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Ascorbic acid encapsulation in a glassy carbohydrate matrix via hot melt extrusion: Preparation and characterization

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Abstract

Hot melt extrusion technology using a twin-screw extruder was employed to obtain maltodextrin, maltodextrin-gum arabic and maltodextrin-trehalose based glassy extrudates containing ascorbic acid (dispersed phase). Ascorbic acid payload of all three formulations was more than 15.67 g/100 g extrudates while the ascorbic acid yield was above 97%. The glass transition temperature (T*g*) of all extrudates was above 40 °C. The expansion ratio of the extrudates and T*g* reduced due to the incorporation of trehalose and gum arabic to maltodextrins, respectively. The results of Scanning Electron Microscopy, X-ray diffraction and Fourier-transform Infrared Spectroscopy confirmed that the formulated feed material turned into a glassy state, whereas, ascorbic acid was uniformly dispersed throughout the glassy matrix. Extruded formulations showed a steady dissolution rate, therefore, having a role in controlling the dissolution rate of ascorbic acid.

Keywords: ascorbic acid; encapsulation; melt-extrusion; maltodextrins; glass transition temperature.

Practical Application: Carbohydrate matrices in a glassy state offer protection to the encapsulated ascorbic acid in it, allowing the use of this vitamin in different food formulations.

1 Introduction

Ascorbic acid (AA) is a water-soluble compound which is essential for the normal regulatory functions of a human body. Humans have lost the ability to synthesize AA. Thus, AA must be obtained through the diet for healthy life. Although fruits and vegetables are good sources of AA, it is partially destroyed due to oxidation during post-harvest and processing conditions. To compensate this, food is often fortified with AA to meet Recommended Daily Allowances (Carr & Frei, 1999; Silva et al., 2018). However, benefits of fortification are spoiled by the fact that AA is highly unstable and interactive towards other food components, thus, destabilizing the whole food system.

Variety of encapsulation techniques has been introduced for the protection and delivery of AA, as reviewed by Abbas et al. (2012). Among these, hot-melt extrusion (HME) technology is being widely used by the pharmaceutical industry to preserve labile bioactives, including AA (Gouin, 2004; Chang et al., 2010; Tackenberg et al., 2014; DiNunzio et al., 2016). HME is a continuous and cost-effective process that involves feeding polymeric materials to extruder with a rotating screw at temperatures above their glass transition temperature (T_g). The basic idea behind this technique is to exploit the T_g of carbohydrates in which the active agents (gas, liquids, solids) are dispersed or dissolved. Therefore, HME can be used to encapsulate unstable bioactives in glassy carbohydrate matrices (Yılmaz et al., 2001; Chang et al., 2010; Emin et al., 2012; Emin & Schuchmann, 2013; Chuah et al., 2014; Al-Kasmi et al., 2017).

However, to our knowledge, no work has been reported to produce maltodextrin-gum arabic and maltodextrin-trehalose based glassy matrices (through HME technology) for the encapsulation of AA. Therefore, aim of the present study was to develop new carbohydrate blends and to investigate their influence on the solid state of the processed matrices for AA encapsulation. In this context, major objective is to stabilize AA in carbohydrates matrices prepared from biopolymer-based novel formulations. We hypothesize that the glassy matrices of selected carbohydrate material may offer improved barrier properties to dispersed AA, thereby, decreasing the chance of unwanted interactions of AA with its environment. This acquired stability would allow food processors to use encapsulated AA as a fortificant in different food formulations.

2 Material and methods

2.1 Materials

Maltodextrins of DE 10-15 was obtained from Baolingbao Biology Co., Ltd, Yucheng, China. Hangzhou Jinchengzhuji Co., Ltd, Hangzhou, China provided the medium chain triglycerides (decanoic acid ester with 1, 2, 3-propanetriol octanoate). Soy lecithin was the product of Solae Company, US. Ascorbic acid was purchased from CSPC Pharmaceutical Group Lid, Shijiazhuang, China. CNI provided gum arabic while Hayashibara Co., Ltd, Okayama, Japan supplied trehalose. All other chemicals were of analytical grade (Sinopharm Chemical Reagent (SCR) Co., Ltd, Shanghai, China).

