Journal of Molecular Modeling (2026) 32:95
https://doi.org/10.1007/s00894-026-06679-7

RESEARCH

Impact of excipient composition and environmental humidity on the physicochemical properties of ondansetron orally disintegrating tablets: experimental and molecular simulation study

Alaa Aldabet[1]

Received: 23 December 2025 / Accepted: 27 February 2026

Abstract

Context Orally disintegrating tablets (ODTs) are highly sensitive to environmental humidity due to their hydrophilic excipients, which impact critical quality attributes like hardness, friability, and disintegration time. This study integrates molecular simulation with experimental analysis to investigate how excipient composition governs the moisture affinity and physicochemical stability of two ondansetron ODT formulations (gelatin-based vs. microcrystalline cellulose (MCC)-based) under varying humidity conditions. Molecular dynamics simulations predicted higher hygroscopicity for the MCC-based formulation, which correlated with experimental observations of increased friability and faster disintegration at elevated humidity. The gelatin-based formulation exhibited greater stability across humidity levels. These findings validate MD simulation as a predictive tool for screening excipient interactions with moisture during ODT pre-formulation.

Methods Molecular dynamics simulations were performed using Materials Studio 6.0.0 (BIOVIA, 2012) with the COMPASS force field. All molecular structures were energy-minimized, and amorphous cells for both formulations were constructed using the Amorphous Cell module with the COMPASS force field. Henry's constants and isosteric heats of adsorption were calculated using the Sorption module via Grand Canonical Monte Carlo simulations at 298 K. Experimental evaluations included hardness, friability, loss on drying, and disintegration time tests conducted according to USP 43–NF 38 guidelines at 29% and 57% relative humidity. Statistical analysis was performed using one-way ANOVA in JMP 13.2.0.

Keywords Henry's constant · Hygroscopicity · Moisture sorption · Molecular dynamics simulation · Orally disintegrating tablets

Introduction

Orally disintegrating tablet (ODT) is a solid dosage form that dissolves rapidly in the mouth without water [1]. This characteristic makes them ideal for pediatric, geriatric, and psychiatric patients who may have difficulty swallowing conventional tablets or capsules [2]. Over the past two decades, ODT has attracted significant attention due to its quicker onset of action, enhanced patient compliance, and convenience [2, 3]. Despite their benefits, ODT presents critical formulation challenges. Their rapid disintegration necessitates the use of hydrophilic excipients, which actually increases their sensitivity to moisture uptake [4, 5]. Moisture can strongly affect the mechanical, physical, and stability properties of ODT [6]. Therefore, excipient selection is essential to balance mechanical strength, moisture resistance, and rapid disintegration [7]. Humidity can influence multiple critical quality attributes (CQAs) of ODTs. At high relative humidity (RH), hygroscopic excipients absorb moisture, leading to changes in tablet weight, hardness, friability, and disintegration time [2, 8] Many excipients are used to achieve rapid disintegration of ODT. Mannitol is the most widely used diluent in ODT formulation due to its cooling sensation and rapid solubility [9, 10], while lactose monohydrate is less suitable for patients with lactose intolerance [11]. Binders such as microcrystalline cellulose (MCC) offer good compressibility and disintegration properties [12], while gelatin improves the physical properties of ODT but may increase moisture sensitivity [13]. Understanding the interaction

✉ Alaa Aldabet
alaa.aldabet@au.edu.sy; alaa.aldabet@gmail.com

[1] Faculty of Pharmacy, Al-Andalus University for Medical Sciences, Qadmus, Tartus, Syrian Arab Republic

Published online: 10 March 2026

between moisture and ODT excipients is crucial as it directly affects the physical and mechanical properties [2].

