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Review of The Use of Croscarmellose Sodium and Crospovidone Superdisintegrants in Orally Disintegrating Tablets (ODT)

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ABSTRACT

ODT (Orally Disintegrating Tablet) is an orally disintegrating tablet that dissolves in saliva within a few seconds without the need to chew the tablet or drink additional water. ODT can be made by direct compression (DC), lyophilization, and molding technology. For ODT produced by the Direct Compression process, disintegration time depends on disintegrant, matrix, tablet weight, and tablet hardness. The use of different super disintegrants will result in different ODT characteristics, particularly disintegration time and dissolution profile. Superdisintegrants that are often used in ODT formulas that produce good tablet physical characteristics are croscarmellose sodium and crospovidone. This research is literature review research using a systematic review method. Data is obtained through several databases such as Google Scholar; PubMed; Science direct; and Willey. The data that has been obtained will go through a selection process based on inclusion and exclusion criteria. The data obtained will be arranged in a table. Data will be evaluated and synthesized systematically. The results of this review study reported that the physical properties of ODT with superdisintegrant croscarmellose sodium and crospovidone had significant differences in the results of disintegration and tablet hardness and dissolution of ODT tablets with superdisintegrant croscarmellose sodium and crospovidone had different disintegration times and Q values. This is because the mechanism of action of disintegration of croscarmellose sodium and crospovidone is different, croscarmellose sodium disintegrates by swelling and crospovidone undergoes wicking, followed by swelling and then ending with restoration of stretch.

INTRODUCTION:

ODT (Orally Disintegrating Tablet) is an orally disintegrating tablet that dissolves in saliva within a few seconds without the need to chew the tablet or drink additional water. This dosage form is specially designed for patients with dysphagia (difficulty swallowing), for example pediatric, geriatric, psychiatric, bedridden patients, or patients with persistent nausea. Using ODT for these groups can reduce the risk of choking. ODT is also ideal for patients who need immediate action such as patients who have had a stroke. ODT is a dosage form that is very suitable because it does not require additional water to consume the drug [1].ODT can be made by direct compression (DC), lyophilization, and molding technology. Of these manufacturing processes, DC is the most economical because it uses conventional equipment, commercially available excipients, and relatively simple process steps. The degree of disintegration of ODT is a critical success factor. For ODT produced by the DC process, disintegration time depends on disintegrant, matrix, tablet weight, and tablet hardness. In many cases, the disintegrant has a major role in the disintegration process, and the level of use of the disintegrant will have an impact on tablet hardness and taste in the mouth. Therefore, the selection of an appropriate disintegrant and an optimal level of use is very important to ensure a high disintegration rate. ODT will undergo rapid disintegration followed by rapid dissolution and absorption, which can result in a rapid onset of action. Increased bioavailability is expected for drugs that are absorbed from the mouth and esophagus when saliva enters the stomach. Ease of administration, accurate dosing when compared to liquids, liquid drugs in solid form, no need for water to swallow, and good taste in the mouth are some of the other prominent features of ODT[2].

Previous studies have shown that ODT formulated with different super disintegrants can produce different physical characteristics of tablets. The use of different superdisintegrants will result in different ODT characteristics, particularly disintegration time and dissolution profile. Superdisintegrants that are often used in ODT formulas that produce good tablet physical characteristics are croscarmellose sodium and crospovidone. Croscarmellose sodium can expand well in a watery environment and has a fibrous form that supports water capillarity and easy disintegration. Thus, the tablet will disintegrate quickly, so that it can then be dissolved properly [3]. Meanwhile, tablets formulated with crospovidone can quickly draw saliva into the tablet which will result in an increase in volume and hydrostatic pressure which promotes rapid disintegration and can be dissolved immediately[4.5]. The mechanism of action of super disintegrants maybe by wicking, swelling, which was found to be especially influential for tablet disintegrants, while other mechanisms, such as deformation recovery, particle repulsion theory,

the heat of wetting, and gas evolution could be the working mechanism of tablet disintegration [6].In this study, we will discuss the superdisintegrant croscarmellose sodium and crospovidone which was carried out with a literature study.