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2.2 Material preparation and mixing process

Initially, oil-water emulsion was prepared for the development of each formulation. MCT was used as an oil phase while soy lecithin acted as an emulsifier. Briefly, oil phase was prepared by slowly adding the liquid emulsifier into MCT oil, while stirring continuously using a mixer (RW20 Digital, Germany) at 200 rpm for 5 minutes at room temperature. To this mixture, distilled water was slowly added and stirred at 200 rpm for 30 minutes until the emulsion was formed. Next, the prepared emulsion was mixed with the rest of solid ingredients (maltodextrins, gum arabic, and/or trehalose) in a high-speed mixer (DFY-500, China) for 1 min at 10,000 rpm to ensure the uniform dispersion of ingredients. MCT in the formulation was meant to enhance the melt rheology and slippage of the molten mass during extrusion process. The composition of each formulation is shown in Table 1. Prior to extrusion, all formulations were passed through a 30-mesh screen sieve to remove lumps.

2.3 Extrusion trials

Experiments were performed using a co-rotating twin-screw extruder (Die diameter: 3 mm) consisting of four barrels with a length-to-diameter ratio of 24 with intermeshing screws (HAAKE PolyLab System, PTW24/25D, USA). The obtained premix in each formulation were fed into the extruder inlet port by a screw feeder (DDSR20N-PRISM, Germany). The measuring feeder was set to obtain a flow rate of 1.1 kg h-1 of feed mixture and screw speed was maintained at 60 rpm for all the runs. For all experiments, temperature along the extruder barrel was set at 85 °C (zone 1), 105 °C (zone 2), 120 °C (zone 3) and 105 °C (zone 4), respectively. The barrel section's temperature and die head pressure, torque, torque percent, material temperatures between zone 2 and zone 3 (TM1), material temperature between zone 3 and zone 4 (TM2) of extruded material for each formulation were recorded to assess the ease of extrusion. After extrusion, the obtained extrudates were subsequently air-cooled at room temperature and crushed at 6000 rpm in a centrifugal mill (Retsch ZM 200, Haan, Germany). The powder was divided into three fractions (<20 mesh, 20-40 mesh and >40 mesh) by sieving and stored for further analysis.

2.4 Differential scanning calorimetry

A device equipped with a nitrogen cooling system (PerkinElmer Pyris 1, US) was used to record the differential scanning calorimetry (DSC) curves. Ultrahigh purity nitrogen was used as the purge gas at a flow rate of 20 mL/minute. Samples (around 10 mg) were pre-sealed into aluminum pans of 40 μL before thermal analysis. Samples were first heated at 10 °C/minute to 90 °C. The glass transition range was determined, and T*g* midpoint was taken as the characteristic value. All determinations were performed in duplicate, and an empty pan served as reference.

Table 1. Composition (%, w/w) of each formulation prepared for extrusion.

	Composition (%)		
	Formulation 1	Formulation 2	Formulation 3
Maltodextrin	80.5	78.5	70.5
Gum Arabic	-	-	10
Trehalose	-	2	-
AA	16	16	16
MCT	1	1	1
Added Water	2	2	2
Soya Lecithin	0.5	0.5	0.5
Total	100	100	100

2.5 Moisture content

The extruded samples were ground into powder. Moisture analysis was performed using "loss on drying instrument." The pre-weighed samples were placed on the aluminum pans and the drying was performed at 130 °C under atmospheric pressure for 165 minutes (Massaux et al., 2008). The percent weight loss of the samples was recorded as the percent moisture content.

2.6 Determination of AA

Iodometric titration method was used to determine the AA content. Starch solution (0.5%) acted as an indicator. Sodium thiosulphate ($Na_2S_2O_3$) solution (0.07M) was prepared and standardized with 50 mL of 0.01M pure potassium iodate containing 2 g of solid potassium iodide. Iodine solution (0.05M) was prepared and standardized with the standard sodium thiosulphate solution (0.07M).

