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NEW TRENDS IN SUNSCREEN –AN OVERVIEW

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ABSTRACT

Continuous exposure to sunlight induces severe skin damage including immune suppression, early skin ageing, melanoma, erythema, skin pigmentation, skin cancer, sun burn, precancerous skin growth, formation of fine and coarse wrinkles. Use of sunscreen reduces incidence of UVradiation associated skin damage and disorder by their ability to absorb, reflect or scatter UV rays. Many sunscreen products are available in the market which contain organic and inorganic, botanical or hybrid sunscreen agent but the use of sunscreen faces so many challenges like photo irritation, contact dermatitis, blockage of pores, acne, systemic and local toxicity, allergic reaction and deficient vitamin D synthesis. Conventional sunscreen are available in the form of lotion, gels, emulsion and cream but the demand of consumers required sunscreen product which has ease of application, sustain release of actives, lack of side effect, and protect the skin from all harmful damage of UV radiation. Novel formulations is emerging need in the field of sunscreen to avoid all side effect of existing conventional sunscreen which would satisfy the demand of consumer has been reviewed in this article.

KEYWORDS: Melanoma, Pigmentation, Immunesuppression, Hybrid sunscreen.

INTRODUCTION

Sunlight emits visible light, UV radiation and heat which are essential for our daily life, it also stimulate production of vitamin D and helps to control some chronic diseases like Psoriasis. The skin is one of the largest organs in the body in surface area and weight, it shield the rest of body from sunlight. Prolong exposure to UV radiation causes immune suppression, early skin ageing, melanoma, erythema, skin pigmentation, skin cancer, sun burn, damaged to the skin, precancerous skin growth, formation of fine and coarse wrinkles, and photosensitivity reaction.[1]

Sunscreen are the agent used to protect the skin from harmful effect of sunlight, aids the body's natural defense mechanism to protect the skin from harmful radiation. Sunscreen agent act by any one mechanism as to absorb, scatter or reflect sunlight. Several sunscreen are available in the market which contain synthetic photoprotective agent which produces various sensitizing reactions like photo irritation, contact dermatitis, blockage of pores, acne, systemic and local toxicity and allergic reaction because of that they have limited use.[2,3] Main purpose of sunscreen to protect skin from harmful effect of UVA and UVB radiation and to preserve moisture content of skin, the sunscreen should be chemically inert, nontoxic, photostable, non-irritating and protective.[4]

UV- Radiation

UV light are classified according to its wavelength broadly in to three types-

1. **Ultraviolet A (UVA):** 320-400 nm this rays cause skin ageing, wrinkles, damage to cells DNA and play role in some skin cancer.
2. **Ultraviolet B (UVB):** 280-320 nm this rays has slightly more energy than UVA rays they can damage directly DNA in skin cells, sun burns and skin cancer
3. **Ultraviolet C (UVC):** 280-200 nm This rays have more energy and more dangerous than UVA and UVBrays but they blocked by ozone layer and don't reach to the ground and skin normally hence they are not at risk of skin cancer but they can also man made source like welding torch, mercury lamps and UV sanitizing bulbs which are used to kill bacteria and germs[5,6]

Harmful effect of sunlight

1. **Premature aging**– Exposure to sun rays causes premature skin aging called as photo aging, associated with freckling, fine wrinkling, dilation of capillaries, irregular pigmentation and loss of elasticity. Sun exposure is the significant factor in development of wrinkles in early age, UV rays damage collagen and elastic tissues of skin, which becomes fragile and sagging which does not spring back in to shape.sun exposure also causes white cysts and blackheads on the cheekbones and dark white spot on skin.[7,8]

2. **Suppression of Immune system-** Overexposure to to UV radiation it alter the immune systegoogm functions which reduces the body"s ability to fight with certain diseases and interfere with effectiveness of immunization given through the skin.[9]
3. **Cataract and eye disorder**- Excessive exposure to UV radiation increase the risk of cataract and other eye problem. Cataract. Corneal sunburn grows on the outer surface of

the eye and causes retinal tissue damage and development of cloudy bumps along the cornea, Hellwhich can grow over the cornea and prevent clear vision.

4. **Heat exhaustion**- People working in hot environment are at risk of heat exhaustion which is associated with excessive water and salt loss, it includes nausea, dizziness, headache, weakness, thirst, elevated body temperature, decreased urine output.

5. **Heat stroke**- If heat exhaustion not treated then it then it can lead to heat stroke which cause death or permanent disability, symptoms are confusion, slurred speech, loss of consciousness, seizure, hot and dry skin with profuse sweating.

6. **Sunburn**- Sunburn cause due continuous exposure to sunlight symptoms include redness of skin, swelling, tenderness, blisters, nausea, fever, chills and headache

Heat rash- Heat rashes develop at elbow creases, skin folds, on the neck and upper chest occurs due to sweat ducts trap perspiration under the skin, looks like red clusters of pimples or small blisters.

