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A Review of Natural vs. Synthetic Disintegrants: Comparative Study and Future Perspectives

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KEYWORDS

Natural superdisintegrants, Synthetic superdisintegrants, Comparative analysis, Oro dispersible tablets.

ABSTRACT:

Introduction: This article compares natural and synthetic superdisintegrants used in tablet and capsule formulations for quick dissolution of tablets. Superdisintegrants like mucilage, croscarmellose, sodium starch glycolate, and poly vinyl pyrrolidone increase mechanical strength and dissolution efficiency at lower concentrations. Oro-dispersible technology has gained attention due to its rapid disintegration time, facilitating swallowing and reducing choking risks. The review evaluates performance, compatibility with API, cost effectiveness, biocompatibility, regulatory considerations, toxicity, safety, and quality standards. The focus is on performance, compatibility, cost effectiveness, biocompatibility, regulatory considerations, toxicity, safety, and quality standards

Objectives: This review aims to provide a comprehensive comparison of natural and synthetic disintegrants in pharmaceutical formulations. It examines their effectiveness, mechanism of action, compatibility with different drug types, and impact on formulation properties. Additionally, the review discusses the current trends, challenges, and future perspectives in the use of disintegrants, providing valuable insights for researchers and pharmaceutical professionals.

Conclusions: The study compares synthetic and natural superdisintegrants in drug formulations, revealing their unique functions and characteristics. Natural superdisintegrants, sourced from plants, offer biocompatibility, biodegradability, and sustainability, making them ideal for quick dissolution. However, they have drawbacks like allergenicity and batch variability. Synthetic superdisintegrants, on the other hand, provide consistency, homogeneity, and high disintegration efficiency, making them suitable for formulations with poorly soluble active components. Despite their advantages, formulation development must consider potential toxicity and environmental effects. The study offers hope for further advancements in pharmaceutical formulation technology.

1. Introduction

Disintegrants are excipients used in the formulation of tablets and capsules that aid in the dissolution of tablets into smaller, more surface-area particles, thereby promoting faster drug release. Excipients known as superdisintegrants are added to formulations for rapid drug release, which makes tablets dissolve more quickly and improves absorption. They are more effective intragranular, have a higher disintegrating capacity, exhibit superior activity, and are effective at low concentrations *(1)*. Small amounts of disintegrants in solid dosage forms have an impact on tablet binders and compression forces. Instant tablets contain natural disintegrants such as karaya gum, psyllium husk, agar, and modified starch. Because of benefits like ease of use, dose accuracy, self-medication, flexibility, and patient compliance, oral solid formulations are recommended. Fast Dissolving Tablets are solid dosage forms that increase the bioavailability of drugs by dissolving in

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saliva *(2)*. Oral disintegrating tablets are solid dosage forms that can be swallowed without water because they dissolve in saliva. Oro-dispersible technology has garnered attention in the last ten years due to its rapid disintegration time. These tablets dissolve into a smooth paste or liquid, which facilitates swallowing and lowers the chance of choking *(3)*. After examining the behaviour of the wetting and disintegration times in the oral cavity using surface free energy, we discovered that a molecule needs a high polar component to wet more quickly. Agents that satisfy these unique requirements are called as superdisintegrants *(4)*.

Factor on disintegration

1. Percentage of disintegrants contained in the mixture
2. Proportion of disintegrants used
3. compatibility with additional excipients.
4. Presence of surfactant.
5. Hardness of the tablets.
6. Nature of Drug substances.
7. Mixing and types of addition *(4)*.

Superdisintegrants are used to facilitate delivery methods and offer instant tablet disintegration. Examples of these include mucilage, croscarmellose, sodium starch glycolate, and poly vinyl pyrrolidone. When these materials come into contact with water, they help tablets and capsules dissolve more quickly by breaking them up and dispersing them into smaller pieces. Superdisintegrants increase disintegration and dissolution by promoting wettability and dispersibility. For the creation of tablet formulations, disintegrants must be carefully chosen and consistent. Superdisintegrants have higher mechanical strength and disintegration efficiency at lower concentrations, making them more effective *(5)*.

