

## ADVANCES IN NOVASOME TECHNOLOGY- A REVIEW

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## ABSTRACT

Novasome was created a few years back in an attempt to modify the liposomal drug delivery and other similar systems. It offers a seven bilayer membrane which has the ability to incorporate both water soluble and insoluble drugs. It has an excellent entrapment efficiency which provides better medication. Formulation of Novasomes is achieved in a high shear device. Due to its numerous advantages, Novasomes have found their applications in various fields like cosmetics, chemical, personal care, foods, pharmaceuticals and agrochemicals. Many products have already been introduced in the market using this technology with a proposal of further more launches. Novasomes has become one of the most advanced derma cosmetics because of its penetration depth. Novasomes are continuously being researched upon in an attempt to obtain enhanced release characteristics.

**Keywords:** Innovation, Bilayered, Non phospholipid, Paucilamellar, Micro vesicles, Advances, Novasome.

## INTRODUCTION

Novasome micro vesicles are the paucilamellar vesicles that are formed from many biocompatible phospholipids and single tailed amphiphiles. Novasome is an effective drug delivery system for a variety of drugs. Novasome is a patented technology developed by the IGI laboratories Novavax. Novasomes are an innovation of the liposomal drug delivery system or a variation of other similar drug delivery systems. Novasome can be defined as paucilamellar vesicles of 200 to 700 nanometres in diameter consisting of 2 to 7 bilayered membrane each composed of amorphous core and amphiphilic molecule. The core accounts for most of the Novasome vesicular volume thus accommodating a high capacity of water immiscible and water soluble drugs. The Novasome micro vesicles are inherently stable and are tailored to be stable at pH range of 2-13 and the temperature ranges from the liquid nitrogen to the temperature above the boiling point of water.[1].

Novasome offers sustained release action. There is no proper array arrangement of the Novasome bilayers. Novasomes can bear any charge and thus function accordingly. For example, if the charge on the Novasome microvesicles is positive, it can combine with the skin, hair or mucous membrane of negative charge. They can also adhere to the hair shafts. Incompatibility problems can be avoided with the

use Novasome technology by incorporating the incompatible drugs between the bilayers. Novasomes increase the efficacy and efficiency of the treatment with almost no side effects. They are natural and do not cause any kind of cytotoxicity. Because of the wide range of pH offered by Novasomes, they can be used for a wide range of applications. Novasomes can be formulated to the desired release action and absorption level. Novasome can be considered as one of the most effective method to treat skin disorders.[1]

Novasome molecules have a hydrophobic tail group attached to a hydrophilic head group. These molecules include long chain acids, long chain fatty alcohol derivatives and long chain amino and glycerolipids. They are prepared from a mixture of cholesterol, free fatty acids and monoester of polyoxyethylene fatty acids. They have a uniform size distribution that depends upon a wide variety of membrane constituents that are chosen individually for each purpose with encapsulation efficiency of 99-100% for lipid materials and 78-88% for aqueous materials [2].

The water soluble materials get incorporated into the aqueous spaces and the lipid soluble materials gets incorporated inside the core of the vesicle. The greater part of the vesicle is occupied by the amorphous core that incorporates finely divided insoluble particles like diamonds and titanium dioxide, water soluble particles.[2]

