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Recent Advancement in Ocular Drug Delivery System: A Systematic Review

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ABSTRACT

Recent scientific and technological advancements have made ophthalmology a top priority for the study of therapeutic products, including the creation, preclinical testing, and clinical evaluation of novel medications, medical devices, and drug-medical device combinations. In order to decrease metabolism and elimination and increase residence time in ocular tissues and compartments, sustained-release drug delivery systems such as liposomes, micelles, nano-emulsions, nanoparticles with colloidal structures, and intraocular implants have been developed. Research is also being conducted in the area of cutting-edge medicines, including those based on gene or cell systems, both of which are considered high-risk products because to their intricate structures. Regarding the definition of drug (medicinal product) and recent changes in regulation, this article reviews recent advancements in ophthalmic drug, gene, and cellular delivery systems and related goods as well as breakthroughs in advanced therapeutic medicinal Products.

Keywords- ODDS, Chitson, nanotechnology, Drug therapy.

I. INTRODUCTION

Since its introduction in the field of biomedicine, microtechnology has been making rapid progress into the realm of pharmaceutical sciences and technology [1–4]. It offers completely new opportunities to develop very sophisticated and precise drug delivery tools [5–6], thanks to the impressive evolution of new manufacturing techniques. A significant number of concepts and implemented projects, which is reflected in a large number of scientific papers, continually pushes pharmaceutical technology to a new level of coping with various diseases, including those related to the eye [7–10]. Inserts are another form of administration that is possible for ophthalmic medications. They are typically solid or semi-solid forms with the appropriate size and shape, and their primary purpose is to be inserted into the conjunctival sac. They are made up of a reservoir for the active substance along with a matrix structure or a film that controls the rate at which the active ingredient is released. Inserts are used less commonly since their application is difficult, they may cause visual abnormalities, and the feeling of the presence of a foreign body in the eye causing pain of the patients [11–12].

There have been many developments in ocular drug delivery systems recently, with the goal of improving the efficacy of drugs administered

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intraocularly. Based on the intraocular drug dose increase performed in the HARBOR and SAVE clinical trials for neovascular AMD, limiting intravitreal injections has been advocated to decrease the socioeconomic treatment load [13,14,15,16]. Figure 1 displays different ocular medication delivery routes, including topical, subconjunctival, suprachoroidal, subretinal, and trans-scleral, and intravitreal. In this review, we aim to summarize (1) intraocular pharmacokinetics of current intravitreal drugs; (2) efforts to enhance the intraocular pharmacokinetics and pharmacodynamics of intravitreal drugs: dose escalation of intravitreal drugs, increasing the molecular weight of intravitreal drug molecules, sustained-release Intravitreal implants, micro- and nanoparticles, hydrogels, combination drug delivery systems, port delivery systems; and (3) Drug administration routes besides the intravitreal route.

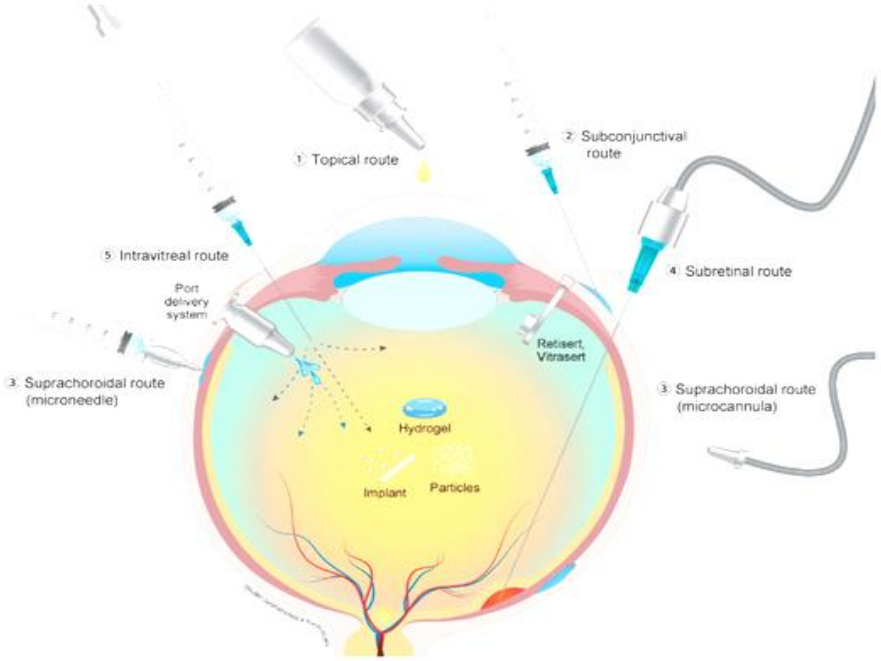

Figure 1: The following is a schematic representation of the many ways of ocular drug administration: (1) the topical route, (2) the subconjunctival route, (3) the suprachoroidal route with microcannula and microneedle, (4) the subretinal route, and (5) the intravitreal injection and port delivery system.

II. OCULAR GENE THERAPY

Gene treatments in this sector have been on the rise over the past few decades, driven by developments in viral vector technology and discoveries in the genetic foundation for ocular ailments. This trend culminated in the FDA approval of LuxturnaTM in 2017, the first medicine of its kind to treat ocular conditions using gene therapy. This landmark achievement strengthens the research and clinical interests in gene therapy for a wider variety of ocular illnesses than it had previously. There are about 350 hereditary ocular illnesses, including a wide variety of genetic loci, such as retinitis pigmentosa, choroideremia, Stargardt disease, and Leber's congenital amaurosis (LCA) [18,19]. Some of these diseases include retinitis pigmentosa, Stargardt disease, and Leber's congenital amaurosis (LCA). The engineering of vectors and the packaging of transgenes have made significant contributions to the enhancement of transgene expression and the phenotypic rescue following intraocular administration. Even though viral vectors have been used successfully in ocular gene therapy, there are still concerns regarding the heterogeneity of viral genomes throughout the manufacturing process, as well as packaging capacity and immunological reactions. In order to circumvent these constraints, non-viral vectors are currently in the process of being designed for gene therapy. In this article, we take a look at the growing corpus of research and clinical trials that include gene therapy for hereditary and acquired eye illnesses. We also discuss the recent developments in viral and non-viral vectors that have been made in this area of research.

