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NANOCOSMECEUTICALS: AN IMMERGING TREND IN PHARMACY

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ABSTRACT: The global market size was valued at $ 380.2 billion in 2019 and is projected to reach $463.5 billion by 2027, registering a CAGR of 5.3% from 2021 to 2027. Cosmetics have become an in-dispersible feature of the modern lifestyle. The use of cosmetics has increased in males and women in daily routine, which complements the growth of global cosmetic market demand. The skin care industries are trying to develop and market new and efficient products with advanced features that will affect appearance and therapeutic effects. The new development in cosmeceuticals has emerged in the form of Nanocosmeceuticals with the aid of nanotechnology in cosmeceuticals. Since, extrinsic factors like sunlight, dry weather, pollutants, stressful life, poor diet and inadequate sleep are leading to dull and diseased skin, nails and hair can be efficiently treated to get the good looking appearance, flawless complexion and blemish-free skin with the help of nanocosmeceuticals with various nanomaterials like liposomes, niosomes, transfersomes, cubosomes, ethosomes, dendrimers, solid lipid nanoparticles, nanoemulsions, gold nanoparticles, fullerenes, nanocapsules potentially utilized in Sunscreens, antiaging creams, toothpaste, hair growth promoters and mineral cosmetics for myriad superficial and epidermal benefits. The current consolidate various nanomaterials used in the development of nanocosmeceuticals along with their structure, advantages, disadvantages, and utility in skin care products to enhance skin-based therapy.

INTRODUCTION: According to the Food and Drugs Act (FDA), cosmetics can be defined as any product/article to be rubbed, poured, sprinkled or sprayed on, introduced to or otherwise applied to the human body or part of it, except soap, intended for cleansing, beautifying, promoting attract-tiveness, or altering the appearance [1]. The variety of products that belongs to the class cosmetics are shampoos, hair colors, nail lacquers, lipsticks, preparations meant to be applied on the eye and face to beautify them, toothpaste and deodorants, *etc* [2]. Within the last 2- 4 decades' cosmetics have gained tons of recognition in both males and females and are considered essential parts of life. They are attracting people towards it and imparting the physiological effect [3]. Cosmetics are not medicines nor still governed and regulated by FDA (2); however, some cosmetic products could contain ingredients that can impart a biological effect with mild therapeutic action or drug-like benefit on the skin, hence termed "Cosmeceuticals" [1] which improves the appearance of the skin, prevent wrinkles, skin dryness, dark spots, uneven complexion, hyperpigmentation, photoaging and hair damage [4]. It is a midway between cosmetics and drugs as these contain medicinal agents to mitigate, prevent or change any biological function of the skin [2].

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Nanocosmeceuticals: Nanotechnology has the potential to enhance the effectiveness and affect the cellular responses associated with various cosmetics with extensive applications such as enhancement in physicochemical properties and the

visual appeal of the cosmetic, enhancement instability of the actives, modulation in penetration of actives, alteration of the route of penetration (intercellular, transcellular or appendageal), cause site-specific accumulation, modulation in systemic toxicity of actives and enhancement in the intrinsic photostability of the cosmetics [5]. Furthermore, they offer targeted delivery, painless remedies, customized therapies, and simplified solutions over conventional therapies [4].

Nanoparticles are sub-micron-sized particles in the size range of 1–100 nm[4], influencing their dermal penetration and cellular internalization. Size dependant accumulation of the nanocarriers may be obtained in various layers of the skin where the effects are specific to each type of nanoparticle, and hence there is no common cellular effect of all nanoparticles [5].

Various non-scientific approaches actively involved in beauty enhancement with better entrapment, dispersibility, performance, quality, protection, penetration and patient compliance are Liposomes, Niosomes, Transferosomes, Cubosomes, Ethosomes, Dendrimers, Solid lipid nanoparticles, Nanoemulsion, Gold nanoparticles, Fullerene, Nanocapsules and Nanosphere, *etc*.

Liposomes: A liposomeis tiny artificial vesicles of spherical shape made up of the same material as a cell membrane that is cholesterols also from non-toxic surfactants, glycolipids, long-chain fatty acids, sphingolipids, and even membrane proteins [6, 7] first described by British haematologist Dr. Alec D Bangham FRS in 1961 (published 1964), at the Babraham Institute, in Cambridge [8]. Liposomes are used as carriers for both lipophilic and water-soluble molecules because of their unique bilayer structure where hydrophilic substances are encapsulated in the interior aqueous compartments while lipophilic drugs are mainly entrapped within lipid bilayers and their sub-cellular size allows relatively higher intracellular uptake than other particulate systems; improving *in-vivo* drug bioavailability [7]. The structure of liposome is shown in **Fig. 1.**

