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Transferosomes as a Novel Therapeutic Delivery System: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The poor penetration rate of the skin as a natural barrier makes transdermal drug delivery problematic. To increase transdermal dispersion of bioactives, electrophoresis, iontophoresis, chemical permeation enhancers, microneedles, sonophoresis, and vesicular systems such as liposomes, niosomes, elastic liposomes such as ethosomes, and transferosomes have all been used. Among these, transferosomes appear to be a promising option. Transferosomes are elastomeric or deformable vesicles that were originally discovered in the early 1990s. They're novel vesicular drug carrier system composed of phospholipid, surfactant, and water that improves transdermal drug delivery. Because of their low toxicity, biodegradability, ability to encapsulate both hydrophilic and lipophilic molecules, ability to prolong the drug's existence in the systemic circulation by encapsulation in vesicles, ability to target organs and tissues, and ability to reduce drug toxicity while increasing bioavailability, these vesicles are preferred over others. These vesicles undergo deformation, changes its shape and easily penetrates through the skin pores. There are two phases in any technique for preparing transferosomes. First, a thin film is hydrated before being sonicated to the required size; next, sonicated vesicles are homogenized by extrusion

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through a polycarbonate membrane. Transferosomes are evaluated for its entrapment efficiency, their drug content , in-vitro drug release, degree of deformability, turbidity, surface charge and morphology. Transferosomes are said to have a number of applications like delivery of vaccines,proteins, Anti-cancer drugs,anesthetics,herbal drugs and has better patient compliance,improved bio-availability and site-specific delivery and can serve as an emerging tool for transdermal delivery of almost all drugs and bio-actives.

Keywords: Transferosomes; deformable; transdermal delivery; bioavailability.

1. INTRODUCTION

Transdermal medication delivery has emerged as a viable alternative to the traditional oral drug delivery method, as well as a viable option to hypodermic injections [1]. Its administration is difficult due to the skin's low penetration rate as a natural barrier. Due to the efficient barrier qualities of intact skin, which are predominantly linked with the epidermis' outermost layers, notably the stratum corneum, the number of molecules that can achieve therapeutic levels at their target site after application to the skin is severely limited [2]. Electrophoresis, iontophoresis, chemical permeation enhancers, microneedles, sonophoresis, and vesicular systems such as liposomes, niosomes, elastic liposomes such as ethosomes, and transferosomes have all been utilized to improve transdermal distribution of bioactives. Transferosomes appear to be a viable strategy among them. They are a new vesicular drug carrier system made up of phospholipid, surfactant, and water that allows for better transdermal drug delivery [3]. Surfactant serves as an edge activator, destabilizing lipid bilayers and increasing the vesicle's deformability [4]. Transferosomes are a type of elastomeric or deformable vesicle that first appeared in the early 1990s [5]. These vesicles are preferred over others because of their low toxicity, biodegradability, ability to encapsulate both hydrophilic and lipophilic molecules, ability to prolong the drug's existence in the systemic circulation by encapsulation in vesicles, ability to target organs and tissues, and ability to reduce drug toxicity while increasing bioavailability [6].

When the carrier is introduced to the skin, it seeks for and exploits hydrophilic channels or 'pores' between the skin's cells, which it opens wide enough to allow the entire vesicle to pass through with its drug payload, deforming itself significantly to do so without losing its vesicular integrity. The vesicle is self-regulating and self-optimizing because the local composition and shape of the bilayer are interdependent. As a result, the Transferosomes are able to efficiently navigate across numerous transport obstacles. Intracellular or transcellular pathways allow transferosomes to reach the stratum corneum. As the vesicle is pulled from the dry surface to the water-rich region under the skin, each vesicular carrier crosses the skin barrier on its own to deposit the medication into deep tissues.“Transferosomes”, which has been discovered to be one of the main breakthroughs in vesicle research, has led the way for reducing the faulty Transdermal penetration of variety of low and high molecular weight drugs [7].

