Review on

ADVANCED APPLICATIONS OF BIOACTIVE EXCIPIENTS

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INTRODUCTION:

Pharmaceutical excipients play a critical role in drug formulations by enhancing stability, bioavailability, and patient acceptability without altering the therapeutic efficacy of the active pharmaceutical ingredients (APIs) [1]. Traditionally, synthetic excipients have been preferred for their consistent performance and ease of manufacturing. However, growing concerns about the safety, environmental impact, and sustainability of synthetic excipients have shifted the focus toward herbal excipients, derived from plants and natural sources. Herbal excipients,

Table no: Difference between the synthetic excipients and herbal excipients[3].

Key aspects	Synthetic excipients	Herbal excipients
Source	These are chemically manufactured.	Derived from natural sources like plants ,animals etc.,
Bio compatibiliy	Synthetic excipients may involve chemicals that could lead to irritation, allergies, or toxicity.	These are more biocompatible and less toxic and reduce the risk of adverse reactions
Bio degradablility	Synthetic excipients often consist of non-biodegradable materials, which may contribute to environmental pollution.	Natural excipients are usually biodegradable and without causing any environment harm.
sustainability	Synthetic excipients are made from non-renewable resources, like petroleum derivatives, which are less sustainable and may involve environmental concerns during manufacturing.	These are made from renewable resources, like plants, making them sustainable in long run if harvested responsibly.
Non Toxic & Eco friendly	Synthetic excipients may involve hazardous chemicals in their production and disposal potentially affecting human health and the ecosystem.	Natural excipients are often less processed and contain fewer harmful chemicals. Their eco- friendly nature is beneficial for both the human and the environment.
Regulatory approval	Synthetic excipients are often scrutinized more heavily, especially	Regulatory bodies more favour to natural excipients due to customer demand for **“clean-label”** products.

	ingredients like artificial colorants or preservatives	
Functional versatility	It provides more controlled functionality but often lack the versatility and natural safety profile of their natural counterparts	These are offer multifunctionality(eg: gums) while being safer

encompassing a wide range of plant-based polymers, gums, oils, and fibres, offer significant advantages, including biocompatibility, reduced toxicity, and multifunctionality. As consumers and regulatory bodies increasingly demand "natural" and "clean-label" products, the incorporation of herbal excipients into drug formulations is gaining momentum[4]. Appreciated characters of herbal excipients over the synthetic excipients were listed in the table no: 1.

2. Types of Herbal Excipients[6, 8,9,11]:

Herbal excipients can be broadly classified based on their source and functional roles in pharmaceutical formulations.

2.1. Starches:

Source: Derived from fruits (like corn, and rice) and roots like potatoes.
Functions:

Binder: Helps hold the substances of a pill together.

Disintegrate: Facilitates the breakdown of capsules in the digestive tract to launch the drug.

Filler/Diluent: it may bulk to the formulation, making sure uniform distribution of the energetic ingredient.

Applications: Starch is extensively used in tablet and tablet formulations for its splendid binding and disintegration properties. Pregelatinized starch is frequently used for direct compression.

2.2. Cellulose Derivatives (Microcrystalline Cellulose - MCC):

Source: Derived from plant fibers, primarily wood pulp.
Functions:
Binder and Diluent: Used in pills and drugs to supply structure.
Disintegrate: Helps the pill disintegrate rapidly after administration.
Stabilizer: Enhances the stability of sensitive drugs.
Applications: MCC is many times used in stable dosage forms, such as drugs and capsules, for its greatest compressibility and binding characteristics. It's a key excipient in direct compression pill formulations.

2.3. Gums (e.g., Acacia, Xanthan Gum, Guar Gum):

Source: Natural polysaccharides derived from plant seeds, algae, or bacterial fermentation.
Functions:
Binder: Provides a cohesive matrix in tablet formulations.
Suspending Agent: Helps in keeping insoluble particles suspended in liquids.
Emulsifier: Stabilizes emulsions in liquid formulations.
Applications: Gums are broadly used in oral suspensions, emulsions, and controlled-release formulations for their potential to structure secure gels and beautify drug delivery.

2.4. Alginates:

Source: Extracted from brown seaweed (algae).

Functions:
Thickening Agent: Increases the viscosity of liquid formulations.
Stabilizer: Prevents the separation of ingredients in suspensions.
Disintegrant: Helps drugs wreck down in the gastrointestinal tract.
Applications: Alginates are used in controlled-release formulations to regulate the release of the drug over time. They are additionally used in wound dressings and dental influence materials.

