



Comparative Physical Stability Observations of Co-Amoxiclav TSS Residual Vacuum Dust at Various Relative Humidity (RH) Levels

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Abstract. This study descriptively compared physical stability observations of residual vacuum-molded dust collected from a Co-Amoxiclav TSS process under different relative humidity (RH) conditions and packaging configurations. The source study did not document the exact amoxicillin-to-clavulanate ratio, batch composition, or whether the residual material was representative of a finished pharmaceutical product or of isolated active pharmaceutical ingredients; therefore, the findings are restricted to the material tested. Nine 5-g samples were allocated to low (22–30%), moderate (50–65%), and high RH (65–80%) environments, with one sample for each RH–packaging combination: parchment paper (P1), parchment paper plus a zip-lock bag (P2), and parchment paper plus a zip-lock bag with silica gel (K1). Samples were observed on Days 0, 3, and 5 using organoleptic assessment and gravimetric weight measurement. Because each RH–packaging combination had only one experimental unit and no independent replication, results were interpreted descriptively without inferential statistical testing. Greater visible and gravimetric changes were observed in P1 and P2 at moderate and high RH, whereas K1 generally showed smaller changes and preserved a fine white powder appearance. These observations support the practical importance of moisture-protective packaging for hygroscopic pharmaceutical materials, but they do not establish chemical degradation because no assay of active substances, degradation products, or moisture content was performed. Appropriate storage and preservation of medicine quality support SDG 3 (Good Health and Well-Being); reducing avoidable quality loss and pharmaceutical waste may also contribute to SDG 12 (Responsible Consumption and Production) when supported by broader lifecycle evidence.

Keywords: Co-Amoxiclav TSS; Physical Stability; Relative Humidity; Hygroscopic Material; Pharmaceutical Packaging

1. Introduction

The availability of safe, effective, and good-quality medicines depends not only on manufacturing quality but also on appropriate storage and packaging throughout the product lifecycle. International stability guidance emphasizes evaluation under defined environmental conditions, while pharmaceutical packaging must provide protection that is appropriate to the moisture sensitivity of the material (ICH, 2003; WHO, 2019; Waterman & MacDonald, 2010). Beta-lactam products containing amoxicillin and clavulanate are particularly relevant to storage research because clavulanate is less stable than amoxicillin under several conditions. Published analytical studies have demonstrated sensitivity of clavulanate-containing formulations to environmental conditions, while humidity-focused formulation studies have shown that barrier design can materially affect stability outcomes (Wardrop et al., 1998; Mack et al., 2021).

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Moisture is an important factor in the handling of hygroscopic pharmaceutical solids. Moisture uptake can alter powder flow, texture, mass, and other physical properties, while the extent to which moisture causes chemical degradation must be established with chemical analytical methods rather than visual inspection alone (Heidemann & Jarosz, 1991; Ng et al., 2022). For moisture-sensitive drug products, packaging performance is therefore commonly considered in relation to moisture-vapor transmission, the humidity inside the package, and the use of desiccants or barrier systems. Studies of pharmaceutical packaging show that container material, barrier characteristics, and desiccant configuration can affect internal humidity and the physical or chemical stability of hygroscopic products (Lehto & Erling, 2007; Waterman & MacDonald, 2010; Mwesigwa & Basit, 2016). In tropical production and storage environments, broad fluctuations in temperature and RH may increase the practical importance of moisture control. However, observed discoloration, caking, stickiness, or weight change should be interpreted as physical evidence of environmental exposure unless degradation is confirmed using a validated assay, chromatographic analysis, moisture-content testing, or another stability-indicating method. This distinction is especially important when the tested material is a process residual rather than a finished dosage form. The general relevance of package barrier properties and hygroscopic-material handling is also supported by pharmaceutical storage literature (Tu et al., 1988; Płotkowiak & Nogowska, 1989; Yang et al., 2019; Yoshida et al., 2026).

Accordingly, this study aimed to descriptively compare organoleptic appearance and gravimetric weight changes of Co-Amoxiclav TSS residual vacuum dust stored under three RH ranges and three simple packaging configurations over five days. The study did not aim to quantify amoxicillin or clavulanate content or to establish chemical degradation. By focusing on practical moisture-control observations, the study relates primarily to SDG 3 (Good Health and Well-Being) through preservation of medicine quality and safe pharmaceutical handling. A potential link to SDG 12 (Responsible Consumption and Production) is limited to the principle that preventing avoidable quality loss may reduce waste; no lifecycle or waste-reduction analysis was conducted in this study.

