

CD spectra of pharmaceutical substances - Steroids (4)

In this and the following two reports, adrenocortical hormones (glucocorticoid) related to the carbohydrate metabolism are examined.

1. Hydrocortisone

Hydrocortisone is one of the typical adrenocortical hormones with carbohydrate metabolism activity and is also important as a mineralocorticoid.¹⁾ Hydrocortisone is used orally for problems such as adrenocortical insufficiency.²⁾

The CD/UV spectra of hydrocortisone shown in Figure 1 closely resemble those of progesterone.³⁾

2. Hydrocortisone acetate

Hydrocortisone acetate, a longer acting drug than hydrocortisone, is used as a water-based suspension for topical application for problems such as rheumatoid arthritis and periarthritis.²⁾

The CD/UV spectra of hydrocortisone acetate shown in Figure 2 closely resemble those of hydrocortisone (Figure 1). The positive CD of the 17 β -acetyl group at approximately 295 nm shows a bathochromic shift of about 5nm in comparison with hydrocortisone. This shift reflects that as the result of the acetylation of the 21-hydroxyl group in hydrocortisone, the intramolecular hydrogen bonding with the 20-ketone group was released.

3. Cortisone

Cortisone is a kind of adrenocortical hormone. It is not described in the Japanese Pharmacopoeia.

Figure 3 shows the CD/UV spectra of cortisone in dioxane and ethanol, nonpolar and polar solvents, respectively. As the result of the ketonization of the 11-hydroxyl group in hydrocortisone (Figure 1), the following changes are observed in the CD/UV spectra of cortisone in dioxane:

UV: An increase in intensity for the saturated carbonyl R-band at approximately 290 nm, due to the overlap of the two absorptions assigned to the 20- and 11- ketones, and a hypsochromic shift of the K-band (230 to 240 nm) assigned to the α , β -unsaturated ketone (enone).

CD: A remarkable decrease in intensity for the negative R-band of enone. (A reversal of the sign to positive is observed in the polar solvent as the result of the phenomenon that the negative component accompanying a vibration structure decreases remarkably, and consequently the positive continuum appears more effectively.)

Disappearance of the shoulder peak is observed in the positive K-band region of the enone in hydrocortisone.

The approximate two-fold increase of the peak maximum at approximately 222 nm.

The spectral behaviors observed above indicate non-bonded interaction between the two chromophoric groups, the Δ^4 -en-3-one and 11-ketone.⁴⁾

On the other hand, the chirality of the enone itself is the same as that of Δ^4 -en-3-one-type steroids.^{3,5)} The positive CD for the saturated carbonyl R-band (at approximately 295 nm) can be explained by the comparatively dominant contribution of the 17 β -acetyl group due to the smaller contribution of the 11-ketone.⁴⁾

4. Cortisone acetate

Cortisone acetate is used orally as an adrenocortical hormone for systemic application.³⁾

The CD/UV spectra of cortisone acetate shown in Figure 4 closely resemble those of cortisone (Figure 3). Concerning the positive CD at approximately 295 nm assigned to the 17 β -acetyl group, the effect of the acetylation of the 21-hydroxyl group is similar to the effect observed in hydrocortisone acetate (Figure 2), except for a little higher intensity in cortisone acetate.