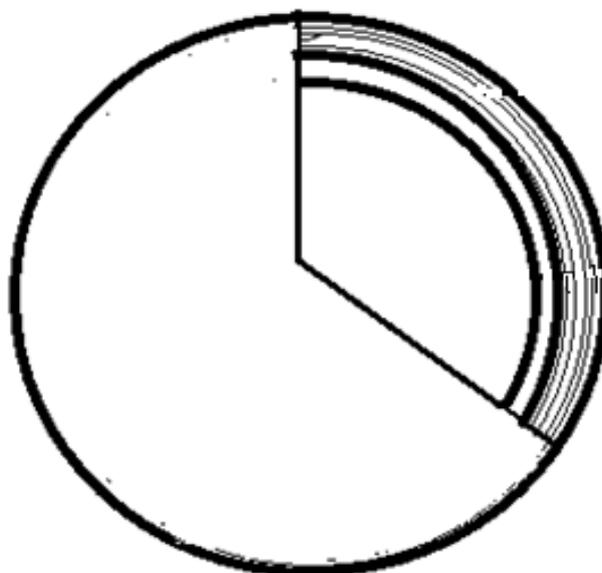


Fig. 1: Diagrammatic representation of Novasome

**Table 1: Characteristics and Advantages of Novasome**

Characteristics	Advantages
<ul style="list-style-type: none"> <li>• The ability to have a negative, positive or neutral charge.</li> <li>• A large volume of water soluble drugs can be incorporated.</li> <li>• Uniform sized vesicles can be predicted.</li> <li>• Depending on the various conditions it can adhere to skin or hair shaft</li> <li>• The release rate is predictable</li> <li>• Up to 80% of the drug can be loaded in the Novasome</li> <li>• Frequent applications can be allowed</li> <li>• It contains a high capacity core with seven membered bilayer surrounding.</li> <li>• Prevents the skin from drying away</li> <li>• Smaller volume can accommodate large amounts of drug [3]</li> </ul>	<ul style="list-style-type: none"> <li>• Residues are not left on the skin and they are rehydrated over extended periods of time.</li> <li>• Improved aesthetics</li> <li>• Higher stability</li> <li>• Rinsing is resisted due to the enhanced adherence to the skin.</li> <li>• Enhanced product stability</li> <li>• Cost effective</li> <li>• Both hydrophilic and hydrophobic drugs can be incorporated.</li> <li>• Reduces product irritation</li> </ul>

**Mechanism of drug release**

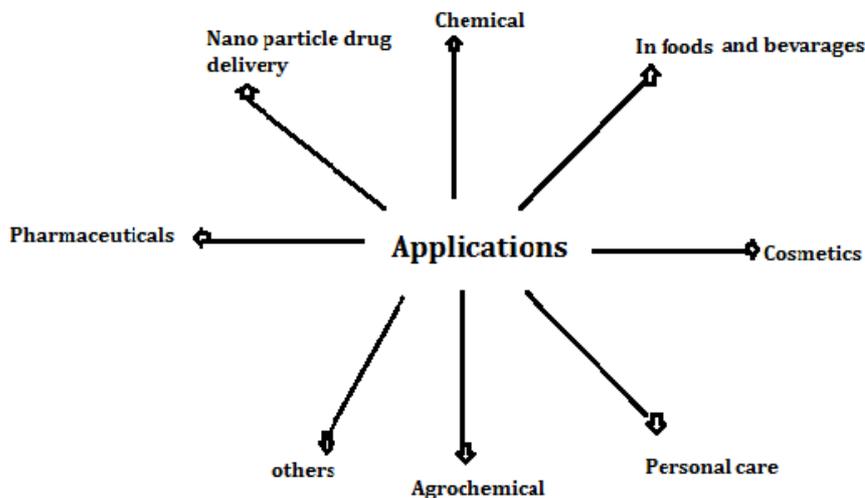
The particles move within the bilayers by making random jumps between the channels contained within the bilayers offering continuous release. The charge on the micro vesicles can be made net positive, net negative or no net charge. The drug is entrapped in a protected manner in the core making it effective and efficient delivery system. This also improves the stability and storage of the micro vesicles.[4]

**Formulation of Novasome**

A high shear device that produces high shear rates is required for the formulation of Novasomes. The devices that can be used for the formulation of Novasomes are French pressure cell and Micro fluidizer. Other devices can also be used that produces high shear rates and have the ability of handling semi viscous and heated lipids.

An advanced device is used now a day to manufacture Novasomes. It includes a mixing chamber that is cylindrical with an inlet orifice located tangentially. The other orifices lead to a reservoir that contains the different phases. The phases include the aqueous phase and the lipophilic phase. A turbulent flow is produced inside the chamber when the reservoir is connected to the pumps. The mixture taken is usually a charge producing agent, a non-phospholipid surfactant a target molecule and an antioxidant. This mixture is first heated and then blended. This mixture is again blended with the aqueous phase containing an aqueous soluble collagen and an aqueous buffer. The micro vesicles are formed in less than a second and can be removed from the axially located discharge orifice of the chamber. Now a new technology has been proposed to prepare the Novasomes using N-acyl sarcosinates by Wallach et.al[5]. This technology has been used for controlled and sustained delivery of emollients or fragrant oils.

**Applications of Novasome**



**Fig. 2: Applications of Novasome**

**Advances in Novasome Technology**

Novasome technology is the most advanced derma cosmetics technology that expands the boundary of dermatology science. Novasome vesicles not only penetrate the deepest layers of the skin easily (figure 3), but they also penetrate into the targeted cell as pre-programmed.

Novasome based dermatological products were studied at Cornell University in two common clinical situations. The first study evaluated the effectiveness of Novasomes based versus non

encapsulated emollients in the management of winter time dry skin in dogs, in which 20 affected dogs were treated with both type of products. The results showed that the Novasome based emollient was the superior agent in 80 percent of the Dogs. This study proved that Novasome can serve as potent Humectants. The second study evaluated Novasome and Non- Novasome based shampoos that contained Benzoyl peroxide. The test results showed that Novasome based shampoos decreased scaling in 70 percent of the subjects while the Non-Novasome based shampoos showed decreased scaling in only 20 percent [6].

