CHAPTER 4

4.0 RESULTS

4.1 Microencapsulation of Tienam®

After the freeze drying processed, the microencapsulated product was transferred out from the freeze drying container into a new amber glass container for storage. The microencapsulated product was very light yellowish coloured. The appearance of these microencapsulated products can be seen in the Figure 4.1.

Figure 4.1: Microencapsulated products of Tienam® in PEG 2000, Sample A (left), and in the PEG 35000, Sample B (right).

4.2 Differential Scanning Calorimeter Analysis.

4.2.1 Analysis of data from DSC themogram.

All the pure materials and samples were scanned under DSC in three different days. All the DSC measurements have been carried out using a Perkin-Elmer DSC-6000(Perkin-Elmer, Norwalk, CT, USA). Data are treated mathematically using the Pyris Software Version 7.0(Perkin-Elmer, Norwalk, CT, USA). Then, the raw data were entered and calculations of mean and standard deviation value were calculated by using Microsoft Excel Software. Based on DSC thermo gram, we could see that thermal transition started with a crystalline event, but only two pure materials had shown this profile.

The crystalline event only happened in Imipenem and Tienam® antibiotic. The values shown in Table 4.1 were an average of sample size, onset temperature, crystalline temperature and heat of fusion.

Table 4.1: The results for DSC scanning for samples on crystallization profile:

Sample Name	Average Sample size (mg) (Mean±SD)	Onset Crystalline Temperature (^{0}C) (Mean±SD)	Crystalline Temperature, T_C(^{0}C) (Mean±SD)	Heat of fusion, ΔH(J/g) (Mean±SD)
Imipenem	1.35 ± 0.19	168.23 ± 1.03	171.77 ± 1.14	133.33 ± 6.70
Tienam	1.37 ± 0.27	148.24 ± 5.77	157.36 ± 5.64	58.70±11.92

Another set of data that we obtained revealed the second thermal transition characteristic that was called melting event.

Table 4.2: The results for DSC scanning for samples on melting profile:

Sample Name	Sample size (mg) (Mean±SD)	Onset Melting Temperature (^{0}C) (Mean±SD)	Melting Temperature, T_m(^{0}C) (Mean ±SD)	Enthalpy of fusion, ΔH(J/g) (Mean ±SD)
Imipenem	1.35 ± 0.19	194.70 ± 6.45	195.90 ± 6.03	58.98±10.89
Tienam	1.37 ± 0.27	189.14 ± 3.83	190.46 ± 3.99	84.51 ± 16.66
PEG 2000	1.66 ± 0.17	49.11± 1.87	52.77 ± 1.26	212.77 ± 8.95

Sample A	1.53 ± 0.36	56.37 ± 1.08	60.99± 0.30	230.37 ± 9.07
PEG 35000	1.72 ± 0.12	61.17 ± 1.19	66.92 ± 1.01	228.05 ± 3.90
Sample B	1.44 ± 0.09	60.78 ± 0.61	65.00 ± 0.26	224.65 ± 7.53

Sample A: Microencapsulated product of Tienam® in PEG 2000

Sample B: Microencapsulated product of Tienam® in PEG 35000

After that, all the necessary calculation had been focused for data obtained from scanning of Sample C and Sample D. Data from the DSC plots shown three thermal transition characteristics, which were two event of melting and one event of crystalline. The results were shown in a few tables below.

Table 4.3: Result obtained from the DSC plots for first melting profile in Sample C and Sample D.

Sample Name	Sample size (mg) (Mean±SD)	Onset Melting Temperature (^{0}C) (Mean±SD)	Melting Temperature, T_m(^{0}C) (Mean±SD)	Enthalpy of fusion, ΔH(J/g) (Mean±SD)
Sample C	1.53 ± 0.36	42.17 ± 0.63	49.22± 0.94	115.52 ± 2.38
Sample D	1.72 ± 0.12	56.04 ± 0.50	63.48 ± 1.32	105.11 ± 3.40

Sample C: Microencapsulated product of Tienam® in PEG 2000 with ratio 1:1(50%:50%)

Sample D: Microencapsulated product of Tienam® in PEG 35000 with ratio 1:1(50%:50%)

Data shown in the above table (Table 4.3) was an average of sample size, onset temperature, melting temperature and heat of fusion for Sample C and Sample D that had been scanned three times within the same day under the DSC instrument.

Table 4.4: Result obtained from the DSC plots for crystallization profile in Sample C and Sample D.

Sample Name	Average Sample size (mg) (Mean±SD)	Onset Crystalline Temperature (^{0}C) (Mean±SD)	Crystalline Temperature, T_C(^{0}C) (Mean±SD)	Enthalpy of fusion, ΔH(J/g) (Mean±SD)
Sample C	1.35 ± 0.19	132.99 ± 4.31	145.54 ± 3.81	9.15 ± 1.22
Sample D	1.37 ± 0.27	144.35 ± 3.48	154.01 ± 3.72	6.14±0.80

Sample C: Microencapsulated product of Tienam® in PEG 2000 with ratio 1:1(50%:50%)

Sample D: Microencapsulated product of Tienam® in PEG 35000 with ratio 1:1(50%:50%)

Table 4.5: Result obtained from the DSC plots for second melting profile in Sample C and Sample D.

Sample Name	Sample size (mg) (Mean±SD)	Onset Melting Temperature (^{0}C) (Mean±SD)	Melting Temperature, T_m(^{0}C) (Mean±SD)	Heat of fusion, ΔH(J/g) (Mean±SD)
Sample C	1.53 ± 0.36	201.98 ±8.06	203.33±8.00	59.69 ±6.17
Sample D	1.72 ± 0.12	216.59 ±6.02	218.00 ±6.10	47.34 ±7.56

Sample C: Microencapsulated product of Tienam® in PEG 2000 with ratio 1:1(50%:50%)

Sample D: Microencapsulated product of Tienam® in PEG 35000 with ratio 1:1(50%:50%)

