
The Effect Of Different Binder Types On The Results Of Hardness Evaluation Tests And Tablet Disintegration Time Using The Wet Granulation Method: Literature Review

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Abstract

Tablets are a widely used pharmaceutical dosage form due to their stability, ease of use, and dosage accuracy. In tablet manufacturing, particularly using the wet granulation method, the use of binders is a critical factor influencing the tablet's physical properties, particularly hardness and disintegration time. Various types of binders, both natural and synthetic, such as polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), gelatin, starch, and sodium carboxymethylcellulose (CMC-Na), have different characteristics in forming bonds between particles. This literature review aims to analyze the effect of different binder types on tablet hardness and disintegration time test results. The method used was a literature review of various scientific journals related to tablet formulations with various binders. The results indicate that increasing binder concentration generally increases tablet hardness but can also prolong disintegration time. Synthetic binders such as HPMC and gelatin tend to produce tablets with high mechanical strength, while binders such as PVP and starch provide more moderate hardness with faster disintegration times. Thus, the selection of the type and concentration of binder must be adjusted to the formulation objectives to obtain an optimal balance between tablet hardness and disintegration time.

Keywords: Tablets, Binder, Wet Granulation, Tablet Hardness, Disintegration Time

INTRODUCTION

Tablets are the most widely used solid pharmaceutical dosage form in clinical practice due to their good stability, ease of use, and accurate dosing. They also offer advantages in production and distribution compared to other dosage forms. Tablet quality is strongly influenced by the composition of the ingredients and the manufacturing method (Hadisoewignyo & Fudholi, 2016). The wet granulation method is widely used in tablet manufacturing because it produces granules with good flowability and compressibility. This process involves the addition of a binder solution to form larger, more uniform particle aggregates. The resulting granules will determine the quality of the final tablet, particularly its mechanical strength and physical stability (Nurhaliza et al., 2024).

Binders are important excipients in tablet formulations, increasing interparticle cohesion, resulting in compact granules. Binder use significantly impacts tablet physical parameters, particularly hardness and disintegration time. Variations in binder type and concentration will result in different tablet characteristics (Aulton & Taylor, 2018). Tablet hardness indicates the tablet's ability to withstand pressure during production and distribution. Too low a hardness value can cause the tablet to become brittle, while too high a hardness can inhibit disintegration. Disintegration time is an important parameter related to the rate of release of active ingredients in the body (USP, 2020).

The relationship between hardness and disintegration time is interdependent in tablet formulation. Tablets with a more compact structure tend to have a longer disintegration time because liquid penetration is more difficult. This condition indicates the importance of balancing these two parameters in tablet development (Hadisoewignyo & Fudholi, 2016). Various types of binders commonly used in tablet formulations include hydroxypropyl methylcellulose (HPMC), gelatin, polyvinylpyrrolidone (PVP), starch, and sodium carboxymethylcellulose (CMC-Na). HPMC is known to form a strong matrix that increases

tablet hardness, but can prolong disintegration time (Ningsih et al., 2020; Sari et al., 2024). Gelatin has high adhesion properties that produce tablets with good compactness, but often causes longer disintegration times (Pratiwi et al., 2017).

PVP is an inert synthetic binder capable of producing granules with good flow properties. The use of PVP tends to produce tablets with moderate hardness and relatively faster disintegration times compared to other binders. Starch, as a natural binder, has limitations in binding strength and compressibility, so it often requires modification to improve its performance (Sakinah & Kurniawansyah, 2018). CMC-Na is a cellulose derivative that is hydrophilic and can significantly increase particle cohesion. The use of CMC-Na can increase tablet hardness, but can also prolong disintegration time due to the formation of a more compact structure (Asyiva et al., 2024). The differences in the characteristics of each binder indicate the importance of selecting the right binder according to the formulation objectives. These differences in properties between binders indicate that no single type of binder is ideal for all tablet formulations. Binder selection must be tailored to the type of active ingredient and the desired tablet characteristics (Pratiwi et al., 2017). A literature review is needed to comprehensively analyze the effect of various binders on tablet hardness and disintegration time.

