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Short communication

Solubilization of the neutral and charged forms of 2,4,6-trichlorophenol by hydroxypropyl-β-cyclodextrin, or methyl-β-cyclodextrin in water

Yan He*, Samuel H. Yalkowsky

College of Pharmacy, The University of Arizona, Tucson, AZ 85721, USA

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Abstract

The solubility of 2,4,6-trichlorophenol (TCP) in hydroxypropyl-β-cyclodextrin (HPβCD), or methyl-β-cyclodextrin (MeβCD) at pH 3.0 and 8.8 reported by Hanna et al. [J. Hazard. Mater. B100 (2003) 109] is reevaluated in this paper.

The complexations of the individual dissolved forms were examined. As expected, the neutral TCP complexes more strongly with the cyclodextrins than the charged species. However, in spite of its lower complexation constant, the charged form of TCP forms more complex with each CD, and thus is solubilized to a greater extent.

Keywords: Solubilization; Complexation; 2,4,6-Trichlorophenol (TCP); Hydroxypropyl-β-cyclodextrin (HPβCD); Methyl-β-cyclodextrin (MeβCD)

1. Introduction

Cyclodextrins (CDs) have the tendency to form inclusion complexes by reversibly incorporating a nonpolar compound moiety into their hydrophobic central cavities. They are widely used in environmental sciences, agriculture, biotechnology, and pharmaceutics to increase the water solubility of nonpolar compounds. The complexation with CDs can potentially be used to remove 2,4,6-trichlorophenol (TCP) from contaminated soils, surface waters, or groundwater [1].

The objective of this paper is to reevaluate the TCP solubility data reported by Hanna et al. [1] under both unionized and ionized conditions in the presence of hydroxypropyl-β-cyclodextrin (HPβCD), or methyl-β-cyclodextrin (MeβCD).

2. Background

β-cyclodextrin (β-CD) is a cyclic oligomer containing seven α-D-glucose units. β-CD and its derivatives have 6.0–6.5 Å lipophilic cavities that are optimal for incorporating many environmentally or biomedically relevant molecules [3].

When the solution pH is above the pK_a of a weak acid, such as TCP, both unionized and ionized forms will be present. The equilibrium concentrations of the unionized form, [C_u], and the ionized form, [C_i], are described in the Henderson–Hasselbalch equation:

$$[C_i] = [C_u] \cdot (10^{pH-pK_a}) \quad (1)$$

Therefore, the concentration of the ionized compound is determined by the concentration and pK_a of the unionized compound, and the solution pH.

The total aqueous solubility is the sum of the concentrations of the ionized and unionized forms:

$$[C_{tot}] = [C_u] + [C_i]$$
$$[C_{tot}] = [C_u] \cdot (1 + 10^{pH-pK_a}) \quad (2)$$

According to Wightman and Fein [2], TCP is a weak acid with a pK_a of 6.1. Its solubility is constant at 0.3 mg/ml in solutions with pH below 5, and it increases 10-fold for each pH unit increment when the pH is above the pK_a.

As reported by Hanna et al. [1], both neutral and ionized TCP form 1:1 complex with β-CD, HPβCD, and MeβCD. However, the low solubility of unsubstituted β-CD precluded its use as a solubilizing agent.

* Corresponding author. Tel.: +1-520-626-2014; fax: +1-520-626-4063.

E-mail address: he@pharmacy.arizona.edu (Y. He).

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The formation of a [CD–TCP] complex depends on the complexation equilibrium constant K, the CD concentration, and the amount of the free compound in the solution:

$$[\text{CD–TCP}] = K \cdot [\text{CD}] \cdot [\text{TCP}] \quad (3)$$

For a neutral compound,

$$[\text{TCP}_\text{u}^\text{tot}] = [\text{TCP}_\text{u}] + [\text{CD–TCP}_\text{u}] \quad (4)$$

If a weak electrolyte dissociates, both the dissolved neutral form and the charged form can complex with a CD. As for the charged compound,

$$[\text{TCP}_\text{i}^\text{tot}] = [\text{TCP}_\text{i}] + [\text{CD–TCP}_\text{i}] \quad (5)$$

The total solubility is the sum of the four species [4–7]:

$$[\text{TCP}^\text{tot}] = [\text{TCP}_\text{u}] + [\text{TCP}_\text{i}] + [\text{CD–TCP}_\text{u}] + [\text{CD–TCP}_\text{i}] \quad (6)$$

Since the concentration of the ionized compound is determined by the Henderson–Hasselbalch equation, both unionized and ionized complex concentrations can be calculated from the complexation equilibrium constants.

3. Data

Wightman and Fein [2] reported the water solubility of TCP as a function of pH, and Hanna et al. [1] reported the apparent complexation equilibrium constants, K_app, for TCP in β-CD, HPβCD, MeβCD solutions at pH 3.0 and 8.8. The TCP solubility, $[\text{TCP}_\text{tot}]$, was calculated from their data by:

$$[\text{TCP}^\text{tot}] = [\text{TCP}^\text{free}] + K_\text{app} \cdot [\text{CD}] \cdot [\text{TCP}^\text{free}] \quad (7)$$

Upon comparing this equation to Eq. (6), $[\text{TCP}^\text{free}]$ equals to $[\text{TCP}_\text{u}] + [\text{TCP}_\text{i}]$, and $K_\text{app}\cdot[\text{CD}]\cdot[\text{TCP}^\text{free}]$ equals to $[\text{CD–TCP}_\text{u}] + [\text{CD–TCP}_\text{i}]$.

