# EXPLORING THE POTENTIAL OF MANNITOL IN THE DEVELOPMENT OF A NOVEL CO-PROCESSED EXCIPIENT

**MIR ASHFAQ ALI MIR MUSHTAQ ALI**
Research Scholar
Shri JJT University,
Rajasthan.

**Dr.DISHA**
Professor
Shri JJT University,
Rajasthan.

**Dr. SHAHZAD AHMED ABDUL RAZZAQUE**
Professor
JMCT INSTITUTE OF PHARMACY, WADALA ROAD NASHIK

## Abstract

*Mannitol is FDA-approved for the reduction of intracranial pressure associated with cerebral edema and the reduction of intraocular pressure. Mannitol is also administered via inhalation as adjunctive therapy in cystic fibrosis. Its dehydrating properties at the cellular and tissue levels increase plasma osmotic pressure, which is studied for its potential to reduce ICP through osmotic diuresis. While clinical guidelines support mannitol use in these cases, the best approach for its application continues to be debated. Mannitol has many side-effects including initial volume expansion (increasing the risk of heart failure), subsequent hypovolaemia and hypotension, metabolic acidosis, and electrolyte imbalance, including hypernatraemia and hypokalaemia. Mannitol's advantages as an excipient are reasonably well-explored at this point, but less well-known is its capacity to deliver therapeutic benefits of its own. Across multiple scientific and clinical studies, mannitol has been shown to impart pharmaceutic effects.*

*Keywords-Excipient, Mannitol*

## Introduction

The demands on the functionality of excipients are increasing day by day because of the emergence of high-speed tableting machines and the use of direct compression methods for tableting. Co-processing plays an important role in the development of a stable excipient with multifunctional activity. The combinations of one or two natural or synthetic polymers have been explored widely to develop novel stable co-processed excipients. In recent years, the co-processing of plant-based components has proved to be a boon for large no of pharmaceutical industries worldwide. The current review article highlights the general description of co-processing, techniques employed, and advantages of using natural components in co-processing. Also, the recent developments in excipient technology with special emphasis on natural combinations that could be used as co-processed excipients are briefly discussed. Mannitol is a sugar alcohol commonly used in the pharmaceutical industry for various purposes. It is a white, crystalline powder with a sweet taste and is known for its ability to act as an osmotic diuretic. Mannitol finds applications in pharmaceuticals due to its unique properties, including solubility, stability, and low toxicity. This article will delve into the sources, manufacturing process, and pharmaceutical uses of mannitol, along with pertinent information from the United States Pharmacopeia-National Formulary (USP-NF) and European Pharmacopoeia (EP) monographs.

## Manufacturing of Mannitol

Mannitol can be naturally found in a variety of plants, fungi, and bacteria. Common sources include seaweed, fruits like apples, and certain types of mushrooms. However, for pharmaceutical purposes, mannitol is often commercially produced through chemical synthesis.

The industrial manufacturing of mannitol typically involves the hydrogenation of fructose or glucose. The process begins with the catalytic hydrogenation of glucose to sorbitol, which is then further hydrogenated to yield mannitol. The resulting product is then purified and crystallized to obtain the desired pharmaceutical-grade mannitol.

**Function of Mannitol as Excipients**

Mannitol is a sugar alcohol commonly used in pharmacy for various purposes. Some of its important functions include:

- Osmotic Diuretic: Mannitol is often used as an osmotic diuretic in medical settings. When administered intravenously, it increases the osmotic pressure of the glomerular filtrate, leading to increased urine production. This can be beneficial in the treatment of conditions such as cerebral edema and acute kidney injury.
- Reducing Intraocular Pressure: Mannitol is employed to reduce intraocular pressure in certain eye conditions, particularly in the treatment of glaucoma and before intraocular surgery. Its osmotic properties help draw fluid out of the eye, reducing pressure.
- Intravascular Volume Expansion: In some medical situations, mannitol is used to expand intravascular volume. It works by drawing fluid from the interstitial space into the vascular system, helping to increase blood volume.
- Excipient in Pharmaceuticals: Mannitol is widely used as an excipient in the pharmaceutical industry. It serves as a bulking agent, diluent, and sweetening agent in various oral dosage forms, including tablets, capsules, and powders.
- Stabilizing Agent: Mannitol is used as a stabilizing agent for certain drugs, particularly proteins and peptides. It helps prevent denaturation and aggregation of these substances, maintaining their stability during storage.
- Inhalation Therapy: In respiratory medicine, mannitol can be used as an inhalation powder to diagnose and manage conditions such as asthma. It is known as a bronchoconstrictor challenge agent.
- Cryoprotectant: Mannitol is employed as a cryoprotectant in the preservation of certain biological materials, such as cells and tissues. It helps prevent damage during freezing and thawing processes.
- Diagnostics: Mannitol is sometimes used in diagnostic tests, particularly in renal function studies. Its ability to increase urine production makes it useful in assessing kidney function.
- Sugar Substitute: Mannitol is also used as a sugar substitute in some sugar-free or reduced-calorie products. It has a sweet taste but is not metabolized in the same way as sugar, making it suitable for individuals with diabetes.