MATERIALS AND METHODS:

Determination of inclusion and exclusion criteria

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Research conducted in 2000- 2020	Research that does not specifically explain the final results of the research.
Research using Language Indonesian and English	
Original research journals available in full text.	Research that does not have completeness of data.
Research with the creation of Orally Disintegrating Tablets (ODT)	Research journals that are not full text and have no conclusion.
Research with the use of variations superdisintegrant composition	Studies not using the superdisintegrant croscarmellose sodium, crospovidone, and the superdisintegrant combination croscarmellose sodium and crospovidone.
Studies using the superdisintegrant croscarmellose sodium, crospovidone, and combined use croscarmellose sodium and crospovidone	
Research that discusses in vitro dissolution in the manufacture of tablets with variations of the superdisintegrant croscarmellose sodium and crospovidone.	

Literature Search

The literature search strategy that will be used for this research is to search journals, articles, and other literature (books and other libraries) related to research topics in databases such as Google Scholar; PubMed; Scopus; and Willey. The keywords used in this search are variations in the use of the words Superdisintegrant, ODT, Croscarmellose Sodium, and Crospovidone.

Data Extraction and Synthesis

The data obtained from the literature has been screened using inclusion-exclusion criteria and a critical assessment is carried out then extracted and arranged in a table to facilitate a synthesis process. The data that has been compiled in the table will be evaluated and synthesized narratively so that a conclusion can be drawn to answer the existing problem formulation.

RESULTS AND DISCUSSION:

Physical Properties of ODT

Orally Disintegrating Tablet (ODT) is a tablet that is made to disintegrate in the mouth and makes it easier to use when used by children and the elderly with dysphagia. Superdisintegrants that are often used in the manufacture of ODT are croscarmellose sodium and crospovidone either alone or in combination. Previous studies have shown that ODT formulated with different superdisintegrants can produce different physical characteristics of tablets. The use of different superdisintegrants will result in different ODT characteristics, particularly disintegration time and dissolution profile. Superdisintegrants that are often used in ODT formulas that produce good tablet physical characteristics are croscarmellose sodium and crospovidone[3].

The physical properties of ODT in the weight uniformity test, the size uniformity did not experience a significant difference in increasing the superdisintegrant concentration, while in the hardness test, disintegration time and tablet friability were different. Tablet hardness is generally inversely proportional to tablet porosity. High tablet porosity is associated with low hardness. The hardness and mechanical strength of the tablets formulated in this study were found to be a function of the type of disintegrant used. Tablet hardness was found to be inversely related to tablet porosity [3]. Increasing the amount of one superdisintegrant and reducing the other is where the tablet disintegration time increases[13]. The ODT was made by direct compression using the superdisintegrants croscarmellose sodium (10%) and crospovidone (2% 4%, 5%, 10%) which gave the results of the brushiest disintegration time was crospovidone. with a concentration of 10%. The results of this study indicate that the use of croscarmellose sodium superdisintegrant makes the disintegration time of ODT longer than the disintegration time of the use of crospovidone superdisintegrant. This effect is more pronounced for compositions containing crospovidone acting almost entirely through shapeshifting, while croscarmellose sodium shows its main mechanism by swelling[12]. Most of the deformation is already due to precompression if the deformation is the main disintegration mechanism[11]. But there is one study from which gives different results, namely that the results of hardness, disintegration time,

and dissolution of croscarmellose are better than crospovidone with the same concentration. The results of the hardness of crospovidone ODT were greater than that of croscarmellose, followed by the results of the disintegration time of ODT showing an increase in the use of crospovidone, and lower dissolution of crospovidone ODT than croscarmellose ODT. The high porosity of the superdisintegrant, when used to increase the disintegration rate of ODT, is undesirable for tablet hardness.

