Research Article

Shadi F. Gharaibeh*, Wasfy M. Obeidat, and Nizar Al-Zoubi

Effect of post-compaction heating on characteristics of microcrystalline cellulose compacts

Abstract: Compacts of microcrystalline cellulose were prepared at applied compression pressures of 21, 32, 43, 53, and 64 MPa. Compacts were subjected to elevated temperatures of 125°C, 150°C, and 175°C according to a 5-min heating program. The effect of these thermal treatments on compact volumes, densities, porosities, tensile strengths, and weight loss was determined. There was no change in the volumes of the compacts due to thermal treatments in most of the conditions. However, the densities of the compacts decreased while the porosities increased as a consequence of weight loss. Moreover, there was no difference ($p > 0.05$) between the tensile strengths of the compacts without heat treatment and those subjected to heat treatment in most of the conditions. This was indicative of the preservation of the magnitude of the interparticulate bonds in the compacts. Weight loss of the compacts was affected by the heat treatment temperature and their porosities.

Keywords: tensile strength, microcrystalline cellulose, heat treatment, porosity, compact

1 Introduction

The compression of a powder results in particle deformation and possibly a consolidation into a compact. The characteristics of the formed compact are affected by the nature and properties of the compacted powder, moisture content, and applied compression pressure (1–3). In addition, post-compaction heating of tablets could influence their properties. Heating could induce the transition of amorphous components into a crystalline structure, leading to an increase in the tensile strength of a tablet (4–6). In addition, the evaporation of the moisture available in the tablet could enhance tensile strength by the crystallization of any dissolved components leading to the formation of additional interparticulate bridges (7,8). Therefore, a wet compression method was suggested in which a wet mass of lactose was compressed at relatively low pressure followed by an appropriate heat exposure to form rapidly disintegrating tablets (9). Moreover, tablet porosity and disintegration time could be influenced by post-compaction heating. It was found that tablet pore size, hardness, and disintegration time increased after heating erythritol and xylitol compacted mixtures at the melting point of xylitol (5). The increase in tablet hardness was attributed to the melting and post-heating crystallization of xylitol in the compacts. In addition, the heating of tablets containing a polymer above the glass transition temperature was shown to improve the polymer networking, thus enhancing the retardation of drug release (10,11).

Microcrystalline cellulose (MCC) powder is used as a binder in the manufacturing of tablets by direct compression. According to the United States Pharmacopeia-National Formulary, MCC contains less than 0.25% of its weight as water-soluble substances (12). MCC deforms under pressure predominantly by plastic behavior (2). It has also been suggested that the degree of crystallinity affects its compaction behavior. It was reported to have apparent crystallinity values in the range of 37–93% depending on the used X-ray method (13). Dry powder of MCC has been reported to have three glass transition temperatures at 132°C, 159°C, and 184°C (14). Moreover, it was found that adsorbed water affects the mechanical properties of compacts of MCC by acting as a plasticizer (1).

* **Corresponding author: Shadi F. Gharaibeh,** Faculty of Pharmacy, Jerash University, Jerash 26150, Jordan,
e-mail: shadi.gharaibeh@jpu.edu.jo, tel: +962-79-6302889,
fax: +962-2-6350520
Wasfy M. Obeidat: Department of Pharmaceutical Technology, Jordan University of Science and Technology, Irbid, P.O. Box 3030, Jordan, e-mail: obeidatw@just.edu.jo
Nizar Al-Zoubi: Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, The Hashemite University, Zarqa, Jordan, e-mail: nzoubi@hu.edu.jo

Several properties of MCC compacts were previously investigated. For example, it was found that compacts of MCC powder prepared at compression pressures between 8 and 106 MPa had tensile strength values in the range between 2 and 12 MPa depending upon the applied compression pressure and the used grade of MCC powder (15). In addition, it was found that the porosity under pressure of compacted MCC powder decreased as the compaction pressure increased. Moreover, the porosity under pressure was reported to reach below 0% at compaction pressures above 150 MPa. This was indicative of interparticulate changes along with increased density under pressure (16). Researchers also investigated the thermal properties of compacted MCC powder. It was found that MCC powder did not show morphological change in the crystal structure during heating to a temperature of 200°C. In addition, it was found that thermal conductivity and volumetric heat capacity of the compacts were dependent upon the relative density and temperature (17). To the best of the authors' knowledge, no research prior to this study investigated the effect of post-compaction heating on the characteristics of MCC compacts.

