Detection of poor acid resistance of enteric coats using the Sirius SDI

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Introduction

The acid resistance of an enteric coat is affected by both formulation and processing conditions. As part of a QbD approach to developing a tablet coat many formulation and processing parameters are investigated to understand which factors could be classed as a Critical Quality Attribute (CQA).

Currently, the acid resistance of the applied coat is determined by dissolution in a compendial dissolution apparatus with 0.1M Hydrochloric acid. Typically such methods require a prolonged running time (e.g. 2 hours) to understand the effect of prolonged exposure to acid and to establish a suitable solution concentration that can be measured. Also it is not possible to determine where the tablet defects are (i.e. the embossed region).

Failure modes of enteric coats

Plasticizer

Both the level and type of plasticizer can affect the acid resistance of an enteric coat. Incorrect selection of these two factors can result in poor acid resistance.

Addition of the correct ratio of polymer and plasticizer results in a coat that is not brittle and has very low water permeability. Too little plasticizer results in a very brittle coat that comes away from the tablet surface.

Coat weight

Typically, formulators avoid using embossed logos on tablets as there are concerns that this could lead to defects and poor coat uniformity. This results in the tablets being printed with the required logos. There is no clear test available that confirms defects with the embossed region.

Processing conditions

The coating temperature should be carefully controlled during the coating process. If the process temperature is too cool then the polymer does no coalesce evenly over the tablet surface. Too high a temperature and the droplets become too viscous to obtain an even coat.

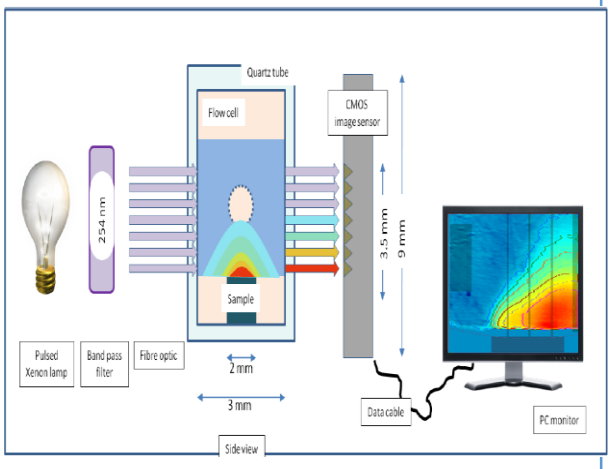
Storage conditions

Some polymers, i.e. cellulose acetate phthalate (CAP) when stored at elevated temperatures can be hydrolysed. This has the opposite effect of forming the insoluble cellulose acetate. Therefore acceptable acid resistance would occur, however no release at elevated pH would occur.

Surface Dissolution Imaging

The Surface Dissolution Imager (SDI) is an instrument marketed by Sirius Analytical. It uses ultra-violet light to monitor the dissolution of active pharmaceutical ingredients (APIs) at the surface. It has been used to study the dissolution behavior of APIs, co-crystals, salts, solid dispersions and stents.

The basic principle is that an API is compressed into a 2 mm diameter compact, which is inserted into the base of a flow cell. Dissolution medium is flowed through the cell, with a laminar flow pattern maintained. UV light, at a selected wavelength, is then transmitted through the flow cell. The UV light is then detected by a CMOSIS chip, where the light intensity is measured. The CMOSIS chip records images every 0.5 seconds and these images are subsequently 'stitched' together to form a film of the dissolution process.

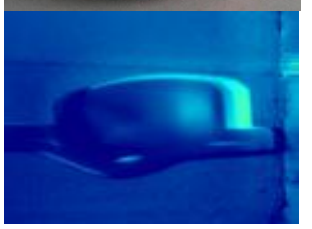


The flow cell was adapted so that the surface of a full dosage form could be analyzed. This resulted in a path length of 25 mm for the UV light; therefore improving the limit of detection of the API. To distinguish between dissolved and undissolved material two wavelegths were used: visible (550 nm) and UV (254 nm). It is proposed that any dissolved material would only be detected by the UV wavelength, undissolved would be observed using both wavelengths.

What can we learn from the SDI?

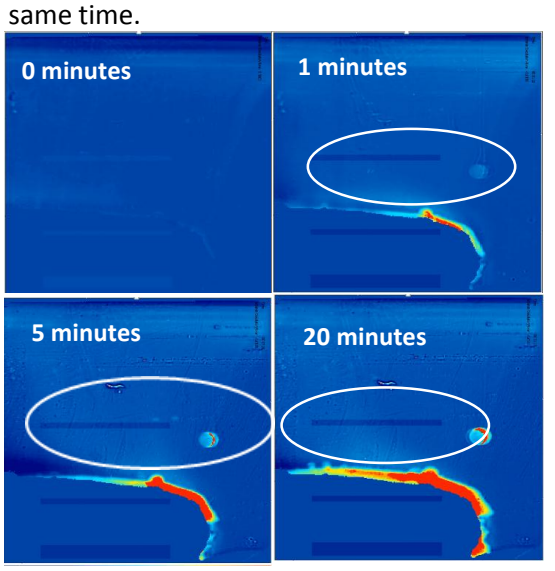
A 50 mg diclofenac sodium tablet coated with HPMCP (which dissolves from pH 5.5) was exposed to 0.1M HCl for 30 minutes.

After 30 minutes of acid exposure the tablet, as anticipated, was unaffected.

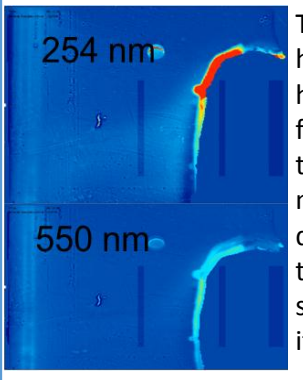


UV imaging of the tablet in acid showed no changes at the surface of the tablet.

To test the ability of the SDI to detect poor acid resistance, a small pinhole was added to the coat. The tablet was then subjected to 20 minutes of dissolution and imaged at the same time.



After only 1 minute of exposure to the acid swelling at the surface was already observed. This was in the exact area that the pinhole was placed. Over the 20 minutes, this swelling got progressively more prominent.



The white circles highlight areas of higher absorbance flowing away from the tablet surface, this is most likely due to dissolved diclofenac as there was no significant evidence of it at 550 nm.

Conclusion

The use of UV surface imaging was able to detect poor acid resistance of an enteric coat. Within 1 minute, changes were observed in the coat and after 5 minutes API leached from the core. Further investigations are planned on development samples.