

THERMAL CHARACTERISTIC EVALUATION OF DIFFERENT ASCORBIC ACID CRYSTAL HABITS

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ABSTRACT

Melting temperature (T_{melt}) and enthalpy of fusion (ΔH_f) are important parameters to determine the quality and the thermal stability of active pharmaceutical ingredient (API) crystals. In this study, different habit of ascorbic acid was prepared by using different polar solvents namely water, methanol, ethanol and 2-propanol. Ascorbic acid crystal was then been physically and thermally characterised by using microscopic analysis, thermo gravimetric analysis (TGA) and differential scanning calorimetry analysis (DSC). This provides an insight into the formation of crystal habit across four different polar protic solvents. The ascorbic acid is found to grow as a cubic or prism crystal when grown in water that provides high hydrogen bond between solvent and solute. As the polarity of the solvents decrease, the hydrogen bond weaken and the width of the crystal become narrower, forming almost a needle like crystal. The thermal stability of ascorbic acid crystal is found to be the most stable when ascorbic acid is crystallized from water (prism) and the weakest from 2-propanol (needle) due to the molecule arrangement in crystal lattice in which resulted from decreasing intermolecular forces in the liquid phase.

Keywords: ascorbic acid, crystal habit, thermal analysis, intermolecular forces

1.0 INTRODUCTION

L-ascorbic acid ((5*R*)-[(1*S*)-1,2-dihydroxyethyl]-3,4-dihydroxyfuran-2(5*H*)-one, C₆H₈O₆) shown in Figure 1, is commonly used as an antioxidant, pharmaceutical compound, cosmetic ingredient, and dietary supplement (Christina, Taylor, & Mauer, 2015). This compound is classified as a polar organic molecule due to the presence of four hydroxyl groups. The habit of ascorbic acid crystals are reported to be either cubic, plate or needle-like depending on the solvent used (Hvoslef, 1968). The selection of solvents may also determine whether the ascorbic acid can exist in the same crystal system or with some habit modification (Eggers et al., 2009; ter Horst, Geertman, & van Rosmalen, 2001).

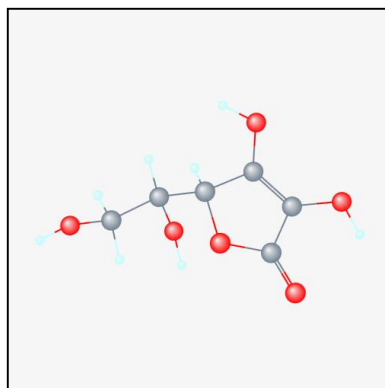


Figure 1: Molecular structure of ascorbic acid

It has been reported that, intermolecular interaction energies such as hydrogen bond and van der Waals between solute and solvents play an important role in determining habit of a crystals and it's thermochemical properties (Nie et al., 2007; Shah et al., 2014). During crystallization process, the interaction between solute and solvent determine influence the formation of crystal habit. The stronger the interaction between solute and solvent will result in a better arrangement crystals habit in system lattice, and so otherwise. Properly aligned molecules in crystal lattice will give better thermal stability compared to loosely packed molecule arrangement (Fahlman, 2011). This study uses thermal analysis to study the effect of different ascorbic acid crystal habit on the degradation pattern at an elevated temperature. Ascorbic acid used was prepared by using evaporation method in the vacuum oven from different polar solvents to produce different crystal habit. Degradation process of ascorbic acid is expressed by thermogravimetric plots by showing the percentage mass loss against temperature in degrees Celsius. In this paper, the effect of different ascorbic acid crystal habits on the thermal properties and their relation to intermolecular forces at the liquid phase are presented. The ascorbic acid crystals of different habits were prepared by evaporation from different polar solvents. Thermal properties of the ascorbic acid crystals were obtained by using DSC and TGA.

2.0 METHODS AND MATERIALS

2.1. Materials

The crystalline powder of ascorbic acid (99.9 wt% purity) (Fisher Scientific International, Inc., New Hampshire, USA) was used in this work and considered as a standard for basis of comparison for the experimental products. Analytical grade solvents used was methanol, ethanol, and 2-propanol with purity of 99.8 wt% (Fisher Scientific). Double distilled water used in the experimental work was prepared in laboratory. Table 1 tabulates some physical properties of the solvent used. The relative polarity values of solvents tabulated in Table 1 is referring to water polarity value.

