Pharmacosomes: Revolutionizing Drug Formulation and Novel Drug Delivery

Samrin R. Pathan[1], Shraddha M. Khaladkar[2], Sanket V. Dhamale[3],
Saniya D. Pathan[4], Sayali A. Wagh[5]

Students, B. Pharmacy, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India[1,3,4,5]
Assistant Professor, Pharmaceutics, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra, India[2]

Abstract: *Pharmacosomes are drug delivery systems that can enhance the bioavailability and protect the GI tract of drugs like poorly soluble ones. They resemble liposomes but with a significant increase in drug loading which makes them more effective for clinical application. The advantage over liposomes is that pharmacosomes do not require any special techniques to improve their loading capacity for drugs. Pharmacosomes, tiny drug-carrying particles, can boost the effectiveness of various medications, such as amoxicillin, bupranolol hydrochloride, and pindolol. By designing and testing pharmacosomes for drug delivery, scientists can enhance drug availability, prevent degradation, and improve overall treatment results. Pharmacosomes are amphiphilic phospholipid complexes of drugs bearing active hydrogen that bind to phospholipids. Pharmacosomes exhibit fusion, aggregation and hydrolysis when stored which affect their stability. Nevertheless, they have various merits such as enhanced biopharmaceutical properties, controlled release, reduced toxicity and cost of therapeutics*

Keywords: Pharmacosomes, vesicular drug delivery, Amphiphilic, Phospholipid, bioavailability

I. INTRODUCTION

Pharmacosomes are a type of drug delivery system that can improve the bioavailability and gastrointestinal safety of drugs, including poorly soluble drugs. They are similar to liposomes but have a higher percentage of drug loading, which makes them more suitable for clinical use. Unlike liposomes, pharmacosomes do not require any special methods for improving drug loading. They can be prepared using two methods: ether-injection and hand-shaking. An analytical grade organic solvent is required for their preparation, and they must be of high purity and volatile in nature. The pharmacosomes undergo fusion, aggregation, and hydrolysis when stored, which can affect their stability. However, they have several advantages, including improved biopharmaceutical properties, controlled release, and reduced toxicity and cost of therapeutics.

Pharmacosomes are a novel drug delivery system that has been gaining attention in recent years. They are defined as "the colloidal dispersion of drug covalently bond to lipids, and many exist as an ultrafine vesicular micelle or hexagonal aggregates depending upon the chemical structure of drug-lipid complex." Pharmacosomes are formed by covalently, electrostatically, or hydrogen bond binding drugs with lipids, providing advantages over conventional vesicles. They exhibit high loading capacity, leakage resistance, ease of preparation, storage, and high stability compared to liposomes. The term "Pharmacosomes" is derived from the two words "pharmacon," which means active principle, and "soma," carrier. The preparation of pharmacosomes involves the covalent bonding of the drug to lipids, and the resulting complex can exist in various forms depending on the chemical structure. The methods of preparation typically include[9] techniques such as the hand shaking method. Pharmacosomes have been evaluated for various characteristics such as drug solubility, drug content, surface morphology, and phase transition behaviour. They have shown high drug loading capacity, which is a prime advantage over liposomes. The preparations do not require special methods like coating for improving drug loading, and they have been found to improve the bioavailability.

ADVANTAGES

- Pharmacosomes are a novel vesicular drug delivery system that offer several advantages over other conventional vesicle systems. According to, some of the advantages of pharmacosomes over other vesicular systems include:
- They are less tedious and time-consuming than liposomes.
- The process of drug release is hydrolysis rather than bilayer diffusion, surface desorption, or degradation as in the case of liposomes.
- Unlike liposomes, the entrapment efficiency of pharmacosomes remains unaffected by the volume of inclusion.
- Pharmacosomes have a greater degree of selectivity for action on specific target cells.
- Additionally, pharmacosomes have a high percentage of drug loading, which is a prime advantage over liposomes, making the delivery of drugs possible for clinical use.
- Compared to other liposomal drug delivery systems, pharmacosomes have advantages such as minimized drug degradation and increased drug bioavailability.

