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Formulation and characterization of hard gelatin capsule with apple lyophilisate

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Introduction and Methods

The aim of our study was to model hard gelatin capsules with lyophilized apple powder by using different excipients and to evaluate the release kinetics of phenolic compounds.

METHODS

Object of study the cultivar 'Ligol' of apple. The slices of apples were lyophilized. The samples of apples extracted with 70% (v/v) ethanol in the ultrasonic bath for 20 min. at room temperature.

The capsule dissolution test was performed using a dissolution tester. The acceptor medium was an ethanol-water mixture at the ratio of 1:1, the volume 250 ml. The temperature being $37.0 \pm 0.5^\circ\text{C}$. The samples were taken after 15, 30, 60, 75 and 90 min.

The capsule disintegration medium was 0.1 M hydrochloric acid solution, temperature $37 \pm 0.50^\circ\text{C}$, observed for 30 min.

Phenolic compounds analysis was performed by HPLC method (Waters 2998 PDA detector, YMC-Pack ODS-A (5 μm , C18, 250 \times 4.6 mm i.d.) column. The mobile phase consisted of 2% (v/v) acetic acid (solvent A) and acetonitrile (solvent B). Gradient variation: 0–30 min 3–15% B, 30–45 min 15–25% B, 45–50 min 25–50% B, and 50–55 min 50–95% B.

Results

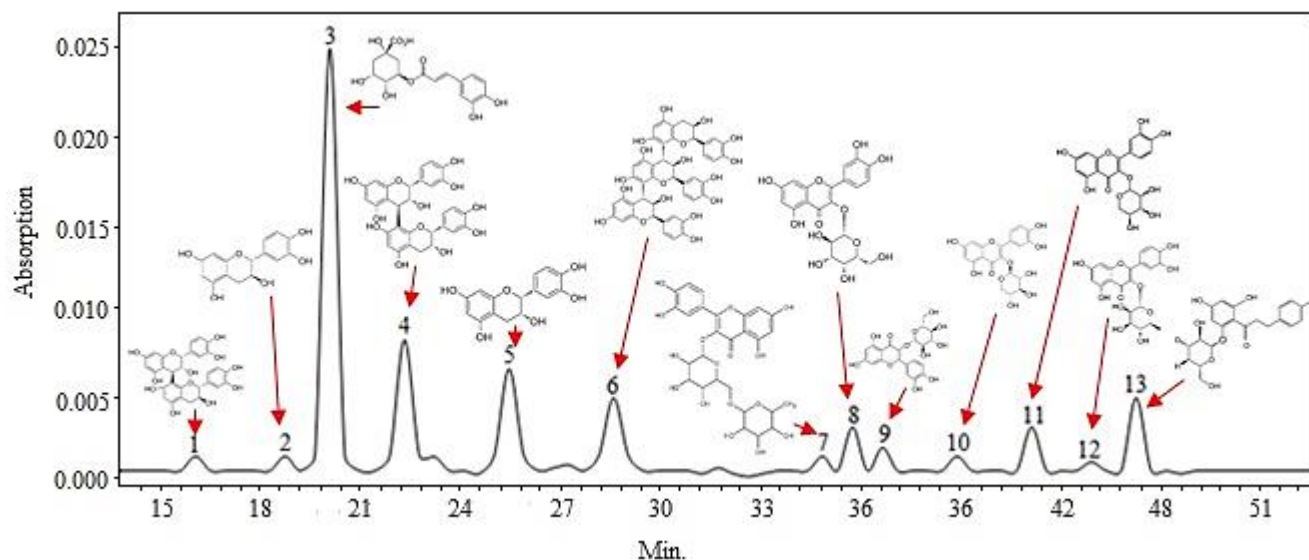


Figure 1. Chromatogram of the ethanol extract of the apple lyophilisate. Analytes determined at $\lambda=280$ nm wavelength: 1-procyanidin B1; 2-(+)-catechin; 3-chlorogenic acid; 4-procyanidin B2; 5-(-)-epicatechin; 6-procyanidin C1; at $\lambda=360$ nm wavelength: 7-rutin; 8-hyperoside; 9-isoquercitrin; 10-reynoutrin; 11-avicularin; 12-quercitrin; at $\lambda=280$ nm wavelength: 13-phloridzin

