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CURRENT REVIEW ON TRANSFEROSOME: A NOVEL DRUG DELIVERY SYSTEM

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Abstract:

A unique drug delivery system is an innovative approach to medication delivery that solves the shortcomings of standard drug delivery systems. Our country has a vast Ayurvedic knowledge base whose potential has just recently been exploited. If innovative drug delivery technology is used in herbal medicine, it may improve the efficacy and reduce the negative effects of diverse herbal compounds and herbs. Due to a lack of scientific explanation and processing problems, such as standardisation, extraction, and identification of specific medication components in complex polyhedral systems, development as innovative formulations. This review will provide a thorough understanding of the various types of bioactive chemicals, as well as those specifically involved in skin and topical application, novel methods to TDDS, specifics of transferosome, comparison of phytososme, liposome, and transferosome, and widespread application of transferosme.

Keywords: *Phytochemicals, Bioactive compounds, Novel drug delivery systems, Transferosome,*

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INTRODUCTION:

Most therapeutic therapies are ineffective or ineffective for a variety of reasons, including hepatic first-pass metabolism, unpleasant side effects, rejection of invasive treatments, and poor patient compliance. As a result, numerous medication delivery systems have been created and investigated over the last several decades to address these issues. Transdermal delivery systems, which are minimally invasive and do not have first-pass effects, are one possible technique. However, the skin's barrier function, which inhibits or dampens transdermal distribution of medicinal substances, must be addressed (Alavi *et al*., 2017; Paolino *et al*., 2006).
Transfersomes are made up of phospholipids and an edge activator (EA), which is a membrane-softening substance (such as Tween 80, Span 80, and sodium cholate) that allows the transfersomes to be ultra-deformable. When transfersomes reach the skin pores, they might change their membrane flexibility and pass through the pores on their own. The difference in transdermal water activity caused by the natural transdermal gradient generates a significantly strong force that acts on the skin via transfersomes vesicles, which force the widening of intercellular junctions with the least resistance and thus generate transcutaneous channels 20-30 nm in width. These channels enable the movement of ultra-deformable, slimed transfersomes across the skin in relation to the hydration gradient (Modi and Bharadia, 2012; Chaurasiya *et al*., 2019).

Furthermore, the osmotic gradient forms as a result of evaporation of skin surface water due to body heat, and it acts as a driving force to facilitate flexible transport across the skin to delivery therapeutic agents from the site of application to the target area for local or systemic treatments at effective therapeutic concentrations with minimal systemic toxicity. Transfersomes outperform typical liposomes in terms of penetration efficiency (through microscopic skin channels), but they share a bilayered structure that allows for the encapsulation of lipophilic, hydrophilic, and amphiphilic drugs. Transfersomes differ from liposomes principally due to their softer, more adaptable, and ultra-deformable artificial membranes. Because of the interdependence between the local composition and the form of the lipid bilayer, the vesicles are both self-optimizing and self-regulating. This feature allows transfersome vesicles to efficiently cross a variety of transport obstacles (Pawar, 2016; Darajat *et al*., 2023).

Additionally, nature has been a source of medical substances for thousands of years, and an astounding number of modern medications have been identified from natural sources, many based on their usage in traditional medicine. Various medicinal plants have been utilised to treat disease all around the world for many years. They have been used as a medical source. The presence of natural items with therapeutic characteristics has been linked to the widespread usage of herbal treatments and healthcare preparations, such as those documented in ancient books like the Vedas. Plants, in reality, create a wide spectrum of bioactive chemicals, making them a rich source of various sorts of medications (Baker *et al*., 1995).

Herbal medicines have attracted a lot of attention in recent years as an alternate option to compensate for perceived flaws in mainstream pharmacotherapy all over the world. Despite a lack of medical data to back up their therapeutic efficacy and toxicological effects, the use of herbal medicine has grown significantly. Traditional medicines have gained increased appeal in Africa as a result of the unavailability, undesired side effects, and high costs associated with orthodox medicines, as well as poor health facilities and healthcare experts, as well as inadequate health worker training (Piero *et al*., 2012). The phytochemicals in these medicinal plants, particularly flavonoids, alkaloids, sterols, terpenoids, phenolic acids, stilbenes, lignans, tannins, and saponins, are responsible for their therapeutic benefits (Ali and Alqurainy, 2006).

