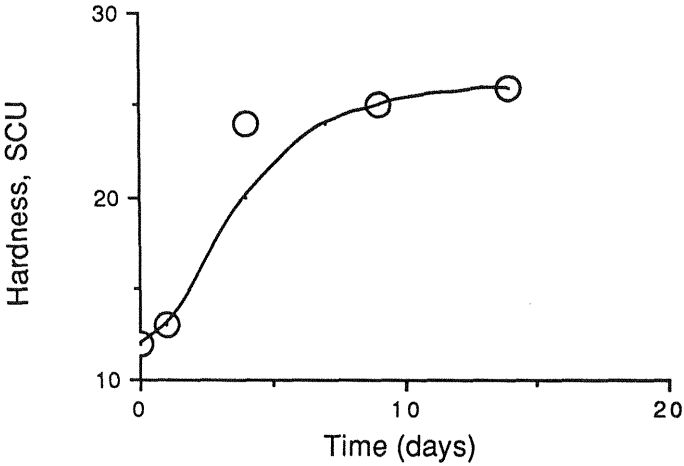

Fig. 20 Hardness as a function of time in pharmaceutical tablets. (Figure constructed from data published by Chowhan, 1979.)

On storage, this expansion can continue (Gucluyildiz et al., 1977), i.e., a tablet may become softer on standing for simple expansion reasons. Expansion is rarely checked as part of a stability program, and the cited article is one of the few published attempts to measure porosity as a function of time.

Frequently tablets will become either softer or harder within short periods of time after manufacture. Figure 20 shows hardness as a function of time for a series of tablets reported by Chowhan (1979).

Aside from the quoted instance of porosity changes and expansion, there are cases where crystallization of a soluble compound has occurred via the sorbed amounts of moisture in the tablet. This happens most often with very soluble compounds, and in such cases it is important to ascertain storage in a dry environment. A test that is now a requirement in the ICH Guidelines is storage in the final container at 40°C, 75% RH. During this test moisture is usually adsorbed by the tablets, and this can then cause softening of the binder bridge because of moisture uptake. At times, redrying will reinstitute the original hardness. Sometimes hardening occurs when the sorbed moisture causes recrystallization of a compound or excipient.

8.2. Softening

Softening can be associated with chemical interaction. Several furoic acids (Carstensen and Kothari, 1983), when tableted with microcrystalline cellulose, will cause a specific interaction leading to the formation of carbon monoxide (rather than decarboxylation of the acid). This interaction is not slow at 55°C, and it causes the tablets to crumble. At room temperature the effect is less pronounced yet significant.

Since a tablet, when produced, is not in equilibrium, there will be a redistribution of moisture. This could make the bonds of a lower or a higher moisture content, and there may for this reason be a change in hardness during a fairly short period of time after manufacture.