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# EFFORTS IN IMPROVING TABLETS' TENSILE STRENGTH WITH A COATING SYSTEM AND BRITTLE EXCIPIENT: A REVIEW

Ahmad Ainurofiq<sup>\*</sup>, Chalimatussa'diyah Wuslatush Sholekah, Dzakiyyatul Hanifah, Eka Nurulita Susanti, Meila Tunjung Suryaningrum and Meyliana Adhitya Kusumawardhani

Department of Pharmacy, Sebelas Maret University, Ir. Sutami 36A, Surakarta 57126, Indonesia

Tablets are the most in-demand pharmaceutical preparation by pharmaceutical companies or users because they provide the best capabilities from all oral preparations. Maintaining the grade and quality of tablets need to be of great concern. Factors affecting the physical quality of tablets must always be evaluated, including tensile strength. Tensile strength directly affects the process of distribution, storage, disintegration, and dissolution of tablets. Tensile strength problem is often found during tablet production with the wet granulation method, in which overgranulation often occurs, especially in high-shear wet granulation (HSWG). The solution for over granulating is the addition of brittle excipients to form a strong bond when combined, thus increasing tensile strength. An ideal tensile strength may be achieved because the mechanical strength of the tablet is increased proportionally to the increased area of the bond. Another solution to increase tensile strength is by using a coating system using the Multiple Unit Pellet Systems (MUPS). The MUPS coating system often experiences problems such as caking. This problem can be overcome using a coating polymer that is stable on high RH and supports a strong tablet formulation. The solution to the tensile strength problem with the addition of brittle excipients and coating will be reviewed in this article to increase tensile strength.

Keywords: Tablet, wet granulation, tensile strength, brittle excipient, coating system

#### **INTRODUCTION**

A tablet is a solid preparation containing drug material with or without fillers. Tablets are the most widely used preparation due to various advantages, including dosage accuracy, ease of use, ease of transport, and relatively compared other affordable to drug preparations<sup>1</sup>. Tablet formulation usually consists of an active ingredient and excipients, although a small number of tablets can be formulated without excipients. Other than that, the method used for tablet formulation molding needs to be considered. Tablets are made in various sizes, shapes, and surface markers depending on mold design. The results of tablet formulation must fulfill the predetermined parameters. The mechanical strength parameter is an important factor to be considered. The mechanical strength of a tablet can be

determined from tensile strength. Tensile strength is defined as the maximum bearable stress prior to fracture and is computed from the tablet dimension and breaking force. Tensile strength is especially useful for finding the maximum strength limit of a material before the material becomes damaged/broken. By knowing the tensile strength, we can know the properties of a material such as flexibility (elongation), strength, bending, so that the right mechanical strength can be obtained. Tensile strength on the tablet will affect the physicochemical properties of the tablet. Tensile strength can determine the choice of the right material to obtain the appropriate physicochemical properties of tablets such as weight uniformity, drug content, friability, disintegration time, crushing strength, tensile strength and dissolution. Tablets will have maximum tablet hardness as indicated by their

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<sup>\*</sup>Corresponding author: Ahmad Ainurofiq, E-mail: rofiq@mipa.uns.ac.id

resistance to various mechanical shocks during manufacture, packing and transportation<sup>2</sup>.

Tensile strength is a function of physicomechanical properties caused by particles (shape, size, and surface), particle mechanical properties (elasticity, plastic deformity, and brittleness), and formation conditions (e.g., compaction pressure and speed). Tensile strength describes a tablet's durability, ease of handling, and resistance to crushing of tablets under a predetermined load. In general, a tablet is considered good if it has a hardness between 4-8 kg. Tablet hardness of less than 4 kg can still be tolerated as long as the brittleness does not exceed the set limit<sup>3</sup>. Factors affecting tensile strength include excipients, tablet formation method, and coating system. Tablet with low tensile strength, which makes them unable to fulfill the parameters of tabletability, compressibility, and compactibility. Therefore, efforts to improve tensile strength are needed. Usually, there are two methods to improve tensile strength, i.e., particle engineering and crystal engineering. Particle engineering can be done with a coating system and choosing excipients in the formulation of wet granulation. This review is conducted to gain deeper knowledge of the two types of particle engineering.