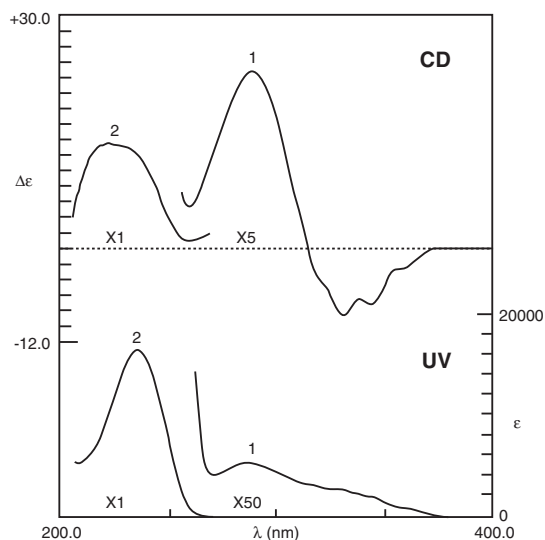
References

- 1) Imabori, K., Yamakawa, T. Ed.: The Dictionary of Biochemistry, Tokyo Kagaku Dojin, 1st Edition, 1984.
- 2) The Manual of Japanese Pharmacopoeia, 12th Edition, Hirokawa Shoten, 1991.

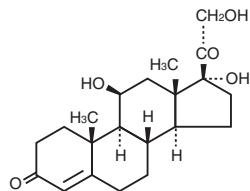
Takashi, Takakuwa, Department of Applied Technology

- 1] Sample: SIGMA H4001
- 2] Measurement apparatus
CD: J-720 Circular Dichroism Spectrophotometer
UV: Ubest V-550 Ultraviolet and Visible Light Spectrophotometer
- 3] The structure of hydrocortisone
- 4] IR spectrum (KBr tablet method)
- 5] Measurement apparatus: FT/IR-300
- 6] Figure 1. The CD/UV and IR spectra of hydrocortisone
- 7] Sample: Tokyo Kasei Kogyo TCI-GR H184
- 8] The structure of hydrocortisone acetate
- 9] Figure 2. The CD/UV and IR spectra of hydrocortisone acetate
- 10] The structure of cortisone
- 11] Figure 3. The CD/UV and IR spectra of cortisone
- 12] The structure of cortisone acetate
- 13] Figure 4. The CD/UV and IR spectra of cortisone acetate

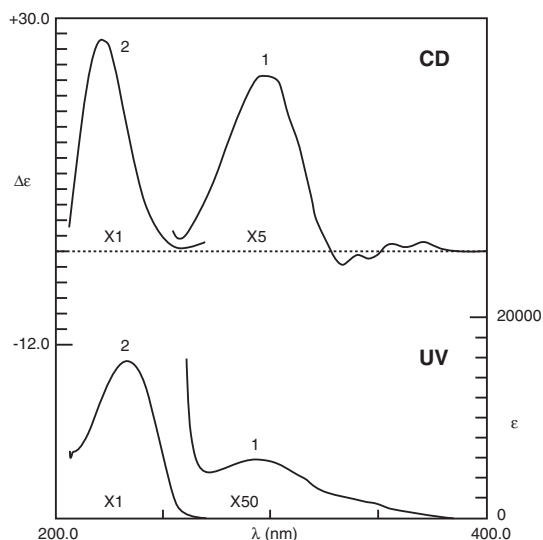
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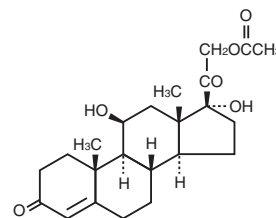
Dioxane Solution (CD/UV)
 1: 5.0 mg/10 ml (1.38 mM), 10 mm Cell
 2: 5.0 mg/20 ml (0.69 mM), 1 mm Cell



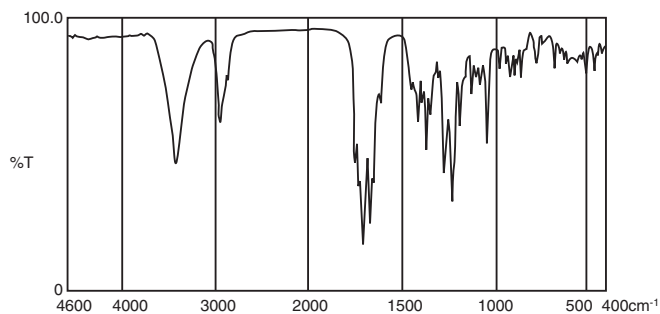
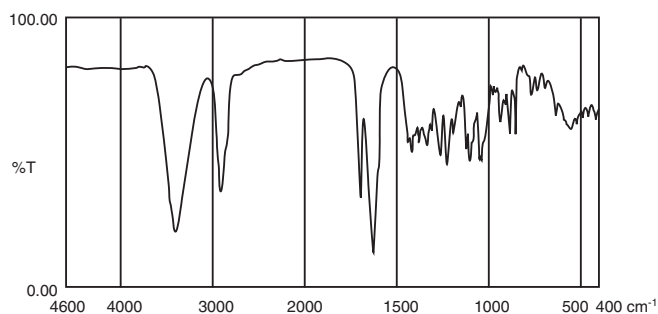
11β, 17α, 21-Trihydroxypregn-4en-3, 20-dione
 (Hydrocortisone)
 $C_{21}H_{30}O_5=362.47$