The Conjunctiva

The conjunctiva can be found on the surface of the eye as well as on the inside of the eyelids' posterior surfaces. It is made up of a few different components, all of which, along with the surface of the cornea, make up what is known as the conjunctival sac [20]. The area of the white of the eye that is discernible or open to view is covered by the bulbar conjunctiva. [20] The palpebral conjunctiva can be seen on the backside of the eyelids. The connection between the bulbar and palpebral conjunctiva is made by the conjunctival fornix, also

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known as the forniceal conjunctiva. The conjunctiva is a tissue that is largely responsible for lubricating the eye [20]. In addition to this function, the conjunctiva also serves to protect the soft tissues that are placed in the eye, supply tissue for the immune system, and allow the eye to move [21]. Microvilli are found within the epithelial cells that make up the conjunctiva. These microvilli are an essential component in the process that allows the tear film to adhere to the surface of the eye [21]. A component of the mucosa-associated lymphoid tissue (MALT) known as the conjunctiva-associated lymphoid tissue (CALT) can be found in the conjunctiva. [21] This system possesses all of the components that are necessary for a comprehensive immune response. This system can help a tissue create tolerance to certain antigens, as well as identify antigens and cause a direct immune response. Additionally, this system can help the tissue recognise antigens. In addition, the conjunctiva is responsible for the secretion of IgA, in addition to other components of the immune system's secretory system [22].

III. OCULAR STRUCTURE & ITS BARRIERS

The human eye has a complex anatomy that can be loosely summarised as being composed of two segments: the anterior and the posterior portions. The former category contains the cornea, the conjunctiva, the iris, the ciliary body, the crystalline lens, and the aqueous humour, while the latter category contains the sclera, the choroid, the retina, and the vitreous (Figure 2) [2]. Because the anterior and posterior segments are influenced by distinct pathogenic variables [13,25], which in turn lead to distinct illnesses, ocular drug delivery is one of the most difficult tasks for researchers to undertake [26]. A concise summary of the relevant ocular structures that influence medication distribution is provided in the next paragraphs.

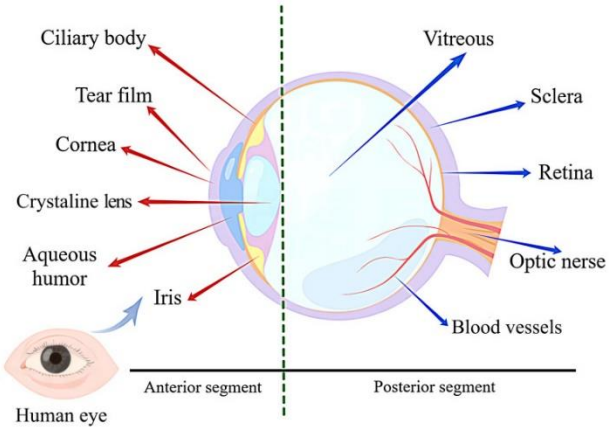

Figure 2: A illustration in schematic form of the structure of the eye. The front part, known as the anterior segment, and the back section, known as the posterior segment, make up the eye. The cornea, the conjunctiva, the iris, the ciliary body, the crystalline lens, and the aqueous humour make up the anterior segment, whereas the sclera, the choroid, the retina, and the vitreous humour make up the posterior segment. They are the most significant obstacles in the way of ocular medication administration.

IV. NANO BASED DRUG DELIVERY SYSTEM FOR GLUCOMA

Glaucoma is a group of eye diseases that damage the optic nerve, leading to progressive vision loss and blindness. It is the leading cause of irreversible blindness globally. To this day, intraocular pressure (IOP) management is the cornerstone of treatment for glaucoma. With the aim of reducing intraocular pressure (IOP), there has been a recent surge in the use of nanocarriers to enhance ocular drug delivery. This development is particularly significant as the long-term use of conventional IOP-lowering agents, which are based on poorly penetrating molecules, can cause frequent ocular toxicity and intolerance due to their adverse effects on the corneal epithelium [45].

Nano-Based DDS Based on Regulating Intraocular Pressure (IOP)

The cornea is a transparent, spherical structure that is made up mostly of avascular connective tissue [27]. It can be found near the front of the eye where it is known as the anterior chamber. The cornea is known as the biggest static barrier in the body and prevents drug molecules from entering the eye [28].

In addition to shielding the eye from microbes from outside environments, the cornea also plays this role. Epithelium, Bowman's membrane, stroma, Descemet's membrane, and the inner endothelium are the five layers that are recognised by researchers as constituting the physiological structure of the cornea [29]. Because the stroma between the epithelium and endothelium is made up of hydrophilic collagen, it blocks the passage of lipophilic molecules but allows the osmotic diffusion of hydrophilic molecules [30]. Both the epithelium and the endothelium are composed of multiple layers of cells that prevent hydrophilic molecules from entering the aqueous humour while allowing lipophilic molecules to pass through. The "sandwich" shape of the cornea, which is hydrophobic on both sides and hydrophilic in the middle, necessitates a large distribution coefficient of medications in both the water and oil phases. As a result, it also dictates the physical and chemical properties of drugs that penetrate the cornea. The cornea is a hydrophobic structure on both sides and a hydrophilic structure in the centre. In addition, the cornea contains a system known as the "tear buffer system" that allows it to self-regulate its pH levels. When the quantity or quality of tear fluids is reduced, the acid–base balance on the corneal surface may be disrupted, and ocular disorders may become even more severe as a result.

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The tear film is located in the outermost layer of the cornea. It is the most important dynamic barrier for ocular medication delivery. The tear film is made up of lipid, aqueous, and mucin layers. Its primary purpose is to nourish and protect the cornea [31,32]. The majority of the tear film is comprised of the aqueous layer, which has a thickness of 7–8 micrometres. It is possible for the active drug to become bound to proteins and enzymes in the aqueous phase, which results in a reduction in the bioavailability of the drug for the eyes [33].