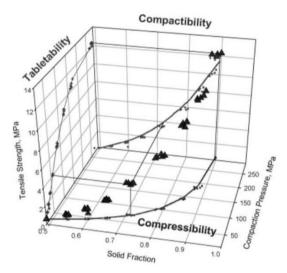
#### **Tensile Strength Parameter**

Tensile strength is a parameter from mechanical properties, which is very important to prevent mechanical damage to the tablet when reaching patients, such as breaking, chipping, and capping<sup>4</sup>. Factors affecting the physical quality of tablets and must always be evaluated include tensile strength. The factors affecting tensile strength include the type of crystal used, particle size, distribution of particle size, polymorphism, amorphism, water level, the shape of salt, tablet compression speed, type of excipient, type of active ingredient, compression force, granulation method, and ultrasonic vibration<sup>5,6</sup>. All of these factors are related to each other and cannot be separated. Other factors, such as moisture, determine the plasticity of a material that can affect viscoelasticity in tensile strength<sup>7</sup>. Tensile strength directly affects the process of distribution, storage, disintegration, and dissolution<sup>8</sup>. Tensile strength keeps increasing along with increased compression strength. The tensile strength value not only must not be too high because the tablet must be able to be destroyed when entering the body but also must not be too low which may hinder the production process. This value can be obtained through several methods, such as the diametral compression test or bending test. Tablet tensile strength is an important component required in film-coating, packaging, distribution, and final use by the patient, which is easily breakable in the body and capable to release active ingredients. In general, a tensile strength of more than 1.7 Megapascal (MPa) is enough to ensure that the tablet resists mechanical processes during manufacture. Tensile strength of fewer than 1 MPa is not recommended for great mechanical stress<sup>9</sup>. Tensile strength  $(\sigma)$  depends on crushing strength (F), diameter (d), and thickness (t) of the tablet calculated according to the following equation<sup>10</sup>:

Tensile strength 
$$\sigma = \frac{2F}{\varpi Adt}$$

Based on the above equation,  $\sigma$  represents tensile strength (MPa), F represents the force required to crush the tablet (Newton), d represents diameter (mm), and t represents tablet thickness (mm).

Another factor that can affect tensile strength is compaction pressure. The correlation between compaction pressure, tensile strength, and solid fraction can be used to determine the characteristics of a material. Fig. 1 depicts a correlation plot of tabletability (tensile strength and compaction pressure), compressibility (compaction pressure and solid fraction), and compactibility (tensile strength and solid fraction). Compressibility is the ability of a material to reduce its volume based on applied pressure, represented by a tablet on compression pressure. porosity plot Compactibility is the ability of a material to produce a tablet with a strength capable to withstand densification and is represented by a tensile strength plot on tablet porosity. Tabletability is the capacity of a powder to be converted into a tablet under certain strength under the effect of compression pressure and is represented by tensile strength on compression pressure<sup>11</sup>. The use of this terminology is suggested in tablet mechanical properties, where the three variables (compaction pressure, tensile strength, and solid fraction) are considered in a study. The densification involving process, especially particle rearrangement, followed by deformation under pressure can be further rearranged, although smaller particles are formed from the fracture of larger particles<sup>12</sup>.



**Fig. 1:** The correlation between compactibility, compressibility, and tabletability in a scheme<sup>13</sup>.

In general, tensile strength increase is proportional to compression pressure. Tablets that are compressed with higher compression pressure showed higher tensile strength. This can be associated with the fact that the average contact area between particles increased proportionally with compression pressure<sup>14</sup>. Understanding the mechanical properties of active ingredients and excipients, such as plasticity, is very important in developing tablet formulation. Plasticity is the ability of a material to form irreversible deformation under pressure and is one of the most important properties that directly affect powder tableting<sup>15&16</sup>.

Tabletability, plasticity, and elasticity are integral components in the process of tablet formation. Elasticity provides direct insight into dispersive interaction, which will regulate the arrangement of solid molecules. Appropriate understanding of mechanical properties and material deformation phenomenon is important in the context of powder densification<sup>17</sup>. Usually, higher compaction pressure creates a stronger tablet. However, several materials with high compaction pressure lead to lower tensile strength due to over compaction. Tabletability provides a good insight into the process of densification and mechanical properties of a material  $^{13}$ .