4.2.2 Review of DSC Plots.

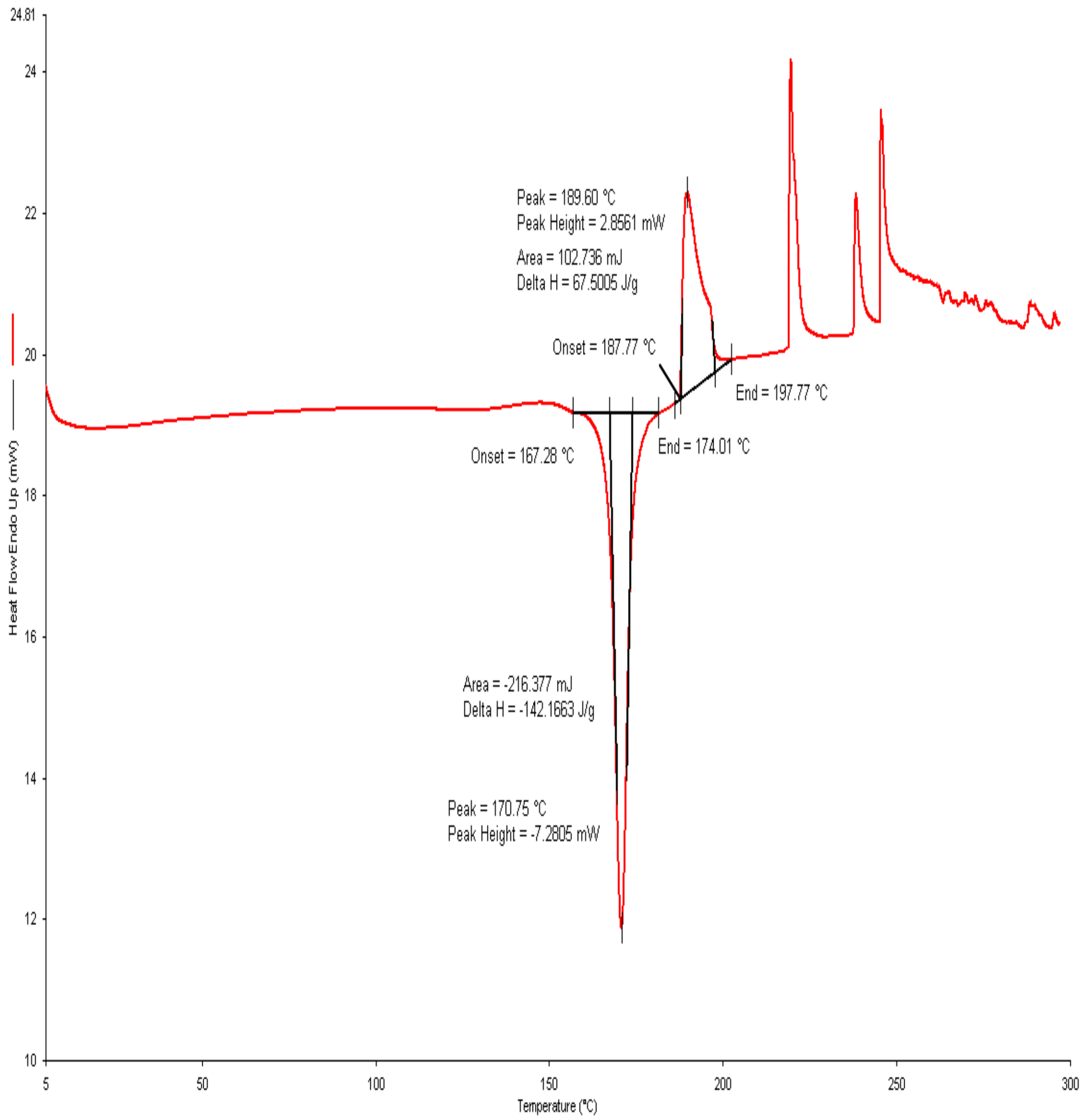

Figure 4.2: Representative one of DSC plot for pure Imipenem.

As we can distinguish from the above thermogram, there are two thermal transitions events. Imipenem thermal transition profiles start with a crystallization event at 168.20 ± 1.03 ^{0}C (crystallization temperature, T_C). In addition to this, the crystallization process has released energy (heat of fusion, ΔH) with the ΔH value was -140.29 ± 9.23 J/g.

Another thermal transition profile appears at 194.73 ± 6.44 ^{0}C and this can be indentifying as melting event(melting temperature, T_m) and enthalpy of fusion is ΔH = 65.43±14.82 J/g. Furthermore, as the temperature increased to 200 ^{0}C a lot of small peak had started to develop which indicates that the Imipenem had started to decompose.

