Analysis of Hydration Processes in Porous Materials Using Terahertz Pulsed Imaging

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***Abstract*— Solvent penetration in porous solids is a very important property that limits the performance of a range of materials in industrial applications. Here we show how terahertz pulsed imaging (TPI) can be used to investigate the uptake of water into materials relevant to the pharmaceutical sciences and catalysis by using depth resolved tracking of the water/solid interface over time upon exposure of the porous solid to water. TPI is an exciting characterisation technique to study such solvent transport processes due to its millisecond time resolution and the transparency of ceramics and polymers to terahertz radiation. These properties make TPI unique to investigate fast processes compared to other measurement modalities.**

I. INTRODUCTION

Mass transport in porous materials is of fundamental importance in chemical engineering applications as it governs both product and process performance. Previous work has shown that it is possible to analyse the ingress of solvents into a range of porous materials, as long as the material is transparent to terahertz radiation [1]. At terahertz frequencies there is typically a relatively large contrast in the refractive index between water (n ≈ 2.4) and the commonly used polymers (n ≈ 1.4-1.8) and ceramics (n < 2) used to make porous solids of industrial significance such as tablets or catalyst pellets. Here we specifically investigate the applicability of terahertz pulsed imaging (TPI) to observe the disintegration kinetics in pharmaceutical immediate release formulations as well as solvent transport in catalysts used for heterogeneous catalysis. The process of solvent penetration into these porous materials controls the rate of swelling and disintegration in pharmaceutical tablets, whilst governing the manufacturing of catalysts and controlling the rate of reaction in an activated catalyst.

II. RESULTS

A commercial TPI Imaga 2000 (Teraview Ltd, Cambridge, UK) was used in conjunction with a custom made flow cell and loop to expose a single face of cylindical sample pellets with water[2,3]. Immediate release tablets were compacted containing either 95 wt. % microcrystalline cellulose (MCC PH102, FMC Biopolymers, Philadelphia, USA) and the disintegrant 5 wt. % croscarmellose sodium (CCS, FMC Biopharmaceutical) or 98 wt. % MCC and 2 wt. % CSS. A second set of pharmaceutical tablets have been compacted containing MCC, CCS, lactose anhydrous (Tablettose 100, Meggle, Wasserburg, Germany) and magnesium stearate (Parchem, New Rochelle, New York, USA) The tablets were compacted using a compaction simulator (Pheonix Calibrations, Pheonix, USA). For the catalyst samples of 100 wt. % γ-alumina (Johnson Matthey, Sonning, UK), 70 wt. % alumina and 30 wt. % silica (Johnson Matthey) or 0.3 wt. % palladium (Johnson Matthey), 30 wt. % silica and 69.7 wt. % alumina were compacted using a manual press (Specac, Slough, UK). All samples were flat-faced discs with a target thickness of 1.5 mm and a diameter of 10 mm. Two liquid temperatures were used: 20 and 37 °C. The effective sampling rate was 3 Hz.

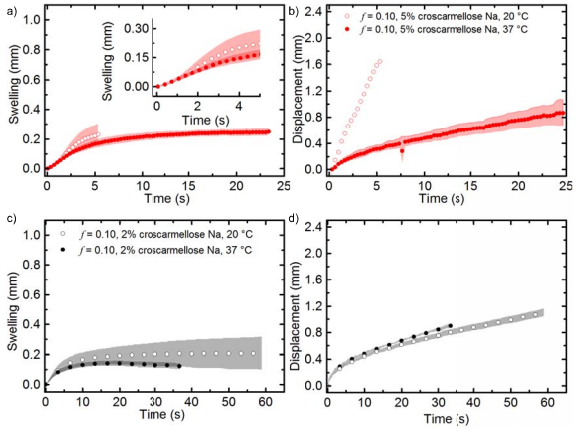

Fig. 1: a) and c) are the swelling kinetics and b) and d) are the transport kinetics in samples containing 5% croscarmellose sodium and 95% MCC and 2% croscarmellose sodium and 98% MCC. All samples have a porosity of 10% ($f = 0.1$)

Using TPI it was possible to assess the change in disintegration kinetics due to changes in temperature and concentration of the disintegrant within the range used for formulations (Fig. 1).

At 5 wt. % disintegrant concentration we observed a drastic change from rapid disintegration (20 °C) to much slower disintegration (37 °C), which we attribute to the formation of hydrogels, changing the transport from Case II to Darcy flow kinetics. At 2 wt. % disintegrant concentration, the hydration is slowed down significantly and only Dracy transport is observed.