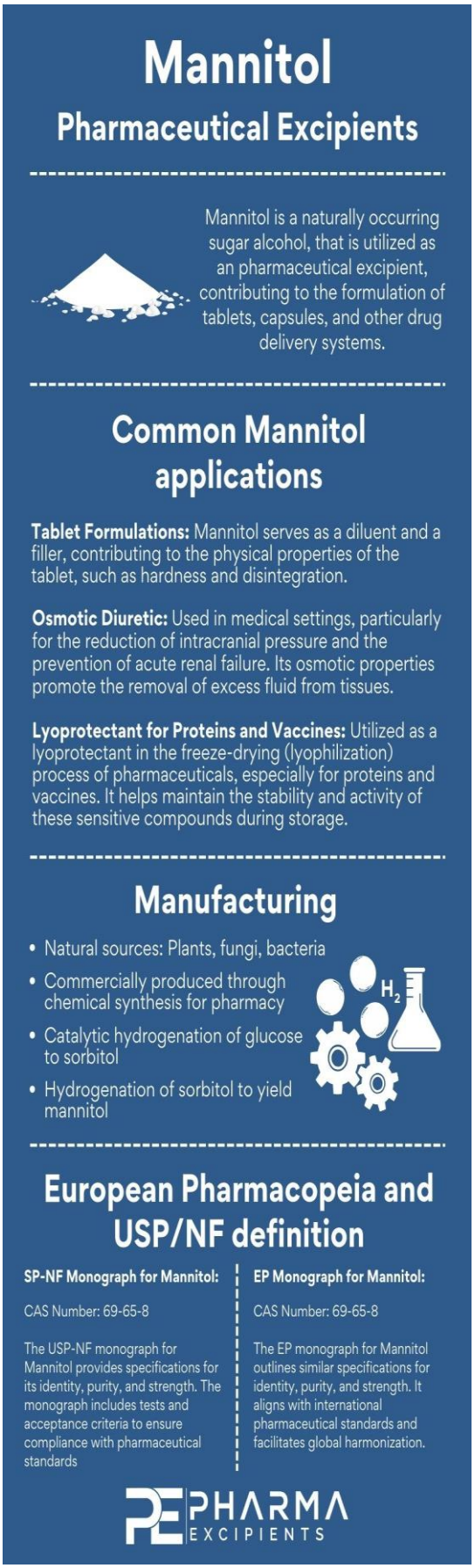
**Factors to consider when selecting Mannitol Excipients**

When selecting a mannitol excipient, several factors should be considered, including:

- Dosage Form: Consider the specific dosage form you are developing (e.g., tablet, capsule, powder, or liquid). Mannitol is versatile and can be used in various formulations, but its properties may be better suited for certain forms over others.
- Physical and Chemical Properties: Assess the physical and chemical properties of mannitol, including its particle size, crystalline structure, and solubility. These properties can impact the formulation's flowability, compressibility, and dissolution characteristics.
- Compatibility with Active Ingredients: Evaluate the compatibility of mannitol with the active pharmaceutical ingredient (API) and other excipients in the formulation. Ensure that mannitol does not interact adversely with the drug substance.
- Stability: Consider the stability of the formulation over time. Mannitol can act as a stabilizing agent for certain drugs, but it's essential to assess its impact on the long-term stability of the entire formulation.
- Manufacturability: Assess the ease of manufacturing with mannitol. Consider its flow properties during processing, compressibility for tableting, and other factors that may affect the efficiency of the manufacturing process.
- Dose Uniformity: Evaluate how well mannitol contributes to dose uniformity within the formulation. It should facilitate the uniform distribution of the active ingredient throughout the dosage form.
- Taste and Palatability: If the dosage form is intended for oral administration, consider the taste and palatability of mannitol. It is often used as a sweetening agent, but excessive amounts may impact the overall taste.
- Regulatory Considerations: Ensure that mannitol complies with regulatory standards and requirements for pharmaceutical excipients. Consider any limitations or restrictions on its use in certain regions or for specific applications.
- Patient Factors: Consider the target patient population and any specific requirements or preferences they may have. For example, if the formulation is for pediatric use, factors like taste and ease of administration become particularly important.
- Cost Considerations: Assess the cost-effectiveness of using mannitol in the formulation. Consider the overall cost of production and how it may impact the final pricing of the pharmaceutical product.
- Specialized Properties: Mannitol has unique properties, such as its ability to act as a bulking agent and its low hygroscopicity. Consider whether these properties align with the desired characteristics of the final dosage form.

By carefully considering these factors, formulators can make informed decisions about the use of mannitol as an excipient, ensuring that it contributes positively to the

overall quality and performance of the pharmaceutical product.



*Mannitol pharmaceutical excipients*

**Definitions according to the European Pharmacopeia and USP/NF**

The United States Pharmacopeia-National Formulary (USP-NF) and the European Pharmacopoeia (EP) have established standards for mannitol to ensure their quality and safety in pharmaceutical applications.