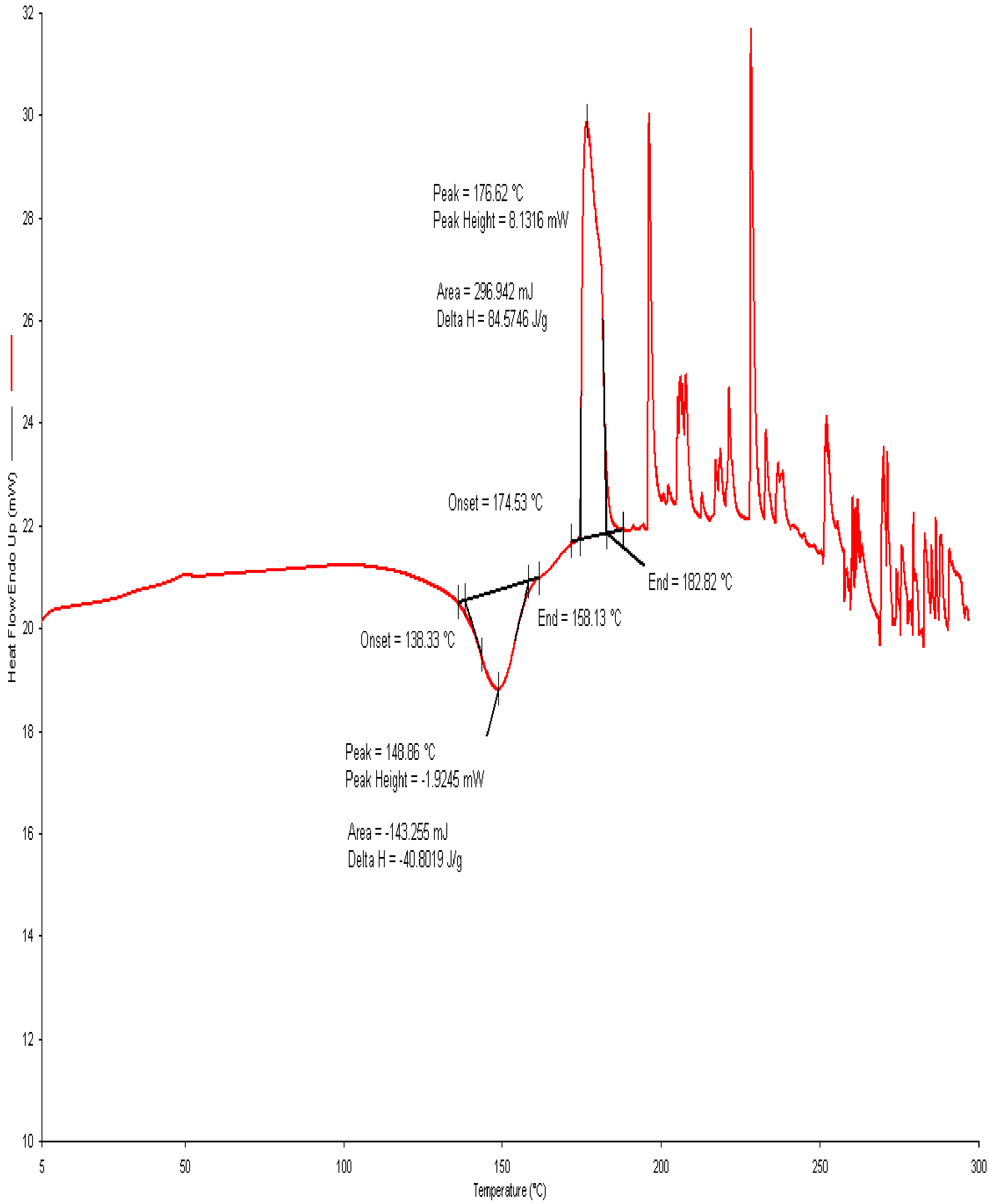

Figure 4.3: Representative one of DSC plot for Tienam® Antibiotic.

In Tienam® antibiotic, there are also two thermal transition events. It start with crystallization, T_C at 146.25 ± 6.69 ^{0}C. The heat of fusion, ΔH is -81.87±13.03 J/g. Afterthat, the second thermal transition profile so call melting start at 189.13 ± 3.83 ^{0}C. The melting event has absorbed lot of energy with ΔH, 91.14 ± 22.33 J/g.

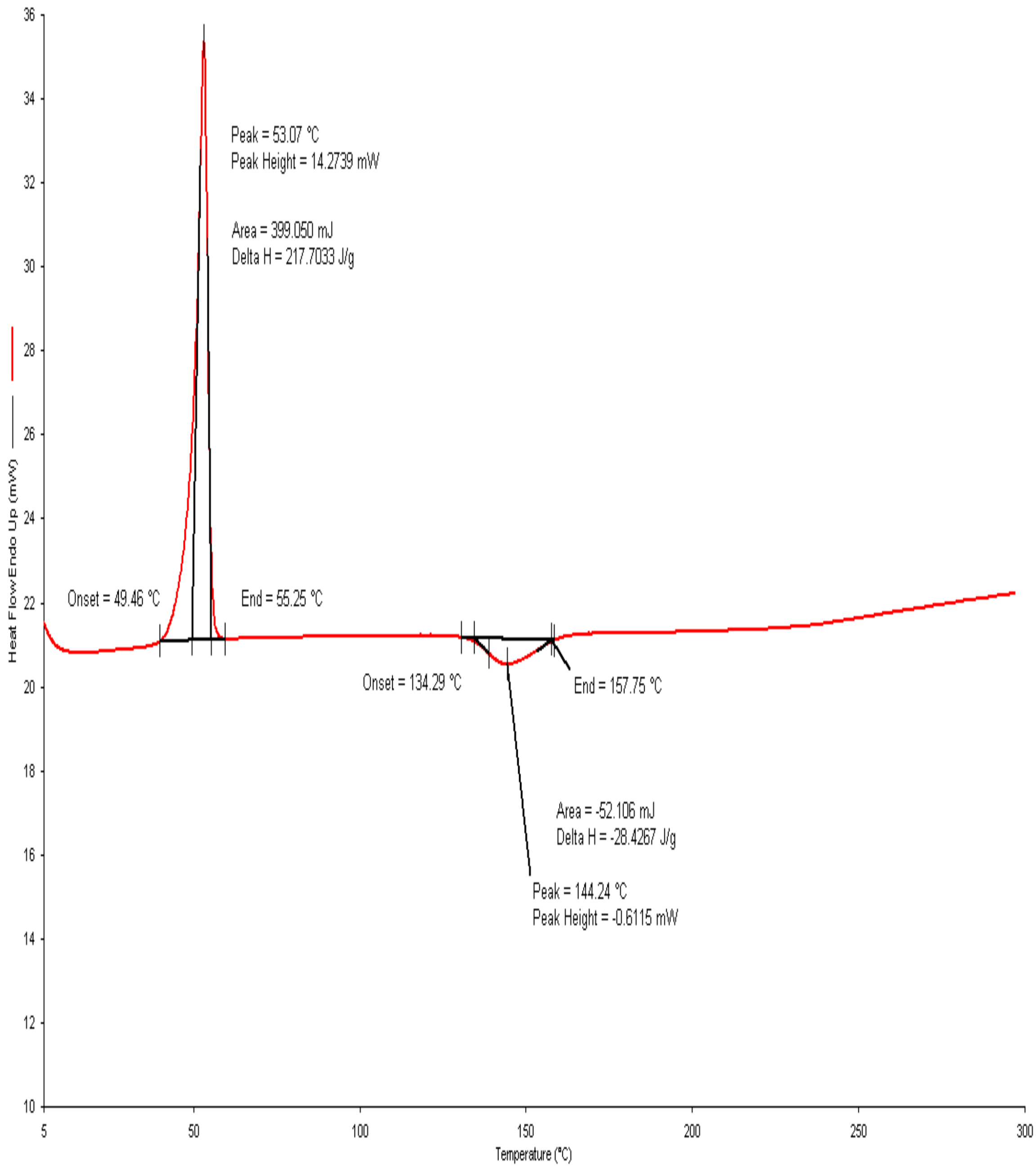

Figure 4.4: Representative one of DSC plot for PEG 2000.