2. Methods

2.1. Research Design

This study used a descriptive comparative experimental design to compare physical appearance and gravimetric weight changes among samples exposed to different RH ranges and packaging configurations. The observations were not treated as a chemical stability assay and no inferential statistical hypothesis testing was performed.

2.2. Study Location and Time

The study was conducted at PT Meprofarm Pharmaceutical, West Java, Indonesia, in April 2026. Samples were stored in production-room environments categorized by the source study as low RH (22–30%), moderate RH (50–65%), and high RH (65–80%). A room hygrometer was used to observe environmental conditions. Detailed temperature profiles, hygrometer calibration records/accuracy, measurement frequency, and evidence that all environmental variables other than RH were comparable across rooms were not documented in the source study; these factors are therefore treated as methodological limitations.

2.3. Materials and Equipment

Test material: residual vacuum-molded dust collected from a Co-Amoxiclav TSS process. The source study did not document the exact amoxicillin-to-clavulanate ratio, complete formulation status, batch characteristics, excipient composition, or analytical confirmation of the material. Accordingly, the material is referred to as Co-Amoxiclav TSS residual vacuum dust rather than as purified raw amoxicillin and potassium clavulanate.

Equipment: analytical/digital balance, room hygrometer, parchment paper, zip-lock bags, silica gel, spatula, sample labels, and a camera or other documentation device.

2.4. Samples

Sampling was performed by direct collection with a spatula from residual vacuum-molded dust generated during a Co-Amoxiclav TSS process at a pharmaceutical industry facility in Bandung. A total of 45 g was divided into nine 5-g experimental units. Each RH-packaging combination was represented by one 5-g unit only; no independent replicate samples were reported. This limits estimation of variability, reproducibility, and statistical significance, and the findings should therefore be interpreted as preliminary descriptive comparisons rather than population-level estimates.

- a. Three samples in different packaging, stored in a room with low RH (22–30%): P1 (parchment paper only), P2 (parchment paper and zip-lock bag), and K1 (parchment paper, zip-lock bag, and silica gel).
- b. Three samples in different packaging, stored in a room with moderate RH (50–65%): P1, P2, and K1 (as defined above).
- c. Three samples in different packaging, stored in a room with high RH (65–80%): P1, P2, and K1 (as defined above).

2.5. Data Collection

Data collection comprised: (1) obtaining permission from the Production Manager and the pharmacist responsible for penicillin production; (2) collecting the residual process material; (3) allocating one 5-g sample to each of nine RH-packaging combinations; (4) observing sample appearance and recording sample weight on Days 0, 3, and 5; and (5) recording observations in a research worksheet. RH was observed using a room hygrometer. Because the source study did not provide instrument calibration/accuracy records, continuous temperature profiles, or a complete environmental monitoring log, comparisons among rooms may be affected by uncontrolled environmental differences in addition to RH.

2.6. Data Analysis

Data were analyzed descriptively by comparing organoleptic appearance and gravimetric weight across the nine experimental conditions. To ensure a single calculation convention, percentage weight change for both Day 3 and Day 5 was calculated relative to the Day 0 baseline weight of 5.00 g for the same sample:

$$\% \text{ Weight change from Day 0} = [(Observed \text{ weight} - Day 0 \text{ weight}) / Day 0 \text{ weight}] \times 100\%$$

Because there was only one experimental unit per RH-packaging combination, no inferential statistical analysis was conducted and terms such as ‘significant’ are not used statistically. Color, texture, and weight changes were treated as physical observations.

Chemical degradation, hydrolysis, oxidation, active-substance loss, and irreversible structural change were not considered verified outcomes because no HPLC/assay, degradation-product analysis, water-content determination, or other chemical stability-indicating test was performed. This conservative interpretation is consistent with compendial and stability-testing expectations that chemical quality be supported by appropriate analytical evidence (British Pharmacopoeia Commission, 2023; United States Pharmacopeial Convention, 2024; Kementerian Kesehatan Republik Indonesia, 2020).

3. Results and Discussion

Samples were evaluated organoleptically and gravimetrically on Days 0, 3, and 5. Tables 1–9 present all nine RH-packaging combinations. For consistency, all percentage weight changes are calculated from the Day 0 baseline. The findings are descriptive physical observations and should not be interpreted as chemical degradation measurements.

3.1. Sample P1 (Parchment Paper Only) at Low RH (22–30%)

As shown in Table 1, Sample P1 at low RH (22–30%) showed only modest weight variation over five days, with a -0.60% change on Day 3 and a $+1.60\%$ change on Day 5 relative to baseline. A slight yellowish discoloration was visible on Day 5, while the powder remained fine. The observation documents a physical change but does not identify its chemical cause.