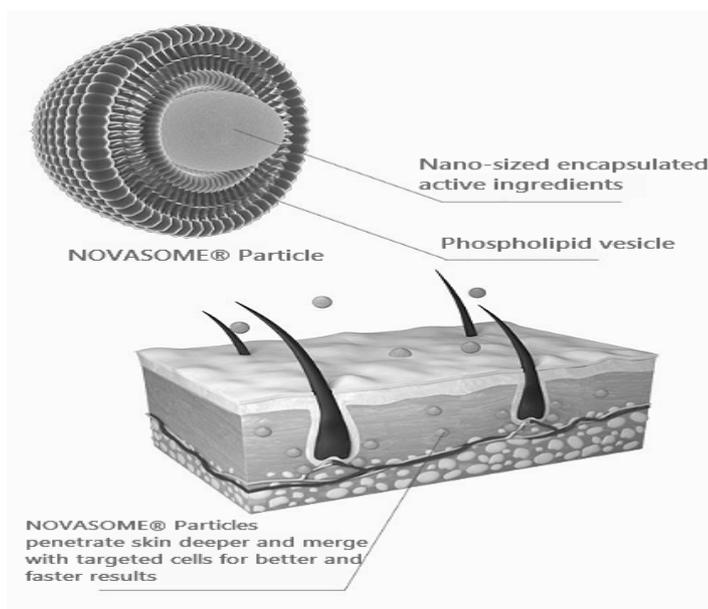


Fig. 3: Novasome penetration to the deepest layer

Recent advances in veterinary topical agents have followed the human field and Novasome based sustained release veterinary products are now available to pets for long lasting skin hydration and delivery of antipyretic agents. Sustained release technology is one such breakthrough that uses Novasome micro vesicles to encapsulate moisture within skin treatments, shampoos and sprays to achieve a hydrating effect. These non-ionic vesicles of glyceryl dilaurate with cholesterol and polyoxyethylene-10-stearyl ether have been known to deliver greater amounts of cyclosporine into and through the mouse skin than phosphatidylcholine or ceramide based vesicles [7].

Mills et al. patented the Novasome technology for the delivery of Mahonia aquifolium extract [4] in the treatment of psoriasis, eczema and other dry skin conditions. The preparation containing 5-20 percent of Mahonia aquifolium extract along with other excipients is used in Novasome (liposomal) delivery system. From the study, it was found to be effectively utilized as lotion or cream in topical application to the affected area [4]. Studies showed that Novasome technology has improved localized delivery of H2 antagonists for the treatment of periodontal diseases due to increased local absorption of the H2 antagonist and enhanced drug action. It also finds applications in the management of inflammatory skin and other disorders [8].

Novasome technology has been extensively used for the preparation of vaccines. Small pox vaccine has been developed based on Novasome. The other Novasome based vaccine is still under development. The Novasome based vaccines have been used for the immunization of fowl against Avian Rheovirus and New castle disease virus [9]. Novasome micro vesicles inactivate viruses such as corona viruses, orthomyxoviruses, retroviruses and paramyxoviruses by fusing with enveloped virus and nucleic acid of the virus that denatures shortly after the fusion. The Novasomes are also used as an adjuvant in the vaccines. It was found that Novasomes has been currently used as potent adjuvant for the

human vaccines (aluminium phosphate) when Gupta et al [10]evaluated the Novasomes composed of cholesterol, oleic acid and dioxyethylene cetyl ether with Diphtheria toxoid and tetanus toxoid. Chambers et al. [11]found that a single dose of formalin-inactivated BCG mixed with Novasome™ when administered to guinea pigs as a single subcutaneous inoculation protected them from lethal tuberculosis. Novasome-WFI diluents (paucilamellar, non-phospholipids liposome encapsulating cherry flavoured oil) have been used in oral vaccine by Wright [12]for prevention against gram negative bacterial infections. In the preparation of oral vaccine the Novasome lipid vesicles are diluted with WFI in a ratio of Novasome: WFI of 1:32(v/v) to maintain 99.2% of water.

The Novasome micro vesicles have also been used as an adjuvant with influenza virus like particles as a candidate for avian influenza by Pushko et al [13]. The Parathyroid hormone analog PTH (1-34) was successfully encapsulated in Novasome(R) cream by Holick et.al enhanced the absorption of this peptide drug into the human skin. The psoriatic lesions treated with PTH (1-34) showed marked improvement in erythema and scaling. This was the first demonstration for the successful encapsulation of a peptide drug for the treatment of skin disease [9]

The topical delivery of Minoxidil was increased by making it more hydrophilic by the use of Novasome micro vesicle and an organic acid or a base such as lactic acid. Fuels enhanced with patented lipid vesicles (Novasome®) and dispersion assistant molecules to deliver water and water soluble fuel additives in fuels has been used that gives enhanced performance characteristics compared to conventional fuels [14].

