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The science of dosage form design

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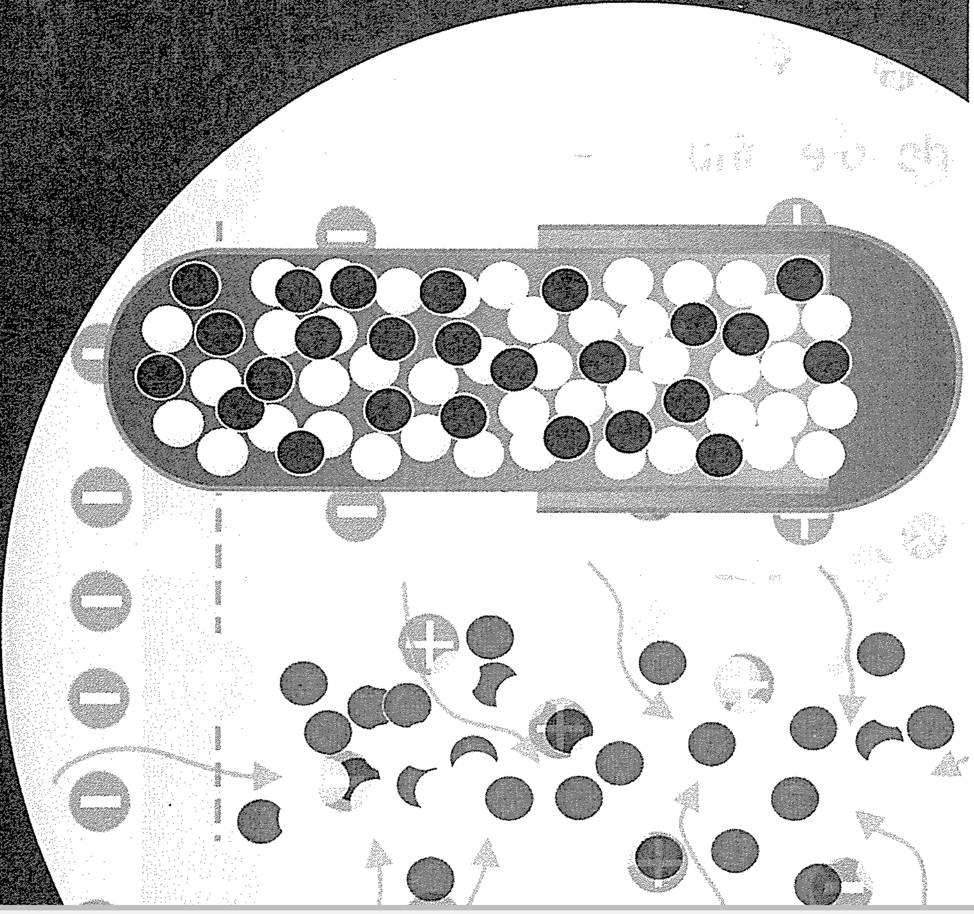

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The Science of Dosage Form Design

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Michael E. Aulton BPharm PhD MRPharmS

Professor of Pharmaceutical Technology, De Montfort University, Leicester, UK

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Mixing

Mixing may be defined as a process where two or more components are treated so as to lie as nearly as possible in contact with a particle of each of the other components. The aim of the process is to produce one of the following:

1 a blend of solid particles (powder mixing),
2 a suspension of an insoluble solid in a liquid,
3 a mixture of miscible liquids,
4 a dispersion of particles in a semisolid as in the preparation of ointments or pastes.

A mixing stage is involved at some time in the preparation of practically every pharmaceutical preparation.

THEORY OF MIXING

Types of mixtures

Miscible liquids, gases and vapours will in time completely mix spontaneously by diffusion and no energy need be used for this to occur. This *positive mixing* may be contrasted with the *negative mixing* of insoluble solid particles with a liquid where the particles will separate out unless work is done by stirring to keep them dispersed. A mixture of powdered constituents is an example of a *neutral* mix. Work must be done to mix them initially but usually there is then no tendency for demixing to occur spontaneously; though demixing is possible in certain circumstances.