Advantages of Superdisintegrants:

- They help in fast disintegration
- They offer reduced friability and increased tablet breaking power.
- Quick disintegration occurs through swelling without gelling, offering a smooth texture.
- There are two particle sizes available, with smaller particles offering a smoother mouthfeel.
- Greater intragranular efficacy.
- Some are anionic and may somewhat bind to cationic medications in vitro.
- Biodegradable *(6)*.

Disadvantages of Superdisintegrants:

- Expensive.
- Time-consuming and delicate.
- Greater sensitivity and hygroscopicity *(7)*.

Ideal Properties of Superdisintegrants:

- It should to result in quick breakdown.
- It should to have acceptable flow characteristics and moulding.
- Its compressibility index, hydration capacity, and particle size should all be good.
- It should to be poorly soluble in water.
- It should to yield less friable, compact tablets.
- Nontoxic and should have good mouth feel *(8)*.

Disintegration Phenomena:

For the majority of solid dosage forms, the disintegration process is essential to guaranteeing, if not optimizing, the API bioavailability. The initial stage of releasing the API from the dosage form is the wetting and subsequent breakdown of the powder compact into the tablets, with the exception of controlled diffusion matrix systems. To ensure consistent clinical performance of the dosage form, total disintegration of the tablet during exposure to the dissolving media is crucial. Without disintegration, only the API near the tablet's surface would be able to dissolve, making it repeatable *(9)*.

Comparative analysis:

1. Performances:

Analysing a variety of factors, including mechanical characteristics, disintegration time, dissolution rate, compatibility with active pharmaceutical ingredients (APIs), cost-effectiveness, and regulatory considerations, is necessary when comparing the performance studies of natural and synthetic superdisintegrants. The potential performance of each kind of superdisintegrants is broken down as follows.

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- **Disintegration Time:**

Natural Superdisintegrants: Natural superdisintegrants with quick water absorption and swelling, such as starches, gums (such as guar gum and locust bean gum), and modified starches, may have good disintegration capabilities.

Synthetic Superdisintegrants: Synthetic superdisintegrants such as croscarmellose sodium and crospovidone (cross-linked polyvinylpyrrolidone) tend to disintegrate faster than their natural counterparts because of their greater capacity to expand and absorb water *(9)*.

- **Dissolution Rate:**

Natural Superdisintegrants: The effect of natural superdisintegrants on dissolving rates might vary depending on the source and modification. Some may be less successful than others in terms of improving dissolving by quickly spreading the dose form.

Synthetic Superdisintegrants: Synthetic superdisintegrants have a high swelling capacity and good particle dispersion, which make them effective at accelerating the rate of dissolution *(3)*.

- **Mechanical Properties:**

Natural Superdisintegrants: When it comes to giving tablets mechanical strength which might be essential for preserving tablet integrity during handling and transit natural superdisintegrants might provide some advantages.

Synthetic Superdisintegrants: In order to ensure the toughness and stability of the dosage form, synthetic superdisintegrants may provide superior mechanical qualities in terms of tablet hardness and friability *(10)*.

- **Compatibilities study with API:**

Natural Superdisintegrants: Natural superdisintegrants are usually considered to be more compatible with a wider range of APIs due to their increased biocompatibility and less likelihood of interaction.

Synthetic Superdisintegrants: Synthetic superdisintegrants may exhibit good compatibility with APIs but could potentially interact with certain sensitive drugs, necessitating careful formulation considerations *(11)*.

2. Cost effectiveness:

Natural Superdisintegrants: Natural superdisintegrants can be less expensive than their synthetic equivalents, particularly if they can be found in large quantities and locally.

Synthetic Superdisintegrants: Synthetic superdisintegrants might cost more due to the costs involved in the manufacturing process and the procurement of raw ingredients *(12)*.

3. Regulatory Consideration:

Natural Superdisintegrants: Depending on the region, obtaining regulatory authorization for some natural superdisintegrants may be simpler due to their perceived safety and natural nature.

Synthetic Superdisintegrants: More thorough safety assessments and regulatory paperwork may be necessary for synthetic superdisintegrants, particularly in the case of innovative formulations *(13)*.