The conjunctiva is a delicate mucous membrane that is thin, translucent, and vascularized. It is located in the front third of the eyeball and is more permeable than the cornea. Additionally, the conjunctiva has 22 times the surface area of the cornea, which allows for more medication to be absorbed [9,34,35]. On the other hand, considering that the conjunctiva contains both capillaries and lymphatics, it is generally agreed that medication absorption through the conjunctiva is an exercise in futility [29]. Large quantities of medications are lost in the systemic circulation, which lowers the bioavailability of ocular drugs and may trigger adverse effects in the systemic circulation. Although the human conjunctival sac has the capacity to temporarily store roughly 30 microliters of tear fluid, the average volume of a single tear is just 7 microliters. Because tear fluids have a high turnover rate, the amount of time that ocular medicines are retained in the eye is restricted [36]. The retina is a delicate sense organ that is located in the deepest layer of the human eye. It is made up of many layers of membranes that have a mean thickness of 249 micrometres and performs complicated activities related to photoconversion and transmission [37,38]. In addition to this, the retina, because it is an essential component of the blood-retinal barrier's architecture, has the ability to shield itself from potentially dangerous compounds that are found in the blood. On the other hand, it forms a considerable barrier to ocular medication delivery, making it difficult for larger drug molecules to reach the retina [29]. This is because the choroid is located in the back of the eye. Crystalline is a translucent tissue that is made up of lens epithelial cells (LECs) and lens fibre cells that are contained by the lens capsule [39]. Crystalline is a part of the lens. The lens, which is located in the anterior portion of the eye, and the cornea work together to concentrate light from external sources onto the retina, which is located in the posterior part of the eye. This allows people to perceive clear images. Vision impairment occurs when the lens's transparency is compromised.

Preclinical Studies

The capacity to modify nanoparticles with biodegradable polymers is one of the benefits of using nanoparticles. This modification can increase the bioavailability of the medicine that the nanoparticles are carrying. This is of utmost significance for glaucoma medications such as brinzolamide, which has poor solubility and, as a result, restricts the effectiveness of its therapeutic effects. PLGA-modified (Polylactic-co-glycolic acid) nanoparticles have been developed in a number of studies to have a prolonged release of brinzolamide. These nanoparticles have been shown to considerably reduce IOP in animal models while exhibiting minimal toxicity [15,46,47]. The researchers Song et al. (2020) employed a technology called coaxial electrospray to coat PLGA nanoparticles with phosphatidylserine (PS), which improved the entrapment efficiency and ocular permeability of brinzolamide when it was delivered topically. However, some systemic absorption was seen in cases where there was a drop in intraocular pressure (IOP) in both the treated and untreated eyes [46]. In the study by Salama et al. (2017), the researchers used subconjunctival injection to increase the extended release of these nanoparticles and provide a more focused drug administration. They discovered that the efficacy of the treatment was dependent on the nanoparticle size. Encapsulating a hybrid chemical known as SA-2, which acts as both a nitric oxide (NO) donor and a superoxide dismutase (SOD) activator, was another application for PLGA nanoparticles [48]. IOP was considerably reduced for up to 72 hours after a single dosage of slow-release SA-2 medication. In addition, raising the activity of the SOD enzyme was found to give cytoprotection in the human trabecular meshwork (TM) cells.

Other polymers that have been employed recently for the formation of nanoparticles include -cyclodextrin [49], chitosan [50], and a natural organic polymer that is based on galactomannans [51]. Angiotensin receptor blockers, candesartan and irbesartan, were administered by the use of cyclodextrin nanoparticles by Lorenzo-Soler et al. (2020). This method avoided the traditional adverse effects that are associated with oral administration of the drugs, while also successfully decreasing intraocular pressure in a manner that was comparable to that of timolol eye drops. In spite of the fact that it looks promising, additional pharmacokinetic profiling is going to be necessary because the researchers identified individual variability in IOP in their rabbit animal model [49]. Nanobrimodine was administered to patients with open-angle glaucoma by the use of ultra-small chitosan nanoparticles, which is a well-known biodegradable polymer with a high capacity for drug loading and gradual release. The research was conducted by Barwar et al. (2019). In vitro tests [50] showed that despite its size, which measured 28 5 nm, this was able to enter cells via a process called receptor-mediated endocytosis. For the purpose of delivering dorzolamide hydrochloride, Mittal et al. (2019) developed a bio-adhesive, non-toxic polymeric nanoparticle that was created utilising galactomannans. When compared to regular eye drops, eye drops with a delayed release have an improved effect on lowering IOP. When compared to synthetic polymers, the safe and cost-effective extraction offered by this formulation is one of its many advantages [51]. Last but not least, Tan

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et al. (2021) administered miRNA using polydopamine-polyethylenimine (PDA/PEI) Nanoparticles by intracameral injection. The drug delivery system was successful in reducing intraocular pressure in living animals [52], in addition to improving its penetration and stability, which allowed for equivalent transfection efficacy to be achieved with lower cytotoxicity.

Even though Mesoporous Silica Nanoparticles (MSNs) have a low degradability due to their pure silica framework, current research has shown that MSNs can be changed to reach a biodegradation that is adequate for clinical applications. Researchers Fan et al. (2021) utilised biodegradable hollow mesoporous organosilica (HOS) nanocapsules to distribute NO in a stimulus-responsive way for the purpose of increased penetration and bioavailability [53]. In spite of the fact that it had an effect on reducing IOP, it had been discovered in the past that extended usage of NO-MSNs led to an increase in IOP elevation after the first decrease [54]. It was hypothesised that this was due to outflow tissue damage as a result of protein nitration, and it was speculated that co-delivery of antioxidants such as MnTMPyP could help mitigate the negative effects of chronic use. Given their high drug-loading capacity and ability to better control drug release, alternative approaches for developing biodegradable hollow polymeric nanocapsules are currently the subject of intensive research [55].

Niosomes are vesicular structures that are based on lipids. When used as a DDS, they offer an enhanced residence time and corneal permeability. with order to more effectively transport carteolol (CT), Zafar et al. (2021) developed a niosome that was coated with chitosan. This improved both its biodegradability and its bioadhesion. In a same fashion, pilocarpine and latanoprost were successfully given to lower intraocular pressure (IOP) in in vivo rabbit models by employing niosomal gels [57,58]. On the other hand, it is common knowledge that niosomes have a short shelf life and a low drug entrapment efficiency. Proniosomes, whether gel or granular, can rapidly transform into niosomes upon hydration, hence minimising niosomal dispersions and providing higher levels of physical stability [59,60]. This can help optimise the process.

The structure of the cell membranes that make up the corneal epithelium is very similar to that of the cubosomes, which are produced by a continuous lipid bilayer. Because of this, it has been looked into as a potential DDS for ocular delivery. Teba et al. (2021) developed an innovative cubosome technique to deliver acetazolamide, which resulted in enhanced corneal penetration, longer ocular residence duration, and no evidence of ocular irritation [61]. In a similar vein, Huang et al. (2017) created a cubosome device that is capable of administering timolol maleate. Both showed an improvement in the drug's bioavailability as well as an enhanced IOP-lowering efficacy [62]. Poloxamer 407 (P407) and GMO (glyceryl monooleate) were the biodegradable polymers that were utilised in the development of the cubosome in both of the experiments [61,62].