The mixing process

To simplify discussion the principles of mixing will be considered by reference to a system consisting of *equal* quantities of two constituents

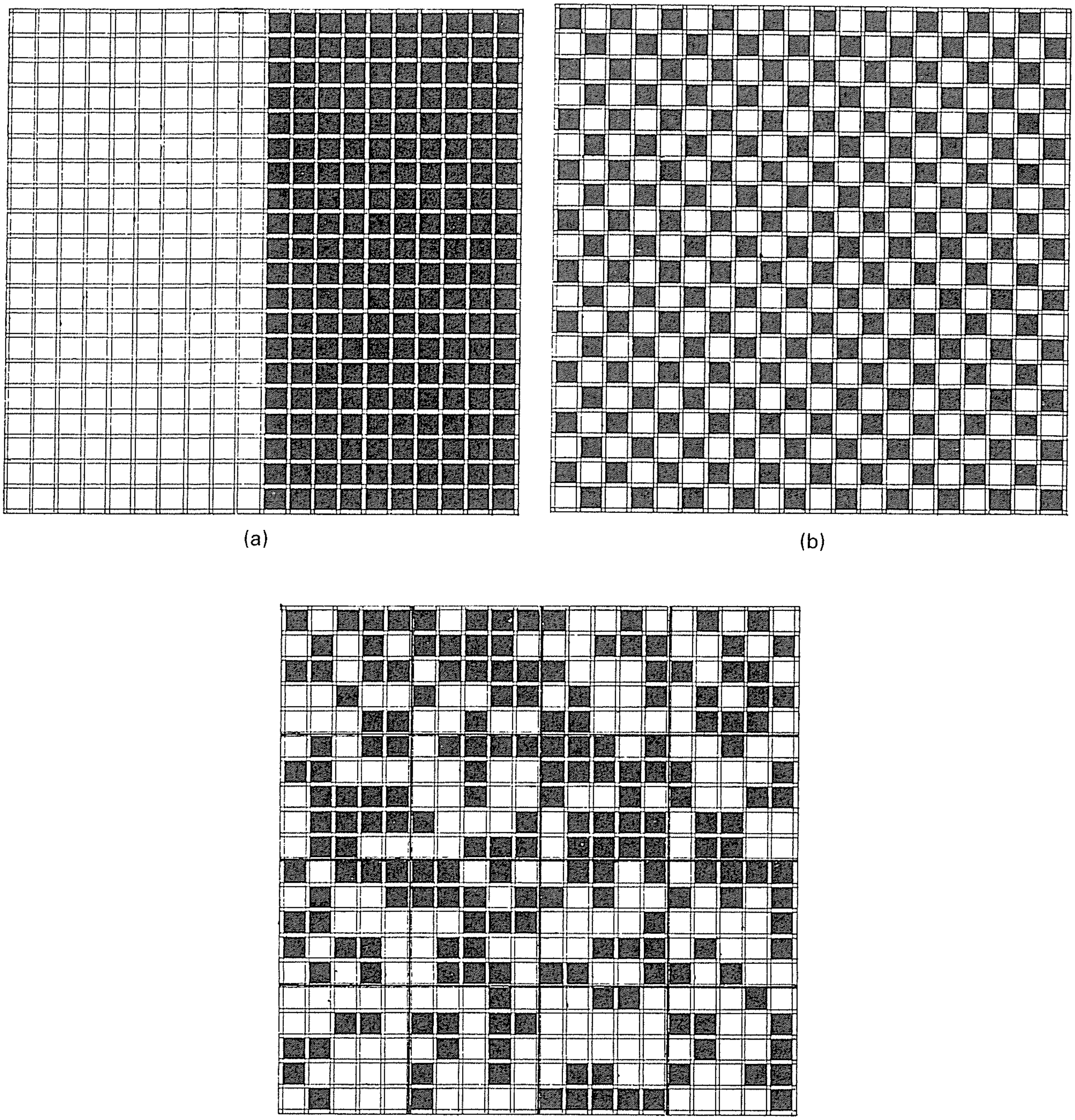

Fig. 32.1 Powder mixing: (a) segregated particles (b) ideal mixing (c) random mixing

A and B of the same size and shape though those conditions are rarely found in practice.

The process can be represented by representing the materials as filled and open squares in Fig. 32.1. Fig. 32.1(a) shows the particles in a completely segregated state prior to mixing. As mixing proceeds it is just conceivable that a so-called *perfect* mix may be produced where each

component (Fig. 32.1(b)). The odds against this happening are so great that the best attainable mix will actually be a *random mix* represented by Fig. 32.1(c). A random mix may be defined as one where the probability of sampling a particular type of particle is proportional to the number of such particles on the total mix. In a large number of trials where single particles were withdrawn there

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