Herbal plants with excellent medical properties are significant in many ways for the existing system of herbal and natural medication identification because they can be used directly as a source of bioactive and medicinal components. Furthermore, these bioactive substances are frequently employed to create more sophisticated semisynthetic chemical compounds based on herbs. The use of medicinal plants has become increasingly important in many developing countries around the world, particularly in primary healthcare for both communities and individuals. The demand for medicinal plants has surged in the marketplace due to their ease of availability, low cost, apparent efficacy, insignificant apparent side effects, and the concept that plant-based products are safer than allopathic drugs. Drug discovery appears to be a challenging task to uncover vigorous and suitable leads, which is actually a process that begins with researching medicinal plants and ends with the identification of bioactive ingredients, which requires patience and experience. Regardless of their compound design variability, breakthroughs in advancements have brought up a revolution in preliminary examination of normal things while searching for novel pharmaceuticals (Fabricant &

Farnsworth, 2001; Balandrin *et al*., 1993; Lahlou and Mouhssen, 2013).

Some chief bioactive compounds are:

Alkaloids

Alkaloids are nitrogenous bases (often heterocyclic) that are the most structurally varied class of secondary metabolites. They range from simple to complicated structures, such as those found in many neurotoxins. In very rare cases, they contain sulphur, as in the diothiolanes isolated from Brugeira species. Their diverse pharmacological properties have always piqued man's curiosity, and alkaloids have been used as poison for hunting, murder, and euthanasia, as euphoriants, psychedelics, stimulants, and medicine. Many basic nitrogen compounds found in higher plants are strong inhibitors of numerous oxidative processes both in vivo and in vitro (Bribi, 2018; Pelletier, 1983).

Flavonoids

Anthocyanins, catechins, flavanones, flavones, isoflavones, and flavonols are phenolic chemicals that belong to the flavonoid family. More than 4,000 flavonoids have been identified, and they are abundant in fruits and vegetables, with the highest concentrations found in berries, citrus fruit, broccoli, cabbage, cucumber, green pepper, and so on. Flavonoids have been found to offer numerous health benefits, including the capacity to prevent cancer, cardiovascular disease, urinary tract infections (UTIs), and other degenerative diseases. These anti-disease effects of flavonoids may be attributed primarily to their strong antioxidant properties, as well as other biological properties such as action against allergies, inflammation, free radicals, hepatotoxins, platelet aggregation, bacteria, viruses, ulcers, and tumours (Nijveldt *et al*., 2001; Grotewold,2006).

Saponins

Saponins are plant chemicals that exist as steroid alkaloids, triterpene glycosides, or steroids. These phytochemicals are recognised to have anticarcinogenic, immunostimulant, and hypocholesterolaemic effects. Saponins are hypoglycemic because they stimulate pancreatic -cells, impede glucose transport across the brush border cells of the small intestines, and reduce glucose transfer from the stomach to the small intestines. Saponins have also been shown to decrease stomach emptying in a dose-dependent fashion. Saponins reduce cholesterol levels by creating big micelles, which are expelled in bile. These chemicals are reported to reduce serum levels of low density lipoprotein cholesterol and cholesterol absorption in the intestines (Tan and Vanitha, 2014; Chung, 2004)

Terpenoids

Terpenes, also known as isoprenoids, are the most abundant phytonutrient class in green foods, soy plants, and grains. Terpenes are important to plants because they are required to ®x carbon through photosynthetic processes employing photosensitizing pigments. This reliance on photoreactive chemistry, along with plants' incapacity to migrate to avoid irradiation, places a heavy emphasis on a range of phytochemical protectants from oxidative processes. Animals have evolved to use these compounds for hormonal and growth regulatory functions (vitamin A), and the presence of these molecules in animal tissues also provides some protection from certain diseases, particularly those associated with chronic damage and growth dysregulation, as is now being discovered. Terpenes have a specific antioxidant activity when they interact with free radicals. Terpenes respond to free radicals by partitioning into fatty membranes due to their long carbon side chain. Tocotrienols and tocopherols are two of the most studied terpene antioxidants (Jahangeer *et al*., 2021; Jaeger *et al*., 2016).

