

CD spectra of pharmaceutical substances - Steroids (6)

1. Triamcinolone

Triamcinolone has a strong effect as an adrenocortical hormone for systemic application, with a minor side effect of potassium depletion. Therefore it is often used to treat extensive symptoms.¹⁾

Figure 1 shows the CD/UV spectra of triamcinolone. Triamcinolone is a derivative of dexamethasone,²⁾ in which the 16 α -methyl group is replaced by the -OH group, therefore both substances have similar CD/UV spectra. Some contamination in the IR spectrum can be expected from the sample used in this experiment when compared with a standard sample.

2. Fluocinolone acetonide

Fluocinolone acetonide, a compound with a steroid structure in which fluorine is introduced at C-6 α and C-9 α , has extremely strong anti-inflammatory properties and is used as a dermatological agent.¹⁾

Figure 2 shows the CD/UV spectra of fluocinolone acetonide. The CD behavior of the cross-conjugated dienone chromophore ($\Delta^{1,4}$ -diene-3-one) in fluocinolone acetonide, a derivative of triamcinolone in which C-6 α is fluorinated (Figure 1), can be interpreted in comparison with triamcinolone: the sign of the R-band ($M-\pi^*$, 400 to 330 nm) reverses to positive and the intensity of the K-band ($\pi-\pi^*$, 280 to 200 nm) decreases. These phenomena can be explained by the interaction between the P-electrons in the 6 α -fluorine and the double bond at C-4 and C-5 in the cross-conjugated dienone.³⁾ On the other hand, both the UV and positive CD spectra for the R-band (320 to 280 nm) of the carbonyl chromophore at C-20 show a bathochromic effect in comparison with triamcinolone. This is due to release from hydrogen bonding as the result of the replacement of the 17 α -OH group.

3. Beclomethasone

Beclomethasone is not described in the Japanese Pharmacopoeia. Its esterified derivative beclomethasone dipropionate (C-17 α and C-21) has a stronger effect and is used to treat dermatitis and as an inhalant.¹⁾

Figure 3 shows the CD/UV spectra of beclomethasone. Beclomethasone is the chloro-substitution product of betamethasone, in which the 9-fluorine is replaced by chlorine. No remarkable change is observed for negative CD absorption for the dienone R-band (400 to 320 nm). On the other hand, a remarkable increase in intensity is observed for the positive CD in the K-band (280 to 200 nm) at approximately 258nm, while the positive CD absorption observed in betamethasone at approximately 220 nm disappears.

4. Santonin

Santonin is used orally to eliminate ascaris.¹⁾ It belongs to the sesquiterpene family but it is discussed here because it contains the same cross-conjugated dienone chromophore in its structure.

Figure 4 shows the CD/UV spectra of santonin. The absorptions in the spectra are all based on the cross-conjugated dienone chromophore, and the presence of γ -lactone is not detected at approximately 220 nm. The negative CD based on the cross-conjugated dienone R-band (400 to 300 nm) is also observed as it is commonly observed for the $\Delta^{1,4}$ -diene-3-one-type steroids shown in this series of reports, except for fluocinolone acetonide. On the other hand, in the K-band region (280 to 200 nm), santonin shows a remarkable difference from these steroids: the UV intensity at approximately 235 nm decreases and a new absorption appears as a clear shoulder at approximately 260 nm. Corresponding to this UV component in the longer wavelength region, a negative CD absorption with a higher intensity appears. The above behaviors in CD/UV in the region of the K-band suggest a strong interaction between the cross-conjugated dienone chromophore and γ -lactone.

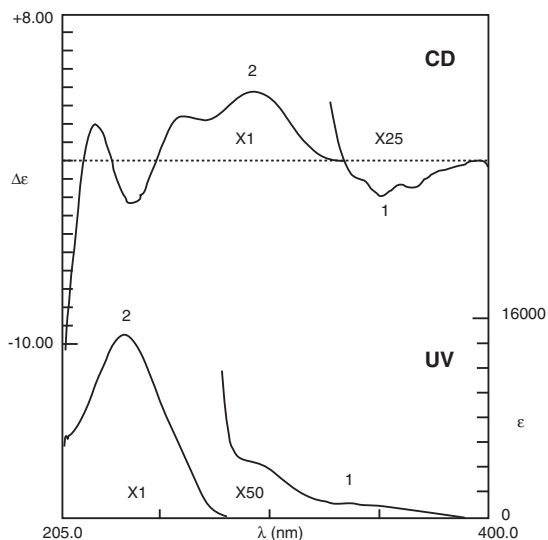
References

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

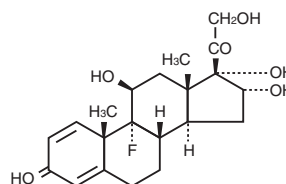
Takashi, Takakuwa, Department of Applied Technology