7. **Skin cancer**- Worldwide more than1milions of people per year are diagnosed with non melanoma skin cancer. Development of Skin cancer is the worst consequence of excessive exposure to sun. Commonly three types of skin cancer occurs due to sun exposure 1) squamous cell carcinoma 2) basal cell carcinoma and 3) malignant melanoma.[10,11]

1) **Squamous cell carcinoma-** occurs due to long term sun exposure, burn scars or form chronic ulcers of the skin. Which can be spread to lymph nodes and other organ
2) **Basal cell carcinoma-** It always occurs in sun damaged skin which is usually pink and shiny, it becomes very soft and may get easily injured, specially common in beard area of men where they used a razor, it get bigger and deeper over the time.
3) **Malignant melanoma-** It occurs in young women especially at the age of 18 and 29 years, it is very dangerous and affected any area of skin where there are pigment producing cells, may include the entire skin.

Photo protection- Photo protection is the biochemical process in which various tools are used to reduce molecular damage caused by sunlight, photo protection is an emerging need to avoid harmful effect of sunlight photocarcinogenesis, photoaging, photosensitivity etc. Full covering garments and use of sunscreen is an effective tool for complete protection from harmful UV radiation.

Classification of UV filters (Sunscreen agent).- Uv filters are broadly categorized into inorganic and organic UV filters.

1) **Organic filters-** Organic filters blocks absorbed high energy UV radiation, they are subcategorized as UVAFilters, UVB filters and broad spectrum uv filters. They are safe, non irritant, non volatile, stable as compared to inorganic uv filters but some organic filters like PABA, PABAderivatives and benzophenone showed skin irritation, photosensitivity, eczema and skin cancer.[12,13]
2) **Inorganic UV filters-** Inorganic UV Filters reflects and scattesr UV radiations, they are stable,less toxic and safe. Now a days nano size Titanium dioxide and Zinc oxideused in sunscreen to avoid undesired effect and better sunscreen effect.[14,15,16]
3) **Hybrid UV filters-** Hybrid UV Filters are the combination of both organic and inorganic uv filters, they are half blended materials which creats ideal UV filter agents promotes high spectrum photoprotection and optical transparency and reduced the toxicity.[17,18]

They are broadly classified as shown in fig1.

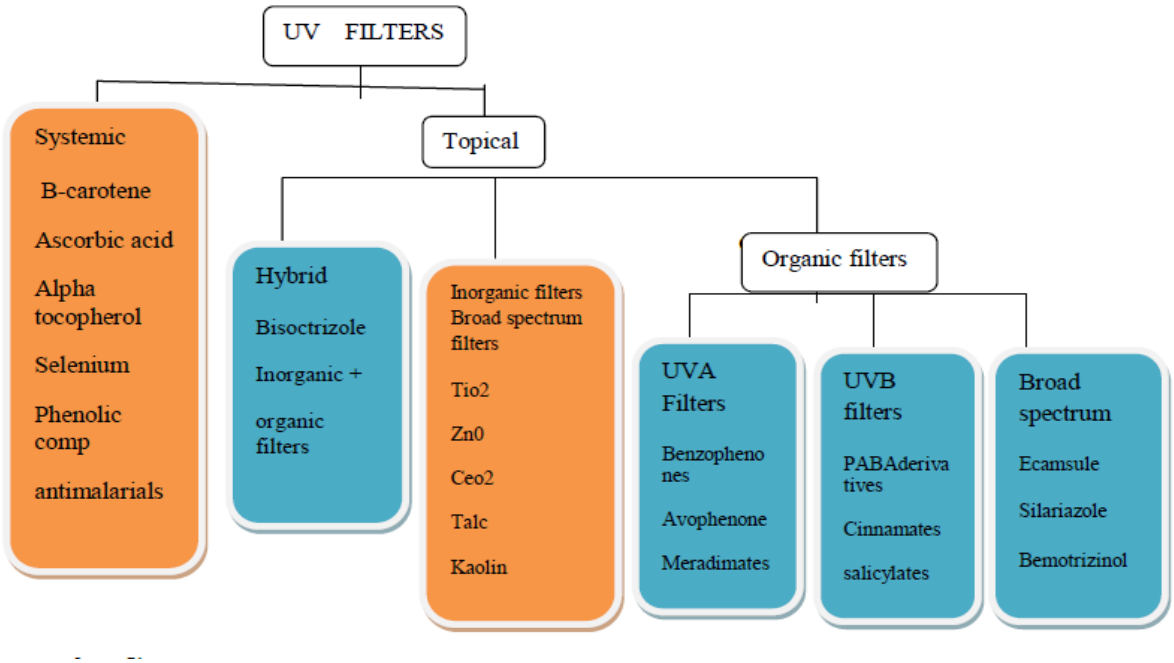

Figure 1: Types of UV filters.