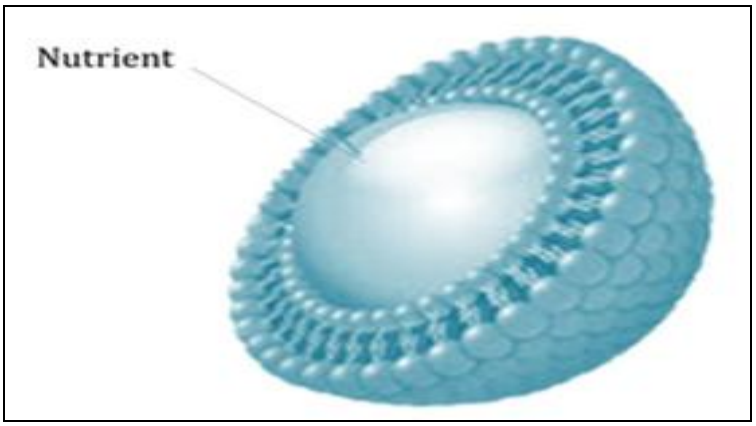

FIG. 1: STRUCTURE OF LIPOSOME

The advantages of liposomes includes selective passive targeting to tumor tissues, increased efficacy and therapeutic index, increased stability *via* encapsulation, reduction in toxicity of the encapsulated agents, site avoidance effect, improved pharmacokinetic effects (reduced elimination, increased circulation lifetimes) and flexibility to couple with site-specific ligands to achieve active targeting while limitations includes cost of phospholipid preparation, liposomes are non-toxic but in the case of cationic liposomes, it tends to be toxic at higher concentrations, sterilization of liposomes is a complicated process as it is unstable in heat and certain methods of radiation while sterilizing with chemicals may affect the stability, as liposomes are prone to oxidation and hydrolysis and they can physically fuse forming larger vesicles, it is very difficult to achieve the stability of liposomal formulation due to chemical and physical degradation, the entrapment efficiency of drug in liposomal system is low and sometimes leakage of drugs takes place while liposomes are rapidly cleared by a phagocytic cell of the Mononuclear Phagocytic System (MPS) which is a major drawback of liposomal systems [9].

Liposomes can encapsulate active ingredients and may be directly applied to the skin cells to transfer and deliver active ingredients to their application site as a cosmetic. As the liposomal walls are physiologically very similar to the material of cell membrane, when cosmetics containing liposomes are applied to the skin, these liposomes are deposited on the skin and begin to merge with the cellular membranes and release their payload of active materials into the cells results in site-specific delivery of actives to the intended cells for a longer period [10].

Niosomes: Niosomes or non-ionic surfactant vesiclesare microscopic lamellar structures of size range between 10 to1000 nm [11] made up of a bilayer of non-ionic surface-active agents and hence the name niosomes [12] and are structurally similar and equiactive to liposomes in drug delivery potential but high chemical stability and economy make Niosomes superior toliposomes [13].

The niosomes are amphiphilic. Both hydrophilic and hydrophobic drugs can be incorporated into niosomes which allows the entrapment of hydrophilic drugs in the core cavity, while hydrophobic drugs in the non-polar region are present within the bilayer, as shown in **Fig. 2** [13].

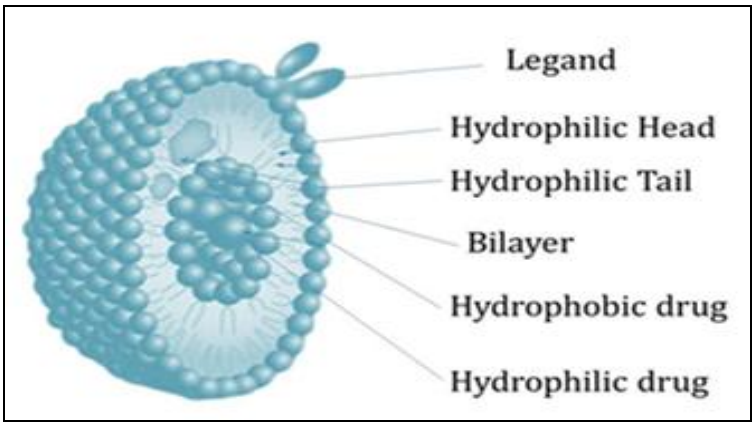

FIG. 2: STRUCTURE OF NOISOME

In niosomes, the vesicles forming amphiphile is a non-ionic surfactant such as Span – 60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as diacetyl phosphate [13]. Niosomes are advantageous as they are chemically stable, osmotically active with long storage time compared to liposomes, non-immunogenic and biodegradable, and hydrophilic head functional groups tend to have very simple surface development and alteration, non-ionic nature of niosomesimpart low toxicity and high compatibility with biological systems, the vesicles can be made to act as a depot, wherein a controlled release of the drug is possible. lipophilic drugs may entrap in vesicular bilayer membranes while hydrophilic drugs in aqueous compartments, exposure to raw material is easy, showing high patient compliance because of the water-based suspension. However, fusion, aggregation, physical instability, leaking of the entrapped drug and hydrolysis of encapsulated drugs that reduce dispersion shelf-life and the time-consuming process of multilamellar vesicle fabrication are some of the limitations associated with niosomes [11, 13, 14, 15]. Niosomescan encapsulates aqueous solutes to act as drug and cosmetic carriers formed by self-assembling non-ionic surfactants in aqueous media. Applying heat or physical agitation helps niosomes attain a closed bilayer structure where the hydrophobic parts are shielded from the aqueous solvent while the hydrophilic head groups are in contact with it. The advantages of using niosomes in cosmetic and skin care applications include their ability to increase the stability of entrapped drugs with improved bioavailability of poorly absorbed ingredients and enhanced skin penetration [16].

Transfersomes: The term “Transferosome” is derived from the Latin word ‘Transfero’ meaning to carry across, and the Greek word ‘soma’ which means a body. A transfersomes is an artificial vesicle designed to be like a cell vesicle or a cell engaged in exocytosis and thus suitable for controlled and potentially targeted delivery of the

drug. Transfersomes is a proprietary drug delivery technology registered by a German company IDEA AG [17]. It is considered an improved form of liposomes with numerous names like ultra-deformable liposomes, deformable liposomes, flexible liposomes, ultra-flexible liposomes, elastic liposomes, *etc*. The basic point of differentiation between the transferosomes and liposomes is that transferosomes have more elasticity and flexibility provided by the edge activator, which modulates the vesicle according to the skin pores and reaches the systemic circulation [18]. Transfersomes have a unique flexible or deformable vesicular structure, colloidal particles with a water-filled core surrounded by a wall of lipids and surfactants (amphiphiles) arranged in a bilayer that is capable of entrapping hydrophilic, lipophilic as well as amphiphilic drugs. Hydrophilic drugs find a place in the internal aqueous environment, while amphiphilic and lipophilic drugs get entrapped in the bilayered wall with electrostatic and/or hydrophobic forces, as shown in **Fig. 3**. If the proportion of water is increased, these amphiphiles can form one or more concentric bilayers [17]. These can spontaneously penetrate the stratum corneum *via* intracellular or transcellular routes and have potential applications in cosmetics and drug delivery [19].