Table 1. Some physical properties of solvents used.

Solvent	Chemical Formula	Boiling point (°C)	Density (g/mL)	Relative Polarity
Water	H ₂ O	100	0.998	1
Methanol	CH ₄ O	64.6	0.791	0.762
Ethanol	C ₂ H ₆ O	78.5	0.789	0.654
2-propanol	C ₃ H ₈ O	82.4	0.785	0.546

2.2 Characterization methods

2.2.1 Sample preparations

Ascorbic acid crystal was prepared by dissolving a certain amount of ascorbic acid in 25 mL solvent until the saturation point was achieved. Then the samples were shaken for 8 hours at 30 °C. After that, the solution is left overnight 30 °C to let the supernatant equilibrate. An aliquot of supernatant from the solutions was filtered using 0.45 µm syringe filter prior to the drying process in vacuum oven at 50 °C. The samples are left to dry and the mass were weighed until a constant mass weight is achieved. The crystal obtained was thermal characterised by using microscopic analysis, Diffraction Scanning Calorimeter (DSC), Thermal Gravimetric Analysis (TGA).

2.2.2 Microscopic analysis

2D images of ascorbic acid crystal were captured using an optical microscope, Nikon Diaphot 300, equipped with DinoXScope camera (Nikon, Tokyo, Japan) operating at standard 4x magnification.

2.2.3 Diffraction Scanning Calorimeter (DSC)

Thermal activity of L-ascorbic acid was studied by using TA Instruments Differential Scanning Calorimetric (DSC, New Castle, USA). It was conducted under a nitrogen atmosphere at a flow rate 25 cm³/min. Approximately 3.5 g of L-ascorbic acid was heated from room temperature 303 K to 773 K at a rate of 10° K/min (Adam, 2012; Juhász et al., 2012). ΔH_{fus} was determined by calculating the area under the curve from when the time the sample started to melt (T_{melti}) until all samples have completely melted (T_{meltf}).

2.2.4 Thermal Gravimetric Analysis (TGA)

TGA was used to measure the changes in the weight of specimen in a controlled nitrogen atmosphere. The analysis was conducted with a Thermo-gravimetric Analyser (TGA) Q500 supplied by TA Instruments (New Castle, USA). Sample with a weight range of 4-6 mg was placed in a platinum pan and heated from 303 K to 573 K at a constant heating rate of 10 K/ min (Adam, 2012; Juhász et al., 2012).

3.0 RESULTS AND DISCUSSIONS

Figure 2 shows ascorbic acid crystals from (a) water; (b) methanol; (c) ethanol; and (d) 2-propanol. The crystal from water was observed under microscope at 4.0x resolution and 10x resolution for crystal from methanol, ethanol and 2-propanol. From the images, the habit of ascorbic acid crystal that is obtained from water was in the form of a prism. This is in agreement with the result obtained by previous (Hvoslef, 1968; Srinivasan & Devi, 2010). Ascorbic acid crystal packing is driven by hydrogen bond and van der Waals due to its polarity. Therefore, ascorbic acid in strong polar solvent has a strong hydrogen bond interaction that helps the ascorbic acid to rearrange its molecule to form prismatic crystal in orderly manner in lattice system. Ascorbic acid that crystallized from other solvents was observed to produce a tree-like formation which is known as dendrites. Dendritic growth commonly happened during evaporation process of high enthalpy crystallization (Mullin, 2001). Individually, the crystal formed from other solvents showed a needle like habit. The width of the crystal was getting smaller as the polarity of solvents used are reduced. The weaker the polarity of the solvents, the weaker the intermolecular interaction between solute and solvent, making the ascorbic acid crystal form smaller needle like crystal.