The effect of post-compaction heating on the mechanical properties of lactose tablets has been previously investigated (8). The researchers subjected lactose tablets to 100°C for a period of 24 h. They noted that the tensile strength of the compacts increased markedly with thermal exposure. They attributed this increase in tensile strength to the transition of amorphous content of lactose to the crystalline form and to the evaporation of water that led to the crystallization of the dissolved materials, thus forming extra interparticulate bonding.

The aim of this study was to investigate the effects on compact volumes, densities, porosities, tensile strengths, and weight loss by subjecting MCC compacts prepared at various compression pressures to elevated temperatures for a relatively short period of time.

2 Materials and methods

2.1 Materials

MCC powder (Avicel PH-101 NF) was obtained from DuPont Nutrition USA, Inc. (USA). Magnesium stearate (magnesium octadecanoate) was purchased from Junsei Chemical Co., Ltd. (Japan). Ethanol (>96%) was obtained from Unicol Limited (Pakistan).

2.2 Characterization of MCC powder

Particle size analysis was performed using a Winner Laser Particle Size Analyzer model 2308C (Jinan Winner Particle Instrument Stock Co., Ltd, China). The analysis was performed using the dry mode. Three grams of the powder were placed in the sample area of the equipment. Multiple particle size distributions were collected for the sample during the run. An average of ten consequent distributions was used to determine the particle size (D10) at which 10% of the particle size distribution lies under, the median (D50), and the particle size (D90) at which 90% of the distribution lies under. The true density of the powder was determined using a gas pycnometer model Ultrapyc 1200e (Quantachrome Instruments, USA). Nitrogen was used as the purging gas. The true densities of three samples were determined and for each sample the result was the average of five runs. The result was presented as the average and standard deviation of the three samples.

Simultaneous thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) were performed on a simultaneous thermal analyzer model STA 409 PC (Netzsch-Gerätebau GmbH, Germany). Five milligrams of each sample were weighed in an aluminum pan and placed in the sample carrier. The thermal analyses were performed under the continuous flow of nitrogen gas at a flow rate of 50 mL·min^{-1}. The heating rate was set at 10 K·min^{-1} with a range between 30°C and 320°C. The TGA data were used to determine the percentage weight loss between the starting point and 175°C. The average and standard deviation of the results of triplicate samples were calculated. Moreover, samples of the powder without heat treatment and heat treated at 125°C, 150°C, and 175°C were analyzed using a multipurpose XRD system model Ultima IV (Rigaku Corporation, Japan). Continuous scanning was performed at a voltage of 40 kV and a current of 20 mA. The scanning range was obtained between 2θ equal to 5° and 80° at 0.02 step.

2.3 Preparation of compacts

Cylindrical compacts were prepared by compression of 0.50 g of MCC powder using a 15T manual hydraulic press (SCO Tech, Germany). The used die had a cavity diameter, outer diameter, and height equal to 14, 70, and 36 mm, respectively. The upper and lower punches were flat faced with lengths of 36 and 10 mm, respectively. The

clearance between the punches and the die wall cavity was less than 0.1 mm. The die wall cavity was lubricated with a 5% magnesium stearate in ethanol suspension prior to each compression. Ethanol was allowed to evaporate leaving a layer of magnesium stearate on the die wall cavity before the die cavity was filled. This lubricant layer would ease the ejection of the compacts from the die cavity after compression. Applied compression pressures were 21, 32, 43, 53, and 64 MPa and the dwell time for each compression was 10 s. Five compacts were produced at each applied compression pressure which were kept at room temperature for 15–30 min before further analyses in order to match the time of the heat treatment procedure. Five other compacts were produced at each applied compression pressure for analyses at each of the heat treatment conditions.

