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ASPASOME: A NOVEL CARRIER FOR DRUG DELIVERY SYSTEM

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ABSTRACT

Novel drug delivery system can significantly improve the performance of bioactive in terms of patient compliance, safety, efficacy and novelty. Aspasomes is a novel carrier for drug delivery; it is an ascorbyl palmitate vesicle with their own biological activity. Ascorbyl palmitate is explored as bilayer vesicle forming material for Aspasomes. Ascorbyl palmitate formed vesicles in combination with cholesterol and a negatively charged lipid (dicetyl phosphate). Aspasomes are capable to suppress pigmentation of the skin and decomposition of melanin; it also improves elasticity of the skin by promoting the formation of collagen. Ascorbyl palmitate is more stable than ascorbic acid and its lipophilic character is beneficial for its skin penetration. This review article focus on the potential applications of Aspasomes as a drug delivery system, their method of preparation, mechanism of formation, Aspasome component and the problems associated with further exploitation of this drug delivery system. This drug delivery system can be characterized by photomicrography, vesicle shape, surface morphology, particle size analysis, scanning electron microscopy, differential scanning calorimetric, transdermal permeation and in vitro (release characteristics).

Keywords: *Aspasome, ascorbyl palmitate, cholesterol, dicetyl phosphate, pigmentation.*

INTRODUCTION

Nowadays, vesicle as a carrier system has become the vehicle of choice in drug delivery and lipid vesicles. Vesicles are found to be of value in immunology, membrane biology and diagnostic technique and most recently in genetic engineering.
Novel drug delivery attempts to either sustain drug action at a predetermined rate it also acts as protecting system which release the drug at target site and also by maintaining a relatively constant, effective drug level in the body with concomitant minimization of undesirable side effects. There has been a tremendous growth in the area of developing various new drug delivery systems. The novel drug delivery system is the most suitable and approachable in developing the delivery system which improves the therapeutic efficacy, drug targeting of new as well as pre-existing drugs. Thus provides controlled and sustained drug delivery to the specific site which meets the real, appropriate and well-timed drug demand of the body [1].

Ascorbyl Palmitate:

Ascorbyl palmitate is derived from corn dextrose fermentation and palm oil. Ascorbyl Palmitate is a highly bioavailable, fat-soluble derivative of ascorbic acid. Ascorbyl palmitate possesses all the benefits of vitamin C, but unlike the water-soluble form, is able to be stored in the lipid cell membrane until the body is ready to put it to use. Vitamin C offers a wide range of support for the human body. It is a potent antioxidant and free radical scavenger supporting cellular and vascular health. Vitamin C has been reported to promote nitric oxide activity as well as to help maintain healthy platelet function. Body's defense system is supported by Ascorbyl Palmitate through enhancing white blood cell function and activity, and increasing interferon levels, antibody responses, and secretion of thymic hormones.

Furthermore, this antioxidant has histamine lowering properties and increases lymphocyte formation. It is also essential for the formation and maintenance of intercellular ground substance and collagen, important for joint health. Vitamin C aids in the absorption of iron and the formation of red blood cells and converts folic acid to its active forms. Ascorbyl palmitate is derived from corn dextrose fermentation and palm oil.

Ascorbyl palmitate is an ester formed from ascorbic acid and palmitic acid creating a fat-soluble form of vitamin C. In addition to its use as a source of vitamin C, it is also used as an antioxidant food additive. Ascorbyl palmitate is known to be broken down (through the digestive process) into ascorbic acidand palmitic acid (a saturated fatty acid) before being absorbed into the bloodstream. Ascorbyl palmitate is also marketed as "vitamin C ester" [2, 3].

Uses of Ascorbyl Palmitate:

Various physiological support properties of ascorbyl palmitate possesses all the benefits of vitamin C, but unlike the water-soluble form, is able to be stored in the lipid cell membrane until the body is ready to put it to use. Vitamin C offers a wide range of support for the human body. It is a potent antioxidant and free radical scavenger supporting cellular and vascular health.