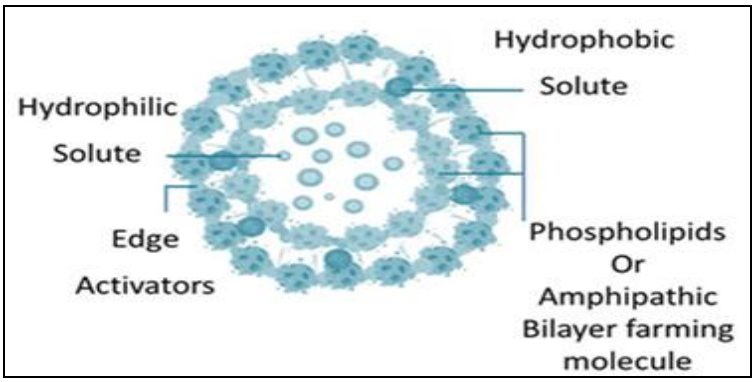

FIG. 3: STRUCTURE OF TRANSFEROSOME

Transferosomes are advantageous as they can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without measurable loss, this high deformability gives better penetration of intact vesicles, gives high entrapment efficiency, in case of lipophilic drug near to 90%, can act as a carrier for low as well as high molecular weight drugs like analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein and albumin *etc*., possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility, act as depot, releasing their contents slowly and gradually, can be used for both systemic as well as topical delivery of drug, biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes, protect the encapsulated drug from metabolic degradation, easy to scale up, as procedure is simple, do not involve lengthy procedure and unnecessary use or pharmaceutically unacceptable additives while limitations of transferosomes include these are chemical instability because of their predisposition to oxidative degradation, Cost effectiveness and purity of natural phospholipids is another question in utilization of transfersomes as drug delivery vehicles [18, 20].

Cubosomes: Cubosomes are discrete, sub-micron, nanostructured particles of the cubic liquid crystalline phase consisting of highly twisted bicontinuous structures, in which a continuous lipid bilayer separates two congruent non-intersecting water channels, and the distinctive internalization of the dispersed particles are built up *via* a highly ordered spontaneous self-assembly process [21, 22]. Cubosomes are nanoparticles, but instead of solid particles, these are self-assembled liquid crystalline particles of certain surfactants with the proper ratio of water with a microstructure that provides unique properties of practical interest [23]. The structure of cubosomes is depicted in **Fig. 4.** The term Cubosomes is coined by Larsson [21, 24] and are generally prepared from a glycerol monooleate (GMO)-water mixture through high-pressure emulsification, using poloxamer 407 as a stabilizer [25].

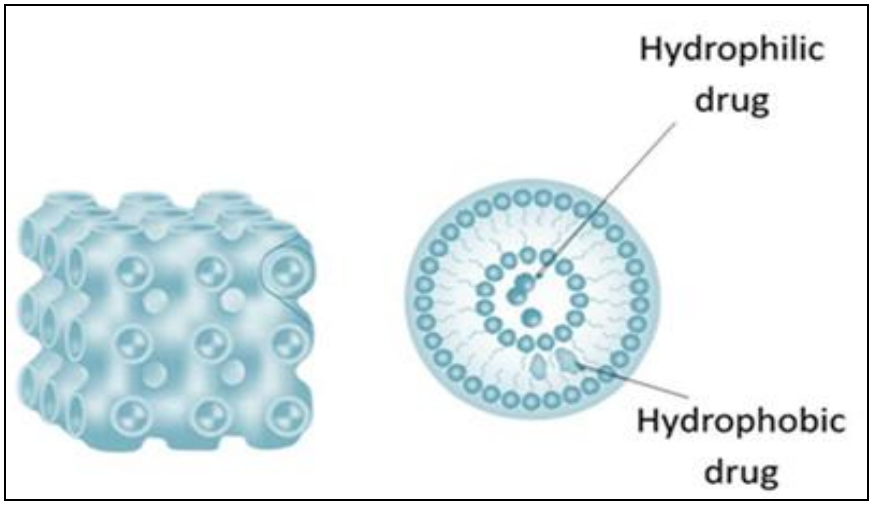

FIG. 4: STRUCTURE OF CUBOSOME

It has the potential to solubilize higher amounts of amphiphilic, hydrophobic, and hydrophilic drugs in their structures [24]. Furthermore, the Cubosomes are also known to be skin-adhesive because they have penetration enhancing effect on the skin as the lipid part of the particles mix with the lipids of the stratum corneum and consequently fluidize the stratum corneum due to the similar cubic phase structure between the cubosomes and the stratum corneum and since this versatile drug nanocarriers can be promising drug carriers to be administrable by transdermal route [22]. Several researchers in association with cosmetic companies like L'Oreal and Nivea are trying to use cubosome particles as oil-in-water emulsion stabilizers and pollutant absorbents in cosmeceuticals [26].