Several studies have explored the effects of excipients and environmental conditions on the performance of ODT. Alyami et al. [14] investigated the impact of moisture content on ODT properties, and the results showed that MCC with 11% moisture content resulted in the most flowable powder and favorable ODT characteristics. Furthermore, Dhewale et al. (2023) studied the effect of relative humidity (RH%), type of excipients, and packaging material on moisture absorption of hygroscopic drugs. The results demonstrated that a high level of RH% reduced the drug bioavailability due to multiple changes in the mechanical properties of ODT [15]. More recently, computational chemistry has been used as a pre-screening tool in developing ODT formulations at the molecular level. This in silico approach could save time and reduce the cost of experimental methods [16]. Qin et al. [17] used Python to model Carr's index and mixing time to determine the suitable mixing time of Carbidopa/Levodopa ODT. Fatima et al. [18] employed the SeDeM-ODT system as a preformulation tool to determine the use of Ludipress in the development of ODT formulation. Ponnammal et al. [19] used MD simulations to determine the miscibility of the drug with the carrier polymer depending on the Hansen parameter. Maus et al. [20] applied MD simulations in predicting the miscibility and glass transition of theophylline and ibuprofen. Koumbogle et al. [21] used the COMSOL multiphysics platform to simulate the effect of moisture behavior of pharmaceutical powders during the tableting process, and the results demonstrated that moisture evaporating from the powder bed accumulates at the punch-tablet surface interface.

There is a lack of reports that combined the MD simulations with macro-scale physicochemical properties of ODT under varying humidity conditions. In this study, two ODT formulations with various excipients were compared using both computational and experimental methods. We aimed to investigate how their composition influences moisture uptake, which in turn affects their mechanical and disintegration properties. Henry's constant and the isosteric heat of adsorption obtained from MD simulations were used as thermodynamic parameters to investigate the interaction between moisture and excipients at the molecular level [22]. The Henry's constant reflects the affinity of excipients to absorb moisture [23], while the isosteric heat of adsorption describes the energetics of sorption as water uptake increases [22]. The MD simulation results were validated by comparing them with experimental results such as hardness, friability, loss on drying (LOD), and disintegration time to better understand ODT stability under different humidity conditions.

Materials and methods

Materials

Two different ODT ondansetron formulations were obtained as a gift from Alpha and Ultramedica pharmaceutical companies (Syria). The excipients used in each formulation are listed in Table 1. The exact quantities of the components are proprietary and therefore not disclosed. However, the listed excipients represent the full formulation basis for comparative purposes.

Molecular dynamics simulation

MD simulations were carried out using Material Studio v.6.0.0 (Accelyres Software Inc., San Diego, CA). Molecular structures for all formulation components were obtained from the PubChem database and energy-minimized using the Forcite Module. The number of geometry optimization iterations was set to 5000 to ensure convergence. The Amorphous module was used to construct three-dimensional periodic structures of the studied formulations using a Monte Carlo fashion [24]. The target density for the amorphous cell was set to 1.2 g/cm^3 to ensure a realistic conformation [25]. Geometry optimization of the constructed amorphous cell was performed using the Forcite module. The COMPASS force field was used in geometry optimization at 298 K. The hygroscopic affinity of amorphous cells of both formulations was investigated using the Sorption module. Water was used as the sorbate. The simulations employed the COMPASS force field with the Metropolis Monte Carlo method at 298 K for 100,000 production steps. Quality convergence tolerance was set to "fine" for the simulations. The sorption module was used to calculate Henry's constant and isosteric heat [24].

The Henry's constant, which relates the equilibrium concentration of sorbate to its partial pressure at low concentrations, was defined in Eq. (1) [22, 26]:

Table 1 Formulation components of ODT

Formulation A	Formulation B
Ondanestron	Ondanestron
Gelatin	MCC
Mannitol	Mannitol
Methyl Paraben Sodium	Cross Povidone
Propyl Paraben Sodium	Lactose Monohydrate
L-Menthol	Magnesium stearate
Aspartam	Aspartame
	Colloidal Silicone Dioxide

$$C = K_H.P \quad (1)$$

where C is the equilibrium concentration of water molecules in the excipient, P is the partial pressure of water vapor, and K_H is the Henry's constant [22].

