Report

Amorphous-to-Crystalline Transformation of Sucrose

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The transformation of amorphous sugar in the form of lyophilized spheres into crystalline sucrose was studied. The lyophilisate, when exposed to moist atmospheres, picks up moisture to a constant weight. The amount of moisture addition is a function of relative humidity of the atmosphere and temperature. The loose "lyophilisate structure" collapses to form a denser amorphous phase ("hydrated amorphate"). After a lag time which varies with relative humidity of the atmosphere and temperature, the hydrated amorphate loses moisture (weight) and, in the process, forms crystalline sucrose. The phase nature of the hydrated amorphate is equivalent to an aqueous solution that is undersaturated with respect to crystalline sucrose. A model was developed for the lag time which accounts for the experimental results.

KEY WORDS: sucrose; rubbery state; amorphous sucrose; crystalline sucrose; amorphous-crystalline transformation.

INTRODUCTION

Amorphous sugar transformation have been previously studied (1,2). Sucrose is difficult to produce completely amorphously and converts to crystalline sucrose at rates that depend on the relative humidity and the temperature. In previous publications (3,4) the general pattern of transformation was described. Lyophilisate spheres that were placed so they did not touch one another in a moist atmosphere, absorbed moisture up to a certain level (1,2). Subsequently the sample loses weight again (Fig. 1), and the phase O-A is the stage where moist lyophilisate is formed, phase A-B is the stage where hydrated amorphate is formed, phase B-C is the lag time, and phase C-D is the phase where hydrated amorphous sucrose converts into anhydrous crystalline sucrose.

Van Scoik (3) and Van Scoik and Carstensen (4) treated the latter part of the curve as a normal cumulative undersize distribution (with mean $t^*$ and standard deviation $s$) of fraction not nucleated versus time. The mean nucleation time, $t^*$, was obtained as the point where $N/N_0 = 0.5$, and the point in time given by $t^* - 3s$ was denoted the lag time. $N$ here is the number of nonnucleated spheres, and $N_0$ the total number of spheres.

Both the percentage water uptake (mg water per mg dry amorphate) at the plateau level and the lag times are plottable by Van't Hoff and Arrhenius plots (Figs. 2 and 3). Use is made of these facts in the following article to develop a theory of the kinetic phenomena in the transformation.

MATERIALS AND METHODS

Amorphous sucrose was produced by preparing 10% sucrose solutions, placing these in a burette, and running drops of the solution into liquid nitrogen. The frozen spheres were placed on petri dishes so that no sphere was in contact with its neighbor; this was then placed in a lyophilizer, and the moist solid was lyophilized.

This method used for producing amorphous sugar worked the best in our hands, whereas other methods (spray drying, bulk lyophilization) never rid the substance completely of crystalline material. Melting followed by cooling does produce good-grade amorphous solid, but poorly reproducible amounts of decomposition products are formed. This method produced material that is free of crystallities as judged by optical microscopy with crossed Nichols and by X-ray diffraction. The produced sucrose spheres are essentially anhydrous [0.2% after outgassing on a high-vacuum rack (<0.5 μm) for 2 days].

Atmospheres of given relative humidities were created by means of supersaturated salt solutions in desiccators. Petri dishes were equilibrated in desiccators and tared, and netted amounts of amorphous sugar beadlets were placed on them. The petri dishes were places open (i.e., both body and lid) in the desiccator. At various times the desiccators were opened, the lid placed on the petri dish, and its weight determined. It was then placed back in the desiccator, the lid removed (but left in the desiccator), and the experiment continued. Experiments were carried out at several other temperatures and humidities.

The dry sucrose lyophilisate spheres will typically have a diameter of $d_n = 4.6 \pm 0.2$ mm. When exposed to the moist atmosphere they will gain weight up to a given plateau level ($q$ g water/100 g sucrose) as shown as point A in Fig. 1. After a while they will visually shrink (point B in Fig. 1).

The weight will stay constant at $q$ until a certain time $t^*$.

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the lag time, at which time weight loss will be experienced (point C in Fig. 1). Once crystallization occurs, the sucrose cannot retain the relatively large amount of moisture of the hydrated amorphate, and the loss of moisture is indicative, both qualitatively and quantitatively, of the conversion. This view has been substantiated by electron micrographs in previous communications (3,4).

X-ray diffraction patterns were conducted on samples at various storage times and have been reported elsewhere (3,4). Surface areas of dry lyophilisate spheres were carried out by nitrogen adsorption and found to be 3.8 m²/g. Differential scanning calorimetry was carried out on anhydrous amorphate (0.2% moisture) from -20 to 210°C.

RESULTS AND DISCUSSION

Figure 1 shows a typical moisture uptake curve at 23°C and 33% RH. The final weight approximates the weight of the anhydrous sucrose at the onset of the experiment. Hence the anhydrous sucrose becomes hydrated and then dehydrates into crystalline sucrose. X-ray diffraction of anhydrous amorphate shows only one broad, noisy band. If spiked with 5% crystalline sucrose, the expected peaks appear.

Modeling analysis of such curves has not been carried out previously, other than the curve-fitting acquisition of parameters reported (4). One logical explanation for the shape of the curve is that once the plateau is reached it consists of a lag period. At a given point in time, a sphere will nucleate; the crystal growth will be rapid, so that a particular sphere, once nucleation starts, will become 100% crystalline in a very short period of time.

The method used here of having isolated spheres of amorphous material thus allows separation of nucleation and crystallization phenomena, which is a great advantage, since otherwise it would be difficult to separate out which of the two phenomena were responsible for the various parts of the curve.

Since the amorphous spheres are independent of one another, the fraction of mass, $\phi$, converted to crystalline material is given by

$$\phi = \frac{(N_o - N)}{N_o} = 1 - \frac{(N/N_o)}$$

If $M$ denotes recorded gross weight of petri dish plus sucrose at time $t$, $M_o$ denotes gross weight right before nucleation, and $M_e$ denotes final gross weight, then it follows that $(N/ N_o) = (M - M_e)/M_o - M_e$.

The first phase (OA in Fig. 1), as mentioned, is presumably the simple collapse of the porous lyophilisate into the more compact, hydrous amorphate form. The diameter of the spheres, during this phase, decreases as a function of time as shown in Fig. 4. No further analysis of this is attempted here, but the fact is recorded that there is an initial contraction event.

The extent to which moisture is taken up ($q$) as a function of relative humidity (at a constant temperature) is tabulated in Table 1. If this is plotted as a BET plot, then the profile in Fig. 5 results. There is a fairly good correlation, but the intercept would correspond to a monolayer coverage of 38 mg of water per g of sucrose. This is two orders of mag-

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**Fig. 1.** Moisture uptake curve for amorphate at 23°C over saturated MgCl₂ solutions.

**Fig. 2.** Van’t Hoff plot of plateau weight values for hydrated amorphate.

**Fig. 3.** Arrhenius plot of lag times of hydrated amorphate.

**Fig. 4.** Shrinkage of moist lyophilisate spheres as a function of time.