2.4 Heat treatment

Heat treatment was performed using a moisture analyzer model BM-60 (Phoenix Instrument, Germany). The heat treatment conditions were programmed with the maximum temperature set at 125ºC, 150ºC, or 175ºC. The heating procedure followed a 5-min heating program from which less than 30 s were needed to reach the maximum temperature. The temperature remained constant for the rest of 5 min. Following the heating program, the temperature dropped down to below 50ºC in approximately 10–25 min depending on the maximum temperature setting. Five compacts prepared at each of the applied compression pressures were analyzed. Each compact was individually heat treated in the analyzer immediately after being produced. The weights of the samples before heat treatment (Wb) and at the end of the heat treatment program (Wh) were recorded. The percentage weight loss (% WL) was calculated using the following equation:

$$\% \, WL = \frac{Wb - Wh}{Wb} \times 100\% \tag{1}$$

Further analyses were performed immediately after the heat treatment procedure. Powder samples of MCC weighing about 0.5 g were also subjected to similar heat treatments at 125ºC, 150ºC, or 175ºC for X-ray diffraction analysis. The % WL of the powder was calculated using Eq. 1.

2.5 Determination of compact dimensions, volumes, densities, and porosities

The diameters and thicknesses of five compacts without heat treatment and of five compacts before and after heat treatment prepared at each of the applied compression pressures were determined using an electronic digital caliper model WT 4171 (Worksite Tools & Equipment, China). The volumes were calculated from the measured dimensions of the cylindrical compacts. Compact density was determined by dividing the weight of the compact by its volume. Porosity (ε) was calculated according to the following equation:

$$\varepsilon = 1 - \frac{\rho_{compact}}{\rho_{true}} \tag{2}$$

where $\rho_{compact}$ is the density of the compact and ρ_{true} is the true density of the powder.

2.6 Determination of Heckel's yield pressure (P_y)

The out-of-die Heckel analysis was performed on MCC compacts based on the following equation (18):

$$\ln\left(\frac{1}{\varepsilon}\right) = KP + A \tag{3}$$

where P is the applied compression pressure, and K and A are constants. P_y is equal to the reciprocal of K. Accordingly, the reciprocal of the slope of the fitted line of $\ln(1/\varepsilon)$ vs P is equal to P_y.

2.7 Determination of compact tensile strengths

A tablet hardness tester model YD-3 (Biobase Group, China) was used to measure the crushing strengths (F) of five compacts prepared at each of the applied compression pressures. The following equation was applied to calculate the tensile strength (TS):

$$TS = \frac{2F}{\pi Dt} \tag{4}$$

where D is the diameter of the compact and t is the thickness.

2.8 Statistical analyses

Results were statistically compared using the *t*-test add-on feature in Microsoft Excel. The mean values of the volumes, densities, and porosities of the compacts before

and after heat treatments were compared using the two-tail paired *t*-test. An independent two tail *t*-test assuming equal variances was used to compare the mean values of the tensile strengths of compacts without heat treatment with those that were heat treated. A *p*-value less than 0.05 was considered a statistically significant difference in the performed tests.