ODT Dissolution Results

Comparing the functionality of the disintegrant, it can be concluded that the disintegration is faster than tablets with croscarmellose sodium superdisintegrant compared to tablets containing crospovidone superdisintegrant. The observations described supporting the assumption that tablets with croscarmellose sodium disintegrate into smaller agglomerates and primary particles, which increases the contact surface to the dissolution medium resulting in faster drug dissolution. As described above, the presence of smaller particle agglomerates may be associated with the smaller primary particle size of croscarmellose sodium compared to crospovidone[11]. This is the same as what was stated by Gulsun et al., 2018 that whose research gave greater dissolution results, namely in ODT with croscarmellose sodium superdisintegrant, not in ODT with crospovidone superdisintegrant. However, according to research by Abd-El Bary et al., 2014 the results showed that the greater dissolution results were in ODT with crospovidone superdisintegrant than ODT with croscarmellose sodium superdisintegrant.

The results of the dissolution of the tablet are affected by the disintegration time of the tablet, if the tablet has a short disintegration time due to the entry of water into the drug particles so that the particles of the superdisintegrant will expand and then break, making the tablet disintegrate into fine particles, it will affect the release of the active substance in the dissolution medium which is faster and has an effect on the greater dissolution efficiency in the early minutes of ODT entering the dissolution medium.

Superdisintegrant Mechanism of Action

Croscarmellose sodium has a high swelling capacity with minimal gel formation resulting in rapid disintegration. Due to its fibrous structure, croscarmellose sodium particles also exhibit a hollow appearance. Unlike croscarmellose sodium which has a swelling mechanism in crospovidone, crospovidone uses a combination of swelling and wicking, namely the process of entering liquid by capillary action into microstructured cracks in the tablet to displace air. The crospovidone particles were found to be granular and highly porous which facilitates the entry

of liquid into the tablet and particles for rapid disintegration. Larger particles provide faster disintegration than smaller particles [8]. The mechanism of crospovidone is sustained, good swelling efficiency or high swelling pressure as the mechanism of crospovidone disintegration. Later, strain recovery was also proposed and validated as a disintegration mechanism of crospovidone[9]. The ODT depends on the nature of the superdisintegrant, the concentration in the formulation, and the source. Even if the superdisintegrant meets USP standards, there may be differences between manufacturers in terms of performance. This is not only limited to in-vitro studies but also continues at the time of disintegration in the human population [10].

Effective disintegration does not form swelling to enhance its disintegration, it is believed that the action of porosity and capillarity can promote disintegration. The porosity of the tablet allows the liquid to enter the tablet. When the tablet is inserted into a suitable medium, the medium will penetrate the tablet and fill the air voids in the particles so that the intramolecular bonds will break and break the tablet into small particles.

Table 2. Result of Physical Properties Affected By Superdisintegrant Croscarmellose Sodium and Crospovidone

Research	API	Superdisintegrant	Weight Uniformity (mg)	Size uniformity (thickness) (cm)	Hardness	Friability (%)	Disintegration Time (s)	Wetting Time(s)
Abd-El Bary *et al*., 2014	Olmesartan	Croscarmellose 5%	350.53 ± 0.71	0.3351	4.51 kg/cm^2	0.91	156±2.41	
		crospovidone5%	349.15 ± 1.64	0.3445	3.51 kg/cm^2	0.89	113±4.95	
Kim*etal*.,2013	Donepezil HCl	Crospovidone20 % Crospovidone10 % Croscarmellose 20% Croscarmellose 10%	281.3 ± 1.2	0.412	5.4±0.56kg/cm^2	0.87	10	
			280.7 ± 1.4	0.414	5.9±0.72kg/cm^2	0.62	15	
			279.7 ± 2.1	0.409	5.3±0.44kg/cm^2	0.53	70	
			280.9 ± 2.4	0.408	5.2±0.83kg/cm^2	0.76	78	