1.2 Mechanism of Action

The bio membrane’s primary component is phosphatidyl choline, which is made up of a hydrophilic polar head group comprising a phosphate group and two hydrophobic fatty acid chains. Edge activator is a structure that is both hydrophilic and hydrophobic, and it is usually a single chain surfactant with a significant curvature that destabilizes the lipid bilayer of the vesicles and enhances its ultra deformability by reducing its interfacial tension. The major driving factor for the movement of transferosomes into the deeper epidermal layers is the osmotic gradient. It also has a small impact on the transferosome’s physical characteristics. As a result, it easily enters skin pores much smaller than itself to achieve transdermal penetration, prolonging the drug's release and increasing its action [8,7,10].

1.3 Different Additives used in Transferosome Formulation

Different additives used in transferosome preparation is given in the Table 1 [11,12].

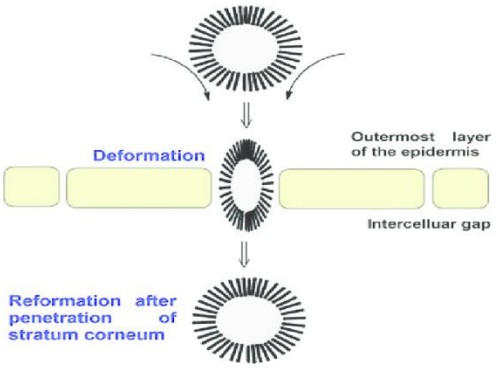

Fig. 1. Mechanism of action of transferosomes [10]

Table 1. Additives used in transferosomes

Class	Examples	Uses
Phospolipids	Soyaphosphatidyl choline Egg Phosphatidyl Choline Dipalmitoyl phosphatidyl choline Distearoylphosphatidyl choline	Vesicles forming component
Surfactants	Sod. Cholate Deoxy cholate Tween-80 Span-80	For providing flexibility
Alcohols	Ethanol Methanol	As a solvent
Dyes	Rhodamine 123 Rhodamine DHPE Fluorescein- DHPE Nile-red 6 Carboxyflourescence	For CSLM study
Buffering agent	Saline Phosphate buffer (pH 6.5) 7% v/v Ethanol Tris Buffer (pH 6.5)	As a hydrating medium

2. METHODS OF PREPARATION OF TRANSFERSOMES

Various process factors, such as lecithin, surfactant ratio, impact of various solvents, effect of various surfactants, and hydration medium, are all involved in the creation of transfersomes. There are two phases in every technique of preparing transfersomes. First, a thin film is hydrated and then sonicated to the required size; subsequently, sonicated vesicles are homogenized via a polycarbonate membrane.[13]. Fig. 2. [13].

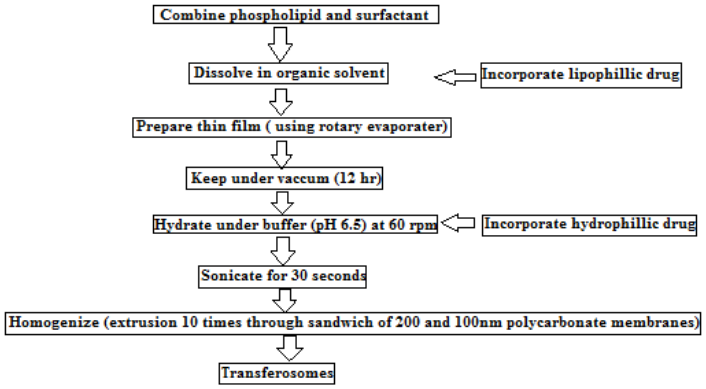

Fig. 2. Method of preparation of transferosomes

2.1 Rotary Film Evaporation Method

The measured quantity of phospholipids and edge activators are utilized to produce a thin film in this approach. In an organic solvent, such as a combination of chloroform and methanol, a solution of phospholipids and edge activators is produced. The prepared solution is transferred to a round bottom flask that is rotated at a constant temperature (above the lipids' glass transition point) and low pressure. On the flask's walls, a coating of lipids and edge activator forms. The drug-infused aqueous medium is then used to hydrate the produced film. Lipids expand and produce bilayer vesicles as a result. Extrusion or sonication of bigger vesicles can produce vesicles of desired size [14,15].

2.2 Vortexing-sonication Method

In a phosphate buffer, the phospholipids, edge activator, and medication are combined. After that, the mixture is vortexed till it forms a milky transferosomal suspension. It's then sonicated for a certain amount of time at room temperature in a bath sonicator before being extruded through polycarbonate membranes (example: 450 and 220 nm) [14,15].