**USP-NF Monograph for Mannitol:**

- CAS Number: 69-65-8
- Description: The USP-NF monograph for Mannitol provides specifications for its identity, purity, and strength. The monograph includes tests and acceptance criteria to ensure compliance with pharmaceutical standards.

**EP Monograph for Mannitol:**

- CAS Number: 69-65-8
- Description: The EP monograph for Mannitol outlines similar specifications for identity, purity, and strength. It aligns with international pharmaceutical standards and facilitates global harmonization.

**Mannitol Excipients**

Mannitol, a sugar alcohol (polyol), finds extensive use in the pharmaceutical industry due to its unique properties and diverse applications. Here is a list of some common uses of mannitol in the pharmaceutical field:

- Excipient in Tablet Formulations: Mannitol is frequently employed as an excipient in tablet formulations. It serves as a diluent and a filler, contributing to the physical properties of the tablet, such as hardness and disintegration.
- Osmotic Diuretic: Mannitol is used as an osmotic diuretic in medical settings, particularly for the reduction of intracranial pressure and the prevention of acute renal failure. Its osmotic properties promote the removal of excess fluid from tissues.
- Lyoprotectant for Proteins and Vaccines: Mannitol is utilized as a lyoprotectant in the freeze-drying (lyophilization) process of pharmaceuticals, especially for proteins and vaccines. It helps maintain the stability and activity of these sensitive compounds during storage.
- Diagnostic Imaging Agent: In radiology, mannitol can be used as a contrast agent in certain imaging studies. It is employed to enhance visualization in procedures like magnetic resonance imaging (MRI) and computed tomography (CT) scans.
- Pulmonary Drug Delivery: Mannitol is sometimes utilized in inhalable formulations for respiratory conditions. It can be incorporated into dry powder inhalers to improve drug dispersion and lung deposition.
- Oral Care Products: Mannitol is found in some oral care products, such as sugar-free chewing gum and lozenges. Its sweet taste and sugar-like properties make it a suitable sugar substitute.
- Diagnostics and Testing: Mannitol can be used in certain diagnostic

tests, such as the Mannitol Salt Agar test, which is employed for the selective isolation of Staphylococcus aureus bacteria.

- Wound Care Products: Mannitol may be included in certain wound care products, contributing to the formulation of gels or creams used in the treatment of burns or skin injuries.

## Conclusion

Mannitol's role in the pharmaceutical industry as a versatile excipient underscores its significance in drug formulation. With defined standards provided by the USP-NF and EP monographs, mannitol continues to be a reliable and indispensable component in the development of pharmaceutical products. As technology advances and industry standards evolve, mannitol's applications are likely to expand, further cementing its place in the realm of pharmaceutical science and medicine.

## References


- *Liew, Kai Bin & Bin, & Hui, Hii & Helal Uddin, A. B. M. & Sarker, Zaidul & Chew, Yik-Ling & Ling,. (2023). Co-processed Excipients: A Revisit of Its Development in the Past Two Decades; A Review. 13. 96-103. 10.47750/pnr.2022.13.S07.015.*
- *Loke, Ying & Chew, Yik-Ling & Kumar, Ashok & Lee, Siew-Keah & Helal Uddin, A. B. M. & Goh, Choon Fu & Kee, Phei Er & Ng, Hui Suan & Ming, L C & Liew, Kai Bin. (2023). Development of a novel direct compressible co-processed excipient and its application for formulation of Mirtazapine orally disintegrating tablets. Drug Development and Industrial Pharmacy. 50. 1-9. 10.1080/03639045.2023.2294095.*
- *Noorani B, Chowdhury EA, Alqahtani F, Ahn Y, Patel D, Al-Ahmad A, et al. LC-MS/MS-based in vitro and in vivo investigation of blood-brain barrier integrity by simultaneous quantitation of mannitol and sucrose. Fluids Barriers CNS 2020;17:61.*
- *Rafaela Cristina TurolaBarbi., Gerson Lopes Teixeira., Polyanna Silveira Hornung., Suelen Avila., Rosemary Hoffmann-Ribani. Eriobotrya japonica seed as a new source of starch: Assessment of phenolic compounds, antioxidant activity, thermal, rheological and morphological properties. Food Hydrocolloids 77 (2018) 646e658*
- *Parmar, P.K., Rao, S.G., & Bansal, A.K. (2021). Co-processing of small molecule excipients with polymers to improve functionality. Expert Opinion on Drug Delivery, 18, 907 - 928.*
- *Singh, R., Kumar, P., Chaudhary, R., Kumar, A., Bahadur, S., & Garg, G. (2022). Development and Characterization of Novel co-processed excipients to enhance compressibility profile for Formulation of Tablet Dosage Form. Research Journal of Pharmacy and Technology.*
- *https://www.pharmaexcipients.com/mannitol-pharmaceutical-excipient/#:~:text=Excipient%20in%20Tablet%20Formulations%3A%20Mannitol,such%20as%20hardness%20and%20disintegration.*