Densification is an important manufacturing stage in tablet formation, which reduces volume and rearranges particles, and is a consolidation of the formation of inter particulate bonds. The success of the densification process does not only depends on the physicotechnical properties of drugs and excipients, especially deformation behavior, but also on the regulation process of the tablet machine in regards to the rate and magnitude of force transfer. Several studies have proven that the properties of drugs and excipients, such as particle size and distribution, water level, crystal habit, polymorphism, amorphism, hydration, amount of lubricant, and binder highly affect powder densification<sup>5&6</sup>. Tablet compression speed and compression force profile also affect the final quality of the tablet. Mechanical aspects of tablet formation can be studied using a tablet-forming machine with a punch and die, and also with a densification simulator. The compression process of a drug from powder to tablet can be seen in Fig.  $2^{18}$ .

In Fig. 2, the pressure against the die-wall reached maximum immediately after the maximum force of the upper and lower punch provide pressure to the tablet material. The residual die-wall pressure is constant after upper and lower punch forces become zero until the beginning of the ejection process. Residual die-wall pressure is the average value in the constant area when the upper punch force is zero and there is a distance forming a contact area between the tablet and die-wall. The residual die-wall pressure depends on particle deformation after pressure force is applied. For materials with plastic deformation, large residual die-wall pressure is observed, different from a smaller force for elastic materials as a result of large relaxation behavior. Brittle material shows a moderate value of residual die-wall pressure as a result of a large fragmentation and large areas when released. Large residual die-wall pressure during ejection is a sign of powder adhesion during molding, and reduced pressure to die-wall is effective during ejection after the process of tablet forming<sup>20</sup>.

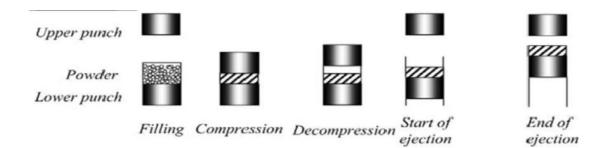


Fig. 2: Compression Process<sup>19</sup>

#### **Coating System**

The use of a coating system can increase the tensile strength of a tablet. The coating material uses polymers with high adhesion that can effectively improve tablets with poor compression. The coating on the tablet surface will provide a strong bond between excipients and drug-active substances, which is proven by the contact bonds between particles as illustrated in **Fig. 3**. In tablets with poor compression, the particle bond in **Fig. 3A** that is not coated showed a less strong bond, while **Fig. 3B** showed stronger particle bonds with coating<sup>21</sup>.

The light brown coating in Figure 3 can control particle bonds, thus improving the bond of a tablet. Therefore, choosing the correct coating is important to improve tensile strength. Coating with high adhesion will create a strong interparticle bond even in low compression pressure. On the contrary, tabletability will be poor in coating with poor bond<sup>23</sup>.

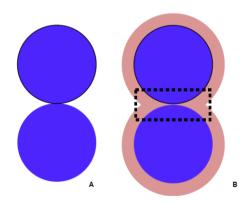


Fig. 3: Profile of tablet bond without coating system (A) and with coating system (B)<sup>22</sup>

The factors affecting coating to improve tensile strength include the interaction between the coating tablet and the ingredients used in the tablet (excipient and active ingredient). A proper selection of excipients in tablet formation will result in a good tablet because excipients can provide sufficient mechanical strength. The effectivity of the tablet formation process is affected by the bond between a physical mixture of excipients and active ingredients, where the bond can be formed when the number of excipients exceeds the critical threshold. Therefore, a strong tablet cannot be obtained unless the formed bond can penetrate all particles, which requires a large number of binders. The tablet will fail if the binder is not effective. Other than that, coating thickness and drying condition of tablet coating also affect the coating system, which implies tensile strength<sup>24</sup>.

Sugar coating is a coating technique that requires 5 days under strict processing conditions, which requires skill and has a high risk of fungi and microbial growth. Therefore, it is mostly substituted by polymer film coating. Abbott Laboratories introduced the first filmlayered tablet to the market in 1954. The availability of various polymers and coating facilitate equipment can batch-to-batch homogeneity, process optimization, good reproducibility, and better process control. Film coating that involves a liquid organic solventbased polymer system is the most commonly used tablet coating technology<sup>25</sup>. This film coating significantly increases tablet tensile strength in low compression.