4. Results and discussion

The aqueous solubilities of TCP at pH 3.0 and 8.8 are 0.3 and 150.7 mg/ml, respectively.

The total TCP solubilities versus HPβCD and MeβCD concentrations reported by Hanna et al. are plotted in Fig. 1. Evidently, it is much more efficient to use CD at pH 8.8 to dissolve TCP than at pH 3.0. The concentrations of TCP in 5% HPβCD or 5% MeβCD at pH 3.0 and 8.8 are listed in Table 1. In 5% MeβCD, the solubility of TCP at pH 8.8 is nearly 100-fold greater than at pH 3. Table 2 shows the concentrations of the individual TCP forms, present in 5% HPβCD or 5% MeβCD at pH 3.0 and 8.8. Note that $[\text{CD–TCP}^\text{tot}]$ at pH 8.8 is the summation of $[\text{CD–TCP}_\text{u}]$ and $[\text{CD–TCP}_\text{i}]$. The total TCP-complexant concentration is 248.6 mg/ml in 5% MeβCD at pH 8.8 and only 4.2 mg/ml in 5% MeβCD at pH 3.0.

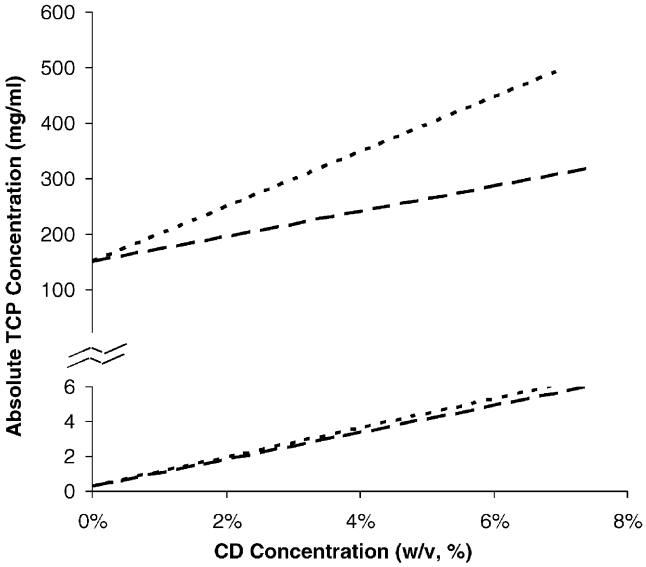

Fig. 1. Absolute solubility of TCP vs. CD concentration in MeβCD (- - -), or HPβCD (— — —) as reported by Hanna et al. The top part is at pH 8.8 and the bottom part is at pH 3.0.

Table 1
Concentration of TCP (mg/ml) in 5% CD

System	pH 3.0	pH 8.8
Water	0.3	150.7
HPβCD	4.1	263.6
MeβCD	4.5	399.2

The formation of complex is dependent on the complexation equilibrium constant, which highly relies on the hydrophobicity of the guest compound. However, it is also dependent on the TCP concentration and the CD concentration. At any given CD concentration, the amount of complex formed is equal to the product of equilibrium constant K and the free compound concentration, [TCP]. The reason that more complex is formed at pH 8.8 is that the concentration of the unbound TCP is 500-fold greater than that at pH 3.0. Since this is much larger than the 17-fold or 9-fold decreases in the equilibrium constants for HPβCD or MeβCD, respectively, the product of K and [TCP] is also larger. In other words: (1) the solute binding constant of the neutral TCP is less than 20× larger than that of the charged form; (2) the solubility of the charged form is 500× larger than

Table 2
Dissolved TCP forms (mg/ml) in 5% CD

Form	pH 3.0	pH 8.8
$[\text{TCP}_\text{u}]$	0.3	0.3
$[\text{HPβCD–TCP}_\text{u}]$	3.8	3.8
$[\text{MeβCD–TCP}_\text{u}]$	4.2	4.2
$[\text{TCP}_\text{i}]$	0	150.4
$[\text{HPβCD–TCP}_\text{i}]$	0	109.2
$[\text{MeβCD–TCP}_\text{i}]$	0	244.4

that of the neutral from; (3) solubilization is proportional to the product of the solute binding constant and the solute concentration; (4) therefore, solubilization of the charged form is over 25× greater than the solubility of the neutral form. This is clearly seen in Fig. 1.

5. Conclusion

The solubility of TCP in HPβCD and MeβCD at pH 3.0 and 8.8 are reevaluated. More TCP dissolves at pH 8.8 and therefore more complex is formed even though the binding constant between the charged TCP and CD is small. The solubility of TCP is greater in HPβCD or MeβCD at pH 8.8 than at pH 3.0. Therefore, CD is more able to remove TCP from contaminated environment when it is charged.

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