The Cubosomes are an advantageous and reliable drug delivery approach as it is economic, non-toxic, biocompatible and thermodynamically stable with excellent bioadhesive properties, skin permeation enhancement properties and the capability of encapsulating hydrophilic, hydrophobic and amphiphilic substances, its method of preparation is the simple, targeted and controlled release of bioactive agents is possible, high drug loading capacity due to high internal surface area & cubic crystalline structures [21, 24], structure generally maintains the efficacy and stability of actives such as vitamins and proteins, colloidal dispersions can be stabilized by the addition of polymers, possess a sufficient average degree of molecular orientation order to characterize by structural symmetry [23]. Cubosomes are associated with certain disadvantages like high viscosity hinders large-scale production, and low entrapment of water-soluble drugs due to the presence of large amounts of water inside cubosomes [21].

Ethosomes: Ethosomes are non-invasive soft, malleable vesicles with high ethanol content used to deliver drugs to reach the deep skin layers [27, 28]. These are the modified forms of liposomes composed of phospholipids (Phosphatidylcholine, phosphatidylserine and phosphatidic acid), high concentrations of alcohol (ethanol and isopropyl alcohol) and water [29] as shown in **Fig. 5**. Ethosomes efficiently penetrate the skin and improve the delivery of different active agents to deeper layers of skin with improved systemic circulation as compared to conventional liposomes due to their soft and flexible nature [27].

One of the unique features of Ethosomes is their ability to encapsulate molecules of various physicochemical properties efficiently. The presence of ethanol and the high vesicle lamellarity allow for efficient entrapment of hydrophilic, lipophilic and amphiphilic molecules [30]. The high concentration of ethanol (20-50%) in ethosomal formulation could disturb the skin lipid bilayer organization. Therefore, when integrated into a vesicle membrane, it could give the ability the vesicles to penetrate the SC. Furthermore, due to high ethanol concentration, the ethosomal lipid membrane was packed less tightly than conventional vesicles but possessed equivalent stability [31].

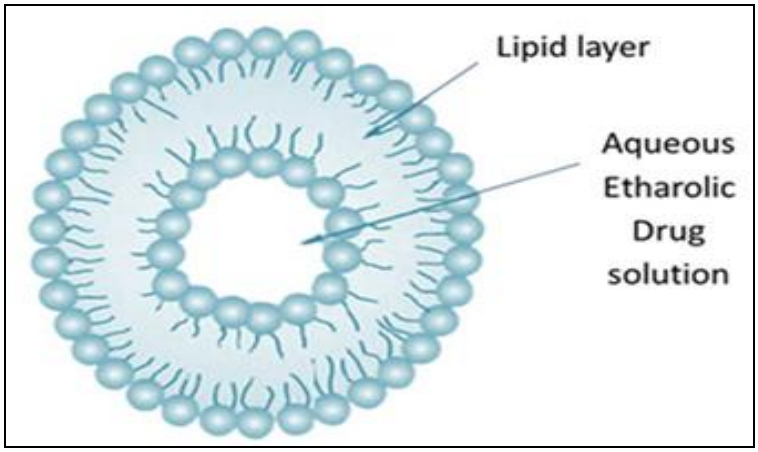

FIG. 5: STRUCTURE OF ETHOSOME

Ethosomes are passive, non-invasive and safe composition with simple technique, non-toxic components and high patient compliance and can efficiently deliver large and diverse group of drugs like peptides, protein molecules, components are approved for pharmaceutical and cosmetic use, available for immediate commercialization, wide range of application in pharmaceutical, veterinary, cosmetic field, more penetration through skin as compared to conventional forms, high deformability, high entrapment capacity and strong transdermal permeation levels in drug delivery systems makes them ideal for transdermal administration while associated with few limitations like it is designed to supply slow, sustained drug delivery, the molecular size of the drug thought to be cheap that is thought to be absorbed percutaneously, adhesive may not adhere well to all types of skin, costly, poor yield, skin irritation or dermatitis due to excipients and enhancers of drug delivery systems, in case if shell protection is ineffective then the ethosomes could coalescence and fall aside on transfer into water, loss of product during transfer from organic to water media [32].

Dendrimers: Dendrimers are defined as nano-sized, radially symmetric molecules with well-defined, homogeneous, and monodisperse structures consisting of tree-like arms or branches as depicted in **Fig. 6**.[33, 34]. The word "dendrimer" originated from two Greek words dendron (tree) and meros, (part). At the same time, Newkome *et al.* independently reported the synthesis of similar macromolecules called 'arborols' from the Latin word 'arbor' also meaning a tree. It can also be called a cascade molecule [35]. Dendrimers possess three distinguished architectural components: an initiator core, interior layers (generations) composed of repeating units, radically attached to the interior core, and exterior (terminal functionality) attached to the outermost interior generations that provide a high degree of surface functionality and versatility [35, 36].