The coating technique has been developed to improve tablet quality, improve tablet esthetics, reduce damage, and control drug release. Effect coating system on tablet disintegration will invariably lead to increase in disintegration time. In several study, coating systems tablet in the ascending colon affect onset time for single-coated tablets has highly variable (45 - 106 min) after gastric emptying, while disintegration time for the double-coated tablets more consistent (20-35 min). The variability in the in vivo disintegration of conventional enteric-coated can be attributed to the inter-subject variability in small intestinal pH, transit and fluid volume. Modified drugs are useful for increasing drug efficacy and patient compliance or prolonging the duration of action. Therefore, tablet film coating with various polymers are actively pursued to achieve modified drug retention by controlling the concentration and/or site of drug concentration. In delayed drug release enteric coating can increase drug stability in the harsh gastric environment and/or reducing undesirable gastric irritation caused by drugs. Drug release rate can be controlled by physicochemical properties and the amount of polymers used for surface coating. It is also controlled by altering the thickness, tortuosity, and permeability of the coating layer. Surface coating approaches are also combined with different mechanism based-drug delivery systems to modify drug release rates. One of the coating techniques available to use is multiple unit pellet systems (MUPS). MUPS is a common method to be used during drug release modified through oral administration with a compressed pellet system. Fig. 4 depicted that MUPS is made from pellets coated with a reservoir. MUPS is formed by several excipients that help perfect pellet compression. Incompatible drugs can be combined into one preparation form and can be designed to produce different release profiles from the same drug or from different drugs. MUPS is made from pellets coated with a reservoir with a characteristic of polymer coating that can withstand compression strength, in which the coating must not be crushed or even change shape<sup>19</sup>.

MUPS is usually developed as a tablet containing bearing beads that act as a coating to modulate drug release. Bearing beads contain active substances coated with polymers to modulate slow drug release. The advantages of this system include reduction of dose-dumping risk, minimizing stomach irritation from irritant drugs, minimizing inter subject variability in drug absorption in the GI tract so that the drug enters the bloodstream slowly and consistently, having flexibility in developing products with different drug release profiles through the combination of beads with different coatings<sup>26-29</sup>.

The process of MUPS coating involves four stages, including functional coating deformation, functional coating densification, fragmentation, and pellet attrition. All of the above stages depend on the core property of pellets, functional coating film, and extra granular excipients used. In a study, a pantoprazole MUPS tablet had an oral rehydration salt-dispersible property, which is made for geriatric and pediatric patients. The pellet was coated with Eudragit L30D-55 and PlasACRYL HTP 20 as plasticizers for enteric release<sup>30</sup>. This tablet was made by maintaining the oral rehydration salts-dispersible property of the tablet such as less than 30 seconds of disintegration time and expected to not give an unpleasant residual taste and texture in the mouth. The coating above and the MUPS coating technique with good compressibility and the good water level were used to increase tablet compactibility and tensile strength, thus increasing hardness and reducing brittleness<sup>31</sup>.

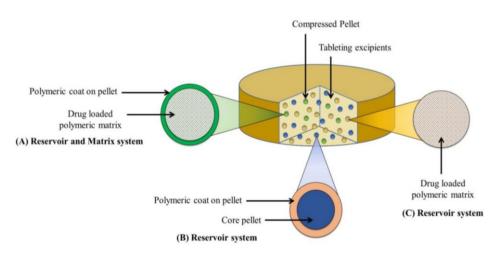
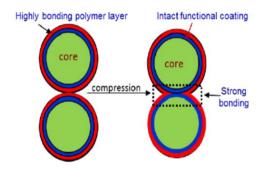


Fig. 4: MUPS constructed from pellets made from the reservoir, matrix, and combined pellet system<sup>19</sup>

#### Success Parameter of the Coating System

The coating system can affect the tablet's physical properties, resulting in a better tensile strength compared to a conventional tablet. There are parameters that determine whether a coating system successfully increases tensile strength. One of the visible parameters is the interparticle contact area after compaction, which is visualized in Fig. 5. If the particles are covered with coating polymers, the existing layers will be deformed during compression, creating a three-dimensional network even under low pressure. Therefore, coating polymer is considered effective to increase tensile strength because it can produce substantial mechanical strength on the tablet with low compression pressure. The top coating method with a strong interpolymer bond is an effective method and has the potential to form a MUPS tablet. Fluid bed coating is a process suitable to produce layered beads free from agglomerates. The combination of moisture activation and silica layer from polymer-coated beads can be used to form MUPS tablets with high mechanical strength and favorable dissolution profile. The success with two coating polymers, i.e., PVP K30 and PVP VA64, is the most common modification used to prove that this method can produce a good result in the controlled administration of oral drugs<sup>32</sup>.