Nanoemulsions are droplets on a nanoscale that are capable of transporting molecules that are either hydrophilic or hydrophobic. It has been demonstrated that they are capable of transporting travoprost and brinzolamide, hence boosting medication absorption and extending the benefits of decreasing intraocular pressure [63,64]. However, the production of nanoemulsions calls for a significant quantity of surfactants, which results in a significant potential for cytotoxicity. This potential for cytotoxicity can be further increased by the incorporation of preservatives [64]. Before using this DDS, longer-term safety testing concerning toxicity are required to be completed.

Optimising ocular inserts by employing nano-based carriers has become a common focus of study in the field of ocular pharmacology. This has been done with the goals of improving treatment adherence and reducing the frequency of administration. Chitosan is a highly biodegradable polymer that has been utilised in a number of experiments to make ocular inserts and films for topical delivery of medications. These modified chitosan inserts were able to lower IOP by delivering 4-aminodiphenylamine (a benzamidine derivative) and dorzolamide, respectively. These modifications were carried out to improve the solubility of chitosan, such as the addition of chondroitin sulphate and hydroxyethyl cellulose [65,66]. It is interesting to note that both medicines displayed a neuroprotective impact towards the retinal ganglion cells (RGC) with a prolonged release of their active ingredient. An environmentally acceptable approach of generating the chitosan polymer dispersed in a water-based film was proposed by Li et al. (2020). This method was able to overcome the solubility issue while maintaining a high cornea permeability [67]. Other biodegradable polymers that have been reported include sodium alginate-ethyl cellulose inserts for the transportation of hydrophilic drugs [68], as well as a cyclodextrin multilayer film incorporating polybutyl acrylate-co-ethylene oxide (PBAE) and graphene oxide, which enabled a time-controlled release of brimonidine that was dependent on the layer thickness in vitro [69].

Xu et al. (2019) [70] produced a drug-loaded contact lens that utilised nanomicelles for the purpose of co-delivering the medications latanoprost and timolol. The authors used biodegradable mPEG-PLA nanomicelles that were generated using thin-film hydration. The ultra-small particle size ensured that the inserted contact lens was transparent and transmitted light. It was claimed that this system may change the physical qualities of the lens, causing it to become rough following drug release. This is the case despite the fact that this DDS delivered a delayed and continuous release of both medications (over 120–144 h), and that the safety of the eye was established. Another method of co-administration was established by Samy et al. (2019),

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who used PCL thin-film implants to deliver timolol and brimonidine [71]. This method was presented by Samy et al. This DDS allowed for a controlled release of both medicines; however, systemic absorption as well as any potential adverse effects were not evaluated. These polymeric films were also employed to deliver a novel hypotensive agent known as DE-117. This agent offered a prolonged IOP-lowering effect; however, because of the bulky size of the implant, it presented a substantial risk of device migration as well as injury to the corneal endothelium [72].

Because of its ability to undergo in situ sol-to-gel synthesis that can be triggered by environmental conditions such as pH and temperature, hydrogels have been the subject of a significant amount of research as a potentially useful ocular delivery mechanism [73]. Recent research has been focusing on the development of hybrid systems, which involve embedding biodegradable nanoparticles into hydrogels, with the goal of achieving a prolonged release of the medicine. Because of this, an effective drug delivery system (DDS) has been created, which has sustained release of brimonidine tartrate [74], timolol maleate [75,76], and bimatoprost [77], as well as co-delivery of curcumin nanoparticles and latanoprost [78] from a thermosensitive in situ hydrogel. Chou et al. (2017) described the administration of pilocarpine loaded with antioxidants GA (gallic acid) through a biodegradable gelatin-based thermogel [79]. This is another example of DDS based on dual functionalities. GA was able to accommodate the regulated release of pilocarpine from the thermogel, in addition to delivering antioxidative effects. Therefore, if controlled, it can produce a prolonged release (found to be optimal at 30 degrees Celsius). The degradation was dependent on the temperatures of the redox radical start reaction, which ranged from 20 to 50 degrees Celsius. This opens up more discussion on the possibility of changing biodegradability in order to optimise the drug's prolonged release. According to the findings of Luo et al. (2019), an increase in the amination degree of gelatin in biodegradable thermogels results in an increase in the material's resistance to biodegradation [80]. Another study conducted by the same group found that increasing the degree of deacetylation in chitosan-based thermogels increased their resistance to biodegradation [81]. This finding was given in the previous article.

Nanocarriers such as liposomes are exceptionally biodegradable and may transport medications that are either hydrophilic or hydrophobic. Jin et al. (2018) revealed a TPGS-modified (tocopheryl polyethylene glycol succinate) liposome carrier for brinzolamide that had a better sustained release and maintained IOP reduction, with no noticeable adverse effects [82]. [TPGS] stands for tocopheryl polyethylene glycol succinate. Liposomes, on the other hand, have a low stability, a low entrapment effectiveness, and a quick release of hydrophilic medicines [83,84]. These are all major disadvantages of employing liposomes. Timolol maleate is a hydrophilic medication, and Hathout et al. (2018) developed gelatinized core liposomes for the sustained release of the drug. This resulted in a considerable improvement in entrapment efficiency without any evidence of ocular discomfort.

In vitro testing of PAMAM (polyamidoamine) dendrimers showed no symptoms of cytotoxicity or ocular discomfort, allowing them to be employed for the sustained release of timolol. In order to optimise drug loading and examine the effects of chronic application, further research utilising in vivo models for safety and pharmacokinetic profiling are required [85]. These investigations should focus on pharmacokinetic profiling. Lancina et al. (2017) employed electrospun dendrimer-based nanofiber mats to distribute brimonidine tartrate (BT) [86]. The effectiveness of this technique in reducing IOP was improved with daily dosing over the course of three weeks, but not with a single dosage.

