8.6.1 Influence of the Transmembrane Flux

The first evidence for polymorph selection promoted by membranes was obtained by Di Profio *et al.* (2007) during glycine crystallization tests.[9] Glycine exhibits three polymorphic forms: α, β and γ.[35] Two additional forms, δ and ε, were obtained under high-pressure conditions.[36]

The relative stability at ambient temperature of the three forms was found to be: $\gamma > \alpha > \beta$.[37]

Figure 8.9 illustrates the selection of glycine polymorphs made by membrane crystallization operated at pH 6.2: experimental results show a preferential crystallization of the γ form for an evaporation rate lower than 1.4×10^{-2} mL h^{-1}, while for an evaporation rate higher than 1.8×10^{-2} mL h^{-1} the kinetic product, α-glycine, is obtained.

Paracetamol (acetaminophen) is a common antipyretic and analgesic drug that can be crystallized in three polymorphic forms: monoclinic form I (space group $P2_1/n$, thermodynamically stable at room temperature), orthorhombic form II (space group *Pcab*, metastable at ambient conditions), and a least stable form III obtained by crystallization from the melt.[38–40]

Since the crystal structure of the commercial monoclinic form shows poor compression properties and requires binding agents for tableting, attention has been focused on the production of the orthorhombic form II,

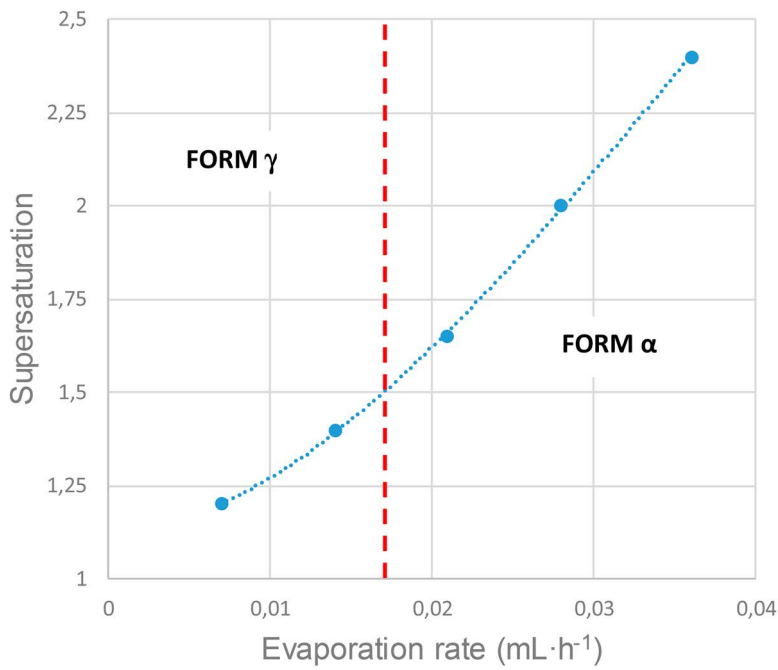

Figure 8.9 Glycine polymorphic selection based on the control of the transmembrane flux in a membrane crystallizer. Reprinted with permission from ref. 9, Copyright 2007 American Chemical Society.