

A Review on Nanoparticles Along With Types

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ABSTRACT

A variety of nanoparticles have been generated and analysed over the last few decades, and there has been a lot of buzz about their potential as diagnostic and therapeutic agents. Despite their potential as diagnostic agents, only one diagnostic nanoparticle formulation, iron oxide nanoparticles, has made it into clinical practise thus far. This is due to the challenges of attaining acceptable pharmacokinetic characteristics and reliable monodispersed nanoparticle manufacturing. Furthermore, biodegradation, elimination, and toxicity are also concerns. The vast majority of nanoparticle formulations now in use in clinics are utilised for medicinal purposes. These therapeutic nanoparticles are primarily based on the "enhanced permeability and retention" (EPR) effect, which aims to more efficiently transfer a (chemo-)therapeutic medication to the diseased site while avoiding buildup in healthy organs and tissues. Nanoparticles also offer tremendous potential for theranostic applications, as they can combine diagnostic and therapeutic elements in a single nanoparticle formulation, and are thought to be extremely effective for personalising nanomedicine-based treatments.

I. INTRODUCTION

The prefix 'nano' refers to a Greek prefix that means 'dwarf' or 'very little,' and represents a thousand millionth of a metre (10⁻⁹). There is a difference between nanoscience and nanotechnology. Nanoscience is the study of structures and chemicals on nanometer scales ranging from 1 to 100 nm, and nanotechnology is the technology that uses it in practical applications such as electronics [1]. Various nanoparticle formulations for diagnostic and therapeutic purposes have been developed as a result of recent breakthroughs in nanotechnology. Diagnostic nanoparticles are designed to aid in the visualisation of pathologies and the better understanding of important (patho-) physiological

principles underlying a variety of diseases and treatments. However, due to the complicated demands on their pharmacokinetic characteristics and elimination, nanodiagnostics are only helpful in a restricted number of clinical settings. As a result, the vast majority of nanoparticle formulations employed in clinics today are for therapeutic purposes. By lowering their location in healthy tissues, therapeutic nanoparticles aim to improve the accumulation and release of pharmacologically active substances at the diseased site, increase therapeutic efficacy, and reduce the occurrence and degree of side effects. [2-5] Nanoparticles' intrinsic properties hold great promise for combining diagnostic and therapeutic agents in a single nanoparticle formulation, allowing for theranostic applications such as monitoring biodistribution and target site accumulation, visualising and quantifying drug release, and assessing therapeutic efficacy longitudinally. By allowing patient selection and adjusting treatment efficacy, theranostic nanoparticles could be used to personalise nanomedicine-based therapeutics. [3-11] The attractiveness of nanomedicines originates from the ability to carefully engineer their physicochemical features, such as size, shape, elasticity, surface charge, and surface functionalization, in order to produce desired in vivo outcomes.[12,13]

TYPES OF NANOPARTICLES

1.NANOSUSPENION:-

As a result, nanosuspension technology has proven to be a novel and profitable method for increasing the bioavailability of poorly soluble medicines. Nanosuspension is the dispersion in an aqueous medium of very fine colloidal solid medication particles that are biphasic in nature and stabilised by surfactants. These are easy to make and have more benefits than other methods. Because of their numerous advantages, such as low toxicity, improved bioavailability, targeted drug delivery to a specific site, reduced dosing

frequency, sustained and controlled release effects, high patient compliance, higher durability, ease of administration through various routes, and so on, nanosuspension has now become an integral part of nano-carriers [14]. Pharmaceutical nanosuspension particles must be less than 1 μ m in size, with an average size range of 200-600 nm [15]. This can be accomplished in a variety of ways, including bottom-up or top-down techniques. The top-down approach involves converting large particles into tiny particles [16-18] using techniques such as high-pressure homogenization and medium milling [19-21]. However, this method is highly costly, and there is a risk of heavy metal contamination [22, 23]. The bottom-up technique entails dissolving the medication in the solvent system, followed by drug precipitation with the addition of an anti-solvent [24-25]. Media milling, nanoedge or high pressure homogenization, nanopure or precipitation method, and various other combinational technologies may be utilised to manufacture nanosuspension, either alone or in combination, to overcome the challenges caused by hydrophobic medications.

Nanosuspension's Benefits and Need

Nanosuspension offers various unique characteristics that can be employed as a potential drug delivery method, as described below [26-27].

- Reduced particle size, increased dissolving rate, and absorption rate and extent.
- Physical stability over time.
- In order to improve bioavailability, drugs with a high log P value can be produced as nanosuspensions.
- Nanosuspension can be made with chemicals that are insoluble in water but soluble in oil.
- Oral, topical, parenteral, ophthalmic, pulmonary, and other routes can be used to administer the medicinal nanosuspension. Nanosuspensions can be used in tablet, pellet, hydrogel, and suppositories, for example.
- Drug nanosuspension can help with passive drug targeting.
- It has the potential to improve in vivo performance because to the drug's high dissolving rate and saturation solubility, as well as ease of manufacture and scale-up for large-scale production.
- The ability to modify the surface of the particles for site-specific drug administration.
- The amorphous fraction in particles can be increased via nanosuspension technology, which could lead to a change in crystalline structure and solubility.

2.POLYMERIC MICELLES:-

Over the last few decades, polymers, one of its most versatile families of materials, have transformed our daily lives. Their increased promise in the realm of polymer and pharmaceutical sciences stems from their capacity to establish either spatial or temporal control of medication administration. To date, a variety of polymer-based nanocarriers have been used to treat posterior ocular disorders, including nanoparticles (NPs), liposomes, solid-lipid nanoparticles (SLNs), and dendrimers [28-29]. However, to overcome ocular barriers, the majority of these formulations are supplied by intracameral, intravitreal, and periocular injections, with frequent injections being necessary, which may cause side effects [30]. Following topical application, polymeric micelles have recently shown increasing evidence as a viable nanocarrier to circumvent such constraints and offer therapeutic drug concentrations in the ocular tissues of the anterior and posterior segments [31-32].

Micelle formation principles

The polymeric components self-assemble form micelles, which have a hydrophobic core and a hydrophilic corona and are nanoscale aggregates (10– 200 nm). A thermodynamic process favours such self-assembly. The hydrophilic chains cover the hydrophobic core to prevent direct contact with water, lowering the polymer-water system's interfacial free energy. The lowering of interfacial free energy is required for micellar formation [33,34]. The degree of self-aggregation is influenced by the concentration of polymer chains, the characteristics of the medication or any targeting agents, and the size and content of the copolymer backbone [35]. Micelles can take a variety of morphologies, including spherical, cylindrical, and star-shaped formations, depending on the molecular weight of the block copolymers [36-37].

Polymeric micelle structures

Polymeric micelles are classified into three categories:

- i. polymer–drug conjugates
- ii. drug-encapsulated carriers,
- iii. polyion complex micelles.

3.DENDRIMERS:-

Dendrimers are nanoscale three-dimensional structures with tree-like branches that are well-defined and homogeneous.[38-39]

Dendrimers have attracted a lot of interest in the field of medication delivery, particularly in the creation of personalised medicine systems [40]. In 1978, Vogtle et al. were the first to attempt to design and synthesise dendritic formations ([41]. Originally, these compounds were known as "cascade molecules." Tomalia's group produced a new category of cascade molecules including amides with considerably smaller structures after several years of this publication ([42,]. The term "dendrimers" was coined by Tomalia et al. to describe this novel class of dendritic macromolecules. The word "dendrimer" comes from the Greek words "dendros," which means "tree or branch," and "meros," which means "part" ([43,44]. At the same time, Newkome's group reported the synthesis of comparable macromolecules, which they dubbed "arborols" after the Latin word "arbour," which means "tree." Dendrimers exhibit molecular chemistry (due to their step-by-step controlled synthesis) and polymer chemistry (owing to their monomer composition) ([45,46].

▪ Types of dendrimers

a. Dendrimers made of polypropylene imine (PPI):

The propylamine spacer moieties were first described by Vogtle [47,41] and the polypropylene imine (PPI) is the oldest known dendrimer. Poly-alkylamines with primary amine terminal groups and numerous tertiary tripropylamineamines are used to make them. PPI dendrimers have been researched in the fields of materials science and biology. As an alternative to PPI dendrimers, the terms "polypropylene amine" (POPAM) and "diamino butane" (DAB) are sometimes used. PEI dendrimers are a type of PPI dendrimer in which the central functional groups are diaminoethane or diamino propane.

b. Dendrimers made of polyamidoamine (PAMAM).