2.5. Gelatin:
Source: Derived from animal collagen, usually from bovine or porcine sources.
Functions:
Capsule Shell: Used to create tender and hard gelatin capsules.
Gelling Agent: Forms gels in a variety of dosage varieties like suppositories and gentle gels.
Coating: Protects tablets from moisture and enhances stability.
Applications: Gelatin is especially used in the manufacturing of tablets and gentle gels, providing a perfect care for liquid and semi-solid drug formulations.

2.6. Pectins:
Source: Extracted from the cell wall partitions of citrus fruits or apples.
Functions:
Gelling Agent: Forms gels in the presence of calcium or acid, used in liquid formulations.
Stabilizer: Prevents ingredient separation in emulsions or suspensions.
Controlled Release: Used in drug transport systems to manage the release of the lively ingredient.
Applications: Pectin are used in oral syrups, lozenges, and in sustained-release formulations where a slower release of the drug is desired.

2.7. Natural Oils and Waxes (e.g., Beeswax, Carnauba Wax, Vegetable Oils):
Source: Extracted from plants (e.g., olive, castor oil) and animals (e.g., beeswax).
Functions:
Lubricant: Reduces friction during pill manufacturing, facilitating tablet release.
Coating Agent: Provides a shielding layer for drugs and capsules.
Controlled Release: Used to gradual down the release of pills in formulations.
Applications: Waxes are in many instances used in coatings to protect tablets and pills from environmental moisture. Oils are additionally used in topical formulations and soft-gel capsules.

2.8. Lactose:
Source: Derived from milk.
Functions:
Diluent/Filler: Adds bulk to tablets and drugs when the dose of energetic ingredient is low.
Binder: Helps bind the elements together in strong dosage forms.
Carrier: Often used in dry powder inhalers to elevate the lively drug to the lungs.
Applications: Lactose is one of the most regularly used excipients in solid dosage varieties like pills and capsules, specifically in oral medications. It's additionally widely used in dry powder inhalers for respiratory drugs.

2.9. Chitosan:
Source: Derived from the exoskeleton of crustaceans like shrimp and crabs.
Functions:
Film Former: Used in coating capsules to furnish controlled release or taste masking.
Bio adhesive: Enhances the adherence of the drug to mucosal surfaces, enhancing drug absorption.
Disintegrate: Helps capsules damage down in the digestive tract.
Applications: Chitosan is used in controlled-release formulations, wound dressings, and nasal or transdermal drug shipping structures due to its bio adhesive residences and potential to improve drug absorption.

2.10. Agar:
Source: Extracted from crimson algae (seaweed).
Functions:
Gelling Agent: Forms gels when dissolved in hot water and cooled.
Thickener: Increases the viscosity of liquid formulations.
Stabilizer: Prevents separation in suspensions and emulsions.
Applications: Agar is used in microbiological media for drug trying out and in topical formulations like creams and ointments. It is also employed in controlled-release drug systems.

3.1. Biocompatibility and Reduced Toxicity[5]:
Herbal excipients are generally safer and less likely to cause adverse reactions compared to synthetic ones. Their natural origin ensures biocompatibility with human biological systems, minimizing risks of allergies, irritation, or toxicity. For instance, Aloe vera and Guar gum are known for their soothing and non-irritating properties, making them ideal for topical applications.

3.2. Biodegradability:
One of the key environmental advantages of herbal excipients is their biodegradability. Plant-based materials like Starch, Agar, and Pectin decompose naturally, reducing the environmental burden associated with pharmaceutical waste disposal.

3.3. Sustainability and Renewable Resources[14]:
Herbal excipients are sourced from renewable plant resources, unlike synthetic excipients, which often rely on non-renewable petroleum derivatives. With proper agricultural practices, the cultivation of plants for excipient production can be both economically and environmentally sustainable.

3.4. Potential Therapeutic Benefits[18]:
Many herbal excipients possess inherent medicinal properties in addition to their functional roles. For example, Aloe Vera not only acts as a binder but also has anti-inflammatory and wound-healing properties, adding therapeutic value to formulations. Similarly, Neem gum and Tragacanth exhibit antimicrobial properties, which can enhance the safety and efficacy of topical and oral formulations.