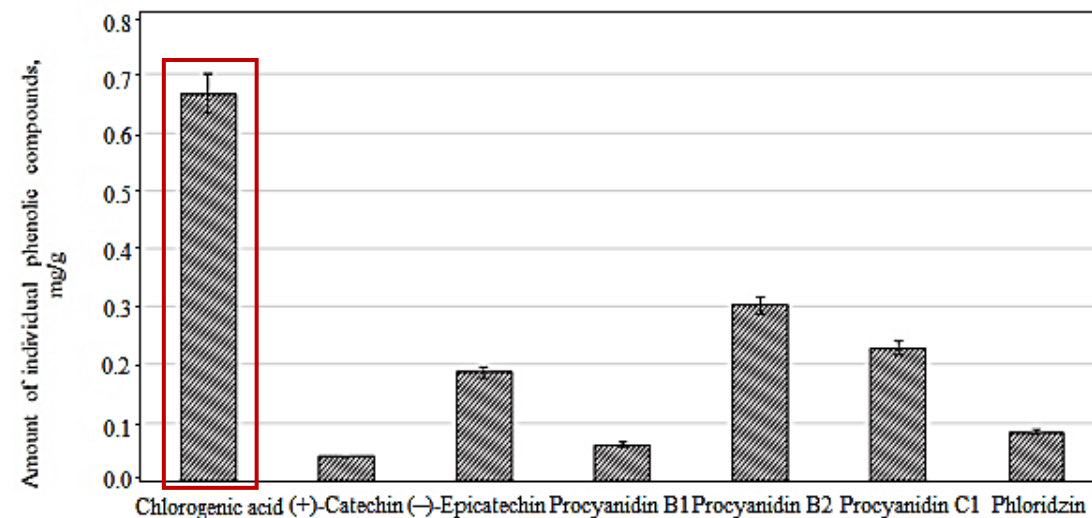


Figure 2. The amount of individual flavan-3-ols, phloridzin, and chlorogenic acid in ethanol extracts obtained from the apple fruit of the "Ligol" cultivar grown in Lithuania

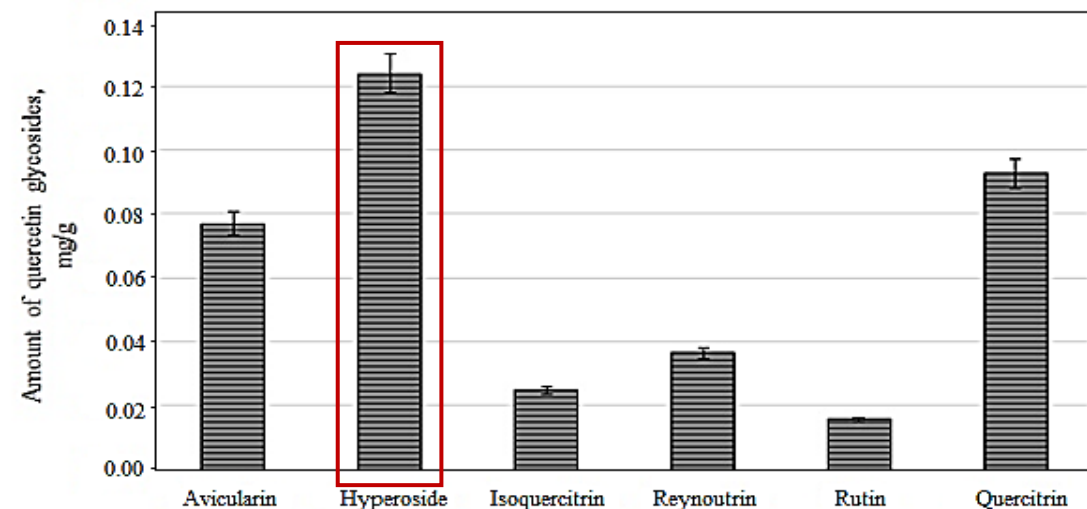


Figure 3. Concentration of individual quercetin glycosides in ethanol extracts obtained from the fruit of the "Ligol" apple cultivar grown in Lithuania.