2.3 Modified Hand Shaking Method

In an ethanol: chloroform (1:1) combination, the drug, lecithin (PC), and edge activator are dissolved. Above the lipid transition temperature (43°C), the organic solvent is evaporated with hand shaking. Rotation causes the formation of a thin lipid layer inside the flask wall. The thin layer is let to dry overnight to ensure complete evaporation of solvent. The film is then hydrated for 15 minutes at room temperature with phosphate buffer (pH 7.4) and moderate shaking. At 2-8°C, the Transferosomal suspension hydrated for a further hour [3,16].

2.4 Reverse Phase Evaporation Method

In a glass beaker, the components such as cholesterol and phospholipids are added. The surfactant is then added to same beaker and dissolved in a separate solvent solution. The beaker is left at room temperature for 24 hours to produce a thin layer. The drug solution is poured over the thin film and sonicated for 2 minutes at a frequency of 20 KHz using a probe sonicator. After that, the film is hydrated in phosphate buffer saline (pH 7.4) with edge activator before being sonicated for 2 minutes to get transferosomal suspension. After that, different transferosomal suspensions should be filtered using Whatman filter paper (No. 40) [16,17].

2.5 Ethanol Injection Method

The organic phase is made by dissolving the phospholipid, edge activator, and lipophilic drug in ethanol and stirring for the appropriate amount of time until a clear solution is obtained. The water-soluble compounds are dissolved in the phosphate buffer to form the aqueous phase. This is the time to incorporate the hydrophilic medication. Both solutions are heated to 45–50 °C. After that, the ethanolic phospholipid solution is injected dropwise into the aqueous solution while stirring continuously for the period specified. Transferring the resulting dispersion into a vacuum evaporator and then sonicating for particle size reduction is how ethanol is removed [9].

3. OPTIMIZATION OF TRANSFERO-SOMES

The preparation and characteristics of the transferosomes can be affected by a number of process factors. As a result, the preparation method was improved and confirmed. The process variables are determined by the manufacturing technique for the formulation [12].

Various process factors are involved in the production of transferosomes, including:

1. The ratio of lecithin to surfactant
2. The impact of different solvents
3. The impact of different surfactants
4. Medium for hydration

The entrapment efficiency of the medication is chosen as the criterion for optimization.

The other variables are kept constant during the development of a specific system.

4. EVALUATION AND CHARACTERI-ZATION OF THE TRANSFERSOMES

4.1 Entrapment Efficiency

The entrapped medication is separated from the un-entrapped drug by centrifuging one milliliter of Transferosomes solution. The sediment is lysed with methanol after the supernatant is removed, and then spectrophotometrically examined with a UV spectrophotometer [18,19].

Using the following equation, the % Entrapment efficiency in the prepared Transferosomes is calculated:

$$\%\ Entrapment\ efficieny = \frac{Amount\ of\ entrapped\ Drug}{Total\ amount\ of\ Drug} \times 100$$

4.2 Number of Vesicles per Cubic MM

This is a critical parameter for optimizing composition and other process factors. Unsonicated transferosome formulations are diluted five times with a 0.9 % sodium chloride solution. For additional investigation, a hemocytometer and an optical microscope are employed [20,21].

The transferosomes in 80 tiny squares are counted and the following formula is used to determine them:

$$\text{Total number of Transferosomes per cubic mm} = \frac{\text{Total number of transferosomes counted} \times \text{dilution factor} \times 4000}{\text{total number of squares counted}}$$

4.3 Degree of Deformability or Permeation Measurement

This is a crucial parameter since it influences the penetration of the transferosomal formulation. The standard used in this investigation is pure water. The solution is passed through a series of microporous filters with known pore diameters ranging from 50 to 400 nanometers. After each pass, DLS measurements are used to record the particle size as well as the size distribution [20,21,22].

The degree of deformability is expressed as:

$$D = J\ \frac{rv}{rp}$$

Where,

D = Degree of deformability
J = amount of suspension extruded within 5 min,
rv = size of vesicle
rp = barrier pore size

4.4 Vesicle Morphology

Photon correlation spectroscopy (PCS) or Dynamic Light Scattering (DLS) can be used to measure the diameter of vesicles [20] [21] (DLS). Samples are prepared in distilled water, filtered using a 0.2 mm membrane filter, and dilutes with filtered saline before being measured using PCS or DLS.