In the Grand Canonical Monte Carlo (GCMC) framework, K_H was obtained from the ensemble average of Boltzmann factors and was demonstrated in Eq. (2) [22, 26]:

$$K_H = \frac{1}{RT}\left(exp\left(-\frac{U}{RT}\right)\right) \quad (2)$$

where R is the universal gas constant, T is the absolute temperature, U is the interaction energy between water and the excipient, and exp is the exponential function [22, 26].

The isosteric heat of adsorption Q_{st} was calculated using the Clausius–Clapeyron relation Eq. (3) [22, 26]:

$$Q_{st} = -R\left(\frac{\partial(\ln p)}{\partial\left(\frac{1}{T}\right)}\right)_q \quad (3)$$

where Q_{st} is the isosteric heat of adsorption, R is the universal gas constant, p is the equilibrium vapor pressure of water at a given sorbed amount, T is the absolute temperature, and q is the amount of sorbate adsorbed [22].

Experimental procedure

Samples from the same batch number of each formulation were collected from two different regions with mean relative humidity (29% and 57% RH). The following tests were conducted in accordance with the United States Pharmacopeia (USP 43–NF 38) [27]. ODT formulations were tested at 29% and 57% RH, respectively.

Hardness

Tablet hardness was determined using a tablet hardness tester, Erweka TBH125 (Langen, Germany). Ten tablets from each formulation were tested randomly, and the results were recorded in kilopascals (kPa) [27].

Friability

The friability test was performed according to USP <1216> using a friability tester Erweka TAR II (Langen, Germany). Initially, ten tablets or a sample equivalent to 6.5 g were weighed and transferred into the friabilator. The apparatus was operated at 25 rpm for 4 min (100 revolutions). Tablets were then dedusted and reweighed. The percentage weight loss was calculated. A friability of less than 1% is considered acceptable. The test was performed in triplicate, and the values are reported as mean ± standard deviation. [27].

Loss on drying (LOD)

An infrared moisture analyzer Precisa 530 (Dietikon, Switzerland) was used to determine LOD based on USP <731> guidelines. A known weight of powdered ODTs was heated, and the percentage weight loss due to moisture evaporation was calculated [27]. The test was performed in triplicate at 29% and 57% RH separately.

Disintegration time

The disintegration time was measured using a wetting test, where ODT samples were immersed in 10 ml of distilled water at 37 ± 0.5 °C, and the time to complete disintegration was recorded [28]. Six ODTs from each formulation were tested separately at 29% and 57% RH.

Statistical analysis

Data are presented as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) with JMP version 13.2.0 (SAS Institute, Cary, NC, USA). A p-value < 0.05 was considered statistically significant.

Results and discussion

Molecular dynamic simulations results

The geometry optimization for all formulation components was performed by setting the optimization parameters using the SMART algorithm with medium quality and an energy convergence tolerance of 10^{-3} kcal/mol. A force convergence tolerance was set to 0.5 kcal mol/Å, while the maximum number of iterations was 5000. The COMPASS force field was used in all MD simulations. The geometry-optimized molecular structures were used to build three-dimensional periodic structures with (29.05 × 29.05 × 29.05 Å) for formulation A and (38.4 × 38.4 × 38.4 Å) for formulation B using the Amorphous Cell module. The amorphous cells were energy minimized and then used in the Sorption module to calculate Henry's constant and isosteric heat of adsorption. The calculated parameters at 298 K are shown in Table 2.

The affinity for water absorption is presented in Fig. 1. The red color indicates H_2O molecules.

The sorption profiles visually showed a denser cluster of water molecules within the MCC-based formulation (B).

