Available Online at www.ijpscr.info
International Journal of Pharmaceutical Sciences and Clinical Research 2021; 1(1):4-8

REVIEW ARTICLE

Formulation of Algosome – A Novel Carrier for Drug Delivery

Moguloori Sai Sowmya, A. Krishna Sailaja

Department of Pharmaceutics, RBVRR Women's College of Pharmacy, Affiliated to Osmania University, Hyderabad, Telangana, India

Received: 01-11-2020; Revised: 15-12-2020; Accepted: 10-01-2021

ABSTRACT

1-O-alkylglycerols (ALKGs) have exhibited several biological activities and a prominent effect on blood-brain barrier permeability. They have markedly improved brain uptake of cancerostatic agents. Since ALKG are amphiphilic, we explored their tendency to assemble into bilayer vesicles, which can be applied as carriers for drugs. Vesicles (Algosomes) were formed by film hydration method. A novel or vesicular drug delivery system is that delivers drug at predetermined rate decided as per the requirement, pharmacological aspects, drug profile, physiological conditions of body, etc. In current conditions not a single, novel drug delivery system behaves ideally those high goals with fewer side effects.

Keywords: 1-O-alkylglycerol, Algosomes, Drug release studies, Entrapment efficiency, Vesicle size determination

INTRODUCTION

In recent years, vesicles have become the vehicle of choice in drug delivery. Lipid vesicles were found to be of value in immunology, membrane biology, diagnostic techniques, and most recently, genetic engineering. Vesicles can play a major role in modeling biological membranes, and in the transport and targeting of active agents.[1]

Biological membranes form the ubiquitous delimiting structures that surround all cells and organelles. The bilayer arrangement of lipids is perhaps the only organizational feature that is common to all biological membranes. Numerous theoretical models of membrane structure have appeared since the publication of the cell theory by Schleiden and Sehwann in 1839. Experimental models provide insight into the motional dynamics and static structures of some isolated compartments of biological membranes.[2] Lipid vesicles are just one type of the many experimental models of bio membranes. Although developed for basic research, many technological innovations have arisen from the applications of these models. Lipid vesicles have evolved successfully, as vehicles for controlled delivery.[3]

Consequently, a number of vesicular drug delivery systems are present. It includes the following:

- Algosomes – Herbosomes
- Liposomes – Colloidosomes
- Noisomes – Sphinosomes
- Ethosomes – Proliposomes
- Pharmacosomes – Electrosomes
- Transferosomes – Layerosomes
- Ufosomes – Cubosomes
- Proniosomes – Coated vesicles
- Transdermal drug delivery system.

Future prospective in vesicular drug delivery system includes:

- Aquasomes – Virosomes
- Cryptosomes – Vesosomes

***Corresponding Author:**
A. Krishna Sailaja,
E-mail: shailaja1234@rediffmail.com

- Discomes – Proteasomes
- Emulsomes – Erythrosomes
- Enzymosomes – Archaeosomes
- Genosomes – Hemosomes
- Photosomes – Bilosomes.[4]

ALGOSOMES DEFINITION

- Algosomes are one of the novel carriers used for delivering the drugs and comes under vesicular drug delivery system.
- They form spherical vesicles for transporting the drugs to their specific target site.
- Algosome is a drug or a carrier delivery mechanism consisting of small and multi lamellar vesicle incorporating drug derived proteins to allow the algosomes to fuse with target cells.
- The prospect of drug delivery and targeting using algosomes is an interesting field of research and development.

COMPOSITION OF ALGOSOMES

- Algosomes are prepared in the form of vesicles by film hydration method using 1-O-Alkylglycerols (ALKG) [tetra, penta, hexa, hepta, octa, and nona-decylglycerols] in combination with cholesterol (CHOL) and dicetyl phosphate (DCP), consisting in the ratio of (ALKG:CHOL:DCP in 45:45:10 molar ratio).
- Optimum quantity of CHOL is used for the membrane formation and it maintains stability, integrity of the membrane.
- DCP is a phospholipid used for the vesicle formation.
- No polymer is required in vesicular drug delivery system.

PREPARATION OF ALGOSOMES

Algosomes were prepared using film hydration method. ALKG, CHOL, and DCP (Phospholipid) are dissolved in a suitable organic solvent (chloroform, ethanol, and acetone); these are placed under rota evaporator by keeping pressure which is depending on its boiling point, dry it such that the solvent is evaporated.

