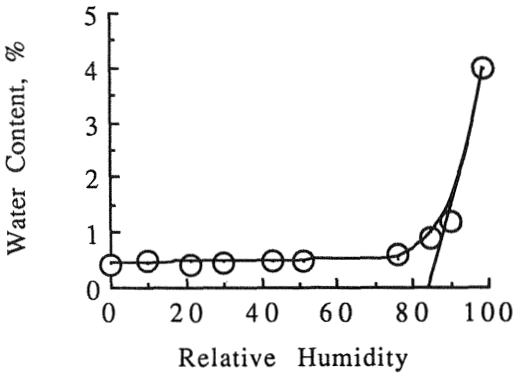


**Fig. 10** Sorption isotherm of anhydrous droloxifene citrate. (Graph constructed from data published by Burger and Lettenbichler, 1993.)

It can be shown that if the air space is sufficiently agitated to prevent vapor pressure gradients, the initial uptake rate (g $H_2O$/g solid per hour) is related to the relative humidity by

$$L = a_{21}[\mathrm{RH} - \mathrm{RH}_0] \tag{9.24}$$

where $\mathrm{RH}_0$ is the vapor pressure of a saturated solution of the drug substance in water. An example of this is shown in Fig. 10.

$X_s$ can be estimated by an ideality assumption; that is, if the solubility is expressed as a mole fraction $X_s$, the vapor pressure over a saturated solution will be $P'$ given by

$$P' = (1 - X_s)P_0 \tag{9.25}$$

where $P_0$ is water's vapor pressure at that temperature.

The experiments above are rather easy to carry out and should always be part of a preformulation program, since hygroscopicity can be so important that it will dictate whether a particular salt should be used. Dalmane, for instance, is a monosulfate, and is used as such since the disulfate, desirable in many other respects, is so hygroscopic that it will remove water from a hard-shell capsule and make it exceedingly brittle.

## 9. COMPATIBILITY TESTS

Prior to attempting the first formulation with a new drug, most research groups carry out compatibility testing (Carstensen et al., 1964). The principle is to make up reasonably ratioed mixtures of drug and excipient, to ascertain which excipients may be reasonably used with the drug. The original method used in the 1960s (Carstensen, 1964) consisted of visual observation of such mixtures, spectrophotometric assay, and TLC. The methods used nowadays have followed in step with analytical developments and are (a) chemical assay, (b) TLC, (c) HPLC, (d) DSC, and (e) microcalorimetric methods. The latter two have been of special interest in recent years and will be treated separately.