4. Biocompatibility:

Origin and composition:

Natural Superdisintegrants: Natural superdisintegrants are mostly proteins or polysaccharides derived from plant or animal sources. Starches, gums (such as locust bean gum and guar gum), and modified celluloses are a few examples. Because these materials are often well-tolerated and resemble compounds found in food, they are frequently biocompatible with the human body *(14)*.

Synthetic Superdisintegrants: Chemically produced substances such as crospovidone (cross-linked polyvinylpyrrolidone, or PVP) and croscarmellose sodium (cross-linked sodium carboxymethylcellulose) are examples of synthetic superdisintegrants. Even if they are made to have particular qualities that aid in disintegration, their artificial origin could make them less biocompatible *(15)*.

5. Toxicity:

Natural Superdisintegrants: Natural superdisintegrants are usually seen as less hazardous because they originate from natural sources. Notwithstanding the use of stringent quality control protocols, it is possible for contaminants or impurities present in raw materials to pose a risk.

Synthetic Superdisintegrants: The potential toxicity of synthetic superdisintegrants can vary based on their chemical structure and any added contaminants during manufacture. Nonetheless, a great deal of testing has been done on those authorized for use as pharmaceuticals to guarantee their safety within predetermined bounds *(16)*.

6. Biological Interaction:

Natural Superdisintegrants: The body often tolerates natural superdisintegrants well, and they could even offer extra health advantages like increased dietary fiber or prebiotic effects. They are less likely to interact negatively with biological systems or produce unfavourable effects.

Synthetic Superdisintegrants: Synthetic superdisintegrants may act differently in biological systems due to their synthetic nature. Questions may arise regarding interactions or long-term effects with specific patient populations, even though many have been shown to be biocompatible *(17)*.

7. Biodegradability:

Natural Superdisintegrants: Natural superdisintegrants frequently decompose into safe components in the body or environment through biodegradation. From the standpoints of biocompatibility and the environment, this feature is preferred.

Synthetic Superdisintegrants: The chemical structure of synthetic superdisintegrants determines whether or not they can break down naturally. For improved biocompatibility and less environmental effect, biodegradable synthetic polymers are recommended *(18)*.

8. Clinical Studies:

Natural Superdisintegrants: There is a long history of safe usage of natural superdisintegrants in pharmaceutical formulations. Their minimal frequency of adverse effects and biocompatibility have been proven through clinical investigations.

Synthetic Superdisintegrants: In clinical settings, synthetic superdisintegrants have also been thoroughly investigated, and the majority of formulations have demonstrated high biocompatibility. Rare reports of intolerances or allergic responses have been made, though *(19)*.

9. Cost consideration:

Raw Material:

Natural Superdisintegrants: Natural superdisintegrants are frequently made from plant or animal sources, and the price of these resources varies according to availability, harvesting techniques, and location. Certain natural resources could be cheap and plentiful, while others might cost more because of things like cultivation costs or seasonal differences.

Synthetic Superdisintegrants: Chemically manufactured synthetic superdisintegrants are expensive raw materials because of the expense of reagents, starting ingredients, and synthesis procedures. Based on variables including chemical complexity, purity standards, and production volume, these expenses may differ *(20)*.

10. Production Process:

Natural Superdisintegrants: The extraction, purification, and modification techniques that may be included in the production processes for natural superdisintegrants can have an effect on the final cost. Depending on the source material and the intended superdisintegrants qualities, these procedures might vary in complexity.

Synthetic Superdisintegrants: Chemical synthesis techniques are used in the production of synthetic superdisintegrants, necessitating the use of specific reagents, equipment, and knowledge. Synthetic processes may frequently be scaled up and adjusted for efficiency, which can eventually lower manufacturing costs even if the initial setup costs may be greater *(21)*.

11. Regulatory Requirements:

Natural Superdisintegrants: More thorough safety assessments and regulatory paperwork may be needed for synthetic superdisintegrants, particularly when it comes to new substances. This may result in higher expenses for regulatory compliance, especially when it comes to getting permissions and keeping up with changing requirements.