On microscopic examination, the algosomes were found to be conspicuously (in a clearly visible way) spherical and the dispersion was a mixture of multi and small lamellar vesicles. Then, 7.4 phosphate buffer was prepared at 55°C, that is, phase transition temperature, where no pressure and no heating (temperature) are applied. Only rotation time should be observed, where number of cycles per rotation is calculated.

Phase transition temperatures of 1-O-hexadecylglycerol (HXDG) and CHOL mixtures were tested by differential scanning calorimetry (DSC). The changes in phase transition temperatures indicate the vesicle forming tendency of ALKG in presence of CHOL.

Alkyl chain length dependent variation in vesicle size, zeta potential (ZP), and capture volume (CV) could not be observed. Vesicles of 1-O-tetradecylglycerol showed improvement in CV with increase in CHOL content from 15 to 55 mol%. However, the vesicle size decreased as shown in Figure 1.

On challenging algosomes with hypertonic salt solution (potassium iodide in water), vesicle size decreased, and thus, algosomes were found to be osmotically sensitive. Algosome dispersions on addition of higher concentration of potassium iodide, that is, KI (40–100 mM) brought about increases in vesicle size and at concentration 60 mM and above showed aggregation.

ADVANTAGES AND DISADVANTAGES

Advantages

- Increased bioavailability
- Increased solubility
- Dose can be reduced
- More entrapment efficiency (EE).

Disadvantages

- Vesicular toxicity
- Stability problems
- Skilled persons are required

- Preparation process is economical
- Oxidation occurs due to presence of phospholipid, that is, drug degradation and drug leakage.

CHARACTERIZATION OFALGOSOMES

Projection or binocular microscopy

On microscopic examination, the algosomes were found to be conspicuously (in a clearly visible way [or] in a way that attracts notice or attention) spherical and the dispersion was a mixture of multi-lamellar and small-lamellar vesicles. The Projection Microscope image was shown in Figure 2.

DSC analysis

Phase transition temperatures of HXDG and CHOL mixtures were tested by DSC. The instrument was shown in Figure 3

Vesicle size analysis

Vesicle size analysis is also called as particle size analysis. It is used to determine mean vesicle diameter.

Zeta-sizer

Zeta-sizer is used to determine the ZP, which identifies stability.

EVALUATION TESTS

Drug content

$$\text{Drug content} = \frac{\text{Pratical drug content}}{\text{Theoritical drug content}} \times 100$$

- Methanol is used for the vesicle destruction.
- 1 ml of suspension +9 ml of methanol (1 mg theoretical part)leave it for 30 min, then take supernatant and observe under UV-spectroscopy (practical part).[4]

EE

EE gives an idea about the % drug that is successfully entrapped/absorbed into nanoparticles. It is calculated as follows:

$$\%EE = \frac{\text{Drug added-Free unentrapped drug}}{\text{Drug added}} \times 100 / \frac{W - w}{w} \times 100$$

- The product and pH 7.4 buffer are added and kept under ultracentrifugation method using 17,000 rpm for 40 min and for a temperature of –4°C and then observe under UV-spectroscopy.