Gulsun *et al*.,2018	Terbutaline sulfate	Crospovidone 5%		0.271	173.03±7.34N	0.27	176	
		Croscarmellose 5%		0.257	212.58±5.61N	0.12	150	
Maheswarappa & Desai, 2011	Olanzapine	Crospovidone 2% Crospovidone 4% Crospovidone 6% Crospovidone 8% Croscarmellose 2% Croscarmellose 4% Croscarmellose 6% Croscarmellose 8%	52.75±0.60 50.61±0.52 51.96±0.86 47.26±1.55 52.64±1.23 50.27±0.97 51.46±0.65 49.07±0.88	0.224±0.06 0.225±0.07 0.221±0.02 0.222±0.06 0.223±0.02 0.220±0.05 0.222±0.04 0.221±0.01	28±0.26 N 25±0.24 N 26±0.49 N 27±0.48 N 27±0.54 N 29±0.26 N 30±0.75 N 32±0.37 N	0.284 0.290 0.287 0.285 0.275 0.267 0.261 0.259	28.00±2.00 25.12±2.08 24.48±1.15 24.32±1.00 35.38±0.58 30.12±1.00 33.41±2.52 34.10±1.53	32.12±1.02 29.23±2.08 28.52±1.15 28.12±1.00 39.51±0.58 35.21±1.00 38.48±2.52 40.53±1.53
S. Desai *et al*., 2016	Eliscarbazepine	Crospovidone 3% Crospovidone 5% Croscarmellose 3% Croscarmellose 5%	1205.41±1.85 1214.74±1.05 1186 ± 1.47 1206 ± 1.69	1,6 1,6 1,6 1,6	3.83 ± 0.21 3.66 ± 0.16 3.83 ± 0.20 3.83 ± 0.22	0.85 0.75 0.76 0.82	45.33 ± 3.51 24.66 ± 1.52 61.66 ± 2.51 69.33 ± 2.58	23 ± 2.47 21 ± 1.41 34 ± 1.41 37 ± 3.82

Table 3. Dissolution Results Affected By Superdisintegrant Croscarmellose Sodium and Crospovidone

Research	Year	API	Superdisintegrant	Result of Dissolution
A.Abd-El Bary,D. Louis, S. Sayed	2014	Olmesartan	Croscarmellose5% Crospovidone 5%	79.36 % (p = 0.001) 86.56 % (p = 0.000)
Tugba Gulsuna, Yagmur Akdag Cayli , Nihan Izat, Meltem Cetin, Levent Oner, Selma Sahin	2018	Terbutaline Sulfat	Crospovidone 5% Croscarmellose 5%	DE 95% = 45min DE 95% = 30min
Manjunatha Kattalagere Maheswarappa, Priyankabahen Dineshchandra Desai	2011	Olanzapine	Crospovidone 2% Crospovidone 4% Crospovidone 6% Crospovidone 8% Croscarmellose 2% Croscarmellose 4% Croscarmellose 6% Croscarmellose 8%	Q30 = 97 Q30 = 98 Q30 = 98 Q30 = 97 Q30 = 96 Q30 = 97 Q30 = 96 Q30 = 97

Table 4. Results of Superdisintegrant Mechanism Affected by Croscarmellose Sodium and Crospovidone Superdisintegrant

Research	Year	Superdisintegrant used	Mechanism
Jong-Il Kima,1, Sang-Min Choa,b,1, Jing-Hao Cui, Qing-Ri Caoc, Euichaul Oh, Beom-JinLee	2013	Crospovidone and croscarmellose sodium	Formulas using crospovidone showed rapid disintegration due to rapid capillary activity and a low tendency to form gels.

