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Unlocking the Potential of Naturosomes: A Comprehensive Study on Phytoconstituent Encapsulation and Evaluation.

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ABSTRACT
In order to improve the solubility and oral bioavailability of hesperidin, in this study phospholipid complex of hesperidin and phospholipid is prepared by solvent evaporation method. QbD approach is used to optimize the formulation and finally optimized formulation is evaluated for various parameters like solubility in aqueous as well as organic solvent. The Entrapment efficiency and percentage yield were also considered for the optimization of the formulation. This study shows that the solubility of the complex as compared to the pure drug there was a three-fold increment both in water as well as n-octanol. The dissolution study shows that pure drug shows 31.24% drug release in 8 hours, whereas complex shows 95.93% release in the same time. So, these results show that the phospholipid complex of drug and lipid is useful to enhance the solubility and oral bioavailability of pure hesperidin.

Keywords: Hesperidin; Box-Behnken design; naturosomes; Solubility.

I. INTRODUCTION

Naturosomes are complexes between natural phospholipids and natural products. The behavior of Naturosomes is managed in physical and biological systems by factors such as physical size, membrane permeability, percent entrapped solutes, quantity, purity as well and chemical composition of starting material. Naturosomes can be used for systematic drug targeting as they are able to move from the hydrophilic environment of absorptive cells and from there into cells. Naturosomes are more bioavailable as compared to herbal extract, it helps to enhance their capacity to cross the lipid-richbio membranes and finally reach the system circulation. A Naturosomes complex is a chemical entity or drug that contain phosphorus along with lipid. A phospholipid is amphipathic in nature, so it is used to increase the absorption of drugs like flavonoids, terpenoids, tannins, triterpenes, saponins, and flavonoids. Phospholipids, phosphatidylcholine is an integral part of the cell membrane, exist in zwitterionic form, and play a major role in drug delivery due to its amphiphilic nature that can modify the rate of drug release for controlled delivery of the active ingredients. It is compatible with pharmaceuticals and also exerts its own therapeutic benefits like hepatoprotection. Moreover, it is also an excellent with which it is co-administered. Many factors affect the bioavailability of orally administered drugs such as solubility, permeability in blood, permeability in tissue, and transit time to release the drug from the dosage form to overcome these problems mainly phospholipid complex formulation is used. The bioavailability of orally administered drugs is governed by several factors like solubility across gastrointestinal transit, release from the dosage form, gut permeability, metabolism, and drug liability to efflux. Hesperidin, a polyphenolic bioflavonoid, is the predominant flavonoid in orange peel and other citrus fruits. The highest concentration of hesperidin can be found in the white parts and pulps of the citrus peels. Hesperidin can also be found in green vegetables. Hesperidin is a flavanone glycoside consisting of the flavone hesperitin bound to the disaccharide rutinose. The sugar causes hesperidin to be more soluble than hesperidin. Formulation and Evaluation of Naturosomes of phytoconstituent 6 ACOP, Vita. Naturosomes showa molecular weight is 610.1898 g/mol and a molecular formula is C28H34O15, Naturosomes contain phosphorous in the form of

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phosphoric acid groups amphipathic in nature. The human body uses phospholipids as emulsifiers. The bioavailability of orally administered drugs is governed by several factors like solubility across gastrointestinal transit release from the dosage form. Phospholipid complexation techniques by chemically reacting polyphenolic plant actives with polyphenolic plant actives with phospholipids containing phosphatidylcholine (PC) and later patented the technology with the name Naturosomes. Phospholipids are the main structural component of all our body's cell membranes. Phospholipids are small lipid molecules in which the glycerol is bonded only to two fatty acids, instead of three as in triglycerides, with the remaining site occupied by a phosphate group.

Advantages:

1. Natural chemical compound
2. Low cost
3. Beneficial anti-inflammatory and Immunomodulatory effects
4. Urinary disease
5. Diabetes
6. Bone protection
7. Lipid metabolism and obesity

Disadvantages:

1. The effect of metabolite hesperidin on the ACE2 receptor is unknown at this time
2. Low bioavailability

Prerequisite for Phyto-phospholipid complex formation:

a. Standardized extract or an active Naturosomes
b. Carrier phospholipid
c. Solvent.

a. Standardized extract or an active Naturosomes:

- Phospholipid complex formulations are prepared according to weight basis for standardized extract, whereas molar ratios for active constituents.
- Selection of hesperidin drug depends on its phytochemical and pharmacokinetic Formulation and Evaluation of Naturosomes of phytoconstituent
- A drug that contains an active hydrogen atom like -COOH, -OH, -NH2, - NH, etc., which has the ability to form a hydrogen bond between the drug and N-(CH3) of PC molecules. • Any drugs that possess pi electrons can be formulated into different complexes with phospholipid molecules. • Both hydrophilic and lipophilic actives can be complexes to improve bioavailability.

II. MATERIALS AND METHODS

Materials

Hesperidin was purchased from TCI. VAV Life Science in Mumbai gifted the Phospholipid. All other compounds were of an analytical grade.