RESEARCH METHODS

This study employed a literature review method utilizing secondary data obtained from various relevant scientific journals. This method aimed to systematically examine the effect of different binder types on the hardness and disintegration time test results of tablets made using the wet granulation method. Data sources were obtained through systematic searches of scientific databases such as Google Scholar, PubMed, and ScienceDirect. The journals used were then selected based on inclusion and exclusion criteria, where inclusion criteria included articles discussing the use of binders in tablet formulations using the wet granulation method and reporting the results of hardness and disintegration time tests. Furthermore, the selected journals were full-text articles published within the last ten years. Exclusion criteria included articles that were irrelevant to the topic, did not use the wet granulation method, or had incomplete data.

Data collection was conducted by identifying, reading, and thoroughly reviewing journals to obtain important information, such as binder type and concentration, granule production method, and tablet evaluation test results. The data obtained were then analyzed descriptively and qualitatively by comparing results between studies, grouping data based on binder type, and identifying the relationship between binder type and tablet hardness and disintegration time. Furthermore, an evaluation of the consistency of the data and methods used in each study was conducted to increase the reliability of the results. The analysis results are presented in a systematic narrative description to provide a clear and easy-to-understand picture of the effect of different binders on the quality of the resulting tablets.

RESULTS AND DISCUSSION

Table 1. Comparison of Binder Type and Concentration on Tablet Hardness and Disintegration Time in Various Studies

Reference Source (Year)	Active Ingredients	Binder Types	Optimal Concentration	Hardness Test Results (kg)	Time Destruction Test Results (minute)
Hidayati et al., 2020	Acetosal 80 mg	PVP	Formula II: PVP (3%)	F1 (1%): 4.898 ± 0.404 F2 (3%): 4.549 ± 0.306 F3 (5%): 4.077 ± 0.194	F1 (1%): 16.74 ± 0.697 F2 (3%): 14.20 ± 0.255 F3 (5%): 08.27 ± 1.681
Cahyani et al., 2023	Paracetamol 500 mg	PVP + Porang Tuber Flour	Formula I: PVP 0% + Porang Tuber Flour 5%	F1 (PVP 0% : Porang 5%): 7.30 F2 (PVP 1% : Porang 0%): 14.37 F3 (PVP 3% : Porang 6%): 8.88 F4 (PVP 5% : Porang 7%): 10.09	F1 (PVP 0% : Porang 5%): 9.6 F2 (PVP 1% : Porang 0%): 30.34 F3 (PVP 3% : Porang 6%): 31.57 F4 (PVP 5% : Porang 7%): 34.31
Rijal et al., 2022	Tacklean leaf extract (Chromolaena odorata (L.)) 56 mg	PVP K-30	Formula III: PVP K-30 5%	F1 (1%): 3.1667 ± 0.145 F2 (3%): 3.584 ± 0.745 F3 (5%): 4.4167 ± 0.850	F1 (1%): 05.09 ± 0.675 F2 (3%): 07.33 ± 0.825 F3 (5%): 08.11 ± 0.975
Khabibah & Ermawati, 2023	Green betel leaf extract (Piper betle L.) 300 mg	Gelatin	Formula II: Gelatin 2%	F1 (1%): 0.60–1.16 F2 (2%): 3.48–3.82 F3 (3%): 4.84–5.28	F1 (1%): 2.29–4.18 F2 (2%): 10.39–11.26 F3 (3%): 19.02–20.07
Singha	Paracetamol	Gelatin	Formula F2:	Formula F2	Formula F2