Glycosides

The term glycoside refers to a class of natural compounds made up of two molecules: a sugar and an aglycone. The sugar molecule is mostly D-glucose, although it can also be L-rhamnose or L-fructose. Any natural substance, such as a flavonoid or terpene, can be used as the aglycone (Gerges *et al*., 2022).

Phenolic acid

Phenolic acids are aromatic secondary plant metabolites found in a wide range of plants. Natural phenolic acids are classified into two groups: cinnammic acid derivatives such as ferulic acid and caffeic acid, and benzoic acid derivatives. Ferulic acid, a phenolic acid, has been shown to have a wide range of therapeutic effects in the treatment of diseases such as diabetes, cancer, neurodegenerative, cardiovascular, and inflammatory diseases. These therapeutic effects are thought to be due in part to this phenolic acid's antioxidant activity. Ferulic acid inhibits lipid peroxidation and scavenges free superoxide radicals. The structural features of phenolic acids contribute to their antioxidant activities. These compounds feature a phenolic nucleus and an unsaturated side chain that can generate a phenoxy group that is resonance stabilised. When reactive radicals interact with these chemicals, they gain a hydrogen atom and produce a phenoxy

radical. TNF-alpha, prostaglandin E2, and other inflammatory mediators are reduced by phenolic acids and their ester derivatives (Joshi *et al*., 2001; Iwase *et al*., 2000).

Essential oil

An essential oil is a complex mixture of volatile plant constituents with low molecular weight components such as terpenes, terpenoids, and other aromatic and aliphatic chemical compounds associated with the plant material from which the oil is extracted, the harvesting time, and the extraction procedure. Because essential oils are lipophilic, they can pass the cell membrane and reach the cytoplasm, where they interact with organelles and cytoplasmic molecules to play an active biological role. Many medicinal plants contain beneficial essential oils that have long been used in traditional medicine to treat respiratory tract infections, anticancer treatment, anti-inflammatory action, antibacterial capabilities, antioxidant activity, and analgesic-like activity (Buchbauer, 2010).

Herbal compounds specifically employed in skin/topical application

Anthocyanins

Anthocyanins are natural water-soluble pigments derived from plants and vegetables that suppress oxidation via a variety of processes. Anthocyanins derived from black raspberry have been shown to prevent tumour cell advancement and progression. These delay the progression of premalignant cells by increasing cell turnover, thereby causing infected cells to die, and by decreasing provocative mediators that initiate tumour formation (McDougall, 2011).

Retinol

Retinol is an important element in anti-aging products. The ability of retinol to accelerate skin-rejuvenation is critical to improving the skin's overall appearance. Retinol may help with skin regeneration by increasing cell turnover rate. It also aids in the appearance of facial wrinkles. Topical application of retinol-containing products (e.g., retinol skin cream) demonstrates significant antioxidant activity, which aids in the elimination of free radicals in the environment (Zouboulis, 2001).

Proanthocyanidin

Proanthocyanidin (oligomeric proanthocyanidins [OPC]) acts as a DNA transformation inhibitor. Furthermore, proanthocyanidin inhibits elastase and keeps the skin's elastin firm and reliable. OPC works in tandem with Vitamins C and E to preserve and energise them (Korać and Khambholja, 2011).