- 1] Sample: SIGMA T6376
- 2] Measurement apparatus
CD: J-720 Circular Dichroism Spectrophotometer
UV: Ubest V-550 Ultraviolet and Visible Light Spectrophotometer
- 3] The structure of triamcinolone
- 4] IR spectrum (KBr tablet method)
- 5] Measurement apparatus: FT/IR-350
- 6] Figure 1. The CD/UV and IR spectra of triamcinolone
- 7] The structure of fluocinolone acetonide
- 8] Figure 2. The CD/UV and IR spectra of fluocinolone acetonide
- 9] The structure of beclomethasone
- 10] Figure 3. The CD/UV and IR spectra of beclomethasone
- 11] Sample: Aldrich 22308-5
- 12] The structure of santonin
- 13] Figure 4. The CD/UV and IR spectra of santonin

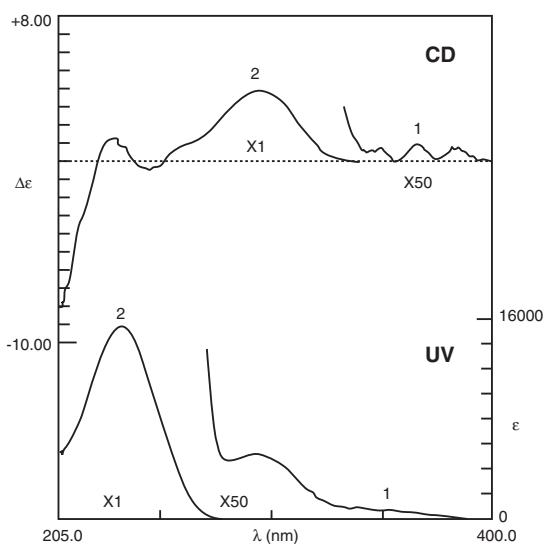
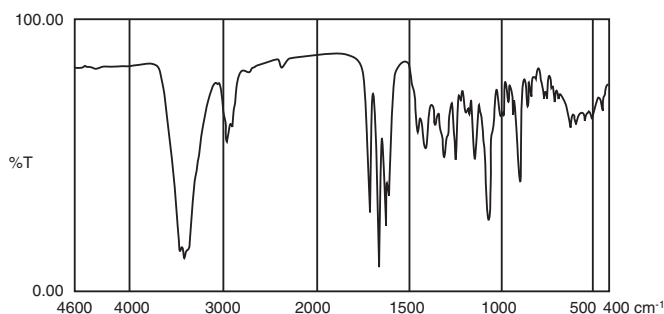
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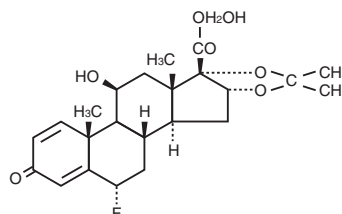
Sample: SIGMA T6376
 Dioxane Solution
 1: 5.0 mg/10 ml (1.3 mM), 10 mm Cell
 2: 5.0 mg/20 ml (0.63 mM), 1 mm Cell



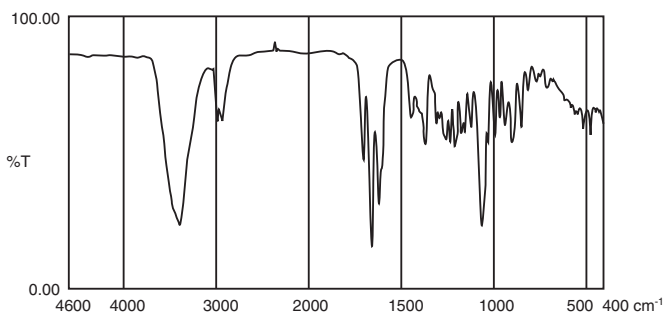
9-Fluoro-11b, 16a, 17, 21-tetrahydroxy-1, 4-pregnadiene-3, 20-dione (Triamcinolone)
 $C_{21}H_{27}O_6F=394.44$