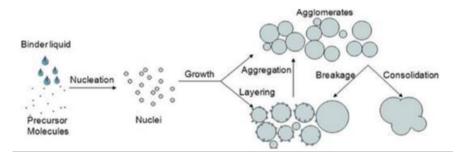
**Fig. 5:** The contact area between particles after coating and compression<sup>35</sup>

Choosing the correct coating material in the coating system will produce a good tablet with high adhesion, making it strong even under low compression pressure. Modification can be done based on the problems existing in the MUPS tablet. For example, a combination of pyridoxine tablets and caffeine beads coated with PVP. There was a significant increase in the ability of pyridoxine and caffeine beads after PVP coating. At high RH, a more plastic PVP coating can naturally form a higher bond area and strength under identical compression conditions. A thicker PVP coating also supports the formation of a stronger tablet. Meanwhile, beads coated with kollicoat have smooth surfaces after the tablet is crushed with low mechanical strength because of low bond areas between the beads. Low tabletability is produced with kollicoatcoating<sup>33</sup>.

MUPS can be problematic when there is an increase of polymer mobility on the upper layer and caking, although this mobility increase makes it easier to form strong bonds between adjacent beads. Therefore, antiadherent silica is added on particle surfaces that can produce lower tensile strength. However, the tablet's ability is enough to form a strong tablet and the loss of tensile strength is recovered after a considerable amount at 75% RH. There is a long equilibrium condition where beads are highly compressible and can flow freely<sup>34</sup>.

#### **Choosing Excipient in Wet Granulation**

Wet granulation is a tablet-forming method with a process of changing from smooth powder into granules with the help of an appropriate binder solution. In this wet granulation method, the binder material should be in the correct amount because a slightly different amount can produce inappropriate granules that may affect the final result of the tablet<sup>36</sup>. The granulation process will produce particle enlargement as seen in **Fig. 6**.



**Fig. 6:** Over granulating process<sup>35</sup>

In general, the granulation process involves critical stages such as preparing the materials for granulation, adding granulation solution, agglomeration process, and drying process. The problem with wet granulation lies in overgranulating, especially when using a high-shear wet granulation (HSWG). The shaping method for granulation known as HSWG has been improved for use in the pharmaceutical sector. The pharmaceutical process known as HSWG is said to be complex and multivariate and is affected by a great deal of factors including equipment, formulations, processes. High-shear and mixers are meticulously built in comparison to conventional mixers, taking into account the phase of the dispersed particles, the fluid viscosity, the needed particle size, and so on. HSWG is mainly used to improve the flow ability of the powder. Nucleation and growth kinetics of the powder during HSWG is complex because of related factors, such as binder type, binder concentration, the surface energy of the drug and excipient, and process parameter. Although manv are known regarding the process of HSWG, а comprehensive understanding of HSWG is highly required. One of the substantial problems that continuously occurs in HSWG is the loss of powder's ability to be compressed into a solid tablet, a phenomenon known as overgranulation. It is a phenomenon characterized by the loss of the tablet's ability to maintain its form. If a tablet has overgranulation, it can be destroyed during the process of formation and distribution. The criteria for overgranulation include the inability of powder to be compressed into a tablet with a tensile strength under 2 MPa with a compaction pressure of 50-400 MPa. These criteria were based on an observation that tablets usually have an adequate mechanical strength to withstand a tensile strength of 2 MPa or higher during handling<sup>37</sup>. The correct endpoint of granulation must be able to prevent overgranulation while maximizing the handling properties of the powder. Several techniques based on process parameters, such as torsion and power consumption have been developed to observe the granulation process and to determine the appropriate end point<sup>35</sup>. An ideal tensile strength is when the tablet is solid during the mechanical process and easily disintegrates in the body. An ideal tensile strength increases in proportion to the increased

bond area because the mechanical strength of the tablet increases with the increased bond area. The solution to overgranulation is the addition of brittle excipients that suppress granular brittle fracture after compaction<sup>37</sup>.