Roy et al., 2025	500 mg		Gelatin 5%	(5%) : 5.0 ± 0.2	(5%) : 3.5 ± 0.3
Abdullahi et al., 2024	Metronidazole 200 mg	Gelatin	Formula F2: Gelatin 3%	Formula F2 (Gelatin 3%) : 9.80 ± 1.10	Formula F2 (Gelatin 3%) : 11.05 ± 3.42
Zilhadia et al., 2021	Paracetamol 500 mg	Goat skin gelatin	TFII (Goat skin gelatin 3%)	TFI (2%): 12.41 ± 0.52 TFII (3%): 15.07 ± 0.67 TFIII (4%): 17.22 ± 0.71	TFI (2%): 2.94 ± 0.82 TFII (3%): 3.71 ± 1.00 TFIII (4%): 4.56 ± 1.14
Lestari & Eliana, 2025	Paracetamol 300 mg	Cassava starch	F2 (Starch 2.0%)	Formula 2: 5.13 ± 0.06 kP	Formula 2: 0.70 ± 0.02 minutes
Singha Roy et al., 2025	Paracetamol 500 mg	Starch	Formula F1: Starch 5%	F1 (Starch 5%): 3.2 ± 0.1	F1 (Starch 5%): 2.8 ± 0.2
Cahyani et al., 2023	Paracetamol 500 mg	PVP + Porang tuber starch	Formula I: PVP 0% + Porang Tuber Flour 5%	F1 (PVP 0% : Porang 5%): 7.30 F2 (PVP 1% : Porang 0%): 14.37 F3 (PVP 3% : Porang 6%): 8.88 F4 (PVP 5% : Porang 7%): 10.09	F1 (PVP 0% : Porang 5%): 9.6 F2 (PVP 1% : Porang 0%): 30.34 F3 (PVP 3% : Porang 6%): 31.57 F4 (PVP 5% : Porang 7%): 34.31
Dewi et al., 2021	Red sweet potato leaf extract (Ipomoea batatas L.)	PVP K-30 + Manihot starch	Formula II: Intragranular 5% : Extragranular 5%	F1 (10% : 0%): 6.58 ± 0.90 F2 (5% : 5%): 5.82 ± 0.63 F3 (0% : 10%): 4.82 ± 0.71	F1 (10% : 0%): 16.66 ± 0.57 F2 (5% : 5%): 9.91 ± 0.58 F3 (0% : 10%): 13.71 ± 0.43
Singha	Paracetamol	HPMC	Formula F5:	F5 (HPMC	F5 (HPMC

Roy et al., 2025	500 mg		HPMC 5%	5%): 6.0 ± 0.3	5%): 5.6 ± 0.4
Hadinugroho et al, 2017	Ketoprofen 100 mg	HPMC	10% (3g binder in 30g mass)	HPMC 10%: 9.94 ± 0.47	HPMC 10%: 23.44
Magfirah et al, 2025	Jatropha curcas L. leaf extract 150 mg	HPMC + Xanthan gum	Formula III: HPMC : Xanthan gum (2:1)	FI (HPMC 25 mg : Xanthan gum 50 mg): 11.10 FII (HPMC 37.5 mg : Xanthan gum 37.5 mg): 10.18 FIII (HPMC 50 mg : Xanthan gum 25 mg): 13.83	FIII: 113 minutes
Siswanto & Adibah, 2025	Aloe vera extract 150 mg	HPMC K100M	Formula 3: HPMC K100M 10%	F1 (5%): 4.46 ± 0.20 F2 (7.5%): 5.30 ± 0.16 F3 (10%): 6.23 ± 0.24	F1 (5%): >60 F2 (7.5%): >60 F3 (10%): >60
Muntaza et al., 2025	Gnetum gnemon L. (Gnetum gnemon L.) peel extract	CMC-Na	Formula I: CMC-Na (5%)	F1: 5.74 (qualified) F2: 3.03 F3: 1.31	F1: 8.48 F2: 4.02 F3: 1.08
Utami et al., 2024	Ethanol extract of shallot bulbs (Allium cepa L.)	CMC-Na	Formula III: CMC-Na (5%)	F1: 4.4 F2: 5.5 F3: 6.8	F1: 11.26 F2: 12.72 F3: 14.25
Anindhita et al., 2022	Polyalthia longifolia leaf extract	CMC-Na	Formula II: CMC-Na (3%)	F1: 4.50 F2: 7.02 F3: 9.33	F1: 22.07 F2: 24.36 F3: 26.59