Table 1. Organoleptic Observation of Sample P1 at Low RH (22–30%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	4.97	-0.60%	Small weight decrease; no visible texture change
5	Slightly yellowish white, fine powder	5.00	5.08	$+1.60\%$	Visible discoloration with weight above baseline; chemical cause not assessed

Initial Phase (Day 0–3):

On Day 3, P1 weighed 4.97 g (-0.60% from Day 0) and remained a fine white powder. The small decrease may reflect moisture exchange or measurement/environmental variation; the study did not directly measure water content.

Subsequent Phase (Day 3–5):

By Day 5, P1 weighed 5.08 g ($+1.60\%$ from Day 0) and appeared slightly yellowish white. Discoloration and weight change indicate reduced physical consistency under the test condition, but oxidation or chemical degradation cannot be confirmed from organoleptic and gravimetric data alone.

3.2. Sample P2 (Parchment Paper and Zip-Lock Bag) at Low RH (22–30%)

Table 2 shows that P2 at low RH (22–30%) remained a fine white powder throughout the observation period. Weight changed from 5.00 g to 5.01 g on Day 3 ($+0.20\%$) and 5.02 g on Day 5 ($+0.40\%$) relative to baseline.

Table 2. Organoleptic Observation of Sample P2 at Low RH (22–30%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	5.01	+0.20%	Small weight increase; RH reported at 24–25%
5	White, fine powder	5.00	5.02	+0.40%	Small cumulative weight increase; no visible change

Initial Phase (Day 0–3):

On Day 3, P2 showed a small +0.20% weight change while retaining its original appearance. This is consistent with limited moisture exchange under the observed low-RH condition.

Subsequent Phase (Day 3–5):

By Day 5, the cumulative weight change was +0.40% and no visible color or texture change was recorded. This descriptive result suggests that the zip-lock configuration limited physical change under low RH during the five-day period.

3.3. Sample K1 (Parchment Paper, Zip-Lock Bag, and Silica Gel) at Low RH (22–30%)

Table 3 summarizes K1 at low RH (22–30%). The sample remained a fine white powder on all observation days, with cumulative weight changes of +0.20% on Day 3 and +0.40% on Day 5.

Table 3. Organoleptic Observation of Sample K1 at Low RH (22–30%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	5.01	+0.20%	Small weight increase; RH reported <25%
5	White, fine powder	5.00	5.02	+0.40%	Small cumulative weight increase; fine powder preserved

Initial Phase (Day 0–3):

The Day 3 observation showed a small increase to 5.01 g (+0.20%) without visible change. The source study recorded RH below 25% around this condition.

Subsequent Phase (Day 3–5):

On Day 5, K1 weighed 5.02 g (+0.40% from baseline) and remained a fine white powder. Within the limitations of a single sample, the physical result is consistent with the moisture-control role expected from a closed bag plus desiccant system (Lehto & Erling, 2007; Waterman & MacDonald, 2010).

3.4. Sample P1 (Parchment Paper Only) at Moderate RH (50–65%)

Table 4 shows that P1 at moderate RH (50–65%) displayed greater physical variability than the low-RH P1 sample. The sample became slightly damp by Day 3, with weight first increasing and then decreasing below baseline by Day 5.

Table 4. Organoleptic Observation of Sample P1 at Moderate RH (50–65%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder, slightly damp	5.00	5.06	+1.20%	Weight gain accompanied by slight dampness
5	White, fine powder, slightly damp	5.00	4.87	–2.60%	Weight below baseline; physical appearance remained slightly damp

Initial Phase (Day 0–3):

On Day 3, P1 weighed 5.06 g (+1.20% from Day 0) and became slightly damp. This combination of weight gain and dampness is consistent with moisture exposure in a hygroscopic material, although the contribution of individual formulation components was not chemically determined.

Subsequent Phase (Day 3–5):

By Day 5, P1 weighed 4.87 g (–2.60% from Day 0) and remained slightly damp. The reversal in weight direction emphasizes that a single gravimetric measurement cannot be equated directly with chemical degradation and may reflect dynamic moisture exchange or other uncontrolled environmental factors.

3.5. Sample P2 (Parchment Paper and Zip-Lock Bag) at Moderate RH (50–65%)

As presented in Table 5, P2 at moderate RH (50–65%) showed the largest cumulative weight gain among the moderate-RH conditions and developed cream-yellow discoloration, stickiness, and caking over five days.