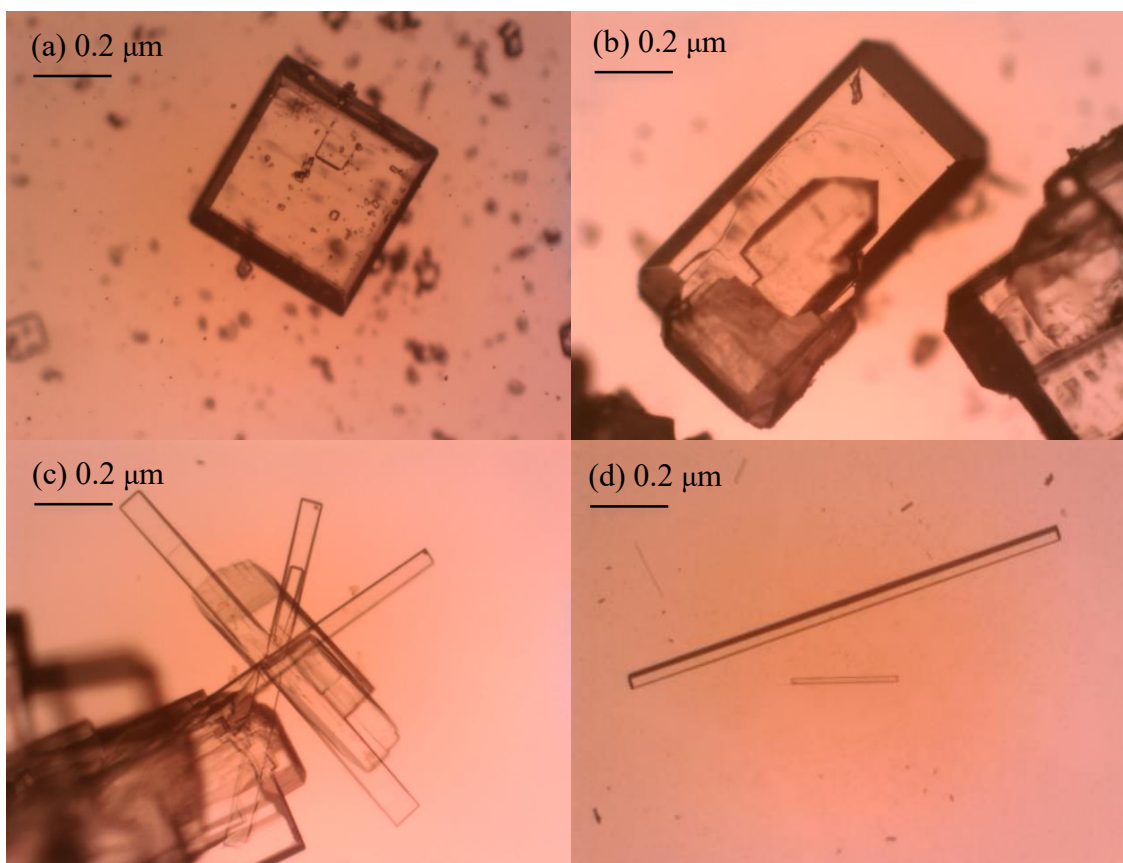


Figure 2: Ascorbic acid crystal by evaporation from (a) water, (b) methanol, (c) ethanol, and (d) 2-propanol

Figure 3 shows a comparison of DSC analysis conducted on ascorbic acid crystals from water, methanol, ethanol, and 2-propanol. The DSC curve of ascorbic acid in Figure 3

has a single endothermic peak, which matches the characteristic of a crystalline compound. The onset melting temperature (T_{melt}) of the first endothermic peak of ascorbic acid varies from 188.9 to 185.6 °C. Enthalpy of fusion (ΔH_f) decreased in the same pattern as T_{melt} . ΔH_f value decreases from 282.6 kJ/mol to 270.5 kJ/mol from prismatic crystal to needle like crystal respectively. The prism habit of ascorbic acid is more stable than the needle by having higher T_{melt} and ΔH_f . This shows that even though ascorbic acid crystals have different habits due to different packing of the molecules the thermal characteristic show identical trend but with weaker in magnitude as the habit of the crystal change from cubic prism to needle like prism. This observation suggests that the crystal formed from water, methanol, ethanol, and 2-propanol despite exhibiting different physical habit, they are having similar quality because the T_{melt} is in agreement to its published T_{melt} , which is 186 °C with percentage differences less than 3% (Srinivasan & Devi, 2010). These differences may due to the strength of intermolecular forces during the formation of the crystal. Neto & Pires reported that smaller molecular size and higher polarity solvent molecules such as water is easier to achieve equilibrium compared to ethanol because of the hydroxyl groups that exist in ascorbic acid can establish stronger hydrogen bonds, resulting in higher ΔH_f and melting temperature (Neto & Pires, 2009). The T_{melt} is lower in crystal formed in weaker polarity solvent due to imperfect crystal that tends to melt first, followed by larger, more stable crystal (Plato, 1969). It may also suggested that the crystal from ethanol and 2-propanol is not properly formed due to observation of broader melting peaks. Broader melting peaks are the results of various size distribution of imperfect crystal. Up until the onset temperature, the crystal does not show any addition endothermic or exothermic peaks, which demonstrate that ascorbic acid retains its phase until the melting process started. The bump after the melting point region indicated that ascorbic acid decomposed after the melting process.

