galenIQ™721-
A Novel Excipient for Orodispersible Minitablets

Ard Lura [1], Oliver Luhn [2], Jörg Breitkreutz [1]

[1]Institute of Pharmaceutics and Biopharmaceutics, Heinrich Heine University, 40225 Düsseldorf, Germany
[2] BENEO-Palatinit GmbH, Maximilanstraße 10, 68165 Mannheim, Germany
☎ +492118114891 ✉ ard.lura@hhu.de

INTRODUCTION

The benefit of orodispersible minitablets (ODMT) for treating pediatrics has been demonstrated [1]. The aim of this study is to determine the feasibility of a direct compression grade isomalt galenIQ™721, (BENEO-Palatinit) for producing ODMTs with hydrochlorothiazide (HCT) and enalapril-maleate (EM) as model drugs. The therapeutic need of these drugs for children is well known [2]. Isomalt (Ph.Eur., USP-NF, JP) is a disaccharide alcohol and belongs to the group of polyols. galenIQ™721 represents an agglomerated type isomalt manufactured by a fluid bed process followed by a sieving operation.

MATERIALS AND METHODS

Six formulations of ODMTs based on galenIQ™721 were directly compressed with 2 mm 19-tips punches on a rotary die press (Pressima, IMA-Kilian) at a speed of 10 rpm containing either 30.8% of HCT (UNICHEM LABORATORIES) or 16% of EM (Kraemer & Martin Pharma) (Figure 1). The influence of 4% of the disintegrants Kollidon CL and CL-SF (BASF) on the disintegration time was evaluated.

The ODMTs were analyzed regarding disintegration time by a modified method [3]: an ODMT was put into a hull of Plexiglas with a height of 21 mm and 10 mm inside diameter. The top and bottom of the hull were locked with mesh sieves of 710 µm. The locked hull was put into a conventional disintegration apparatus according European Pharmacopoeia (Ph.Eur.) and weighted with a hull made of metal (Figure 2).

Content uniformity was analyzed using HPLC according to European Pharmacopoeia 9 (Ph.Eur. 2.9.6) and dissolution profile according to USP methods in 37.5 ± 0.5°C phosphate buffer pH 6.8 for EM and 0.1N HCL for HCT using a basket apparatus. The drug release was measured by UV-Vis spectrophotometry (Lambda 40, PerkinElmer). Tensile strength was analyzed using a Texture Analyser (Stable Micro Systems) with a flat punch of 5 mm in diameter and a pre speed of 0.1mm/s.

Figure 1. ODMT based on galenIQ™721

Figure 2. Modified disintegration basket

RESULTS AND DISCUSSION

Disintegration time [s], mean ± SD					
Without disintegrants		**Kollidon CL**		**Kollidon CL-SF**	
HCT	EM	HCT	EM	HCT	EM
105 ± 46	51 ± 25	38 ± 34	9 ± 2	8 ± 6	20 ± 9

Table 1. Disintegration times of ODMTs in 37.5 ± 0.5°C demineralized water, n=6

ODMTs based on galenIQ™721 were produced successfully. Mechanical properties of the ODMTs were acceptable and the content uniformity requirements according Ph.Eur. 2.9.4 were achieved for all formulations.
It was feasible to produce ODMTs without disintegrants to fulfill the requirements of Ph.Eur. regarding disintegration time. Even better results were obtained when using disintegrants (Table 1). The use of the modified method proved to be a promising tool for analyzing the disintegration of minitablets. A further advantage is the adaptability to the disintegration apparatus of the Ph.Eur. Dissolution studies showed full drug release of EM-ODMTs within 20 minutes. HCT-ODMTs show 60% drug release within one hour fulfilling USP criteria for HCT (Figure 3 and 4). The differences in the dissolution profiles can be explained by the dissolution rate of the drug in the media and influence of the excipients.

In further studies ODMTs based on galenIQ™721 with HCT and EM will be compared to existing formulations for ODMT. Furthermore, content uniformity according to Ph.Eur. 2.9.40 should be obtained.
Stability data will be collected and analyzed regarding disintegration, tensile strength and dissolution.