Table 2 Henry's constant and isosteric heat for tested formulation

Formulation	Henry's constant (kPa^{-1})	Isosteric heat (kcal/mol)
A (gelatin-based)	1184.96	8.69
B (MCC-based)	16,285.5	11.95

The MD simulation results indicated that the gelatin-based formulation (A) had a lower Henry's constant (1184.96 kPa^{-1}) and isosteric heat (8.69 kcal/mol), reflecting weaker interactions with water and lower hygroscopicity [24]. This behavior is related to gelatin's molecular structure, which absorbs water into a stable gel matrix, preventing excessive binding of additional water molecules [29]. Gelatin can act as a moisture buffer, absorbing 5–10 times its weight in water gradually [29]. In contrast, the MCC-based formulation (B) showed a significantly higher Henry's constant (16,285.5 kPa^{-1}) and isosteric heat (11.95 kcal/mol), indicating stronger water-excipient interactions [24]. This is attributed to the hygroscopic properties of lactose monohydrate and MCC. Consequently, formulation B is more sensitive to moisture absorption than formulation A. The MD simulation results correlated with the experimental mechanical and functional properties.

Hardness results

The hardness of ten tablets from each formulation was tested at 29% and 57% RH using an Erweka TBH125 apparatus. The results are shown in Table 3.

According to the hardness data, the MCC-based formulation (B) demonstrated greater hardness under both RH conditions, likely due to the crystalline packing of lactose and the fibrous structure of MCC, which enhance particle bonding [30]. Mild plasticization in the presence of small amounts of water may lower particle surface energy and promote closer interparticulate bonding, explaining the slight increase in hardness at 57% RH for both formulations [30]. The ANOVA test indicated that the formulation type had a significant effect on ODT hardness (p-value < 0.05).

Table 3 The hardness of formulation A and B

Relative humidity	Formulation A (kPa)	Formulation B (kPa)
29% RH	5.24 ± 0.37	6.73 ± 0.71
57% RH	5.64 ± 0.36	7.61 ± 0.77

Table 4 The friability results of formulation A and B

Relative humidity	Formulation A (%)	Formulation B (%)
29% RH	0.45 ± 0.02	0.43 ± 0.01
57% RH	0.14 ± 0.01	0.87 ± 0.05

Friability results

A sample of ten tablets, or 6.5 g, from each formulation was tested at both RH levels using an Erweka TAR II friabilator. The apparatus was operated at 25 rpm for 4 min (100 revolutions). After testing, the tablets were dedusted and reweighed to calculate the percentage weight loss. The results are shown in Table 4.

Both formulations met the USP 43-NF 38 friability limit (< 1%). However, the MCC-based formulation (B) showed a significant increase in friability (0.87%) at 57% RH, likely due to lactose recrystallization and partial disruption of MCC's microfibrillar structure [31]. Water can replace hydrogen bonds between cellulose chains, loosening the structure until capillary condensation occurs [31].

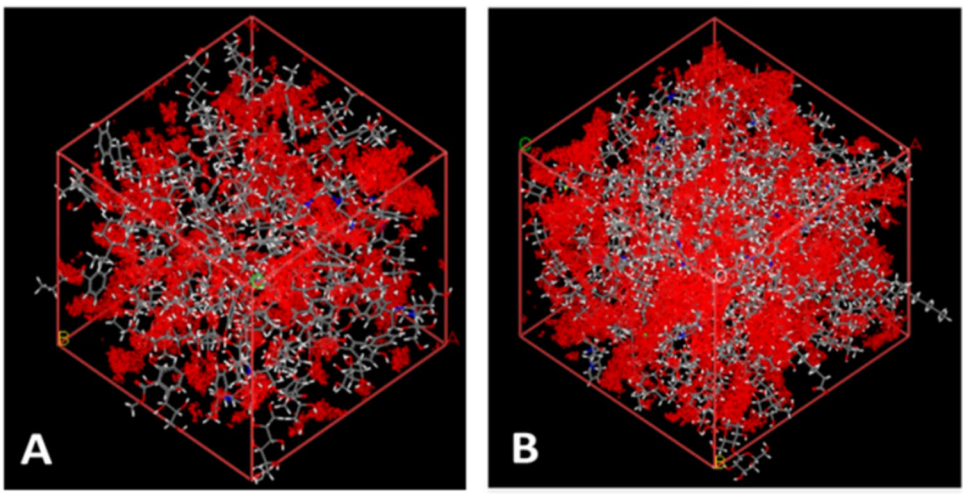

Fig. 1 Simulated amorphous cells of water sorbate absorption of formulation (**A**) and (**B**)

