Porosity and Its Influence on Pharmaceutical Tablet Dissolution Profiles

Drug delivery as solid dosage forms is complex with a number of factors that can noticeably influence their therapeutic benefit. The drug must be stabilized in the tablet and at the same time be available for absorption in a short time after dosing [1]. The formulation and design of soluble oral tablets needs several factors to be considered:

- Time of release (rapid release or slow/timed release)
- Providing optimum bioavailability for actives
- The stability of the active compound (shelf-life and inside the patient)

Porosity is a key attribute of tablets that can strongly influence their performance. By measuring porosity, the manufacturer can design tablets to satisfy critical parameters including:

- Deformation properties during compression
- Pharmacokinetic behavior
- Shelf life
- Moisture ingress during dissolution
- The bioavailability of the active component
- The dissolution rate of the tablet

Porosity is a good prediction of how liquids enter into the tablet matrix, and the expectations can be validated by experiment [2]. Dissolution rates do not exclusively depend upon porosity; other predictors are also valid include solubility, surface area, and particle size. In addition to carrying out dissolution testing, establishing porosity, surface area and other characteristics are key to establishing the optimal dissolution rate.

Rapid disintegration

Solid dosage forms used to deliver analgesics tend to focus on rapid-release, as the onset of action has to be almost immediate. 'Immediate' is actually defined as disintegration within a set period, normally 2.5 min but no longer than 10 min [2,3]. Immediate-release formulations incorporate hydrophilic and hygroscopic excipients to aid the access of fluids and swelling of the tablet and thus successful dissolution. Disintegrants and superdisintegrants (2-5% w/v) including: croscarmellose sodium (CCS), sodium starch glycolate, and crospovidone are commonly necessary to provide enhanced rapid release properties [2].

The Influence of Porosity

Tablet porosity is not just a predictor of dissolution and solvent ingress. With the growing importance of Quality by Design (QbD) porosity is also an important Critical Quality Attribute (CQA) for both disintegration and bioavailability properties [4]. These parameters are vital to provide data to allow the prediction of API and excipients behavior in formulations. The physical properties of granules and their porosity are generally excellent influencers of compatibility that can be adjusted during the manufacturing process by modifying the formulation. Changes in porosity or compression shear strength are extremely significant in the compaction characteristics of granules [5,6].

Case Study

Using pore characteristics to predict tablet dissolution can have difficulties, a study published in 1998 by Riipi et al [1] examined the dissolution rate and porosity of compressed erythromycin acistrate tablets. High-pressure mercury porosimetry was used to determine total porosity of the tablets, pore size distribution and pore specific surface area. The results indicated that even with pore size distribution

data and differences in pore structure, the dissolution behavior of erythromycin acistrate tablets required other analytical techniques to provide a full explanation[1,7].

A 2013 Bristol Myers Squibb study showed that pore size was one of the key factors influencing the release rate of the API. The mercury porosimetry based study also examined the role of water and recrystallization of the API on dissolution slowdown. Dissolution and recrystallization of the test API was shown to be due to a change of pore size distribution following moisture conditioning of the tablet The drug release mechanism connected the spatial distribution of tablet porosity to the dissolution profile. This proved the impact of tablet porosity on the drug release mechanism[8].

Autopore V from Micromeritics

Mercury porosimetry analysis is based on the ingress of mercury into pores under strict pressure control. The technique offers speed, accuracy, and a wide measurement range . Benefits include the calculation of numerous sample properties such as:

- Pore size distributions,
- Total pore volume,
- Total pore surface area,
- Median pore diameter,
- Sample densities for bulk and skeletal samples
- Resolution in the intrusion profile of 0.1 pL.

The AutoPore V Series mercury porosimeter is a safe and automated method for high precision intrusion studies on powdered and solid materials.

References

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