Silymarin

Silymarin is extracted from milk thistle seeds (*Silybum marianum*). It is a flavonoid compound that comprises flavonolignans, which suppress the formation of superoxide radicals. Silymarin has antioxidant, sun damage protection, anti-acne, anti-inflammatory, lightning, and brightening properties. Silymarin is also used to treat hyperpigmentation. Silymarin is an excellent antioxidant because it scavenges free radicals that can harm cells exposed to pollutants. (Kaur *et al*., 2011).

Carotenoids sun damage can be prevented by the topical application of this antioxidant. When applied topically, only the natural part of Vitamin E– tocotrienol and alpha-tocopherol – viably diminish skin roughness. It also reduces the extent of facial lines and the intensity of the wrinkles.

Topical application of Vitamin E improves hydration of the stratum corneum (outermost layer of the epidermis) and expands its water-restriction limit. Alpha-tocopherol or Vitamin E diminishes the harmful collagen-destructive enzyme collagenase. Level of this enzyme gets increased in matured skin. Vitamin E is an emollient and free radical scavenger as well

Ascorbic acid (Vitamin C)

Vitamin C (L-ascorbic acid) is the most important extracellular and intracellular aqueous phase oxidation inhibitor agent in the body. Ascorbic acid has several skin benefits, the most important of which are increased photoprotection and collagen formation. Ascorbic acid's anti-inflammatory effect improves photoprotection. Photoprotection allows the skin to recover from earlier photodamage; collagen formation and MMP-1 suppression have been shown to reduce face wrinkles. Vitamins E and C work together to prevent the damaging UV radiation by greatly reducing cell apoptosis and the creation of thymine dimers (Grosso *et al*., 2013).

Resveratrol

Resveratrol is a fat-soluble molecule that belongs to the polyphenolic chemical class known as stilbenes. It is a polyphenolic phytoalexin that occurs naturally. Resveratrol was discovered to mediate anti-inflammatory action, to be an antioxidant, and to intervene in moderating effects. Topical application of resveratrol SKH-1 bald mice prior to UVB light resulted in a significant decrease in UVB-age of H2O2, invasion of leukocytes, and inhibition of skin edoema. Long-term studies have revealed that topical administration of resveratrol (both pre- and post-treatment) reduces the frequency of UVB-

initiated tumours and delays the onset of skin carcinogenesis (Ratz-Łyko *et al*., 2019).

Novel drug delivery system in topical application

To minimize drug degradation and loss, to prevent harmful side effects and to increase drug bioavailability and the fraction of the drug accumulated. Novel drug delivery system is the method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, nonspecific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated (Mukherjee *et al*., 2009; Muller-Goymann, 2004).

Importance of novel drug delivery systems in herbal medicines

A unique drug delivery system is an innovative approach to medication delivery that solves the shortcomings of standard drug delivery systems. Our country has a vast Ayurvedic knowledge base whose potential has just recently been exploited. However, the medication delivery technology employed to administer the herbal medicine to the patient is outdated, resulting in diminished therapeutic efficacy. If innovative drug delivery technology is used in herbal medicine, it may improve the efficacy and reduce the negative effects of diverse herbal compounds and herbs. This is the core concept behind introducing innovative drug delivery methods into natural remedies. To fight this, it is critical to integrate innovative drug delivery systems and Indian Ayurvedic remedies (Patwardhan *et al*., 2004).

Due to a lack of scientific reason and processing problems, such as standardisation, extraction, and identification of individual medicinal components in complicated polyherbal systems, herbal medicines were not considered for development as innovative formulations for a long time. However, modern phytopharmaceutical research can address the scientific needs of herbal medicines to be incorporated in novel drug delivery systems, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles, and so on (Vaidya,2006).