3 Results and discussion

3.1 Characteristics of MCC powder

The true density of MCC powder was found to be equal to 1.597 ± 0.005 g·cm^{-3}. According to the particle size analysis, the powder had D10 = 44 μm, D50 = 74 μm, and D90 = 103 μm. A noticeable percentage weight loss of the powder between the starting temperature and 175°C was observed on the TGA plot (Figure 1). This percentage weight loss was found to be equal to 5.61 ± 0.08%. In addition, there were no peaks on the DSC plot (Figure 1) that would indicate melting or decomposition of the powder at temperatures below 200°C. The diffractograms of MCC powder without heat treatment and heat treated at 125°C, 150°C, and 175°C (Figure 2) had peaks at similar 2 theta locations with similar intensities. This is indicative of the powder maintaining its crystallinity after the heat treatments. Crystallization from the amorphous form and polymorphic transitions were reported for cellulose when heat treated at elevated temperatures (19). However, such transitions were reported for heat treatments under pressure and for longer periods of time compared to our study. The slope of the fitted line of the out-of-die Heckel plot
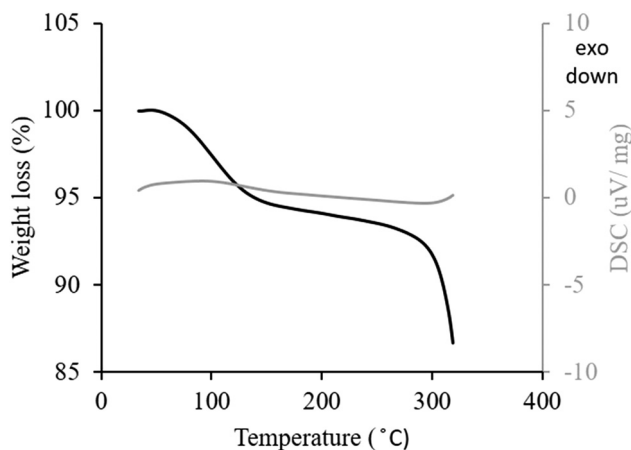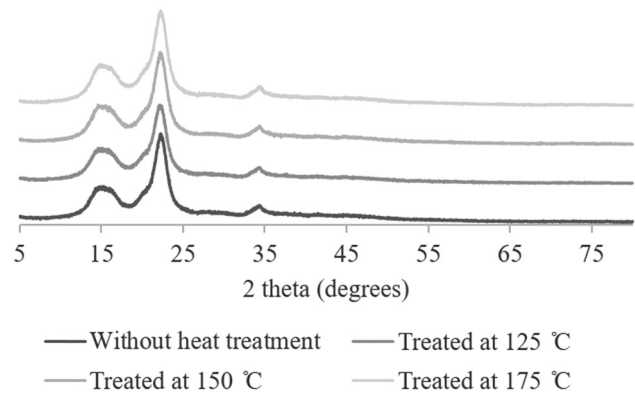

Figure 2: Diffractograms of MCC powder without heat treatment and heat treated at 125°C, 150°C, and 175°C.

(Figure 3) was found to be equal to 0.013 (1/MPa). The yield pressure (P_y) was calculated to be equal to 77 MPa.

3.2 Effect of heat treatment on volumes, densities, and porosities of compacts

Statistical comparison between the mean values of the volumes of the compacts before and after heat treatment showed no significant difference ($p > 0.05$) in almost all the cases. Statistically significant differences were obtained when the compacts were heat treated at 125°C and the applied compression pressures were 43 MPa ($p < 0.05$) and 64 MPa ($p < 0.05$). In both of these cases, the differences between the averages of the volumes of the compacts before and after heat treatment were less than 1.6%. A change in volume after heat exposure was not observed for almost all of the heat-treated compacts. It
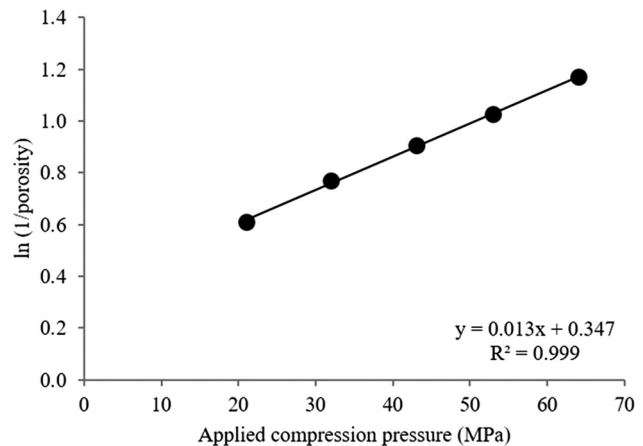

Figure 1: A representative plot of overlaid TGA-DSC analyses of MCC powder.
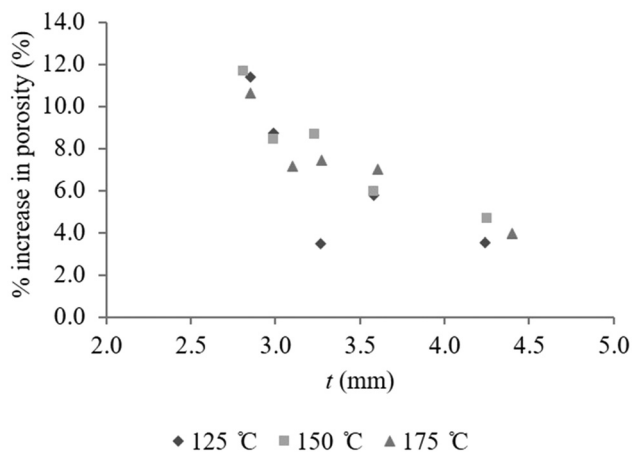

Figure 3: Out-of-die Heckel plot of MCC compacts.