Distilled water (100 mL), 2 mol/L acetic acid (1 mL) and starch solution (2 mL) added into the 250 mL conical flask. The 0.2 g powder of each extrudate in triplicates, added into the conical flask and dissolved. The prepared solution was titrated with the standard iodine solution to a stable blue end-point using freshly prepared starch solution. One mL of 0.05M iodine was equivalent to (8.806 mg) of ascorbic acid. The results were the average of the triplicates in each sample.

2.7 Expansion properties

Radial expansion was determined by measuring the diameter of extrudates through digital calipers. Expansion ratio was calculated as the extrudate diameter divided by the die diameter. The results were the average of the twenty readings in each sample (Yuliani et al., 2006; Milani et al., 2014).

2.8 Scanning Electron Microscopy (SEM)

Electron microscopy (QUANTA-200, PHILIPS, Netherlands) conducted to observe the cross sections of extrudates, under high vacuum and operating potential of 5 kV. The prepared specimens previously coated with a thin gold layer.

2.9 AA yield of the extruded product

AA yield of extrudate was calculated as the amount of AA in extrudate divided by the amount of AA added in initial formulation prior to extrusion.

2.10 X-ray diffraction analysis

A D-8 Advance X-ray Diffractometer (Bruker AXS) was used for X-ray diffraction (XRD) analysis. The generator voltage and current were 40 kV and 40 mA, respectively. The X-ray

pattern was collected in the angular range of 3°< 2θ< 70° in the step-scan mode with step width of 0.02° and scan rate of 4°/min.

2.11 Fourier-transform Infrared Spectroscopy (FTIR)

Nicolet Nexus 470 FTIR spectrometer (Nicolet American) helped to obtain the FTIR spectra of AA, maltodextrins, premix material and extrudates. Hydraulic press was helpful in compressing the Sample-KBR-blends into KBr disks.

2.12 Dissolution testing

Dissolution testing was performed using the reciprocating cylinder method (modified USP Apparatus 2, paddle), in 900 mL of 0.1 N HCl, at rotation of 125rpm. The temperature of the medium (900 mL) was kept at 37 ± 0.5 °C and all experiments were run in six replicates. Samples of 5 mL were withdrawn at appropriate time intervals and immediately replaced by a fresh dissolution medium. The amount of AA released from milled extrudates was quantified by Iodimetric titration method.

2.13 Storage trial

The extrudates were ground into powder and 20 g powder of each extrudate was put into 250 mL air-tight glass bottle and sealed. Afterwards, the samples were stored at 40 °C for 3 months to analyze their storage stability.

2.14 Statistics

Data were analyzed using Microcal Origin V.7.0 software (Microcal software, Northampton, USA).

3 Results and discussion

3.1 Effect of the formulations on the extrusion processing parameters

In the glassy carbohydrates, the low water content is needed to guarantee a T_g above 40 °C at constant formulations while the extruder must work with high viscosity systems and provide considerable mixing. As given in Table 2, the torque percent of the premix materials ranged 13.82-15.09%, which were found to be desirable for the extrusion of the formulations. Incorporation of trehalose to the maltodextrins could decrease the torque during extrusion, making extrusion more efficient. Die head pressures ranged from 10.56 to 13.19 bar, which is higher than that previously observed (~ 6.89 bar) in the flavor encapsulation studies. In the current work, temperature of the hot molten material ranged 108.73 °C to 111.92 °C and residence time of material in the extruder was less than 3 minutes for all the samples (not shown in the Table).

Similar temperature conditions were recorded when sunflower oil-starch material was extruded (Yılmaz et al., 2001) in which the mix was treated at lower temperatures (less than 115 °C) compared to spray drying.

3.2 Effect of the formulations on the physical characteristics of the extrudates

AA content, moisture, AA yield, T_g and expansion ratio of the extrudates were recorded (Table 3).

As shown, AA yield of all samples was above 97%, which indicated that this method can be employed to encapsulate AA with minimal losses as compared to other contemporary techniques (Desai & Park, 2005; Pierucci et al., 2006). The Tg of glassy matrices determines its chemical stability, and physical stability, as well as viscoelastic properties (Hancock & Zografi, 1994; Li et al., 2018).