In PEG 2000, it starts with melting event at 49.04 ± 1.87 ^{0}C with ΔH of 216.52 ± 9.59 J/g. As the temperature increase above 130.00 ^{0}C there is small exothermic reaction started to appear.

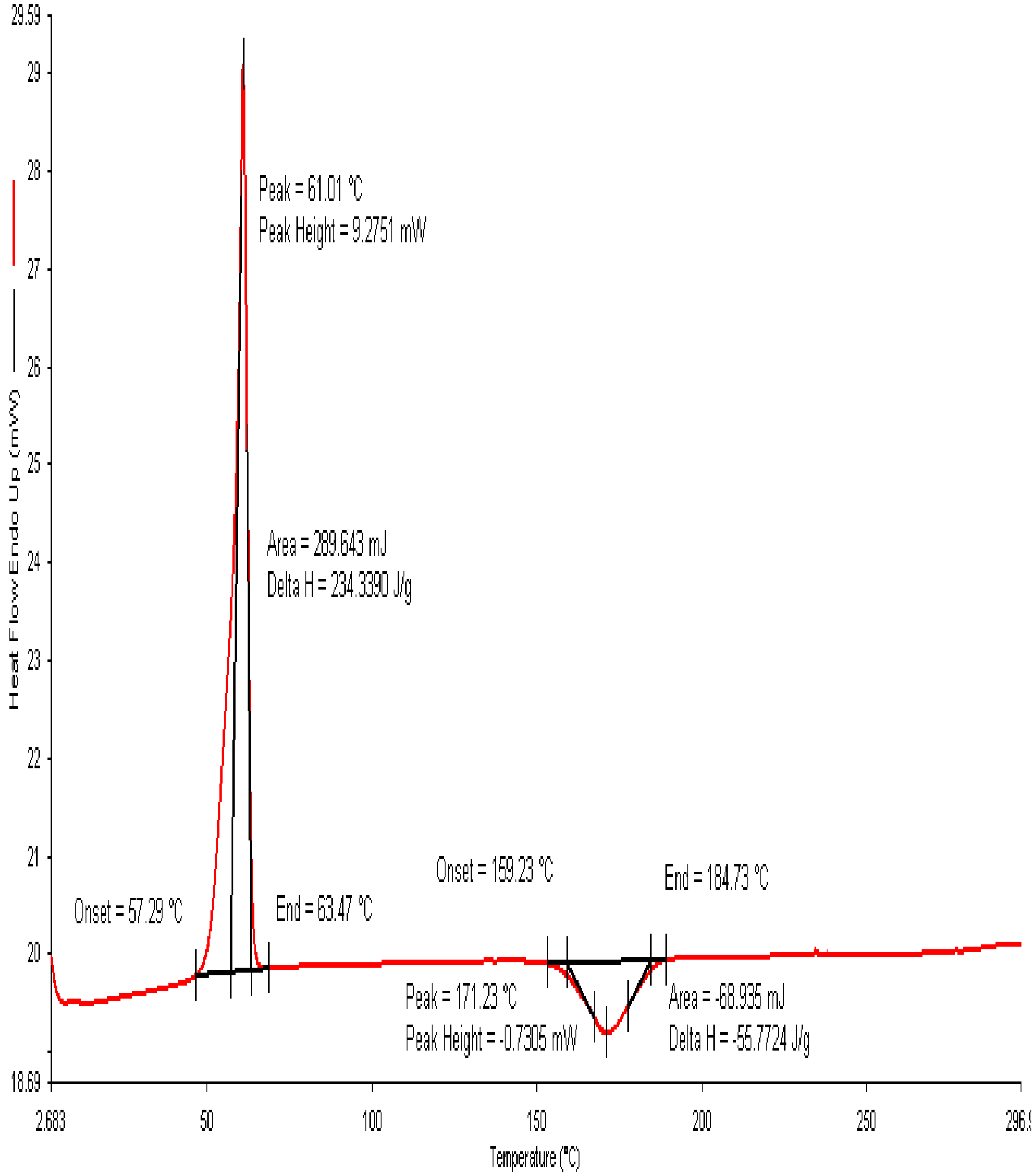

Figure 4.5: Representative one of DSC plots for Sample A (Microencapsulated product of Tienam® in PEG 2000).

In Sample A, melting event begin at 56.36 ± 1.10 ^{0}C with ΔH of 230.37 ± 9.07 J/g. Later when the heating process is continued, again the exothermic reaction appeared at a temperature above 150.00 ^{0}C.