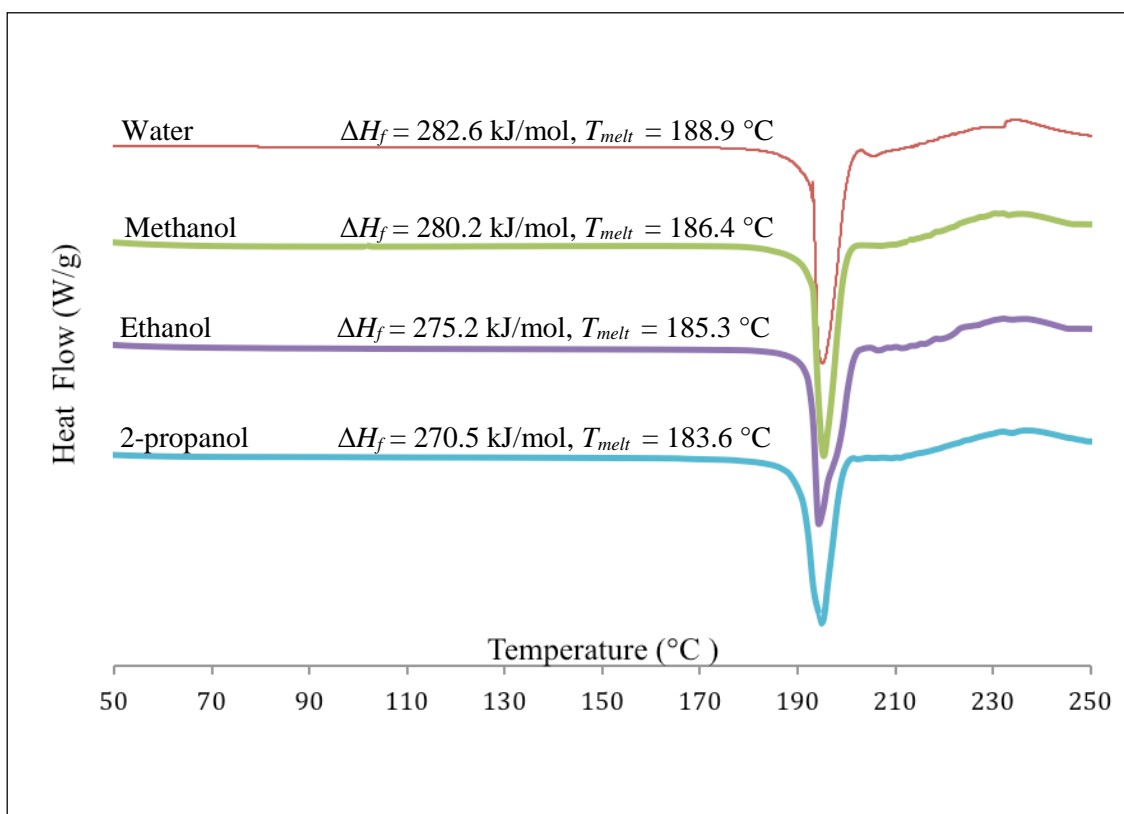
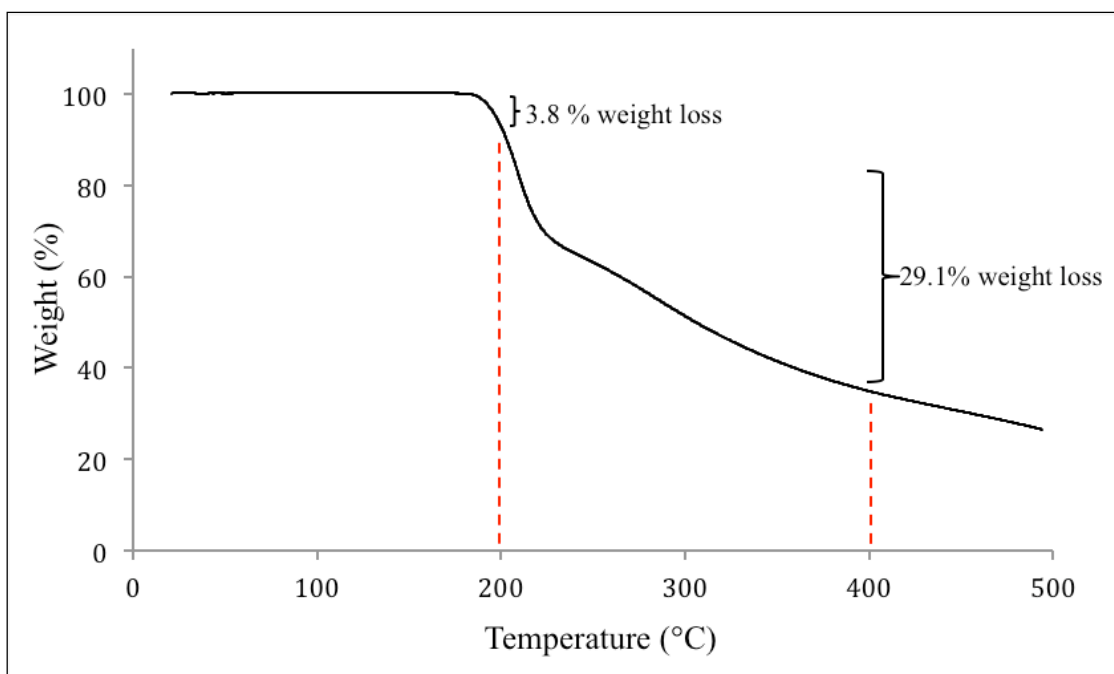