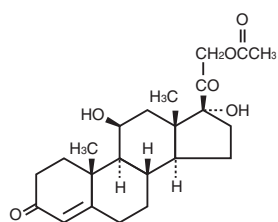
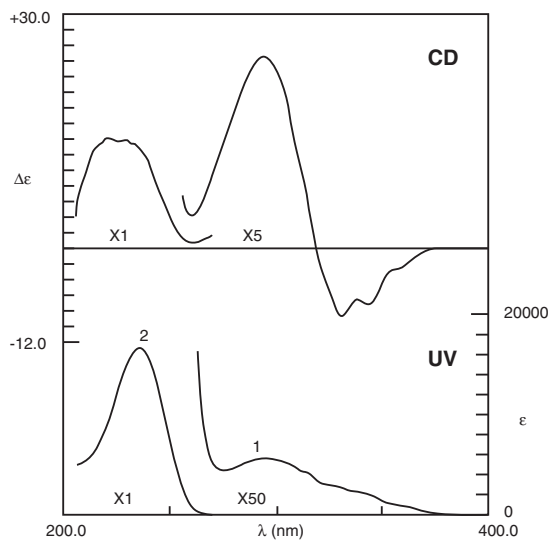
Sample: Tokyo kasei TCI-GR C389
 Dioxane Solution (CD/DV)
 1: 5.0 mg /10 ml (1.2 mM), 10 mm Cell
 2: 5.0 mg /20 ml (0.62 mM), 1 mm Cell



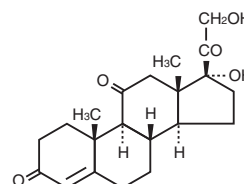
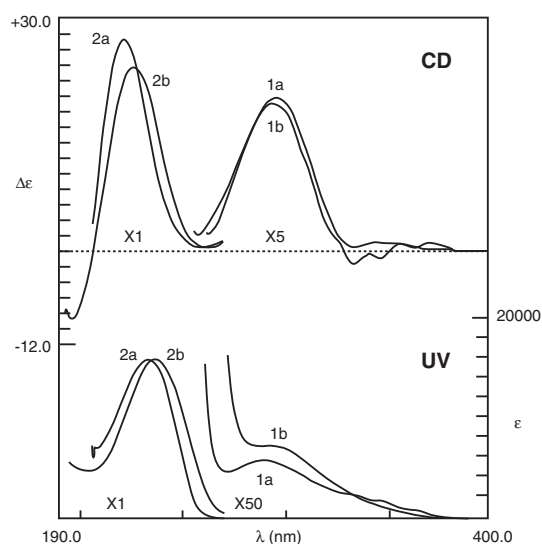
17α, 21-Dihydroxypregn-4en-3, 11, 20-trione21-acetate (Cortisone acetate)
 $C_{23}H_{36}O_6=402.49$



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11 β , 17 α , 21-Trihydroxypregn-4-en-3, 20-dione 21-acetate (Hydrocortisone acetate)
C₂₃H₃₂O₆=404.50



17 α , 21-Dihydroxypregn-4-en-3, 11, 20-trione (Cortisone)
C₂₁H₂₈O₅=360.45