#### The Effect of Brittle Excipient to Overcome Overgranulation

Choosing excipients is a critical process that also affects the resulting tablet tensile strength. The excipients used usually involve diluent, binder, disintegrant, lubricant, and glidant. These five components can be the determinant factors for tablet quality. A diluent is a main component that acts to increase the bulk volume and flowability of the active ingredients used in tableting. A diluent is required to ensure that the tablet has the required size or mass during molding to provide sufficient mechanical strength<sup>38</sup>.Correct use of diluent can produce a compact tablet, with a structure of strong particles and physical shape<sup>39</sup>. Common examples of diluent are microcrystalline cellulose (MCC), calcium phosphates, e.g., dibasic calcium phosphate, polydextrose, pregelatinized starch, sugar, lactose, and mannitol<sup>40</sup>.

MCC is an important excipient that has been extensively investigated. A study stated that tablets with MCC are harder because of increased water levels, while the lack of moisture is responsible for tablet lamination due to the condition of the recovery of the material to its original position as the elastic property of the material. Another study reported the effect of moisture in MCC on density, compaction, and tensile strength, and related to changes in the mechanical properties of MCC by way of water absorption into cellulose structure. The tensile strength of MCC tablets is observed at 8% water level. This effect is associated with hydrostatic resistance to consolidation caused by the existence of water<sup>13</sup>.

Figure 7 showed that the tensile strength profile of MCC tablets in the same pressure compaction is not significantly different between four different dwell times (8 ms, 27 ms, 20 s, and 90 s). This result showed that compaction behavior in MCC is mostly independent of dwell time during compression. The same goes for lactose, which is not affected by dwell time during compression. Based on Figure 7, MCC produced higher tensile strength compared to lactose within the same compaction pressure. This shows that MCC excipient provides better tensile strength compared to lactose. Therefore, the resulting tablet with MCC is harder and better<sup>13</sup>.

One of the problems in the granulation method with the HSWG system is the overgranulation phenomenon. Therefore, a solution is needed to overcome overgranulation. Size enlargement in dry powder is known to reduce tabletability of a material. The combination of brittle excipients such as lactose and dibasic calcium phosphate (Dical)in the MCC matrix can increase tabletability. More brittle excipients are more effective to overcome the problem of overgranulating during the production process with HSWG<sup>41</sup>.

A test was conducted with the combination of MCC binder with lactose and Dical as brittle excipients (Figure 8), both of them represent various ingredients because lactose is water soluble while Dical is not. When lactose is dissolved during the wet granulation process, some lactose crystallized due to the drying process. However, not all formed crystals are lactose, but also Dical. It is important to note that Dical has very low solubility in water. This condition can cause structural differences and affect the tendency of fragmentation from the produced granules<sup>13,42</sup>.

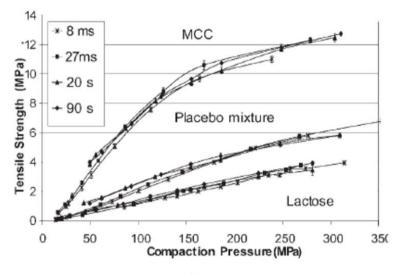


Fig. 7: Tabletability of MCC, lactose, and placebo<sup>19</sup>.

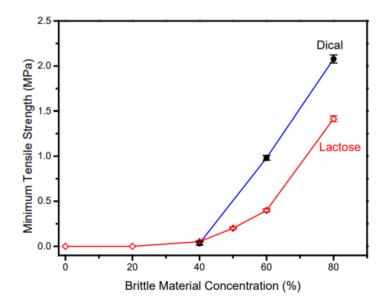


Fig. 8: The effect of MCC binder combined with lactose and Dical excipients on tensile strength<sup>35</sup>

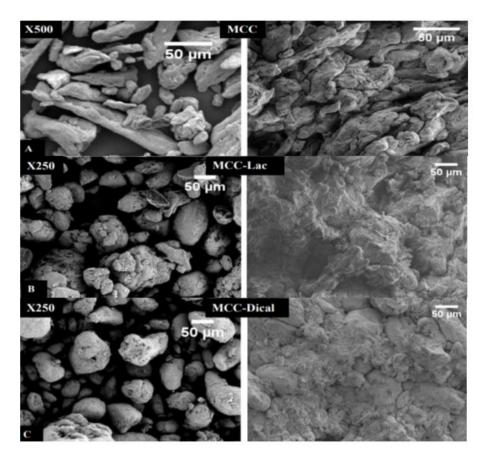
## CorrelationBetweenFormulationComposition and Tableting Performance