Tugba Gulsuna, Yagmur Akdag Cayli , Nihan Izat, Meltem Cetin, Levent Oner, Selma Sahin	2018	Crospovidone and croscarmellose sodium	The natural pores of croscarmellose sodium make it easy for water to enter and make for a good wicking process. and cross-linking provides outstanding swelling properties by making the superdisintegrant hydrophilic and high absorption. This increase in formulation volume leads to faster disintegration as a result of the increase in hydrostatic pressure in thein ODT.
Andreas Gryczke, Silke Schminke, Mohammed Maniruzzaman, Julien Beck, Dennis Douroumis	2011	Crospovidone and croscarmellose sodium	Swelling is not the primary disintegration mechanism for crospovidone and can rapidly absorb water (wicking), due to its porous particle size morphology, and results in rapid volume expansion by increasing hydrostatic pressure leading to tablet disintegration. On the other hand, croscarmellose has a non-porous fiber particle structure that swells at a speed
Rajendar K Mittapalli, Sha Qhattal, H. S., Lockman, P. R., & Yamsani, M.R.	2010	crospovidone	This study indicates that the tablets disintegrate orally depending on the nature of the superdisintegrant, the concentration in the formulation, and the source. Even if the superdisintegrant meets USP standards, there may be differences between manufacturers in terms of performance. This is not only limited to in-vitro studies but also continues at the time of disintegration in the human population.

CONCLUSION:

The physical properties of ODT with differences in superdisintegrant croscarmellose sodium and crospovidone did not experience large differences in weight balance, size uniformity, but had significant differences in tablet hardness, friability, and disintegration time. The smallest friability is owned by crospovidone. The results of the dissolution of ODT depended on the disintegration time of ODT and the superdisintegrant crospovidone. Most researchers said that the dissolution value with the highest dissolution was obtained by ODT with crospovidone although there were researchers who said that croscarmellose could obtain a higher dissolution value than crospovidone. The mechanism of the superdisintegrant croscarmellose sodium is by swelling and the mechanism of crospovidone is by liquid by capillary action into the microstructured crevices in the tablet to displace air then swelling and ending with strain recovery.

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Abbreviations

ODT: Orally Disintegrating Tablet; DC: Direct Compression.

REFERENCES

1. Almukainzi, M., Araujo, G. L. B., & Löbenberg, R. (2019). Orally disintegrating dosage forms. Journal of Pharmaceutical Investigation, 49(2), 229–243. https://doi.org/10.1007/s40005-018-0408-2.
2. Zhang, Y., Wrzesinski, A., Moses, M., & Bertrand, H. (2010). Comparison of superdisintegrants in orally disintegrating tablets. Pharmaceutical Technology, 34(7), 54–61.
3. Bhardwaj, V., Bansal, M., dan Sharma, P.K., 2010. Formulation and Evaluation of Fast Dissolving Tablets of Amlodipine Besylate Using Different Super Disintegrants and Camphor as Sublimating Agent. Am.-Eurasian J. Sci Res, 5: 264–269.
4. Kulkarni, S.V., Kumar, R., Patel, N., Rao, S., Ramesh, B., dan Kumar, A., 2011. Formulation and Evaluation of Fast Disintegrating Meloxicam Tablets and Its Comparison with Marketed Product. Int J Pharm Pharm Sci, 3: 91–94.
5. Prajapati, B.G. dan Patel, S.N., 2010. Formulation, Evaluation, and Optimization of Orally Disintegrating Tablet of Cinnarizine. e-Journal of Science & Technology, 5: 9–21.
6. Kumar, A., & Saharan, V. A. (2017). Salbutamol Sülfatın Oral DağılanTabletlerininFormülasyonuveDeğerlendirilmesi: SüperDağıtıcılarınFarklıOranlarınınKarşılaştırmalıÇalışması. Turkish Journal of Pharmaceutical Sciences, 14(1), 40–48. https://doi.org/10.4274/tjps.74946.
7. Pabari, R. M., &Ramtoola, Z. (2012). Effect of a disintegration mechanism on wetting, water absorption, and disintegration time of orodispersible tablets. Journal of Young Pharmacists, 4(3), 157–163. https://doi.org/10.4103/0975-1483.100021.
8. Gandhi, L., & Akhtar, S. (2019). Comparative study on effect of natural and synthetic superdisintegrants in