Both self-assembly drug nanostructures (SADN) [87] and phase transition microemulsions (PMEs) [88] are examples of important other DDS systems. Both of them are innovative systems that contributed to a sustained effect of decreasing IOP. Cytotoxicity and systemic consequences have not yet been looked into for either of these delivery strategies. Cell-softening agents such as ligands targeting FLT-4/VEGFR3 receptors were administered by modified micelles, which improved receptor targeting and resulted in a decrease in intraocular pressure (IOP) [89]. Because the benefits only lasted for a maximum of forty-eight hours, there is a pressing need for further advancement in corneal permeability and sustained release. It was also reported by Donia et al. (2020) that nanosuspensions could deliver acetazolamide. In this study, the authors demonstrated that the nanosuspensions prolonged drug release, enhanced acetazolamide solubility, and consequently improved bioavailability [90]. The nanosuspension was stabilised using hyaluronic acid (HA), although this alteration could only keep the dispersion parameters stable for a maximum of six months. As a result, the widespread challenge of enhancing the stability of nanosuspensions needs to be investigated further.

It is interesting to note that Chae et al. (2020) have presented a way of lowering IOP that does not involve the use of drugs and does not involve surgery. In this method, the suprachoroidal space is expanded using a hyaluronic acid hydrogel microneedle injection [91]. This treatment establishes a temporary route between the anterior chamber and the suprachoroidal area. It is similar in theory to suprachoroidal minimally invasive glaucoma surgeries (MIGS) such as Cypass and iStent Supra, but it does not result in the loss of endothelial cells like those procedures do. This makes it easier for aqueous humour to drain down the channel that leads out of the uveoscleral opening. They were able to prolong

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the reduction of IOP without the use of medicines or surgical intervention, and there were no major issues that arose as a result. In order to confirm this strategy, additional mechanistic investigations are necessary, and there is a pressing need to investigate ways to avoid fibrosis through the use of numerous injectable treatments.

Recent research has seen a number of different DDS, such as microspheres [92,93], solid lipid nanoparticles (SLNs) [94], and chitosan nanoparticles, modified by embedding montmorillonite (Mt) [95] in a biodegradable hybrid polymer. These modifications have been carried out by a number of different researchers. A silicate with high biocompatibility, Mt, has an overall negative surface charge and can form an ion complex with cationic medicines such as betaxolol hydrochloride (BH) and brimonidine. Mt has a high level of compatibility with biological systems. This makes it possible to have a controlled release of the medicine using a hybrid nanocarrier, as evidenced by a persistent reduction in intraocular pressure (IOP).

Solid formulations for ocular delivery, such as gels, contact lenses, implants, and the like, provide a number of advantages, including prolonged ocular residence; nonetheless, it is imperative that these formulations do not interfere with patients' vision and that they provide adequate comfort. Recent DDS studies have suggested the use of electrospinning biodegradable polymers. These polymers, which have a highly porous structure, are more adaptive and dissolve in the cornea more quickly than other biomaterials. Similar to how Morais et al. (2021) developed electrospun ocular implants for acetazolamide delivery [97], Andreadis et al. (2022) developed an in situ electrospun film gel for the delivery of timolol maleate [96]. Both had a strong and sustained effect on IOP reduction, as well as an increase in local delivery. However, additional optimisation of the sterilisation procedures for the implant is required in order to prevent infection and adverse effects without affecting the efficiency of the polymer. This is because: 1.

Rubiao et al. (2021) carried out a Phase 2 controlled trial in which they compared a bimatoprost topical chitosan-based insert to traditional bimatoprost eyedrops (LumiganTM). The goal of this investigation was to improve sustained release while simultaneously reducing systemic exposure. Notably, 16 patients with Primary Open Angle Glaucoma (POAG) and 13 individuals with ocular hypertension were participated in the study. On the other hand, the sample size for the control group was just five patients. Because chitosan is capable of biodegradation, the insert did not have to be withdrawn from the patients after the procedure was complete. This was a safety research, and the insert did not result in any significant adverse effects, changes in visual acuity, or increases in the thickness of the central cornea. A reduction in intraocular pressure (IOP) of 30% was achieved with the insert by the third week, whereas a reduction of 35% was achieved with eye drops. This study verified a more effective therapeutic regimen by demonstrating that using inserts at three-week intervals rather than daily dosing improved patient compliance with the treatment [98]. According to their previous statements, the next step will be to carry out Phase 3 confirmatory tests.

DurystaTM is a bimatoprost implant that will receive FDA approval in the year 2020. It is made up of poly-lactic acid and poly-lactic-co-glycolic polymers, which are similar to biodegradable sutures that are utilised in clinical settings [99]. It is meant to deliver a non-pulsatile release of 10 micrograms of bimatoprost and is implanted intracamerally before administration. It is currently being tested in a number of Phase 3 clinical trials to determine its long-term safety and effectiveness in patients who have open-angle glaucoma (OAG) or ocular hypertension (OH) [100]. It has been demonstrated to be non-inferior to timolol eye drops in terms of enhancing adherence and lowering the treatment burden that is associated with glaucoma [101]. There is a possibility of corneal adverse effects, inflammation of the intraocular space, or endophthalmitis. Following up on its Phase 1/2 patients [102,103], the researchers found that implant biodegradation varied among patients, with clinically substantial degradation by the end of 12 months. Despite this, the IOP-lowering effect was sustained. Patients diagnosed with glaucoma who are unable to be relied upon or who suffer from dementia and who are not good candidates for incisional glaucoma surgery may be good candidates for this implant.

In randomised, double-masked Phase 2 clinical trials, Brandt et al. (2017) [104] looked into the possibility of achieving a sustained release of bimatoprost by administering it via an ocular ring. The long-term effectiveness was evaluated in a total of 65 and 63 patients, respectively, seven and thirteen months after initial exposure. Mucus discharge was revealed to be a negative effect of using bimatoprost ocular rings, despite the fact that these rings were shown to be safe and well tolerated overall. It has been hypothesised that a reduction in IOP that is clinically significant can be achieved by doing treatments at intervals of six months. Due to the fact that the ocular ring is made up of a silicone matrix that is placed on top of a polypropylene framework, research into the biodegradability of the material could shed light on potential areas of development in terms of biocompatibility.

Patients with OAG and OH participated in a randomised controlled trial that was done by Kouchak et al. (2017) to explore the effects of dorzolamide nanoliposomes (DRZ-nanoliposome) on IOP [105]. A control group that received dorzolamide eye drops (BiosoptTM) was used as a comparison for the efficacy and safety of the DRZ-nanoliposomes, which were administered to a total of twenty patients. A significant decrease in intraocular pressure (IOP) was discovered in

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the DRZ-nanoliposomes group after being evaluated at days 14 and 28. This was theorised to be owing to improved adhesion and corneal permeation with the liposome delivery method, which was shown to have an extended release and higher intensity. Any irritation or redness that was reported was comparable between the two groups, and it was most often attributed to the dorzolamide itself. This has the potential to improve treatment outcomes by lowering the dosage and administration times while maintaining the same level of effectiveness.

