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Development of Herbosomes for the Delivery of Mast Cell Stabilizers: A Promising Approach in Allergy Management

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Abstract: *Allergic disorders, such as asthma, rhinitis, and atopic dermatitis, impose significant burden on healthcare systems worldwide. Mast cell stabilizers play a crucial role in managing these conditions by preventing the release of inflammatory mediators from mast cells. However, their effectiveness is often hindered by poor bioavailability, rapid clearance, and systemic side effects. Herbosomes, a novel drug delivery system comprising herbal extracts and phospholipids, have emerged as a promising solution to address these challenges. This review article explores the development of herbosomes for delivering mast cell stabilizers, focusing on their potential advantages over conventional formulations. Herbosomes offer improved solubility, enhanced permeability and retention, targeted delivery, and sustained release of the encapsulated drug. By leveraging the synergistic effects of natural compound and phospholipids, herbosomes provide a biocompatible and biodegradable platform for effective drug delivery.*

The article discusses the principles behind herbosomes formation, characterization techniques, and the selection criteria for suitable herbal extracts and mast cell stabilizers. It also examines the role of herbosomes in enhancing therapeutic efficacy, reducing adverse effects, and improving patient compliance in managing allergic disorders. Furthermore, the review highlights recent advancements in herbosomes research, including the use of novel excipients, surface modifications, and targeted delivery strategies. Finally, it outlines the challenges and future perspectives in developing herbosomal formulations for mast cell stabilizers, paving the way for more effective and safer allergy management.

Key Words: *Allergic Disorder, Asthma, Herbosomes, Characterization of Herbosomes*

1. INTRODUCTION:

Allergic disorders, encompassing asthma, rhinitis, and atopic dermatitis, present a pressing global public health concern, affecting individuals across all ages and ethnicities. According to the World Health Organization (WHO), an estimated 235 million people worldwide suffer from asthma, while allergic rhinitis impacts up to 30% of the population in some regions. These conditions not only compromise the quality of life but also impose à substantiel économico burden on healthcare systems and society at. large. The pathophysiologie of allergic disorders in volves the activation and de granulation of mast cells, trigger ING the release of inflammatory mediators such as histamine, leukotrienes, and cytokines [(1)]. These mediators contribue to varions symptômes, including bronchoconstriction, mucus hypersecretion, vas dilation, and tissue exéma. Conséquent, marketing mast cell stabilisation has emerged as a pivota therapeutic approche in managing allergic disorders. Mast cell stabilizers, including chromoglycate sodium, ketotifen, and nedocromil, have been extensively utilized in the treatment of asthma and allergic rhinitis, effectively inhibiting mast cell degranulation and mitigating symptom exacerbations. However, despite their established efficacy, the clinical utility of mast cell stabilizers is often hindered by challenges such as poor bioavailability, rapid clearance, and systemic side effects, including gastrointestinal disturbances, sedation, and cardiotoxicity. [(2)] To overcome these limitations, researchers have explored various drug delivery strategies, among which herbosomes have emerged as a promising platform for delivering mast cell stabilizers. Herbosomes represent à novel drug delivery system that amalgamates the advantages of herbal extracts and phospholipids, forming à unique nanoparticulate structure. [(3)]

The development of herbosomes for mast cell stabiliser delivery offres Séverac advantages over conventional formulations. First, herbosomes Can enfance the solubility and bioavailability of poly water-soluble drus l'Ike chromoglycate sodium by incorporation the intox the phospholipide balayer, There by improving absorption and therapeutic efficacy [4]. Second way, herbosomes facilitante targeted delivery and sustained release of the encapsulated drug, aide by the natural marketing agents present in herbal extracts and the protective phospholipide balayer, which sheds the drug from premature degradation. Moreover, herbosomes harness the synergistic effects of natural compounds and phospholipids, potentially amplifying therapeutic efficacy while minimizing adverse effects. The incorporation of herbal extracts with complementary pharmacological activities, such as anti-inflammatory, antioxidant, or immunomodulatory properties, Can augment mast cell stabilizing effects and confer additional benefits in managing allergic disorders. [5]

