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Effect of relative humidity and temperature on moisture sorption and stability of sodium bicarbonate powder

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Abstract

The effects of relative humidity and temperature on moisture sorption rate and stability profile of sodium bicarbonate powder exposed to various storage conditions were investigated using gravimetrical and acid-titration methods. In the study, samples were placed in desiccators, which contained various saturated salt solutions to generate desired levels of relative humidity, denoted as RH, ranging from 30–93% RH. The weight of each sample was determined periodically. The results show that both the temperature and relative humidity are key factors in moisture sorption isotherm and decomposition kinetics. The threshold relative humidity RH_{th} is defined as the relative humidity above which sodium bicarbonate powder starts to rapidly gain weight. The critical relative humidity RH_c is defined as the relative humidity above which sodium bicarbonate powder either starts to rapidly gain weight or starts to rapidly hydrolyze (resulting in losing weight). The moisture sorption isotherm shows an unusual phenomenon at high RH, where the weight of the sodium bicarbonate powder either increases or decreases with time, depending on the storage temperature. When the powder is exposed to a lower temperature and high humidity level (e.g. at 25°C and 93% RH), the weight increases rapidly, due to the fact that the relative humidity exceeds the RH_{th} at this temperature. On the other hand, when the powder is exposed to higher temperature and high humidity levels (e.g. at 40°C, 89% RH and at 55ºC, 82% RH), the weight of the powder decreases with time since the relative humidity is below the RH_{th} at these temperature levels and the decomposition rate is higher than the moisture sorption rate. The decomposition of sodium bicarbonate results in the release of carbon dioxide. The values of RH_c at 25 and 40°C were determined to be between 76 and 88% RH and between 48 and 75% RH, respectively. The accurate moisture content and the stability profiles of sodium bicarbonate were determined using a titration-drying-titration procedure. The results of determination show that sodium bicarbonate powder is stable below 76% RH at 25°C and below 48% RH at 40°C, respectively. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Critical relative humidity; Moisture sorption; Sodium bicarbonate; Equilibrium moisture content; Decomposition kinetics; Hydrolysis; Titration–drying–titration

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1. Introduction

Sodium bicarbonate is an important component in various pharmaceutical solid and liquid dosage forms. Because of its widespread use, the stability of sodium bicarbonate in solid state, both as a raw material and as a formulation component, is of high interest to the pharmaceutical scientists. When sodium bicarbonate is stored as a powder, it degrades over time to carbon dioxide and sodium carbonate after sorption of moisture at lower temperature, or degrades directly to carbon dioxide and sodium carbonate without sorption of moisture at elevated temperature (Shefter et al., 1975). Therefore, it is critical to maintain appropriate temperature and relative humidity during the storage of the raw material and finished product as well as during manufacturing.

Several studies regarding the thermal decomposition of sodium bicarbonate under various conditions have been reported. Krupkowski (1938) investigated the decomposition of sodium bicarbonate powder in an open system, by means of a heating curve and reported a temperature decomposition of 124°C. Shefter et al. (1975) reported the kinetics of solid state transformation of sodium bicarbonate to sodium carbonate in an open system at 82–95°C. Studies conducted by Usui and Cartensen (1985) included sodium bicarbonate stability at 70°C in open and closed systems. Ahlneck and Alderborn (1989) investigated moisture sorption of sodium bicarbonate at 25°C and relative humidity ranging from 33–100% but did not study the stability of sodium bicarbonate at these conditions.

The rate of sodium bicarbonate decomposition to sodium carbonate is dictated by the moisture sorption kinetics at given temperature and humidity conditions. The release of carbon dioxide results in a decrease of powder mass and therefore, the moisture sorption isotherm of sodium bicarbonate is unique compared with other pharmaceuticals. For example, at room temperature and high humidity, a rapid increase in powder mass would be expected because of significant moisture gain and relatively low rate of carbon dioxide formation; however, at elevated temperature, a decrease in powder mass would be expected due to rapid formation and release of carbon dioxide with relatively low rate of moisture sorption. A review of literature shows lack of information on moisture sorption and related stability of sodium bicarbonate at controlled temperature and humidity conditions. Therefore, the purpose of this study was to investigate the moisture sorption of sodium bicarbonate and associated stability at various temperature and humidity conditions and to determine the critical humidity at given values of storage temperature.