V. CONCLUSION

We have reached much more advanced stages today, where the cell itself is a drug, biological medicinal product, or advanced therapy product, or is given advanced therapy medicinal status in regenerative medicine and is defined as a regenerative medicine. These developments stem from studies of drug delivery systems that began with liposomes, which are known to have a lengthy development and approval process. In the context of this procedure, dosage forms such as liposomes and nanoparticles, which were formerly referred to as colloidal delivery systems, are now known as "nanodrugs" or "nano pharmaceuticals" and fall under the purview of the field of nanotechnology. Studies are currently being conducted on the creation of new nanodrugs for the treatment of eye illnesses using a variety of products, and ocular implants are currently being utilized in the treatment process. The treatment of ocular disorders continues to be the top priority, and research on ATMP and other systems comprising cells that permit the release of medications with high molecular weight is still being conducted. This process, which involves the development of numerous nanodrugs, gene and cellular delivery systems, and ATMPs, each of which involve their own dangers, involves a time of change and harmonisation among national and international legislation. When developing high-risk medications from modified cells that show promise in the treatment of chronic diseases or eye diseases that cannot be treated currently, it is of the utmost importance to comply with all applicable national and international standards. The production of these products during the development stages within the framework of a pharmaceutical quality assurance system is an essential step towards achieving a more rapid transition from the research and development stage to the clinical stage. In order to accomplish this goal, multidisciplinary research teams and infrastructure with GMP conditions that are compliant with the legal criteria of pharmaceutical quality systems are required to be established.

REFERENCES

[1] Fenton, O. S., Olafson, K. N., Pillai, P. S., Mitchell, M. J., & Langer, R. (2018). Advances in biomaterials for drug delivery. *Advanced Materials*, *30*(29), 1705328.

[2] Dhiman, N., Awasthi, R., Sharma, B., Kharkwal, H., & Kulkarni, G. T. (2021). Lipid nanoparticles as carriers for bioactive delivery. *Frontiers in chemistry*, *9*, 580118.

[3] Lerch, M. M., Hansen, M. J., van Dam, G. M., Szymanski, W., & Feringa, B. L. (2016). Emerging targets in photopharmacology. *Angewandte Chemie International Edition*, *55*(37), 10978-10999.

[4] Khosa, A., Reddi, S., & Saha, R. N. (2018). Nanostructured lipid carriers for site-specific drug delivery. *Biomedicine & Pharmacotherapy*, *103*, 598-613.

[5] Varela-Fernández, R., Díaz-Tomé, V., Luaces-Rodríguez, A., Conde-Penedo, A., García-Otero, X., Luzardo-Álvarez, A., ... & Otero-Espinar, F. J. (2020). Drug delivery to the posterior segment of the eye: Biopharmaceutic and pharmacokinetic considerations. *Pharmaceutics*, *12*(3), 269.

[6] Zennifer, A., Senthilvelan, P., Sethuraman, S., & Sundaramurthi, D. (2021). Key advances of carboxymethyl cellulose in tissue engineering & 3D bioprinting applications. *Carbohydrate Polymers*, *256*, 117561.

[7] Tran, L., Xiao, J. F., Agarwal, N., Duex, J. E., & Theodorescu, D. (2021). Advances in bladder cancer biology and therapy. *Nature Reviews Cancer*, *21*(2), 104-121.

[8] Begines, B., Ortiz, T., Pérez-Aranda, M., Martínez, G., Merinero, M., Argüelles-Arias, F., & Alcudia, A. (2020). Polymeric nanoparticles for drug delivery: Recent developments and future prospects. *Nanomaterials*, *10*(7), 1403.

[9] Gedde, S. J., Vinod, K., Wright, M. M., Muir, K. W., Lind, J. T., Chen, P. P., ... & Mansberger, S. L. (2021). Primary open-angle glaucoma preferred practice pattern®. *Ophthalmology*, *128*(1), P71-P150.

[10] Li, W., Tang, J., Lee, D., Tice, T. R., Schwendeman, S. P., & Prausnitz, M. R. (2022). Clinical translation of long-acting drug delivery formulations. *Nature Reviews Materials*, *7*(5), 406-420.

[11] Zhang, X., Wei, D., Xu, Y., & Zhu, Q. (2021). Hyaluronic acid in ocular drug delivery. *Carbohydrate Polymers*, *264*, 118006.

[12] Peng, C., Kuang, L., Zhao, J., Ross, A. E., Wang, Z., & Ciolino, J. B. (2022). Bibliometric and visualized analysis of ocular drug delivery from 2001 to 2020. *Journal of Controlled Release*, *345*, 625-645.

[13] Gupta, B., Mishra, V., Gharat, S., Momin, M., & Omri, A. (2021). Cellulosic polymers for enhancing drug bioavailability in ocular drug delivery systems. *Pharmaceuticals*, *14*(11), 1201.

[14] Marchesi, N., Fahmideh, F., Boschi, F., Pascale, A., & Barbieri, A. (2021). Ocular neurodegenerative diseases: interconnection between retina and cortical areas. *Cells*, *10*(9), 2394.

ISSN: 2583-4053

Volume-2 Issue-3 || June 2023 || PP. 238-249

https://doi.org/10.55544/jrasb.2.3.32

[15] Mohamed, H. B., Abd El-Hamid, B. N., Fathalla, D., & Fouad, E. A. (2022). Current trends in pharmaceutical treatment of dry eye disease: A review. *European Journal of Pharmaceutical Sciences*, *175*, 106206.

[16] Lin, P. H., Jian, H. J., Li, Y. J., Huang, Y. F., Anand, A., Huang, C. C., ... & Lai, J. Y. (2022). Alleviation of dry eye syndrome with one dose of antioxidant, anti-inflammatory, and mucoadhesive lysine-carbonized nanogels. *Acta Biomaterialia*, *141*, 140-150.

[17] Ye, J., Fu, S., Zhou, S., Li, M., Li, K., Sun, W., & Zhai, Y. (2020). Advances in hydrogels based on dynamic covalent bonding and prospects for its biomedical application. *European Polymer Journal*, *139*, 110024.