Vitamin C has been reported to promote nitric oxide activity as well as to help maintain healthy platelet function.

It supports the body's defense system by enhancing white blood cell function and activity, and increasing interferon levels, antibody responses, and secretion of thymic hormones. Furthermore, his antioxidant has histamine lowering properties and increases lymphocyte formation. It is also essential for the formation and maintenance of intercellular ground substance and collagen, important for joint health. Vitamin C aids in the absorption of iron and the formation of red blood cells and converts folic acid to its active forms [3].

Applications of Ascorbyl Palmitate (ASC-P):

1. Cosmetic ingredients
2. Solubilization of drug
3. Decrease viscosity of gel formulation
4. Skin moisturizing and penetration effect of ASC-P entrapped in SLN, NLC, and NE incorporated into hydrogel
5. Antioxidant
6. Stabilization of ASC-P by encapsulation in PLA nanoparticles
7. Skin permeation enhancer
8. Cytotoxicity against cancer cell
9. ASC-P vesicles (Aspasomes)

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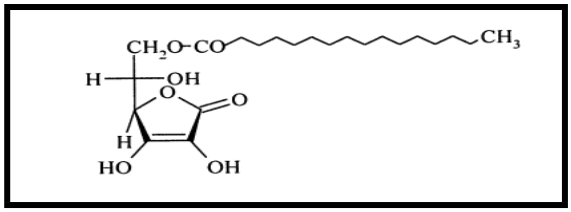

Fig 1. Chemical structures of ascorbyl palmitate

Physical and Chemical Properties:

Table No. 1: Physical and Chemical Properties of Ascorbyl Palmitate

S. No.	Nature	Physical and Chemical Properties
1	Form	Powder
2	Color	white - pale yellow
3	Odour	Odorless
4	Chemical name	2,3-Didehydro-L-threo-hexono-1,4-lactone-6-palmitate
5	Molecular weight	414.54 g/mol
6	Melting point/range	107 - 117 °C
7	Boiling point/boiling range	> 250 °C Decomposes on heating.
8	Bulk density	ca. 240 kg/m3
9	Water solubility	<= 1.8 mg/l (20 °C) practically insoluble
10	Partition coefficient	6.0 (n-octanol/water)
11	Solubility in other solvents	Methanol:183g/l(ca.22°C)
		Ethanol: 125 g/l (ca. 22°C)
		Peanut oil: 0.3 g/l (ca. 22°C)
12	Requirements for storage areas and containers	Protect from humidity, Protect against light. Keep container tightly closed and dry.
13	Storage temperature	< 77 °F (< 25°C)

Skin Whitening:

Ascorbic acid and ascorbyl palmitate play a major role in skin whitening, Conventionally what we mean by whitening is the elimination of the melanin that acts as a self defense mechanism for the human skin against the exposure to Ultraviolet light. The meaning of the expression "whitening", however, has evolved to mean far more. It entails inhibiting the further synthesis of melanin. Functional, natural cosmetics are in vogue recently, which carries the skin whitening function, for example, retinal and collagen. Cosmetics that contain the retinal, which is vitamin A, is quite good for removing freckles and stretch marks by retarding the skin's aging process and reliving it of pigmentation. Whitening cosmetics that contain vitamin C, on the other hand, are popular because they are effective in whitening and wrinkle elimination.

Products that help enhancing the skin's immunity are also recommended with best skin permeation rate. It is important not to forget that those products are just supplementary for the inhibiting pigmentation. Mainly the skin whitening ingredients works in three ways:-

1. By absorbing the UV rays, thus preventing the sun from darkening your skin.
2. By reducing the production of melanin, the skin pigment found in your skin which is responsible for skin darkening.
3. Most skin whiteners currently in the market contain ingredients- Hydroquinone, Ascorbic acid, Kojic acid, Glycyrrhetinic acid acts as direct inhibitors of tyrosinase, the enzyme in the skin pigment cells which produce melanin [4-6].