DISADVANTAGES

- Synthesis of compound depends on its amphiphilic nature.
- Required surface and bulk interaction of lipids with drugs.
- Required covalent bonding to protect the leakage of drugs.
- On storage, undergo fusion and aggregation, as well as chemical hydrolysis.

Applications:-

1. Pharmacosomes have a broader range of stability and greater shelf life.

2. Pharmacosomes can improve drug absorption and delivery. Geniposide pharmacosomes that were designed using the response surface methodology and characterized by our colleagues. The ratios of lipid to drug, temperature during reaction mixture, and concentration of drugs were 3, 50 C, and 5.5 mg / mL respectively.

3. Pharmacosomal formulations were prepared for few anti-inflammatory drugs that are poorly soluble, non-steroidal such as Aceclofenac, Diclofenac, Aspirin and Fenoprofen. These researchers also show how pharmacosomes can help in solubilizing and enhancing penetration through any substance. There was an increase in dermal permeation when tested by penetration with fenoprofen over time.

4. Pharmacosomes can enhance membrane fluidity to accelerate permeation rate across membranes. The transition temperature of vesicles in the form of vesicles or micelles could significantly affect the interaction between them with biomembrane which improves transfer of drug across the membrane.

5. The phase transition temperature of pharmacosomes is another issue that greatly affects their interactions with membranes both bilayered and interacting with bio membranes thereby allowing better transdermal delivery.

COMPONENTS OF PHARMACOSOMES:

Component	Requirements
Drugs	Functional hydrogen atom from amino, carboxyl, or hydroxyl group that can be esterified.
Solvents	High purity, volatile, and intermediate polarity
Lipids	Phospholipids-phosphoglycerides or Sphingolipids

DRUGS

Any drug containing active hydrogen atom (-COOH, -OH, -NH2, etc) can be esterified with the lipid, with or without spacer chain. Facilitates membrane, tissue, cell wall transfer in the organisms is due to its amphiphilic nature.

LIPID

Phospholipids are the major components of biological membrane; majorly two types of phospholipids are used namely phosphoglycerides and sphingolipids.

The most common type of phospholipids is Phosphatidylcholine moiety.

Phosphatidylcholine is an amphiphilic molecule in which a glycerol bridges links a pair of hydrophobic acyl hydrocarbon chains with hydrophilic polar head group phosphocholine.

SOLVENTS:-

They should be high pure and volatile in nature, and should be selected based on the intermediate polarity for their preparations

METHODS FOR FORMULATION OF PHARMACOSOMES

There are various methods which have been employed to prepare vesicles;

1. Solvent evaporation method

In the solvent evaporation method of preparing the pharmacosomes, the drug is first acidified so that the active hydrogen might be available for complexation. The drug acid is then extracted into chloroform and subsequently recrystallized. The drug-PC complex is prepared by associating drug acid with PC in various molar ratios. The accurately weighed PC and drug acid are placed in a 100 ml round bottom flask and dissolved in sufficient amount of dichloromethane. The mixture is refluxed for one hour.

Then the solvent is evaporated off under vacuum at 40 ° C in a rotary vacuum evaporator. The dried residues are then collected and placed in vacuum desiccator for complete drying.

2. Hand –shaking method

In the hand-shaking method, a mixture of drug and lipids are dissolved in volatile organic solvent such as dichloromethane in a round bottom flask. The organic solvent is removed at room temperature using a rotary vacuum evaporator, which leaves a thin film of solid mixture deposited on walls of flask. The dried film can then be hydrated with aqueous media and gives a vesicular suspension.

3. Ether injection method

In this method solution containing drug-lipid complex is slowly injected into a hot aqueous medium through gauze needle and vesicle is formed readily.