It is believed that chemical stability of active materials is a direct function of the T_g of the dried product (Hatley & Blair, 1999; Li et al., 2018). In our formulation, both water and AA are the potent plasticizers for extruded glassy products, which indicated that water content and AA loading percentage compromised the stability of extruded material. Maltodextrins based extrudate containing 15.59% (w/w) of AA at 6.28% (w/w) water level showed T_g of 44.84 °C. The incorporation of trehalose reduced the T_g while gum arabic had a slight effect on T_g. All formulations had a low expansion ratio while the gum arabic-based extrudates offered reduced expansion ratio. Higher expansion ratio is undesirable as it is linked to the increased hygroscopicity of the extruded material.

Table 2. Pressure, torque, torque percent and material temperature in the extruder (TM1, TM2) during production of glassy extrudates using different formulations at the same processing conditions.

Series	*Torque (Nm)*	*Torque percent (%)*	*TM_1 (°C)*	*TM_2 (°C)*	*DHP[a] (bar)*
Formulation 1	25.04±1.30	14.73±0.77	109.39±0.21	111.92±0.38	10.56±2.92
Formulation 2	23.49±1.15	13.82±0.68	109.33±0.24	111.38±0.11	12.76±2.88
Formulation 3	25.65±1.44	15.09±0.84	108.73±0.22	111.52±0.07	13.19±3.11

Note: Results were means±SD of all the data recorded during extrusion; [a] Die Head Pressure.

Table 3. AA content, moisture, AA yield, T_g and expansion ratio of the extrudates.

[A]Series	*Water content of the extrudate (%)*	*AA yield (%)*	*AA content (g/100g extrudate)*	*T_g (°C)*	*Expansion ratio*
1	6.28	98.50	15.96	44.84	1.125
2	6.57	98.36	15.89	40.89	1.127
3	6.59	97.02	15.67	43.02	1.098

[A]1, 2, 3 represents the formulation 1, formulation 2 and formulation 3, respectively.

3.3 X-ray diffraction analysis

XRD studies helped to confirm whether the crystalline structure of the extruded AA was retained. The X-ray diffractograms of pure AA, premixed mixture of formulation 1, extruded products of formulation 1, 2, 3 after extrusion, extruded products of formulation 1, 2, 3 after 3 months storage at 40 °C are given in Figure 1. The characteristic crystalline peaks of AA were obtained at 2θ of 10.3, 14.09, 17.3, 25.24, 40.29, 48.19 and 54.3.

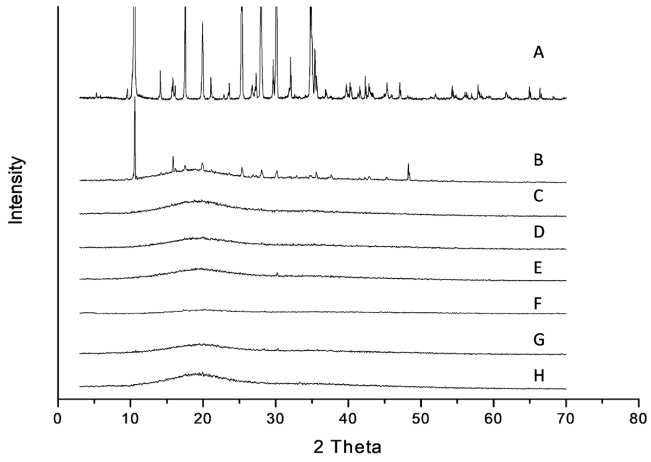

Figure 1. XRD spectra of (A) pure AA, (B) premix of formulation 1 (C) extruded product of formulation 1 (D) extruded product of formulation 2 (E) extruded product of formulation 3 (F) extruded product of formulation 1 after 3 months storage at 40˚C (G) extruded product of formulation 2 after 3 months storage at 40˚C, (H) extruded product of formulation 3 after 3 months storage at 40˚C.