4. Challenges in the Use of Herbal Excipients[17, 19]:
Despite the numerous advantages, there are some challenges associated with the use of herbal excipients in pharmaceutical formulations:

4.1. Variability in Composition:

Herbal excipients can exhibit batch-to-batch variability due to factors such as climate, soil conditions, and harvesting techniques. This variability can affect the performance and consistency of the final drug product.

4.2. Limited Availability:

The cultivation of plants for excipient production can be resource-intensive, and certain herbal excipients may not be available in large quantities year-round. This can lead to supply chain challenges and affect scalability for large-scale production.

4.3. Regulatory Challenges[5, 14]:

Regulatory approval of herbal excipients can be complex due to the lack of standardized testing protocols and limited historical data on their use in pharmaceutical formulations. In some regions, herbal excipients may face stringent regulatory scrutiny, delaying their incorporation into mainstream drug products.

4.4. Potential for Allergic Reactions[3]:

Although herbal excipients are generally safe, there is a risk of allergic reactions in sensitive individuals. For example, Guar gum and Shellac have been known to cause hypersensitivity reactions in some patients.

5. Applications of Herbal Excipients[22]:

Herbal excipients have found diverse applications across pharmaceutical dosage forms:

Applications of Natural Excipients in Drug Formulations:

1. Tablets and Capsules: Natural excipients like starch, cellulose, and gums are crucial for binding, disintegration, and managed drug release.

2. Suspensions and Emulsions: Gums and alginates stabilize formulations to ensure even distribution of the drug.

3. Topical Formulations: Natural oils and waxes act as carriers and protectants for pores and skin applications.

4. Controlled Release Systems: Natural excipients like alginates, pectins, and chitosan are key in modulating the release of active ingredients over time.

5. Biocompatible and Biodegradable Formulations:

Natural excipients are favoured for their security and biocompatibility in sensitive formulations like eye drops, nasal sprays, and transdermal patches. Nutraceuticals: Given the "natural" appeal of nutraceuticals, herbal excipients are increasingly being used to develop clean-label products that align with consumer preferences for minimal synthetic ingredients.

6. Global Market Growth:

The global natural excipients market is expanding, driven by increasing consumer preference for eco-friendly, clean-label products. Major players include Ashland, Dow Chemical, and BASF, among others, investing in R&D and partnerships for plant-based excipients. Asia-Pacific is emerging as a key market, with countries like India and China capitalizing on their rich biodiversity to supply raw materials for natural excipients production. Europe and North America also maintain strong market shares, driven by stringent regulations and advanced pharmaceutical industries.