Aspasomes:

Aspasome is a ascorbyl palmitate vesicle with biological activity, Ascorbyl palmitate (ASP) is explored as bilayer vesicle forming material. It formed vesicles (Aspasomes) in combination with cholesterol and a negatively charged lipid (dicetyl phosphate).

Ascorbyl palmitate is Ascorbic acid esters which are amphiphilic in nature and a study delineating their surface active properties. It is capable to suppress pigmentation of the skin and decomposition of melanin; it can be used to whiten the skin. It also improves elasticity of the skin by promoting the formation of collagen. Ascorbyl palmitate is more stable than ascorbic acid. Its lipophilic character is beneficial for its skin penetration [7,8].

Rational for Using Aspasomes as Novel Drug Delivery System:

Many drugs which are used for skin whitening purpose is a hydrophilic or hydrophobic in nature, hydrophilic drugs are slowly penetrate through the skin, less stable and produce side effect when it is in direct contact to the skin hence we will need a carrier which enhance drug penetration and provide stability with reduce its side effect with the following rationales [7] :-

1. Aspasome Vesicles posses biological activity or with a targeting function in addition to carrier properties will have an added advantage.
2. They are capable to suppress pigmentation of the skin and decomposition of melanin; it can be used to whiten the skin.
3. They also improve elasticity of the skin by promoting the formation of collagen.
4. They are more stable than ascorbic acid. Its lipophilic character is beneficial for its skin penetration.
5. The Vesicles prepared with amphiphiles having antioxidant property may have potential applications towards disorders implicated with reactive oxygen species.
6. They Produce skin hydration effect and Penetration through skin are easier.

Method of Preparation of Aspasomes:

Film Hydration Method:

Formulation Ingredients for Aspasomes:

Table No. 1: Ingredients of Aspasomes [7]

S. No.	Ingredients	Uses
1.	Ascorbyl palmitate	Vesicles forming component
2.	Dicetyl phosphate	As a stabilizer
3.	Cholesterol	Provide strength to vesicle
4.	Chloroform and methanol	As an organic solvent
5.	Phosphate buffer (pH 7.4)	As a hydrating medium

Aspasomes is prepared by film hydration method under nitrogen atmosphere in which lipid mixture (ascorbyl palmitate: cholesterol) dissolved in chloroform and methanol (9:1 Ratio) in a round bottom flask and is kept under reduced pressure in rotary evaporator (Rotavapour Popular lab India) at 50°C till it formed a thin dry film on the walls of the flask. The dried thin lipid film is hydrated with 10 ml of phosphate buffered saline (PBS, pH 7.4) at the same temperature. The vesicles are then sonicated for 2 min using ultrasonicator. The Aspasomes is stored in nitrogen-purged vials [7].

Characterization of Aspasomes:

Photomicrography:

Photomicrographs of unsonicated Aspasomes is taken using LABORLUX S microscope fitted with camera at various magnifications, so as to confirm the formation and to understand the nature of vesicles [9].

Vesicle Shape and Surface Morphology:

Images of aspasome vesicle are record by using Scanning electron micrograph with different magnification; Analysis is performed at 25 ± 2°C. The lyophilized sample of aspasomal dispersion is placed on the grid and the image is capture [10, 11].

Determination of Vesicle Size, Zeta potential, and Polydispersity Index (PI) of Aspasomal dispersion:

The vesicle size, zeta potential and size distribution of ASP is measured by using Malvern Zetasizer. Vesicular dispersion are mixed with the appropriate medium (PBS, pH 7.4) and the measurements is taken in triplicate in a multimodal mode. All measurements are performing at 25˚C after 5min of thermal equilibration [12].