PAMAM is a dendrimer with polyamide branches as branching points and tertiary amines as branching points. PAMAM dendrimers were first developed by Tomalia and colleagues in the mid-1980s ([42,48], and they have since been extensively researched by researchers. The heart of "Starburst" dendrimers, a trademark of the PAMAM sub-class, is a tris-aminoethylene-imine group. The name comes from the fact that these high-generation dendrimer structures have a star-like appearance when viewed in two dimensions (2D).

c. Dendrimers of the Frechet type

Hawker and Frechet [49,50] recently discovered a form of dendrimer with a hyper-branched poly-benzyl ether architecture. Frechet dendrimers have $-COOH$ groups as terminal groups, providing a convenient branching point for terminal group functionalization modification. Furthermore, the presence of these polar terminal groups aids in the solubility of this family of dendrimers in both aqueous and polar solvents ([51].

d. Dendrimer with a core and a shell

These are dendritic structures in which a dendrimer molecule serves as the core and is surrounded by dendrimer shells that are covalently attached. The core usually has a higher generation number than the dendrimers around it. Synthetic processes govern the attachment of additional shells, allowing the development of a nanoscale region of 1–100 nm [52].

e. Chiral dendrimers

These dendrimers are made from branches that are constitutionally different but chemically similar to the chiral core. Chirality runs parallel to the functional group axis. Seebach and coauthors [53] constructed chiral dendrimers to investigate the effect of chiral building blocks on dendritic chirality and to demonstrate the potential of enantioselective host complexation using these structures. Dendrimers with merely a chiral core lose their chirality, and hence their optical activity, as their size grows. [52,53,54] are among the many scientists focusing on the development of chiral dendrimers.

f. Dendrimers made of liquid crystalline dendrimers

Many academics have looked at the synthesis of liquid crystals because it has potential industrial uses. Mesogenic liquid crystalline monomers make up these dendrimers. These liquid crystalline phases, or mesophases, are generated by rodlike (calamitic) or disklike (discotic) molecules, such as carbosilane dendrimers with mesogenic functional groups such as cyanobiphenyl and cholesteryl [55-56]. Percec and co-authors report the synthesis of the racemic AB₂ rod-like mesogenic monomer 13-hydroxy-1-(4-hydroxyphenyl)-2-(4-hydroxy-4'-p-terphenyl)tridecan(e5), as well as the creation of its first four generations of monodendrons and dendrimers, utilising a convergent strategy [57]. Amino terminated carbosilane dendrimers, according to Pedziwiatr-Werbicka and colleagues, have the ability to deliver short chain siRNA and anti-HIV

oligodeoxynucleotide to HIV-infected blood cells. These dendrimers had limited utility in the delivery of long-chain double-stranded nucleotides, but dendrimplexes of carbosilane dendrimers and anti-HIV nucleic acid were more stable and less cytotoxic to blood cells than plain dendrimers, indicating their utility in the delivery of bioactives [58-59].

g. Dendrimers of peptides

These are branched macromolecular structures with a peptidyl branching core and covalently attached terminal functional groups that are radial or wedge-like. Divergent and convergent methods of synthesis are often used to make peptide dendrimers. Because of their precise composition and simplicity of production, they have been investigated for a variety of biotechnological and biochemical applications. Peptide dendrimers are used as surfactants and as multiple antigen peptides protein mimics and carriers for medication and gene delivery in the biomedical area.[60-61]

h. Dendrimers with several antigen peptides

Described the construction of multiple antigen peptide (MAP) dendrimers with a polylysine skeleton. The monomer unit of alkyl amino side-chain of lysine is used to introduce branching points in the dendrimer structure. The MAP dendrimer has been extensively researched in biological research, including vaccination and diagnostic studies.[62-63]

i. Glycodendrimers

Glycodendrimers are monodispersed macromolecular dendritic structures containing carbohydrate moiety. [64,65] The terminal groups of most glycodendrimers are saccharide residues, and the middle group is a sugar unit. Glycodendrimers are classified as carbohydrate centered, carbohydrate-based, or carbohydrate-coated.[66,67] These dendrimers bind to lectin-attached systems better than mono-carbohydrate-attached systems. They're utilised to deliver drugs to lectin-rich organs at specified sites.[68,69]

j. Hybrid dendrimers

Hybrid dendrimers are a mixture of linear and dendritic polymers that can be found as a hybrid block or graft copolymer. Due to the spherical shape and huge number of terminal functional groups of dendrimers, dendritic hybrids are likely to arise. Surface active agents, adhesives or compatibilizers, or hybrid dendritic linear polymers can all benefit from the small dendritic fragments' association with the various reactive chain ends. Dendritic hybrids have a compact,

rigid, consistently formed globular structure that has been studied in the field of drug delivery for a variety of purposes.[70-72]

k. Dendrimers made of polyester

Drug therapeutic index development is a crucial area in diseases including cancer, inflammatory diseases, and infectious diseases like HIV. Polyester dendrimers have a lot of promise in this field because of their biocompatibility and biodegradability. They have lower toxicity than other dendrimers due to reduced drug exposure to healthy tissue, which is a desirable attribute in any molecule used as a drug delivery system. These dendrimers have interior void spaces that are similar to those found in common dendrimers, allowing them to be used as a carrier for small molecule drugs, metals, or imaging moieties.[73-77]

4.LIPOSOMES:-

Liposomes are excellent biomembranes and cell models.[78-79] They are known as the excellent model in studies studying the origin, function, and development of primitive cell membranes because of their similarities to biological membranes.[80-81] Furthermore, they are used as carrier systems by the cosmetic, culinary, pharmaceutical, and agricultural industries to protect and distribute various materials such as nutraceuticals, medications, and genetic material. The phospholipid molecules used in the structure of lipid vesicles are the most important component of these naturally occurring bilayers. The major shared trait of bilayer-forming compounds is their amphiphilicity. It's also worth noting that not all phospholipid-based nanostructures are liposomes. Nonliposomal shapes, such as hexagonal, lamellar, micellar, or cubic phases, can also be generated by certain combinations of lipid or phospholipid molecules[82]. Liposomes, on the other hand, are continuously sealed vesicular structures made mostly of phospholipid bilayer(s) in an aqueous medium.[83]. Since the introduction of liposomes to the scientific community 35 years ago, there have been significant advancements in liposomal formulation optimization and engineering techniques .[84] As a result of these advancements, smart plans for tissue and cell targeting are being developed, as well as a longer liposomal half-life in blood flow and the elimination of harmful solvents used during their manufacturing.[85] Nanoliposomes and liposomes have chemical, structural, and thermodynamic features that are

almost identical. In comparison to liposomes, nanoliposomes have a larger surface area and can improve solubility, control release, boost bioavailability, and give precision targeting of the encapsulated substance.[86] Liposomes could be created by using natural ingredients such as soy, milk, or egg .[87] As a result, they can obtain regulatory approval to be used in food-grade products. According to recent research, lipid vesicles can be found in our first natural food, breast milk.[88-89] Humans benefit from phospholipid components of liposomes and liposomes, including liver protection and memory enhancement.[90-92]

The ability of lipid vesicles to target availability is a very useful feature. It is critical to target bioactive molecules to the location where their action is required in order to achieve sufficient concentrations of bioactives at the target site for optimal effectiveness. Liposomes can be used to encapsulate, distribute, and release lipid-soluble and amphiphilic substances, medicines, and biological molecules such as peptides and genes due to the presence of both hydrous and lipid phases in their structure. Liposomes have a lot of potential applications in the food business, current medication delivery systems, and gene therapy systems because of their unique features.[93]

5. QUANTUM DOTS:-

Quantum dots are a type of nanomaterial used for fluorescent labelling and imaging in nanomedicine.[94-97] Quantum dots with different emission bands can be made by altering the particle size. Quantum dots emission bands are narrow and constantly tunable, allowing for multiplexed read-out, and wide absorption bands simplify the excitation source's use circumstances. Quantum dots have a long fluorescence lifetime and outstanding fluorescence stability, which is worth mentioning. These benefits make it easier to observe biomolecules that have been labelled in vivo and provide a valuable tool for nanomedicine. The quality of the synthesis process is determined by the parameters control, which determines the possible application of Quantum dots materials in nanomedicine. As a result, for steerable manufacture and practical applications, accurate Quantum dots synthetic techniques are required.[98-99]