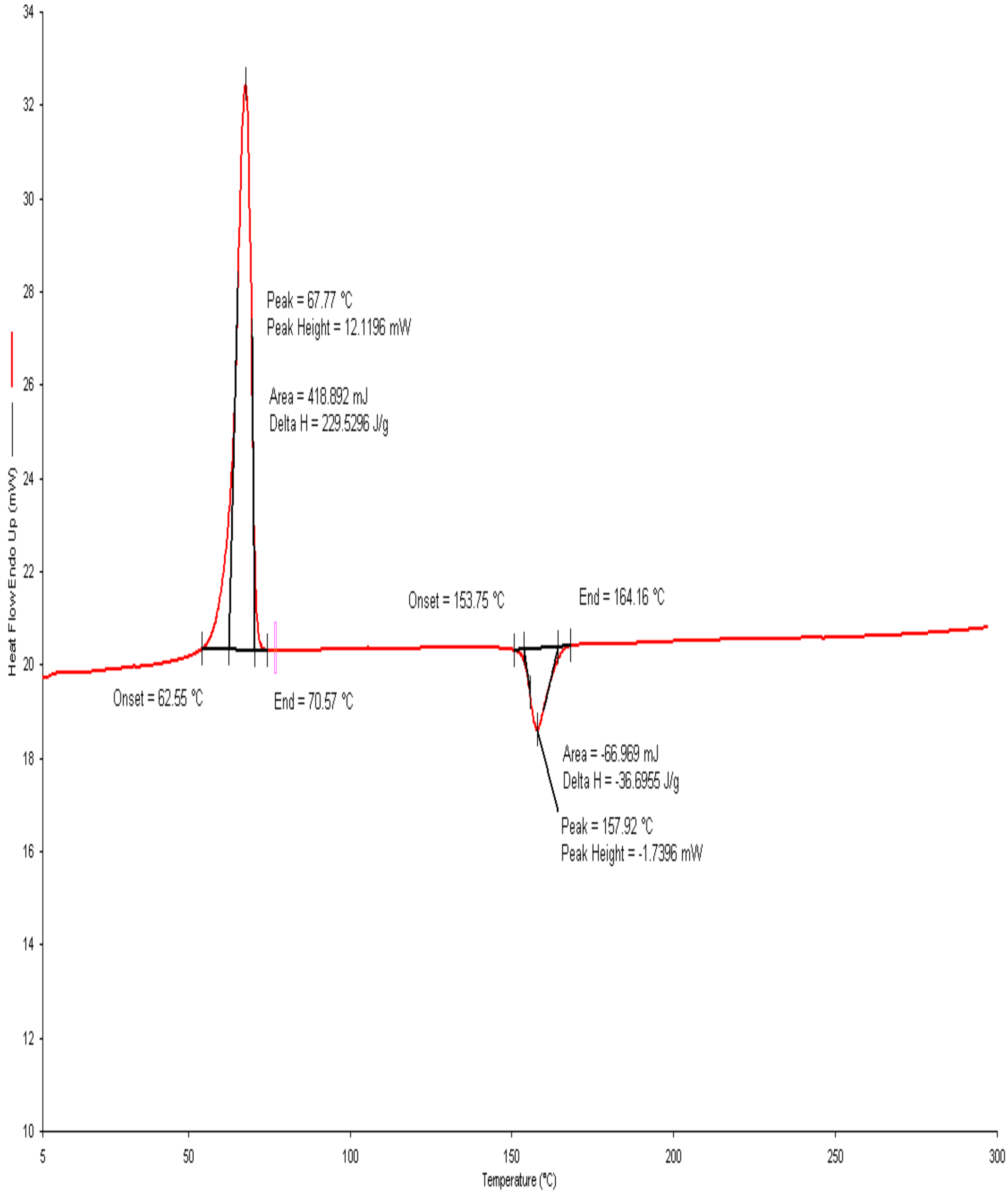

Figure 4.6: Representative one of DSC plot for PEG 35000.

Thermal transition in PEG 35000 start with melting at 61.13 ± 1.20 ^{0}C with enthalpy of fusion, ΔH 233.92 ± 4.24 J/g. Same as in PEG 2000 material, there is a small exothermic reaction started at a temperature above 150.00 ^{0}C.

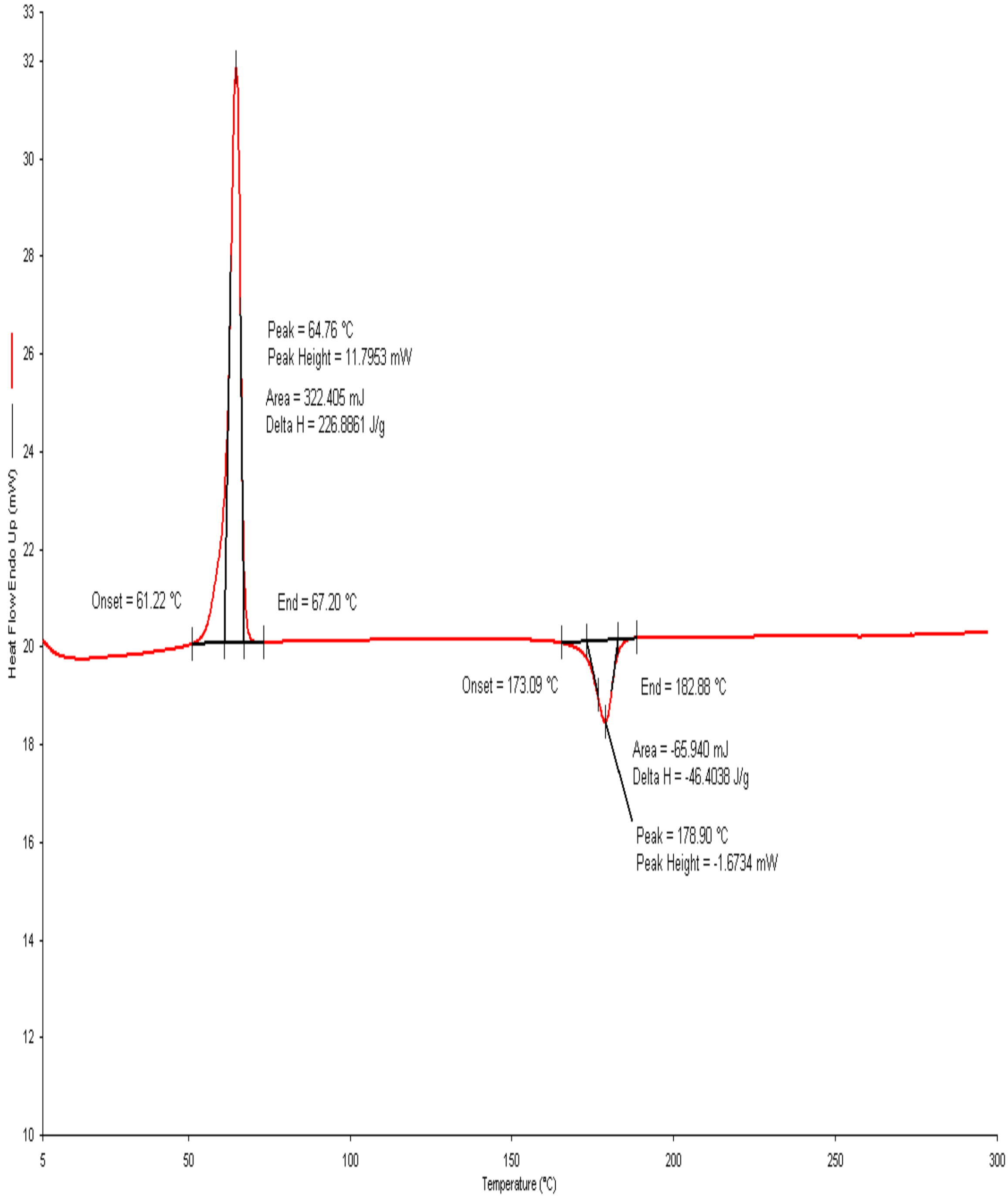

Figure 4.7: Representative one of DSC plot for Sample B (Microencapsulated product of Tienam® in PEG 35000).