4.5 Measurement of Turbidity

The turbidity sample in an aqueous solution is measured using a nephelometer [17,21].

4.6 Surface Charge and Charge Density

The surface charge and charge density of transferosomes are measured using a zeta sizer [17,21].

4.7 Vesicle Size Distribution and Zeta Potential

For determining vesicle size, size distribution, and zeta potential, researchers utilized the dynamic light scattering method (DLS) with a computerized inspection system from Malvern Zeta sizer [20,21]

4.8 Drug Content

Depending on the analytical method of the pharmacopoeial drug, the drug content is determined using one of the instrumental analytical methods such as a modified high performance liquid chromatography method using an ultraviolet detector, column oven, auto sample, pump, and computerized analysis program [20,21].

4.9 Occlusion Effect

In the case of conventional topical treatments, occlusion of the skin is thought to be beneficial for drug penetration. The blockage, on the other hand, is detrimental to elastic vesicles. The primary driving factor for vesicle penetration through the skin is hydrotaxis (water flow in a direction) from the comparatively dry surface to the water-rich deeper areas. It has an effect on hydration forces because it stops water from evaporating from the skin [20,21]

4.10 *In vitro* Drug Release

A penetration rate is determined by conducting an in vitro drug release study. Before more expensive in vivo investigations, the time required to achieve steady state permeation and the permeation flux at steady state are utilized to improve the formulation. The free drug is isolated by mini column centrifugation after the

Table 2. Evaluation and Characterization of the Transferosomes [23,24,25]

Parameter	Method
Vesicle shape morphology	Transmission electron microscopy
Entrapment efficiency	Mini column centrifugation method
Vesicle size and size distribution	Dynamic light scattering method Photon correlation spectroscopy
Skin permeation potential	Confocal laser scanning microscopy Fluorescence Microscopy Transmission electron microscopy Thin layer Chromatography
Degree of deformability	Extrusion method
Surface charge and charge density	Zeta Sizer
Turbidity	Nephelometre
In vitro drug release study	Side by side diffusion with artificial or biological membrane Dialysis bag diffusion
Stability study	Transmission electron microscopy Dynamic light scattering method
Comparison study with other vesicles	Confocal scanning laser microscopy (CSLM) study
Drug content	High performance liquid chromatography

transferosomes suspension has been incubated at 32°C for several hours [21,22]. The amount of drug released is then determined indirectly by multiplying the amount of drug entrapped by zero (100 percent contained and 0% released).

4.11 Physical Stability

The amount of drug entrapped in the formulation (percentage) was measured and kept in sealed glass ampoules. For at least three months, the ampoules are kept at 42°C (refrigeration), 25.2°C (room temperature), and 37.2°C (body temperature). After 30 days, samples from each ampoule are examined to see if there is any medication leakage [21,22]. The percentage drug loss is determined by maintaining the initial drug entrapment at 100%.

4.12 Comparison Study with other Vesicles

Confocal scanning laser microscopy (CSLM) study allows researchers to compare transferosomes to liposomes, niosomes, and other types of nanoparticles, as well as investigate the process of transferosome penetration. The process involves the use of a lipophilic fluorescent marker that can produce light. The light that is emitted is used for additional detection [22].

5. APPLICATIONS [17,18,23,25,26]

- Transferosomes offer the potential to provide regulated medication release while also enhancing the stability of labile drugs.
- Insulin encapsulation in transferosomes (transfersulin) solves the difficulties of inconvenient administration, greater size (making it inappropriate for transdermal distribution using traditional methods), and a 50% response rate as compared to subcutaneous injection.
- Interferons, such as INF-, have been carried by transferosomes. INF- is a naturally occurring protein with antiviral, anti-proliferative, and immunomodulatory properties. As a drug delivery method, transferosomes offer the potential to provide regulated drug release and increase the stability of labile substances.
- Transferosomes containing soluble proteins such as integral membrane protein, human albumin, and gap junction protein are used in transdermal vaccination. By adjusting the epicutaneously given medication dosage, transferosomes enhance the site specificity and overall drug safety of corticosteroid administration into skin.
- The adjuvant immunogenic bovine albumin in transferosomes, for example, induces a robust immune response after repeated percutaneous application and is immunologically as active as the equivalent injectable proteo-transferosomes preparations after multiple skin challenges.