Types of quantum dots

Quantum dots are a sort of low-dimensional substance whose dimensions in all three dimensions are no more than twice the

exciton Bohr radius of the material to which they correspond. Quantum dots have a diameter of 2 to 20 nm and are spherical or quasi-spherical in shape. Semiconductor Quantum dots , carbon Quantum dots, two-dimensional (2D) Quantum dots , and perovskite Quantum dots are the four categories. Wide absorption band and narrow emission band, continuous tunable emission spectrum creation, long fluorescence life, significant Stokes shift, and outstanding biocompatibility are just a few of the optical features of Quantum dots . As a result, Quantum dots are quickly becoming one of the most important materials in nanomedicine.[100-105]

a.) Quantum dots in semiconductors

QDs manufactured of semiconductor materials have come a long way in the last two decades, with their emission band spanning the ultraviolet to near infrared.[94,95] Semiconductor Quantum dots are divided into groups:

- II–VI (CdS, CdSe, CdTe, ZnO, ZnS, ZnSe, and ZnTe)
- III–V (InN, InP, InAs, InSb, GaN, GaP, GaAs, and GaSb)
- IV–VI (PbS, PbSe, and PbTe), IV–VI (PbS, PbS.[106-97]

b.) Quantum dots made of carbon

Carbon Quantum dots (C-QDs) are a type of nanomaterial made up of monodisperse quasispherical nanocarbon dots with a diameter of less than 10 nanometers.[107] The emission band of C-QDs is usually size dependent and excitation wavelength dependent, as it is a new type of Quantum dot. Researchers are quite interested in these qualities.[108-109] Because of their heavy metal composition, conventional semiconductor Quantum dots are hazardous, limiting their use in nanomedicine. C-QDs have the advantages of low toxicity, low cost, and good biocompatibility in addition to similar fluorescence properties. As a result, they can be used in nanomedical applications instead of semiconductor Quantum dots.[110] Researchers have created two types of C-QD synthesising methods in the last decade: "top-down" and "bottom-up."

c.) Quantum dots in two dimensions

In recent years, graphene, a two-dimensional substance, has become a research hotspot in a variety of sectors. Researchers discovered that when the size of a graphene sheet is less than 20 nm, it begins to glow. Nano-scale graphene (graphene Quantum dots) retains the

inherent advantages of graphene while also exhibiting certain new properties, such as a greater specific surface area, improved solubility, and ease of assembly and modification, thanks to the quantum constraint effect. Graphene Quantum dots offer fresh perspectives on graphene research and show the way for future research into additional 2D- Quantum dots. 2D- Quantum dots are rapidly being used in nanomedicine due to their superior physical and chemical properties. The utilisation of microfluidic technology for batch stable synthesis is critical.[111]

d.) Quantum dots made of perovskite

CaTiO₃ was first identified in the Ural Mountains by mineralogist Gustav Rose, who dubbed it perovskite.[112] In the last five years, perovskite quantum dots have been a rising star in scientific study.[113-118] It has been pursued by researchers universally due to its remarkable photoelectric capabilities and predictable application potential. Perovskite is a type of ceramic oxide with the formula ABX₃ as its general formula. [119-121] A-site ions are metal elements with a high ion radius that coordinate with 12 oxygen elements to produce the densest cubic accumulation, primarily maintaining the perovskite structure. B-site ions are transition metal elements (Mn, Co, Fe, etc.) with a small ionic radius that coordinate with six oxygen and occupy the octahedron centre in the cubic dense accumulation. It is frequently the major component determining many aspects of perovskite structure materials due to the flexibility of its valence state. Both A-site and B-site ions can be partially replaced by other metal ions of similar radius, allowing the perovskite to maintain its crystal structure.[122-125] Hybrid organic-inorganic perovskites (HOIPs) Quantum dots [125,126] and all-inorganic perovskites (AIPs) Quantum dots are two types of perovskite Quantum dots.[127-129]

6.) SOLID LIPID NANOPARTICLES

When [130] proposed the terms solid lipid nanoparticles and nanostructured lipid carriers in the 1990s, it seemed like a natural fit: combine the benefits of NPs (mostly metallic and polymeric at the moment) with those of lipid-based parenteral emulsions, which are made up of non-toxic and biodegradable lipid components.[131] These lipid NPs were marketed as a safer alternative to other nanosystems since they are made up of a solid matrix that allows for regulated drug release while being more stable (and surely less expensive) than previous phospholipid-based liposomes.[132]

Solid lipid nanoparticles were first described as tiny, spherical particles made of solid lipids at room temperature, which may be viewed of as ideal crystal lipid matrices capable of accommodating a medicine or other molecules between fatty acid chains.[133] However, it is now recognised that this is not always the case, as disc-like shapes and flat ellipsoidal geometry also were described. Furthermore, instead of being immersed in the solid core, the loaded medicine may be largely adhered to the carrier matrix surface [134-136]

▪ **application of Solid lipid nanocarriers in drug delivery**

Solid lipid nanocarriers have showed considerable promise in drug delivery, particularly in terms of drug release control and targeting to specific tissues. [137-141] With the right excipients and particle manufacturing processes, solid lipid particles can carry both small molecule drug substances and biomacromolecules; solid carriers limit drug mobility, and the lipid digestion product increases drug solubility in vivo. [142-143]

a.) Oral presentation

Poorly water-soluble compounds are a challenge for oral drug administration since their low aqueous solubility is the rate-limiting stage for several compounds' absorption. Oral bioavailability has been found to be improved by lipid-based drug delivery methods. [144,145] Even though different lipid excipients were utilised, oral administration of drug-loaded nanostructured lipid carriers improved bioavailability for poorly water-soluble medicines. Atorvastatin is used to treat dyslipidemia and coronary heart disease Olmesartan medoxomil is being used to treat hypertension and luteolin has been used to treat respiratory disorders. When compared to drug suspension, the bioavailability of those drug compounds from drug-loaded nanostructured lipid carriers increased by approximately 5-fold in rats. T_{max} values reported from drug-loaded nanostructured lipid carriers and drug suspension were not significantly different [146-149]. In beagle dogs, drug-loaded nanostructured lipid carriers increased the oral bioavailability of sirolimus and silymarin by 2 to 3 times compared to control pill or pellets. The T_{max} for both sirolimus and silybin in the in vivo investigation of drug-loaded nanostructured lipid carriers in beagle dogs was smaller than that of the control group, i.e. the marketed goods, which was an interesting finding. The size of solid lipid nanocarriers has an impact on the absorption and

oral bioavailability of compounds that are low water soluble. [150-151]

b.) Parenteral

The colloidal dimensions of solid lipid nanoparticles and the regulated release behaviour of this nanoparticulate carrier enable drug protection and administration by both parenteral and non-parenteral routes, highlighting the versatility of this nanoparticulate carrier. The use of solid lipid nanocarriers via parenteral methods has been documented in publications, including biodistribution and pharmacokinetic investigations on i.v. and i.p. dosing. [152-158] The lipid matrices utilised in solid lipid Nanoparticles produce a sustained release profile that can last for several weeks.[154-156,158] This release profile is most likely influenced by the lipid matrix's composition as well as the integrated molecule's affinity for certain formulation component. Because hydrophilic peptides and proteins tend to collect at the o/w interface during particle formation, a burst release of the drug may be observed after in vivo injection of peptides and proteins delivered by solid lipid nanocarriers. [159-162] During particle preparation, hydrophilic peptides and proteins tend to concentrate at the o/w interface.[163] Although burst release can be effective for delivering an initial dose, [164] it is frequently seen as a substandard controlled release formulation, and there is a desire to prevent it through formulation optimization in general. The burst release of integrated compound is often followed by a well-defined slow release period,[159,160] during which the compound from the particle's core is released.

c.) Dermal drug delivery

Because of their biocompatibility and lipophilicity, lipids have been widely employed as functional excipients in cosmetic formulations and for cutaneous medication delivery. The advantages of solid lipid nanocarriers include the ability to stabilise both drug molecules and labile components in formulations and at the application site, as well as regulating drug release. Using certain excipients and particle preparation procedures in solid lipid nanocarriers formulations may improve both occlusive behaviour at the skin surface and drug molecule penetration across the skin barrier, having adequate drug retention locally to ensure therapeutic effects [164,165-167].