Binder Characteristics on Physical Properties of Tablets

Wet granulation is a tablet manufacturing method that involves converting a powder mixture into compact granules by adding a binder solution, thus significantly improving the flow properties, mixture homogeneity, compressibility, and mechanical strength of the tablet compared to the direct compression method. The selection of the type and concentration of the binder is a crucial factor because it greatly affects the final physical characteristics such as hardness, friability, and disintegration time of the tablet, where synthetic binders such as polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), and sodium carboxymethylcellulose (CMC-Na) are generally superior in adhesion ability, polymer film formation, and produce granules with high density and low porosity that provide superior mechanical strength, although at high concentrations often prolong the disintegration time due to the matrix structure being too compact. In contrast, natural binders such as starch (including variants such as cassava starch or porang) and gelatin are more economical and have good swelling and water penetration capabilities to support rapid disintegration, although their compactibility and flowability are relatively lower unless through modifications such as pregelatinization or intragranular-extragranular combinations. Specifically, PVP produces high tablet hardness (4-6.8 kg/cm²) with good flowability but elasticity increases at doses >3%; HPMC provides 6-13 kg hardness with low friability and a stable gel matrix ideal for sustained-release formulations; starch offers the fastest disintegration time (<3 minutes) but low hardness (3-5 kg); gelatin achieves very high hardness (9-17 kP) due to strong protein cohesion; and CMC-Na provides a balance with a hardness of 5-9 kg through the formation of a hydrophilic viscous mass. Optimal binder concentrations are usually in the range of 1-5%, where increasing the dosage tends to increase hardness but slow disintegration, and its effectiveness is influenced by the nature of the active ingredient, compression pressure, and other supporting excipients, so the selection must be tailored to the formulation objectives—synthetic for mechanically strong tablets and natural for rapid release—and requires optimization through experimental testing to achieve the ideal balance between physical properties and tablet performance.

Binder Working Mechanism in Wet Granulation

The mechanism of action of binders in wet granulation involves a complex physicochemical process that converts fine powders into compact granules through three main stages: wetting/nucleation, consolidation/growth, and drying. In the wetting stage, the binder solution wets the particle surface forming liquid bridges through capillary forces, adhesion, and cohesion, resulting in stable granule nuclei; consolidation involves densification and granule growth due to mechanical agitation (coalescence, layering, breakage), where medium binder viscosity ensures homogeneous distribution while low viscosity causes friability and high viscosity triggers overgranulation; drying solvent evaporation forms permanent solid bridges via hydrogen bonding, van der Waals, electrostatic, and mechanical interlocking for stable cohesion.

Binders also influence particle deformation during compression—plastic increases contact area for high tensile strength, excess elastic triggers capping/recovery, fragmentation aids compaction—and final porosity: strong bonds reduce pores (slow disintegration), porous increases disintegration. PVP works via film-forming and H-bonding for high compactibility (hardness 4-6.8 kg/cm²), HPMC viscoelastic hydrogel for sustained-release (6-13 kg, >20 minutes), starch mucilage swelling/interlocking for fast disintegration (3-5 kg, <3 minutes), gelatin protein network adhesive (9-17 kP), CMC-Na hydrophilic viscous gel increases density (5-9 kg).

Optimization of 1-5% concentration, intra/extra-granular distribution, and combination (e.g. PVP-porang adhesion-swelling synergy) is essential for the balance of flow, compression, and disintegration; synthetic binders have superior mechanical strength

but are slow to disintegrate, while natural binders, on the other hand, are influenced by active ingredients/excipients, making this understanding crucial for optimal tablet formulation.