- Delivery of Anticancer Drugs: In 2018, Jiang et al. published a study that linked transferosome-embedded oligopeptide hydrogels containing paclitaxel produced by the thin-film dispersion technique to topical treatment of melanoma. Phosphatidylcholine, tween80, and sodium deoxycholate-based transferosomes have been demonstrated to enter tumour tissues efficiently.
- Delivery of herbal drugs: Transferosomes may enter the stratum corneum and deliver nutrients locally, resulting in skin maintenance. In this regard, Xiao-Ying et al. developed Transferosomes of Capsaicin, which exhibit greater topical absorption than pure capsaicin.
- Delivery of Anesthetics: The use of anesthetics in the suspension of highly deformable vesicles, transferosomes, causes topical anesthesia in less than 10 minutes under the right circumstances. The maximum pain insensitivity is almost as powerful (80%) as a similar subcutaneous bolus injection, although transferosomal anesthetics have a longer duration of action.
- Corticosteroid Administration: Cevc and Blume investigated the biological activity and properties of halogenated corticosteroid triamcinolone-acetonideloaded transferosomes produced using the traditional thin-film hydration method in 2003 and 2004. Transferosomes boosted biological potency and extended impact, as well as lowered therapeutic dose, according to the findings.
- Transfersomes have a bioavailability that is comparable to injection. When given transdermally and encapsulated in Transfersomes, human albumin was found to be effective in inducing an immunological response.
- Transferosomes containing soluble proteins such as integral membrane protein, human albumin, and gap junction protein are used in transdermal vaccination. These methods have at least two advantages: first, they are non-injectable, and second, they produce a reasonably high titer and, perhaps, quite high IgA levels. Corticosteroids have also been delivered via transferosomes. By adjusting the epicutaneously given medication dosage, transferosomes enhance the site specificity and overall drug safety of corticosteroid administration into skin.
- The ability of transfersomes to target peripheral subcutaneous tissues is due to the little carrier-associated drug clearance through blood arteries inside the subcutaneous tissue.
- Since phospholipids are incorporated into transfersomes, they have the potential to regulate the release of the given medication and increase the stability of labile medicines.
- Transdermal immunisation has shown to be effective in the treatment of hepatitis B. When compared to usual control administration, zidovudine had a 12 times greater AUC. The selectivity of HIV deposition in RES (the typical location for HIV residency) was also improved.
- Anticancer Drug Administration: Using transfersome technology, anticancer medicines like methotrexate were attempted for transdermal delivery. The outcomes were positive. This provides a novel therapeutic option, particularly for skin cancer.
- Delivery of NSAIDs: NSAIDs are connected with a variety of gastrointestinal adverse effects. Transdermal delivery of ultra-deformable vesicles can solve these issues. Diclofenac and Ketoprofen have both been the subject of research. In 2007, the Swiss regulatory body (SwissMedic) approved ketoprofen in a Transfersome formulation for marketing.

6. ADVANTAGES [27,28]

- Transferosomes can transport both low and large molecular weight molecules such analgesics, insulin, protein, anesthetics, corticosteroids, sex hormones, anticancer agents, and albumin.
- Sustained drug delivery ensures a consistent plasma profile, which is especially important for medicines with short half lives, as well as regulated input kinetics and less systemic adverse effects.
- Transferosomes have a high entrapment efficiency, up to 90% in the case of lipophilic drugs.

- They prevent metabolic breakdown of the encapsulated medication.
- Improved patient compliance
- For medicines with a low oral bioavailability, First-Pass metabolism can be avoided.
- They are biocompatible and biodegradable since they are produced from natural phospholipids, comparable to liposomes.
- They're simple to scale up because the technique isn't complicated.
- In comparison to the oral route, it is preferred for unconscious patients.
- Self-administration is feasible, and medication delivery can be easily stopped in the event of toxicity.
- There is no interference with the fluids in the stomach and intestines.