Sun protection factor- The efficacy of sunscreen is usually express by sun protection factor which is defined as-"UV energy required to produce minimal erythemal dose (MED) in protected skin divided by UV energy required to produce MED in unprotected skin."

$$SPF = \frac{\text{Minimal erythema dose in sunscreen protected skin}}{\text{Minimal erythema dose in non sunscreen protected skin}}$$

The minimal erythemal dose (MED) is defined as "The lowest time interval or dosage of UV light radiation sufficient to produce a minimal, perceptible erythema on unprotected skin.[22-24]

The in-vitro methods are in two types

1) Methods that involve measurement of absorption or transmission of UV radiation through sunscreen product films in quartz plates or biomembrane.
2) Methods in which absorption characteristics of sunscreen agent are determined based on spectrophotometric analysis of dilute solution.[25-28]

$$SPF = CF \times \sum_{290}^{320} EE(\lambda) \times 1(\lambda)\, Abs(\lambda)$$

Where

CF= correction Factor

EE= Erythmogenic effect of radiation with wavelength λ

Abs (λ)= Spectrophotometric absorbance values at wavelength λ

The observed absorbance values at 5nm interval (290 nm-320nm) were calculated by using above formula.

Future trends in sunscreen- Due to number of side effects of chemical and synthetic sunscreen agent there is need of safe photo protective agent to be incorporate in sunscreen, Natural sunscreen agent such as antioxidants vit. A, E, C, polyphenols, flavonoids, plant oligosaccharides acts as free radical scavangers, prevents UV induced immunosuppression and other harmful effect,[19,20,21]

Novel sunscreen formulations – Commercially Sunscreens are available in the form of cream, lotion, gel but due drawback of this conventional topical drug delivary system there is need sunscreen to be formulated by using novel drug delivary system.

Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems.

Emulsion – An emulsions are heterogeneous system in which one phase (Liquid) is dispersed in to another phase(liquid) in the form of droplet with help of emulsifying agent The droplet size is 0.5-50 µm. Emulsion further dispersed in to another emulsion is called as double emulsion or multiple emulsion. Emulsion is stable more cost effective, easily spread uniformly over the skin and minimize interaction among the ingredient.[29] Emulsion is unstable at higher temperature.[30] The inner droplet size distribution of w/o emulsion in multiple emulsions is smaller than 0.5µm, while the outer, external multiple emulsions is quite large exceed upto10µm. Emulsions are thermodynamically unstable, they may remain stable for long periods of time, will ultimately undergo phase separation on standing to attain a minimum in free energy. Emulsion when kept for longer periods of time or in case of absence of an emulsifying agent, results in cracking of emulsion or phase inversion.

Types of emulsion

1) **O/W type of emulsion-** In which oil phase is dispersed in a continuous aqueous phase with the help of emulsifying agent the emulsion is known as "oil in water".
2) **W/O type of emulsion-** In which water phase is dispersed in a continuous oily phase with the help of emulsifying agent the emulsion is known as "water in oil".
3) **Multiple emulsion**

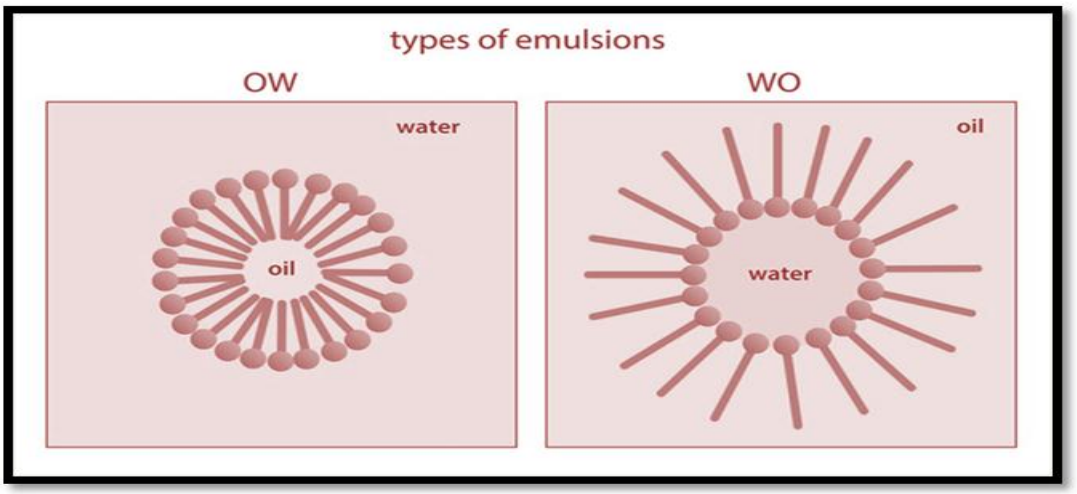

Fig. 2: Emulsion.