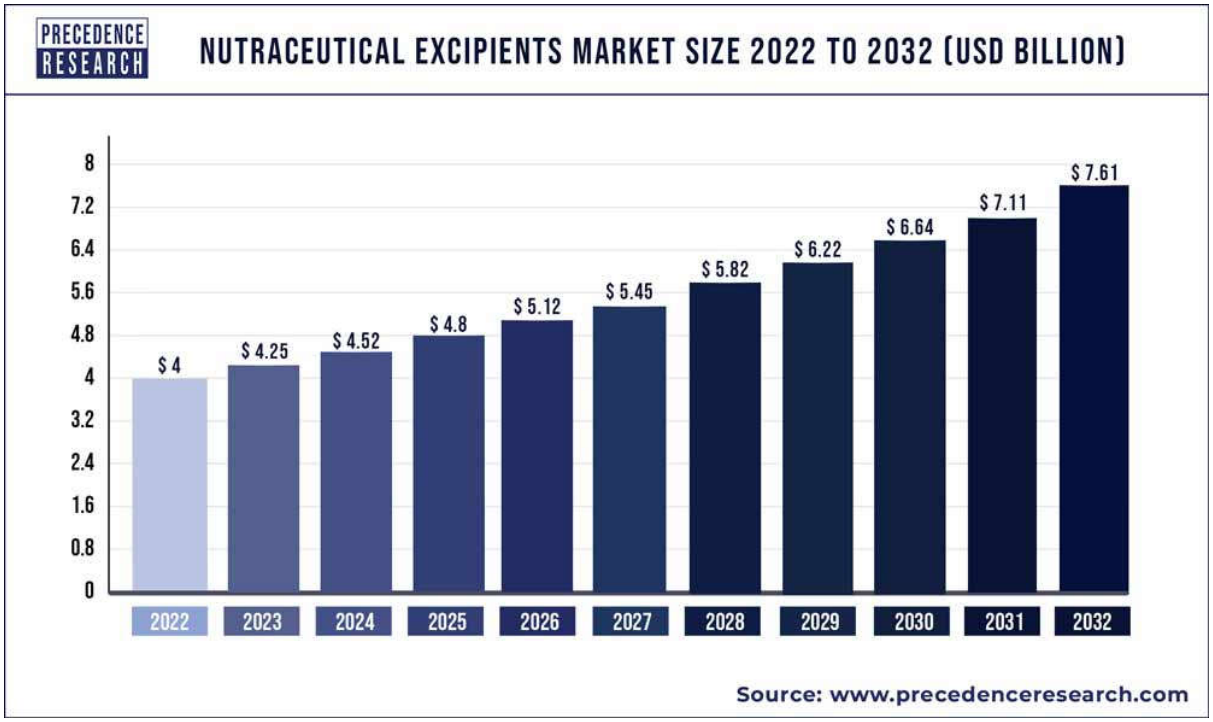

Figure no: 1 market size of natural excipients around the world[23].

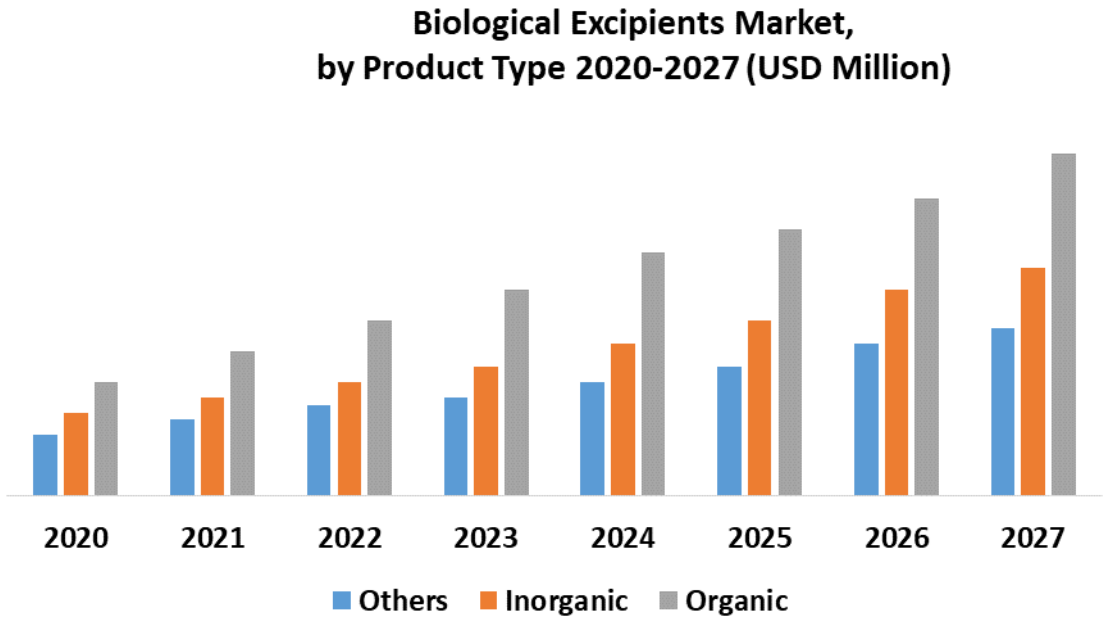

Figure no: 2 market size of natural excipients around the world[18].

7. Future Prospects:

The future of herbal excipients looks promising, driven by consumer demand for natural, sustainable, and safe pharmaceutical products. Ongoing research and development efforts are focused on improving the standardization, extraction techniques, and characterization of herbal

excipients to overcome the challenges associated with variability and regulatory approval. With advances in biotechnology and green chemistry, novel plant-derived excipients with enhanced functionality and therapeutic benefits are likely to emerge. Additionally, the growing interest in personalized medicine may open new avenues for the tailored use of herbal excipients in individualized formulations.

8. Conclusion:

Herbal excipients offer significant advantages over synthetic excipients in terms of biocompatibility, biodegradability, and sustainability, making them an attractive option for pharmaceutical formulations. While challenges related to variability, availability, and regulatory hurdles exist, ongoing research and innovation are poised to address these issues, paving the way for broader adoption of herbal excipients in the pharmaceutical industry. As the demand for natural and clean-label products continues to rise, herbal excipients will play a crucial role in the development of safer, more sustainable, and therapeutically beneficial drug formulations.

Conflict of interest:

No conflict of interest by author.

Funding sources:

Self-funding support was received.

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