a 1:2 complex) (■). (Inset) Dependence of emission fluorescence intensities of *trans*-stilbene (30 μM) on HP-β-CD concentrations.

Table 1. K_F Values and Correlation Coefficients Arising from Eqs 4 and 5 (for 1:1 and 1:2 Stilbenoids−HP-β-CD Complexes, Respectively) at 25 °C at pH 7.0

			correlation coefficient	
complex	K_F (M^{-1})	K_{F12} (M^{-2})	1:1 using eq 4	1:2 using eq 5
trans-resveratrol−HP-β-CD	24880 ± 1020		0.99	0.91
pterostilbene−HP-β-CD	17520 ± 981		0.99	0.86
trans-stilbene−HP-β-CD		$1.01 \times 10^9 \pm 0.67 \times 10^6$	0.88	0.99

than 0.99) (**Table 1**), which indicates that the stoichiometry of the inclusion complex was 1:2.

These results can be explained by the symmetrical structure of *trans*-stilbene. As is shown in **Scheme 1**, this stilbenoid presents a symmetrical structure not present in the other guest molecules studied. This means that one molecule of *trans*-stilbene may be complexed by two molecules of HP-β-CD, each one of which complexed to *trans*-stilbene through one of the sides of its symmetrical structure. Finally, the K_{F12} value determined for the *trans*-stilbene by HP-β-CD is shown in **Table 1**.

CONCLUSIONS

Although the number of works concerning the benefits of pterostilbene for human health have increased in recent years, its use as a functional ingredient (as a fortifier) or as a nutraceutical compound has been limited because of problems associated with its low solubility and bioavailability and the ease with which it is oxidized by pro-oxidant agents. For this reason, we propose its complexation with CDs, a type of molecule that facilitates the "solubilization" of this stilbene and protects it against pro-oxidant agents. Our results show that the K_F values for the pterostilbene−CD complexes are strongly dependent upon several factors, such as temperature, pH, type of CD, and structure of the guest molecule. However, the stoichiometry of the complex is 1:1 for all of the conditions used, except for the *trans*-stilbene−CD complexes, where 1:2 complexes were formed. Potential applications of the resulting pterostilbene−CD complexes can be found in the pharmaceutical and food ingredient industries as nutraceuticals because of their high solubility and stability. Moreover, the use of pterostilbene−CD complexes could slow down the rapid metabolism and elimination of pterostilbene, improving its bioavailability, as demonstrated for other stilbenoid complexes.

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