Wet Granulation Process via Foams and Drops

Melvin X.L. Tan and Karen P. Hapgood

Monash Advanced Particle Engineering Laboratory
Chemical Engineering Department, Monash University, Clayton, VIC, 3800
Email address: melvin.tan@eng.monash.edu.au

ABSTRACT

Wet granulation using foaming binder solution is a new approach of liquid delivery to create granules. This study compares wet granulation via foamed binder addition method and sprayed binder addition method by studying the kinetics of foam and drop penetrations into loosely packed powder beds.

Foam and drop nucleation kinetics were compared by examining specific penetration time (penetration time per unit mass of liquid drop or foam) and nucleation ratio (ratio of mass of nuclei granules to mass of liquid binder).

The mechanisms of foam decay such as liquid drainage and bubble coalescence are critical to the process of foam penetration into the powder pores. Foam penetration rate cannot be completely revealed until the foam characteristics are clearly determined. Nucleation ratio results suggest that foam nucleation method allows more efficient liquid usage and liquid distribution to induce nucleation of powder compared to drop nucleation method.

INTRODUCTION

A new liquid delivery method – foam granulation has been developed as an alternative to the traditional application of atomized liquid spray in pharmaceutical wet granulation processes. Unlike spray granulation, the liquid binder is sent through a foam generator and distributed to the powder bed as aqueous foam to induce granulation. This novel approach has been shown to produce granules and tablets in the pharmaceutical processing. Initial experiments indicate that foam granulation uses less liquid binder; discards the need for nozzles which subsequently eliminates the problems associated with nozzles; and has better liquid dispersion and wetting through the powder mass (Keary and Sheskey, 2004). Scale-up studies has also demonstrated the technical operating potential of this technology (Sheskey, et al., 2007).

Research on foam granulation technology has focused on a series of foam granulation industrial case studies (Keary and Sheskey, 2004). However, there is still lack of understanding on how nucleation and granulation occur when foamed addition method is used. This paper investigates the penetration kinetics of foam by depositing a single foams on a loosely packed powder bed, and it was compared to that of using single drops of the same fluid. The nucleation kinetics of foams and drops are compared by examining the penetration time and nucleation ratio. Both parameters are useful in quantifying the liquid distribution efficiency and the nuclei formation kinetics (Hapgood, et al., 2002, Schaafsma, et al., 2000).

The penetration time is defined as the time required for a drop or foam to completely penetrate into the powder bed. Studying the penetration kinetics of liquid can be useful to understanding nucleation kinetics (Hapgood, et al., 2002). Due to variations of foam mass dispersed, specific penetration ($\hat{t}_p$), defined as the penetration time (t_p) per unit mass of binder (m) is introduced in this study:

$$\hat{t}_p = \frac{t_p}{m} \quad [1]$$

Nucleation ratio is defined as the amount of powder nucleated per unit mass of liquid binder required. This ratio of liquid binder mass to nucleus mass reflects the efficiency of liquid binder distribution through the powder mass to create granule (Schaafsma, et al., 2000). In this paper, nucleation ratio is calculated in terms of mass ratios:

$$K_m = \frac{M_n}{M_b} \quad [2]$$

where M_n and M_b are the nucleus mass and liquid binder mass respectively.

EXPERIMENTAL

Materials

Lactose monohydrate was used in the experiments. A loosely packed powder bed was prepared by sieving the particular powder into a petri dish and the bed surface was scraped smooth using a metal spatula. Several concentrations of hydroxylpropyl cellulose, HPC were used in the experiments. The binders were prepared by dispersing the HPC powders in distilled water according to the required concentration (3% w/w HPC and 6% w/w HPC).

Procedures

Drop and foam penetration experiments are performed with a 6ml syringe or a handheld Airspray 150ml foam dispenser. The amount of binder added can be measured by placing the powder bed on the balance.

Penetration time is measured using a stopwatch. A small amount of food dye was added to the solutions to assist visibility of liquid penetration. Nucleus collection was performed by sieving method. Excavated nuclei were weighed using the balance.

RESULTS AND DISCUSSION

Comparisons of Foam and Drop Specific Penetration Times

The plot of specific penetration time against binder mass for both foam and drop yields similar trends, where decreasing foam and drop mass increase specific penetration time. This similar trend may be attributed to the fact that liquid drains from the foam will also penetrate into the powder mass, which is similar to the drop penetration process.

The results show that 3% HPC foam penetration on lactose powder requires a longer specific penetration time compared to a drop of the same fluid. Longer specific penetration time indicates that foam dispersion will have to be controlled by mechanical mixing during foam granulation process. This may presumably due to the extra time needed for the occurrences of bubble coalescence and liquid drainage to induce liquid penetration into the powder pores. However, the results for 6% HPC binder penetration on 100mesh lactose do not clearly show whether foam or drop has a shorter or longer penetration time. As both liquid binder and foam properties are interactively affecting the penetration behaviour of foam on the powder surface, we cannot reach any general conclusions until the effects of liquid binder properties and foam properties on the penetration process are clearly determined.

Comparisons of Foam and Drop Nucleation Ratios

For lactose powder, foamed addition method has generated a larger nucleation ratio compared to drop addition method. This implies that nucleation via foamed addition method requires less liquid binder; which supports a key finding of Keary and Shesky (2004), who found that foam granulation used lower amount of fluids to achieve similar average granule size. A larger nucleation ratio also indicates that foamed addition method provides better liquid distribution within the non-uniform powder beds to create a lager final nucleus size. Nucleation of powder particles is often restricted due to the presence of macrovoids in lactose powder beds with irregular packing structure (Hapgood, et al., 2002), while foamed addition method offers better liquid distribution efficiency within the powder bed to form nuclei.

CONCLUSIONS

Comparisons were made between foam and drop penetration kinetics by examining the penetration time and nucleation ratio. The properties of foam are critical to the rate at which foam penetrates into the powder pores. This was seen from the microscopy observation that the foam penetration process was largely influenced by the liquid drainage and bubbles movement mechanisms. Comparisons of foam and drop nucleation ratios have shown that foam dispersion provides better liquid distribution efficiency and uses less liquid binder to nucleate the same number of powders.

REFERENCES

Hapgood K. P., Litster J. D., Biggs S. R., Howes T., 2002. Drop penetration into porous powder beds. Journal of Colloid and Interface Science 253 (2)**,** 353-366.

Keary C., Sheskey P., 2004. Preliminary report of the discovery of a new pharmaceutical granulation process using foamed aqueous binders. Drug Development & Industrial Pharmacy 30 (8)**,** 831-845.

Schaafsma S. H., Vonk P., Kossen N. W. F., 2000. Fluid bed agglomeration with a narrow droplet size distribution. International Journal of Pharmaceutics 193 (2)**,** 175-187.

Sheskey P., Keary C., Clark D., Balwinski K., 2007. Scale-up trials of foam-granulation technology--high shear. Pharmaceutical Technology 31 (4)**,** 94-108.