In Sample B, as we heat it, the thermal transition begins with melting process. It start at 60.77 ± 0.61 ^{0}C with ΔH, 227.43 ± 4.76 J/g. The exothermic reaction also occur at a temperature above 170.00 ^{0}C.

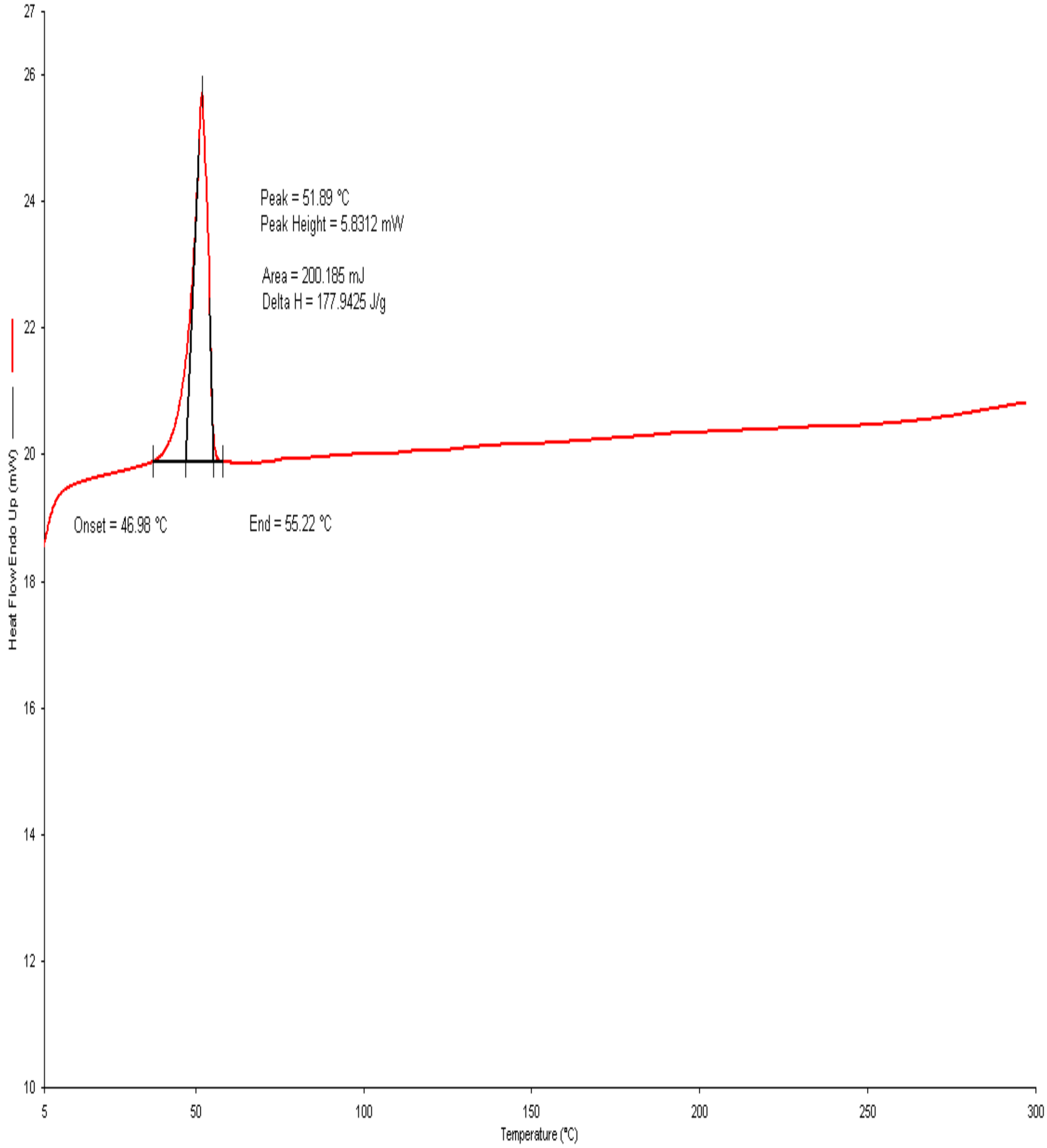

Figure 4.8: DSC plot of PEG 2000 re-scanning under DSC in none hermetically sealed pans.

From Figure 4.8, we can see the thermal transitions of PEG 2000 begin with a melting process start at 46.98 ^{0}C with ΔH 177.94 J/g. The heating process is continued and there is no other thermal transition profile observed.