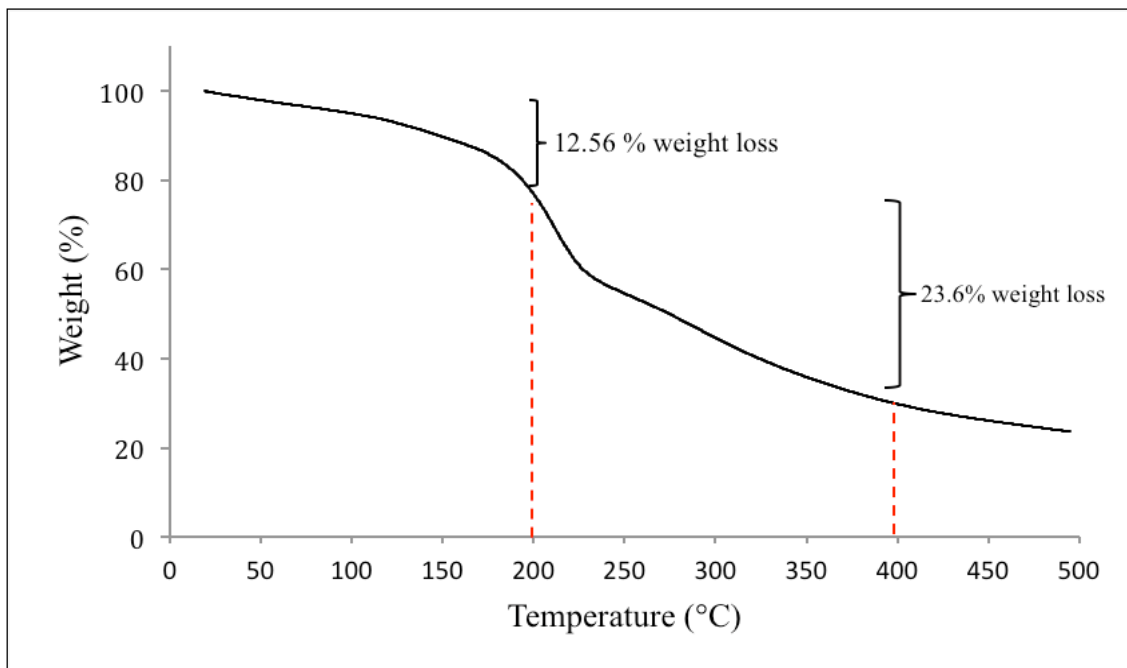