Relationship between Hardness and Tablet Disintegration Time

Tablet hardness, ideally 4-10 kg, measures mechanical resistance to the stresses of packaging, distribution, and everyday handling, while disintegration time (<15-30 minutes as per pharmacopoeia) assesses the ability to rapidly disintegrate into small particles upon contact with biological fluids for optimal release of active ingredients; these two parameters are inversely related because the wet granulation process produces high granule density through liquid/solid bridges, shear densification, and interparticle consolidation, which increases tight packing but reduces pore connectivity, thus slowing liquid penetration via wicking and swelling mechanisms.

Gelatin binder significantly increases hardness (range 0.6-17 kg in studies such as Khabibah 2023, Zilhadia 2021, Abdullahi 2024) through the formation of a rigid protein network and stable film during hydration/drying, resulting in dense granules with narrow pores that increase tensile strength but prolong disintegration time (2-20 minutes) due to hydration inhibition; on the other hand, PVP provides a superior balance (3-5 kg hardness, 5-17 minutes disintegration in Hidayati 2020, Rijal 2022) due to high wettability, low surface tension, and homogeneous distribution that maintains a connected pore network; starch produces a porous structure for very fast disintegration (0.7-3 minutes, low hardness 3-5 kg such as Lestari 2025, Singha Roy 2025) via swelling pressure and wicking action; HPMC forms a viscoelastic hydrogel barrier for sustained-release (hardness 6-14 kg, disintegration >20-113 minutes in Hadinugroho 2017, Magfirah 2025); CMC-Na triggers a viscous gel that increases hardness (4-9 kg) & disintegration (8-27 minutes in Utami 2024, Anindhita 2022).

Combinations such as PVP-porang (Cahyani 2023) create an adhesion-swelling synergy that triggers extreme density and slow disintegration (up to 34 minutes), while optimizing the 1-5% concentration, compression pressure, super disintegrant, and intra/extra-granular distribution are essential for the balance of the granule microstructure; these factors determine fluid transport, hydration kinetics, and release profiles, as wet granulation uniquely changes the pore morphology and cohesiveness of the wet mass compared to other methods.

Comparison of Effectiveness Between Binders

The effectiveness of binders in wet granulation is evaluated from the balance of tablet hardness (ideal 7-14 kgf) and disintegration time (<30 minutes for conventional), where strong binders create a compact/high-density structure via liquid/solid bridges, granule density, and shear densification that increase mechanical stability but reduce porosity/pore connectivity, thus slowing liquid penetration/wicking; wettability, binder distribution, compression pressure, and pore size determine the overall performance for immediate/sustained-release purposes (Hadisoewignyo & Fudholi, 2016; Jange et al., 2023; Kotamarthy et al., 2024).

PVP has superior balance (hardness 3-5 kg, disintegration 5-17 minutes in Hidayati 2020, Rijal 2022) due to high hydrophilic/wettability for homogeneous distribution and connected pores; gelatin effectively improves mechanics (0.6-17 kg, disintegration 2-20 minutes in Khabibah 2023, Zilhadia 2021, Abdullahi 2024, Singha Roy 2025) via protein network adhesive but source/viscosity varies trigger solid dens; superior starch disintegration is fast (hardness 3-5 kg, disintegration 0.7-3 minutes in Lestari 2025, Singha Roy 2025) through porous/swelling structure; HPMC ideal sustained-release (6-14 kg, >20-113 minutes in Hadinugroho 2017, Magfirah 2025, Siswanto 2025) with hydrogel barrier;

CMC-Na good compactibility (4-9 kg, 8-27 minutes in Utami 2024, Anindhita 2022) but viscoelastic gel inhibits hydration.