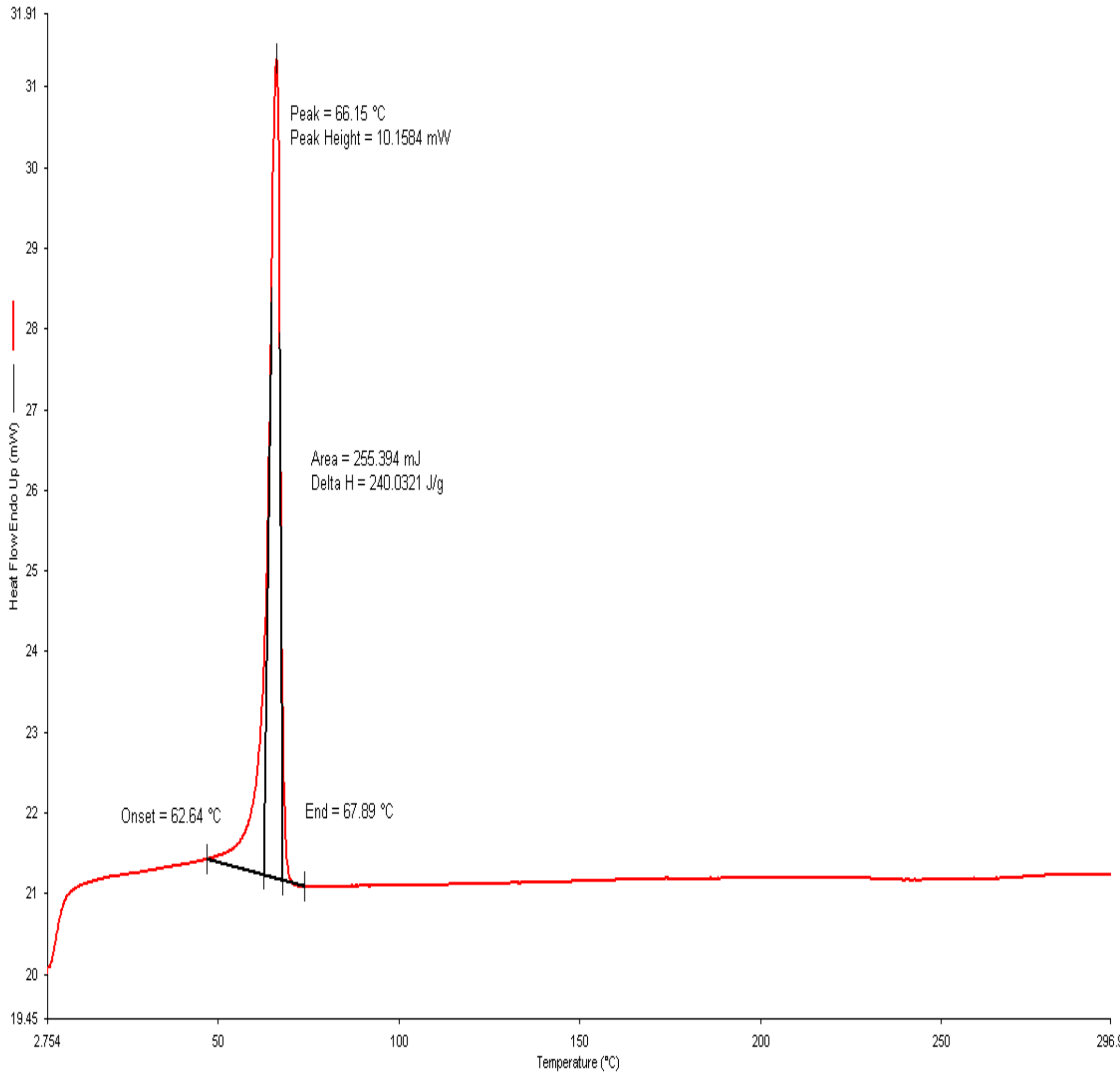

Figure 4.9: DSC plot of PEG 35000 re-scanning under DSC in none hermetically sealed pans.

From Figure 4.9, we can see the thermal transitions of PEG 35000 begin with a melting process start at 62.64 ^{0}C with ΔH 240.03 J/g. The heating process is continued and there is no other thermal transition profile observed.

The next result shows DSC plot obtained after scanning both Sample C and Sample D. In both sample we manage to get two melting profile and one crystalline profile. These are shows in the Figure 4.10 and Figure 4.11.

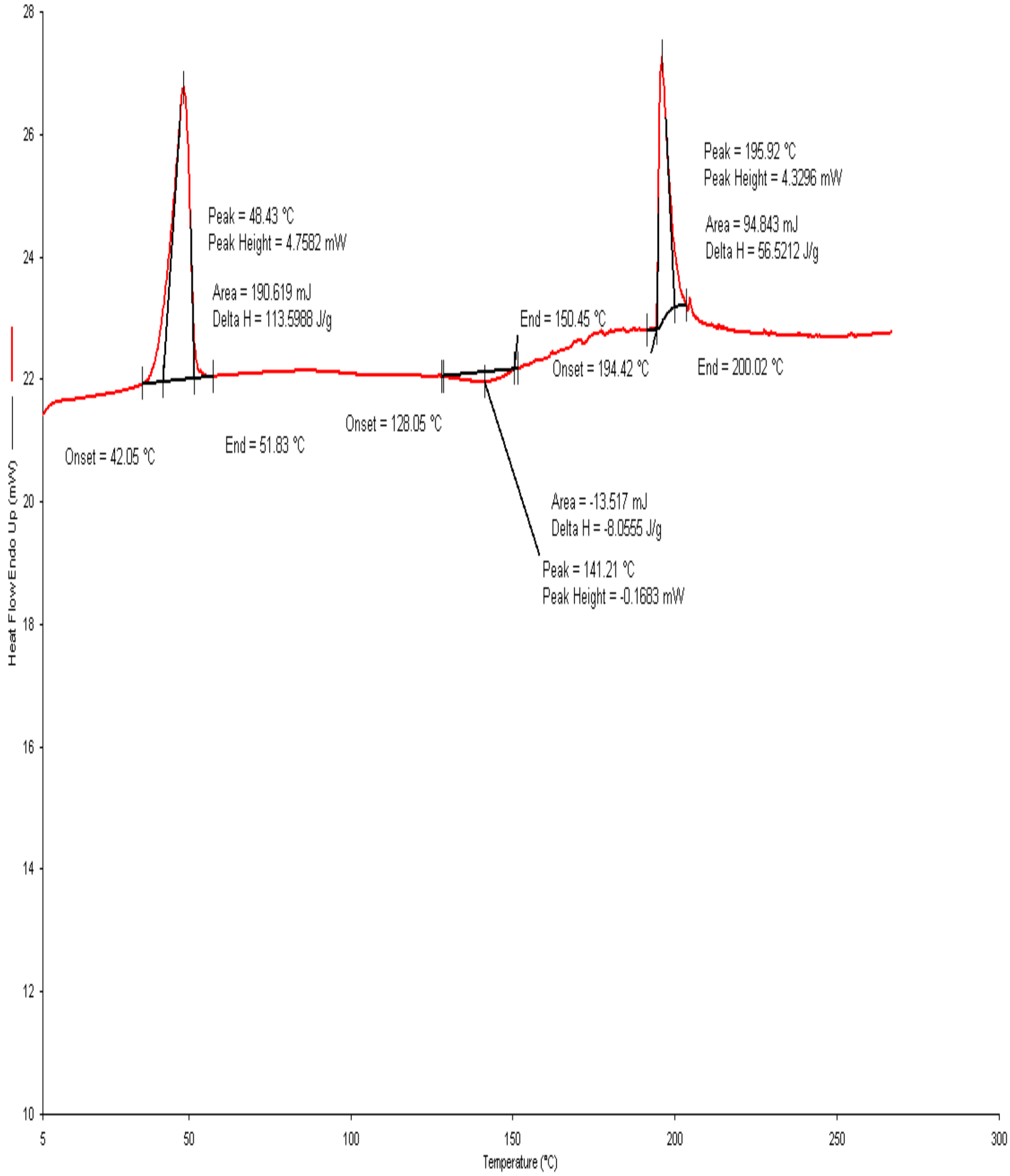

Figure 4.10: Representative one of DSC plot for Sample C [Microencapsulated product of Tienam® in PEG 2000 with ratio 1:1(50%:50%)].