Table 5 LOD for formulation A and B

Relative humidity	Formulation A (%)	Formulation B (%)
29% RH	0.24 ± 0.005	0.16 ± 0.01
57% RH	0.24 ± 0.005	0.21 ± 0.01

Table 6 The disintegration time of formulation A and B

Relative humidity	Formulation A (s)	Formulation B (s)
29% RH	37.67 ± 1.51	33.5 ± 2.59
57% RH	34.0 ± 1.41	23.5 ± 2.81

Conversely, the gelatin-based formulation (A) exhibited decreased friability at higher RH, probably due to gelatin's capacity to absorb and retain moisture, enhancing cohesion and plasticity [29]. ANOVA indicated that the formulation type had a significant effect on the friability of the tested formulations (p-value < 0.05).

Loss on drying (LOD) results

A determined amount of powdered ODT was heated using a Precisa 530 infrared moisture analyzer, and the LOD was calculated for each formulation at 29% and 57% RH. The results are shown in Table 5.

Formulation A had a consistent moisture content (0.24%) under both conditions, suggesting it reached saturation at 29% RH and could not absorb additional water at 57% RH. Similar moisture-buffering properties of gelatin-based systems have been reported in other contexts. This behavior is related to gelatin's molecular structure, which absorbs water into a stable gel matrix, preventing excessive binding of additional water molecules. Gelatin can act as a moisture buffer in ODT [29]. The LOD results aligned with MD simulations, which indicated that the gelatin-based formulation (A) had a lower Henry's constant (1184.96 kPa^{-1}) and isosteric heat (8.69 kcal/mol), reflecting weaker interactions with water and lower hygroscopicity. In contrast, formulation B showed a 31% increase in moisture uptake at 57% RH, indicating greater hygroscopicity and potential stability issues in variable conditions. The ANOVA test indicated that the formulation type had a significant effect on LOD (p-value < 0.05). Therefore, the formulation type has a significant effect on the LOD of the tested formulation, while RH% did not (p-value > 0.05).

Disintegration time results

Six ODTs from each formulation were tested separately at 29% and 57% RH by immersing them in 10 ml of distilled water at 37 ± 0.5 °C and recording the time required for complete disintegration. The results are shown in Table 6.

Both formulations disintegrated more rapidly at 57% RH. Formulation B disintegrated faster, with times decreasing significantly at higher RH (from 33.5 s to 23.5 s) due to the water-wicking properties of MCC and lactose monohydrate, reflecting the hygroscopic nature of its excipients, while formulation A showed consistent disintegration times (37.67 s at 29% RH vs. 34.0 s at 57% RH). ANOVA showed that both formulation components and RH% had a significant effect on disintegration time (p-value < 0.05). The disintegration time results confirmed the MD simulation results.

In summary, the MD simulations reveal a strong correlation between sorption parameters and experimental performance. The high Henry's constant of the MCC-based formulation accounts for its pronounced sensitivity to relative humidity, whereas gelatin's diminished sorption values are consistent with its robust stability under humidity conditions.

Conclusion

This study highlights the importance of MD simulations as a rapid screening tool in ODT pre-formulation studies. MD simulations help to understand the intermolecular interactions between excipients and water under varying humidity conditions. Two ODT formulations were compared: a gelatin-based formulation (A) and an MCC-based formulation (B). The Sorption module in Materials Studio was used to calculate Henry's constants and isosteric heats, which accurately predicted the moisture affinity of each formulation. The MD simulations demonstrated a strong correlation between predicted and observed behavior of ondansetron ODT under different humidity conditions. The MCC-based formulation (B) exhibited significantly higher water sorption, with higher Henry's constant and isosteric heat values, and displayed RH-sensitive changes in hardness, friability, and disintegration time. In contrast, the gelatin-based formulation (A) showed weaker sorption and maintained greater stability across humidity conditions.