The combination increases synergy, e.g., PVP-porang (hardness 7-14 kg, disintegration 9-34 minutes, Cahyani 2023) via glucomannan swelling/strong hydration increases cohesion but risks a solid matrix; PVP-starch (Dewi 2021) optimizes intra/extra-granular for balanced porosity; starch modification (pregelatinization) increases effectiveness; the choice of synthetic/natural/combination binders depends on the release profile, with an optimization of 1-5% concentration essential to avoid over-compaction/brittleness (Latifah & Lukman 2025).

Potential Pharmaceutical Applications

The potential pharmaceutical applications of various types of modified binders and excipients continue to grow along with the increasing need for more effective, stable, and specific drug delivery systems for therapeutic purposes. The development of tablet formulation technology is no longer solely focused on the ability to produce hard and stable tablets, but is also directed at controlling drug release, increasing bioavailability, production efficiency, and the use of safer and more sustainable raw materials. Various studies have shown that binder characteristics such as hydration ability, swelling, gel formation, wettability, compactibility, and matrix formation significantly determine their potential applications in various types of pharmaceutical preparations (Wang et al., 2025; Jange et al., 2023). Therefore, the selection of binders in modern tablet formulations takes into account not only the physical parameters of the tablet, but also the therapeutic purpose, type of drug release, stability of the active ingredient, and manufacturing process efficiency.

One of the most developed pharmaceutical applications is the use of hydrophilic polymers as a sustained-release matrix in slow-release tablets. Binders such as Hydroxypropyl Methylcellulose (HPMC) are known to form a hydrogel matrix and diffusion barrier that slows the penetration of liquids into the tablet core so that the release of active substances occurs gradually (Magfirah et al., 2025). Research by Magfirah et al. (2025) showed that the combination of HPMC and xanthan gum with a ratio of 2:1 produced tablets with a high hardness of 13.83 kg and a disintegration time of up to 113 minutes due to the formation of a very stable hydrophilic matrix. Similar results were also shown by Siswanto and Adibah (2025), where HPMC K100M produced a disintegration time of more than 60 minutes in all formulas due to the formation of a thick gel layer during tablet hydration. In addition, Hadinugroho et al. (2017) showed that HPMC is able to maintain tablet integrity and produce a more controlled drug release. According to Fatma et al. (2024), the formation of a gel barrier in hydrophilic polymers allows controlled drug diffusion and an erosion-controlled release mechanism, making it highly suitable for use in long-term therapy such as hypertension, diabetes mellitus, and cardiovascular disease. Therefore, HPMC has enormous application potential in controlled drug delivery systems.

In addition to sustained-release systems, developments in pharmaceutical technology have also led to the use of binders for immediate-release formulations, fast-dissolving tablets, and orally disintegrating tablets (ODT). Binders such as starch and PVP have great potential in fast-disintegrating systems because they are able to maintain a balance between compactibility and liquid penetration into the tablet. Research by Lestari and Eliana (2025) showed that cassava starch produced a very fast disintegration time of 0.70 ± 0.02 minutes, making it very potential for application in ODTs and fast-dissolving tablets. Similar results were also reported by Singha Roy et al. (2025), where starch produced a disintegration time of 2.8 ± 0.2 minutes. According to Handayani et al. (2023), the more porous structure of starch-based granules causes liquid penetration to occur more quickly, thus accelerating tablet disintegration. In addition, Hidayati et al. (2020) showed that the use of PVP in acetosal chewable tablets resulted in tablets that were quite compact but still easily

disintegrated, making them suitable for chewable tablet formulations. Research by Rijal et al. (2022) also demonstrated that PVP K-30 was able to maintain a balance between mechanical strength and disintegration time in herbal extract tablets, making it potentially suitable for use in conventional and immediate-release tablets.