In Sample C, thermal transitions begin with melting process. It starts at 60.77 ± 0.61 ^{0}C with ΔH 227.43 ± 4.76 J/g. The first melting profile belongs to PEG 2000. As we continue to heat Sample C, the crystalline reaction occurs starting at 132.99 ± 4.31 ^{0}C with Δ H 9.15 ± 1.22 J/g. Later, as the temperature reaches 200 ^{0}C, there is another melting profile observed which start at 201.98 ±8.06 ^{0}C, with Δ H 59.69 ±6.17 J/g. This melting profile is belonging to Tienam® antibiotic.

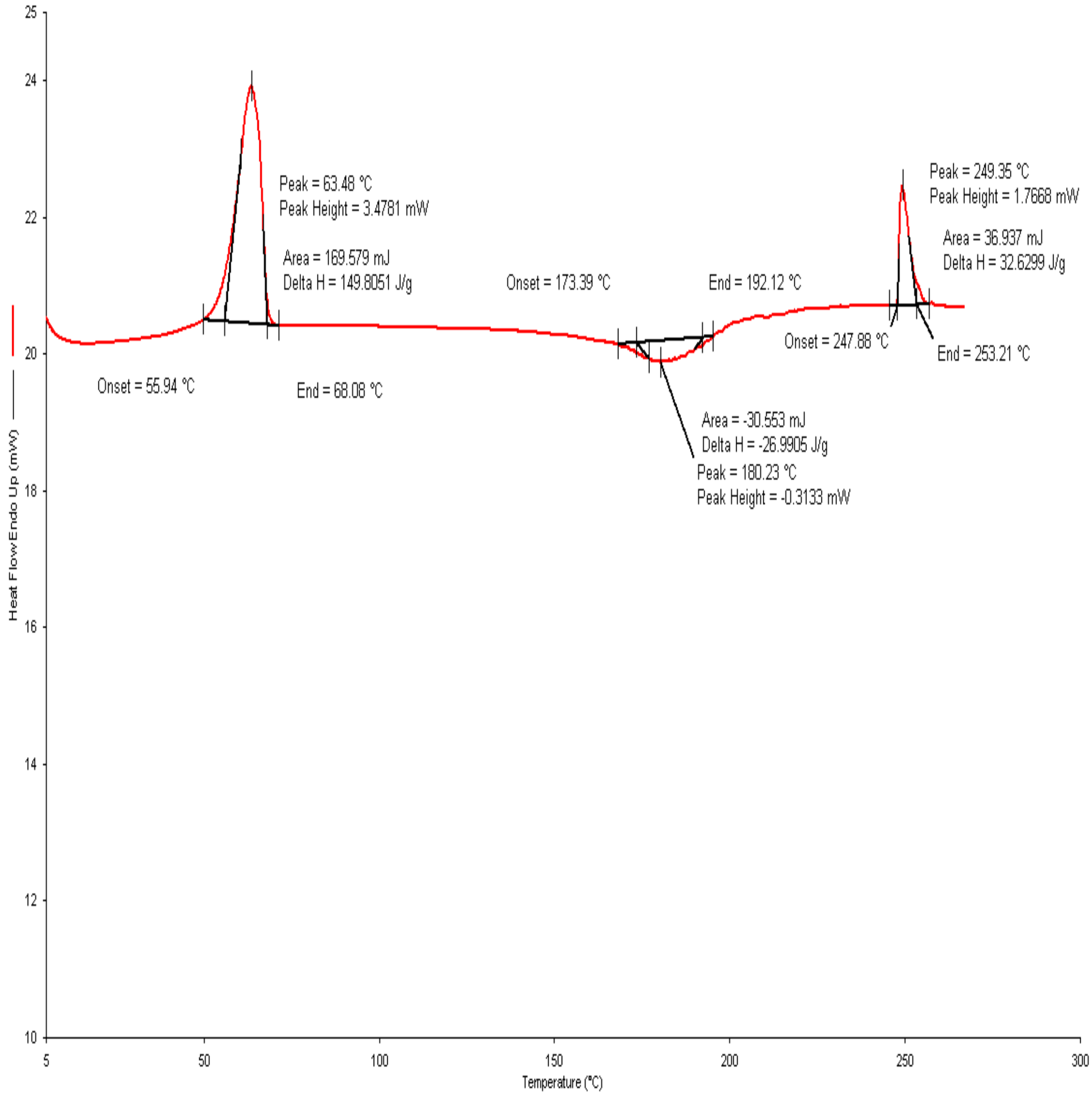

Figure 4.11: Representative one of DSC plot for Sample D [Microencapsulated product of Tienam® in PEG 35000 with ratio 1:1(50%:50%)]

In Sample D, thermal transitions begin with the first melting profile. It starts at $56.04 \pm 0.50\ {}^{0}C$ with ΔH 105.11 ± 3.40 J/g. This melting profile is belonging to PEG 2000. As we continue to heat Sample C, the crystalline reaction occurs starting at $144.35 \pm 3.48\ {}^{0}C$ with Δ H 6.14 ± 0.80 J/g. Later, as the temperature reaches 200 ${}^{0}C$, there is another melting profile observed which start at $216.59 \pm 6.02\ {}^{0}C$, with Δ H 47.34 ± 7.56 J/g. This melting profile is belonging to Tienam® antibiotic.