Ocular drug delivery

The advancement of nanotechnology presents a significant opportunity for the effective delivery of ocular drugs and the treatment of anterior segment illnesses[168-169]. The

development of specific nanotherapeutics for different drugs and diseases using a lipid-based nanocarrier strategy offers another option, with the added benefit of solid lipid nanocarriers in regulating drug release and increasing the residence time of both drug molecules and formulations in the precorneal area, improving efficacy. The hydrophobic ion pairing method has been utilised to improve drug loading and control drug release in nanoparticles[170]. As ion-pair complexes, pilocarpine and tobramycin were successfully integrated into solid lipid nanocarriers. [171-173]

II. CONCLUSION

Formulators are having a lot of problems developing pharmaceutical formulations that contain poorly soluble medicines. Nanosuspension is now a potential technique for delivering a variety of therapeutically active chemicals due to a number of significant advantages. This method has the potential to overcome difficulties associated with hydrophobic pharmaceuticals, such as poor solubility and bioavailability. Oral administration necessitates the encapsulation of therapeutic agents in nanosized carriers with a particularly stable structure, as leaking of the payload before it reaches the intended sites might decrease medication bioavailability and efficiency dramatically. The major hurdles for designers of surface-modified liposomes for oral drug administration are still enhancing oral bioavailability and stability, as well as minimising adverse effects; hence, the size and surface charge are the most significant concerns. It's critical to keep developing nanocarrier systems for oral delivery that meet the demands for stability, solubility, and permeability. These nanocarrier systems should be efficient, easy to use, safe, and inexpensive. Solid lipid nanoparticles are a stronger carrier for managing drug release than nanostructured lipid carriers; the composition of lipid particles can be chosen based on the needed drug release profile, delivery route, and application site. The addition of functional excipients to lipid carriers, and also particle surface modification, may expand the range of solid lipid nanocarriers and target pharmaceuticals that can be delivered to specific organs and tissues. A deeper knowledge of the mechanisms driving nanoparticle molecular interactions and biological obstacles would aid future drug carrier design and translation to clinical uses. Ultimately, ARTIFICIAL CELLS, NANOMEDICINE, AND BIOTECHNOLOGY 9 liposomes have cemented their place in current

medication delivery, gene therapy systems, and the food sector. Quantum dots are semiconductor nanocrystals with variables significantly spectra, limited emission spectra, adjustable emission peaks, extended fluorescence lifetimes, low photobleaching, and the capacity to be conjugated to proteins, making them ideal bioimaging probes.

REFERENCE:-

- [1]. Mansoori, G.; Fauzi Soelaiman, T. Nanotechnology—An Introduction for the Standards Community. *J. ASTM Int.* **2005**, *2*, 1–22.
- [2]. Kiessling F, Mertens ME, Grimm J, Lammers T. Nanoparticles for imaging: top or flop? *Radiology* 2014;273(1):10-28.
- [3]. Duncan R, Gaspar R. Nanomedicine(s) under the microscope. *Mol Pharm.* 2011;8(6):2101-41.
- [4]. Rizzo LY, Theek B, Storm G, Kiessling F, Lammers T. Recent progress in nanomedicine: therapeutic, diagnostic and theranostic applications. *Curr Opin Biotechnol.* 2013;24(6):1159-66.
- [5]. Mohanraj VJ, Chen Y. Nanoparticles – A Review. *Trop J Pharm Res.* 2006;5(1):561-573.
- [6]. Lammers T, Aime S, Hennink WE, Storm G, Kiessling F. Theranostic nanomedicine. *Acc Chem Res.* 2011;44(10):1029-38.
- [7]. Theek B, Rizzo LY, Ehling J, Kiessling F, Lammers T. The Theranostic Path to Personalized Nanomedicine. *Clin Transl Imaging.* 2014;2(1):66-76.
- [8]. Lammers T, Rizzo LY, Storm G, Kiessling F. Personalized Nanomedicine. *Clin Cancer Res.* 2012;18(18):4889-94.
- [9]. Kim BYS, Rutka JT, Chan WCW. Nanomedicine. *N Eng J Med.* 2010;363:2434-43.
- [10]. Sumer B, Gao J. Theranostic nanomedicine for cancer. *Nanomedicine.* 2008;3:137-40.
- [11]. Chen X, Gambhir SS, Cheon J. Theranostic nanomedicine. *Acc Chem Res.* 2011;44:841.
- [12]. Pelaz, B.; Alexiou, C.; Alvarez-Puebla, R. A.; Alves, F.; Andrews, A. M.; Ashraf, S.; Balogh, L. P.; Ballerini, L.; Bestetti, A.; Brendel, C.; et al. Diverse Applications of Nanomedicine. *ACS Nano* 2017, *11*, 2313–2381.
- [13]. Shi, J.; Kantoff, P. W.; Wooster, R.; Farokhzad, O. C. Cancer Nanomedicine: Progress, Challenges and Opportunities. *Nat. Rev. Cancer* 2017, *17*, 20–37.
- [14]. Kreuter J. In: Kreuter J, Eds. *Colloidal drug delivery systems*. New York: Marcel Dekker, Inc 1994.
- [15]. Geetha G, Poojitha U, Khan U. Various techniques for preparation of nanosuspension- A review. *Int J Pharm Res Rev* 2014; *3*: 30-7.
- [16]. Muller RH, Peter K. Nanosuspension for the formulation of poorly soluble drugs: Preparation by size reduction technique. *Int J Pharm* 1998; *160*: 229-37.
- [17]. Zhang D, Tan T, Gao I, Zhao W, Wang P. preparation of azithromycin nanosuspension by high-pressure homogenization and its physicochemical characteristics studies. *Drug Dev Ind Pharm* 2007; *33*: 569-75.
- [18]. Chingunpitak J, Puttipipatkachorn S, Chavalitshewinkoon PP, Tozuka Y, Moribe K, Yamamoto K. Formation, physical stability and in-vitro antimalarial activity of dihydroartemisinin nanosuspension obtained by the co-grinding method. *Drug Dev Ind Pharm* 2008; *43*: 314-22.
- [19]. Moschwitz J, Achleither G, Pomper H, Müller RH. Development of an intravenously injectable chemically stable aqueous omeprazole formulation using nanosuspension technology. *European J Pharm Biopharm* 2004; *58*: 615-19.
- [20]. Xiong R, Lu W, Li J, Wang P, Xu R Cuen T. Preparation and characterization of intravenously injectable nimodipine nanosuspension. *Int J Pharm* 2008; *350*: 338-43.
- [21]. Van Eerdenbrugh B, Van den MG, Augustijns P. Top down the production of drug nanocrystals-nanosuspension, miniaturization, and transformation into Solid Products. *Int J Pharm* 2008;364(1):64-75.
- [22]. Krause KP, Kayser O, Mäder K, Gust R, Müller RH. Heavy metal contamination of nanosuspensions produced by high-pressure homogenization. *Int J Pharm.* 2000; *196*(2): 169-72.
- [23]. Verma S, Gokhale R, Burgess DJ. A comparative study of topdown and bottom-up approaches for the preparation of micro/nanosuspensions. *Int J Pharm.* 2009; *380*: 216-22.
- [24]. Li XS, Wang JS, Shen ZG, Zhang PY, Chen JF, Yun J. Preparation of uniform prednisolone microcrystals by a controlled micro- precipitation method. *Int J Pharm* 2007; *342*: 26-32.
- [25]. Zhang X, Xia Q, Gu N. Preparation of all-trans retinoic acid nanosuspensions using a modified precipitation method. *Drug Dev Ind Pharm* 2006 Aug; *32*(7): 857-63.
- [26]. Nagaraju P, et al. Nanosuspensions: Promising Drug Delivery Systems. *Int J Pharm Sci Nanotech* 2010; *2*(4): 679-84.
- [27]. Prabhakar C, Krishna KB. A review on nanosuspensions in drug delivery. *Int J Pharm Biosci* 2011; *2*(1): 549-58.
- [28]. S.H. Boddu, H. Gupta, S. Patel, Drug delivery to the back of the eye following topical administration: an update on research and patenting activity, *Recent Pat. Drug Deliv. Formul.* *8* (2014) 27–36.
- [29]. T.R. Thrimawithana, S. Young, C.R. Bunt, C. Green, R.G. Alany, Drug delivery to the posterior segment of the eye, *Drug Discov. Today* *16* (2011) 270–277.