Table 5. Organoleptic Observation of Sample P2 at Moderate RH (50–65%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	Cream-yellow, sticky	5.00	5.21	+4.20%	Marked weight gain with discoloration and stickiness
5	Cream-yellow, sticky and caked	5.00	5.24	+4.80%	Further cumulative weight gain and caking; chemical cause not assessed

Initial Phase (Day 0–3):

By Day 3, P2 increased to 5.21 g (+4.20% from baseline), with a cream-yellow color and sticky texture. These are clear physical stability changes under the test condition. However, because no active-substance assay or degradation-product testing was conducted, the observations cannot establish chemical degradation.

Subsequent Phase (Day 3–5):

By Day 5, P2 reached 5.24 g (+4.80% from baseline) and became sticky and caked. The result is consistent with substantial moisture-associated physical change in a hygroscopic

pharmaceutical material. Published studies similarly show that humidity and packaging can strongly influence the behavior of hygroscopic drug products, although chemical stability requires analytical confirmation (Ng et al., 2022; Mwesigwa & Basit, 2016).

3.6. Sample K1 (Parchment Paper, Zip-Lock Bag, and Silica Gel) at Moderate RH (50–65%)

Table 6 presents K1 at moderate RH (50–65%). The sample remained a fine white powder, with a small +0.40% weight change on Day 3 and return to the 5.00-g baseline on Day 5.

Table 6. Organoleptic Observation of Sample K1 at Moderate RH (50–65%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	5.02	+0.40%	Small weight increase; no visible change
5	White, fine powder	5.00	5.00	0.00%	Returned to baseline weight; fine powder appearance preserved

Initial Phase (Day 0–3):

On Day 3, K1 weighed 5.02 g (+0.40%) without visible change. This result indicates relatively limited physical variation compared with P1 and P2 at the same RH range, but the single experimental unit prevents estimation of reproducibility.

Subsequent Phase (Day 3–5):

By Day 5, K1 returned to 5.00 g (0.00% from baseline) and remained a fine white powder. The observation is compatible with the intended moisture-buffering function of silica gel, but no direct moisture-balance measurement was performed to quantify desiccant uptake.

3.7. Sample P1 (Parchment Paper Only) at High RH (65–80%)

Table 7 shows that P1 at high RH (65–80%) underwent pronounced visible and gravimetric changes over five days, including yellowing, caking, stickiness, and progressive weight gain.

Table 7. Organoleptic Observation of Sample P1 at High RH (65–80%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	Yellow, slightly caked	5.00	5.08	+1.60%	Weight gain with visible yellowing and early caking
5	Yellow, sticky and caked	5.00	5.20	+4.00%	Marked cumulative weight gain with worsening visible changes

Initial Phase (Day 0–3):

By Day 3, P1 weighed 5.08 g (+1.60%) and had turned yellow with slight caking. These findings document a physical response to the high-RH environment; they do not, by themselves, prove hydrolysis.

Subsequent Phase (Day 3–5):

By Day 5, P1 weighed 5.20 g (+4.00% from baseline) and was yellow, sticky, and caked. This was the clearest physical instability observed in the high-RH P1 condition. Chemical degradation or irreversible structural change cannot be inferred without a stability-indicating chemical assay.

3.8. Sample P2 (Parchment Paper and Zip-Lock Bag) at High RH (65–80%)

Table 8 presents P2 at high RH (65–80%). The zip-lock configuration limited visible change through Day 3, but by Day 5 the sample showed cream-yellow discoloration and a cumulative +1.20% weight change.

Table 8. Organoleptic Observation of Sample P2 at High RH (65–80%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	5.03	+0.60%	Small weight gain; no visible change
5	Cream-yellow, smooth	5.00	5.06	+1.20%	Cumulative weight gain with discoloration; chemical cause not assessed

Initial Phase (Day 0–3):

On Day 3, P2 weighed 5.03 g (+0.60%) and remained a fine white powder. The modest weight gain suggests some environmental moisture exchange despite the zip-lock barrier, but the mechanism was not directly measured.

Subsequent Phase (Day 3–5):

By Day 5, the weight increased to 5.06 g (+1.20% from baseline) and the sample became cream-yellow. This supports a descriptive association between high-RH exposure and physical change; it does not establish potassium-clavulanate hydrolysis because no component-specific analytical testing was conducted.

3.9. Sample K1 (Parchment Paper, Zip-Lock Bag, and Silica Gel) at High RH (65–80%)

As shown in Table 9, K1 at high RH (65–80%) retained a fine white powder appearance across the five-day observation period. Its weight decreased to 4.96 g on Day 3 and remained at that value on Day 5 (–0.80% from baseline).

