JPP Journal of Pharmacy and Pharmacology

Royal Pharmaceutical Society of Great Britain

JPP Journal of Pharmacy and Pharmacology

JPP 2010, 62: 1517–1518

DOI 10.1111/j.2042-7158.2010.01199.x
ISSN 0022-3573

Editorial

Themed issue: Improve dissolution, solubility and bioavailability of poorly soluble drugs

Yvonne Perrie[a] and Thomas Rades[b]

[a]School of Life and Health Sciences, Aston University, Birmingham, UK and [b]School of Pharmacy, University of Otago, Dunedin, New Zealand

Despite continued research efforts, poor aqueous solubility of active compounds remains a major problem in the design and formulation of medicines. Factors thought to contribute to the increasing number of poorly soluble new chemical entities (NCEs) include the increasing number of lipophilic drugs. These molecules, sometimes referred to as 'grease ball molecules', have low melting points and low water solubility, but have a relatively high solubility in lipophilic environments. A second issue compounding to this increasing number of low solubility NCEs is the trend for drugs to crystallize into very stable crystals with very high melting points (often over 20°C). These drugs are often not particularly lipophilic, therefore neither dissolve in oils or water particularly well and are sometimes termed 'brick dust' molecules.

Therefore, while poor drug solubility is a defined problem, depending on the properties of the molecule, these compounds require different formulation strategies to increase their dissolution rate, solubility, and ultimately bioavailability. In addition to improving solubility and dissolution, other aspects in drug delivery may be considered such as targeting, for example of low solubility drugs to tumour sites after injection. In such instances, an increase in bioavailability is not required but rather an appropriate carrier system, which ensures the drug can reach the target site without precipitating in the circulation. There are a wide range of options available (Figure 1), however, it is clear that no individual strategy can offer solutions to all of these poorly soluble drugs (pun intended!).

Within this special issue of the *Journal of Pharmacy and Pharmacology* we have asked a range of experts in the field to give us an insight into the research that they are applying to tackle improving the solubility and delivery of poorly water soluble drugs. Looking at it

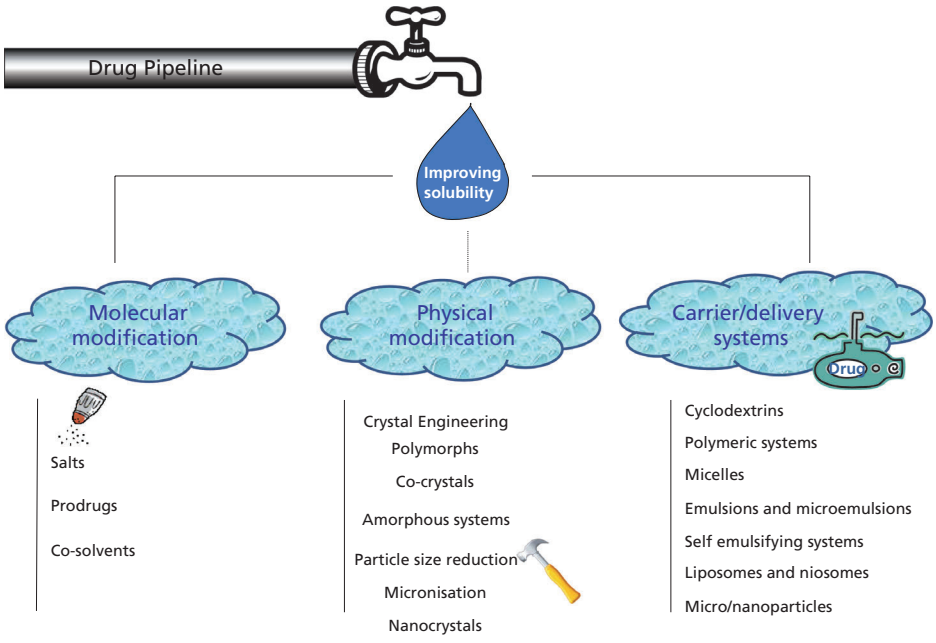

Figure 1 Flow diagram of possible solutions for poorly soluble drugs.

