



CD IN EUROPEAN PHARMACOPOEIA

This is a good news: at last CD is listed in European Pharmacopoeia¹!

We can see it as a good indication of the growing interest for *chirality* and it'll become a reference for testing procedures in the future.

Unfortunately text is very short, just over one page. It gives an indication on what CD is and how a typical hardware is built (a picture shows the optical layout of the J.Y. CD6).

Testing procedures are very short and limited to:

CD scale calibration

Method suggests a solution of 10.0 mg of iso-Androsterone R in 10.0 ml Dioxane R.

Spectra should be collected from 360 to 280 nm and $\Delta\epsilon$ at the maximum at 304 nm should be of + 3.3.

$$\Delta\epsilon = \epsilon_L - \epsilon_R = \Delta A / (c \cdot l)$$

where *c* is concentration in mole/liter

l = path of the cell in cm

As an alternative a solution of (1S)-(+)-10-Camphorsulfonic acid can be used, see below.

Modulation linearity

Method suggests a solution of 10.0 mg of (1S)-(+)-10-Camphorsulfonic acid in 10.0 ml of water R.

Collecting spectra from 340 to 185 nm a positive band should be detected at 290.5 nm (with $\Delta\epsilon$ of $2.2 \div 2.5$ and a negative band should be detected at 192.5 with $\Delta\epsilon$ of $-4.3 \div -5$).

As an alternative (1S)-(+) or (1R)-(-)-Ammonium-10-Camphorsulfonate is accepted.

Comments:

1. it's good to see that test of modulator linearity is included, wavelength range of CSA or ACS solution is very proper for protein analysis in the low UV
2. CSA widely replaced Androsterone² for CD scale calibration since solvent is water
3. As a matter of fact ACS solution is now widely accepted as the best choice also for scale correction since less hygroscopic³
4. There is no attempt to extend the check of calibration in the visible part of the spectra (with Co complex for example)
5. No reference is given on enantiomeric purity of the compounds used, which must be detected by other methods (with a polarimeter validated with certified sucrose solutions)
6. There is no reference on how to check other important parameters such as wavelength accuracy, stray-light, resolution, stability, sensitivity etc, while it's true that a CD spectrometer is basically a UV-VIS spectrophotometer and related testing procedures can be applied, this is not written and furthermore not so direct

Since the forecasted impact of the European Pharmacopoeia is relevant, at least at industrial level, a more ample treatment of these matters is very necessary, otherwise incomplete procedures will not fill the practical needs.

Manufacturers are trying to fill the gap offering *validation software* (a good example is the Jasco JWVAL-486 for the J-800 series). Here too however while tests are more complete (photometric accuracy, baseline flatness, wavelength accuracy, wavelength precision, baseline stability and RMS noise), the overall target seems to be matched only partially: a more systematic approach seems to be necessary.

¹ European Pharmacopoeia (Addendum 2001) 2.2.41

² Schippers P.H., Dekkers H.J.M. *Anal.Chem.* 53 (1981) 778

³ Takakuwa T., Konno T., Meguro H. *Anal.Sciences* 1, 1985, 215