Nano emulsion- Nano emulsion are nano sized isoropic dispersed system thermodynamically stable, two immiscible phase are mixed to form single phase by using surfactant and co-surfectants. Nanoemulsion droplet ranges from 50-1000nm.[31,32] Nanoemul sion are having advantages like protection from oxidation and hydrolysis of active ingredient, increased rate of absorption, increased bioavaibility of active medicament, proper drug delivery of lipid soluble drug, incorporate both hydrophilic and lipophilic drug, increase rate of absorption, non toxic, non irritant.[33,34]

In contrast to microemulsion, nanoemulsion are thermodynamically unstable and creats big problem during storage as they required higher energy during preparations of nanoemulsion, prepared by three method high-pressure homogenization, micro fluidization, and phase-inversion temperature method. Nanoemulsion are expensive method as size reductuion of droplet is very difficult and process methods and Ostwald ripening is another factor.[35]

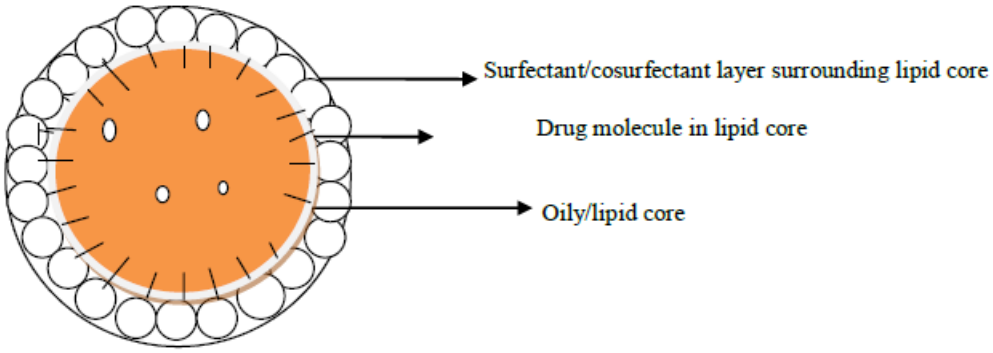

Fig. 3: Structure of nanoemulsion.

Microemulsion – Microemulsion is a transparent, thermodynamically stable, single optically isotropic system consists of water, oil and mixture of surfactant and cosurfectant.[36] Microemulsion are prepared by simple mixing of the components and do not require specific preparation conditions. There are three types of microemulsions 1) oil dispersed in water (o/w), 2)water dispersed in oil (w/o), and 3) bicontinuous.[37,38] Droplets of microemulsion ranges from 0.1-1.0 µm[39] .Microemulsion increase solubility of both hydrophilic -lipophilic active ingredients, microemulsion are thermodynamically stable, long shelf life, formation of microemulsion is reversible process,increased bioavaibility of drug.[40] Limitation of microemulsion are as it required mixture of surfactant and cosurfectant in large concentration, microemulsion has limited solubility of high melting point drugs, stability of micro emulsion depends upon temperature and pH.[41]

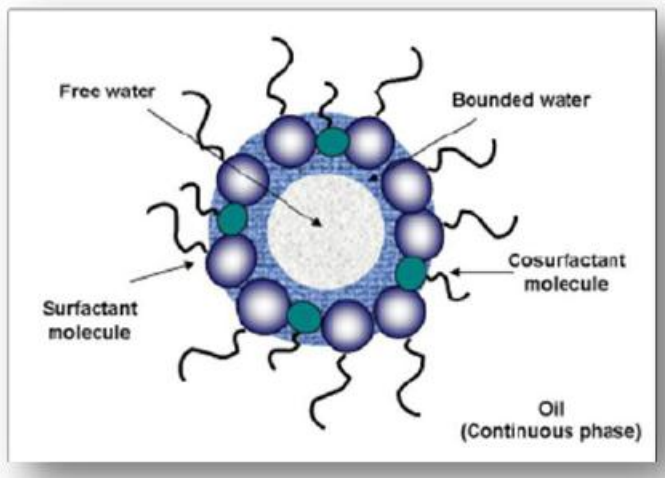

Fig. 4: Structure of microemulsion.

Phytosomes- Phytosomes are complex of phytoconstituents and phospholipids, which increased absorption of conventional herbal extract.[43] Phyto-phospholipid complex has promising strategy to enhance the bioavaibility of phytoconstituents. Water soluble phytoconstituents like flavonoids, tannins, glycosidic aglycones etc are poorly absorbed either due to their large molecular size which cannot absorb by passive diffusion, or due to poor lipid solubility, which limit their ability to pass across the lipid-rich biological membranes, resulting poor bioavailability[42] Phytosomes showed promising drug delivary due to increase in bioavaibility and solubility of poorly soluble or absorbed phytoconstituents. Due to extract- phospholipid complexes, the membrane permeability and O/W partition coefficient of phytoconstituents are greatly improved.[44,45] Phytosomes has greater therapeutic value as it enhances the absorption and bioavaibility of lipid insoluble polar phytoconstituents through oral as well as topical route. Due to increased in absorption of active constituents dose requirement is reduced. Phytosomes shows better stability than liposomes. Phytosome improve percutaneous absorption of plant extract. While limitation of Phytosomes are phytoconstituent from phytosomes are rapidly eliminated.