Figure 4: Relations between percentage increase in compact porosity and thickness of compacts at different heat treatment temperatures.

Figure 5: Comparisons between the averages of the tensile strengths of compacts without heat treatment and compacts heat treated at 125°C, 150°C, and 175°C prepared at various applied compression pressures. Error bars represent + standard deviation, $n = 5$.

seems like the distances between the consolidated particles did not change as a result of the heat treatment. However, there was a statistically significant difference ($p < 0.05$) between the mean values of the densities of the compacts before and after heat treatment in all of the cases. A decrease in the compact densities after heating was observed. This change in the densities was due to the compacts losing weight as a result of moisture evaporation during heat treatment while maintaining their volumes. In addition, there was a statistically significant difference ($p < 0.05$) between the mean values of the porosities of the compacts before and after heat treatment in all of the cases. An increase in porosity after heat treatment was observed. The increase in porosity was also due to the weight loss of the compacts as a result of the heat treatment. Therefore, the volume of the voids in any given compact relative to its volume increased. Figure 4 shows relations between the percentage increase in compact porosity after thermal exposure and compact thicknesses at different heat treatment temperatures. It can be seen that the highest percentage increase in porosity (10–12%) was obtained for the compacts with the smallest thicknesses. This increased effect of evacuation of pores was due to the smaller volumes of the compacts.

3.3 Effect of heat treatment on tensile strength of compacts

The tensile strengths of the compacts heat treated at 125°C, 150°C, and 175°C were comparable to those of the compacts without heat treatment for most of the applied compression pressures (Figure 5). The statistical comparison
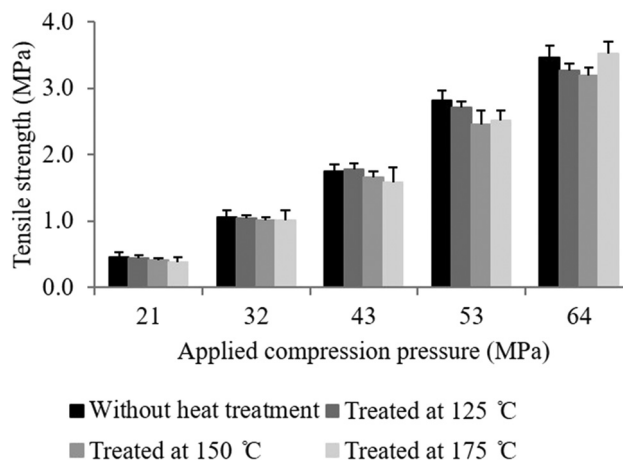
between the mean values of the tensile strengths of the compacts without heat treatment and those heat treated showed no significant difference ($p > 0.05$) for most of the heat treatment and applied compression pressure conditions. This finding indicates no change in the extent of interparticulate bonding. This is probably due to the preservation of the crystal structure of MCC (Figure 2) during the heat exposure and lack of any dissolved substance that might have crystallized during moisture evaporation. Nevertheless, statistical significance was obtained when the compacts were heat treated at 150°C and prepared at 53 MPa ($p < 0.05$) and 64 MPa ($p < 0.05$) with a decrease in the average tensile strength for the heat-treated compacts equal to 13% and 8%, respectively. Furthermore, statistical significance between the mean values of the tensile strength of compacts without heat treatment and those heat treated at 175°C was also obtained for compacts prepared at an applied compression pressure of 53 MPa ($p < 0.05$) with a decrease in the average tensile strength for the heat-treated compacts equal to 11%. The decrease in tensile strength after heat exposure is indicative of a reduction in the overall magnitude of interparticulate bonding. It is possible that the evolution of entrapped air in the compacts led to this finding. Researchers estimated that entrapped air in tablets could have pressure values that reach up to 20 times the atmospheric pressure (20). Upon heating, this pressure could increase to a point where it is sufficient to break the surrounding bonds to be released. This effect would be more pronounced at higher heat treatment temperatures (150°C and 175°C) and applied compression pressures (53 and 64 MPa).