Acknowledgements The author thanks Al-Andalus University for medical science for their support in providing the required equipment for this research.

Author contributions The author designed the study and performed the MD simulation, the physical experiments and wrote the paper.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

References

1. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A et al (2011) Orally disintegrating tablets: formulation, preparation techniques and evaluation. J Appl Pharm Sci (Issue):35–45
2. Ghourichay MP, Kiaie SH, Nokhodchi A, Javadzadeh Y (2021) Formulation and quality control of orally disintegrating tablets (ODTs): recent advances and perspectives. Biomed Res Int 2021(1):6618934. https://doi.org/10.1155/2021/6618934
3. Chinwala M (2020) Recent formulation advances and therapeutic usefulness of orally disintegrating tablets (ODTs). Pharmacy Basel 8(4):186. https://doi.org/10.3390/pharmacy8040186
4. Al-khattawi A, Mohammed AR (2013) Compressed orally disintegrating tablets: excipients evolution and formulation strategies. Expert Opin Drug Deliv 10(5):651–663. https://doi.org/10.1517/17425247.2013.769955
5. Haider R, Das GK, Ahmed Z, Zameer S (2025) Orally disintegrating tablets {ODT} and related formulation. Clin Res Clin Rep 6(6). https://doi.org/10.31579/2835-8325/167
6. Khan A, Khan A, Nazir S, Khan NR, Ullah M, Shahbaz N et al (2025) An evaluation of the effect of aging on the quality attributes of orodispersible tablets prepared by the direct compression technique. Drug Dev Ind Pharm 51(4):309–318. https://doi.org/10.1080/03639045.2025.2469800
7. Yee KM, Mohamad N, Kee PE, Chew Y-L, Lee S-K, Lakshminarayanan V et al (2024) Recent advances in orally disintegrating tablet: properties, formulation and production. Drug Deliv Lett 14(3):211–225. https://doi.org/10.2174/0122103030319091240317162755
8. Koner J (2017) Formulation strategies and engineering processes for orally disintegrating tablets: the importance of robustness and disintegration. Aston University
9. Ohrem HL, Schornick E, Kalivoda A, Ognibene R (2014) Why is mannitol becoming more and more popular as a pharmaceutical excipient in solid dosage forms? Pharm Dev Technol 19(3):257–262. https://doi.org/10.3109/10837450.2013.775154
10. Nayak AK, Manna K (2011) Current developments in orally disintegrating tablet technology. Journal of Pharmaceutical Education and Research 2(1):21
11. Dominici S, Marescotti F, Sanmartin C, Macaluso M, Taglieri I, Venturi F et al (2022) Lactose: characteristics, food and drug-related applications, and its possible substitutions in meeting the needs of people with lactose intolerance. Foods Basel 11(10):1486. https://doi.org/10.3390/foods11101486
12. Goel H, Rai P, Rana V, Tiwary AK (2008) Orally disintegrating systems: innovations in formulation and technology. Recent Pat Drug Deliv Formul 2(3):258–274. https://doi.org/10.2174/187221108786241660
13. Kumar ML, Shree KJ, Mounika N, Akhila T, Bhargavi NM, Bonthagarala B (2024) Formulation and quality control of orally disintegrating tablets (ODTS): recent advances and perspectives. https://doi.org/10.20959/wjpr202417-33721
14. Alyami H, Koner J, Dahmash EZ, Bowen J, Terry D, Mohammed AR (2017) Microparticle surface layering through dry coating: impact of moisture content and process parameters on the properties of orally disintegrating tablets. J Pharm Pharmacol 69(7):807–822. https://doi.org/10.1111/jphp.12623