2. Materials and methods

2.1. Experimental design

For convenience of discussion, the threshold relative humidity RH_{th} is defined as the relative humidity above which sodium bicarbonate powder starts to rapidly gain weight. The critical relative humidity RH_c is defined as the relative humidity above which sodium bicarbonate powder either starts to rapidly gain weight or starts to rapidly hydrolyze (resulting in losing weight). With these definitions, the value of RH_c is always lower than or equal to RH_{th}. A stagewise approach was undertaken to determine the critical relative humidity of sodium bicarbonate at 25, 40 and 55°C. In stage 1 study, the approximate range of RH_c was determined using the three saturated salt solutions, $MgCl_2$, $Mg(NO_3)_2$ and KNO_3, which corresponds to the three levels of relative humidity at 25°C, 33, 52 and 93% RH, respectively. In stage 2 study, the range of the RH_c was further refined using the additional two saturated salt solutions NaCl and Li_2SO_4, which generated the two levels of relative humidity at 25°C, 76 and 88% RH, respectively.

2.2. Moisture sorption

The five saturated salt solutions, $MgCl_2$, $Mg(NO_3)_2$, NaCl, Li_2SO_4, and KNO_3, were chosen to control various levels of relative humidity. Since the relative humidity of these solutions somewhat varies with temperature, the actual relative humidity levels for these solutions obtained from the literature (Greenspan, 1977; Callahan et al., 1982; Umprayn and Mendes, 1987) are listed below: (33, 52, 76, 88 and 93% RH) at 25°C, (32, 48, 75, 88 and 89%) at 40°C, and (30, 44, 74, 88, and 82%) at 55°C. It is noted that the three relative humidity values at 55°C, 44, 88, and 82%, were estimated in this work from the above literature data at 15–50°C using regression equations, since the experimental data at this temperature are not available. A thin layer ($\approx$0.5 g) of sodium bicarbonate powder (Mallinckrodt analytical reagent, Lot #7412 KMPT) was spread in each glass drying dish ($\approx$4.5 cm in inside diameter and 3.1 cm in height) using a brush. The dishes were placed in the desiccator which contained a saturated salt solution that generated a desired relative humidity. The desiccator was then stored in a constant temperature chamber of 25, 40 or 55°C. At predetermined time intervals, each sample dish was removed and covered with aluminum foil to prevent moisture exchange with the ambient during the transportation. After weighing, the dish was immediately placed back into the desiccator for the next time interval use. The net weight of the sodium bicarbonate powder in each dish was then calculated.

2.3. Stability evaluation of sodium bicarbonate by titration with hydrochloric acid

A known amount of sodium bicarbonate powder from each sample dish, $\approx$0.5 g, was dissolved using CO_2-free distilled and deionized water and transferred to a 100 ml volumetric flask, followed by bringing to volume. A total of 10 ml of the above solution was withdrawn and transferred to a 100 ml beaker, and two drops of phenolphthalein indicator solution were added to the solution with stirring. If the solution turned to pink, it indicated that the amount of decomposition was significant. This is referred to as the phenolphthalein test. If the test appeared to be negative, the sodium bicarbonate solution was titrated with a standardized hydrochloric acid solution using methyl red indicator. The hydrochloric acid ($\approx$ 0.05 N) was pre-standardized using pre-dried sodium carbonate (The US Pharmacopeia 23, 1995). Each solution was titrated until the appearance of pink color, boiled on a hot plate until the pink color disappeared, followed by cooling in an ice bath. This titration–boiling–cooling cycle was repeated until the pink color no longer disappeared after boiling. The amount of sodium bicarbonate in each sample was then calculated.

