

of temperature and supersaturation ratio.<sup>203</sup> The scraping process at a given frequency would have created local heat due to friction, leading to a small temperature gradient between the scraping and non-scraping parts in the OBC. Consequently, the generation of nuclei of an opposite chirality on scraping would be faster, which competes in the solution with those nuclei from the spontaneous nucleation due to excess supercooling. This could have led to the close to racemic EEs in the OBC as shown in Table 3.7.

The *third summary* is that scraping in the mixed and supersaturated system prevented chiral symmetry from breaking in unseeded crystallisation.

A patent arose from these studies, as the scraping could be utilized as a means to generate primary nucleation when the amount of nuclei could be quantified and controlled. It should be emphasized that the scraping only happens in batch OBRs where the string of baffles moves up and down the column driven by a linear motor. In COBC, baffles are stationary and there is no scraping effect.

### 3.5.4 Encrustation

The increased specific surface areas in COBC are the unique feature for the enhanced heat transfer processes but are also prone to encrustation in crystallisation when operated incorrectly. Some investigations on fouling were undertaken on other devices.<sup>167,204</sup> Numerical simulation of crystallisation fouling on heat exchanger surfaces was also reported, outlining that fouling layers exhibit complicated structures, which essentially affect flow hydrodynamics, fouling kinetics and heat transfer performance.<sup>205</sup> Fouling resistances, defined as the decrease of efficiency due to fouling, were evaluated for brass, copper, aluminium, bronze and stainless steel surfaces; the energy at the interface of fluid and surface was a key factor in surface crystallisation, besides the surface roughness of the materials.<sup>206</sup>

In terms of cooling crystallisation in NiTech DN15 crystallisers, the following are the culprits for fouling encountered for processes involving industrial compounds: (a) local temperature or local supersaturation; (b) incorrect seeding strategy; (c) insufficient mass of nuclei; (d) suboptimal hardware; (e) oil out; (f) intrinsically sticky compounds.

We shall eliminate the category of compounds that are intrinsically sticky, *e.g.* sucrose. When compounds stick on the walls and impellers of stirred tank crystallisers, these would be amplified in DN15 crystallisers due to the larger specific surface area. We should be confident to say that these are NOT the compounds for continuous crystallisation.

Here Are Some Industrial Challenging Project Examples

#### 3.5.4.1 Case 1 – Due to Local Temperature

In a seeded cooling crystallisation of an API from a pharma company, the seed tank was heated to 50 °C and seeds were pumped into a NiTech DN15 Standard crystalliser *via* an 8 mm pipe. It was anticipated that the temperature