15. Dhewale S, Kale B, Chivte V, Dhakne R, Shep S (2023) The preparation of orodispersible tablet & study effect of processing condition on Tablet. International Journal of Scientific Development and Research (IJSDR) 8(1):115–131
16. Ponduri TK, Budha RR, Paliwal D, Siripurapu K, Alavala RR, Rao GSK (2025) Computational Modelling for Formulation Design. In: Applications of computational tools in drug design and development. Singapore: Springer Nature Singapore, pp 55–98
17. Qin F, Wan C, Zhang Y (2024) Computer-aided optimization of carbidopa/levodopa orally disintegrating tablets. Drug Dev Ind Pharm 50(4):331–340. https://doi.org/10.1080/03639045.2024.2327475
18. Fatima SS, Zafar F, Ali H, Raees F, Naqvi GR, Alam S et al (2024) Development and characterisation of orally disintegrating flurbiprofen tablets using SeDeM-ODT tool. PLoS ONE 19(10):e0309894. https://doi.org/10.1371/journal.pone.0309894
19. Ponnammal P, Kanaujia P, Yani Y, Ng WK, Tan RBH (2018) Orally disintegrating tablets containing melt extruded amorphous solid dispersion of tacrolimus for dissolution enhancement. Pharmaceutics 10(1):35. https://doi.org/10.3390/pharmaceutics10010035
20. Maus M, Wagner KG, Kornherr A, Zifferer G (2008) Molecular dynamics simulations for drug dosage form development: thermal and solubility characteristics for hot-melt extrusion. Mol Simul 34(10–15):1197–1207. https://doi.org/10.1080/08927020802411695
21. Koumbogle K, Gosselin R, Gitzhofer F, Abatzoglou N (2023) Moisture behavior of pharmaceutical powder during the tableting process. Pharmaceutics 15(6):1652. https://doi.org/10.3390/pharmaceutics15061652
22. Siderius DW, Hatch HW, Shen VK (2022) Temperature extrapolation of Henry's law constants and the isosteric heat of adsorption. J Phys Chem B 126(40):7999–8009. https://doi.org/10.1021/acs.jpcb.2c04583
23. Veronica N, Heng PW, Liew CV (2024) Understanding the roles of excipients in moisture management in solid dosage forms. Mol Pharm 21(5):2484–2500. https://doi.org/10.1021/acs.molpharmaceut.4c00031
24. BIOVIA DS (2012) Materials Studio, version 6.0. San Diego, CA, USA
25. Klancke J, Payne P, Nordholm C (2018) Application of a modified disk for testing orally disintegrating tablets by USP< 701>. Dissolution Technol May 2018 10–13. https://doi.org/10.14227/DT250218P10
26. Mackay D, Boethling RS (2000) Henry's law constant. Handbook of Property Estimation Methods for Chemicals. CRC Press, pp 91–110
27. Convention USP (2019) USP 43, NF 38: The United States Pharmacopeia, the National Formulary: United States Pharmacopeial Convention
28. Bafail RS (2023) Disintegration testing for orally disintegrating tablets (ODTs): an overview. Trop J Pharm Res 22(11):2399–2406. https://doi.org/10.4314/tjpr.v22i11.21
29. Rowe RC, Sheskey PJ, Quinn ME (eds) (2006) Handbook of pharmaceutical excipients, vol 6. London: Pharmaceutical press
30. Alderborn G, Ahlneck C (1991) Moisture adsorption and tabletting. III. Effect on tablet strenght-post compaction storage time

profiles. Int J Pharm 73(3):249–258. https://doi.org/10.1002/jps.20411
31. Airaksinen S, Karjalainen M, Shevchenko A, Westermarck S, Leppanen E, Rantanen J et al (2005) Role of water in the physical stability of solid dosage formulations. J Pharm Sci 94(10):2147–2165. https://doi.org/10.1002/jps.20411