2.4. Determination of moisture content and decomposition products of sodium bicarbonate using the titration–drying–titration procedure

If the phenolphthalein test indicated that the amount of carbonate was not negligible, the titration–drying–titration procedure was performed to accurately determine the moisture content and decomposition products simultaneously. The amounts of moisture content and decomposition products were determined by combining the drying and acid titration methods. In the pre-drying titration, the samples were titrated with the standardized hydrochloric acid. In the drying step, the samples were dried in a 40 ± 0.2°C chamber to remove the moisture. The weight loss of each sample was recorded for a period of time, and the amounts of moisture and carbon dioxide removed were calculated. In the post-drying titration, the dried samples were again titrated with the standardized hydrochloric acid. The amounts of moisture content, sodium bicarbonate, and sodium carbonate were derived using mass balance before and after titration.

3. Results and discussion

3.1. Moisture sorption profiles

The conventional moisture sorption isotherms of pharmaceuticals indicate that at a given temperature, the amount of moisture sorption constantly increases with the relative humidity, and reaches a plateau at the critical humidity (Carstensen, 1993). It will be seen that the moisture sorption profiles of the sodium bicarbonate powder investigated in this work appear to be significantly different. The results obtained from the two stages of study are discussed below.

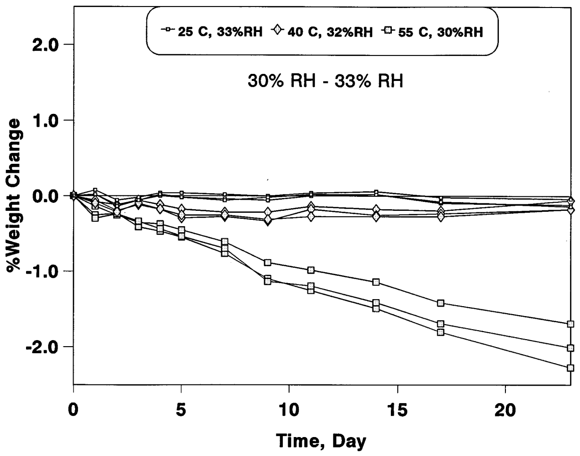

Fig. 1. Weight change profiles of sodium bicarbonate powder stored at 30–33% RH and various levels of temperature—stage 1 study.

3.1.1. Stage 1 study

The effects of temperature on percent weight change, denoted as %(weight change), at the humidity levels of 30–52% RH are shown in Figs. 1 and 2. For the cases of 25 and 40°C, it is noted that after the initial induction period, each of these profiles reaches a plateau at the end of storage. Also the value of %(weight change) for each profile is nearly negligible over 23 days of storage, indicating that the moisture sorption rate or decomposition rate is very slow. On the other hand at 55°C, the powder continuously loses weight over the storage period. From these profiles, it is postulated that the decomposition kinetics of sodium bicarbonate at 55°C appears to be different than that at 25 and 40°C. It is also noted from the profiles at 55°C that the rate of weight loss in Fig. 1 is higher than that in Fig. 2. This phenomenon may be explained by the following scenario. The decomposition of sodium bicarbonate to sodium carbonate in the absence of water molecules per Eq. (1), as described in Section 3.2.1, is commenced at $\sim$50°C (Handbook of Pharmaceutical Excipients, 1986), which is lower than the 55°C investigated in this work. Thus, the decomposition kinetics of sodium bicarbonate powder at 55°C may be a combination of: (1) the absence of water molecules per Eq. (1); and (2) with the presence of moisture per Eqs. (2)–(7) described in Section 3.2.1. The weight change of the powder is then determined by the competing effect of these two mechanisms.