The potential for pharmaceutical applications is also growing in the use of a combination of natural and synthetic binders through the concept of excipient co-processing. The combination of PVP and porang tuber flour in the study of Cahyani et al. (2023) showed that the formula with 5% porang produced a hardness of 7.30 kg with a disintegration time of 9.6 minutes, thus meeting the requirements of conventional tablets. These results indicate that the binder combination is able to produce a synergistic effect between compactibility and swelling. Glucomannan in porang is known to have high hydration and gel-forming capabilities, thereby increasing granule cohesion and tablet stability (Sun et al., 2023). In addition, Aanisah et al. (2022) explained that glucomannan has great potential as a novel natural excipient because it can function as a binder, filler, and gelling agent simultaneously. According to Hu et al. (2025), the hydrophilic structure of glucomannan allows the formation of a stable viscoelastic matrix so that it can be utilized in hydrogel-based drug delivery systems. The research of Dewi et al. (2021) also showed that the combination of PVP K-30 and manihot starch with a balanced intragranular and extragranular distribution was able to produce more optimal tablet characteristics compared to the use of a single binder. Thus, the development of co-processed excipients has the potential to increase formulation efficiency and produce tablets with an optimal balance between compactibility and disintegration ability.

The use of local natural materials as pharmaceutical excipients also has enormous economic and industrial potential. The use of porang glucomannan, taro starch, and cassava starch can reduce the pharmaceutical industry's dependence on imported excipients while increasing the added value of local agricultural commodities (Cahyani et al., 2023). Kelana et al. (2018) explained that starch modification through pregelatinization can improve compactibility and flowability, bringing its characteristics closer to those of commercial synthetic excipients. Furthermore, Lestari and Eliana (2025) demonstrated that cassava starch has the ability to maintain compactibility after recompaction, making it potentially useful in tablet reworking processes in the pharmaceutical industry. This potential supports production efficiency because granules or tablets that fail to meet physical specifications can still be reprocessed without causing significant damage to the active ingredients. Therefore, the development of excipients based on local natural resources has great prospects in supporting the independence of the national pharmaceutical industry.

In herbal formulations, the use of binders is also crucial because most plant extracts are hygroscopic, have poor flow, and have low compactibility. Research by Muntaza et al. (2025), Khabibah and Ermawati (2023), and Rijal et al. (2022) shows that the use of binders such as CMC-Na, gelatin, and PVP can improve the physical integrity of herbal extract tablets, preventing them from becoming brittle during distribution and storage. Gelatin has significant application potential in herbal tablet formulations because it produces high cohesiveness and mechanical strength due to the formation of a protein network during the granule drying process (Abdullahi et al., 2024). Furthermore, the use of goatskin gelatin in the research by Zilhadia et al. (2021) demonstrates the potential for developing halal excipients, which are crucial for the global pharmaceutical industry. The development of halal-based gelatin also supports the circular economy concept, as biological waste can be utilized as high-value excipient products.

Other pharmaceutical applications are developing in mucoadhesive systems and lozenges. Na-CMC is known to have high swelling and gel-forming capabilities, thereby increasing tablet adhesion to the oral mucosa. Research by Anindhita et al. (2022) showed

that the use of CMC-Na in lozenges results in a longer disintegration time, allowing the active ingredient to be gradually released to the target area in the oral cavity. Such mucoadhesive systems have great potential for the delivery of oral antiseptics, local anti-inflammatories, and throat infection therapy. Furthermore, Utami et al. (2024) showed that the use of CMC-Na in chewable shallot extract tablets produced tablets with good mechanical strength and disintegration characteristics that were still suitable for herbal oral preparations. According to Nurhaliza et al. (2024), cellulose polymers such as CMC-Na have the ability to extend the residence time of the preparation, thus increasing the effectiveness of local therapy without the need for a significant increase in the drug dose.