the formulation of orodispersible tablets. Journal of Drug Delivery and Therapeutics, 9(2), 507–513. https://doi.org/10.22270/jddt.v9i2.2404.
9. Desai, P. M., Liew, C. V., & Heng, P. W. S. (2016). Review of Disintegrants and the Disintegration Phenomena. Journal of Pharmaceutical Sciences, 105(9), 2545–2555. https://doi.org/10.1016/j.xphs.2015.12.019.
10. Mittapalli, R. K., Sha Qhattal, H. S., Lockman, P. R., &Yamsani, M.R. (2010). Varying efficacy of superdisintegrants in orally disintegrating tablets among different manufacturers. Pharmazie, 65(11), 805–810. https://doi.org/10.1691/ph.2010.0162.
11. Berkenkemper, S., Keizer, H. Lou, Lindenberg, M., Szepes, A., &Kleinebudde, P. (2020). Functionality of disintegrants with different mechanisms after roll compaction. International Journal of Pharmaceutics, 584, 119434.https://doi.org/10.1016/j.ijpharm.2020.119434.
12. Kande, K. V., Kotak, D. J., Degani, M. S., Kirsanov, D., Legin, A., & Devarajan, P. V. (2017). Microwave-Assisted Development of Orally Disintegrating Tablets by Direct Compression. AAPS PharmSciTech,18(6), 2055–2066. https://doi.org/10.1208/s12249-016-0683-z.
13. Kumar, A., & Saharan, V. A. (2017). Salbutamol Sülfatın Oral DağılanTabletlerininFormülasyonuveDeğerlendirilmesi: SüperDağıtıcılarınFarklıOranlarınınKarşılaştırmalıÇalışması. Turkish Journal of Pharmaceutical Sciences, 14(1), 40–48. https://doi.org/10.4274/tjps.74946.
14. Allen, L., V., Popovisch, N.G. dan Ansel, H.C., 2011, Ansel's Dossage Forms and Drug Delivery Systems, 9th Ed., Lippinkott Williams and Wilkins, Philadelphia
15. Ashish, P., Harsoliya, M.S., Pathan, J.K, dan Shruti, S., 2011. A Review Formulation of Mouth Dissolving Tablet. Int J Pharm Clin Sci, 1: 1-8..
16. Aulton, M.E. dan Taylor, K.M.G., 2007. Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 3e, 3 edition. ed. Churchill Livingstone, Edinburgh ; New York.
17. Babu, G., Mayuri, G., & Chemistry, P. (2014). FORMULATION AND EVALUATION OF RIFAMPICIN FAST. 3(12), 675–691
18. Bestari, A. N., Sulaiman, T. N. S., &Rohman, A. (2016). Formulasi Orally Disintegration Tablet (Odt). MajalahFarmaseutik, 12(2), 453–465.
19. Desai, S., Poddar, A., & Sawant, K. (2016). Formulation of cyclodextrin inclusion complex-based orally disintegrating tablet of eslicarbazepine acetate for improved oral bioavailability. Materials Science and Engineering C, 58, 826–834. https://doi.org/10.1016/j.msec.2015.09.019.
20. Essa, E., Zin Eldin, E. E., Abouzeid, A. F., & Essa, E. A. (2019). Formulation and Evaluation of Mouth Dispersible Tablets of Simvastatin Using Novel Excipients. European Journal of Biomedical AND Pharmaceutical Sciences, 6(6), 532–541. Retrieved from https://www.researchgate.net/publication/334122203.
21. FB, A., & T, U. (2015). Orally Disintegrating Tablets: A Short Review. Journal of Pharmaceutics and Drug Development, 3(3). https://doi.org/10.15744/2348-9782.3.303.
22. Gandhi, L., & Akhtar, S. (2019). Comparative study on effect of natural and synthetic superdisintegrants in the formulation of orodispersible tablets. Journal of Drug Delivery and Therapeutics, 9(2), 507–513. https://doi.org/10.22270/jddt.v9i2.2404.
23. Jain, C.P. dan Naruka, P.S., 2009, 'Formulation and Evaluation of Fast Dissolving Tablets of Valsartan', International Journal of Pharmacy and Pharmaceutical Sciences, 1, 219-221.
24. Kayastha, R.R., Bhat, N.M., Phatak, N.L., Chadasma, A.R.H. and Darediya, A.A.,2011, Formulation and Evaluation of Fast Disintegrating Tablet of Diclofenac Sodium, International Journal of Pharmaceutical Research and Development, 3 (6): 17-22.
25. Lv, H. X., Zhang, Z. H., Hui-Jiang, Waddad, A. Y., & Zhou, J. P. (2012). Preparation, physicochemical characteristics and bioavailability studies of an atorvastatin hydroxypropyl-β- cyclodextrin complex. Pharmazie, 67(1), 46–53. https://doi.org/10.1691/ph.2012.1082.
26. Manjunath, P. N., Satish, C. S., Vasanti, S., Preetham, A. C., &Naidu,R. (2017). Formulation and evaluation of simvastatin gastroretentive drug delivery system. International Journal of Applied Pharmaceutics, 9(3), 55–60. https://doi.org/10.22159/ijap.2017v9i3.18763.
27. Maheswarappa, M. K., & Desai, P. D. (2011). Design and in-vitro evaluation of mouth dissolving tablets of olanzapine. Asian Journal of Pharmaceutics, 5(2), 107–113. https://doi.org/10.4103/0973-