- [30]. R. Bisht, J.K. Jaiswal, Y.S. Chen, J. Jin, I.D. Rupenthal, Light-responsive in situ forming injectable implants for effective drug delivery to the posterior segment of the eye, *Expert Opin. Drug Deliv.* 13 (2016) 953–962.
- [31]. K. Cholkar, A. Patel, A.D. Vadlapudi, A.K.Mitra, Novel nanomicellar formulation approaches for anterior and posterior segment ocular drug delivery, *Recent Pat. Nanomed.* 2 (2012) 82–95.
- [32]. S. Liu, L. Jones, F.X. Gu, Nanomaterials for ocular drug delivery, *Macromol. Biosci.* 12 (2012) 608–620.
- [33]. T.F. Tadros, Microemulsions, *Applied Surfactants*, Wiley-VCH Verlag GmbH & Co. KGaA 2005, pp. 309–334.
- [34]. H.M. Aliabadi, A. Lavasanifar, Polymeric micelles for drug delivery, *Expert Opin. Drug Deliv.* 3 (2006) 139–162.
- [35]. S.C. Owen, D.P.Y. Chan, M.S. Shoichet, Polymeric micelle stability, *Nano Today* 7 (2012) 53–65.
- [36]. V.P. Torchilin, Structure and design of polymeric surfactant-based drug delivery systems, *J. Control. Release* 73 (2001) 137–172.
- [37]. C. Deng, Y. Jiang, R. Cheng, F. Meng, Z. Zhong, Biodegradable polymeric micelles for targeted and controlled anticancer drug delivery: promises, progress and prospects, *Nano Today* 7 (2012) 467–480.
- [38]. Srinivasa, G.S., Yarena, K.J., 2007. *Nanotechnologies for the Life Sciences: Dendrimers in Cancer Treatment and Diagnosis*. Wiley, New York.
- [39]. Elham, A., Sedigheh, F.A., Abolfazl, A., Morteza, M., Hamid, T.N., Sang, W.J., Younes, H., Kazem, N., Roghiyeh, P., 2014. Dendrimers: synthesis, applications, and properties. *Nanoscale Res. Lett.* 9, 247.
- [40]. Dendrimers, Jain K., 2017. In: *Smart Nano-Engineered Polymers for Bioinspired Applications in Drug Delivery*. Elsevier Ltd, pp. 169–220.
- [41]. Vogtle, F., Buhleier, E.W., Wehner, W., 1978. Cascade and nonskid-chain-like syntheses of molecular cavity topologies. *Synthesis* 2, 155–158.
- [42]. Tomalia, D.A., Baker, H., Dewald, J., Hall, M., Kallos, G., Martin, S., Roeck, J., Ryder, J., Smith, P., 1985. A new class of polymers: starburst-dendritic macromolecules. *Polym. J.* 17, 117–132.
- [43]. Madaan, K., Kumar, S., Poonia, N., Lather, V., Pandita, D., 2014. Dendrimers in drug delivery and targeting: Drug-dendrimer interactions and toxicity issues. *J. Pharm. Bioallied Sci.* 6 (3), 139–150.
- [44]. De Brander, E.M.M., Berg, van den, Meijer, E.W., 1993. Poly (propylenimin)-dendrimer: synthese in gro Derem MaBstab durch heterogen katalysierte Hydrierungen *Angew. Chemistry* 105, 1370.
- [45]. Caminade, A.M., Laurent, R., Majorel, J.P., 2005. Characterization of dendrimers. *Adv. Drug Delivery Rev.* 57, 2130–2146.
- [46]. Malik, A., Chaudhary, S., Garg, G., Tomar, A., 2012. Dendrimers: a tool for drug delivery. *Adv. Biol. Res.* 6 (4), 165–169.
- [47]. Buhleier, E., Wehner, W., Vögtle, F., 1978. “Cascade”- and “nonskid-chain-like” syntheses of molecular cavity topologies. *Synthesis* 155–158.
- [48]. Tomalia, D.A.; Dewald, J.R.; Hall, M.R.; Martin, S.J., Smith, P.B., 1984. In: 1st SPSJ International Polymer Conference, Kyoto, Japan, 65.
- [49]. Hawker, C., Frechet, J.M.J., 1990. A new convergent approach to monodisperse dendritic macromolecules. *J. Chem. Soc., Chem. Commun.* 15, 1010–1013.
- [50]. Hawker, C.J., Wooley, K.L., Frechet, J.M.J., 1993. Unimolecular micelles and globular amphiphiles: dendritic macromolecules as novel recyclable solubilisation agents. *J. Chem. Soc. Perkin Trans. 1* (12), 1287–1297.
- [51]. Elham, A., Sedigheh, F.A., Abolfazl, A., Morteza, M., Hamid, T.N., Sang, W.J., Younes, H., Kazem, N., Roghiyeh, P., 2014. Dendrimers: synthesis, applications, and properties. *Nanoscale Res. Lett.* 9, 247.
- [52]. Li, J., Swanson, D.R., Qin, D., Brothers, H.M., Piehler, L.T., Tomalia, D., Meier, D.J., 1999. Characterizations of core-shell tecto-(dendrimer) molecules by tapping mode atomic force microscopy. *Langmuir* 15, 7347–7350.
- [53]. Seebach, D., Beat, R.P., Greiveldinger, G., Butz, T., Sellner, H., 1998. In: *Chiral Dendrimers – Dendrimers. Topics in Current Chemistry*. Springer, Berlin, Heidelberg, pp. 125–164.
- [54]. Kremers, J.A., Meijer, E.W., 1994. Synthesis and characterization of a chiral dendrimer derived from pentaerythritol. *J. Org. Chem.* 59, 4262–4266.
- [55]. Lorenz, K., Holter, D., Stuhn, B., Mulhaupt, R., Frey, H., 1996. A mesogen-functionalized carbosilane dendrimer—a dendritic liquid-crystalline polymer. *Adv. Mater.* 8, 414–416.
- [56]. Frey, H., Lorenz, K., Mulhaupt, R., 1996. Dendritic polyols based on carbosilanes-lipophilic dendrimers with hydrophilic skin. *Macromol. Symp.* 102, 19–26.
- [57]. Percec, V., Chu, P., Ungar, G., Zhod, J., 1995. Rational design of the first nonspherical dendrimer which displays calamitic nematic and smectic thermotropic liquid crystalline phases. *J. Am. Chem. Soc.* 117, 11441–11454.
- [58]. Pedziwiatr-Werbicka, E., Fuentes, E., Dzmitruk, V., Sánchez-Nieves, J., Sudas, M., Drozd, E., Shakhbazov, A., Shcharbin, D., de la Mata, F.J., Gomez-Ramirez, R., Munoz-Fernandez, M.A., Bryszewska, M., 2013. Novel ‘SiC’ carbosilane dendrimers as carriers for anti-HIV nucleic acids:

- studies on complexation and interaction with blood cells. *Colloids Surf. B.* 109C, 183–189.s
- [59]. Jorg, I., Rolf, M., Dendrimers, Fritz V., 1994. From generations and functional groups to functions. *Angew. Chem. Int. Ed.* 33, 23/24.
- [60]. Sadler, K., Tam, J.P., 2002. Peptide dendrimers: applications and synthesis. *Mol. Biotechnol.* 90, 195–229.
- [61]. Kinberger, G.A., Cai, W., Goodman, M., 2002. Collagen mimetic dendrimers. *J. Am. Chem. Soc.* 124, 15162–15163.
- [62]. Tam, J.P., 1988. Synthetic peptide vaccine design: synthesis and properties of a high density multiple antigenic peptide system. *Proc. Natl. Acad. Sci. U.S.A.* 85, 5409.
- [63]. Tam, J.P., 2000. In: Goodman, M. (Ed.), *Peptide Dendrimers and Protein Mimetics*. Thieme, Stuttgart.
- [64]. Boas, U., Sontjens, S.M., Jensen, K.J., Christensen, J., Meijer, E.W., 2002. New dendrimerpeptide host-guest complexes: towards dendrimers as peptide carriers. *ChemBioChem* 3, 433–439.
- [65]. Choi, J.S., Joo, K.D., Kim, C.H., Kim, K., Park, J.S., 2000. Synthesis of a barbell-like triblock copolymer, poly (L-lysine) dendrimer-block-poly(ethylene glycol)-block-poly (L-lysine) dendrimer, and its self-assembly with plasmid DNA. *J. Am. Chem. Soc.* 122, 474–480.
- [66]. Nanjwade, B.K., Bechra, H.M., Derkara, G.K., Manvi, F.V., Nanjwade, V.K., 2009. Dendrimers: emerging polymers for drug-delivery systems. *Eur. J. Pharm. Sci.* 38, 185–196.
- [67]. Woller, E.K., Cloninger, M.J., 2001. Mannose functionalization of a sixth generation dendrimer. *Biomacromolecules* 2, 1052–1054.
- [68]. Roy, R., Baek, M.G., 2002. Glycodendrimers: novel glycotope isosteres unmasking sugar coding. case study with T-antigen markers from breast cancer MUC1 glycoprotein. *J. Biotechnol.* 90, 291–309.
- [69]. Oliveira, J.M., Salgado, A.J., Sousa, N., Mano, J.F., Reis, R.L., 2010. Dendrimers and derivatives as a potential therapeutic tool in regenerative medicine strategies-a review. *Prog. Polym. Sci.* 35, 1163–1194.
- [70]. Roy, R., Zanini, D., Meunier, S., Romanowska, A., 1993. Solid phase synthesis of dendrimeric sialoside inhibitors of influenza A virus hemagglutinin. *Chem. Commun.* 24, 1869–1872.
- [71]. Pushechnikov, A., Jalisatgi, A.A., Hawthorne, M.F., 2013. Dendritic closomers: novel spherical hybrid dendrimers. *Chem. Commun.* 49, 3579–3581.
- [72]. Kesharwani, P., 2014. Dendrimer as nanocarrier for drug delivery. *Prog. Polym. Sci.* 39 (2), 268–307.
- [73]. Twibanire, K. Jean-d'Amour, Grindley, T. Bruce, 2014. Polyester dendrimers: smart carriers for drug delivery. *Polymers* 6, 179–213.
- [74]. Gillies, E.R., Dy, E., Frechet, J.M.J., Szoka, F.C., 2005. Biological evaluation of polyester dendrimer: poly (ethylene oxide) “Bow-Tie” hybrids with tunable molecular weight and architecture. *Mol. Pharm.* 2, 129–138.
- [75]. Morgan, M.T., Carnahan, M.A., Immoos, C.E., Ribeiro, A.A., Finkelstein, S., Lee, S.J., Grinstaff, M.W., 2003. Dendritic molecular capsules for hydrophobic compounds. *J. Am. Chem. Soc.* 125, 15485–15489.
- [76]. Antoni, P., Hed, Y., Nordberg, A., Nyström, D., von Holst, H., Hult, A., Malkoch, M., 2009. Bifunctional dendrimers: From robust synthesis and accelerated one-pot post-functionalization strategy to potential applications. *Angew. Chem. Int. Ed.* 48, 2126–2130.
- [77]. Jain, K., Kesharwani, P., Gupta, U., Jain, N.K., 2010. Dendrimer toxicity: let's meet the challenge. *Int. J. Pharm.* 394, 122–142.
- [78]. Khosravi-Darani K, Pardakhty A, Honarpisheh H, Rao VM, Mozafari MR. 2007. The role of high-resolution imaging in the evaluation of nanosystems for bioactive encapsulation and targeted nanotherapy. *Micron.* 38:804–818.
- [79]. Mozafari MR, Flanagan J, Matia-Merino L, Awati A, Omri A, Suntres ZE, et al. 2006. Recent trends in the lipid-based nanoencapsulation of antioxidants and their role in foods. *J Sci Food Agric.* 86:2038–2045.
- [80]. Allison SD. 2007. Liposomal drug delivery. *J Infus Nurs.* 30:89–95.
- [81]. Mehrabi M, Esmaeilpour P, Akbarzadeh A, Saffari Z, Farahnak M, Farhangi A, et al. 2016. Efficacy of pegylated liposomal etoposide nanoparticles on breast cancer cell lines. *Turk J Med Sci.* 46:567–571.
- [82]. Siegel D, Tenchov B. 2008. Influence of the lamellar phase unbinding energy on the relative stability of lamellar and inverted cubic phases. *Biophys J.* 94:3987–3995.
- [83]. Mozafari M, Mortazavi S. 2005. *Nanoliposomes: from fundamentals to recent developments*. Oxford, UK: Trafford Pub. Ltd.
- [84]. Golkar N, Samani SM, Tamaddon AM. 2016. Data on cell growth inhibition induced by anti-VEGF siRNA delivered by Stealth liposomes incorporating G2 PAMAM-cholesterol versus Metafectene(R) as a function of exposure time and siRNA concentration. *Data Brief.* 8:1018–1023.
- [85]. Mozafari MR. 2005. Liposomes: an overview of manufacturing techniques. *Cell Mol Biol Lett.* 10:711.
- [86]. Mozafari MR. 2006. *Nanocarrier technologies: frontiers of nanotherapy*. The Netherlands: Springer.
- [87]. Thompson AK, Mozafari MR, Singh H. 2007. The properties of liposomes produced from milk fat globule membrane material using different techniques. *Le Lait.* 87:349–360.

- [88]. Sanchez-Purra M, Ramos V, Petrenko VA, Torchilin VP, Borros S. 2016. Double-targeted polymersomes and liposomes for multiple barrier crossing. *Int J Pharm.* 511:946–956.
- [89]. Nasrabadi HT, Abbasi E, Davaran S, Kouhi M, Akbarzadeh A. 2016. Bimetallic nanoparticles: Preparation, properties, and biomedical applications. *Artif Cells Nanomed Biotechnol.* 44:376–380.
- [90]. Sonali RP, Singh G, Sharma L, Kumari B, Koch S, Singh, et al. 2016. RGDTPGS decorated theranostic liposomes for brain targeted delivery. *Colloids Surf B Biointerfaces.* 147:129–141.
- [91]. Luo L, Bian Y, Liu Y, Zhang X, Wang M, Xing S, et al. 2016. Gold nanoshells: combined near infrared photothermal therapy and chemotherapy using gold nanoshells coated liposomes to enhance antitumor effect (*Small* 30/2016). *Small.* 12:4102.
- [92]. Daraee H, Eatemadi A, Abbasi E, Aval SF, Kouhi M, Akbarzadeh A. 2016a. Application of gold nanoparticles in biomedical and drug delivery. *Artif Cells Nanomed Biotechnol* 44:410–422.
- [93]. Gregoriadis G, Bacon A, Caparrós-Wanderley W, McCormack B. 2002. Plasmid DNA vaccines: entrapment into liposomes by dehydration/rehydration. *Methods Enzymol.* 367:70–80.
- [94]. Mingyong Han, Xiaohu Gao, Jack Z. Su & Shuming Nie (2001). Quantum-dot-tagged microbeads for multiplexed optical coding of biomolecules. *Nature Biotechnology,* 19, 631–635.
- [95]. Igor L Medintz, H Tetsuo Uyeda, Ellen R Goldman, (2005). Quantum dot bioconjugates for imaging, labelling and sensing. *Nature Materials,* 4, 435–446.
- [96]. Peter Reiss, Myriam Protière, Liang Li (2009). Core/shell semiconductor nanocrystals. *Small,* 5, 154–168.
- [97]. Julie A. Smyder, Todd d. Krauss (2011). Coming attractions for semiconductor quantum dots. *Materials Today,* 14, 382–387.
- [98]. Kim E. Sapsford, Thomas Pons, Igor L. Medintz, Hedi Mattoussi (2006). Biosensing with luminescent semiconductor quantum dots. *Sensors,* 6, 925–953.
- [99]. Lijia Shao, Yanfang Gao and Feng Yan (2011). Semiconductor quantum dots for biomedical applications. *Sensors,* 11, 11736–11751.
- [100]. AL Efros, M Rosen, M Kuno, M Nirmal, DJ Norris, M Bawendi (1996). Band-edge exciton in quantum dots of semiconductors with a degenerate valence band: Dark and bright exciton states. *Physical Review B,* 54, 4843–4856.
- [101]. A. L. Efros, Al. L. Efros, “Interband Absorption of Light in a Semiconductor Sphere, *Soviet Physics - Semiconductors.* Vol. 16, No. 7, 1982, pp. 772-775.
- [102]. A.I.Ekimov, Al.L.Efros, A.A.Onushchenko (1985). Quantum size effect in semiconductor microcrystals. *Solid State Communications,* 56, 921–924.
- [103]. A. I. Ekimov & A. A. Onushchenko (1982). Quantum size effect in the optical-spectra of semiconductor micro-crystals. *Soviet Physics Semiconductors-Ussr,* 16, 775–778.
- [104]. R. Rossetti, J. L. Ellison, J. M. Gibson, and L. E. Brus (1984). Size effects in the excited electronic states of small colloidal CdS crystallites. *The Journal of Chemical Physics,* 80, 4464–4469.
- [105]. Rossetti, R., Nakahara, S., & Brus, L. E. (1983). Quantum size effects in the redox potentials, resonance Raman spectra, and electronic spectra of CdS crystallites in aqueous solution. *The Journal of Chemical Physics,* 79, 1086–1088.
- [106]. Peter Reiss, Myriam Protière, Liang Li, (2009). Core/shell semiconductor nanocrystals. *Small,* 5, 154–168.
- [107]. Dr. Sheila N. Baker, Dr. Gary A. Baker Luminescent carbon nanodots: Emergent nanolights. *Angewandte Chemie International Edition,* 49, 6726–6744.
- [108]. Shi Ying Lim, Wei Shen and Zhiqiang Gao (2015). Carbon quantum dots and their applications. *Chemical Society Reviews,* 44, 362–381.
- [109]. Mahasin Alam Sk, Arundithi Ananthanarayanan, Lin Huang et.al (2014). Revealing the tunable photoluminescence properties of graphene quantum dots. *Journal of Materials Chemistry C,* 2, 6954–6960.
- [110]. Hui Ding, Shang-Bo Yu, Ji-Shi Wei et.al (2015). Full-color light-emitting carbon dots with a surface-state-controlled luminescence mechanism. *ACS Nano,* 10, 484–491.
- [111]. Xuewan Wang, Gengzhi Sun, Nan Li, Peng Chen (2016). Quantum dots derived from two-dimensional materials and their applications for catalysis and energy. *Chemical Society Reviews,* 45, 2239–2262.
- [112]. Rose, G. (1839). De novis quibusdam fossilibus quae in montibus Uraliis inveniuntur. *Schade.* Retrieved from <https://books.google.com/books?id=fhSAAAACAAJ&printsec=frontcover&hl=en#v=onepage&q&f=false>.
- [113]. Mingyang Cha, Peimei Da, Jun Wang, Zhanghai Chen et.al (2016). Enhancing perovskite solar cell performance by interface engineering using CH₃NH₃PbBr_{0.912}. 1 quantum dots. *Journal of the American Chemical Society,* 138, 8581–8587.
- [114]. Dibyendu Ghosh, Md Yusuf Ali, Dharendra K Chaudhary, Sayan Bhattacharyya (2018). Dependence of halide composition on the stability of highly efficient allinorganic cesium lead halide perovskite quantum dot solar cells. *Solar Energy Materials and Solar Cells,* 185, 28–35.
- [115]. Jacob B. Hoffman, Gary Zaiats, Isaac Wappes, Prashant V. Kamat (2017). CsPbBr₃ solar cells: Controlled film growth through layer-by-layer