Results

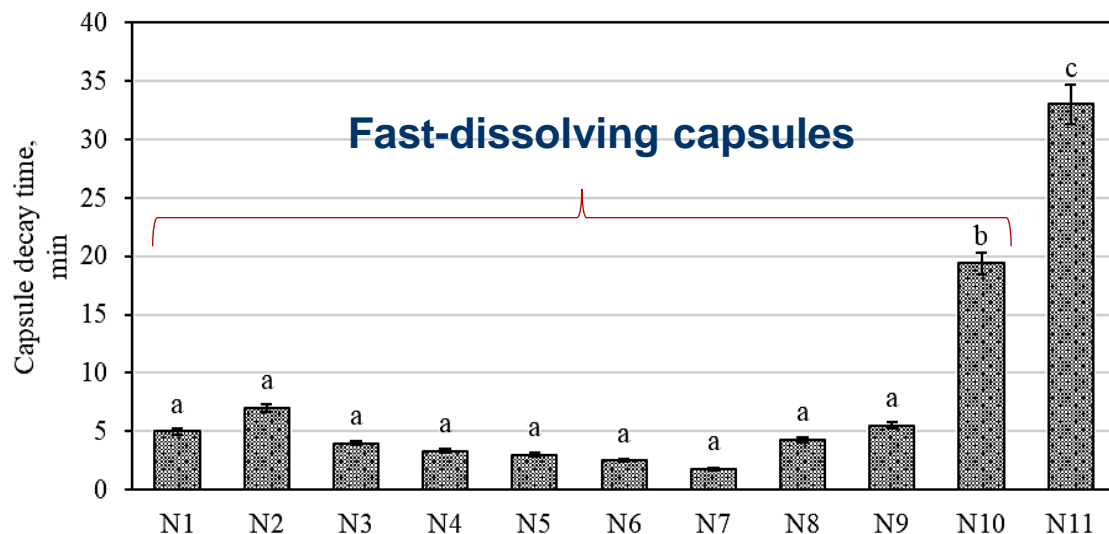


Figure 4. Results of the capsule disintegration test. The means followed by different letters are significantly different at $p < 0.05$.

Table 1. Results of the *in vitro* dissolution test after 30 min. The means followed by different letters in the columns are significantly different at $p < 0.05$.

	Chlorogenic acid	Rutin	Hyperoside	Isoquercitrin	Quercitrin	Avicularin	(-)-Epicatechin	Phloridzin
CC	µg/mL							
N1	372.5 ^B	160.0 ^B	144.5 ^B	7.0 ^A	97.5 ^B	149.0 ^B	17.5 ^A	122.5 ^B
N2	367.5 ^B	157.5 ^B	140.0 ^B	6.0 ^A	89.5 ^B	142.5 ^B	9.5 ^B	117.5 ^B
N3	372.5 ^B	149.5 ^B	139.0 ^B	7.5 ^A	91.5 ^B	148.5 ^B	10.0 ^B	121.5 ^B
N4	367.5 ^B	152.5 ^B	140.5 ^B	5.5 ^A	92.5 ^B	142.0 ^B	14.5 ^A	125.0 ^B
N5	385.0 ^B	155.0 ^B	132.5 ^B	4.9 ^A	87.5 ^B	141.5 ^B	8.5 ^B	110.0 ^B
N6	589.5 ^A	265.6 ^A	240.4 ^A	5.0 ^A	170.7 ^A	253.7 ^A	6.3 ^{B,C}	140.5 ^A
N7	640.3 ^A	268.3 ^A	241.8 ^A	4.9 ^A	166.5 ^A	254.3 ^A	10.2 ^B	119.9 ^B
N8	167.9 ^C	62.1 ^C	60.9 ^C	2.3 ^B	40.3 ^C	61.8 ^C	1.2 ^D	50.6 ^C
N9	128.3 ^C	60.8 ^C	59.6 ^C	2.3 ^B	39.4 ^C	59.6 ^C	1.1 ^D	49.5 ^C
N10	126.4 ^C	39.9 ^C	49.4 ^C	2.9 ^B	33.3 ^C	50.4 ^C	3.8 ^C	40.9 ^C
N11	68.4 ^D	32.4 ^D	31.7 ^D	1.2 ^C	21.0 ^D	31.8 ^D	0.6 ^D	26.4 ^D