Table 1: Averages of % WL of MCC powder at different heat treatment temperatures, *n* = 5

Heat treatment temperature	% WL (%)	Standard deviation
125°C	5.20	0.14
150°C	5.27	0.20
175°C	5.56	0.31

3.4 Effect of heat treatment on % WL

The magnitude of the weight loss of MCC powder at the heat treatment temperature of 175°C (Table 1) was comparable to that obtained from the TGA analysis. However, it was found that the heat treatment temperature and porosity of compacts affected the magnitude of % WL (Figure 6 and Table 1). Some compacts had lower % WL compared to that of the powder. At the heat treatment of
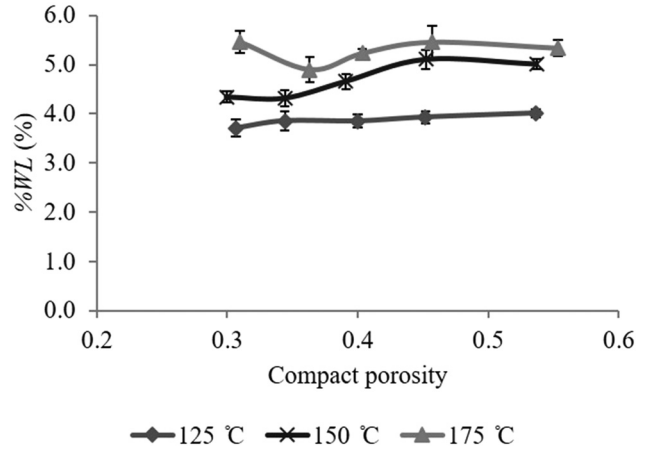

Figure 6: Relations between average values of % WL of compacts and compact porosity before heat treatment at different heat treatment temperatures. Error bars represent ±standard deviation, *n* = 5.
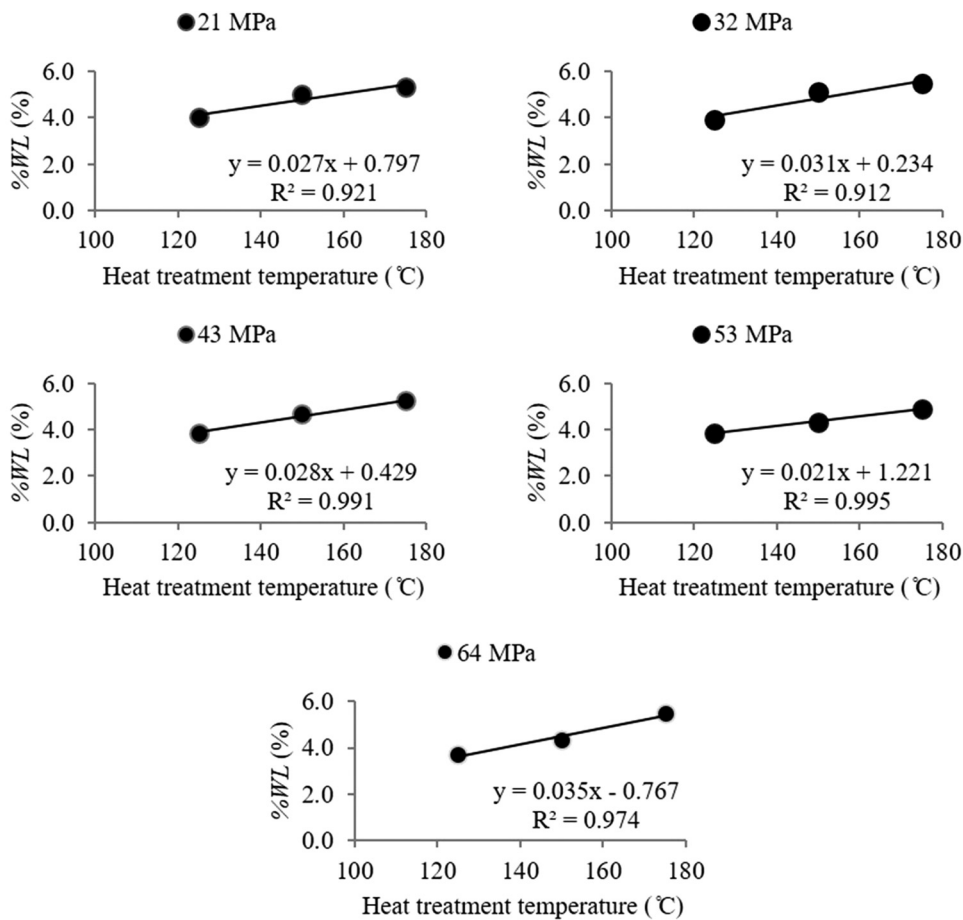