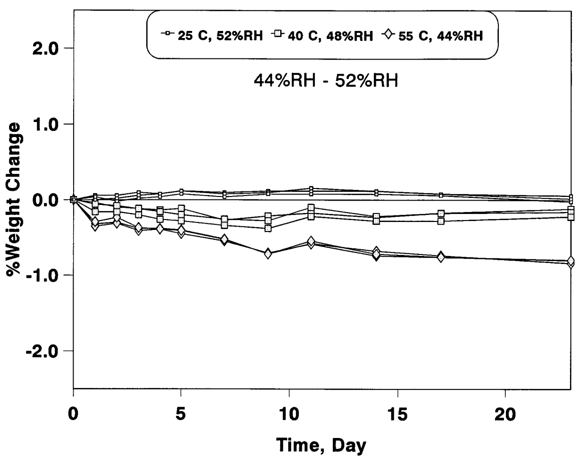

Fig. 2. Weight change profiles of sodium bicarbonate powder stored at 44–52% RH and various levels of temperature—stage 2 study.

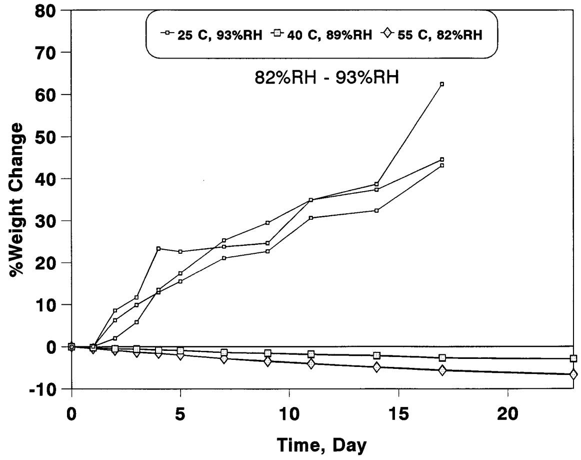

Fig. 3. Weight change profiles of sodium bicarbonate powder stored at 82–93% RH and various levels of temperature—stage 1 study.

The effects of temperature on moisture sorption and sodium bicarbonate decomposition at a very high relative humidity, ranging from 82–93% RH, are depicted in Fig. 3. A dramatic difference between these profiles is observed in Fig. 3. At 25°C, the powder gains as much as 65% moisture over 17 days of storage. At 40°C, the powder loses about 3% weight over 24 days of storage. This phenomenon may be attributed to the scenario that the relative humidity 93% RH at 25°C has exceeded the threshold relative humidity RH_{th}, so that the powder starts to rapidly absorb moisture. At 40°C, 89% RH, however, the relative humidity is below the RH_{th}, and the hydrolysis rate rapidly increases and exceeds the moisture sorption rate. At 55°C, 82% RH, the powder constantly loses weight with a higher decreasing rate than that at 40°C, 89% RH. It is noted that none of the moisture sorption profiles in Fig. 3 has reached an equilibrium over the storage period. The results indicate that both temperature and relative humidity contribute important roles on moisture sorption and the accompanied sodium bicarbonate hydrolysis and decomposition.

The results of Stage 1 study show that the critical relative humidity is probably between 52 and 93% RH for samples stored at 25°C, and between 48 and 89% RH for samples stored at 40°C. For samples stored at 55°C, as shown in Figs. 1–3, the powder continuously loses weight over the storage period, and therefore the critical humidity could not be determined.

3.1.2. Stage 2 study

In order to refine the range of the critical humidity, the stage 2 study was performed, where two additional saturated salt solutions, NaCl and Li_2SO_4, were chosen to control two levels of humidity, 76 and 88% RH (at 25°C), respectively. The values of weight change over ≈1 month of storage are plotted in Figs. 4 and 5, respectively. For the samples stored at 25°C, the powder loses weight and reaches a plateau for both levels of humidity. Also the value of %(weight change) for each profile is nearly negligible over 27 days of storage, indicating that the moisture sorption rate or decomposition rate is very slow. At 40°C, however the powder constantly loses weight over the entire period of storage.