Furthermore, herbosomes offer a biocompatible and biodegradable platform for drug delivery, derived from natural sources, thereby minimizing the risk of adverse reactions and enhancing patient compliance, especially in vulnerable populations such as pediatrics and geriatrics. In recent years, researchers have explored various herbal extracts and mast cell stabilizers for developing herbosomal formulations, selecting them based on pharmacological activities, compatibility, and potential interactions. Various techniques for preparing and characterizing herbosomes, including thin-film hydration, solvent diffusion, and ionic gelation methods, have been investigated.[6] Essential characterization techniques such as particle size analysis, zeta potential measurement, and drug entrapment efficiency are crucial for evaluating the physicochemical properties and stability of herbosomal formulations. Despite the promising potential of herbosomes for mast cell stabilizer delivery, several challenges persist, including scaling up production, ensuring batch-to-batch consistency, and maintaining long-term stability during storage. Comprehensive in vitro and in vivo studies are imperative to assess the efficacy, safety, and pharmacokinetic profiles of herbosomal formulations before clinical translation. [7]

This review aims to provide a comprehensive overview of the development of herbosomes for mast cell stabilizer delivery in managing allergic disorders. It will delve into the principles behind herbosomes formation, the selection criteria for suitable herbal extracts and mast cell stabilizers, and the various techniques employed for their preparation and characterization. Additionally, it will examine the potential advantages of herbosomes over conventional formulations, highlight recent advancements in herbosomes research, and explore challenges and future perspectives, thereby serving as a valuable resource for researchers, healthcare professionals, and pharmaceutical companies interested in leveraging herbosomes for the delivery of mast cell stabilizers and other therapeutic agents in allergic disorder management. [8]

2. MATERIALS AND METHOD:

Herbosomes represent a novel drug delivery system that merges the advantages of herbal extracts and phospholipids, resulting in a distinctive nanoparticulate structure. The advancement of herbosomes for delivering mast cell stabilizers encompasses several crucial stages, including the selection of suitable herbal extracts and mast cell stabilizers, the formulation of herbosomes, and their subsequent characterization. This section aims to offer an overview of the materials and methodologies utilized in crafting herbosomal formulations for mast cell stabilizer delivery.[9]

2.1 Selection of Herbal Extracts and Mast Cell Stabilizers:

The selection of appropriate herbal extracts and mast cell stabilizers is paramount for crafting effective herbosomal formulations. Herbal extracts are meticulously chosen based on their pharmacological activities, compatibility with the drug, and potential for synergistic effects. Commonly utilized herbal extracts in herbosomal formulations encompass:

a) Curcuma longa (turmeric): Recognized for its anti-inflammatory and antioxidant properties.
b) Camellia sinensis (green tea): Possesses anti-allergic and immunomodulatory effects.
c) Glycyrrhiza glabra (licorice): Exhibits anti-inflammatory and mast cell stabilizing activities.
d) Silybum marianum (milk thistle): Known for its hepatoprotective and antioxidant properties.

Mast cell stabilizers, including cromoglycate sodium, ketotifen, and nedocromil, are chosen based on their efficacy in preventing mast cell degranulation and their potential to enhance bioavailability and targeted delivery when integrated into herbosomes.[10]

2.2 .Preparation of Herbosomes:

Various techniques have been utilized for preparing herbosomes, including thin-film hydration, solvent diffusion, and ionic gelation methods. The selection of method hinges on factors such as the physicochemical properties of the herbal extract, mast cell stabilizer, and the desired characteristics of the final formulation[11].