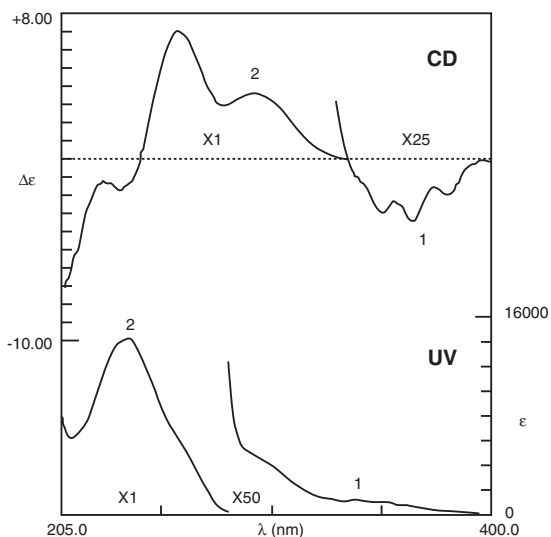
Sample: SIGMA F8880
 Dioxane Solution
 1: 5.0 mg/10 ml (1.1 mM), 10 mm Cell
 2: 5.0 mg/20 ml (0.55 mM), 1 mm Cell



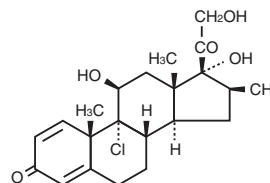
6a, 9-Difluoro-11b, 21-dihydroxy-16a, 17-isopropylidenedioxy-1, 4-pregnadiene-3,20-dione (Fluocinonone Acetonide)
 $C_{24}H_{30}O_6F_2=452.50$



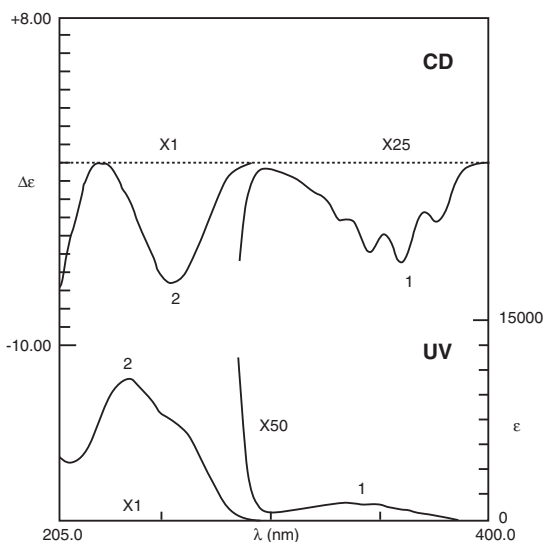
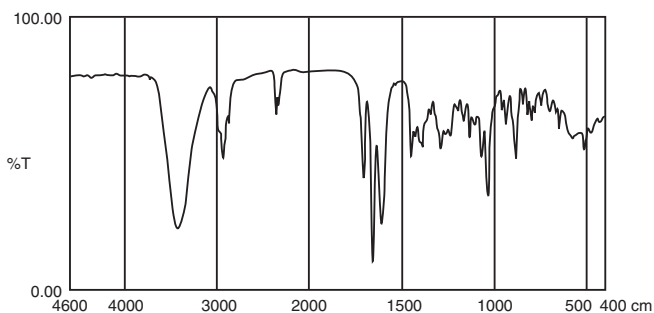
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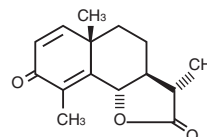
Sample: SIGMA B0385
Dioxane Solution
1: 5.0 mg/10 ml (1.2 mM), 10 mm Cell
2: 5.0 mg/20 ml (0.61 mM), 1 mm Cell



9-Chloro-11 β , 17, 32-trihydroxy-16 β methyl-1, 4-pregnadiene-3,20-dione (Beclomethasone)
C₂₂H₂₅O₅Cl=408.92



Sample: Aldrich 22308-5
Dioxane Solution
1: 3.5 mg/10 ml (1.4 mM), 10 mm Cell
2: 3.5 mg/20 ml (0.7mM), 1mm Cell



1, 2, 3, 4, 7-Hexahydro-1-hydroxy- α , 4a,8-trimethyl-7-oxo-2-naphthaleneacetic acid γ -lactone (α -Santonin)
C₁₅H₁₈O₂=246.31