Figure 3: DSC analysis for crystallized ascorbic acid from water, methanol, ethanol, and 2-propanol.

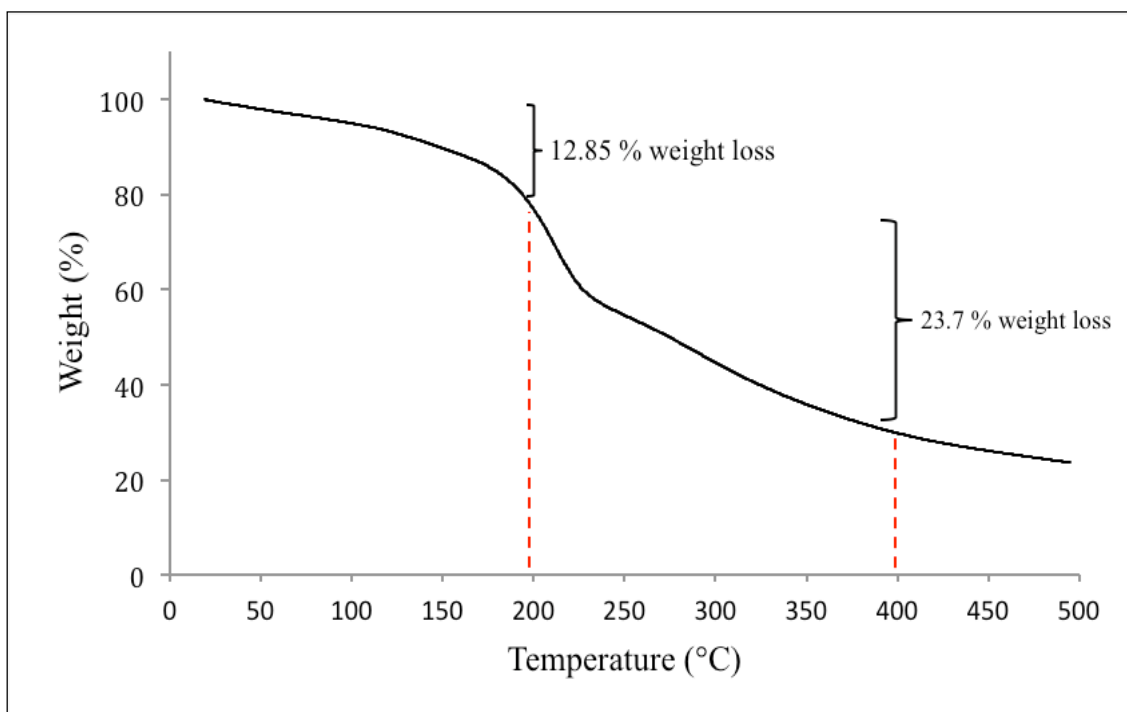
The thermal degradation of the ascorbic acid crystal from four solvents were studied using thermogravimetric techniques at temperature range of 20 to 500 °C. Figure 4 shows thermal gravimetric analysis (TGA) curves of ascorbic acid crystal obtained from (a) water, (b) methanol, (c) ethanol, and (d) 2-propanol. The TG derivative curves were presented to provide the percentage weight loss at 200 °C and 400 °C temperature. The ascorbic acid TGA curves had several distinct weight loss transitions. In the lower temperature range between 20 to 200 °C, there was a small weight loss that indicated moisture or low boiling point solvents evolving out of the matrix. From Figure 4, only crystal from water show very small weight loss during this stage. Crystals from methanol, ethanol and 2-propanol show more than 10% weight loss at temperature less than 200 °C. This indicates that there are still traces of solvent in the ascorbic acid crystal which may related to imperfect crystal formation. This may due to dendritic growth that hinder the release of trapped solvent. This also may due to the structure of ascorbic acid itself which consist of four hydroxyl groups. During this step, ascorbic acid tend to loose water and carbon dioxide molecules (Jingyan et al., 2013). The major weight loss transition occurred between 200 to 400 °C. This is when the ascorbic acid was further decomposed. The final was small weight loss transition from 400 to 500°C. The curves show a significant weight change from 165°C to 245°C. The changes in weight is due to the decomposition of ascorbic acid crystals or volatilization of residual solvents during the melting process. (Craig and Galwey, 2007).



