The Mechanics of Inhaled Pharmaceutical Aerosols

AN INTRODUCTION

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ACADEMIC PRESS

A Harcourt Science and Technology Company

San Diego San Francisco New York Boston
London Sydney Tokyo

This book is printed on acid-free paper.

Academic Press
A Harcourt Science and Technology Company
Harcourt Place, 32 Jamestown Road, London NW1 7BY, UK
http://www.academicpress.com

Academic Press
A Harcourt Science and Technology Company
525 B Street, Suite 1900, San Diego, California 92101-4495, USA
http://www.academicpress.com

ISBN 0-12-256971-7

Library of Congress Catalog Number: 2001090350

A catalogue record for this book is available from the British Library

Typeset by Paston PrePress Ltd, Beccles, Suffolk, UK
Printed and bound in Great Britain by Bookcraft, Bath, Somerset

01 02 03 04 05 06 BC 9 8 7 6 5 4 3 2 1

Here, ν is the kinematic viscosity of the fluid surrounding the particle and is given by

$$\nu = \mu/\rho_{\text{fluid}} \tag{3.8}$$

where μ and ρ_{fluid} are the dynamic viscosity and mass density, respectively, of the fluid surrounding the particle. Various empirical equations for $C_d(Re)$ based on experimental data are normally used (Crowe *et al.* 1998), one such correlation being

$$C_d = 24(1 + 0.15\, Re^{0.687})/Re \tag{3.9}$$

However, most inhaled pharmaceutical aerosol particles have very small diameters d and low velocities v_{rel}, so that Re is small. If $Re \ll 1$, the drag coefficient of a sphere is given by

$$C_d = 24/Re \tag{3.10}$$

which for $Re < 0.1$, gives a value of C_d that is accurate to within 1%.

Combining Eqs (3.4)–(3.10), for $Re \ll 1$ we can write

$$\mathbf{F}_{\text{drag}} = -3\pi d\mu(\mathbf{v} - \mathbf{v}_{\text{fluid}}) \tag{3.11}$$

Equation (3.11) is often referred to as Stokes law[1]. It is derived from the continuum equations of fluid motion (since Eq. (3.10) comes by solving the Navier–Stokes equations), and so is valid only for particle diameters that are much greater than the mean free molecular path (which in air at typical inhalation conditions is near 0.07 μm). Extension of Eq. (3.11) to particles with diameter d near the mean free path is considered later in this chapter, while extension to larger Reynolds number is readily accomplished with correlations such as Eq. (3.9).

3.2 Settling velocity

A particle in stationary air will settle under the action of gravity, and reach a terminal velocity quite rapidly. The settling velocity (also referred to as the 'sedimentation velocity') is defined as the terminal velocity of a particle in still fluid.

Because the particle's velocity does not change once it reaches the settling velocity, the acceleration on the particle is zero at this velocity, so that the net force on the particle must also be zero. Assuming the only forces on the particle are the aerodynamic drag and gravity, then for a solid, nonrotating, spherical particle only a vertical drag force will be present, which must balance gravity, i.e.

$$mg = F_{\text{drag}} \tag{3.12}$$

where F_{drag} is the magnitude of the drag force. Assuming the Reynolds numbers $Re \ll 1$, we can use Eq. (3.11) for F_{drag}, in which the air velocity is zero ($\mathbf{v}_{\text{fluid}} = 0$), so that Eq. (3.11) reduces to

$$F_{\text{drag}} = 3\pi d\mu v_{\text{settling}} \tag{3.13}$$

Also, the gravity force is

$$mg = \rho_{\text{particle}} V g \tag{3.14}$$

[1] It is named after George Stokes, who first determined the flow field due to a rigid sphere in translational motion through a fluid for very low Reynolds number flow (Stokes 1851).

where $V = \pi d^3/6$ is the volume of the spherical particle and g is the acceleration of gravity. Equation (3.14) can thus be written

$$mg = \rho_{\text{particle}}(\pi d^3/6)g \qquad (3.15)$$

Substituting Eqns (3.13) and (3.15) into Eq. (3.12), we have

$$3\pi d\mu v_{\text{settling}} = \rho_{\text{particle}}(\pi d^3/6)g \qquad (3.16)$$

or

$$v_{\text{settling}} = \rho_{\text{particle}}\, gd^2/18\mu \qquad (3.17)$$

Equation (3.17) gives the settling velocity for a spherical particle settling under the action of gravity under the condition that $Re \ll 1$ and diameter $\gg$ mean free path. Most inhaled pharmaceutical aerosols readily satisfy the condition diameter $\gg$ mean free path, and many inhaled pharmaceutical aerosols also satisfy the condition that $Re \ll 1$, as seen in the example below. Exceptions to the condition $Re \ll 1$ are uncommon with inhaled pharmaceutical aerosols, but do occur in the entrainment of large carrier particles that occur in dry powder particles (discussed in Chapter 9), and high-speed metered dose propellant droplets (discussed in Chapter 10).

Example 3.1

What is the Reynolds number of a 10 micron diameter spherical, budesonide powder particle (a drug used in treating asthma, specific gravity = 1.26) settling in room temperature air?

Solution

We have

$$\rho_{\text{particle}} = 1.26 \times \text{density of water} = 1260\ \text{kg m}^{-3}$$

$$\text{viscosity of air } \mu = 1.8 \times 10^{-5}\ \text{kg m}^{-1}\ \text{s}^{-1}$$

$$d = 10 \times 10^{-6}\ \text{m}$$

which gives

$$\begin{aligned} v_{\text{settling}} &= (1260\ \text{kg m}^{-3})(9.81\ \text{m s}^{-2})(10 \times 10^{-6}\ \text{m})^2/(18 \times 1.8 \times 10^{-5}\ \text{kg m}^{-1}\ \text{s}^{-1}) \\ &= 3.8 \times 10^{-3}\ \text{m s}^{-1} \\ &= 3.8\ \text{mm s}^{-1} \end{aligned}$$

This gives us a Reynolds number of

$$\begin{aligned} Re &= U_{\text{rel}} d/\nu \\ &= (3.8 \times 10^{-3}\ \text{m s}^{-1}) \times (10 \times 10^{-6}\ \text{m})/(1.5 \times 10^{-5}\ \text{m}^2\ \text{s}^{-1}) \end{aligned}$$

where we have used Eq. (3.8) for the kinematic viscosity of air with the density of air being $\rho = 1.2\ \text{kg m}^{-3}$. Calculating the numbers, we have

$$Re = 0.0025$$

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