Phytosomea are prepared by three method

1) **Solvent evaporation method** – In this method mixture of drug-polymer and phospholipid reflux with specific solvent for 2 hours at a temp. 50-60^{o} c, then the mixture concentrated for 5-10 ml, filtered ,collected and dried and stored in amber color bottle at room temp.[46]
2) **Antisolvent precipitation method**-– In this method mixture of drug-polymer and phospholipid reflux with specific solvent for 2 hours at a temp.60^{o} c, then the mixture concentrated for 5-10 ml, add N hexane with continuous stirring to get precipitate,

filtered, collected and keep overnight in vacuum desicator, dried precipitate crushed in mortar and stored in amber color glass bottle at room temperature.[47]

3) **Rotary Evaporation method**-In this method mixture of drug-polymer and phospholipid dissolve in specific solvent in rotary spherical bottom flask with continuous stiring for 3 hours at a temp. not exceeding 40^{o} c then add N hexane with continuous stirring with magnetic stirrer,the precipitate of phytosome loaded drug can be collected and dried and stored in ambar color glass bottle at room temp.[46]

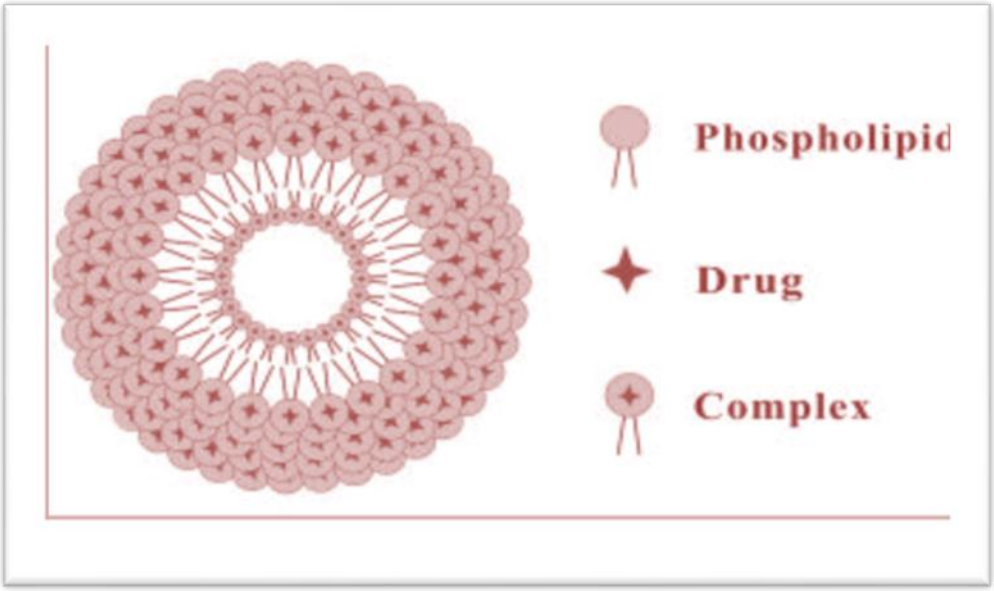

Fig. 5: Structure of phytosome.

Liposomes- Liposomes are spherical shape vesicle consist of one or more phosopholipid bilayers transport lipid or aquous drug to the target site. liposomes are the promising novel drug delivery system to the target tissues used in pharmaceutical and cosmetic field. Liposomes entrapped unstable active drug, avoid degradation and release to target cells. Liposomes form the barrier around the active drug and resists the enzyme in stomach, mouth, alkaline media, intestinal flora, digestive fluid and free radicals, protect the drugs from degradation and oxidation.[48,49] Liposomal encapsulation technology, the novel drug delivery system used to deliver drug to the desired organ. It acts as sustain release drug locally as well as systemically, increase solubility of amphiphilic and lipophilic drug, increase penetration of drug into the cell or tissues. Limitations of liposomes are short shelf life undergoes sometime oxidation and hydrolysis reaction, leakage of fusion of encapsulated drug, lows stability and production cost is high.[50]