Figure 8 depicted that the physical mixture of MCC-lactose has lower tabletability compared to lactose and Dical. The results of the study on all mixtures showed that tensile strength decreased in line with the increased water level. In MCC, this might be due to the process of surface smoothing, particle rounding, compaction, and agglomeration. This is in line with a study that a mixture containing more MCC tends to be more sensitive to water addition, with tensile strength decreasing rapidly with increased water level during the granulation process. However, in pure MCC, tensile strength is increased with increased water level during the granulation process. The higher the water level, the larger the area that can be granulated, thus enabling a larger fragmentation during the compaction process to form bonds on the tablet. Another condition occurring in MCC granules that provide zero tensile strength during the granulation process is when the water level is at 55%. Tablets are not fragmented under pressure because hard, large, and elastic granules resist deformation. Under high pressure, MCC granules can only crack, instead of being crushed into fragments. On the other hand, brittle lactose granules with various sizes, shapes, and porosities produced with different methods showed a comparable ability of tableting with non-granulated lactose. For certain conditions, a higher concentration of brittle excipients has lower sensitivity to changes in water level during the granulation process. The same is seen in the effect of magnesium stearate, which is not dissolved in water but can reduce tensile strength with the reduction mechanism of interparticle bonding between particles. In other words, lower water levels during the granulation process produced a stronger result for a granule mixture containing brittle excipients. In this event, higher brittle excipient concentration, although effective in overcoming overgranulation, still has a possible error in the amount of water used during the granulation process<sup>43</sup>.

Dry granules provide a different result between lactose and Dical-based granules, where lactose is expected to mix tighter with MCC compared to Dical because of the dissolution of the crystallization  $process^{13}$ . Figure 8 showed that the expected difference in the structure of lactose and Dical-based granules insignificantly affects the number of brittle excipients required to have an impact on overgranulation. More than 40% of brittle excipients are needed for both. The minimum tensile strength of Dical granules showed higher results from lactose granules (Figure 8), implying that Dical is more effective than lactose in overcoming overgranulating. The minimum tensile strength of a mixture containing 80% of brittle excipients is 1.4 MPa for lactose and 2.1 MPa for Dical. There are at least two possible explanations for this: a) Dical-based granules are more brittle, and b) Dical has a higher bond strength than lactose<sup>44</sup>.

#### Correlation Between Formulation Composition and Tablet Structure

The formulation strategy to overcome overgranulating is also supported by direct observation to fragmentation granules in tablets. Scanning Electron Microscope (SEM) can be used to observe the fracture surface of the tablet (Figure 9). Each granule in pure MCC after compression (right image) has similar pattern to individual granules before compression (left image) with no fractured granules. A different condition is seen in the mixture between MCC and lactose and MCC and Dical. For granules containing 80% of lactose and Dical, most granules are destroyed on the fracture surface after compression. A few fragments are spread around the fracture surface, showing extensive fragmentation from the granules. This condition supports the hypothesis that the combination of brittle excipient forms brittle granules, promoting size reduction during compaction, thus overcoming overgranulating during HSWG in laboratory scale setting or production scale setting which can increase tensile strength<sup>44&45</sup>.



**Fig. 9:** Scanning Electron Microscope (SEM) before compression (left panel) and after compression (right panel) from (A) MCC (B) MCC-lactose (C) MCC-Dical granules<sup>35</sup>.

