- Many different commercial size separation methodologies and apparatus exist – their designs are dependent on the final required particle size and the size of the commercial batch. These methodologies include: sedimentation, sieving elutriation and cyclone methods.
- As with size reduction, the pharmaceutical scientist must understand the parameters for the selection of the best method for the material in question.

Introduction to size reduction

The significance of particle size in drug delivery has been discussed in Chapter 9 and some of the reasons for carrying out a size reduction operation have already been noted. In addition, the function of size reduction (also called *comminution*) may be to aid efficient processing of solid particles by facilitating powder mixing or the production of suspensions. There are also some special functions of size reduction, such as exposing cells in plant tissue prior to extraction of the active principles or reducing the bulk volume of a material to improve transportation efficiency.

Influence of material properties on size reduction

Crack propagation and toughness

Size reduction or comminution is carried out by a process of *crack propagation*, whereby localized stresses produce strains in the particles that are large enough to cause bond rupture and thus propagate the crack. In general, cracks are propagated through regions of a material that possess the most flaws or discontinuities. Crack propagation is related to the strain energy in specific regions according to Griffith's theory. The stress in a material is concentrated at the tip of a crack and the stress multiplier can be calculated from an equation developed by Inglis:

$$\sigma_K = 1 + 2\left(\frac{L}{2r}\right) \tag{10.1}$$

where σ_K is the multiplier of the mean stress in a material around a crack, L is the length of the crack and r is the radius of curvature of the tip of the crack. For a simple geometric structure such as a circular discontinuity $L = 2r$ and the stress multiplier σ_K will have a value of 3.

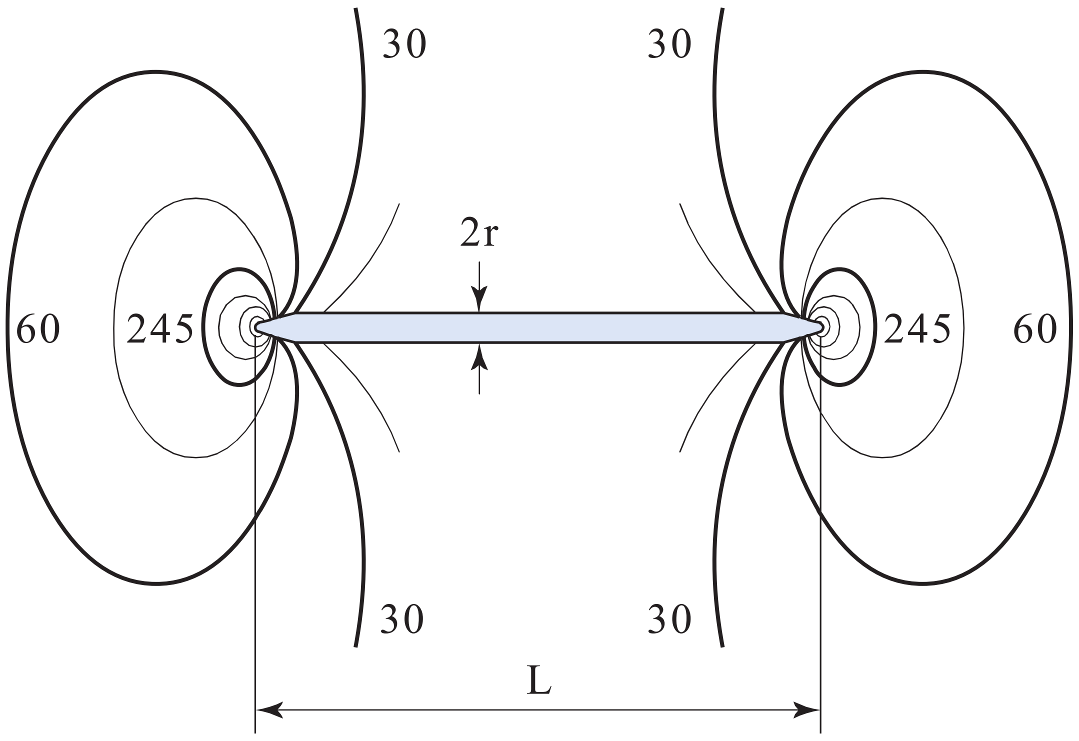

Fig. 10.1 • Stress concentrations at the edges of a disc-shaped crack; r is the radius of curvature of the crack tip; L is the crack length.

In the case of a thin disc-shaped crack, shown in cross-section in Figure 10.1, the crack is considered to have occurred at molecular level between atomic surfaces separated by a distance of 2 × 10^{-10} m for a crack 3 μm long, which gives a stress multiplier of approximately 245. The stress concentration diminishes towards the mean stress according to the distance from the crack tip (Fig. 10.1). Once a crack is initiated, the crack tip propagates at a velocity approaching 40% of the speed of sound in the solid. This crack propagation is so rapid that excess energy from strain relaxation is dissipated through the material and concentrates at other discontinuities, where new cracks are propagated. Thus a cascade effect occurs and almost instantaneous brittle fracture occurs.

Not all materials exhibit this type of brittle behaviour and some can resist fracture at much larger stresses. This occurs because these tougher materials can undergo *plastic flow*, which allows strain energy relaxation without crack propagation. When plastic flow occurs, atoms or molecules slip over one another and this process of deformation requires energy. Brittle materials can also exhibit plastic flow and Irwin and Orowan suggested a modification of Griffiths' crack theory to take this into account. This relationship has a fracture stress, σ, which varies inversely with the square root of crack length, L:

$$\sigma = \frac{E_p}{\sqrt{L}} \tag{10.2}$$