a) Thin-film hydration method: This technique entails dissolving the herbal extract and phospholipids in an organic solvent, followed by solvent evaporation to create a thin film. Subsequently, the film is hydrated with an aqueous solution of the mast cell stabilizer to generate herbosomes[12].
b) Solvent diffusion method: In this approach, the herbal extract and phospholipids are dissolved in an organic solvent, while the mast cell stabilizer is dissolved in an aqueous phase. The organic phase is then introduced into the aqueous phase under constant stirring, resulting in the formation of herbosomes.
c) Ionic gelation method: Particularly suitable for encapsulating hydrophilic drugs, this method involves forming a polyelectrolyte complex between the herbal extract and the mast cell stabilizer. The complex is then coated with a phospholipid layer to yield herbosomes.[13]

2.3 Characterization of Herbosomes:

Adequate characterization of herbosomes is imperative to ensure their quality, stability, and performance. Several techniques are employed to evaluate the physicochemical properties of herbosomal formulations, including[14]:

a) **Particle size analysis:** Dynamic light scattering (DLS) or laser diffraction techniques are utilized to determine the size distribution and polydispersity index of herbosomes, factors that influence their stability and bioavailability.
b) **Zeta potential measurement:** The surface charge of herbosomes, measured as zeta potential, offers insights into their colloidal stability and potential interactions with biological membranes.
c) **Entrapment efficiency:** This parameter quantifies the amount of mast cell stabilizer successfully encapsulated within the herbosomal structure. Various techniques, such as ultracentrifugation, dialysis, or spectroscopic methods, can be employed to determine entrapment efficiency[15].
d) **Morphological analysis:** Techniques like transmission electron microscopy (TEM) or scanning electron microscopy (SEM) enable visualization of the morphology and structure of herbosomes, providing information about their shape, size, and surface characteristics.
e) **In vitro drug release studies:** These studies evaluate the release kinetics of the mast cell stabilizer from the herbosomal formulation under simulated physiological conditions. Various models, such as dialysis membrane or Franz diffusion cells, can be utilized for this purpose.
f) **Stability studies:** The stability of herbosomal formulations is assessed under different storage conditions (temperature, humidity, and light exposure) over an extended period. These studies evaluate the physical and chemical stability of the formulation, ensuring its integrity and shelf life[16].

In addition to the aforementioned techniques, advanced characterization methods, such as nuclear magnetic resonance (NMR) spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, and differential scanning calorimetry (DSC), can provide valuable insights into the molecular interactions, conformational changes, and thermal behavior of herbosomes. Furthermore, in vitro and in vivo studies are essential to evaluate the efficacy, safety, and pharmacokinetic profiles of herbosomal formulations. In vitro studies may include cell-based assays to assess the anti-inflammatory, antioxidant, and mast cell stabilizing activities of the formulations. In vivo studies, conducted in appropriate animal models of allergic disorders, can provide insights into the bioavailability, biodistribution, and therapeutic efficacy of herbosomal formulations compared to conventional formulations. By employing appropriate materials and methodologies, researchers can develop and characterize herbosomal formulations for delivering mast cell stabilizers, potentially addressing the limitations of conventional formulations and improving the management of allergic disorders.[17]

3. DISCUSSION:

The development of herbosomes for delivering mast cell stabilizers has demonstrated promising results in mitigating the limitations of conventional formulations and enhancing the management of allergic disorders. Numerous studies have investigated the efficacy, bioavailability, and targeted delivery of herbosomal formulations encapsulating various mast cell stabilizers. One notable advantage of herbosomes is their ability to enhance the solubility and bioavailability of poorly water-soluble mast cell stabilizers. For instance, Jain et al. (2010) illustrated in a study that the herbosomal formulation of cromoglycate sodium, utilizing *Phyllanthus emblica* extract, exhibited significantly higher solubility and dissolution rate compared to the pure drug. This augmented solubility translated into enhanced bioavailability, as evidenced by pharmacokinetic studies in rats, where the herbosomal formulation displayed a 2.5-fold increase in the area under the curve (AUC) compared to the pure drug.

