CD spectra of pharmaceutical substances - Steroids (7)

1. Cholic acid

Cholic acid, one component of bile acid,[1] is a homologue of ursodeoxycholic acid described below, as both are OH-substitutes of 5β-cholanic acid. Cholic acid is not described in the Japanese Pharmacopoeia

Figure 1 shows the CD/ORD/UV spectra of cholic acid. UV absorption from 250 to 200nm is assigned to the carboxyl group and the corresponding negative CD reflects the effect of the adjacent asymmetric field of the steroid ring to the carboxyl group side chain. On the other hand, the broad ORD background curve reflects the 5β-cholanic acid structure and hydroxyl substitution.

2. Ursodeoxycholic acid

Ursodeoxycholic acid, known as the chief ingredient of "bear' s gall",[1] a Chinese medicine, is described as a cholagogue in the Japanese Pharmacopoeia.[2] Figure 2 shows the CD/ORD/UV spectra of ursodeoxycholic acid. The CD/UV spectra assigned to the carboxyl group closely resemble those of cholic acid (Figure 1). On the other hand, the intensity increase in ORD sharply reflects the difference in the substitution state of the hydroxyl group.

3. Dehydrocholic acid

Dehydrocholic acid is a strong cholagogue and synthesized by the oxidation of cholic acid.[2]

Figure 3 shows the CD/ORD/UV spectra of dehydrocholic acid. The UV absorption in the wavelength region from 350 to 250nm is assigned to the n-π* transition (R-band) of the ketone group, where the hypsochromic effect (blue shift) is observed with the increasing polarity of the solvent. The corresponding negative Cotton effect can be explained by the result of the additive property among the 3-keto(-), 7-keto(-) and 12-keto(+), after applying the octant rule to the 5β-series-ketosteroid. On the other hand, in the region of wavelengths of less than 250nm, the absorption, located at less than 200nm and assigned to the far-ultraviolet transitions (such as n-σ*) of the carbonyl group, shows the bathochromic effect (red shift)[3] in the polar solvent, and consequently the UV absorption and CD of the carboxyl group is concealed and is not observed. In the nonpolar solvent, however, the UV absorption and negative CD for the carboxyl group are clearly observed.

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 and Chihiro, Jin, Department of Applied Technology

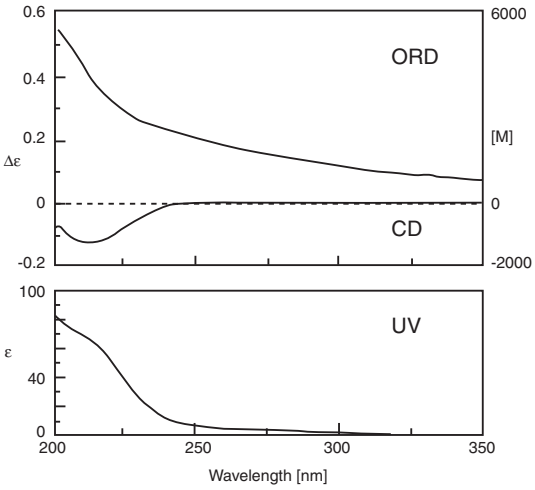
1] Wavelength (nm)
2] Sample: Fluka 27010
Ethanol solution: 5.0 mg / 5 ml (2.4 mM), 10mm Cell
3] Measurement apparatus
CD: J-720W Circular Dichroism Spectrophotometer
UV: Ubest V-560 Ultraviolet and Visible Light Spectrophotometer
4] The structure of cholic acid
5] IR spectrum (KBr tablet method)
6] Measurement apparatus: FT/IR-350
7] Figure 1. The CD/ORD/UV and IR spectra of cholic acid