Synthetic Superdisintegrants: More thorough safety assessments and regulatory paperwork may be needed for synthetic superdisintegrants, particularly when it comes to new substances. This may result in higher expenses for regulatory compliance, especially when it comes to getting permissions and keeping up with changing requirements *(13)*.

12. Formulation Economics:

Natural Superdisintegrants: A formulation's total cost-benefit analysis may be impacted by a number of variables, including market demand, performance standards, and dosage form features. While there may occasionally be financial benefits to using natural superdisintegrants, other factors to take into account include formulation stability, effectiveness, and patient acceptability.

Synthetic Superdisintegrants: Synthetic superdisintegrants have constant properties and predictable performance, making them useful in formulation economics since they operate well in a range of dosage forms. These advantages can contribute to the total cost-effectiveness of formulation development and production, even though the initial cost of the components may be higher *(22)*.

13. Cost Benefits:

Natural Superdisintegrants: Natural superdisintegrants should have their formulation performance, regulatory compliance, supply chain stability, and market dynamics taken into account when doing a cost-benefit analysis. Natural superdisintegrants could be more affordable in some circumstances, but choosing them should be based on a thorough evaluation of these variables.

Synthetic Superdisintegrants: Analyses of the costs and benefits of synthetic superdisintegrants should also take long-term economic sustainability, industrial scalability, regulatory compliance, and formulation performance into account. Although synthetic superdisintegrants may initially cost more, their benefits in terms of performance and formulation optimization could make the investment worthwhile *(22)*.

14. Regulatory Aspects:

Regulatory Approval Process:

Natural Superdisintegrants: Natural superdisintegrants may have an edge in people's sense of safety and familiarity since they originate from natural sources. However, several regulatory clearance procedures can be applicable based on the specific natural resource and its planned use. Generally speaking, using natural superdisintegrants in pharmaceutical formulations may need regulatory clearance; this approval necessitates evidence of the materials' safety, purity, and efficacy.

Synthetic Superdisintegrants: Synthetic superdisintegrants are subject to rigorous regulatory clearance procedures due to their manufacturing process, which involves chemicals. A product typically has to show its safety, efficacy, and quality through preclinical and clinical research, as well as comprehensive documentation of the production process and control methods, in order to be approved. Synthetic superdisintegrants are governed by regulatory bodies such as the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) *(16)*.

15. Safety Consideration:

Natural Superdisintegrants: Natural superdisintegrants are generally seen as safer because they are derived from nature. There are still valid safety concerns about the potential for impurities, allergenicity, and interactions with other formulation constituents. To support regulatory clearance, toxicological studies and further safety proof may be required.

Synthetic Superdisintegrants: In depth safety analyses of synthetic superdisintegrants are necessary to determine any possible hazards related to their manufacture and chemical makeup. In order to determine

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acceptable exposure levels, this may involve investigations on genotoxicity, carcinogenicity, and other safety factors. Regulations must be met for safety data to be approved *(23)*.

16. Documentation Requirements:

Natural Superdisintegrants: Documentation requirements for natural superdisintegrants may include proof of identity, purity, and quality, as well as data on safety and efficacy. This typically involves providing information on the source material, extraction methods, characterization, and testing to ensure compliance with regulatory standards.

Synthetic Superdisintegrants: Synthetic superdisintegrants need substantial documentation that covers everything from synthesis pathways to impurity profiles, analytical techniques, and quality control procedures. To prove uniformity, purity, and safety throughout the production process, this data is required.

17. Quality Standards:

Natural Superdisintegrants: Natural superdisintegrants may have different quality criteria according on the regulatory jurisdiction, particular monographs, and compendial needs. It could be necessary to adhere to pharmacopeial standards like the USP (United States Pharmacopeia) or EP (European Pharmacopoeia).

Synthetic Superdisintegrants: Strict quality requirements set by regulatory bodies must be met by synthetic superdisintegrants. This involves following pharmacopeial criteria for purity, identity, and potency as well as adhering to Good Manufacturing Practices (GMP) for medicines *(24)*.