[18] Melo, G. B., da Cruz, N. F. S., Emerson, G. G., Rezende, F. A., Meyer, C. H., Uchiyama, S., ... & Rodrigues, E. B. (2021). Critical analysis of techniques and materials used in devices, syringes, and needles used for intravitreal injections. *Progress in Retinal and Eye Research*, *80*, 100862.

[19] Melo, G. B., da Cruz, N. F. S., Emerson, G. G., Rezende, F. A., Meyer, C. H., Uchiyama, S., ... & Rodrigues, E. B. (2021). Critical analysis of techniques and materials used in devices, syringes, and needles used for intravitreal injections. *Progress in Retinal and Eye Research*, *80*, 100862.

[20] Kumar, R., Saha, P., Kahwa, I., Boateng, E. A., Boateng, P. O., & Nyarko, R. O. (2022). Biological Mode of Action of Phospholipase A and the Signalling and Pro and Anti Inflammatory Cytokines: A Review. *Journal of Advances in Medicine and Medical Research*, *34*(9), 1-10.

[21] Keshri, S., Kumar, R., Kumar, D., Singhal, T., Giri, S., Sharma, I., & Vatsha, P. (2022). Insights Of Artificial Intelligence In Brain Disorder With Evidence Of Opportunity And Future Challenges. *Journal of Pharmaceutical Negative Results*, 10853-10867.

[22] Bist, V. L., & Faruk, A. (2023). Recent Advancement in Self Emulsifing Drug Delivery System. *Journal for Research in Applied Sciences and Biotechnology*, *2*(2), 89-101.

[23] Shukla, S., Rawat, N., Rana, S., Rana, V., Mittal, C., Kumar, R., & Sood, P. (2023). Clinical Features Present, Past & Future Prospective of Monkey Pox: A Orthopoxvirus. *Journal for Research in Applied Sciences and Biotechnology*, *2*(3), 134-146.

[24] Kumar, A., Uniyal, Y., & Kumar, R. (2022). Recent Advancement of Colorectal Cancer and Their Herbal Essential Oil Treatment. *Journal for Research in Applied Sciences and Biotechnology*, *1*(5), 133-144.

[25] Kohli, A., & Kumar, R. (2023). Role of Antioxidants of Natural Herbs in Management of Male Infertility. *Journal for Research in Applied Sciences and Biotechnology*, *2*(1), 55-80.

[26] Butola, K., Bisht, V., & Kumar, R. (2023). Recent Approaches of Ocular Disease and Its Herbal Product Treatment: An Updates. *Journal for Research in Applied Sciences and Biotechnology*, *2*(2), 102-114.

[27] Mazet, R., Yaméogo, J. B., Wouessidjewe, D., Choisnard, L., & Gèze, A. (2020). Recent advances in the design of topical ophthalmic delivery systems in the treatment of ocular surface inflammation and their biopharmaceutical evaluation. *Pharmaceutics*, *12*(6), 570.

[28] Desai, N., Rana, D., Salave, S., Gupta, R., Patel, P., Karunakaran, B., ... & Kommineni, N. (2023). Chitosan: A Potential Biopolymer in Drug Delivery and Biomedical Applications. *Pharmaceutics*, *15*(4), 1313.

[29] Attia, S. A., & MacKay, J. A. (2022). Protein and polypeptide mediated delivery to the eye. *Advanced Drug Delivery Reviews*, 114441.

[30] Cheng, K. J., Hsieh, C. M., Nepali, K., & Liou, J. P. (2020). Ocular disease therapeutics: design and delivery of drugs for diseases of the eye. *Journal of Medicinal Chemistry*, *63*(19), 10533-10593.

[31] Cheng, K. J., Hsieh, C. M., Nepali, K., & Liou, J. P. (2020). Ocular disease therapeutics: design and delivery of drugs for diseases of the eye. *Journal of Medicinal Chemistry*, *63*(19), 10533-10593.

[32] Amador, C., Shah, R., Ghiam, S., Kramerov, A. A., & Ljubimov, A. V. (2022). Gene therapy in the anterior eye segment. *Current gene therapy*, *22*(2), 104.

[33] Cheng, K. J., Hsieh, C. M., Nepali, K., & Liou, J. P. (2020). Ocular disease therapeutics: design and delivery of drugs for diseases of the eye. *Journal of Medicinal Chemistry*, *63*(19), 10533-10593.

[34] Attia, S. A., & MacKay, J. A. (2022). Protein and polypeptide mediated delivery to the eye. *Advanced Drug Delivery Reviews*, 114441.

[35] Chatterjee, S., Upadhyay, P., Mishra, M., Srividya, M., Akshara, M. R., Kamali, N., ... & Misra, S. K. (2020). Advances in chemistry and composition of soft materials for drug releasing contact lenses. *Rsc Advances*, *10*(60), 36751-36777.

[36] Sun, X., Sheng, Y., Li, K., Sai, S., Feng, J., Li, Y., ... & Tian, B. (2022). Mucoadhesive phenylboronic acid conjugated chitosan oligosaccharide-vitamin E copolymer for topical ocular delivery of voriconazole: Synthesis, in vitro/vivo evaluation, and mechanism. *Acta Biomaterialia*, *138*, 193-207.

[37] Ryu, J. (2022). New aspects on the treatment of retinopathy of prematurity: currently available therapies and emerging novel therapeutics. *International Journal of Molecular Sciences*, *23*(15), 8529.

[38] Fan, X., Torres-Luna, C., Azadi, M., Domszy, R., Hu, N., Yang, A., & David, A. E. (2020). Evaluation of commercial soft contact lenses for ocular drug delivery: A review. *Acta Biomaterialia*, *115*, 60-74.

[39] Qiao, H., Xu, Z., Sun, M., Fu, S., Zhao, F., Wang, D., ... & Sun, J. (2022). Rebamipide liposome as an effective ocular delivery system for the management of dry eye disease. *Journal of Drug Delivery Science and Technology*, *75*, 103654.

ISSN: 2583-4053

Volume-2 Issue-3 || June 2023 || PP. 238-249

https://doi.org/10.55544/jrasb.2.3.32

[40] Tian, B., Bilsbury, E., Doherty, S., Teebagy, S., Wood, E., Su, W., ... & Lin, H. (2022). Ocular drug delivery: advancements and Innovations. *Pharmaceutics*, *14*(9), 1931.

[41] Tian, B., Bilsbury, E., Doherty, S., Teebagy, S., Wood, E., Su, W., ... & Lin, H. (2022). Ocular drug delivery: advancements and Innovations. *Pharmaceutics*, *14*(9), 1931.