3.1.3. Summary of moisture sorption profiles—critical relative humidity

The rate of weight change, in percent per day, for each of the profiles presented in Figs. 1–5 is equal to the slope of the profile. It appears that after the initial induction period of moisture sorption and/or decomposition, each of these profiles tends to approach a straight line. The slope of the straight line was determined using linear regression. At 25°C and below 88% RH, the values of the slope are negative, but are only slightly less than zero. For example, the weight loss calculated from Table 1 ranges from 0.099% per month to 0.157% per month. These values indicate that

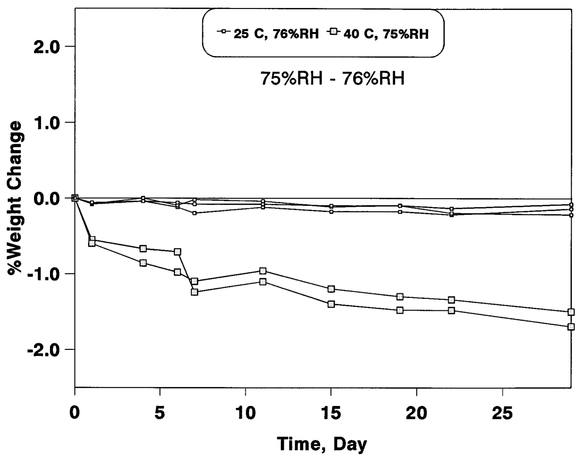

Fig. 4. Weight change profiles of sodium bicarbonate powder stored at 75–76% RH and various levels of temperature—stage 2 study.

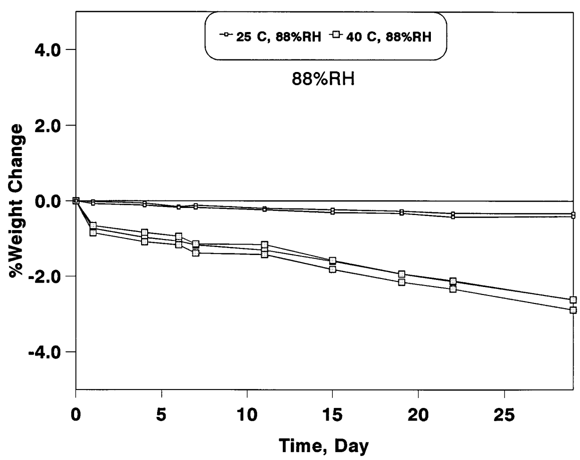

Fig. 5. Weight change profiles of sodium bicarbonate powder stored at 88% RH and various levels of temperature—stage 2 study.

Table 1
Summary of the rate of weight change (% per day) of sodium bicarbonate powder at various storage conditions

	Storage temperature					
	25°C		40°C		55°C	
	Storage humidity (%RH)	Weight change (% per day)	Storage humidity (%RH)	Weight change (% per day)	Storage humidity (%RH)	Weight change (% per day)
	93	2.6	89	−0.11	88[a]	Not tested
	88	−0.011	88	−0.071	82[a]	−0.24
	76	−0.0033	75	−0.023	74	Not tested
	52	−0.0042	48	0.0068	44[a]	−0.015
	33	−0.0052	32	0.0067	30	−0.078
Critical %RH	Between 88 and 93%		Between 48 and 75%		Not applicable	

[a] The three relative humidity values at 55°C, 44, 82 and 88% are estimated from the literature data of 15–50°C using regression equations, since the experimental data at these temperature values are not available.

moisture sorption or weight loss under these storage conditions is negligible. At 40°C and below 75% RH, the values of the slope become positive, but are only slightly greater than zero. For example, the weight change calculated from Table 1 ranges from 0.202% per month to 0.204% per month. These values indicate that moisture sorption or weight loss under these storage conditions is negligible. At 55°C and at the three levels of relative humidity tested, the values of the slope are significantly less than zero, indicating considerable weight loss due to decomposition. The critical humidity is evaluated when the value of each slope changes from a negligible (near zero) value to a significantly positive value (indicating rapid moisture sorption) or to a significantly negative value (indicating considerable decomposition). Thus, it can be seen from Table 1 that at 25°C, the critical relative humidity is possibly between 76 and 88%, whereas at 40°C the critical relative humidity is considerably lower, possibly between 48 and 75%. These values will be confirmed in Section 3.2.