In addition, prepared premix of materials also exhibited the crystalline peaks (Figure 1B). While any characteristic crystalline peaks of AA were not observed in the extruded products, which indicated that AA was dispersed at the molecular level in the carbohydrate matrices. In a similar study, ketoconazole was dispersed in the extruded matrix (Dong et al., 2008). After storage at 40 °C for 3 months, no recrystallization could be detected in the milled extrudates, thus, indicating a good physical stability.

3.4 FTIR analysis

The FTIR spectrograms of pure AA, maltodextrin, premix of formulation 1, and extruded products of formulation 1, 2, 3 are shown in Figure 2. The characteristic peaks of pure AA were obtained at 1025, 1321, 1661, 1747, 3315, 3409 and 3525 cm-1 (Figure 2A). The peaks at 3525, 3409, 3315, 3216 cm-1 were assigned to the O-H stretching vibration.

In the spectrum of the carbohydrates/AA extrudates, the peaks corresponding to O-H stretching of AA become diffused and broadened (Figure 2D, 2E, 2F), which indicated that the formulation was in an amorphous form, and no significant chemical changes occurred. These findings were corresponding to that of extrudates containing celecoxib compound (Chawla et al., 2003; Sarode et al., 2013; Malaquias et al., 2018).

3.5 Scanning electron microscopy

The SEM images of the cross-section morphology of the extrudates are displayed in Figure 3. It was found that the pure AA existed as crystals with sharp edges (Figure 3A). The images

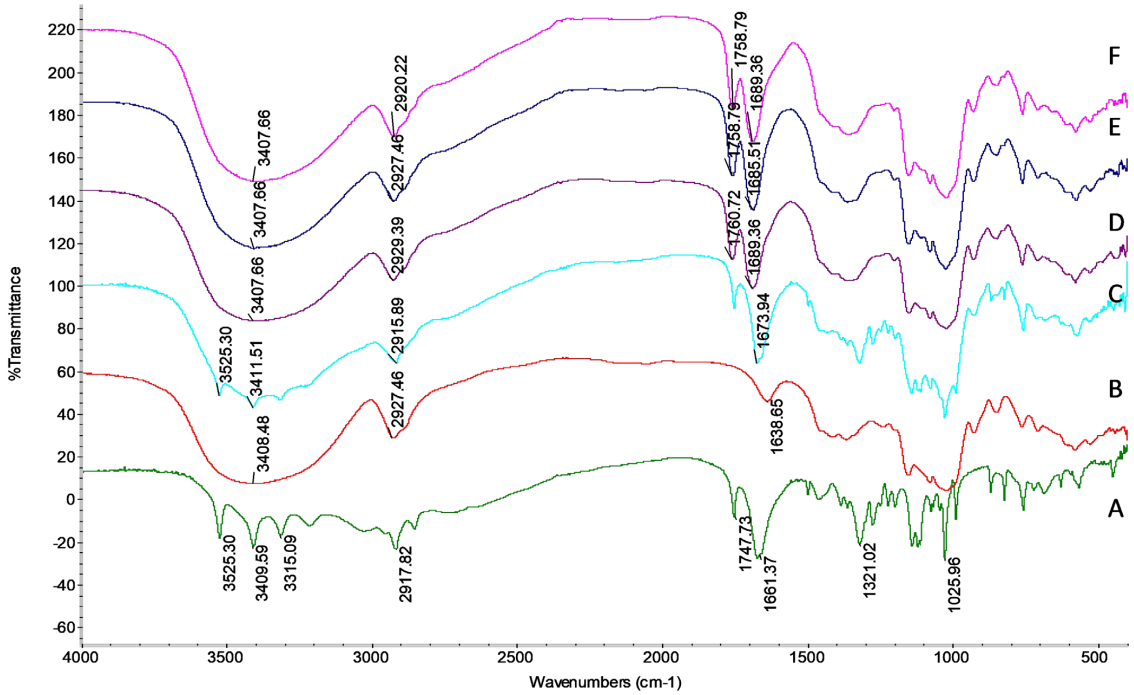

Figure 2. FTIR spectra of (A) pure AA (B) maltodextrin (C) premixed mixture of formulation 1 (D) extruded product of formulation 1 (E) extruded product of formulation 2 (F) extruded product of formulation 3.