7. LIMITATIONS [29,30,31,32]

- Transferosomes are chemically unstable and oxidatively degraded.
- They are costly.
- The purity of natural phospholipids has an influence on vesicles, making transferosome formation more challenging.

Table 3. Recent advancements in Transferosome preparations

Sl.No.	Drug	Drug category	Study conducted	Results obtained
1	Pioglitazone	Anti-diabetic	Skin permeation study	Enhanced delivery of Pioglitazone via skin [33]
2	Amphotericin	Anti-fungal	Nasal membrane permeation study	Enhanced permeation of Amphotericin through nasal membrane [34]
3	Ebastine	2nd generation Anti-Histamine	Invitro-Invivo characterizations and physiochemical considerations	Ebastine's bioavailability and antihistamine efficacy were significantly enhanced using highly flexible transferosomal oral films. [35]
4	Curcumin	Herbal drug (Anti-inflammatory agent)	Skin penetration study	Improved penetration to arthritic skin tissue and exhibited potential effectiveness in the treatment of Freud's adjuvant-induced arthritis. [36]
5	Mulberry leaf extract (Quercetin)	Bio-active compound (anti-oxidant)	Anti-oxidant activity	Transferosome gel filled with Mulberry leaf extract containing Quercetin is a promising and stable long-term delivery method for Quercetin. [37]
6	Catechin	Herbal Drug (anti-oxidant)	In-vivo skin whitening study	The formulation was shown to be efficient in inhibiting Tyrosinase and to be compatible with the skin of guinea pigs in a study. It might be regarded as a therapeutic option for UV-induced oxidative damage to the skin. [38]
7	Vancomycin	Anti-bacterial	ex-vivo studies	The drug's penetration and bioavailability might be improved with a vancomycin-HCl loaded transferosome. [39]
8	Chrysin	Flavanoid	Intranasal administration	The incorporation of chrysin into transfersomes and chitosan composite vesicles significantly improved its therapeutic efficacy in rats with doxorubicin-induced cognitive impairment.

Sl.No.	Drug	Drug category	Study conducted	Results obtained
				Doxorubicin-induced histological alterations and neurodegeneration were reversed by chrysin vesicles. Additionally, they increased cholinergic transmission, which improved cognitive function as measured by the acetylcholinesterase enzyme. Furthermore, chrysin reduced oxidative stress and apoptosis, counteracting the cognitive impairment caused by doxorubicin. [40]
9	Retinyl palmitate	Vitamin A palmitate	Skin penetration study	The findings suggest that transferosomes might be an effective vehicle for delivering retinoids to the skin's inner layers, such as the epidermis. [41]
10	Lornoxicam	NSAID	Skin permeation study	Lornoxicam transferosomal hydrogel is a potential topical product for treating local inflammatory disorders effectively. [42]
11	Rifampicin	Antibiotic	Ex-Vivo and in-vivo permeation study	In cutaneous leishmaniasis, a rifampicin-loaded Nano-Transferosomal gel might be an effective carrier for anti-leishmanial medicines. The NTs had a three-fold greater penetration rate than the RIF solution. Passive targeting by the NTs enhanced cellular internalization, which was verified by macrophage uptake analysis. [43]
12	Stavudine	Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Skin permeation study	The findings showed that transferosomes may be used to enhance Stavudine transdermal administration [44].
13	Itraconazole	Anti-Fungal	Skin permeation study	The findings revealed that transferosomal gel is a viable option for transdermal administration of a medication with targeted and sustained release. It also improves the penetration of many medicines through the skin. [45]
14	Ivabradine HCl	Hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers	Skin permeation study	When compared to pure medication, films containing Ivabradine transferosomes had improved permeability and skin retention, as well as improved pharmacokinetic characteristics. [46]

Sl.No.	Drug	Drug category	Study conducted	Results obtained
15	Tocopherol acetate	Tocopherols (Vitamin E)	In-vitro Biocompatibility, Anti-Oxidant activity In-vitro wound closure study	Transferosomes containing tocopherols have the potential to be used as a topical delivery method with antioxidant and wound-healing effects. [47]

8. MARKETTED FORMULATIONS OF TRANSFEROSOME

8.1 Diractin

Manufactured by IDEA AG,Munich.The active medication ketoprofen, with a label claim of 22.9 mg per gm, was manufactured by Idea AG and was claimed to treat infammation and pain associated with osteoarthritis. Ketoprofen is a nonsteroidal anti-rheumatic medication that works by inhibiting cyclooxygenase and lowering prostaglandin levels, both of which are linked to pain and inflammation. Diractin was a new carrier transfersome-based formulation for epicutaneous medication administration that was targeted to the deeper layers of skin. The Swiss regulatory agency (SwissMedic) approved the Transfersome® formulation Diractin®, which contains the non-steroidal anti-inflammatory medication (NSAID) ketoprofen, for the treatment of osteoarthritis in 2007 [48,49,50].