3.2. Stability profiles of sodium bicarbonate

3.2.1. Decomposition kinetics

In the absence of water molecules, the decomposition kinetics of sodium bicarbonate at an elevated temperature is well known, as given by Barrall and Rogers (1966) and Handbook of Pharmaceutical Excipients (1986).

$$2\,NaHCO_3 \Leftrightarrow Na_2CO_3 + CO_2 + H_2O \qquad (1)$$

where each sodium bicarbonate molecule loses carbon dioxide and water molecules and becomes sodium carbonate. On the other hand, when the sodium bicarbonate powder is placed under high humidity, the decomposition schemes can be postulated as

$$NaHCO_3\,(s) \overset{+H_2O,\,k_s}{\Leftrightarrow} NaHCO_3(aq) \qquad (2)$$

$$2NaHCO_3\,(aq) \Leftrightarrow 2Na^+ + 2HCO_3^- \qquad (3)$$

$$HCO_3^- \Leftrightarrow H^+ + CO_3^{-2} \qquad (4)$$

$$HCO_3^- + H^+ \Leftrightarrow H_2CO_3 \qquad (5)$$

$$H_2CO_3 \Leftrightarrow H_2O\,(aq) + CO_2\,(aq) \qquad (6)$$

and

$$CO_2\,(aq) \Leftrightarrow CO_2\,(g)\uparrow \qquad (7)$$

Eq. (2) indicates that the bicarbonate powder in the solid phase, denoted as $NaHCO_3$ (s), after absorbing moisture from the ambient (with a sorption rate constant k_s), is dissolved into the sorbed moisture layer, denoted as $NaHCO_3$ (aq). The equilibrium reactions Eqs. (3)–(6) are subsequently established in the aqueous phase. Eq. (7) shows that the CO_2 molecules produced in the aqueous phase migrate to the ambient through a mass transfer process. This process will continue until the concentration of CO_2 in the gas phase increases to a sufficient level (for the case of placing samples in the desiccator) to establish an

Table 2
Stability profiles of sodium bicarbonate under various storage conditions, based on total weight[a]

Storage temperature (°C)	% Relative humidity	% Of intact sodium bicarbonate after:			
		0 Month	1 Month	2 Months	3 Months
25	33	100.0	95.51	99.56	99.79
	52	100.0	NA	NA	99.79
	76	100.0	100.2	100.3	99.97
40	32	100.0	100.0	99.52	99.81
	48	100.0	NA	NA	99.70
	75	100.0	100.5	NA	90.81[b]

NA, not applicable, test was not performed at this interval.
[a] Each data point represents an average of three observations.
[b] Data generated using the titration–drying–titration method to quantify sodium bicarbonate after the phenolphthalein test was positive indicating bicarbonate decomposition. All other data were generated by direct titration with HCl as the phenolphthalein test was negative indicating absence of significant bicarbonate decomposition.

equilibrium with the dissolved CO_2. At higher temperature, the solubility of CO_2 in the aqueous moisture layer is lower. Thus, the mass transfer rate of CO_2 increases, resulting in higher hydrolysis and decomposition rates of bicarbonate powder. It is noted that Eqs. (2) and (7) are physical processes, whereas Eqs. (3)–(6) are chemical equilibrium equations. The overall chemical reaction, from Eqs. (3)–(6), becomes

$$2\ NaHCO_3\ (aq) \Leftrightarrow 2Na^+ + CO_3^{-2} + CO_2 + H_2O \quad (8)$$

which is similar to Eq. (1).