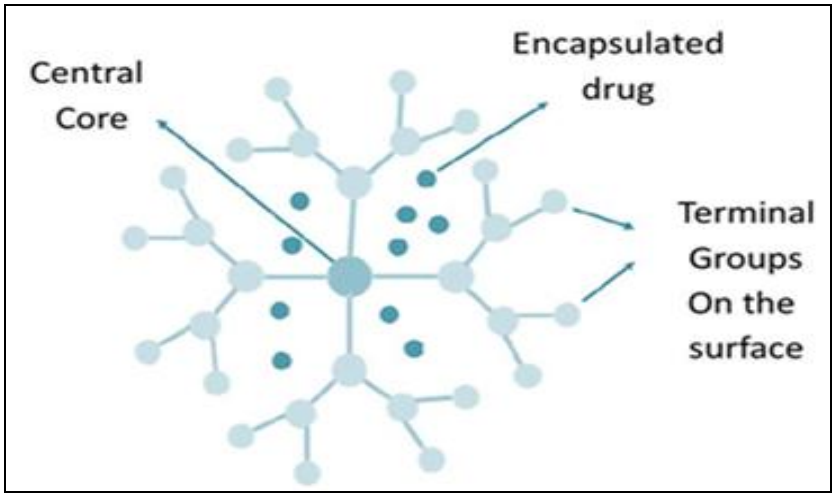

FIG. 6: STRUCTURE OF DENDRIMER

The important properties of dendrimer includes Nanoscale sizes that have similar dimensions to important bio-building blocks for example, proteins, DNA, availability of numbers of terminal surface groups (Z) suitable for bio-conjugation of drugs, signaling groups, targeting moieties or biocompatibility groups, Surfaces that may be designed with functional groups to augment or resist transcellular, epithelial or vascular permeability, an interior void space which can be used to encapsulate small molecule drugs, metals, or imaging moieties which reduces the drug toxicity and facilitates controlled release, Positive biocompatibility patterns that are associated with lower generation anionic or neutral polar terminal surface groups as compared to higher generation neutral apolar and cationic surface groups, Non- or low-immunogenicity associated with most dendrimer surfaces modified with small functional groups or polyethylene glycol (PEG), Surface groups that can be modified to optimize bio-distribution, receptor-mediated targeting, therapy dosage or controlled release of drug from the interior space [35].

The dendrimers are advantageous because of their particle size in the nanometer range (1- 100 nm) and hence easily cross cell membranes with reduced clearance through Reticulo-Endothelial System (RES). It is a perfect carrier for an unstable drug that can be protected in the core and also improves the solubility of the poorly soluble drug. It shows monodispersity. Its Multiple functional groups impart attachments to vector devices for targeting a particular site in the body while the reasons which limit the use of dendrimer are the drug dendrimer complex requires a new construct for clinical testing as it is considered a new chemical entity and shows unsuitability for oral drug delivery as it does not cross gut wall [34, 37].

The drug dendrimer skin interactions propose three potential mechanisms for some drugs, dendrimers may act as a drug release modifier and speed up the drug dissolution, which is the rate-limiting step of percutaneous drug absorption. Secondly, via particle engineering the properties of dendrimers can be tailored to preferably penetrate the skin *via* the follicular route and finally, certain low generation dendrimers may impair the stratum corneum barrier function, particularly in the presence of potent vehicles, which promotes effective delivery of drug to skin and the same phenomenon can be used in Nanocosmeceuticals [38].

Solid Lipid Nanoparticles: Colloidal carriers made up of natural or synthetic polymers with a size range between 10 and 1000 nm are called nanoparticles, and they are ideally used to optimize drug delivery and reduce toxicity [39]. But the major hurdle in the application of nanoparticles to clinical medicine is the shortage of safe polymers and their regulatory approval high cost [40]. To overcome these limitations of polymeric nanoparticles, lipids have been effectively used as an alternative career, particularly for poorly water-soluble drugs [39]. Enhanced oral bioavailability, reduced plasma profile variability, better characterization of lipoidal excipients and improved ability to address the key issues of technology transfer and manufacture scale-up are the few reasons for the increasing interest in lipid-based systems [40, 41].

Furthermore, Liquid lipids are limited in use because of the liquid state of the oil droplets. This limitation can be overcome by the replacement of liquid lipids with solid lipid, which eventually transformed into solid lipid nanoparticles with enormous advantages like good biocompatibility, low toxicity, better delivery of lipophilic drugs and physical stability of the system [39, 41]. The system consists of spherical solid lipid particles dispersed in water or an aqueous surfactant solution, made of a solid hydrophobic core having a monolayer of phospholipids coating in the nanometer ranges. The solid core contains the drug dissolved or dispersed in the solid high melting fat matrix with the potential to carry lipophilic or hydrophilic drugs or diagnostics [42] as shown in **Fig. 7.**

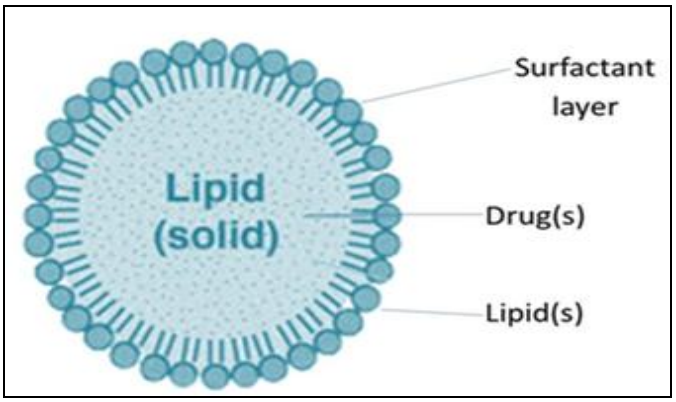

FIG. 7: STRUCTURE OF SOLID LIPID NANOPARTICLES

Advantages of solid lipid nanoparticles include controlled and targeted release of the drug, excellent biocompatibility, improved stability of pharmaceuticals, high and enhanced drug content, easy to scale up and sterilization, better control over release kinetics of encapsulated compounds, enhanced bioavailability of entrapped bioactive compounds, chemical protection of labile incorporated compounds, easy manufacturing than biopolymeric nanoparticles, no requirement of special solvent, long-term stability, application versatility. While particle growth, unpredictable gelation tendency, the unforeseen motion of polymeric transition, poor drug loading capacity, drug expulsion after polymeric transition during storage, and relatively high water content of the dispersions (70-99.9%) are a few limitations of solid lipid nanoparticles [40, 41]. Topical applications of solid lipid nanoparticles are relatively unproblematic with the major advantage of the protective properties for chemically labile drugs against degradation and the occlusion effect due to film formation on the skin [43]. The SLNs have been applied in the preparation of sunscreens and as an active carrier agent for molecular sunscreens and UV blockers with increased skin hydration by 31% after 4 weeks by the addition of 4% SLN to a conventional cream while SLN and NLCs have proved to be controlled release innovative occlusive topicals [44].

