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CIRCULAR DICHROISM STUDY ON INCLUSION COMPLEXES OF SOME PROSTAGLANDINS WITH α- AND β-CYCLODEXTRINS

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The interaction of some prostaglandins with α- and β-cyclodextrins in aqueous solution has been investigated by circular dichroism (CD) spectroscopy. The changes of the intrinsic CD of prostaglandins and the induced CD of cyclopentanone following the binding to cyclodextrins were largely dependent upon the geometry of guest and host molecules.

The prostaglandins (PGs) are fatty acids of 20 carbon atoms having a cyclopentanone ring with two adjacent side chains. The β-hydroxyketo moiety of E-type prostaglandins (PGEs) is susceptible to dehydration in acidic and alkaline conditions to form A-type prostaglandins (PGAs), which are isomerized consecutively to form corresponding B-type prostaglandins (PGBs) in alkaline conditions.[1] In the preceding paper,[2] it was shown that some naturally occurring PGs such as prostaglandin E_1, E_2, A_1, A_2, B_1, and B_2 (PGE_1, PGE_2, PGA_1, PGA_2, PGB_1, and PGB_2) formed soluble complexes with cyclodextrins (CyDs) in water, which were relatively stable in neutral pH range. Since circular dichroism (CD) provides useful informations for complexation of CyDs,[3] it is the aim of this paper to show that these PGs actually form inclusion complexes and to gain clear insight into the mechanism and geometry of the inclusion process. The CD and UV spectra were measured by a Jasco J-40 AS recording spectropolarimeter and a Shimadzu 200 type spectrophotometer, respectively. All measurements were carried out in 0.1 M sodium phosphate buffer of pH 6.0 at 25°. The CD spectra were expressed in terms of molar ellipticity, $[\theta]$.

Figure 1 shows the CD spectra of PGs in the presence and absence of CyDs in phosphate buffer. PGEs exhibit a negative CD band around 292 nm due to $n - \pi^*$ transition of C-9 carbonyl chromophore.[4] PGAs show a strong positive peak around 238 nm and