- quantum dot deposition. *Chemistry of Materials*, 29, 9767–9774.
- [116]. Jeong-Hyeok Im, Chang-Ryul Lee, Jin-Wook Lee, et.al. (2011). 6.5% efficient perovskite quantum-dot-sensitized solar cell. *Nanoscale*, 3, 4088–4093.
- [117]. Huan Wang, Luoran Shang, Xiaoxiao Gu, Fei Rong, Yuanjin Zhao(2017). The preparation and biomedical applications of encoded microcarriers. *Progress in Chemistry*, 29, 1159–1172.
- [118]. Lance M. Wheeler, Erin M. Sanehira, Ashley R. Marshall, et.al. (2018). Targeted ligand-exchange chemistry on cesium Lead halide perovskite quantum dots for high-efficiency photovoltaics. *Journal of the American Chemical Society*, 140, 10504–10513.
- [119]. Michael A Carpenter, Christopher J Howard (2009). Symmetry rules and strain/order-parameter relationships for coupling between octahedral tilting and cooperative Jahn–Teller transitions in ABX₃ perovskites. I. Theory. *Acta Crystallographica Section B: Structural Science*, 65, 134–146.
- [120]. Chonghea Li, Xionggang Lu, Weizhong Ding, et.al. (2008). Formability of ABX₃ (X= F, Cl, Br, I) halide perovskites. *Acta Crystallographica Section B: Structural Science*, 64, 702–707.
- [121]. Yi, C, Luo, J., Meloni, S., Boziki, A., Ashari-Astani et.al.(2016). Entropic stabilization of mixed A-cation ABX₃ metal halide perovskites for high performance perovskite solar cells. *Energy & Environmental Science*, 9, 656–662.
- [122]. Giles E. Eperon, Samuel D. Stranks, Christopher Menelaou et.al. (2014). Formamidinium lead trihalide: A broadly tunable perovskite for efficient planar heterojunction solar cells. *Energy & Environmental Science*, 7, 982–988.
- [123]. Jing Feng (2014). Mechanical properties of hybrid organic-inorganic CH₃NH₃BX₃ (B= Sn, Pb; X= Br, I) perovskites for solar cell absorbers. *APL Materials*, 2, 081801.
- [124]. Hyun Suk Jung, Nam-Gyu Park (2015). Perovskite solar cells: From materials to devices. *Small*, 11, 10–25.
- [125]. Constantinos C. Stoumpos, Christos D. Malliakas, Mercouri G. Kanatzidis (2013). Semiconducting tin and lead iodide perovskites with organic cations: Phase transitions, high mobilities, and near-infrared photoluminescent properties. *Inorganic Chemistry*, 52, 9019–9038.
- [126]. Li, Wei Wang, Zheming Deschler, Felix Gao, (2017). Chemically diverse and multifunctional hybrid organic-inorganic perovskites. *Nature Reviews Materials*, 2, 16099.
- [127]. Yongchao Fan, Huanhuan Xing, Qingfeng Zhai et.al (2018). Chemiluminescence of CsPbBr₃ perovskite nanocrystal on the hexane/water interface. *Analytical Chemistry*, 90, 11651–11657.
- [128]. Jie Lei, Fei Gao, Haoxu Wang, et.al.(2018). Efficient planar CsPbBr₃ perovskite solar cells by dual-source vacuum evaporation. *Solar Energy Materials and Solar Cells*, 187, 1–8.
- [129]. Nikolay S. Makarov, Shaojun Guo, Oleksandr Isaienko, et.al (2016). Spectral and dynamical properties of single excitons, biexcitons, and trions in cesium-lead-halide perovskite quantum dots. *Nano Letters*, 16, 2349–2362.
- [130]. R H Müller, M Radtke, S A Wissing (2002). Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Adv. Drug Deliv. Rev.* 54, S131–S155. doi: 10.1016/S0169-409X(02)00118-7
- [131]. C.Schwarz, W.Mehnert, J.S.Lucks, R.H.Muller (1994). Solid lipid nanoparticles (SLN) for controlled drug delivery I. Production, characterization and sterilization. *J. Control. Release* 30, 83–96. doi: 10.1016/0168-3659(94)90047-7.
- [132]. Susana Martins, Bruno Sarmento, Domingos C Ferreira, Eliana B Souto Lipid-based colloidal carriers for peptide and protein delivery-liposomes versus lipid nanoparticles. *Int. J. Nanomed.* 2, 595–607.
- [133]. Anu Puri, Kristin Loomis, Brandon Smith et al. (2009). Lipid-based nanoparticles as pharmaceutical drug carriers: from concepts to clinic. *Crit. Rev. Ther. Drug Carrier Syst.* 26, 523–580. doi: 10.1615/CritRevTherDrugCarrierSyst.v26.i6.10.
- [134]. Jaroslaw Mazuryk, Tobiasz Deptuła, Alice Polchi, Jacek Gapinski et al. (2016). Rapamycin-loaded solid lipid nanoparticles: morphology and impact of the drug loading on the phase transition between lipid polymorphs. *Colloids Surf. A Physicochem. Eng. Asp.* 502, 54–65. doi: 10.1016/j.colsurfa.2016.05.017.
- [135]. Rohan M. Shah, Jitendra P. Mata, Gary Bryant et al. (2019). Structure analysis of solid lipid nanoparticles for drug delivery: a combined USANS/SANS study. *Part. Part. Syst. Charact.* 36:1800359. doi: 10.1002/ppsc.201800359.
- [136]. Demi L. Pink, Orathai Loruthai, Robert M. Ziolk, et al. (2019). On the structure of solid lipid nanoparticles. *Small* 15:e1903156. doi: 10.1002/sml.201903156.
- [137]. Schwarz C, Mehnert W, Lucks JS, Muller RH. Solid Lipid Nanoparticles (SLn) for Controlled Drug-Delivery .1. Production, Characterization and Sterilization. *Journal of Controlled Release* 1994;30(1):83-96.
- [138]. Maretti E, Rossi T, Bondi M, Croce MA, Hanuskova M, Leo E, et al. Inhaled Solid Lipid Microparticles to target alveolar macrophages for tuberculosis. *International Journal of Pharmaceutics* 2014;462(1-2):74-82.
- [139]. Zhao SN, Van Minh L, Li N, Gararnus VM, Handge UA, Liu JW, et al. Doxorubicin hydrochloride-oleic acid conjugate loaded nanostructured lipid carriers for tumor specific