Correspondence: Yvonne Perrie, School of Life and Health Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, UK.
E-mail: y.perrie@aston.ac.uk

from the molecular level, we have work investigating a range of gemfibrozil salts, imidafenacin polymorphs, and work looking at the influence of hydrate formation on solubility.[1–3] This is followed by an update on how we can apply hydrates and co-crystallisation to improve solubility and bioavailability.[4,5] From a physical modification side the critical process parameters to manufacture nanocrystals to improve dissolution are investigated, followed by two contributions on the preparation of amorphous forms by holt-melt extrusion in terms of physicochemical characterisation and in-vitro permeability screening, and a microwave-induced approach to enhance solubility of a poorly water soluble drug.[6–9] Approaches to improve solubility by the application of carrier systems are considered with the pharmaceutical application of cyclodextrins from the basics to product development, lipid and surfactant based drug delivery systems, and new developments in the formulation of lipid nanoparticles and liposomes for the delivery of poorly soluble drugs.[10–13] Finally considerations are given to new biorelevant media that we should consider using for the characterisation of poorly water soluble drugs – a vital consideration given how this can influence solubility and dissolution parameters.[14] Hopefully you will find this collection of papers as useful as we do.

References

1. David SE *et al*. Comparative physical, mechanical and crystallographic properties of a series of gemfibrozil salts. *J Pharm Pharmacol* 2010; 62: 1519–1525.
2. Otsuka M *et al*. Application of a novel combination of near-infrared spectroscopy and humidity controlled 96-well plate to the characterization of the polymorphism of imidafenacin. *J Pharm Pharmacol* 2010; 62: 1526–1533.
3. Tian F *et al*. Factors affecting crystallization of hydrates. *J Pharm Pharmacol* 2010; 62: 1534–1546.
4. Friščić T *et al*. Benefits of cocrystallisation in pharmaceutical materials science: an update. *J Pharm Pharmacol* 2010; 62: 1547–1559.
5. Velaga SP *et al*. Bioavailability of indomethacin-saccharin cocrystals. *J Pharm Pharmacol* 2010; 62: 1560–1568.
6. Peltonen L *et al*. Pharmaceutical nanocrystals by nanomilling: critical process parameters, particle fracturing and stabilization methods. *J Pharm Pharmacol* 2010; 62: 1569–1579.
7. Andrew GP *et al*. Physicochemical characterisation and drug release properties of hot melt extruded celecoxib glass solutions. *J Pharm Pharmacol* 2010; 62: 1580–1590.
8. Brandl M *et al*. In-vitro permeability screening of melt extrudate formulations containing poorly water-soluble drug compounds using the phospholipid vesicle-based barrier. *J Pharm Pharmacol* 2010; 62: 1591–1598.
9. Tekade AR *et al*. Microwave-induced solubility enhancement of poorly water soluble atorvastatin calcium. *J Pharm Pharmacol* 2010; 62: 1599–1606.
10. Loftsson T *et al*. Pharmaceutical applications of cyclodextrins: basic science and product development. *J Pharm Pharmacol* 2010; 62: 1607–1621.
11. Müllertz A *et al*. New perspectives on lipid and surfactant based drug delivery systems for oral delivery of poorly soluble drugs. *J Pharm Pharmacol* 2010; 62: 1622–1636.
12. Bunjes H *et al*. Lipid nanoparticles for the delivery of poorly water soluble drugs. *J Pharm Pharmacol* 2010; 62: 1637–1645.
13. Ali MH *et al*. Solubilisation of drugs within liposomal bilayers: alternatives to cholesterol as a membrane stabilising agent. *J Pharm Pharmacol* 2010; 62: 1646–1655.
14. Müllertz A *et al*. Characterising the behaviour of poorly water soluble drugs in the intestine: application of biorelevant media for solubility, dissolution and transport studies. *J Pharm Pharmacol* 2010; 62: 1656–1668.