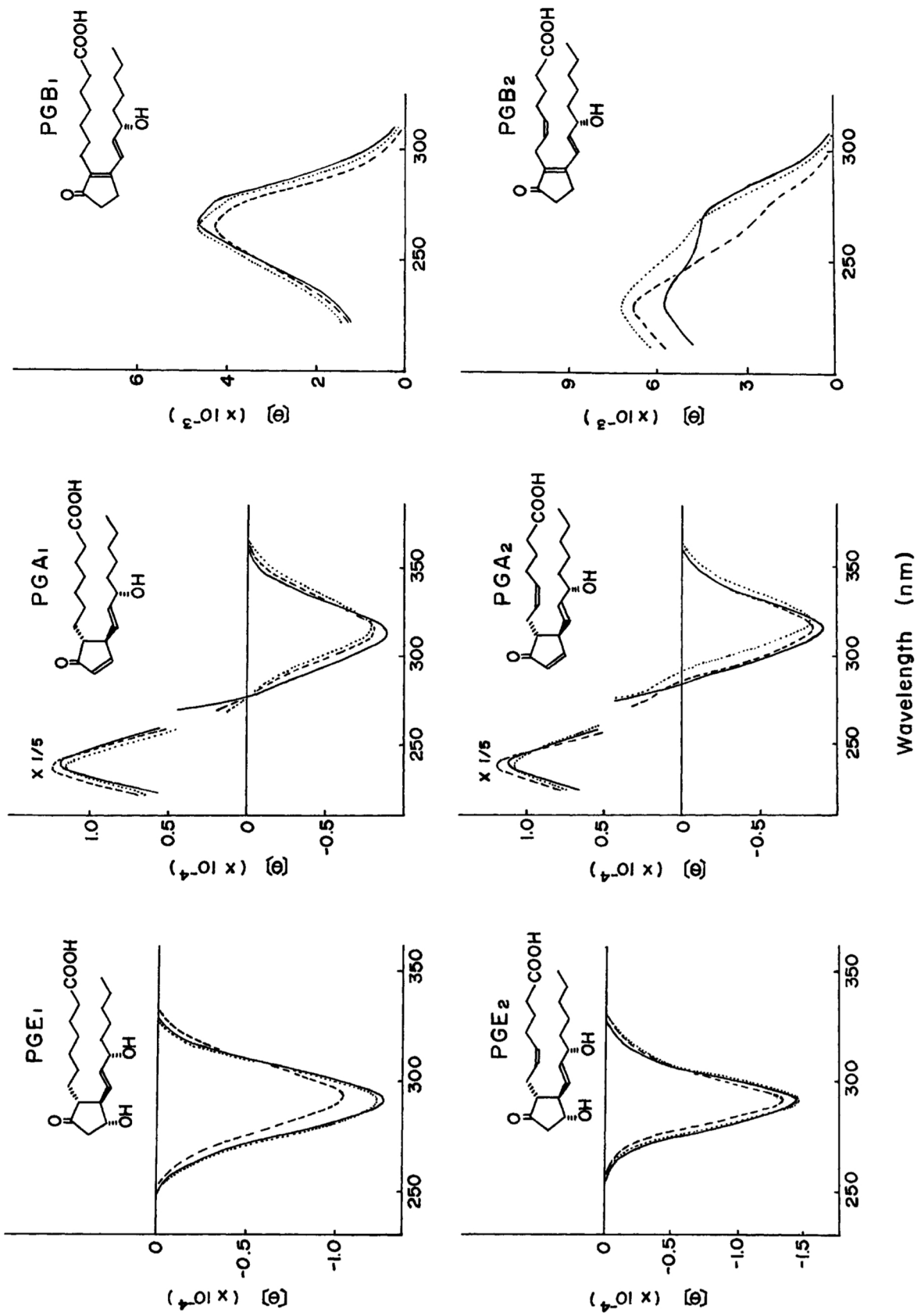

Fig. 1. The CD spectra of prostaglandins in the presence and absence of cyclodextrins (1.0×10^{-2}M) in 0.1 M phosphate buffer of pH 6.0. ——: in the absence of CyD, – – –: in the presence of α-CyD, ·····: in the presence of β-CyD.

a relatively weak negative peak around 314 nm due to $\pi - \pi^*$ and $n - \pi^*$ transition of enone chromophore, respectively.[5] PGBs exhibit weak positive ellipticity bands due to dienone chromophore: PGB_1 shows peak and shoulder at 268 nm and 280 nm, respectively; PGB_2 shows two peaks at 232 nm and 270 nm. By the addition of α-CyD the negative peaks of PGEs and PGAs were shifted to longer wavelength with significant decrease in optical activity, whereas the positive peaks of PGAs and PGBs were shifted to shorter wavelength with increase in optical activity. In all cases the effects of β-CyD on the CD spectra of PGs were small compared to α-CyD. When PGs were dissolved in ethanol-buffer or dioxane-buffer solution, red shift of $\pi - \pi^*$ transition and blue shift of $n - \pi^*$ transition with increasing the solvent polarity were observed. These results apparently suggest that chromophore of PGs were located within hydrophobic cavity of CyDs.

Anticipating a geometry of guest and host molecules, interaction between cyclopentanone and CyDs was investigated. Figure 2 shows the induced CD spectra of cyclopentanone following the binding to CyDs. With α-CyD cyclopentanone showed a negative peak at 286 nm, which located near the UV absorption maximum of carbonyl $n - \pi^*$ transition. In sharp contrast, with β-CyD cyclopentanone showed a weak negative and a weak positive peaks at 265 nm and 290 nm, respectively. The larger induced CD with α-CyD suggests that the smaller cavity gives a more favorable fit for cyclopentanone ring. Similar results were obtained for cyclohexanone-CyDs systems.[6]

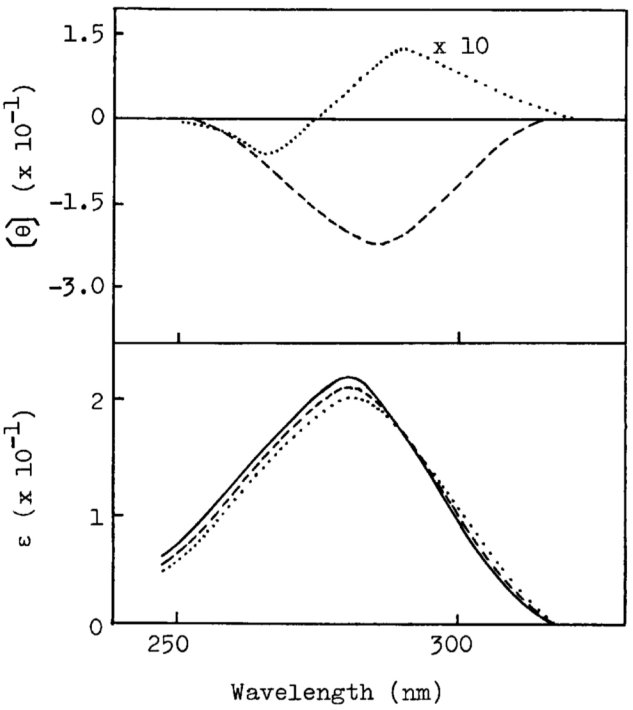

Fig. 2. The induced CD (upper) and UV (lower) spectra of cyclopentanone (1.0 x 10^{-2} M) by the binding to CyDs (1.0 x 10^{-2} M) in phosphate buffer of pH 6.0.

——: in the absence of CyD
----: in the presence of α-CyD
·····: in the presence of β-CyD

Table I. Formation constants (M^{-1})[a] of PGAs - CyDs complexes in 0.1 M phosphate buffer of pH 6.0 at 25°

	Partition coefficient[b]	α-CyD		β-CyD	
		CD	UV	CD	UV
PGA_1	80.8	200	970	180	1200
PGA_2	69.4	160	840	200	1560

a) Accuracy is ± 10 %. b) See ref. 2.

Complex formation constants for PGAs - CyDs assuming 1:1 relationship[2] measured by CD and UV methods[3] are shown in Table I, where importance of the spacial relationship between guest and host molecules is reflected in formation constants. That the values obtained by CD method are smaller than those by UV method may be due to the fact that spectral changes of the intrinsic CD of PGs are compensated by the induced CD of PGs following the binding to CyDs (not only at interior but also at exterior of the cavity),[7] as expected from Fig. 2. No correlations can be obtained between formation constants and partition coefficients of PGs as should be expected for these predominantly hydrophobic interaction.[2] Further study on these problems is in progress and details will be reported elsewhere.

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