Figure 7: Relations between average values of % WL of compacts and heat treatment temperature at the applied compression pressures of 21, 32, 43, 53, and 64 MPa.
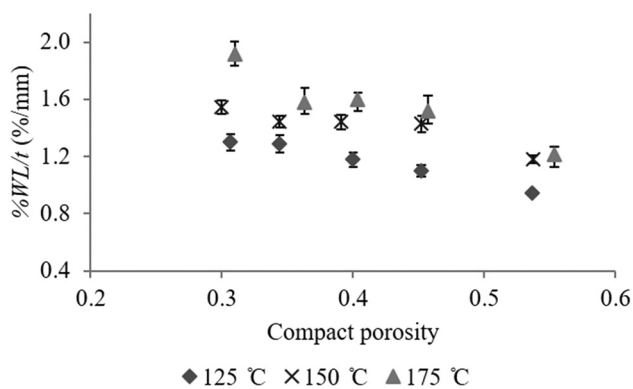
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Figure 8: Relations between average values of % WL/*t* of compacts and compact porosity before heat treatment at different heat treatment temperatures. Error bars represent ± standard deviation, *n* = 5.

125°C, the % WL of all compacts were smaller than that of the powder. This difference reached about 29% when compacts were prepared at 64 MPa. Compaction of the powder resulted in a less porous structure which increased the resistance to moisture escape. For heat treatments of 150°C and 175°C, some compacts had lower % WL while others had similar % WL compared to that of the powder heat treated at the same temperature (Figure 6 and Table 1). At the heat treatment of 150°C, the % WL of compacts decreased at lower values of porosities. The % WL of heat-treated compacts were lower than that of the powder by a magnitude of 18% when the compacts were prepared at 53 or 64 MPa. Additionally, compacts heat treated at 175°C and prepared at 53 MPa had a % WL that was 12% lower than that of the powder subjected to similar heat treatment conditions. Moreover, it was found that linear correlations between the % WL of the compacts and the heat treatment temperature can be made ($R^2 > 0.91$) for the compacts prepared at each of the different applied compression pressures (Figure 7). Compacts were heated in the analyzer which utilizes a heating element located above the sample in the chamber. This element heats up to the designated temperatures for the required period (5 min). The extent of weight loss is expected to depend upon the amount of heat transferred through the compact and the ability of moisture to escape through the porous structure during the treatment time. Compacts prepared at higher compression pressures are expected to have improved heat flow due to smaller thicknesses and lower porosities leading to higher thermal conductivity (17,21). On the other hand, these compacts could offer higher resistance for the moisture to escape. Figure 8 shows the relation between % WL normalized with compact thickness (i.e., % WL/*t*) and compact porosities before heat

treatment. A trend of increased magnitude of % WL/*t* as the porosity decreased can be seen. Therefore, a combination of factors such as the heat treatment temperature, thermal conductivity of the compact, compact thickness, and resistance to moisture escape affected the magnitude of % WL.

4 Conclusion

Heat treatment of compacts of MCC at 125°C, 150°C, and 175°C did not significantly affect their volumes in almost all of the applied compression pressure and heat treatment conditions. However, the densities of the compacts decreased while porosities increased due to weight loss associated with the heat treatments. In addition, the tensile strengths of the compacts did not significantly change for most of the heat treatment and applied compression pressure conditions. Therefore, the interparticulate bonding in the compacts was not affected under most of the conditions. Finally, a combination of factors resulting from both the applied compression pressure and heat treatment temperature affected the magnitude of weight loss of the compacts.

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