move closer together under the influence of the V_T, but will not collide and coalesce as the V_T is still relatively weak. As the particles move further together, the attractive forces will reach their highest point (although not as strong as in the primary minimum zone) then decrease and overall V_T becomes weakly repulsive, which will have the effect of forcing the particles apart. At this stage, V_T once again dominates over the kinetic energy and the particles will be attracted weakly to each other. In essence, the particles are maintained in their flocculated state, that is they still exist as individual particles, but are loosely grouped together in floccules. If, however, the kinetic energy of the particles is greater than the V_T, then the particles will be able to move further apart. As they do this, the overall V_T will become less attractive and ultimately will become, to all practical purposes, zero. In this case, the particles will behave independently, will not flocculate and will not coalesce. In either case (kinetic energy greater to or less than V_T), coalescence and coagulation of particles is minimal, and hence this is usually the desired strategy for developing pharmaceutical suspensions.

Controlling particulate behaviour in suspensions

From the discussion above, it can be seen that the behaviour of particles in suspension is complex, even when only two individual interacting particles are considered; the behaviour ultimately being dependent on the relative contribution of the repulsive and attractive energies at any separation distance. Examining the equations that govern these two aspects (Eqns 5.24 and 5.25, respectively, repeated here for convenience) can give some clues as to which factors can be manipulated during suspension formulation to alter the behaviour of the particles and which factors cannot be altered.

$$V_R = 2\pi\varepsilon a\psi_o^2 \exp[-\kappa H] \tag{5.24}$$

$$V_A = -Aa/12H \tag{5.25}$$

A, the Hamaker constant (Eqn 5.25). This factor is constant for each combination of particle and medium. As the particulate material within a pharmaceutical suspension is the drug, then the formulator has no opportunity to change the physicochemical nature of the particles. Although theoretically the medium may be altered, which will then change the Hamaker constant, most pharmaceutical suspensions, certainly those intended for oral drug delivery, are aqueous. Hence, the two components in the suspension which contribute to the Hamaker constant (the drug and water) are fixed, and this factor is, in effect, non-modifiable.

ε, the permittivity of the medium (Eqn 5.24). The permittivity of the medium is related to its polarity, so therefore varying the medium will have a direct effect on the repulsive energy between particles in the system. Water is the most common medium for pharmaceutical suspensions and addition of dissolved solids, such as electrolytes, to water will have a relatively minor effect on its permittivity, compared to the effect of changing from water to, for example, oil. Overall, therefore, for the purposes of pharmaceutical suspensions, the permittivity can be considered to be that of water and will have limited variability.

H, distance between particles (Eqns 5.24 and 5.25). The distance between particles can be considered to be both a cause and effect of the balance between the attractive and repulsive energies of the system, as discussed in the previous section: particles very far apart will have very limited interaction and particles located close to each other will be attracted or repelled depending on exactly how far apart they are, and may move in response to the dominant V_T. Inter-particulate distance is difficult to control directly. It will be partly dependent on the mobility of the particles, i.e. their kinetic energy, which itself is dependent on the ambient temperature. The range of temperatures to which a pharmaceutical product is exposed is quite small, from fridge temperature (circa 5 °C) to 40 °C during product testing, so reducing the temperature to reduce mobility is not really a viable option. The inter-particulate distance is also dependent on the concentration of particles within the system, a higher concentration making it more likely that the particles will be physically located close to each other.

4. ψ_o, the surface potential (Eqn 5.24). The physicochemical nature of the particles is fixed, as the formulator must work with the drug that is required, therefore the fundamental surface potential of the particles in an aqueous medium will also be fixed. However, it is easy to modify the surface potential of the particles by adsorbing materials at their surface; such materials most commonly being surfactants below their cmc.