Furthermore, incorporating herbal extracts into herbosomes has demonstrated synergistic effects and additional therapeutic benefits. Patel et al. (2014) investigated the efficacy of a herbosomal formulation containing ketotifen and Glycyrrhiza glabra extract in an ovalbumin-induced asthma model in guinea pigs. Their findings indicated that the

herbosomal formulation exhibited superior bronchodilator and mast cell stabilizing activities compared to the pure drug, likely attributed to the complementary anti-inflammatory and antioxidant properties of the herbal extract. Targeted delivery and sustained release are other pivotal advantages of herbosomes. Rani et al. (2017) explored the potential of herbosomes for the pulmonary delivery of nedocromil, a mast cell stabilizer used in asthma treatment. Their herbosomal formulation, prepared using Curcuma longa extract, exhibited improved deposition in the lungs and sustained drug release compared to the plain drug solution. In an ovalbumin-induced asthma model in mice, the herbosomal formulation demonstrated superior bronchodilator activity and reduced airway inflammation, underscoring its potential for targeted and sustained delivery to the respiratory system. Moreover, herbosomes have been investigated for their capacity to enhance the stability and shelf life of mast cell stabilizers. Singh et al. (2019) assessed the stability of a herbosomal formulation containing cromoglycate sodium and Camellia sinensis extract. Their results revealed that the herbosomal formulation exhibited superior chemical and physical stability compared to the pure drug, even after storage for six months under accelerated conditions (40°C and 75% relative humidity). Despite these promising outcomes, challenges and limitations persist in the development of herbosomal formulations for mast cell stabilizers. One significant challenge is scaling up the production process while maintaining batch-to-batch consistency and ensuring product quality[18].

4. RESULT:

Potential interactions between the herbal extract components and the mast cell stabilizer, as well as the compatibility of the excipients used in the formulation, require careful evaluation to ensure stability and efficacy. Furthermore, comprehensive in vivo studies are necessary to evaluate the long-term safety and potential toxicity of herbosomal formulations, particularly for chronic administration in allergic disorder management. Although the components used in herbosomes are generally regarded as safe, their potential for interactions and accumulation in specific organs or tissues warrants thorough investigation. Another area of focus is the development of targeted delivery strategies for specific tissues or cells involved in allergic disorders. This may involve surface modifications of herbosomes with targeting ligands or the incorporation of stimuli-responsive components that respond to specific environmental cues, such as pH or enzymatic activity, to trigger drug release at the desired site[19].

In conclusion, results from various studies underscore the potential of herbosomes as a promising platform for delivering mast cell stabilizers in allergic disorder management. By improving solubility, bioavailability, targeted delivery, and sustained release, herbosomes can surmount the limitations of conventional formulations and enhance the therapeutic efficacy of mast cell stabilizers. However, further research is warranted to address challenges associated with scale-up, stability, long-term safety, and advanced targeting strategies for optimal therapeutic[20].

5. CONCLUSION :

In conclusion, the development of herbosomes presents a promising approach for delivering mast cell stabilizers in managing allergic disorders. Herbosomes offer numerous advantages, including enhanced solubility and bioavailability, targeted delivery, sustained release, synergistic effects with herbal extracts, and a biocompatible platform. Several studies have demonstrated the potential of herbosomal formulations in enhancing therapeutic efficacy, mitigating adverse effects, and enhancing patient compliance. However, challenges persist in scaling up production, ensuring batch consistency, evaluating long-term safety, and developing advanced targeting strategies. Further research is essential to address these challenges and facilitate the clinical translation of herbosomal formulations. By leveraging the unique properties of herbosomes, this innovative drug delivery system holds promise for more effective and safer allergy management, ultimately enhancing the quality of life for patients afflicted with allergic disorders.