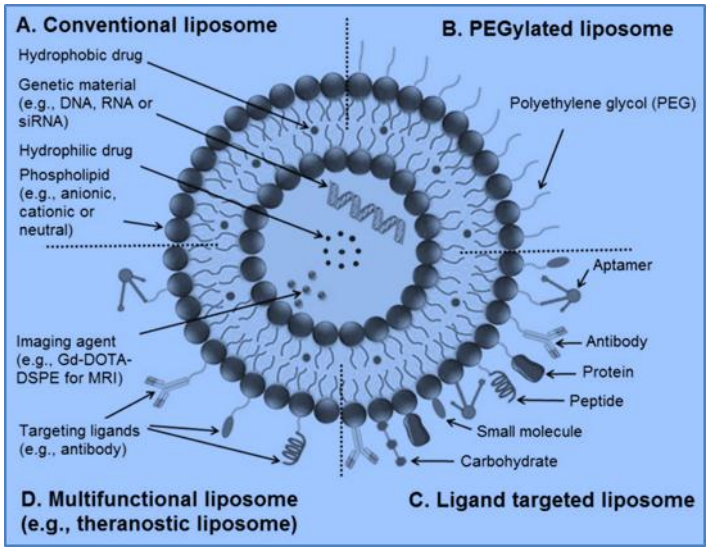

Fig. 6: Structure of liposome.

Niosomes –Niosomes is a nonionic surfactant based vesicle formed by non ionic surfactant and cholesterol. Niosomes are similar to liposomes but they are more stable than liposomes, entrapped both lipophilic and hydrophilic drug either in aqueous or vesicular lipid membrane.[51] .Niosomes constitute non ionic surfactant of the alkyl or dialkyl polyglycerol ether category and cholesterol with subsequent hydration in aqueous medium, lamellar orientation of surfactant lies as hydrophilic ends of the non ionic surfactant point outside and hydrophobic ends face each other to form bilayer. Niosomes may be unilamellar or multilamellar depends upon themethod used for preparation.[52,53] Niosomes used to treats number of diseases like tumor, melanoma, breast cancer, overian cancer, lung cancer,. Localization of drugs encapsulated in niosomes is used to treat tumors of the liver and spleen, leishmaniasis, drug targeting delivary system, studying immune response, transdermal drug delivery system, carriers for haemoglobin, cosmetics and delivery of peptide drug.[54]

Niosomes have many advantages they are chemically stable and long shelf life as compared to liposomes, more compatible with biological system, biodegradable and non immunogenic, low toxicity, protect drug from biodegrading and gives better therapeutic efficacy.[55,56]

Niosomes are having some limitation like noisome show physical stability problems, during storage of dispersion niosomes are at risk of aggregation, fusion, drug leakage, or hydrolysis of encapsulated drugs, during the sterilization of niosomes it needs much effort, while heat sterilization and membrane filtration are unsuitable for niosomes.[57]

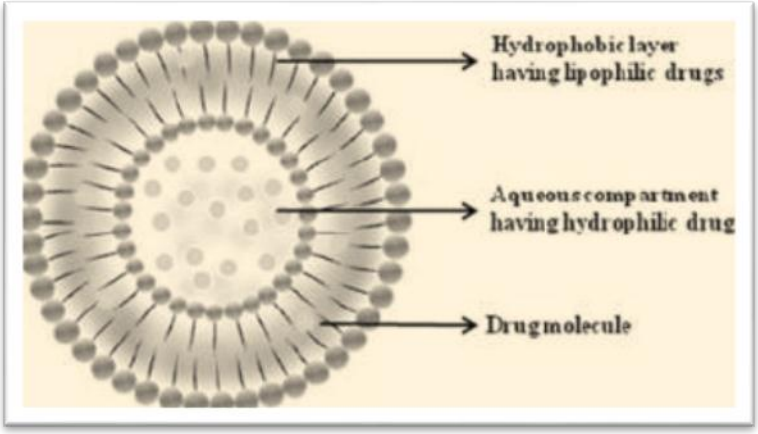

Fig. 7: Structure of niosome.

Transferosomes- Transferosomes are novel vesicular drug delivary system. Transferosomes composed of phospholipid, surfactant, and water, in the form of elastic or deformable vesicle, deliver the drug into or through the skin because of their self optimized and ultra flexible membrane properties. Transferosomes are more elastic than the liposomes which enhance efficient skin penetration of drug.[58,59]

Transferosomes transport large molecule drug across the skin like control release of insulin and interferon by transferosomes across the skin has been efficiently done and increase the stability of labile.[60]

Transferosomes used as a carrier for interferons like leukocytic derived interferon-α (INF-α). It also used as a carrier for the transport of other proteins and peptides.[61,62]

Applications- Transferosomes have the ability to target peripheral subcutaneous tissues is due to minimum carrier associated drug clearance through blood vessels in the subcutaneous tissue. which automatically increases drug concentration locally along with the probability of drug to enter peripheral tissues. Hepatitis B vaccine Transferosomes has been gicen good result. Ketotifen. ketoprofen and diclofenac Transferosomes has been good therapeutic potential than conventional drug delivary system, corticosteroids transferisomes has been proven good therapeuticefficacy at lower doses. Methotrixate transferosome gives better anticancer activity.[63,64]

Advantages

- High penetration power
- High entrapment efficiency for lipophilic drug

- Act as a carrier for large molecular drug e.g. anaesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin.
- Protect metabolic degradation of encapsulated drug
- Biocompatible and biodegradable.