8398.84551.
28. Mohamed, M.B., Talari, M.K., Tripathy, M. and Majeed, A.B.A., 2012, Pharmaceutical Applications of Crospovidone: A Review, International Journal of Drug Formulation and Research, 3 (1): 13-28.
29. Olah, I., Lasher, J., Regdon, G., Pintye-hodi, K., Baki, G., &Sovany,T. (2019). Journal of Drug Delivery Science and Technology Evaluating superdisintegrants for their performance in orally disintegrating tablets containing lysozyme enzyme. Journal of Drug Delivery Science and Technology, 49(September 2018), 396–404. https://doi.org/10.1016/j.jddst.2018.12.012.
30. Saurabh, S., Rajni, B., Baibhav, J., Rana, A.C., dan Vikas, S., 2012. Mouth Dissolving Tablet : A Future Compaction. International Research Journal of Pharmacy, 3: 98-109.
31. Savjani, K. T., Gajjar, A. K., &Savjani, J. K. (2012). Drug Solubility: Importance and Enhancement Techniques. ISRN Pharmaceutics, 2012(100 mL), 1–10. https://doi.org/10.5402/2012/195727.
32. Sheshala, R., Khan, N., Chitneni, M., &Darwis, Y. (2011). Formulation and in vivo evaluation of ondansetron orally disintegrating tablets using different superdisintegrants. Archives of Pharmacal Research, 34(11), 1945–1956. https://doi.org/10.1007/s12272- 011-1115-y.
33. Snyder, H. (2019). Literature review as a research methodology: An overview and guidelines. Journal of Business Research, 104(March), 333–339. https://doi.org/10.1016/j.jbusres.2019.07.039.
34. Zishan, M., Amir, M., Ahmad, Z., Hussain, M. W., Singh, P., & Idris, S. (2017). Review on Application and Factor Affecting and Official Monographs in Dissolution Process. Journal of Drug Delivery and Therapeutics, 7(3), 19–27. https://doi.org/10.22270/jddt.v7i3.1422.

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