#### Conclusion

The development of products with new innovations is a strategy to improve product quality. The specification of product quality must be achieved in the process of formulation development. The overall increase in product quality should be reviewed in every step of choosing development. from materials. screening and formula development, scale-up, and process optimization. Tensile strength evaluation is required to maintain the quality of the tablet's mechanical properties. Not every tablet condition achieves tensile strength due to other factors, such as wet granulation with HSWG which have a critical parameter in over granulating, causing the tablet to be easily crushed. The use of brittle excipients by combining excipients to granule formula successfully overcame over granulation problem. When a brittle excipient is inserted into the matrix, it can effectively increase tablet tensile strength. For a mixture containing higher brittle excipients, water addition during the granulation process usually cause a slower decrease of tabletability before the minimum is reached. After the minimum is reached, the

ability of each tablet mixture increased along with the water level during the granulation process due to higher granule fragmentation. Another solution to increase tensile strength is the coating system. This system can increase the mechanical properties of the tablet, especially by producing tablets with better tensile strength compared to conventional tablets. If the particles are coated with a coating polymer, the existing layers will be deformed when compressed with low pressure. Coating polymer is quite effective to improve tensile strength because, in low compression strength, it can produce a high mechanical strength on the tablet.

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الجهود المبذولة في تحسين قوة شد الأقراص باستخدام نظام تغليف وسواغ هش: بحث مرجعي

أحمد عينوروفيك\* – شاليماتوساديه وسلاتوس شوليكة – دزاكياتول حنيفة – إيكا نوروليتا سوزانتي – ميلا تونجونغ سوريانينغروم، ميليانا أديتيا كوسوموارداراني

قسم الصيدلة ، جامعة سيبيلاس ماريت ، سوراكارتا ٧١٢٩ ، إندونيسيا

الأقراص هي المستحضرات الصيدلانية الأكثر طلبا من قبل شركات الأدوية أو المستخدمين لأنها توفر أفضل القدرات ضمن جميع المستحضرات الفموية. يجب أن يكون الحفاظ على نوعية وجودة الأقراص مصدر اهتمام كبير. لذلك جب دائما تقييم العوامل التي تؤثر على الجودة المادية للأقراص ، الأقراص مصدر اهتمام كبير. لذلك جب دائما تقييم العوامل التي تؤثر على الجودة المادية للأقراص ، بما في ذلك قوة الشد. تؤثر قوة الشد بشكل مباشر على عملية توزيع وتخزين وتفكك وإذابة الأقراص. غالبا ما توجد مشكلة قوة الشد أثناء إنتاج الأقراص باستخدام طريقة التحبيب الرطب ، حيث يحدث إعابا ما توجد مشكلة قوة الشد أثناء إنتاج الأقراص باستخدام طريقة التحبيب الرطب ، حيث يحدث إص بغالبا ما توجد مشكلة قوة الشد أثناء إنتاج الأقراص باستخدام طريقة التحبيب الرطب ، حيث يحدث منابي الزائد غالبا ، خاصة في التحبيب الرطب عالي القص العلامي (HSWG) الحل للتحبيب الزائد هـ وأضافة سواغات هشة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة الشد. يمكن تحقيق قوة شـ إضافة سواغات هشة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة الشد. يمكن تحقيق قوة شـ إضافة سواغات همة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة الشد. يمكن تحقيق قوة شـ وأضافة سواغات همة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة الشد. يمكن تحقيق قوة شـ وأضافة سواغات همة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة الشد. يمكن تحقيق قوة شـ وأضافة سواغات همة لتشكيل رابطة قوية عند دمجها ، وبالتالي زيادة قوة المثلا. يمكن التغلب على هذه المشكلة باستخدام بوليمر طلاء مستقر عنـ وأسبة هو استخدام نظام تغليف باستخدام أنظمة الحبيبات متعددة الوحدات .(MUPS) غالبا ما يواجه نظام تغليف MUPS ألمثلا بينا ما يواجه منظام رطوبة نسبية مرتفعة ويدعم تركينة قرص قوية. سيتم مراجعة حل مشكلة باستخدام بوليمر طلاء مستقر عنـ وأسبة والطلاء في هذه المشكلة باستخدام بوليمر ألم والم المؤمة السواغات المثلاء في هذه المشكلة باستخدام بوليم مثومة الحمان القرة السواغان القوة السرمي مثلاية الرعمة الحبيبات متعددة الوحدات .(MUPS) عالباما يواجه منتقر عنـ وألم منابية مرتفعة ويدعم تركينة قرص قوية. سيتم مراجعة حل مشكلة قوة الشد بإضافة السـ واغات رطوبة نسبية مرتفعة ويدم تركيبة قرص قوية. سيتم مراجعة حل مشكلة قوة الشد بإضافة السـ واغات المشيا المربة الملاه ألموا