Limitations-

- Transferosomes are chemically unstable because of their
- Purity of natural phospholipids is another criteria militating against adoption of transfersomes as drug delivery vehicles.
- Transfersomes formulations are expensive.

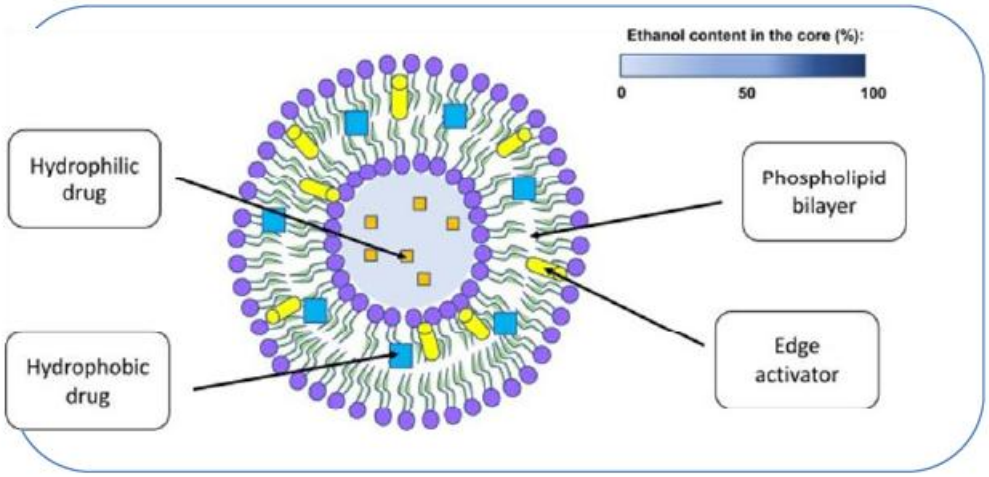

Fig. 8: Strutcture of transferosome.

Nanoparticles (NPS)- Nanoparticles are the microscopic particles with dimension range 1-100nm, can not be seen by optical microscope it require electron microscope. Nanoparticle occurs in various shapes such as nanosphere, nanorods, nanochains, nanostars, nanoflowers, nanoreefs, nanowhiskers, nanoboxes andnanofibers.[68,69] Shape of NPSmay be determined by intrinsic crystal habits. Application of NPS may require specific shapes and sizes, naturally NPS are produces by cosmological, biological, meterological and geological processes.[65,66,67] Nanoparticles are widely used in various field like medicines, drug carrier, contrast photo imaging agriculture, cosmetics, electronics, food, home appliances, printing, textile, petroleum, renewable energy and construction.[70] In medicine NPS areusedin treatment of cancer, tumor, hyperurethemia, Alzheimer's disease, multiple sclerosis and sunscreen.

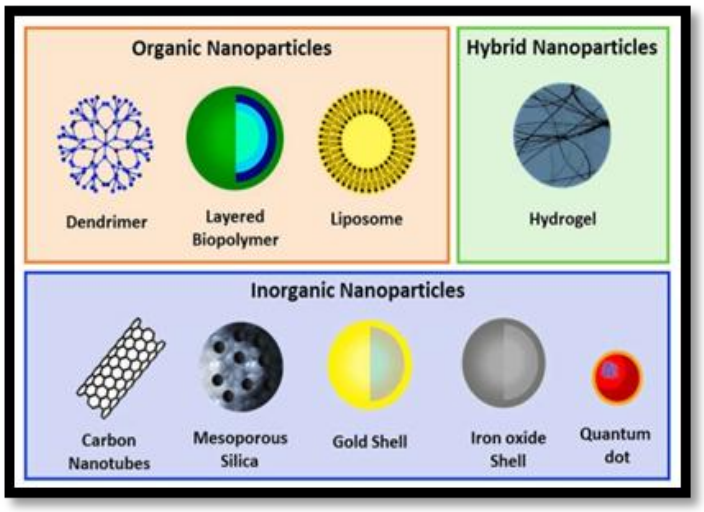

Fig. 9: Structure of nanoparticle.