Novasome is marketed as skin cleansers, skin- protective agents, oil and moisturizers as given in table 2. Novasome offers greater resistance to acidity, alkalinity and temperature. Hence products can be easily incorporated by the use of this technology.

Table 2: Marketed products of Novasomes and their uses

Product name	Ingredients	Use	Reference
Relieva@shampoo	Mahonia aquifolium, Novasome micro vesicles	Psoriatic plaque	[15]
Novasome I	Cyclosporine, a-interferon, Novasome micro vesicles	In hamster Ear model produced high levels of drug	[17]
AcneWorx	2% Salicylic acid, Novasome micro vesicles	Adult Acne and dry skin	[17]
Novasome ®	Small Pox vaccine	Small Pox	[16]
Nova Pearls	Salicylic acid or Sulphur, Novasome micro vesicles	Deodorant, shampoos	[17]
MPA- Seba Hex	2% Chlorhexidine Gluconate, sulfur, salicylic acid, Novasome Micro vesicles	Antibacterial, Antifungal,	[18]

**Novasome® based products on the market today include**

1. Estee Lauder, Pierre Fab, and Neutrogena have marketed lines of cosmetics using Novasomes® for years.
2. Chattem Pharmaceuticals offers Icy Hot, a line of OTC pain therapy creams, lotions and patches as endorsed by Shaquille O'Neal and Mia Hamm. The line is in the process of going worldwide.
3. Complexions by Dr. Watts, a prominent New Jersey plastic surgeon used Home Shopping Network to introduce a line of anti-wrinkle facial beauty creams and treatments. The products sold so well that HSN's website continues offering the line.
4. Super Foods Rx recently introduced its SFRx Complex Age Defying Serum, a line of natural ingredient skin care creams and lotions.
5. Apollo Pharmaceuticals has recently begun marketing Relieva cream, lotion, and shampoo for the treatment of psoriasis.
6. Amore Pacific of Korea, one of the world's 10 largest consumer care products companies recently launched through its Laneige division, a moisturizing cream and gel in its popular Water Bank products line.
7. Vetoquinol USA markets a broad line of animal care products worldwide, including vaccines, pharmaceuticals and grooming.
8. Dermworx has recently begun marketing an adult acne product.
9. Dermatology Associates of Georgia; a physician healthcare group has recently introduced a collection of skin care products for its patient base and available online.
10. Johnson and Johnson has been a long-term IGI customer using Novasomes® in some of its retinoid products.
11. MIAJ anti-wrinkle cosmetics developed by IGI are now available online at MIAJ.com. [19]

**Novasome based products in development**

1. Manhattan Pharmaceuticals recently announced completion of enrolment for its Novasome® based phase 2A clinical trial for (PTH) 1-34 psoriasis treatment.
2. Dermworx is developing a group of products including treatment for psoriasis, and has forwarded to IGI an initial \$250,000 payment as part of a \$1 million licensing agreement.
3. Bharat Biotech of India is developing animal vaccines using Novasomes®.
4. Dr. Mark A. Pinsky, a Florida Board Certified Plastic Surgeon has applied for a patent to administer collagen to human subjects using Novasomes®. In addition Dr. Pinsky has also developed a skin care line he intends to market.
5. Pharmachem Laboratories, a leading manufacturer and supplier of value-added nutritional ingredients for beverages, foods, flavours and fragrances is developing a group of Novasome® based products. Pharmachem has directly invested \$1.5 million in IGI stock.
6. The Company received a grant from the National Cancer Institute to evaluate the safety and therapeutic potential of its Novasome® technology in conjunction with a Parathyroid hormone PTH (7-34) for treating baldness (Alopecia) as a result of chemotherapy for breast cancer. Dr. Michael Hollick, M.D. a Professor of Medicine, at Boston [19]

**CONCLUSION**

From various studies it was found that Novasomes increase product stability, extend shelf life from weeks to sometimes years, prevent oxidation and emulsification, and permits isolating antagonistic ingredients within the formulation until use. Novasomes also enables the control release of active ingredients through heat, pressure and/or time. Time release is especially beneficial, as it has shown to be more therapeutic and significantly less irritating than products that dump a full dosage on the skin at one time. It was shown to have entrapment efficiency. The incremental cost of manufacturing products using Novasomes is minimal. It has applications in the fields of foods, cosmetics, pharmaceuticals, chemical, agrochemical, personal care and others. Continuous advances are being made in Novasome technology. Many Novasome based products are under development to be launched into the market.

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