Comparison between Phytosome, Liposome & Transferosome

Parameters	Phytosome	Liposome	Transferosome
Defination	Phytosomes are natural active component and phospholipid complexes.	Lipososmes are spherical phospholipid bilayer vesicles that surround an aqueous solvent containing specific medications and nutrients.	Transfersome is an artificial vesicle with the features of a cell vesicle that can be used for controlled and potentially targeted drug delivery.
Type of molecule delivery	Mainly deliver plant based molecule that have poor solubility like flavonos & terpenes	Can deliver both hydrophobic & hydrophilic	Proteins and peptides, insulin, corticosteroids, interferons, anesthetics, NSAIDs, anticancer drugs and herbal drugs.
Effectiveness	Cannot reach far beyond GI tract without being filtered by the liver so they don not reach circulatory system	Cn reach beyond GI tract without being filtered by liver	high entrapment efficiency, which is nearly 90% in the case of lipophilic drug.
Size	Large in size	Small in size	below 300 nm
Type of phospholipid & other lipid	Lecithin	Phosphotidyl choline, cholesterol, egg, phosphotidyl ethanolamine	Phospholipids and edge activator (EA),

(Alharbi *et al*., 2021; Duangjit *et al*., 2014)

Lipid based nanocarriers: A new choice for drug delivery

Researchers focusing on the development of new formulations for increased therapeutic efficacy and drug safety are paying close attention to lipid-based delivery systems. Topical drug distribution is required for the treatment of skin, eye, rectum, vaginal, and systemic illnesses with cutaneous symptoms. Because lipid nanocarriers are biocompatible, biodegradable, nontoxic, and nonirritating, they are widely used in topical medication delivery. Microemulsion and nanoemulsion contain nanosized lipids, which can allow drugs to penetrate deeper epidermal layers. Solid lipid nanoparticles and nanolipid carriers work by producing an occlusive layer on the skin, increasing hydration and medication penetration. Liposomes, niosomes, ultradeformable vesicles, cubosomes, and other vesicular carriers have also been shown to improve medication penetration in deeper layers of skin. These carrier systems are mostly made up of lipids, surfactants, and co-surfactants, all of which are considered safe and acceptable by regulatory bodies (Patidar *et al*., 2010).

Transferosome: A novel approach of transdermal drug delivery

Transferosomes are ultradeformable vesicles with an aqueous core and a complex lipid bilayer. The bilayer's local composition and interdependence of shape make it self-regulating and self-optimizing. Transferosomes are suitable candidates for non-delivery of small, medium, and big ones due to their deformability. Transferosomes may deform and pass through constrictions 5-10 times smaller than their own diameter without significant loss' flexibility can be produced by combining appropriate surface active components in the proper ratios. The resultant flexibility of the transferosome membrane reduces the likelihood of full vesicle rupture in the skin and allows transferosomes to follow natural water gradients throughout the epidermis when applied under non-occlusive conditions.They overcome skin penetration by pressing themselves along the sratum corneum's internal lipids (Chauhan *et al*., 2017).

When pressed against or enticed into a narrow pore, the ultra-deformable transferosomes change their membrane composition locally and irreversibly due to the high and self-optimizing deformability of typical composite transferosomes that are adaptable to ambient stress. Transferosome components that can withstand strong deformation preferentially accumulate, whereas less adaptable molecules significantly reduce the energetic cost of membrane deformation, allowing the resulting highly flexible particles to enter and pass through the pore quickly and efficiently (Opatha *et al*., 2020).

Mechanism of penetration

- Transferosomes may transfer 0.1 mg of lipid per hour and square centimetre area across undamaged skin when used properly. This number is significantly higher than what is generally caused by transdermal concentration gradients.

- This high flow rate is caused by naturally occurring "transdermal osmotic gradients," which means that another, far more apparent gradient exists across the skin.

- This osmotic gradient created by the skin penetration barrier limits water loss through the skin and maintains a water activity difference between the living epidermis (75% water content) and the virtually entirely dry stratum corneum near the skin surface (15% water content).

- This gradient is very steady because ambient air is a superb sink for water molecules even when transdermal water loss is abnormally large.

- Water is attracted to all polar lipids. This is because the hydrophilic lipid residues and their proximal water have an energetically favourable interaction. As a result, most lipid bilayers withstand induced dehydration.