Dendrimers- Dendrimers are star shaped highly branched three dimensional macromolecule, having high functionality with very low polydispersity. Dendrimers having three component structure consists of central core, an interior branched structure dendrimer and exterior surface with functional group or active drug. Dendrimers are monodisperse macromolecules containing symmetric branching units around thepolymeric core. Denrimers are prepared by divergent method, hyper cores and branched monomers growth, double exponential growth or convergent method. In divergent method the synthesis starts from the central core of the dendrimer to which the arms are attached by adding building blocks in step-wise manner, while in the convergent method synthesis starts from the exterior branch beginning with the molecular structure that ultimately becomes the outermost arm of the final dendrimer.[81]

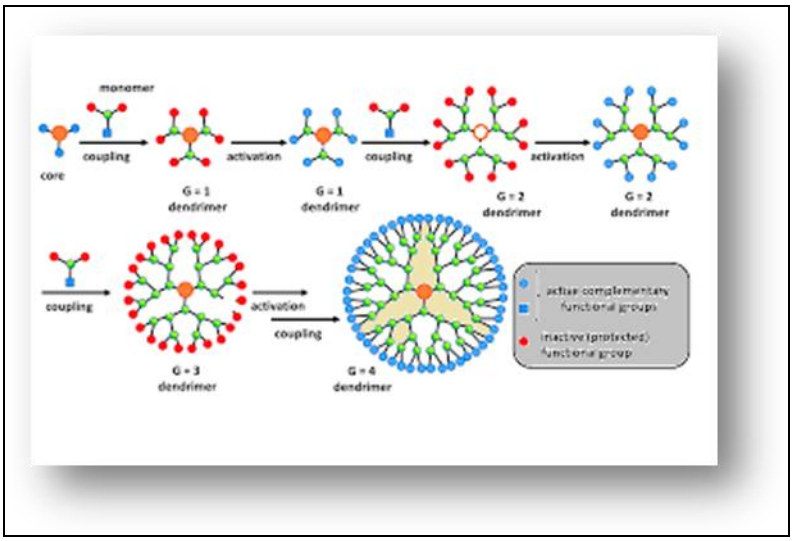

Fig. 10: Structure of dendrimers.

Applications of dendrimers

- Used in treatment of cancer[82]
- Usedin transdermal drug delivery[83]
- Used in Gene delivery[84]
- Used in photodynamic therapy[85]
- Used as magnetic resonance imaging contrast agents[86]
- Used for Boron Neutron capture therapy
- Used as diagnostic MRI contrast agen
- Used as diagnostic X-Ray contrast
- Used in ocular drug delivery
- Used in controlled release drug deliver
- Used in targeted drug delivery
- Used in cosmetics
- Used as solubility enhancer
- Used in pulmonary drug delivery[87,88]

Examples of novel sunscreen formulation

Table 1: Examples of novel sunscreen formulations.

S. no	Name of novel drug delivery system	Sunscreen formulation	Ingredients	References
01	Emulsion	sunscreen emulsion	benzophenone-3, ethylhexyl methoxycinnamate and titanium dioxide	[73]
02	Nanoemulsion	Nanoemulsion sunscreen	Soybean Oil, Avobenzone, and Octyl Methoxycinnamate	[72]
03	Microemulsion	Cistanche tubulosa phenylethanoid glycosides micoremulsion sunscreen	Cremorphor EL and isopropyl myristate (IPM), Millipore, Ethanol, oleic acid (OA) and Tween-80, Ethyl oleate	[71]
04	Phytosomes	Curcumin phytosomal soft gel	Curcumin, soy phos-phatidylcholine (SPC) phospholipid, Polyoxyl 35 castor oil, and Polyoxyl 40 hydro-genated castor, Soya	[74]

			bean oil and capric/caprilic triglyceride,PEG400	
05	Niosomes	Blackteaextract Niosomal sunscreen	Black tea extract,	[75,76]
06	Transferosomes	Transferosomal Gel	Malus domesticaMill extract, phospholipon 90 G, phasphotidyl choline,span80ascorbyl palmitate	[77]
07	Nanoparticles	1.Nanoparticlessunscreen 2. Naringenin nanoparticles sunscreen	Titanium dioxide and Zinc oxide Naringenin NPS	[78] [79]
08	Dendrimers	Polyphenol peptide dendrimers sunscreen	EGCG and silibinin	[80]

CONCLUSION

Immune suppression, photoaging and skin cancer are the major acute and chronic skin disorder cause due to exposure of solar radiation. Use of sunscreen for photoprotection has been increase since from last decade. Large number of conventional sunscreens are available in the market, incomplete sunscreen efficacy of conventional sunscreen due to permeability barrier of the skin by intracellular lipid limits the permeation of UV-filters into the skin. Novel sunscreen approach like nano or micro vesicular drug delivery sunscreen formulation are the advance form of delivery of active sunscreen agent deep into the skin, control drug release, enhance their safety and efficacy. Vesicular drug carrier system encapsulate hydrophilic, lipophilic as well as amphiphilic drugs, prevent their degradation, biocompatible with tissue and organ. This novel technique has got a great potential for overcoming current problems faced by the conventional techniques. Thus, this novel approach has great scope for researcher to formulate novel sunscreen of phytoconstituents which would fulfill the demand of consumers.

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