18. Global Regulatory Harmonization:

Natural Superdisintegrants: Regulations pertaining to natural superdisintegrants may be difficult to harmonize since various areas have distinct botanical sources, extraction techniques, and historic applications. There are continuous attempts to create worldwide rules and standards for botanicals, albeit they might not be as extensive as those for synthetic substances.

Synthetic Superdisintegrants: Synthetic superdisintegrants benefit from a more homogenous regulatory environment due to their chemical nature. International harmonization programs such as the recommendations of the ICH (International Council for Harmonization of Technical criteria for Pharmaceuticals for Human Use) facilitate the alignment of regulatory requirements across many locales *(25)*.

Conclusion:

A comparative analysis of synthetic and natural superdisintegrants illuminates the many functions and characteristics of these essential excipients in drug formulations. A detailed examination reveals that natural and synthetic superdisintegrants have different benefits and drawbacks, providing formulators in the pharmaceutical industry with a range of choices to customize formulations based on particular needs.

Natural superdisintegrants are sourced from plants and provide biocompatibility, biodegradability, and sustainability. This makes them perfect for quick dissolving and disintegration in the production of pharmaceuticals. Although they are inexpensive and easily accessible, they have drawbacks such allergenicity and batch variability. Conversely, synthetic superdisintegrants are appropriate for a range of production circumstances because they provide consistency, homogeneity, and high disintegration efficiency. They work especially well in formulations that contain pharmaceutical active components that are poorly soluble or dissolve slowly. Nevertheless, during formulation development, issues about possible toxicity and environmental effect must be carefully taken into account.

When selecting natural and synthetic superdisintegrants, formulators must carefully take into account elements such formulation needs, performance qualities, regulatory concerns, and cost-effectiveness. The study of synthetic and natural superdisintegrants offers hope for more developments in the field of pharmaceutical formulation technology.