In the manufacturing sector, the development of modern granulation technology also opens up new application opportunities in tablet development using the Quality by Design (QbD) approach and industrial scale-up. Wang et al. (2025) explained that binder properties such as wettability, cohesiveness, adhesiveness, and compactibility significantly influence the overall quality of granules and tablets. Furthermore, de Koster et al. (2019) explained that the mechanisms of wetting, nucleation, consolidation, and granule growth determine the pore distribution and density of granules formed during wet granulation. Research by Abdullahi et al. (2024) showed that gelatin is capable of producing granules with good mechanical strength in the wet granulation process, thus potentially being applied to industrial-scale tablet production. Kotamarthy et al. (2024) also explained that parameters such as liquid saturation, mixing dynamics, and pore distribution can be used as a basis for optimizing modern granulation processes. Thus, the use of modern binders is no longer merely viewed as tablet additives, but has evolved into an important part of pharmaceutical process engineering and continuous manufacturing.

Sustainability is also a major concern in the development of modern pharmaceutical applications. The use of natural excipients such as glucomannan, taro starch, cassava starch, and natural gelatin supports the reduction of synthetic polymers that are difficult to degrade in the environment (Asyiva et al., 2024). Asyiva et al. (2024) explained that the use of natural excipients based on polysaccharides and proteins not only supports the biodegradability of pharmaceutical materials but also has the potential to reduce dependence on synthetic polymers in modern tablet formulations. Furthermore, the use of more environmentally friendly solvents in the wet granulation process and optimization of the production process to reduce powder waste are part of the green pharmacy concept. The development of natural ingredients as pharmaceutical excipients also provides opportunities for integration between the agricultural sector, the food industry, and the pharmaceutical industry to create a more sustainable and economical production system.

Overall, the development of pharmaceutical applications of various types of binders shows that excipients no longer function solely as inert additives, but have evolved into functional components that determine therapeutic performance, stability, production efficiency, and drug release characteristics. Binders such as HPMC have great potential in sustained-release systems, starch in fast-dissolving tablets and ODTs, PVP in chewable and conventional tablets, gelatin in herbal formulations and halal excipients, and CMC-Na in mucoadhesive systems and lozenges. In addition, the development of combinations of natural and synthetic binders shows great potential in producing tablets with an optimal balance between compactibility, porosity, hydration, and disintegration ability. With the support of modern granulation technology, a Quality by Design approach, and the utilization of local natural resources, the development of binder-based pharmaceutical applications is expected to continue to grow towards more effective, safe, economical, and sustainable drug delivery systems.

CONCLUSION

The conclusion of this literature review indicates that differences in binder type and concentration in the wet granulation method significantly affect tablet hardness and disintegration time. Synthetic binders such as HPMC, PVP, and CMC-Na generally produce higher tablet mechanical strength due to their ability to form strong interparticle bonds and a more compact granule structure. HPMC demonstrates the best ability to produce tablets with sustained-release characteristics through the formation of a stable hydrophilic gel matrix, while PVP provides an optimal balance between hardness and disintegration time. Gelatin has high adhesive power, resulting in tablets with high hardness, but tends to prolong disintegration time due to the formation of a dense structure. In contrast, natural binders such as starch provide faster disintegration time due to their good swelling and porosity properties, although tablet hardness is relatively lower. These findings indicate that binder selection must be tailored to the formulation objectives, the type of active ingredient, and the desired drug release profile to achieve an optimal balance between mechanical strength and tablet disintegration ability.

However, this study has limitations because the analyzed data comes from various journals with different formulation methods, compression pressures, types of active ingredients, and evaluation parameters, so that the results between studies cannot be fully compared directly. In addition, some studies are still limited to the evaluation of physical properties without further analysis of dissolution profiles, long-term stability, or the influence of industrial production scale. Therefore, further research is recommended to use a more standardized experimental design, evaluate the combination of natural and synthetic binders, and develop a Quality by Design-based approach to obtain a more optimal and reproducible tablet formulation. Practically, the results of this literature review can provide a scientific basis for the pharmaceutical industry and researchers in selecting the right binder for the development of conventional, sustained-release, and fast-dissolving tablets with better physical quality and therapeutic performance.

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