4. Anhydrous co-solvent lyophilisation method

Drug powder and phospholipids dissolved in 1ml of Dimethyl sulfoxide (DMSO) containing 5% glacial acetic acid, after that agitates the mixture to get clear liquid. Freeze –dried overnight at condenser temperature. Then resultant complex flushed with nitrogen & Stored at 4°C.

5. Supercritical fluid process

This method is known as solution enhanced dispersion by complex supercritical fluid. Drug and lipid complex are premixed in a supercritical fluid of carbon dioxide, then high supersaturation is obtained by passing through the nozzle mixture chamber. The turbulent flow of solvent and carbondioxide results in fast mixing of dispersion leading to the formation of pharmacosomes.

6. Alternative Approach

An alternative approach for producing pharmacosomes is to synthesize a biodegradable micelle-forming drug conjunct from the hydrophobic drug Adriamycin and a polymer composed of polyxyethylene glycol and polyaspartic acid. This approach provides an advantage that all though micelle can be diluted, the drugs probably not precipitate due to the water solubility of the monomeric drug conjuncts.

Evaluation parameters for pharmacosomes:-

1. Complex Determination

The formation of complex and conjugate can be determined by the correlation spectrum observed in complex sample with that of discrete constituents and also with their mixture will be determined in the help of FTIR spectrum.

2. Solubility

With the help of shake –flask Techniques the determination of change in solubility due to complexation can be evaluated .In this techniques solubility of drug acid and drug PC- complex was determined in phosphate buffer 6.8 and n-octanol was also determined. In this technique, the drug acid and n-octanol i.e phosphate buffer at pHofdrug-phospholipid conjugated are mixed after constant shaking , equilibrium is maintanied with the temperature of 37 °C for 24 hrs. The separation of aqueous phase is occurring and concentration is determined using UV or HPLC techniques.

3. Scanning electron microscopy

Scanning electron microscopy detect the surface morphology of pharmacosomes. Drug content To determine the drug content in drug – pc complex , complex is equivalent to drug was weighed and added into volumetric flask with pH 6.8 Phosphate buffer . Then volumetric flask was stirred for 24 hrs on magnetic stirrer. After 24 hrs suitable dilution were made and measured for the drug content at 276nm UV spectrophotometrically.

4. Differential scanning calorimetry

This thermal analytical techniques is used to determine the drug – excipient compatibility interactions were recorded using a 2910 Modulated Differential Scanning Calorimeter V4.4E.The thermal behaviour was studied by heating 2.0+ 0.2 mg of each individual sample in a covered sample pan under nitrogen gas flow. The investigation were carried out over the temperature range 25-250 °C at a heating rate of 10°C min– 1. The interaction can be concludes by the elimination endothermic peaks, appearance of peaks and change in peak shape and its onset , peak temperature melting point and relative peaks area or enthalpy.

5. X-ray power diffraction (XRPD)

It is performed to determine the degree of crystallinity by using the relative integrated intensity of reflection peaks . The integrated intensity is given by the area under curves of the XRPD patterns and it represents the specimen characteristics.

6. Fourier transform infrared spectroscopy (FTIR)

With the help of IR spectroscopy the formation of complex can be confirmed by comparing the spectrum of complex with the spectrum of individual components and their mechanical mixture. In different time interval the stability can be determined by comparing the spectrum of complex in solid form with the spectrum of micro dispersion in water after lyophilisation techniques.

7. In – Vitro Study

Depending upon the expected therapeutic activity of biologically active constituents, model of in –vivo and in- vitro evaluation have been carried out. Surface Morphology With the help of scanning electron microscopy(SEM) or transmission electron microscopy (TEM) , the surface morphology can be observed. Purity grades of Phospholipid affected to shape and size of pharmacosomes and the process variables such as speed of rotation , vacuum applied or the method used.

8. Dissolution studies

Dissolution studies in vitro are done by using various models available using different buffers, then the results obtained are estimated on the basis of activity of the drug.

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