The above discussion can be exemplified by Fig. 3, which shows that at 25°C, 93% RH, the weight of the powder increases rapidly, since the relative humidity exceeds RH_{th}. Also at this temperature, the solubility of CO_2 in water is relatively higher, so that the rate of CO_2 transferred from the aqueous phase to the gas phase is relatively low. This causes the net increase in the weight of powder. At higher temperature, such as 40 or 55°C, the relative humidity is still below RH_{th}. In addition, the solubility of CO_2 is much lower, resulting in rapid removal of CO_2 from the solution. It can be concluded that the rate of weight change of the bicarbonate powder depends on the rate of moisture sorption rate and the rate of losing carbon dioxide and water molecules.

3.2.2. Stability profiles

The stability profiles of sodium bicarbonate for the Stages 1 and 2 studies determined per Sections 2.3 and 2.4 are summarized in Table 2. Each value in the table for 1, 2, and 3 months of storage represents the mean of three observations. The values in Table 2, except the one stored at 40°C and 75% RH, indicate that the intact amount of sodium bicarbonate are close to 100%. In Table 2, only the samples exposed to 40°C, 75% RH appears to be positive to the phenolphthalein test described in Section 2.4. The values in Table 2 confirm that the profiles that had reached 'equilibrium' in Figs. 1–3 at the end of storage, indeed have negligible amounts of decomposition. The values of the moisture content stored at 25°C, 76%RH for 3 months and 40°C, 75% RH for 3 months were determined using the titration-drying-titration procedure described in Section 2.4, and the obtained average values are equal to 0.884 and 2.725%, respectively. The higher moisture content at 40°C seems to be similar to the observations by Umprayn and Mendes (1987), (page 663–667). They studied the moisture uptake of cefaclor for the temperature investigated from 25–55°C and the relative humidity between 26 and 90.2% RH. For this particular compound, they found that an increase in temperature resulted in increasing the rate of moisture uptake

Table 3
Summary of stability profile of sodium bicarbonate stored at various conditions

Storage temperature			
25°C		40°C	
Storage humidity (%RH)	Stability	Storage humidity (%RH)	Stability
76	Negligible decomposition	75	Decompose slightly
52	Negligible decomposition	48	Negligible decomposition
33	Negligible decomposition	32	Negligible decomposition

and also the amount of moisture adsorbed at equilibrium. The moisture content of the sodium bicarbonate powder raw material, prior to storage at various levels of temperature and relative humidity, was also determined using the titration–drying–titration procedure. The average value obtained is only 0.038%. The moisture content values described above are much smaller than those of some common pharmaceutical excipients stored under similar conditions in the literature (Callahan et al., 1982; Umprayn and Mendes, 1987). According to the criteria established by Callahan et al. (1982), sodium bicarbonate may be classified as a non-hygroscopic pharmaceutical excipient.

It can be concluded from Table 2 that at 25°C, the powder is stable below 76% RH. At 40°C, the powder is less stable and started to degrade at 75% RH. The values presented in this table are consistent with the moisture sorption profiles described in Table 1. The results in Table 2 are further summarized in Table 3 to show the overall picture of the stability profile discussed above.

4. Conclusion

The moisture sorption kinetics of sodium bicarbonate powder is dictated by the rate of moisture sorption and the rate of sodium bicarbonate decomposition to sodium carbonate. The weight of sodium bicarbonate powder could increase or decrease, it is highly dependent on the storage humidity and temperature. The moisture sorption profiles can not be generalized by a simple schematic pattern, due to the complexity of the physical and chemical reactions. The values of the critical humidity at 25 and 40°C were determined to be approximately between 76 and 88% RH and between 48 and 75% RH, respectively. The results of acid titration show that sodium bicarbonate powder is stable below 76% RH at 25°C and below 48% RH at 40°C, respectively. At 55°C, the critical relative humidity cannot be determined due to the fact that sodium bicarbonate powder continuously loses weight. A titration–drying–titration approach was used to accurately determine the moisture content and the stability profiles of sodium bicarbonate powder. The results show that the moisture content of the sodium bicarbonate raw material prior to storage is very low, $\approx 0.038\%$. It also shows that the equilibrium moisture content is a function of the relative humidity and temperature.

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