- drug release. *Colloids and Surfaces B-Biointerfaces* 2016;145:95-103.
- [140]. Tapeinos C, Battaglini M, Ciofani G. Advances in the design of solid lipid nanoparticles and nanostructured lipid carriers for targeting brain diseases. *Journal of Controlled Release* 2017;264:306-32.
- [141]. Zhang RX, Ahmed T, Li LY, Li J, Abbasi AZ, Wu XY. Design of nanocarriers for nanoscale drug delivery to enhance cancer treatment using hybrid polymer and lipid building blocks. *Nanoscale* 2017;9(4):1334-55.
- [142]. Almelda AJ, Souto E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. *Advanced Drug Delivery Reviews* 2007;59(6):478-90.
- [143]. Borkar N, Xia DN, Holm R, Gan Y, Mullertz A, Yang MS, et al. Investigating the correlation between in vivo absorption and in vitro release of fenofibrate from lipid matrix particles in biorelevant medium. *European Journal of Pharmaceutical Sciences* 2014;51:204-10.
- [144]. Mu HL, Holm R, Mullertz A. Lipid-based formulations for oral administration of poorly water-soluble drugs. *International Journal of Pharmaceutics* 2013;453(1):215-24.
- [145]. Lin CH, Chen CH, Lin ZC, Fang JY. Recent advances in oral delivery of drugs and bioactive natural products using solid lipid nanoparticles as the carriers. *Journal of Food and Drug Analysis* 2017;25(2):219-34.
- [146]. Khan S, Baboota S, Ali J, Narang RS, Narang JK. Chlorogenic acid stabilized nanostructured lipid carriers (NLC) of atorvastatin: formulation, design and in vivo evaluation. *Drug Development and Industrial Pharmacy* 2016;42(2):209-20.
- [147]. Brunner HR. The new oral angiotensin II antagonist olmesartan medoxomil: a concise overview. *Journal of Human Hypertension* 2002;16:S13-S16.
- [148]. Liu Y, Wang L, Zhao YQ, He M, Zhang X, Niu MM, et al. Nanostructured lipid carriers versus microemulsions for delivery of the poorly water-soluble drug luteolin. *International Journal of Pharmaceutics* 2014;476(1-2):169-77.
- [149]. Kaithwas V, Dora CP, Kushwah V, Jain S. Nanostructured lipid carriers of olmesartan medoxomil with enhanced oral bioavailability. *Colloids and Surfaces B-Biointerfaces* 2017;154:10-20.
- [150]. Yu Q, Hu XW, Ma YH, Xie YC, Lu Y, Qi JP, et al. Lipids-based nanostructured lipid carriers (NLCs) for improved oral bioavailability of sirolimus. *Drug Delivery* 2016;23(4):1469-75.
- [151]. Shangguan MZ, Lu Y, Qi JP, Han J, Tian ZQ, Xie YC, et al. Binary lipids-based nanostructured lipid carriers for improved oral bioavailability of silymarin. *Journal of Biomaterials Applications* 2014;28(6):887-96.
- [152]. Almeida JPM, Chen AL, Foster A, Drezek R. In vivo biodistribution of nanoparticles. *Nanomedicine* 2011;6(5):815-35.
- [153]. Hirsjarvi S, Sancey L, Dufort S, Belloche C, Vanpouille-Box C, Garcion E, et al. Effect of particle size on the biodistribution of lipid nanocapsules: Comparison between nuclear and fluorescence imaging and counting. *International Journal of Pharmaceutics* 2013;453(2):594-600.
- [154]. Fundaro A, Cavalli R, Bargoni A, Vighetto D, Zara GP, Gasco MR. Non-stealth and stealth solid lipid nanoparticles (SLN) carrying doxorubicin: Pharmacokinetics and tissue distribution after i.v. administration to rats. *Pharmacological Research* 2000;42(4):337-43.
- [155]. Manjunath K, Venkateswarlu V. Pharmacokinetics, tissue distribution and bioavailability of clozapine solid lipid nanoparticles after intravenous and intraduodenal administration. *Journal of Controlled Release* 2005;107(2):215-28.
- [156]. Zara GP, Cavalli R, Bargoni A, Fundaro A, Vighetto D, Gasco MR. Intravenous administration to rabbits of non-stealth and stealth doxorubicin-loaded solid lipid nanoparticles at increasing concentrations of stealth agent: Pharmacokinetics and distribution of doxorubicin in brain and other tissues. *Journal of Drug Targeting* 2002;10(4):327-35.
- [157]. Ballot S, Noiret N, Hindre F, Denizot B, Garin E, Rajerison H, et al. Tc-99m(188)relabeled lipid nanocapsules as promising radiotracers for imaging and therapy: formulation and biodistribution. *European Journal of Nuclear Medicine and Molecular Imaging* 2006;33(5):602-7.
- [158]. Bargoni A, Cavalli R, Zara GP, Fundaro A, Caputo O, Gasco MR. Transmucosal transport of tobramycin incorporated in solid lipid nanoparticles (SLN) after duodenal administration to rats. Part II - Tissue distribution. *Pharmacological Research* 2001;43(5):497-502.
- [159]. Garcia-Fuentes M, Prego C, Torres D, Alonso MJ. A comparative study of the potential of solid triglyceride nanostructures coated with chitosan or poly(ethylene glycol) as carriers for oral calcitonin delivery. *European Journal of Pharmaceutical Sciences* 2005;25(1):133-43.
- [160]. Reithmeier H, Herrmann J, Gopferich A. Lipid microparticles as a parenteral controlled release device for peptides. *Journal of Controlled Release* 2001;73(2-3):339-50.
- [161]. Almeida AJ, Runge S, Muller RH. Peptide-loaded solid lipid nanoparticles (SLN): Influence of production parameters. *International Journal of Pharmaceutics* 1997;149(2):255-65.
- [162]. Hu FQ, Hong Y, Yuan H. Preparation and characterization of solid lipid nanoparticles containing peptide. *International Journal of Pharmaceutics* 2004;273(1-2):29-35.

- [163]. Zhang N, Ping QN, Huang GH, Xu WF, Cheng YN, Han XZ. Lectin-modified solid lipid nanoparticles as carriers for oral administration of insulin. *International Journal of Pharmaceutics* 2006;327(1-2):153-9.
- [164]. Muller RH, Mader K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. *European Journal of Pharmaceutics and Biopharmaceutics* 2000;50(1):161-77.
- [165]. Jain S, Patel N, Shah MK, Khatri P, Vora N. Recent Advances in Lipid-Based Vesicles and Particulate Carriers for Topical and Transdermal Application. *Journal of Pharmaceutical Sciences* 2017;106(2):423-45.
- [166]. Lauterbach A, Muller-Goymann CC. Applications and limitations of lipid nanoparticles in dermal and transdermal drug delivery via the follicular route. *European Journal of Pharmaceutics and Biopharmaceutics* 2015;97:152-63.
- [167]. Roberts MS, Mohammed Y, Pastore MN, Namjoshi S, Yousef S, Alinaghi A, et al. Topical and cutaneous delivery using nanosystems. *Journal of Controlled Release* 2017;247:86-105.
- [168]. Janagam DR, Wu LF, Lowe TL. Nanoparticles for drug delivery to the anterior segment of the eye. *Advanced Drug Delivery Reviews* 2017;122:31-64.
- [169]. Sanchez-Lopez E, Espina M, Doktorovova S, Souto EB, Garcia ML. Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye - Part II - Ocular drug-loaded lipid nanoparticles. *European Journal of Pharmaceutics and Biopharmaceutics* 2017;110:58-69.
- [170]. Song YH, Shin E, Wang H, Nolan J, Low S, Parsons D, et al. A novel in situ hydrophobic ion pairing (HIP) formulation strategy for clinical product selection of a nanoparticle drug delivery system. *Journal of Controlled Release* 2016;229:106-19.
- [171]. Cavalli R, Morel S, Gasco MR, Chetoni P, Saettone MF. Preparation and Evaluation In-Vitro of Colloidal Lipospheres Containing Pilocarpine As Ion-Pair. *International Journal of Pharmaceutics* 1995;117(2):243-6.
- [172]. Cavalli R, Gasco MR, Chetoni P, Burgalassi S, Saettone MF. Solid lipid nanoparticles (SLN) as ocular delivery system for tobramycin. *International Journal of Pharmaceutics* 2002;238(1-2):241-5.
- [173]. Chetoni P, Burgalassi S, Monti D, Tampucci S, Tullio V, Cuffini AM, et al. Solid lipid nanoparticles as promising tool for intraocular tobramycin delivery: Pharmacokinetic studies on rabbits. *European Journal of Pharmaceutics and Biopharmaceutics* 2016;109:214-23.