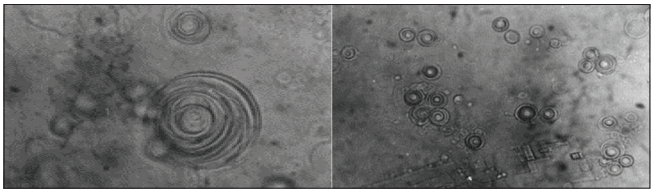

Figure 1: Algosomes in microscopic view

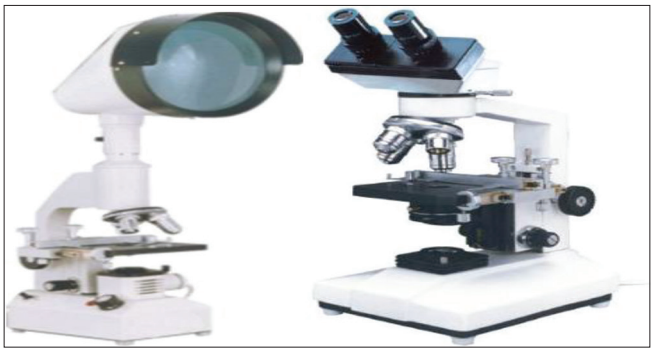

Figure 2: Projection and binocular microscope

Figure 3: Differential scanning calorimetry

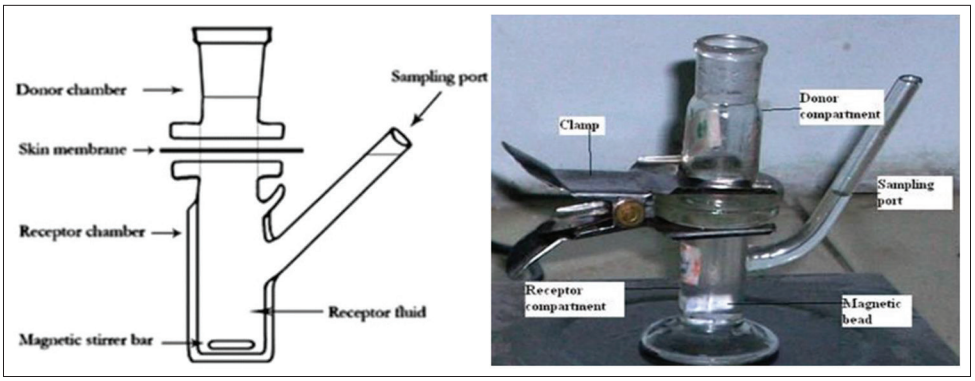

Figure 4: Franz diffusion cell apparatus

Drug release studies (*in vitro* studies)

- Franz diffusion cell is used for the determination of drug release studies.
- In these, 2 compartments are present, namely:

Donor compartment

Receptor compartment

- In donor compartment 1 ml of algosomal suspension is taken.
- In receptor compartment pH 7.4 phosphate buffer is considered.
- In between these 2 compartments, a semi-permeable membrane is present, which consists of an animal skin.
- The drug which is present in the donor compartment will permeable through the membrane and enters into the receptor compartment.[5]
- Then the samples were collected for the estimation of drug release accordingly as shown in Figure 4:
  - For 1st 30 min
  - Then after for every 1 h.

APPLICATIONS

ALKG has exhibited several biological activities. It shows a prominent effect on blood-brain barrier permeability. It also shows anticancer effects.

ALKG is extracted from the hepatopancreas of the crab *Paralithodes camtschaticus*, liver of the squid *Berryteuthis magister*, and liver of the skate *Bathyraja parmifera*, and their anticancer activity on human melanoma cells was observed.

They have markedly improved brain uptake of cancerostatic agents. Since ALKG are amphiphilic, we explored their tendency to assemble into bilayer vesicles, which can also be applied as carriers for drugs.[6]

Stability is considered to be good. Dose can be reduced. Dose regimen can be maintained. It has poor solubility.

It is the best control drug carrier delivery system, that is, sustain release. Vesicular drug delivery systems are particularly important for targeted delivery of drugs due to their ability to localize the activity of drug at the site or organ of action, thereby lowering its concentration at the other sited in body.

Both hydrophilic and hydrophobic drugs can be easily encapsulated. Bioavailability of drugs can also be improved. Elimination of rapidly metabolizable drug can be delayed. Circulation life time of drugs in the body can be prolonged.

Targeted delivery of drugs can often be achieved. Stability issues of liable drugs can be resolved. Toxicity issues of certain drugs can also be resolved.[7]

Scandinavian folk medicine used shark liver oil for the treatment of cancers and other ailments based on the rarity of tumors in sharks and their ability to resist infections. Shark liver oil is a source of ALKG which has been studied as anti-cancer agents in several clinical trials

CONCLUSION

Since ALKG is amphiphilic, we explored their tendency to assemble into bilayer vesicles, which can be applied as carriers for drugs.

Vesicles (Algosomes) were formed by film hydration method using ALKG incombination with CHOL and DCP (ALKG: CHOL: DCP in 45:45:10 molar ratio).

Algosome dispersions on addition with higher concentrations of KI (40–100 mM) brought about increases in vesicle size and at concentrations 60 mM and above it showed aggregation. All vesicular dispersions were stable for only a few days.

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