When lactose is added there is a clear change in disintegration kinetics, where tablet disintegration takes place over a longer period of time, even though disintegrant is present at 5 wt. %. This is due to the strength of the inter-particulate bonds, between the excipients in the tablet. The strength of these sinter bridges are so strong, that the tablets only begin to disintegrate once the lactose begins to dissolve. As there is such a high concentration of lactose in these samples, once the lactose begins to dissolve the water becomes saturated with lactose as it dissolves into the solvent. This saturated solution is more viscous than water and therefore hindered liquid transport will be observed. Therefore the reduction in the rate of liquid transport expected at the lower porosities will be enhanced. .

Figure 2 shows how the rate of liquid penetration is changing with porosity, in samples containing croscarmellose sodium, MCC, magnesium stearate and lactose. As porosity is increasing the rate of liquid penetration is increasing in a non-linear fashion. This is expected based on the Washburn equation.

There is large increase in the rate of tablet hydration and tablet disintegration with a decrease of 300 s from porosities of 5.0% to 7.5% and decrease of approximately 1000 s, when the porosity is increased from 5.0 to 20%. Each porosity corresponds to a different tensile strength of tablet. This is an important physical parameter in pharmacy, which is used to assess the mechanical strength of the tablet to assess whether the tablet is sufficiently strong for subsequent processing. The tensile strength is also used traditionally as an indirect metric to estimate the time it takes for a tablet to disintegrate.

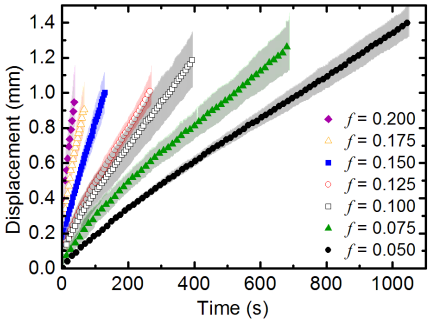

Fig. 2: Transport profiles observed in samples containing, MCC, lactose, CCS and magnesium stearate, with porosities of; 5.0% (black circles), 7.5% (green triangles), 10.0% (hollow black squares), 12.5% (hollow red circles), 15.0% (blue squares), 17.5% (hollow orange triangles) and 20.0% (purple diamonds). The shading in the background is the standard deviation between independent repeats (n = 5).

Figure 2 shows that TPI can easily resolve the changes in transport properties for porosities between 10.0% and 20.0%. These results in pharmaceuticals samples show that TPI is capable of analysing key disintegration parameters in complex tablet formulations, which cannot be measured with any other technology currently available in the field.

Similar transport analysis is carried out for the catalyst samples (Fig. 3). Here a more rigid ceramic structure is being hydrated and no swelling is observed. As shown for the pharmaceutical samples, TPI is sensitive to small changes of concentration of the formulation in the sample mixtures: our results show that the addition of silica and palladium both hinder solvent transport. When silica is added at 30 wt% there is a clear change in the hydration times of the pellets. Hydration times increase from 30 s (100 wt% alumina) to over 100 s (30 wt% silica and 70 wt% alumina). This can be explained by the strong hydrophillicity of the silica particles. Furthermore when an additional 0.3% wt palladium is added there is a further increase in hydration time to 110 s.

III. Summary

We have demonstrated that TPI can be used to measure transport and swelling processes in porous materials. In a pharmaceutical context it has been used to analyse swelling and transport where the technique has been shown to be sensitive to changes in porosity, temperature, excipients and

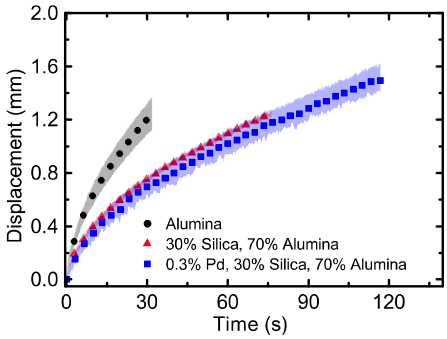

Fig. 3: Transport kinetics observed in catalysts and catalyst supports, where the shading in the background is the standard deviation between 3 repeat experiments.

excipient concentration. By assessing systematically how the tablet disintegration properties change upon variation of the fundamental physical and chemical properties of the formulation it is possible to rationally design tablet formulations, predict their performance and assess the reproducibility of a manufactured batch of products.

In a similar fashion the design of catalysts can be improved using the understanding gained from the TPI analysis. Based on such knowledge it becomes possible to optimise catalyst formulations and their manufacturing processes. The method also provides insight into how the active catalyst components interact with solvents. This information of the liquid-solid interaction might prove useful in the future to further understand reaction control mechanisms.

References

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