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Development and In-vitro characterization of liposphere gel forAntifungal drug econazole.

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1.Introduction:-

The development of multiple-unit drug delivery systems has provided significant advantages over single-unit systems, particularly in ensuring uniform distribution and absorption of drugs in the gastrointestinal tract. However, challenges such as polymer breakdown and residual organic solvents have been observed in these systems, raising concerns about acceptability and toxicity. In response to these issues, a novel fat-based encapsulation technology known as lipospheres has been proposed.

Lipospheres are solid lipid particles with a diameter ranging from 0.01 to 100 µm, consisting of a hydrophobic lipid core containing the active drug moiety dissolved or dispersed in a fat matrix. The core is stabilized by an external layer of phospholipid molecules. Liposphere systems offer several advantages over other particulate delivery systems, including improved stability, controlled particle size, high drug load, controlled drug release, and lack of carrier toxicity.

These lipospheres have shown promise in delivering a variety of medication candidates, including anti-inflammatory substances, local anesthetics, antibiotics, and anticancer medicines. They also demonstrate the potential for delivering lipid-entrapped vaccines with an adjuvant effect. The convenience of various processing techniques, safety, stability, and versatility in drug administration routes make lipospheres a promising option for drug development across pharmaceutical, cosmetic, veterinary, and food additive fields. Additionally, advancements in solvent-free technologies have enhanced the feasibility of lipid-based formulations without the need for surfactants.

1.2 *Drug and excipient profile* *Econazole:-

The antifungal drug econazole belongs to the imidazole class, patent grant in 1968, and

Was approved for therapeutic use in 1974 .

1.3 Chemical and physical data :-

Formula: C18H15Cl3N2O

Molar mass: 381.68g·mol−1

Melting point: 162°C

1.4 Objective :-

To enhance the loading of econazole drug

To enhance the drug release of the econazole from the liposphere.

2 . Riview of Literature

The literature review discussed the role of lipospheres and pro-nanolipospheres as drug delivery carriers, highlighting their benefits such as increased bioavailability, reduced toxicity, and the ability to deliver medications with short half-lives or poor permeabilities. The use of lipid-based carriers, known for their capacity to protect the active pharmaceutical ingredient (API) from degradation and their safety profile, was emphasized. The review also covered analytical methods for determining drug release from liposphere gels, such as the UPLC–MS/MS method, which demonstrated high precision and accuracy in determining dermatokinetics parameters of drugs.

Furthermore, specific studies were discussed, including one that prepared lipospheres containing ibuprofen to enhance its oral delivery. This study evaluated the in vitro and in vivo performance of ibuprofen-loaded lipospheres, demonstrating high encapsulation efficiency and stable morphology. Another study focused on developing phospholipid lipospheres loaded with rifampicin for inhalation to enable deep lung delivery, showing promising characteristics such as amorphous nature and improved flowability.

Overall, the review provided comprehensive insights into the potential of lipospheres and pro-nanolipospheres as versatile drug delivery systems for various routes of administration, emphasizing their potential to enhance drug bioavailability and therapeutic outcomes.

3. Pharmacokinetic

Econazole nitrate, when topically applied, shows minimal systemic absorption in healthy individuals, with high concentrations in the skin's outer layer. It inhibits fungal growth by interacting with 14-α demethylase, disrupting ergosterol synthesis in the cell membrane. Adverse effects are rare, with about 3% of patients experiencing mild symptoms like burning and itching. Econazole is used to treat various skin conditions such as jock itch, athlete's foot, and ringworm, and is also available in Canada as Ecostatin for vaginal thrush. Its mechanism of action includes preventing lipid production, altering membrane structure, and inhibiting cellular processes.

4. Plan of work

Preformulation studies of drug The step involves the evaluation of preformulation properties of the econazole nitrate drug like Organoleptic properties, FT-IR Spectroscopy, UV-visible Spectroscopy, Melting point, Partition Coefficient, Solubility.

