

## CD spectra of pharmaceutical substances - Steroids (5)

### 1. Prednisolone

Prednisolone is used orally as an adrenocortical hormone for systemic and topical application.<sup>1)</sup> Prednisolone has a structure in which a double bond is introduced between C-1 and C-2 of hydrocortisone and consequently shows increased anti-inflammatory activity without affecting the salt metabolism.<sup>1)</sup>

Figure 1 shows the CD/UV spectra of prednisolone. In the wavelength region from 400 to 320 nm, UV absorption of the R-band assigned to the  $\Delta^{1,4}$ -diene-3-one (cross-conjugated dienone) chromophore and a negative CD are observed. This sign of the Cotton effect can be predicted by the usual octant rule, although some attention is necessary when P- or  $\pi$ -electrons are present nearby.<sup>2)</sup> The sign of the Cotton effect is negative for the band of  $11\beta$ -hydroxy-substituted  $\Delta^{1,4}$ -diene-3-ketosteroids such as prednisolone.<sup>3)</sup> On the other hand, in the far-ultraviolet region below 280 nm, the K-band of the cross-conjugated dienone is observed in the UV spectrum. The three corresponding absorptions are also observed in the CD spectrum at 250 nm (-), 225 nm (+), and in the region below 210 nm (-). The signs of the Cotton effect are common in  $\Delta^{1,4}$ -diene-3-ketosteroids.<sup>4)</sup>

The UV absorption and positive CD in the wavelength region from 320 to 280 nm, assigned to the R-band of the acetyl group, are similar to those in hydrocortisone.

### 2. Methylprednisolone

Methylprednisolone is used orally as an adrenocortical hormone for systemic application.<sup>1)</sup> The pharmacological effect of this substance is known to be about three times stronger than that of prednisolone for carbohydrate metabolism activity (using the deposition of glycogen in rat livers as an indicator) and approximately 1.5 to 2 times stronger for anti-inflammatory activity.<sup>1)</sup>

The CD/UV spectra of methylprednisolone shown in Figure 2 are similar to those of prednisolone, except for the increased intensity of the negative CD for the cross-conjugated dienone R-band of the  $6\alpha$ -methyl group at approximately 350 nm.

### 3. Dexamethasone

Dexamethasone is used orally as an adrenocortical hormone for systemic and topical application, and also as a dermatologic agent.<sup>1)</sup> Concerning its pharmacological effect, the anti-inflammatory activity of dexamethasone is known to be remarkably strengthened due to the presence of the  $9\alpha$ -fluorine and its dosage about 1/7 that of prednisolone.<sup>1)</sup>

The UV and CD spectra of dexamethasone shown in Figure 3 are similar to those of prednisolone (Figure 1), except that there are minor observed differences in the Cotton effect for the R- and K-bands of the cross-conjugated dienone. Three differences are observed when compared with prednisolone, which are due to the presence of  $9\alpha$ -fluorine in dexamethasone. First, the negative CD intensity for the R-band decreases. Secondly, a hypsochromic shift of about 13 to 6 nm is observed for the CD absorptions of the K-band. Finally, a new positive CD absorption appears at approximately 263 nm.

### 4. Betamethasone

Betamethasone, like dexamethasone, is also used orally as an adrenocortical hormone for systemic and topical application.<sup>1)</sup>

The CD/UV spectra of betamethasone shown in Figure 4 closely resemble those of dexamethasone (Figure 3).

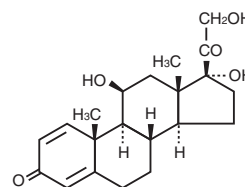
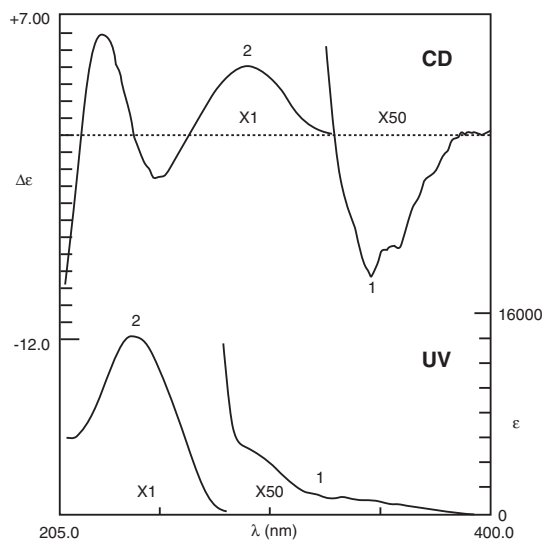
### References