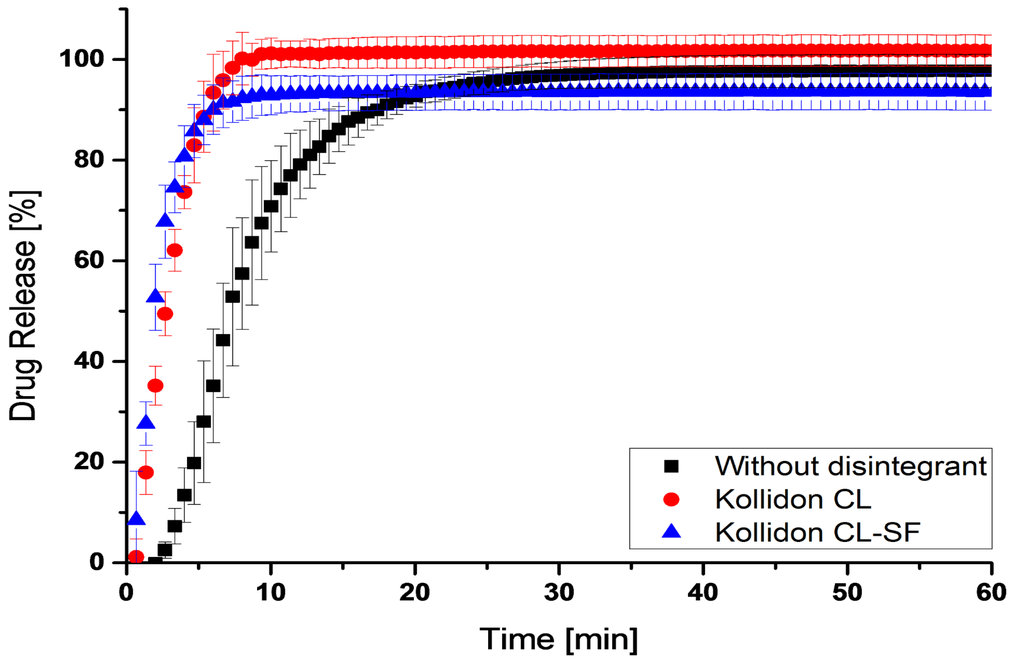

Figure 3. Dissolution profile of EM ODMT; n=6, mean ± SD

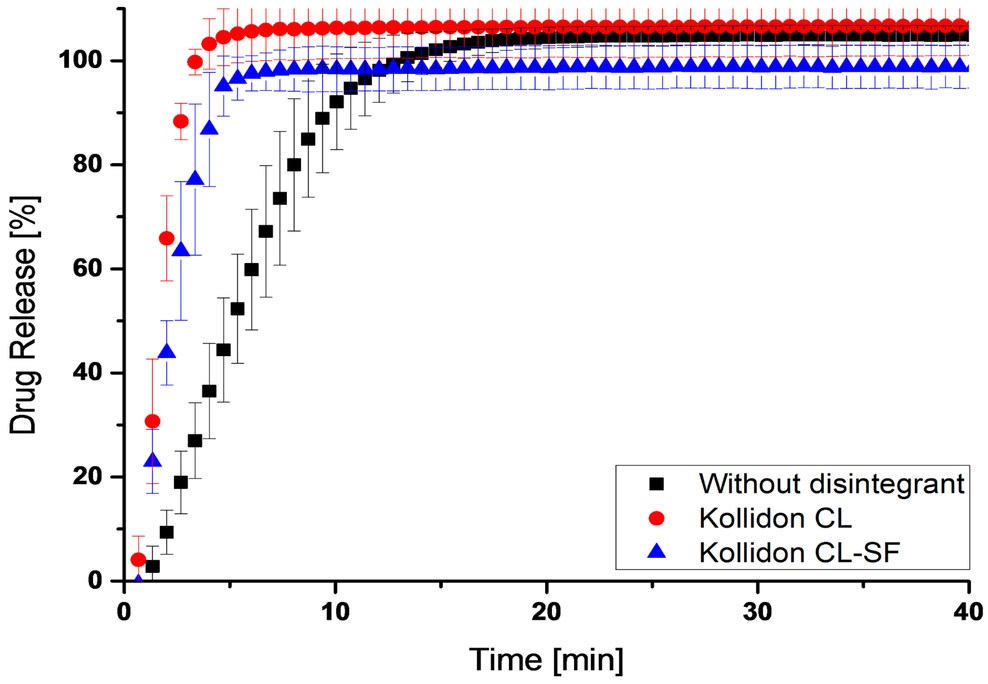

Figure 4. Dissolution profile of HCT ODMT; n=6, mean ± SD

CONCLUSION

For the first time ODMTs based on galenIQ™721 were developed successfully by direct compression. Acceptable disintegration times and dissolution profiles as well as good mechanical properties of the minitablets indicate the suitability of galenIQ™721 for the production of ODMTs. Furthermore, the palatability and non-cariogenic properties of galenIQ™721 can have a benefit for pediatrics [4].

References: [1] Klingmann, V. , Spomer, N., Lerch, et.al. (2013) J.Pediatr. 163, 1728-1732.e.1.
[2] www.who.int/medicines/publications/essentialmedicines/6th_EMLc2017_FINAL_amendedAug2017.pdf?ua=1 (20.05.18)
[3] Stoltenberg, I. Orodispersible Minitabletten-Entwicklung und Charakterisierung einer neuen Darreichungsform für die Pädiatrie, doctoral thesis, Heinrich-Heine-University, Düsseldorf (2012)
[4] www.galeniq.com/galenIQ_Grades/galenIQ721/ (26.04.18.

10th EuPFI Conference 12th – 13th September 2018 London, United Kingdom