Macedonian pharmaceutical bulletin, 69 (Suppl 1) 191 - 192 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.094
Short communication

Preparation and characterization of Glucomannan granules with controlled swelling properties

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Introduction

European authorities are recognizing obesity as chronic metabolic disease with serious consequences (European Court of Justice, 2014). Therefore, a proper management of this disease is needed, where diet is among the most important (Yumuk et al., 2015).

Glucomannan (GLM) is a water-soluble, fermentable dietary fiber which can absorb up to 50 times its weight in water. Due to the swelling properties, GLM is approved as a food for weight loss (Yakubu et al., 2023). However, regarding these characteristics it is highly hygroscopic, which is a problem for its production as dosage form and can affect its stability (Enomoto-Rogers et al., 2013). Therefore, the challenge is to improve the hygroscopic properties of GLM without affecting it's *in vivo* swelling abilities. Literature data suggests several approaches for overcoming the aforementioned issues, *i.e.* by using ethanol for granulation (Tatirat, et al., 2013) or coating of GLM particles with different types of moisture protective polymers (Zhao et al., 2015).

The purpose of this work was to prepare and characterize GLM particles/granules for oral administration using fluid-bed technique in an order to understand the interactions taking place between KLM and granulation agent/polymer, thus affecting their swelling behaviour in water and stomach acid conditions.

Materials and methods

Konjac mannan, glucomannan (GLM, mol. weight 80.000-120.000 Da) was obtained from Straqim S.A., Switzerland, ethanol (96% *v/v*) was purchased from Alkaloid Skopje, N. Macedonia and Eudragit E PO (EPO) was provided from EVONIK Ind., Germany. All other chemicals used were of pharmaceutical grade and were used without further modifications.

Raw GLM was granulated or coated in VFC Lab Micro Fluid bed, Freund-Vector Corporation, USA using ethanol as granulating solvent (sample G-E) or 4% coating ethanolic EPO solution (sample G-EPO). Fluid-bed granulation was performed under the following working conditions: air flow 17 LPM; inlet temperature 45 °C; nozzle air 75 mBar; pump speed 12 rpm and granulation time of 10 min/cycle. For G-EPO, Wurster fluid-bed coating was used under the same process parameters except the pump speed of 10 rpm.

Raw GLM was characterized for mean particle size and particle size distribution (SPAN factor) (Mastersizer 2000, Malvern Instruments Ltd., UK), moisture content (MA100 Moisture Analyzer, Sartorius, Germany), bulk and tapped density (Tapped volumeter, Ph.Eur. method 2.9.34) and compressibility index and Hausner's ratio (calculated values). Viscosity of 1% solution of GLM in purified water and 0.1M HCl pH 1.2 was measured after 1h of samples preparation (Rheometar MCR 92, Anton Paar GmbH, Austria). Prepared granules (samples G-E and G-EPO) were evaluated for mean particle size and particle size distribution (Mastersizer 2000, Malvern Instruments, K). A FT-IR spectrometer (Varian 660 FT-IR, Varian Instruments, USA) was used to record the infrared spectra

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of the GLM and G-EPO using the MIRAcle module with ZnSe crystal and micrometer clamp for low pressure recording under attenuated total reflection (ATR). The spectra were recorded in the range of 4000 - 550 cm^{-1}. Having in mind that the water uptake is an important physiochemical process that ultimately influences the GLM *in vivo* effects, the swelling behavior in purified water and 0.1M HCl pH 1.2 during the period of 15 min was evaluate for all prepared samples. Swelling behaviors of prepared granules were calculated through swelling index (Si %) = [(Dt-Do)/Do]*100), where Dt represents the diameter achieved at defined time point and Do is the initial diameter of raw GLM..

Results and discussion

Main characteristics of GLM as a starting active ingredient are presented in Table 1.

Table 1. Main characteristics of GLM as raw material

Raw GLM	Characteristics
Mean size (D_{50}, µm)±SD	305.4 ±1.16
SPAN factor±SD	1.039±0.0059
Moisture (%)±SD	4.52±0.17
Viscosity in water (mPa·s)	3113
Viscosity in 0.1M HCl (mPa·s)	1872
Bulk density (g/ml)	0.848
Carr index (%)	7.0
Hausner ratio	1.08

After the fluid-bed granulation process with ethanol (sample G-E), no significant differences were observed in mean particle size and size distribution (D_{50} 300,3 µm±2.19 and SPAN factor of 1.08±0.0061) in comparison with the raw GLM. Also, this process did not result in prolonged swelling time (Fig. 1). On the other hand, particles coated with EPO (sample G-EPO) showed significant increase in the mean size (D_{50} 699 µm±9.35) with unimodal narrow distribution (SPAN factor 1.24±0.03).

The coated sample's FTIR spectrum showed similarity to the EPO spectrum and absence of the characteristic GLM bands, thus indicating that the surface of the primary GLM particles were fully coated with EPO polymer. Additionally, sample G-EPO showed significant decreased swelling behavior in purified water and delayed swelling in 0.1 M HCl pH 1.2, compared to those of GLM and G-E (Fig 1).

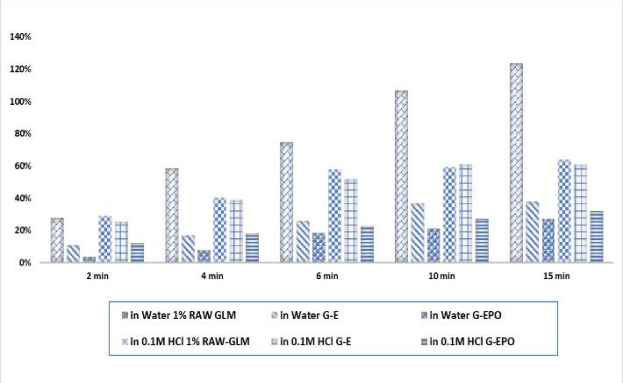

Fig. 1. Swelling index of different samples during time.

Conclusion

From the obtained results it can be concluded that the GLM fluid-bed granulation with ethanol did not show any significance changes in the main characteristics of the basic raw material. Wurster coating of GLM with EPO showed significantly decreased swelling in water and delayed swelling in HCl, thus suggesting the possibility of improvement of the main characteristic of this dietary fiber in one hand, and fulfill its therapeutic/dietary properties on the other hand.

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