As a result, all lipid vesicles formed from polar lipid vesicles migrate from the relatively dry place to sites with a sufficiently high water content. When a lipid solution (transferosome) is applied to a skin surface that is partially dehydrated due to water evaporation loss, the lipid vesicles detect this "osmotic gradient" and attempt to avoid total drying by travelling along it. Transferosomes composed of surfactant have more suitable rheological and hydration properties than that responsible for their greater deformability; less deformable vesicles, including standard liposomes, are confined to the skin surface, where they dehydrate completely and fuse, so they have less penetration power (Benson, 2006).

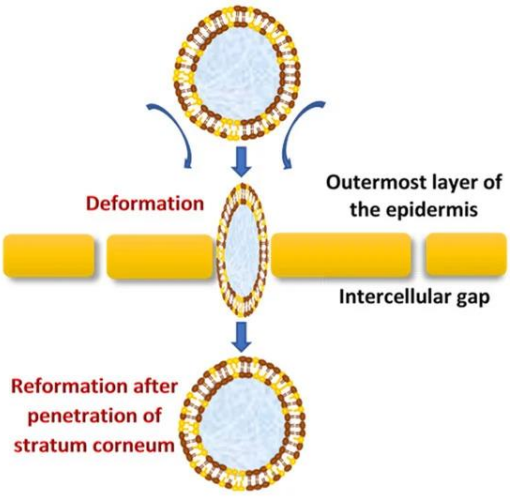

Figure: Mechanism of penetration

Methods of preparation of transferosome

Modified Hand Shaking Method

To create transfersomes, the lipid film hydration technique is also utilised, and it comprises of the some crucial procedures. At first, the medication, lecithin (PC), and edge activator were dissolved in a 1:1 mixture of ethanol and chloroform. To remove it, organic solvent was evaporated during hand shaking at temperatures above the lipid transition point (43°C). A thin lipid coating formed inside the flask wall as it rotated. The thin layer was kept on overnight to allow the solvent to completely evaporate. Further the film was then hydrated for 15 minutes with phosphate buffer (pH 7.4) and moderate shaking at the suitable temperature. The transferosome suspension was hydrated for 1 hour at 2-8°C. (Dhopavkar and Kadu, 2017).

Ethanol Injection Method

To make the organic phase, dissolve the phospholipid, edge activator, and lipophilicdrug in ethanol and mix for the proper period of time until a clear solution is achieved. To generate the aqueous phase, the water-soluble chemicals are dissolved in the phosphate buffer. This is the moment to start using the hydrophilic medicine. Both solutions are warmed to 45-50 °C. The ethanolic phospholipid solution is then injected dropwise into the aqueous solution while stirring continuously for the time given. Ethanol is removed by passing the resultant dispersion through a vacuum evaporator and then sonicating for particle size reduction (Jain and Kumar, 2017).

Reverse Phase Evaporation Method

Components such as cholesterol and phospholipids are introduced to a glass beaker. The surfactant is then added to the same beaker and dissolved in a different solvent solution. To create a thin coating, the beaker is left at room temperature for 24 hours. The medication solution is poured over the thin film and sonicated for 2 minutes with a probe sonicator at a frequency of 20 KHz. The film is then hydrated in phosphate buffer saline (pH 7.4) with edge activator before being sonicated for 2 minutes to obtain transferosomal suspension. Following that, various transferosomal suspensions should be filtered using Whatman filter paper (No. 40) (Guanyu *et al*., 2014).

Vortexing-sonication Method

The phospholipids, edge activator, and medicine are mixed in a phosphate buffer. The mixture is then vortexed until it forms a milky transferosomal suspension. It is then sonicated for a set amount of time at room temperature in a bath sonicator before being extruded through polycarbonate membranes (450 and 220 nm, for example) (Garg *et al*., 2017).

Characterization of Transferosome

Vesicle Structure and Shape:

Vesicle structure and shape can be characterised by various types of microscopy scanning electron microscopy (SEM), Transmission electron microscopy (TEM), Optical Microscopy, etc.