Nanoemulsion: A thermodynamically stable isotropically clear dispersion of two immiscible liquids, such as oil and water, stabilized by an interfacial film of surfactant molecules is called a "Nanoemulsion" [45]. It is one of the Colloidal Particulate nanosystems, an Isotropic mixture of drugs with oil, Surfactant, Cosurfactant (Smix), and water having droplet sizes ranging to submicron size range *i.e.* 50-200 nm acting as carriers of drug molecules [46, 47]. These carriers are the solid spheres with amorphous surfaces and lipophilicnegative charge, enhancing the bioavailability of poorly water-soluble drugs as shown in **Fig. 8** [46].

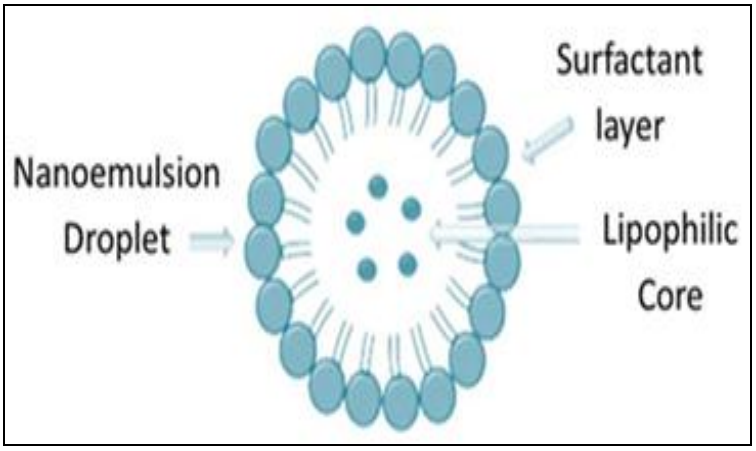

FIG. 8: STRUCTURE OF NANOEMULSION

Nanoemulsions offers several advantages such as it is non-toxic and non-irritant, makes the plasma concentration profiles and bioavailability of drugs more reproducible, deliver peptides that are prone to enzymatic hydrolysis in GIT, higher surface area and higher free energy, avoids creaming or sedimentation effect when stored for long times as because its small size reduces the gravity effect, prevents flocculation and coalescence effect, allows rapid penetration of drug through skin which contributes its efficiency in transdermal drug delivery systems, gives pleasant when applied on skin due to fluidity at optimum concentration of oil and their optically transparent behaviour, feasible with low surfactant concentration, spreadability, moisturizing ability, high stability, can be used instead of liposomes, formulated in numerous dosage foam such as creams, liquids, sprays and foams whereas the limitations are listed as requirement of special instruments for preparation, expensive production cost, role of surfactant, cosurfactant and interfacial chemistry should be studied before formulating the Nanoemulsion, large concentration of surfactant and cosurfactant is required for stabilization of the system, stability can be influenced by environmental parameters such as temperature and pH [45, 48]. Nanoemulsions are becoming a vital area of research in

cosmetology because of their bioactive effects; it acts as a potential vehicle for controlled-release cosmetics. Furthermore, because there is no inherent creaming, sedimentation, flocculation or coalescence observed they can be successfully used as carriers in hair care products, moisturizers, makeup and sunscreens in the form of nanogels, and nanograms [45, 48].

Gold Nanoparticles: Gold nanoparticles (AuNPs) are a promising delivery system used in wide areas like catalysis, bio labelling, nonlinear optical devices, and in the field of drug delivery for efficient transport and release of pharmaceuticals into diverse cell types because of their unique physical and chemical properties compared to either small molecules or other bulk materials [49, 50].

It exhibits different shapes such as spherical, sub-octahedral, octahedral, decahedral, icosahedral multiple twined, multiple twined, irregular shape, tetrahedral, nano triangles, nanoprisms, hexagonal platelets and nanorodsin various sizes ranging from 1 nm to 8 µm as shown in **Fig. 9** [51, 52].

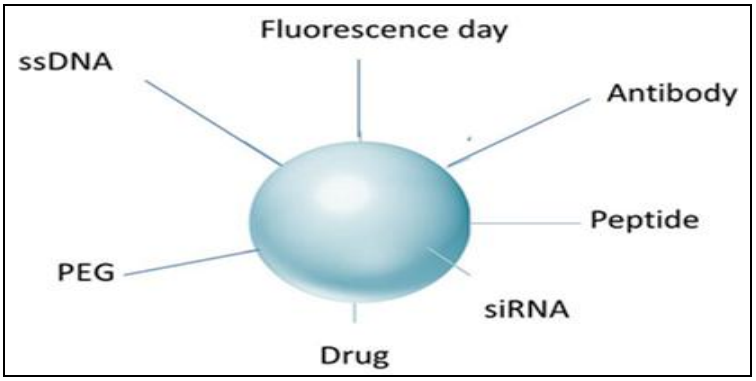

FIG. 9: STRUCTURE OF GOLD NANOPARTICLES

Gold Nanoparticles possess specific intrinsic reactivity because of the increased surface area. Depending upon surface functionalities, particle size and shape, and state of aggregation, cell type can interact with biological systems by employing different uptake routes or targeting different organelles [53]. Gold nanoparticles have been successfully utilized in cosmetics like creams, lotions, face packs, deodorants, and antiaging creams due to their strong antifungal and antibacterial properties. It helps in blood circulation, possesses anti-inflammatory and antiseptic properties, improves the firmness and elasticity of the skin, delays the aging process, and vitalizes skin metabolism [54].