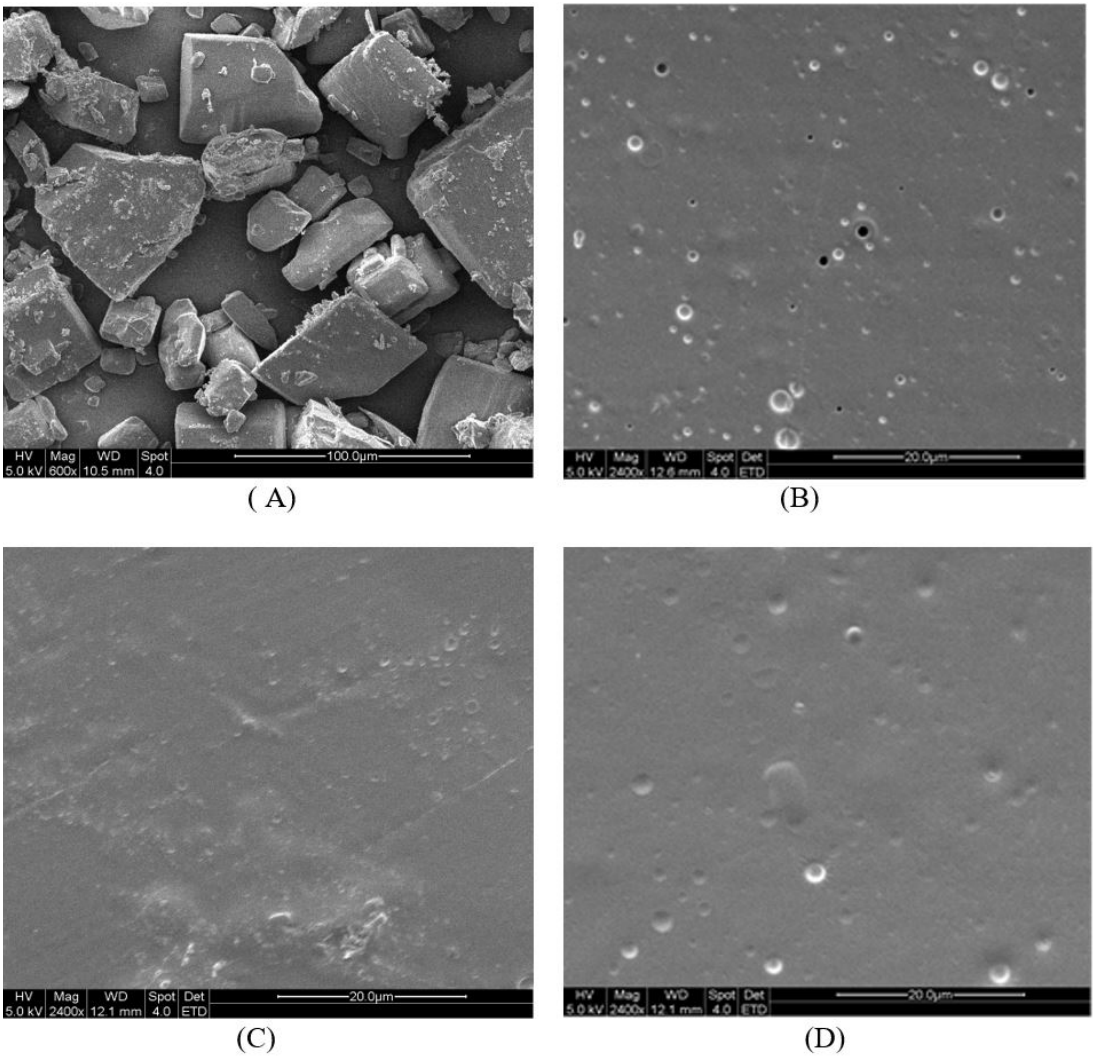

Figure 3. (A) SEM micrographs of the pure AA powder (B) Cross section morphology of the extrudates of formulation 1 (C) Cross section morphology of the extrudates of formulation 2 (D) Cross section morphology of the extrudates of formulation 3.

of all AA loaded extruded glassy products showed that there was no difference among them and did not reveal crystallization of AA (Figure 3B, 3C, 3D). It could be concluded that the AA was most likely molecularly dispersed within the carbohydrates suggesting AA/carbohydrates miscibility. This could be explained by the fact that if AA is in its crystalline form, the cross-section of the extruded glassy products would not have been smooth when viewed with SEM.