Size, Size distribution and vesicle diameter:

Size, size distribution and diameter of vesicle can be detect by dynamic light scattering (DLS) and photon correlation spectroscopy (PCS).

Entrapment efficiency (EE):

The entrapment efficiency expressed as

$$\text{Entrapment efficiency} = \frac{\text{Amount of drug entrapped}}{\text{Total amount of drug added}} \times 100$$

Skin interaction studies:

It is common in-vivo methods are confocal microscopy and tape stripping method.

Degree of deformability or permeability measurement:

Permeability assessment is one of the most important and distinguishing characteristics in the evaluation of transferosmes. Pure water is used as a standard to measure the degree of distortion in transfersome samples. The transferosomes suspension is passed through a sandwich of several micropore filters with pore diameters ranging from 50 nm to 400 nm, depending on the starting transferosomes solution. After each pass, dynamic light scattering (DLS)

measurements are performed to record particle size and size distribution (Jain *et al*., 2003).

Turbidity Measurement:
A nephelometer is used to detect the turbidity of a sample in an aqueous solution.

Surface charge and charge density:
The surface charge and charge density of transferosomes samples are measured using a Zeta sizer

Penetration ability:
The capacity of transferosomes to penetrate is measured using fluorescence microscopy.

Occlusion effect:
The occlusion effect has a deleterious impact on ultradeformable vesicles. The driving mechanism for transferosome vesicle migration through the skin is hydrotaxis, or movement in the direction of water for deeper penetration. Because it keeps water from evaporating from the skin, occlusion has an effect on hydration forces.

In- vitro Drug release study:
In-vitro drug release can be measured using a diffusion cell or a dialysis method.

Drug content
It may be assessed using HPLC or Spectrophotometric techniques, and vesicle stability can be determined by analysing the size and shape of the vesicle over time.

Stability study:
Drug content may be assessed using HPLC or spectrophotometric techniques, and vesicle stability can be evaluated by examining the size and structure of the vesicles over time (Rajan *et al*., 2011).

Transferosme in skin & topical application

Name of drug	Classification	Inference	Reference
Tetracaine, Lignocain	Local anaesthetic	Direct topical medication administration is a suitable method for the noninvasive treatment of local discomfort.	(Maghraby *et al*., 2000)
Triamcinolone, Acetonide	Glucocorticoid	Used for both local and systemic delivery	(Cevc *et al*.,1997)
Capsaicin	Neuropeptide releasing agent and analgesic	Increase skin penetration	(Long *et al*., 2006)
Tamoxifen	Selective Estrogen Receptor Modulators (SERM)	Improved transdermal flux	(Walve *et al*., 2011)
Hydrocortisone	Anti-inflammatory agent	Biologically active at dose several times lower than currently used formulation	(Cevc *et al*., 2004)
Curcumin	Antibacterial, anti-inflammatory, hypoglycemic, agent	Better permeation for anti-inflammatory activity	(Patel *et al*., 2009)
Oestradiol	Steroidal hormone	Improved transdermal flux	(Maghraby *et al*., 2000)
Human serum Albumin	Protein	The antibody titer is comparable, if not slightly higher, than that of subcutaneous injection.	(Sachan *et al*., 2013)
Indinavir sulfate	Protease inhibitors and antiretroviral	Increased inflow for anti-acquired immunodeficiency syndrome (AIDS) activities	(Sheo *et al*., 2010)
Interferon-α	Antiviral and anti - neoplastic agent	Efficient delivery means (because other routes are difficult to provide). Controlled ejection. Solve the stability issue.	(Hafer *et al*., 1999)

CONCLUSION & FUTURE PROSPECT:

Based on our findings, we may conclude that transfersomes have broad future applications and are virtually as efficient as water at overcoming skin barriers. They can be utilised to improve the permeability of medicines with both high and low molecular weight. They are able to travel through microscopic pores in their skin because of their capacity to deform and reform their shape. Transfersomes are proving to be more efficient than liposomes and phytosomes in transporting medications through barriers.

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