8.2 Flexiseq

Manufactured by Pro bono bio. It's a drug-free, drug-free transfersomal pain-relieving gel designed specifically for joint discomfort caused by osteoarthritis. Flexiseq is a lubricant that relieves stiffness and pain by lubricating the cartilage in joints. Sequessome is an aqueous gel containing hydrophilic nano sized lipid vesicles with phospholipid bilayer structure. The word sequessome is a synonym for transfersome, which comprises lipid bilayer vesicles, according to the applicant's pro bono bio. Pro bono bio owns the trademarks Flexiseq and Sequessome technologies. Since Flexiseq is a drug-free placebo gel, it is classified as a medical device. Sequessomes are ultra-deformable vesicles that may pass through Skin's intercellular gaps intact [48].

8.3 TDT-067

Manufactured by Celtic Pharma Development Services. TDT-067 is a novel topical drug that is used to treat antifungal treatments. For the treatment of onychomycosis, terbinafine transfersomes were created to transport the medication to the nail and surrounding tissue. It is a topical terbinafine formulation with a carrier-based vesicular formulation. The medication can reach a deeper layer of infection in the nail, nail bed, and surrounding tissue using Transfersome. Dermatophyte fungus, the most common of which is Trichophyton rubrum, cause onychomycosis [48] [51].

8.4 Transfersulin

Transfersulin is a vesicle that carries insulin-loaded transfersomes and is ultra-deformable. Systemic normoglycemia was established with a single epicutaneous injection of non-invasive transfersulin. The clinical trial was carried out to confirm the efficiency of the treatment in reducing blood glucose levels in a patient with type 1 diabetes. Human volunteers were evaluated on the pharmacokinetic characteristics of transfersulin, and a normal concentration ratio of insulin/C-peptide was discovered in the glucodynamic profle in blood after delivery. This can keep the glucose levels normal for up to 16 hours. A comparison was Ultralente insulin (Ultratard, Novo-Nordisk), which was administered subcutaneously by injection. The findings of the study revealed that transfersomes not only keep blood glucose at an optimal level, but also bring it down to a normal range (below 5.6 mmol/L) [48].

8.5 Triamcinolene Acetonide Transfersome

Eczema, dermatitis, rash, allergies, and other inflammatory skin disorders are commonly treated with gluco corticosteroid topical formulations. The triamcinolene acetonide (TAC) transfersome is capable of penetrating the therapeutic quantity of medication into the deeper layers of the skin. A double-blind placebo-controlled clinical experiment was conducted to assess the efficacy and atrophogenic potential of TAC transfersome, which was compared to commercially available Volon A cream and ointment. TAC transfersome

was found to be bioequivalent to regular cream at a 10-fold lower dosage of 2.5 g cm-2 compared to 25 g cm-2. TAC transfersome was found to enhance the risk-benefit ratio following topical application after 6 weeks of therapy in a clinical trial [49].

9. CONCLUSION

Transfersomes are ultra-deformable carriers that allow for more effective distribution of a wide range of drug compounds through the skin barrier than traditional vesicular systems.The vesicles are flexible and deformable and thus easily passes through the skin pores for the effective delivery of drugs.They are custom-designed vesicular systems that must be adjusted for specific cases of medicines of interest in order to produce the most effective formulations and pharmacological reactions. Tranferosomes are said to have a variety of applications, including the delivery of vaccines, proteins, anti-cancer drugs,cortico-steroids, anaesthetics, and herbal drugs, and also has improved patient compliance, bio-availability,low toxicity and site specific delivery, and can serve as an emerging tool for transdermal delivery of nearly all drugs and bio-actives.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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