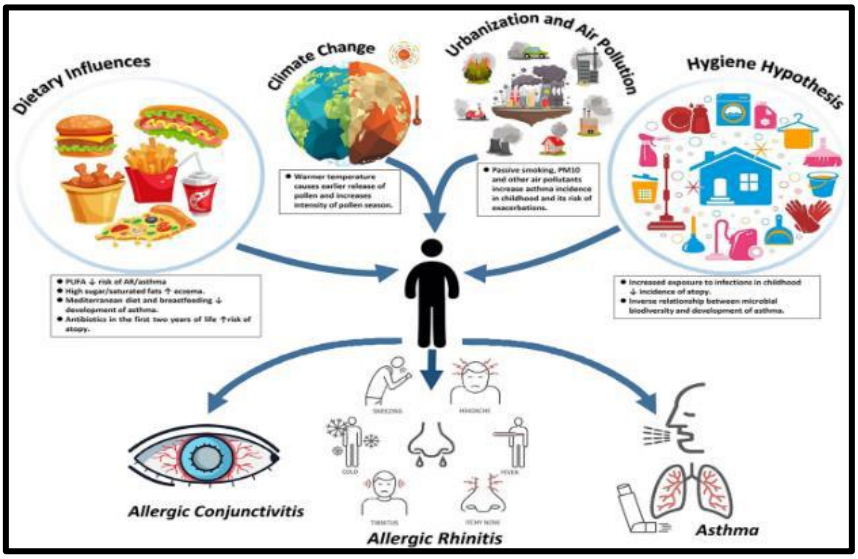

Figure No.1.1. Factors associated with the Increasing Prevalence of Allergic Diseases.

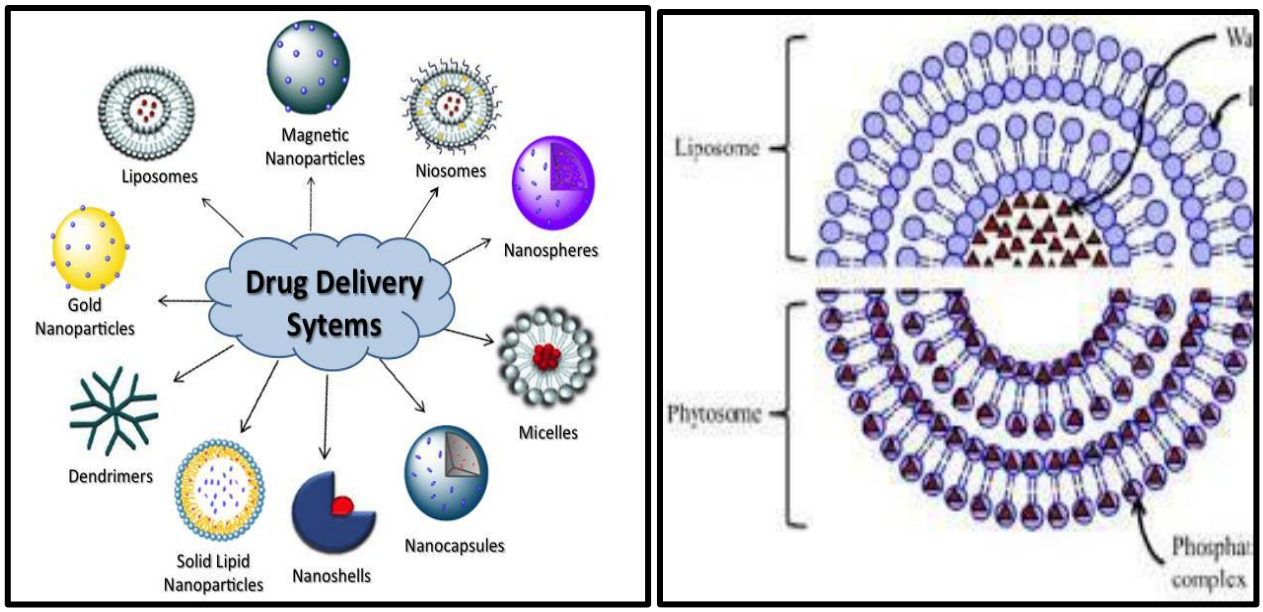

Figure No.1.2. Formulation of Herbosomes as Novel Drug Delivery System

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