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References

1. H, V. R. C.; Lakshmi, P. K.; Bhaskaran, S.; College, G. P.; Pradesh, A. Comparative review of functionality and performance of the natural and synthetic superdisintegrants. *Journal of Pharmaceutical Research* **2011**, *10*(4), 130–143.
2. Kanaujiya, S.; Kumar, S. Comparative study of natural disintegrants, selection criteria for superdisintegrants. *World Journal of Pharmaceutical Sciences* **2022**, *10*(05), 56–63. doi:10.54037/wjps.2022.100503.
3. Dhurjad, L.; Sagle, D.; Deshmukh, A.; Narkhede, M. Asian Journal of Pharmaceutical Research and Development. *Asian Journal of Pharmaceutical Research and Development* **2020**, *8*(3), 92–96.
4. Dhoot, S. N.; Shahane, S. P.; Gaikwad, K. P.; Joge, L. P.; Ambhore, J. P. Superdisintegrants in Orally Administered Products of Pharmaceuticals : A Review. *International Journal of Trend in Scientific Research and Development (IJTSRD)* **2022**, *6*(4), 1482–1486.
5. Shobana, K.; Subramanian, L.; Rajesh, D. M.; Sivaranjani, K. A Review on Superdisintegrants. *International Journal of Pharmaceutical Sciences Review and Research* **2020**, *65*(2), 149–154. doi:10.47583/ijpsrr.2020.v65i02.023.
6. Pahwa, R.; Gupta, N. Superdisintegrants in the Development of Orally Disintegrating Tablets: A Review. *International Journal of Pharmaceutical Sciences and Research* **2011**, *2*(11), 2767–2780.
7. Bhowmik, D. A comprehensive review on superdisintegrants used in orodispersible tablets. *Indian Journal of Research in Pharmacy and Biotechnology* **2014**, No. May, 2320–3471.
8. Omidian, H.; Park, K. Swelling agents and devices in oral drug delivery. *Journal of Drug Delivery Science and Technology* **2008**, *18*(2), 83–93. doi:10.1016/S1773-2247(08)50016-5.
9. Article, R. International Journal Of Pharma Professional ' s Research technologies influencing rapidly disintegrating drug delivery. *International Journal Of Pharma Professional's Research* **2014**, *1*(November), 1–56.
10. Islam, A.; Haider, S. S.; Reza, M. S. Formulation and evaluation of orodispersible tablet of domperidone. *Dhaka University Journal of Pharmaceutical Sciences* **2011**, *10*(2), 117–122. doi:10.3329/dujps.v10i2.11791.
11. Chakraborty, S.; Khandai, M.; Singh, S.; Ch. Patra, N. Comparative study on effect of natural and synthetic superdisintegrants in the formulation of fast dissolving tablets. *International Journal of Green Pharmacy* **2008**, *2*(1), 22. doi:10.4103/0973-8258.39158.
12. Madhulika, G. S. S. V; Kuber, B. R. A review on natural and synthetic polymers employed in the formulation of oral disintegrating tablets. **2019**, *9*, 652–658.
13. Alam, M. T.; Parvez, N.; Sharma, P. K. FDA-Approved Natural Polymers for Fast Dissolving Tablets. *Journal of Pharmaceutics* **2014**, *2014*, 1–6. doi:10.1155/2014/952970.
14. Panda, S.; Sethi, G.; Madhusrota, P. Superdisintegrants from Natural Origin: An Updated Review. *International Journal of Pharmacognosy and Phytochemical Research* **2020**, *12*(1), 1–15. doi:10.25258/phyto.12.1.1.
15. Dalimbe, A.; Pawar, J.; Bhosale, S.; Shinde, N.; Tupe, R. A review: Novel Superdisintegrants. *International Journal of Creative Research Thoughts* **2021**, *9*(7), 31–45.
16. Pradhan, D.; Chakraborty, P.; Halder, S.; Bagchi, A. An overview on FDA-approved natural super disintegrants efficacy in a fast dissolving drug delivery system. *Journal of Applied Pharmaceutical Research* **2021**, *9*(3), 1–7. doi:10.18231/j.joapr.2021.v9.i3.1-7.
17. Pandey, J.; Vimal, K. S.; Shashi, T.; Raja, W. Asian Journal of Research in Biological and. *Asian j. pharm. biol res.* **2019**, *7*(3), 65–70.
18. Soni, A.; Raju, L. An Updated Review on Natural and Synthetic Superdisintegrants. *World Journal of Pharmacological Research and Technology* **2015**, *3*(January 2015), 14–20.
19. Swarnalatha, N.; Maravajhala, V. Formulation, in vitro, and in vivo evaluation of taste-masked oral disintegrating tablets of fexofenadine hydrochloride using semisynthetic and natural superdisintegrants. *International Journal of Applied Pharmaceutics* **2021**, *13*(5), 99–108. doi:10.22159/ijap.2021v13i5.41558.
20. Dave, V. S.; Saoji, S. D.; Raut, N. A.; Haware, R. V. Excipient variability and its impact on dosage form functionality. *Journal of Pharmaceutical Sciences*

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2015, *104*(3), 906–915. doi:10.1002/jps.24299.

21. Pawar, C. V; Mutha, S. S.; Bhise, S. V; Borawake, P. D. Pawar, C., et al. "Formulation and evaluation of mouth dissolving tablet of meloxicam using natural superdisintegrants." Asian J Pharm Clin Res 13.2 (2020): 197-203.*13*, **2020**. (2).
22. Yoon, C. 済無No Title No Title No Title. *Paper Knowledge . Toward a Media History of Documents* **2014**, *15*(1), 120–130. doi:10.13040/IJPSR.0975-8232.15(1).120-30.
23. Domokos, A.; Nagy, B.; Szilágyi, B.; Marosi, G.; Nagy, Z. K. Integrated Continuous Pharmaceutical Technologies - A Review. *Organic Process Research and Development* **2021**, *25*(4), 721–739. doi:10.1021/acs.oprd.0c00504.
24. Pradesh, U. FDA-Approved Natural Superdisintegrants and their comparision in formulation of mouth Dissolving Tablet. **2023**, *8*(2), 339–344.
25. Kar, M.; Chourasiya, Y.; Maheshwari, R.; Tekade, R. K. *Current Developments in Excipient Science: Implication of Quantitative Selection of Each Excipient in Product Development*; Elsevier Inc., 2018. doi:10.1016/B978-0-12-817909-3.00002-9.