Sample: Fluka 94465
Ethanol solution: 5.0 mg / 5 ml (2.5 mM), 10 mm Cell

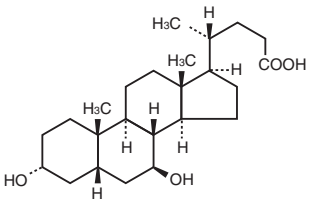
8] The structure of ursodeoxycholic acid
9] Figure 2. The CD/ORD/UV and IR spectra of ursodeoxycholic acid
10] Sample: SIGMA D-3750
1. Dioxane Solution: 5.0 mg / 10 ml (1.2 mM), 10 mm Cell
2. Ethanol Solution: 5.0 mg / 5 ml (2.5 mM), 10 mm Cell
11] The structure of dehydrocholic acid
12] Figure 3. The CD/ORD/UV and IR spectra of dehydrocholic acid

JASCO International Co.,Ltd
4-21, Sennin-cho 2-chome, Hachiouji, Tokyo 193-0835 Japan
Tel: 0426-66-1321 FAX: 0426-65-6512 Web: http://www.jascoint.co.jp Mail: support1@jascoint.co.jp

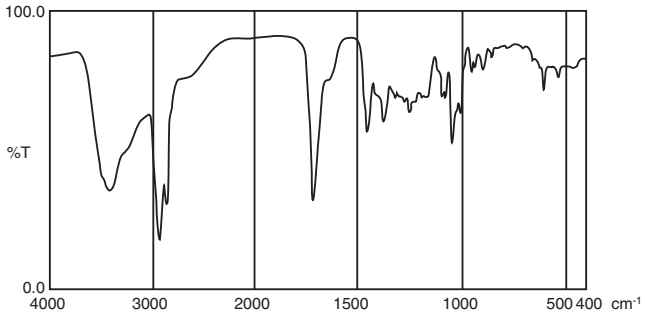
CD spectra of pharmaceutical substances - Steroids (7)



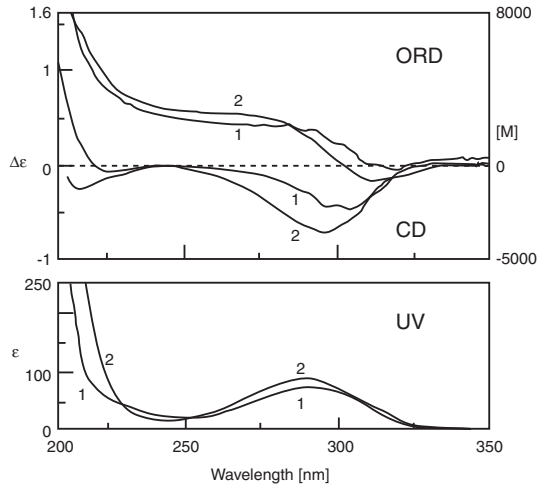
Sample: Fluka 94465
: 5.0 mg/5 ml(2.5 mM), 10 mm Cell

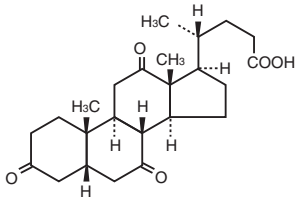


3α, 7β-Dihydroxy-5 β-oholamic acid
(Ursodesoxycholic acid)
$C_{24}H_{40}O_4$=392.58

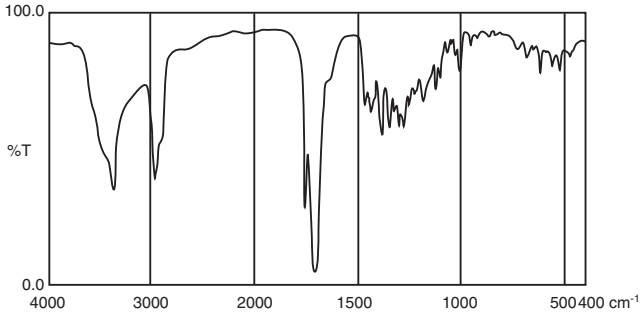


FT/IR-350





3, 7, 12-Trioxo-5 β-cholanic acid
(Dehydrocholic acid)
$C_{24}H_{34}O_5$=402.53



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JASCO International Co.,Ltd
4-21, Sennin-cho 2-chome, Hachiouji, Tokyo 193-0835 Japan
Tel: 0426-66-1321 FAX: 0426-65-6512 Web: http://www.jascoint.co.jp Mail: support1@jascoint.co.jp