Percent Entrapment Efficiency:

To determine the entrapment efficiency, drug loaded aspasomes is to be prepared and the drug entrapment capacity of ASP is determined by using centrifugation method with cooling microcentrifuge (Remi instruments 4˚C at 12000 rpm for 15 min. The supernatant (free drug in PBS pH7.4) and sediment (vesicle entrapping the drug) are collected separately. Supernatant and sediment (After lysis of vesicles by Triton X-100 0.5% v/v) are removed and analyzed for drug quantity. The entrapment efficiency is calculated using the following equation [12, 13].

$$EE\ \% = [(T-S)/T] \times 100$$

Where, T is the total amount of drug detected both in supernatant and sediment; S is the amount of drug detected only in the supernatant.

Lyophilization:

For lyophilization freshly prepared ASP dispersion is used. The ASP dispersion containing the cryoprotectant (Trehalose) is frozen in liquid nitrogen. The samples are freeze-dried for 24 h at a temperature of -25˚C. The lyophilized ASP is used for DSC investigation and for long term storage stability of ASPs [11].

Differential Scanning Calorimetry:

Aspasome dispersions (Lyophilized) and anhydrous mixtures of ascorbyl palmitate, cholesterol and dicetyl phosphate are studied by Differential Scanning Calorimeter (Mettler DSC 821e, Mettler-Toledo, Switzerland) to understand the thermotropic properties and phase transition behavior. Analysis is carried out in conventional aluminium pan with a heating rate of 5˚C/min [14,15] .

In Vitro Release Study:

Aspasomes preparation is subjected to release studies using dialysis apparatus. Prior to release study; maximum extent of unentrapped drug (model drug) is removed by dialyzing the original preparation. A dialysis membrane weight cut off between 12000 and 14000 is used for this study. The membrane is soaked in distilled water for 12 hours before the release study. Five milliliters of dialyzed aspasome preparation is subjected to release studies. 16 ml of PBS pH 7.4 is placed in receptor cell. Dialyzed aspasome preparation (in PBS, pH 7.4) is transferred to donor cell and a two-milliliter sample is drawn from the receptor cell at preset intervals over a period of 18 h. At each time immediately after removal of sample, the medium is compensated with PBS. The samples are analyzed for drug by UV spectrophotometer. Model drug solution (in PBS, pH 7.4) served as control. All experiments are performed in triplicate and values are reported as mean ± standard deviation [16].

In Vitro Transdermal Permeation Study:

The in-vitro skin permeation of drug loaded aspasomal formulations are studied using Franz diffusion cell with an effective permeation area and receptor cell volume of 2.54 cm^2 and 16 ml, respectively. The temperature is maintained at 37 ± 0.5˚C. The receptor compartment contained 16 ml PBS (pH 7.4) and is constantly stirred by magnetic stirrer at 100 rpm. The dorsal skin of albino rat is washed with distilled water and used. The skin then placed on aluminium foil and the dermal side of the skin is gently teased off any adhering fat and/or subcutaneous tissue. The rat skin is mounted on a receptor compartment with the stratum corneum side facing upward into the donor compartment. The aspasomal formulation (200 µl) is applied on the skin in donor compartment. Samples (1 ml) is withdrawn through the sampling port of the diffusion cell at predetermined time intervals over 16 h and analyzed for drug content. The receptor phase immediately replenished with equal volume of fresh diffusion buffer.

The amount of drug deposited in the skin is determined at the end of the In-vitro permeation experiment (16 h). The skin washed 10 times using a cotton cloth immersed in methanol. The skin samples is washed with 5 ml of distilled water and the drug content of the skin is determined by homogenizing it with distilled water (10 ml) and assaying the filtrate (0.22 µm filter), the amount of drug determined by measuring the absorbance using spectrophotometer. The cumulative amount of drug permeated, Transdermal flux (J) µg/cm^2/h, and skin deposition is calculated [16, 17].

CONCLUSIONS

Ascorbyl palmitate formed vesicles (Aspasomes) in the presence of cholesterol and dicetyl phosphate, encapsulating drug solution. The antioxidant potency and its capability to suppress pigmentation of the skin can be used to whiten the skin. Thus, they may find applications as drug delivery system which is use for whitening or brightening the pigmented skin. Aspasomes also enhances the transdermal permeation of drugs. The antioxidant property and lipophilic character indicate it is a promising tool for transdermal drug delivery system. It also improves elasticity of the skin by promoting the formation of collagen.