1) The Manual of Japanese Pharmacopoeia, 12th Edition, Hirokawa Shoten (1991)

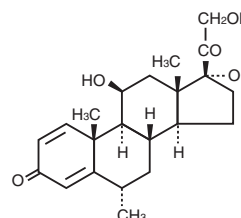
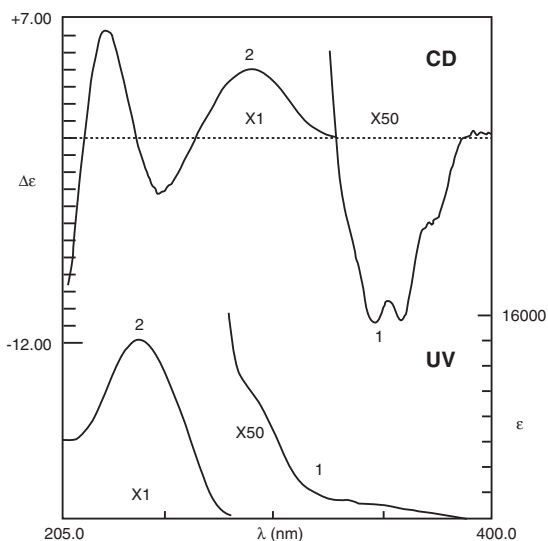
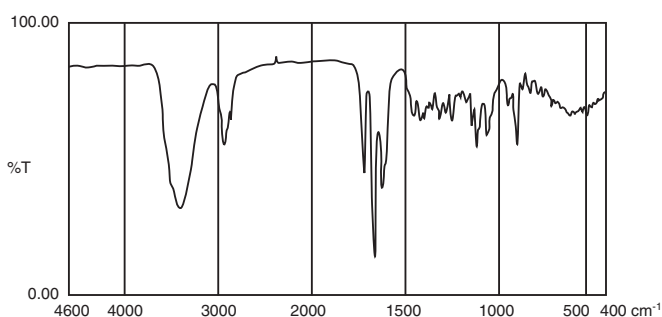
Takashi, Takakuwa, Department of Applied Technology

- 1 ] Sample: SIGMA P6004
- 2 ] Measurement apparatus  
CD: J-720 Circular Dichroism Spectrophotometer  
UV: Ubest V-550 Ultraviolet and Visible Light Spectrophotometer
- 3 ] The structure of prednisolone
- 4 ] IR spectrum (KBr tablet method)
- 5 ] Measurement apparatus: FT/IR-350
- 6 ] Figure 1. The CD/UV and IR spectra of prednisolone
- 7 ] The structure of methylprednisolone
- 8 ] Figure 2. The CD/UV and IR spectra of methylprednisolone
- 9 ] The structure of dexamethasone
- 10 ] Figure 3. The CD/UV and IR spectra of dexamethasone
- 11 ] Sample: Wako Pure Chemical Industries 021-10081
- 12 ] The structure of betamethasone
- 13 ] Figure 4. The CD/UV and IR spectra of betamethasone