3.6 Dissolution behavior of the extrudates

The molecularly dispersed state of the AA might also attribute to the good content uniformity of the extruded glassy products. The SEM result was consistent with the results obtained from XRD and FTIR studies. These results agree with those reported previously in pharmaceutical formulation (Repka et al., 2003; Mididoddi & Repka, 2007; Jaiswar et al., 2016). Dissolution profiles of three milled extrudates with particle size range of 20-40 mesh are shown in Figure 4.

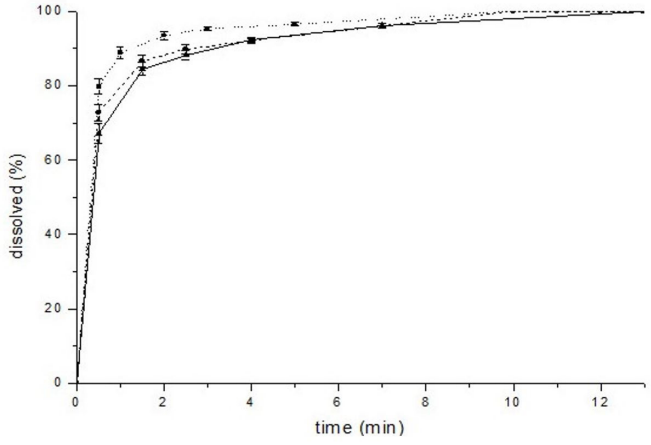

Figure 4. Dissolution profiles of milled extrudates which particle size in the range of 20-40 mesh. formulation 1 (dash line); formulation 2 (dot line) and formulation 3 (solid line).

The pure AA was completely dissolved in less than 20 seconds (not shown). Results showed that three milled extrudates had a fast dissolution rate, and AA was completely dissolved within 10 min. Similarly, Cilurzo et al. (2008) reported that low DE maltodextrins formed fast dissolving films. However, there was difference in the initial release of AA for all three different formulations used. The higher the molecular weight material added to the maltodextrin, the lower dissolution rate of the initial release was. In polymer matrices, the release pattern depends mainly on the geometry of the system, the type of carrier material and the loading of the active agent (Pothakamury & Barbosa-Cánovas, 1995). To describe the drug release mechanism from solid dispersions, two sets of observations were made in this work: carrier-controlled dissolution and drug-controlled dissolution. For the carrier-controlled dissolution, the rate of release was controlled by the carrier and was independent of the drug properties (Albers et al., 2009). In our research work, the dissolution mechanism of the milled extrudates could be explained based on the carrier-controlled dissolution phenomenon.

4 Conclusion

In this study, maltodextrin, maltodextrin-gum arabic and maltodextrins-trehalose microencapsulated AA powders were successfully prepared using the HME technique. Results explained the behavior of AA dispersed in the encapsulating matrix. The nature of the wall matrix affected the physical characteristics of extrudates. For instance, the incorporation of small molecular weight carbohydrate (trehalose) could decrease the T_g, thus, making the extrusion processing more efficient. On the other hand, incorporation of high molecular weight carbohydrate (gum arabic) mainly reduced the expansion ratio. A significantly reduced dissolution rate of the maltodextrin-gum arabic and maltodextrins-trehalose microencapsulated powders compared to non-encapsulated AA suggests potentially good release profiles. FTIR, SEM and X-RD results proved that AA and carbohydrates were miscible, and they formed solid solution during the melt formation process. Overall, the extrusion technique employed in the study demonstrated that AA can be stabilized effectively in carbohydrate matrices. Results of this study also suggest that glassy matrices of maltodextrin-gum arabic obtained through HME can be extended to encapsulate other bioactives, including polyphenols.

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