British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1142

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 13th APS International PharmSci 2022

A Translation of Technology: MicroCoat™ to Sustained Release Orally Disintegrating Tablets

Kavil Patel[a*], Darragh Murnane[a], Craig Richardson[b], Fang Liu[a,b]

[a]Department of Clinical, Pharmaceutical and Biological Sciences, University of Hertfordshire, Hatfield, UK.

[b]Fluid Pharma Ltd., Windsor House, Harrogate, UK.

ARTICLE INFO

Received: 17/06/2022
Accepted: 07/07/2022
Published: 02/11/2022

*Corresponding author.
Tel.: +44 7960 475 333
E-mail: k.patel39@herts.ac.uk

KEYWORDS: sustained release; microparticles, coating, dysphagia

SUMMARY

Orally disintegrating tablets (ODTs) comprising sustained release (SR) coated microparticles smaller than 250 µm provide an appealing dosage form for patients with dysphagia, offering a superior mouthfeel and highly convenient route of administration without the need for water. SR coating for microparticles of the requisite size (<200 µm) is incredibly challenging however the utilisation of the MicroCoat™ technology, whereby various dry powder glidants are added during SR coating, was demonstrated to achieve desirable coating outcomes. ODTs were prepared via direct compression. In addition to conventional USP methods, texture analysis (TA) was applied to determine disintegration. ODTs were shown to disintegrate within an acceptable time (<30s) and drug release was unaffected by compression during tabletting indicating a robust coating.

INTRODUCTION

The provision of patient-centric formulations is of upmost importance considering the ageing population and increasing prevalence of dysphagia, where swallowing is difficult. Oral microparticles smaller than 250 µm can improve swallowability and provide an appealing mouth feel without grittiness. Another challenge for formulation design involves dosing simplification and this can be achieved by applying sustained release (SR) coatings. The SR coating process for microparticles of the necessary size is incredibly challenging due to the tendency of agglomeration and poor powder flow; a MicroCoat™ technology has been demonstrated to successfully produce freely-flowing SR microparticles without agglomeration using Würster fluid bed coating. The aim of this research is to prepare orally disintegrating tablets (ODTs) comprising SR coated microparticles in order to simplify administration and further increase patient centricity.

MATERIALS AND METHODS

Gliclazide layered microcrystalline cellulose (MCC) spheres (Cellets® 100, Pharmatrans Sanaq AG) were coated with ethyl cellulose (Surelease®, Colorcon Ltd.) and hypromellose (Opadry®, Colorcon Ltd.) (80:20) using a fluid bed coater (Mini-Glatt®, Glatt GmbH). During coating, magnesium stearate (MS), sodium stearyl fumarate (SSF) (Pruv®, JRS Pharma) or silicon dioxide (SD) (Aerosil® 200, Evonik AG) were added as dry powder glidants into the coating chamber (0.1 % w/w coating batch per 15 min) (1).

ODTs were prepared by applying 8 kN compression force to co-processed mannitol, MCC, carmellose and crospovidone (Granfiller-D™ 215, Daicel Corporation and Nichirin Chemical Co., Ltd) and SR microparticles (30 %) with MS as lubricant (0.5 %) (both w/w based on ODT weight).

ODT mass (n=20), thickness (n=10), hardness (n=10), friability (n=15) and disintegration (n=6) were

https://doi.org/10.5920/bjpharm.1142

measured according to USP standards. An additional disintegration method was applied using texture analysis (TA) (TA.XTplusC, Stable Micro Systems) with a flat probe and 5 kg load cell. 1 mL deionized water was pipetted onto the tablet surface just before the probe contacted the tablet and the time taken for the gap height to plateau was measured (n=6). Single factor ANOVA tests were carried out to assess the significance of any observed differences.

In vitro drug release from SR microparticles was observed pre- and post-compression using USP II (paddle) method (n=6) and compared using the F2 (similarity factor) statistical model. Scanning electron microscopy (SEM) was used to observe microparticle appearance both before and after compression to assess potential damage to the SR coating.

RESULTS AND DISCUSSION

The application of MicroCoat™ technology led to dramatic coating process improvement with the addition of both MS and SD providing yields of 99% compared to 72 % without glidant addition (Figure 1)

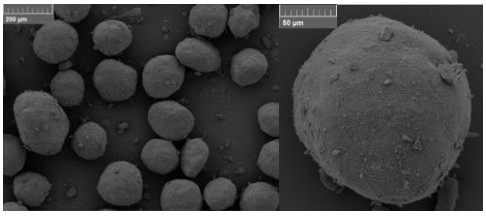

***Fig. 1. SEM images of** 20 % Surelease®:Opadry® coated microparticles with MS addition during SR coating*

ODT mass and thicknesses were equivalent irrespective of glidant added during SR coating ($p>0.05$) however hardness was increased by the addition of SD ($p<0.05$). Overall disintegration using the TA method occurred slower and more gradual compared to the standard USP method (Figure 2). Additionally, the glidant impact on disintegration was method dependent. Differences were observed between each of the formulations tested using the USP method ($p=0.0001$) however the difference between formulations containing SSF and SD were found to be insignificant ($p=0.81$) using the TA method. Both methods showed that formulations comprising MS disintegrated more slowly ($p=0.003$ or 0.002 for USP and TA methods, respectively).

Microparticles comprising MS and SSF provided SR over a 15h duration whereas SD inclusion caused an increase in release rate. Drug release was unaffected during compression indicating a preservation of the SR coating membrane during tableting ($F2>50$). This is supported by SEM images of microparticles within the ODT (Figure 3).

***Table 1.** Summary of ODT properties*

Glidant added during SR coating	MS	SSF	SD
Mass (mg)	454±2	455±2	455±2
Thickness (mm)	4.2±0.04	4.3±0.04	4.3±0.03
Hardness (N)	76±2	76±3	87±4
Friability (%)	0.18	0.13	0.08
Disintegration (s) a	8.5±0.5	6.7±0.9	4.8±1.3
Disintegration (s) b	23.7±3.4	16.7±1.6	16.3±2.5

[a] USP method, [b] texture analysis

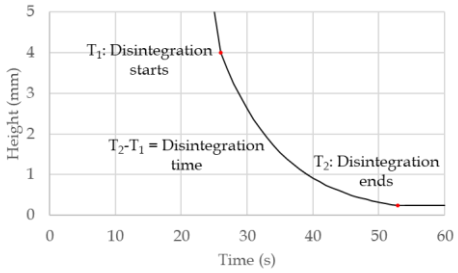

***Fig. 2.** ODT disintegration behaviour using TA*

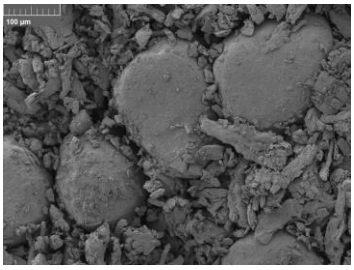

***Fig. 3.** SR coated microparticles within the ODT matrix*

CONCLUSIONS

The development of SR ODTs comprising coated microparticles has been shown to be a viable approach in the development of patient-centric formulations for patients with dysphagia. Prepared ODTs showed promising disintegration times (< 30s) whilst allowing for sustained release and once daily dosing.

REFERENCES

Mohylyuk, V., et al., 2020. Wurster Fluidised Bed Coating of Microparticles: Towards Scalable Production of Oral Sustained-Release Liquid Medicines for Patients with Swallowing Difficulties. AAPS PharmSciTech, 21(1), p.3.

Abdelbary, G., et al., 2005. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. International Journal of Pharmaceutics, 292(1-2), pp.29-41