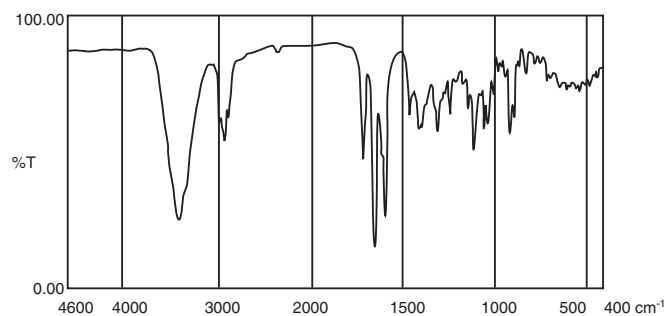
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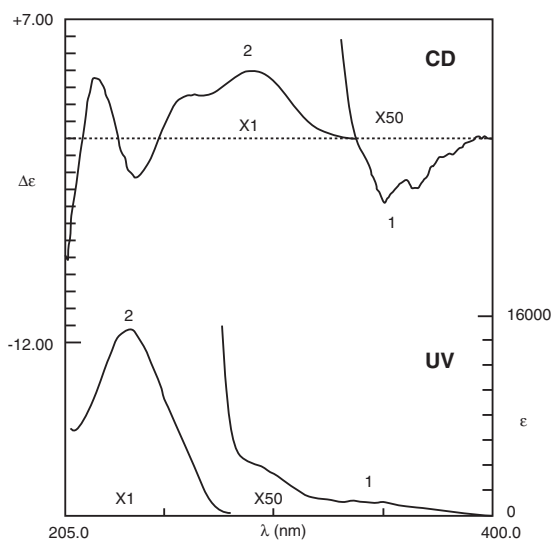
11 $\beta$ , 17, 21-Trihydroxy-14-pregnadiene-3, 20-dione  
(Prednisolone)  
 $C_{21}H_{28}O_5=360.45$



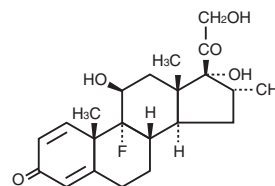
11 $\beta$ , 17, 21-Trihydroxy-6 $\alpha$ -methyl-1, 4-pregnadiene-3, 20dione  
(Methylprednisolone)  
 $C_{23}H_{36}O_5=374.48$



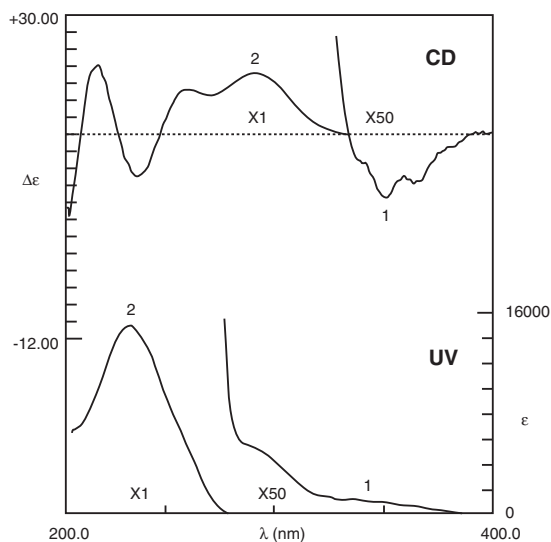
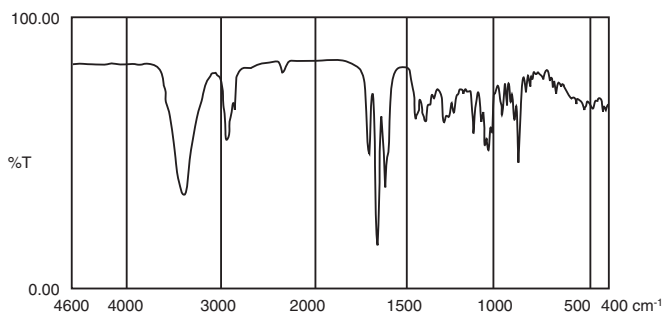
## CD spectra of pharmaceutical substances - Steroids (5)



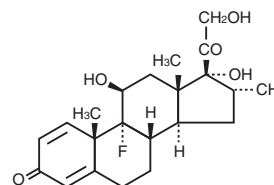
Sample: SIGMA D1756  
Dioxane Solution  
1: 5.1 mg/ 10 ml (1.3 mM), 10 mm Cell  
2: 5.1 mg/ 20 ml (0.64 mM), 1 mm Cell



9-Fluoro-11β, 17, 21-trihydroxy-16α-methyl-1, 4-pregnadiene-3, 20-dione  
(Dexamethasone)  
 $C_{22}H_{29}O_5F=392.47$



Sample:  
Dioxane Solution  
1: 5.0 mg/ 10 ml (1.3 mM), 10 mm Cell  
2: 5.0 mg/ 20 ml (0.64 mM), 1 mm Cell



9-Fluoro-11β, 17, 21-trihydroxy-16β-methyl-1, 4-pregnadiene-3, 20-dione  
(Betamethasone)  
 $C_{22}H_{29}O_5F=392.47$