Fullerene: Carbon is the common element in organic compounds used to exist in two allotropic forms diamond and graphite whereas the third form of carbon was discovered as fullerenes in 1985 by Smalley, Kroto and Curl [55]. Fullerene is any molecule with only carbon atoms in various shapes like hollow spheres, tubes, or ellipsoids with interconnected carbon atoms in hexagonal and pentagonal rings. It is similar to graphite, except these may have pentagonal rings. As fullerenes have interlinked ring structures and a geodesic dome having shape-like interconnected rings as shown in **Fig. 10,** was designed by Richard Buckminster Fuller, an architect, the fullerenes were given the name Buckminsterfullerene (C60).

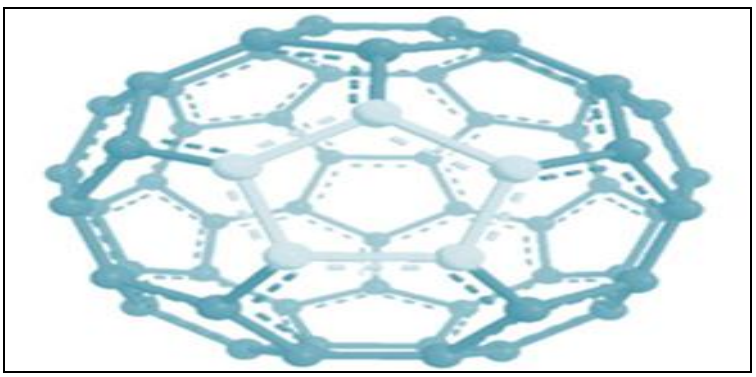

FIG. 10: STRUCTURE OF FULLERENE

The suffix "ene" in the name fullerenes indicates that every carbon atom is bonded covalently to the other three carbon atoms instead of four which shows there are double bonds in fullerenes. The C_{60} has sp2 hybridization as each carbon atom is covalently bonded to three neighboring carbon atoms. It has 20 hexagonal and 12 pentagonal rings. On each polygon's vertices, there is a carbon atom and along the edge of each polygon, there is a bond with two bond lengths and the average bond length of C60 is 1.4 Å. C_{60} is not super-aromatic but it is an alkene having electron deficiency properties. It reacts with species that are rich in electrons [56].

Pure fullerenes have better close packing than impure ones. The C_{60} molecule shows the range of solubility as fluorinated derivatives are more soluble than Bromo derivatives, which have a density of 1.65 g. cm^{-3}, a refractive index of 600 nm, a resistivity of 1014 ohms m^{-1} and a vapor pressure of 5×10^{-6} torr at Room temperature. It is known for its symmetry property and has great resonance energy than the benzene molecule. Hence the molecule was assigned to a new class of aromatic system. It can undergo various reactions such as reduction, oxidation, hydrogenation, halogenation, nucleophilic reactions, radical reaction, transition metal complex reaction and regioselective reactions and could be successfully utilized in the field of medical, electronics, energy, and water treatment/conservation sectors.

The molecule was initially found to be inert, but their unique cage structure and solubility in organic solvents opened up their susceptibility to functionalization via addition and redox reactions, susceptible to degradation or decomposition in presence of light and oxygen. The intersystem crossing of the singlet excited state to energetically lower triplet excited state results in the decaying of the molecule while the triplet excited states are prone to many deactivation processes such as ground state quenching, quenching by molecular oxygen, and transfer of electrons to molecules [57, 58]. Fullerenes display a wide range of different biological activities, strong antioxidant capacities, and effective quenching radical oxygen species (ROS), which are useful in pretoxicity studies. Water and lipid-soluble derivatives can greatly increase their usefulness as antioxidants in health and personal care products, *e.g.*, skin creams, burn creams, and nutritional supplements, which made fullerenes suitable active compounds in the formulation of skin care products [55, 59].

Nanocapsules: Nanocapsules is a class of nanoparticles existing in minuscule size ranging from 10 nm to 1000 nm made up of one or more active materials (core) and a protective matrix (shell)in which the therapeutic substance may be confined [60, 61]. Polymeric nanoparticles are named nanocapsules when they contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids and an oil core [61] as shown in **Fig. 11.**