Table 9. Organoleptic Observation of Sample K1 at High RH (65–80%)

Time (Day)	Appearance (Color/Texture)	Day 0 Baseline Weight (g)	Observed Weight (g)	Weight Change vs Day 0 (%)	Remarks
0	White, fine powder	5.00	5.00	0.00%	Baseline condition
3	White, fine powder	5.00	4.96	–0.80%	Small weight decrease; fine powder appearance preserved
5	White, fine powder	5.00	4.96	–0.80%	Weight unchanged from Day 3; fine powder appearance preserved

Initial Phase (Day 0–3):

On Day 3, K1 showed a -0.80% weight change while retaining its original appearance. The direction of change differs from several other conditions and may reflect moisture exchange, desiccant effects, or measurement/environmental variation; the study cannot distinguish among these possibilities.

Subsequent Phase (Day 3–5):

On Day 5, K1 remained at 4.96 g and continued to appear as a fine white powder. Within this short, unreplicated experiment, K1 showed the least visible deterioration at high RH. This descriptive pattern is consistent with literature indicating that barrier packaging and desiccant strategies can reduce moisture exposure of hygroscopic pharmaceutical materials (Waterman & MacDonald, 2010; Lehto & Erling, 2007).

3.10. Study Limitations

This study has several important limitations. First, each RH–packaging combination was represented by only one 5-g sample, so between-sample variability and reproducibility could not be estimated. Second, the exact composition, amoxicillin-to-clavulanate ratio, batch characteristics, and representativeness of the residual Co-Amoxiclav TSS vacuum dust were not documented. Third, environmental monitoring was reported as broad RH ranges, while detailed temperature profiles, hygrometer calibration/accuracy, measurement frequency, and comparability of the three rooms were not available. Fourth, the study used only organoleptic and gravimetric evaluation; therefore, changes in active-substance content, degradation products, water content, hydrolysis, oxidation, and chemical structure were not measured. These limitations restrict the findings to preliminary descriptive physical observations and prevent generalization to finished Co-Amoxiclav products, isolated active ingredients, shelf-life performance, or chemical stability. Recommendations:

1. Future studies should compare pharmaceutical packaging systems with characterized water-vapor transmission performance, including high-barrier materials, rather than assuming that any specific packaging format is superior without direct WVTR and stability data (Waterman & MacDonald, 2010; Mwesigwa & Basit, 2016).
2. The use of desiccants may be evaluated as part of a defined packaging system, with desiccant capacity, package headspace, seal integrity, and internal RH measured explicitly. Desiccant effectiveness should be confirmed experimentally rather than inferred from external RH alone (Lehto & Erling, 2007).
3. Environmental monitoring should include calibrated instruments, documented measurement frequency, actual temperature and RH profiles, and comparable storage conditions across experimental groups.
4. Visual inspection of discoloration, stickiness, dampness, or caking can be used as an early physical-quality observation, but such findings should not be labeled hydrolysis or chemical degradation unless confirmed with an appropriate stability-indicating analytical method.
5. For finished medicines, patients should follow the manufacturer-approved storage instructions and retain products in their original packaging unless advised otherwise by an authorized healthcare professional. The present experiment on residual process material does not establish storage instructions for marketed products

Conclusions

The study objective was to compare physical appearance and gravimetric weight changes of the tested Co-Amoxiclav TSS residual vacuum dust across RH and packaging conditions. Descriptively, moderate and high RH were associated with greater visible and weight changes in several P1 and P2 samples, whereas the K1 configuration generally preserved a fine white powder appearance and showed smaller or more stable gravimetric changes over five days. The observed pattern is consistent with moisture sensitivity of a hygroscopic pharmaceutical material, especially under moderate and high RH. However, the experiment did not identify which component caused the observed changes and did not measure moisture content or chemical degradation. Among the configurations tested, P1 (parchment paper only) and P2 (parchment paper plus zip-lock bag) showed more visible deterioration in some moderate- and high-RH conditions, while K1 (parchment paper plus zip-lock bag and silica gel) showed the most consistent preservation of a fine white powder appearance. These are descriptive observations from single experimental units and should not be interpreted as statistically proven superiority or as shelf-life validation. The findings support further controlled, replicated studies of moisture-protective packaging for Co-Amoxiclav-related materials. Chemical stability claims require validated assays of amoxicillin and clavulanate, degradation-product testing, defined temperature/RH control, calibrated monitoring instruments, and independent replicates in accordance with stability-testing principles (ICH, 2003; WHO, 2019).

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Conflicts of Interest

The authors declare no conflict of interest.

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