Table 2. Results of the dissolution test for phenolic compounds released from the N1–N11 capsules after 30 min. The means followed by different letters in the columns are significantly different at $p < 0.05$.

Release content, %	Chlorogenic acid	Rutin	Hyperoside	Isoquercitrin	Quercitrin	Avicularin	(-)-Epicatechin	Phloridzin
N1	96.0 ^A	94.0 ^A	88.0 ^A	85.0 ^A	80.0 ^A	90.0 ^A	83.0 ^A	97.0 ^A
N2	94.0 ^A	92.0 ^A	87.0 ^A	84.0 ^A	82.0 ^A	92.0 ^A	80.0 ^A	95.0 ^A
N3	95.0 ^A	85.0 ^A	89.0 ^A	81.0 ^A	80.0 ^A	90.0 ^A	81.0 ^A	94.0 ^A
N4	97.0 ^A	90.0 ^A	89.0 ^A	83.0 ^A	85.0 ^A	88.0 ^A	83.0 ^A	92.0 ^A
N5	94.0 ^A	88.0 ^A	90.0 ^A	85.0 ^A	80.0 ^A	92.0 ^A	85.0 ^A	96.0 ^A
N6	95.0 ^A	96.0 ^A	90.0 ^A	84.0 ^A	84.5 ^A	92.0 ^A	81.0 ^A	94.0 ^A
N7	90.0 ^A	92.0 ^A	88.0 ^A	80.0 ^A	83.0 ^A	91.0 ^A	82.0 ^A	92.0 ^A
N8	55.0 ^B	52.0 ^B	53.0 ^B	35.0 ^B	38.0 ^B	47.0 ^B	35.0 ^B	50.0 ^B
N9	52.0 ^B	55.0 ^B	56.0 ^B	34.0 ^B	37.0 ^B	40.0 ^B	34.0 ^B	54.0 ^B
N10	50.0 ^B	39.0 ^B	42.0 ^B	29.0 ^B	30.0 ^B	40.0 ^B	29.0 ^B	47.0 ^B
N11	29.0 ^C	26.0 ^C	29.0 ^C	19.0 ^C	18.0 ^C	27.0 ^C	19.0 ^C	28.0 ^C

Conclusions

Hypromellose prolonged the disintegration time of the modeled capsules when its amount reached 50–83% of the capsule weight.

The selected fillers did not affect the kinetics of the release of the phenolic compounds from the capsules.

Based on the results of the dissolution test, the capsules can be classified as fast-dissolving preparations since more than 85% of the active substance was released within 30 min.

Chlorogenic acid was the compound that was released in the highest amounts from capsules of different encapsulating content: its released amounts ranged from 68.4 to 640.3 $\mu\text{g}/\text{mL}$.

The results of the solubility and disintegration tests proved that the capsules of the proposed composition are appropriate for internal use. The proposed product could serve as a basis for the development of food supplements with lyophilized apple powder.