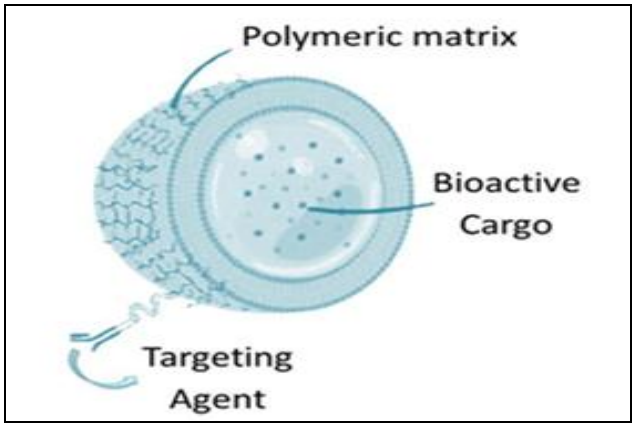

FIG. 11: STRUCTURE OF NANOCAPSULES

The nanocapsules offer various advantages like higher dose loading, reduced irritation of drug at the site of administration, greater protection from degradation during storage, site-specific action, increased bioavailability of the drug, and can be given through various routes of administration including oral, nasal, parenteral, intra-ocular [62] sustained release, incremental drug selectivity and effectiveness, improvement of drug bioavailability and alleviation of drug toxicity, due to submicron size when administered intravenously, reach to the target and release the encapsulated drug. It can be utilized to get controlled release and target drugs against the protection of enzymes, proteins, foreign cells, etc., thus holding biomedical interest. The scope of magnetic nanocapsules has been increased recently because of their intermediate states between mass and atomic materials. Few drugs find difficulty in marketing because of their unpleasant side effects; such drugs, when placed inside the cavity of a nanocapsule, deliver the drug directly to the target site in a reducible dosage (10,000 fold) and lead to the removal of side effects.

It possesses a greater capacity to take on an extensive range of applications with extremely high efficient reproducibility due to itsminuscule size [61]. The major limitations of nanocapsules include very costly formulation with no low yield; productivity is more difficult, technology transfer to commercial production is very difficult, reduced ability to adjust the dose, highly sophisticated technology requires skills to manufacture and stability is big issue owing to its nano size, recycling is very expensive, *etc.* [62]. Nanocapsules are utilized in cosmetics to protect sensitive actives, decrease unwanted odors and remove incompatibility between formulation components [63]. The potential dermatological use of nanocapsules was investigated with the first nanocapsule-based cosmetic product launched by the French company L'Orealin 1995 to improve the impact of their cosmetics [26]. A few examples of nanocosmeceuticals are depicted in **Table 1** as follows.

TABLE 1: EXAMPLES OF NANOCOSMECEUTICAL PRODUCTS

Name of Drug	Type of Nanomaterial	Use	Ref.
Clindamycin	Liposome	In the treatment of acne	64
4-n-butylresorcinol	Liposome	In the treatment of melasma	64
Khellin	Liposome	To treat vitiligo	64
Minoxidil	Liposome	To promote hair growth in alopecia	64
Sodium ascorbyl phosphate	Liposome	As an antioxidant	64
Methotrexate	Liposome	In the treatment of psoriasis	64
Methotrexate	Niosome	In the treatment of psoriasis	65
Tretoin	Niosome	As an anti-acne treatment	65
Ketoconazole	Niosome	As an anti-fungal	65
Fluconazole	Niosome	As an anti-fungal	65
Griseofulvin	Niosome	As an anti-fungal	65
Capsaicin	Transferosomes	Increase skin penetration in the treatment of psoriasis	66
Norgesterol	Transferosomes	Improved transdermal flux	66
Capsaicin	Cubosomes	Used in the treatment of psoriasis, pruritus, and contact allergy	67
Hydroxypropyl β cyclodextrin / minoxidil complex	Cubosomes	It is used for hair growth	67
Erythromycin	Cubosomes	In the treatment and prevention of several types of acne as a result of its bacteriostatic activity against propionibacterium acnes.	67
Palmitoyl peptides (palmitoyl-GHK and palmitoyl- GQPR).	Cubosomes	Pal-GHK and pal-GQPR have anti-wrinkle properties when applied topically to the skin	67
Decorin	Ethosomes	Used as an antiaging cream, treating, repairing, and delaying the visible aging signs of the skin including wrinkle lines, sagging, age spots, loss of elasticity, and hyperpigmentation	68
Minoxidil	Ethosomes	As a hair growth promoter	68
Amphotericin B	Dendrimers	As an antifungal and solubility enhancer	69
Niclosamide	Dendrimers	As an anthelmintic	69
Minoxidil	Solid lipidnanoparticles	Used for enhanced penetration and reduced corrosive action	70
Tacrolimus	Solid lipidnanoparticles	In the treatment of atopic dermatitis	70
Phosphoric acid	Nanoemulsions	In dermatological treatment	03
Ethylene oxide and propylene oxide block copolymers	Nanoemulsions	In dermatological and/or ophthalmological fields	03
Sesame oil raspberry oil	Nanoemulsions	As an antioxidant	71
Rice bran seed oil	Nanoemulsions	In hydration, oiliness, and maintaining normal pH values of skin	71
Vitamin E	Nanocapsules	It reduces the lip bleeding and feathering due to fine lines and wrinkles	26
Perfluorodecalin & Perfluorocarbon	Nanocapsules	In the treatment of skin aging	73
Poly(ε-caprolactone) carrot oil	Nanocapsules	For synergistic SPF activity in sunscreens	74

CONCLUSION: Cosmeceuticals are the rapidly expanding division of beauty and personal care products, combining active pharmaceutical ingredients and cosmetics. Previously it was utilized for conditions such as photoaging, hyperpigmentation, wrinkles, and hair damage to affect appearance. Still, nowadays, it has a therapeutic effect, too, with the evolution of cosmeceuticals to nanocosmeceuticals due to the use of nanotechnology in cosmeceuticals.

In this review, we have discussed a few nanotechnology approaches to preparing nanocosmeceuticals including liposomes, niosomes, transfersomes, cubosomes, ethosomes, dendrimers, solid lipid nanoparticles, nanoemulsions, gold nanoparticles, fullerenes, nanocapsules along with their examples, though few cases of toxicity have been reported in Nanocosmeceuticals. Thus, the safety and efficacy of these Nanocosmeceuticals need to be checked before marketing the same and guidelines regarding production and use is to be regulated. The development, production and marketing of Nanocosmeceuticals need more attention and awareness in the future.

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