Experimental Design and Optimization

The Hesperidin Naturosomes (HN) were optimized using the Box-Behnken design technique (Design Expert software, version 13; Stat-Ease Inc., Minneapolis, MN, USA). This design was used to assess the effectiveness of independent formulation variables, such as the Hesperidin to-phospholipid ratio (A), process temperature (°C, B), and reflux time (h, C), on the dependent variables, such as the percentage of entrapment efficiency (% EE) and, of phytosomes formulations. The design generated 15 runs for HNoptimization, with a center point of 03 and various combinations of the three independent variables at low (-1), middle (0), and high (+1) values, as shown in Table 1.

Table 1. Levels of independent variables, their combination, and dependent variables for Hesperidin Naturosomesas per Box- Behnken design.

Run Number	Independent variables			Dependent variables
	A (H: PC)	B (Temp, °C)	C (Time, hrs.)	% EE
1	1:0.5	60	3	56.66
2	1:0.5	50	2	66.66
3	1:1.5	60	1	44.00
4	1:1.5	70	2	60.00
5	1:0.5	70	2	73.67
6	1:1.5	60	3	66.8
7	1:1.5	50	2	48.00
8	1:1	60	2	44.00
9	1:1	70	3	50.00
10	1:1	50	3	60.00
11	1:1	60	2	56.00

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12	1:1	70	1	59.5
13	1:0.5	60	1	66.66
14	1:1	50	1	42.5
15	1:1	60	2	45.00

Preparation of Hesperidin Naturosomes (HN)

The Hesperidin Naturosomes are created in a straightforward and repeatable manner. According to the experimental design data, precisely weighed Hesperidin and PC were dispersed separately in 30 ml of ethanol, then mixed and refluxed at a given temperature for a specific amount of time. Finally, the organic solvent was evaporated down to 5 ml, and 5 ml of n-hexane was added as an antisolvent to generate the phospholipid complex precipitate. The resulting complex was desiccated and stored at 4 °C until use in an amber-colored container.

III. RESULT AND DISCUSSION

Solubility of Hesperidin

Hesperidin is sparingly soluble in water. It can dissolve to some extent in water due to its polar nature and the presence of hydroxyl (OH) groups in its structure. However, its solubility in pure water is relatively low, which makes it challenging to use in aqueous solutions or beverages. When hesperidin naturosomes were prepared the solubility of Hesperidin was improved by 6-fold.

The partitioncoefficient of Hesperidin

The partition coefficient of hesperidin in n-octanol and water was increased which indicates that the lipophilicity and hydrophilicity ofhesperidinwere increased by forming the naturosomes.

Dissolution study

The USP type II apparatus was used for the dissolution study of Hesperidin in naturosomes. The Phosphate buffer solution of pH 6.8 was used as a dissolution medium. The Hesperidin naturosomes showeda drug release of 91.23% release in 12 hours as compared to pure hesperidin (26.45%)

Entrapment efficiency

The formula for calculating entrapment efficiency is:

Entrapment Efficiency (%) = (Amount of Drug Entrapped / Total Amount of Drug Used) × 100

The entrapment efficiency of the optimized batch was found to be 73.67.

Differential Scanning Calorimetry

DSC measures the heat flow into or out of a sample as it is heated or cooled, and it provides valuable information about the material's thermal behavior, including phase transitions, thermal stability, and heat capacity.A diffractogram of formulated naturosomes revealed the formation of hesperidin naturosomes.

Fourier transform infrared spectroscopy

Fourier Transform Infrared Spectroscopy (FTIR) is a widely used analytical technique for identifying and analyzing the chemical composition of substances based on their interaction with infrared light. It is a powerful tool in various fields, including chemistry, material science, biology, pharmaceuticals, and environmental science. FTIR spectroscopy provides information about the vibrational and rotational modes of molecules, allowing for the identification of functional groups and the determination of chemical structures.

Transmission electron microscope

A Transmission Electron Microscope (TEM) is a powerful microscopy technique that uses a beam of electrons instead of visible light to magnify the details of very small specimens. TEM is one of the most versatile and high-resolution imaging tools available in the field of microscopy and is widely used in various scientific disciplines, including materials science, biology, nanotechnology, and physics. The hesperidin naturosomes reveal the spherical shape of hesperidin naturosomes.

Particle Size, Zeta potential, and Polydispersity index

The particle size of prepared naturosomes was found to be 263 nm, along with a zeta potential of -36 mV and PDI of 0.256. The parameters indicated that the prepared naturosomes are small in size along with ahigh stability and homogenous mixture.

IV. CONCLUSION:

Our study successfully formulated and evaluated naturosomes as a promising drug delivery system for phytoconstituents. Our findings demonstrated improved encapsulation efficiency and sustained release profiles compared to

traditional delivery methods. These results suggest that naturosomes hold great potential for enhancing the therapeutic efficacy of phytoconstituents. However, further research is needed to optimize formulation parameters and assess long-term stability. This study contributes to the growing body of knowledge in the field of drug delivery and opens avenues for future investigations into naturosomes as a versatile drug delivery platform.

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