The Aspasomes is highly efficient in the treatment of skin pigmentation disorders and produce whitening effect on skin, because of its promising feature it is explored as a promising carrier for drug delivery especially in case when the antioxidant activity and whitening effect required.

REFERENCE:

1. Robinson JR and Lee VHL. In Controlled Drug Delivery:Fundamental Applications, **1987**; 2(N4): 7.
2. Ritter E.; Cohen, N; Rubin, SH. "Physiologic availability of dehydro-L-ascorbic acid and palmitoyl-L-ascorbic acid". Science. **1951**; 113(2944): 628 631. doi:10.1126/ science.113.2944.628.PMID 14845692.
3. Moribe K. Limwikrant W. Higashi K. Yamamoto K. Drug nanoparticle formulation using ascorbic acid derivatives. J. of Drug Delivery. **2011**; 1-9.
4. Parvez S. Kang M. Chung H. S. Cho C. Hong MC. Shin MK. Bae H. Survey and mechanism of skin depigmentation and lightening agents. Phytother. Res. **2006**; 20: 921-934.
5. Nikolaou V. Stratigos A J. and Katsambas AD. Established treatments of skin hypermelanoses. J. of Cosmet. Derm. **2006**; 5: 303–308.
6. Nudelmanl A. Ben-Ishail Z. Ruse M. Schamrothz J. Skin-depigmenting prodrugs of hydroquinone. Eur. J. Med. Chem. **1993**; 2: 159-164
7. Gopinath, D., Ravia, D., Raoa, B.R., Apte, S.S., Renuka, D., And Rambhaua, D. Ascorbyl palmitate vesicles (Aspasomes): formation, Characterization and application. Int. J. Pharm., **2004;** 71: 95–113.
8. Doijad R. Manvi F. Godhwani B. Joseph R. Formulation and targeting efficiency of cisplatin engineered solid lipid nanoparticles, Ind. J. Pharm. Sci., **2008**; 70: 7-20.
9. Lau KG. Hattori Y. Chopra S. Ultra-deformable liposomes containing bleomycin: In vitro stability and toxicity on

human cutaneous keratinocyte cell lines. Int. J. Pharm. **2005**; 300: 12-4.
10. Ewoud CA. Winden V. Crommelin DJA. Short term stability of freeze-dried, lyoprotected liposomes. J. of Control. Rel. **1999**; 58: 69–86.
11. Mehnert W. Schwarz C. Freeze drying of drug free and drug loaded solid lipid nanoparticles. Int. J. Pharm., **1997**; 157: 171-79.
12. Castelli F. Sapietro GM. Puglia C. Rizza L. Bonina F. Characterization of indomethacin loaded lipid nanoparticles by differential scanning calorimetry. Int. J. Pharm., **2005**; 304: 231-238.
13. Mohamed MN. In vitro release of hydrophilic and hydrophobic drugs from liposomal dispersions and gels. Act. Pharm., **2006**; 56: 311-324.
14. Dubey V. Mishra D. Jain NK. et. al. Dermal and tarnsdermal delivery of an anti –psoriatic agent via ethanolic liposomes. J. Control Rel., **2007**; 123: 148-54.
15. Castelli F. Sapietro GM. Puglia C. Rizza L. Bonina F. Characterization of indomethacin loaded lipid nanoparticles by differential scanning calorimetry. Int. J. Pharm., **2005**; 304: 231-238.
16. Dragicevic-Curic N. Winter S. Stupar M. Temoporfin-loaded liposomal gels: Viscoelastic properties and in vitro skin penetration. Int. J. Pharm., **2009**; 373: 77-84.
17. Mourtas S. Haikou M. Theodoropoulou M. The effect of added liposomes on the rheological properties of a hydrogel: A systematic study. J. Colloid. Interf. Sci., **2008**; 317: 611-9.

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