INTRODUCTION

Semi-solid formulations are often used to stabilise APIs and prevent crystal growth by locking the API molecules into a matrix [1]. Surfactants and disintegrants are commonly used in solid oral dosage forms to accelerate the rate of disintegration and meet the criteria for an immediate release dosage form. These materials can increase the surface area breaking up tablets or plugs allowing API to be more readily available for absorption. The aim of this work was to improve the disintegration time of semi-solid formulations, encapsulated into hard shell capsules, to achieve a target disintegration time of less than 30 minutes.

MATERIALS AND METHODS

Two semi-solid formulations using the same API, at a concentration of 30%w/w API, were filled into size 0 hard gelatin capsule shells. The formulation compositions were as follows;

1. Miglyol 812N and 2% w/w Aerosil 200.
2. Poloxamer 188.

Disintegration testing was performed using standard Ph. Eur apparatus with 0.1N HCl at 37°C.

The following approaches were used to increase the rate of disintegration:

1. Addition of disintegrants to API/Poloxamer 188 formulation (Ac-Di-Sol (1% w/w), Kollidon CL (2% w/w), Explotab (4% w/w), Starch 1500 (7% w/w), and Avicel PH102 (12% w/w).
2. Addition of surfactants to the API/Miglyol 812N/Aerosil 200 formulation (Lauroglycol 90 and Tween 80 at a concentration of 13.9% w/w).
3. Grinding of the API/Poloxamer 188 plug.

RESULTS

Inclusion of disintegrants to the Poloxamer 188 formulations reduced the disintegration time. Avicel PH102 reduced the disintegration time most significantly, full disintegration was achieved in 34 minutes (formulation plug size ≈ 570mg). Furthermore, increasing the surface area of the API/Poloxamer 188 plug, by grinding the solid formulation matrix, was also shown to accelerate the disintegration time Figure 1).

Addition of surfactants to the Miglyol 812N/Aerosil 200 formulation significantly reduced the disintegration time. In the case of Tween 80, the disintegration time was reduced from >2hours to 3 minutes (formulation plug size ≈ 590mg) with good dispersion observed in the disintegration media . Whilst Lauroglycol 90 was found to reduce the disintegration time it did not disperse well with an oily mass being observed on the surface of the disintegration media (Figure 2).

CONCLUSIONS

Disintegrants and surfactants in conjunction with semi-solid formulations can significantly reduce disintegration time. Semi-solid plugs, formed in the capsule shell may require assistance to disintegrate in a reduced time frame. This work demonstrates that disintegrants commonly used in tablet formulations, and surfactants, can significantly improve disintegration times of capsules filled with semi-solid/paste-like formulations. Work is ongoing to optimise the concentration of Avicel PH102 and Tween 80.

REFERENCES