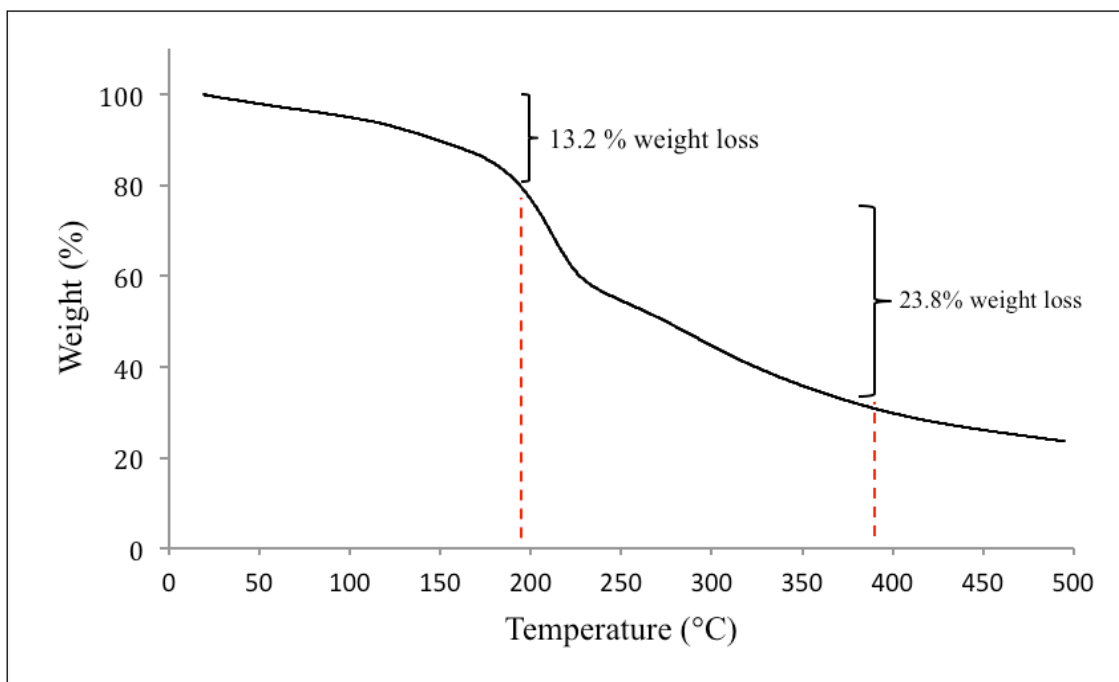
(a) water



(b) methanol



(c) ethanol



(d) 2-propanol

Figure 4: TGA curves of ascorbic acid crystal obtained from (a) water; (b) methanol; (c) ethanol; and (d) 2-propanol and its derivatives.

4.0 CONCLUSION

The thermal properties of different ascorbic acid crystal habits crystallised from different polar solvents namely water, methanol, ethanol and 2-propanol have been studied by using microscope analysis, TGA and DSC. It was found that the ascorbic acid crystal habit change from cubic prism to thinner elongated prism almost needle like as the polarity of solvent decreased. This attribute is due to the intermolecular interaction between ascorbic acid and solvents during liquid phase. DSC and TGA were used to study the differences in thermal properties of different habit of ascorbic acid. The results for crystal formed from water showed that no solvent entrapment in the ascorbic acid crystals and the crystals were completely decomposed during melting process. The crystal in the form of prism shows the highest T_{melt} and ΔH_f at 188.9 °C and 229 kJ/mol respectively due to its stable arrangement from strongly polar solvent. While for crystals that were formed from other solvents, there are trace of solvent entrapment and imperfect crystal formation. The differences in T_{melt} and ΔH_f may due to weak hydrogen bond interaction between solute and solvent during liquid phase. T_{melt} and ΔH_f decreased as the habit of the crystal become more elongated and thinner which suggest loose molecule arrangement in crystal packing.

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