- Preparation of econazole nitrate loaded liposphere
- Characterization of econazole nitrate loaded liposphereThe step involves the evaluation of all prepared econazole nitrate loaded liposphere formulation For their appearance, pH, drug entrapment, particle size and micromeritic properties. Scanning Electron microscopy and, FTIR of selected formulation.
- Preparation of econazole nitrate loaded liposphere gel
- In-vitro characterization of econazole nitrate loaded liposphere gel
- The step involves the evaluation of all prepared econazole nitrate loaded liposphere gel Formulation for their appearance, pH, Percentage drug content, Percentage drug release of selected Formulation, In-vitro drug release kinetic study.

5. Preparation of the econazole nitrate loaded liposphere gel

The current study utilized the melt dispersion method to prepare econazole nitrate-loaded lipospheres. Various lipids as the core material and soybean lecithin as the coat material were melted at 80°C, with econazole nitrate added to the mixture. Simultaneously, an aqueous phase was prepared by adding water to a beaker at 80°C. The two phases were combined using a mechanical stirrer to form a uniform emulsion, which was then rapidly cooled to 20°C for solidification of the liposphere particles.

Subsequently, the econazole nitrate-loaded liposphere gel was prepared by soaking carbopol 934 in water overnight. The liposphere particles were added to the carbopol dispersion along with glycerin and propyl paraben under continuous stirring to achieve a homogeneous dispersion. The pH of the gel formulation was adjusted to 6.8 using 0.1N NaOH, with viscosity increasing as pH was adjusted. The final gel was stored in a beaker for further use.

6. Result & Discussion

6.1 Evaluation of econazole nitrate loaded liposphere Physical Appearance:-

All prepared formulation was evaluated for their physical properties like aggregation of particles that Indicated the liposphere formulation comprises the stearic acid Were spherical and uniform in appearance. While the liposphere prepared form the other lipids were non uniform in appearance.

6.2 Percentage yield:-

The percentage yield of the all prepared liposphere formulations were found to be in range of 50.835±0.979 to 97.099±0.320. The liposphere possess the stearic acid as their core material Revelated the higher percentage yield. In addition, on increasing the amount of the core material The percentage yield of the drug laoded liposphere formulation increases.

6.3Percentage drug content

Percentage drug content of the all three-gel formulation was observed to be in range 89.714±0.451% to 99.089±1.193% indicted the unform distribution of the econazole nitrate loaded Liposphere in the gel matrix.

7. Summary

The aim of this project was to develop an econazole-loaded liposphere gel to enhance drug loading and release. Preformulation studies determined the melting point of econazole nitrate to be in the range of 161.34°C to 164.67°C and its UV spectrum absorption maxima at 271nm. The linearity curve for econazole nitrate was found to be linear and accurate, with good linearity observed at concentrations ranging from 10 µg/ml to 70 µg/ml.

Econazole nitrate was found to have varying solubility in different solvents, being very slightly soluble in water, soluble in methanol and ethanol, sparingly soluble in chloroform, and very slightly soluble in phosphate buffer pH 6.8. The econazole-loaded lipospheres were prepared using the melt dispersion method, with various factors such as different lipids, lipid amounts, and stirring speed screened during formulation. The percentage yield of the prepared lipospheres ranged from 50.835% to 97.099%, with percentage drug entrapment ranging from 23.141% to 89.556%. Particle size of the lipospheres ranged from 1.836 µm to 8.376 µm, with formulation EL8 selected for further evaluation.

Formulation EL8 was incorporated into gel carriers with varying concentrations of carbopol 934 (1%w/w, 1.5%w/w, and 2%w/w). The resulting gel formulations showed uniform distribution of the econazole-loaded lipospheres, with drug content ranging from 89.714% to 99.089%. Viscosity of the gel formulations ranged from 699.000cp to 6314.667cp. Econazole nitrate release profiles from the liposphere gel formulations indicated nearly 100% release for EL8G2, roughly 98% for EL8G3, and around 40% for the control gel after 24 hours. The release of econazole nitrate from the liposphere gel formulation was found to follow the Higuchi model, with a regression coefficient value of 0.931 indicating a good fit.

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