[42] Shekhar, S., Kumar, A., Rana, V., Kumar, R., Mittal, C., & Tariyal, K. (2023). Recent Approaches of Matrix Release Tablet in NDDS System. *Journal for Research in Applied Sciences and Biotechnology*, *2*(3), 64-71.

[43] Kumar, R., Sood, P., Rana, V., & Prajapati, A. K. (2023). Combine Therapy of Gallic Acid and Allicin in Management of Diabetes. *Journal for Research in Applied Sciences and Biotechnology*, *2*(3), 91-99.

[44] Kumar, R., & Saha, P. (2022). A review on artificial intelligence and machine learning to improve cancer management and drug discovery. *International Journal for Research in Applied Sciences and Biotechnology*, *9*(3), 149-156.

[45] Amle, V. S., Rathod, D. A., Keshamma, E., Kumar, V., Kumar, R., & Saha, P. (2022). Bioactive Herbal Medicine Use for Eye Sight: A Meta Analysis. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 42-50.

[46] Kumar, R., Saha, P., Keshamma, E., Sachitanadam, P., & Subramanian, M. (2022). Docking studies of some novel Hetrocyclic compound as Acat inhibitors: A meta analysis. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 33-41.

[47] Subramanian, M., Keshamma, E., Janjua, D., Kumar, D., Kumar, R., Saha, P., ... & Rao, S. (2022). Quality risk management approach for drug development and its future prospectives. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 166-177.

[48] Patel, R. K., Gangwar, D., Gupta, H., Sharma, N., & Kumar, R. (2023). Plants Alkaloids Based Compound as Therapeutic Potential for Neurodegenerative. *Journal for Research in Applied Sciences and Biotechnology*, *2*(2), 14-26.

[49] Kashyap, N., Kumar, R., Rana, V., Sood, P., & Chauhan, T. (2023). Role of Terpenoids Active Ingredients Targeting for Neuroprotective Agents. *Journal for Research in Applied Sciences and Biotechnology*, *2*(3), 22-40.

[50] Gadziński, P., Froelich, A., Wojtyłko, M., Białek, A., Krysztofiak, J., & Osmałek, T. (2022). Microneedle-based ocular drug delivery systems–recent advances and challenges. *Beilstein Journal of Nanotechnology*, *13*(1), 1167-1184.

[51] Gote, V., Ansong, M., & Pal, D. (2020). Prodrugs and nanomicelles to overcome ocular barriers for drug penetration. *Expert Opinion on Drug Metabolism & Toxicology*, *16*(10), 885-906.

[52] Berillo, D., Zharkinbekov, Z., Kim, Y., Raziyeva, K., Temirkhanova, K., & Saparov, A. (2021). Stimuli-Responsive Polymers for Transdermal, Transmucosal and Ocular Drug Delivery. *Pharmaceutics*, *13*(12), 2050.

[53] Arribada, R. G., Behar-Cohen, F., de Barros, A. L. B., & Silva-Cunha, A. (2022). The use of polymer blends in the treatment of ocular diseases. *Pharmaceutics*, *14*(7), 1431.

[54] Almehmady, A. M., El-Say, K. M., Mubarak, M. A., Alghamdi, H. A., Somali, N. A., Sirwi, A., ... & Ahmed, T. A. (2022). Enhancing the antifungal activity and ophthalmic transport of fluconazole from PEGylated polycaprolactone loaded nanoparticles. *Polymers*, *15*(1), 209.

[55] Kanaan, A. F., Piedade, A. P., de Sousa, H. C., & Dias, A. M. (2021). Semi-interpenetrating chitosan/ionic liquid polymer networks as electro-responsive biomaterials for potential wound dressings and iontophoretic applications. *Materials Science and Engineering: C*, *121*, 111798.

[56] Wroblewska, K. B., Jadach, B., & Muszalska-Kolos, I. (2021). Progress in drug formulation design and delivery of medicinal substances used in ophthalmology. *International Journal of Pharmaceutics*, *607*, 121012.

[57] Mobaraki, M., Soltani, M., Zare Harofte, S., L. Zoudani, E., Daliri, R., Aghamirsalim, M., & Raahemifar, K. (2020). Biodegradable nanoparticle for cornea drug delivery: Focus review. *Pharmaceutics*, *12*(12), 1232.

[58] Rebibo, L., Frušić-Zlotkin, M., Ofri, R., Nassar, T., & Benita, S. (2022). The dose-dependent effect of a stabilized cannabidiol nanoemulsion on ocular surface inflammation and intraocular pressure. *International Journal of Pharmaceutics*, *617*, 121627.

[59] Sharma, D. S., Wadhwa, S., Gulati, M., Kadukkattil Ramanunny, A., Awasthi, A., Singh, S. K., ... & Vishwas, S. (2021). Recent advances in intraocular and novel drug delivery systems for the treatment of diabetic retinopathy. *Expert Opinion on Drug Delivery*, *18*(5), 553-576.

[60] Maccarone, R., Tisi, A., Passacantando, M., & Ciancaglini, M. (2020). Ophthalmic applications of cerium oxide nanoparticles. *Journal of Ocular Pharmacology and Therapeutics*, *36*(6), 376-383.

[61] Kesav, N. P., Young, C. E. C., Ertel, M. K., Seibold, L. K., & Kahook, M. Y. (2021). Sustained-release drug delivery systems for the treatment of glaucoma. *International Journal of Ophthalmology*, *14*(1), 148.

[62] O'Brien Laramy, M. N., & Nagapudi, K. (2022). Long-acting ocular drug delivery technologies with clinical precedent. *Expert Opinion on Drug Delivery*, *19*(10), 1285-1301.

[63] Navarro-Partida, J., Castro-Castaneda, C. R., Santa Cruz-Pavlovich, F. J., Aceves-Franco, L. A., Guy, T. O., & Santos, A. (2021). Lipid-based nanocarriers as topical

ISSN: 2583-4053

Volume-2 Issue-3 || June 2023 || PP. 238-249

https://doi.org/10.55544/jrasb.2.3.32

drug delivery systems for intraocular diseases. *Pharmaceutics*, *13*(5), 678.

[64] Gedde, S. J., Lind, J. T., Wright, M. M., Chen, P. P., Muir, K. W., Vinod, K., ... & Mansberger, S. L. (2021). Primary open-angle glaucoma suspect preferred practice pattern®. *Ophthalmology*, *128*(1), P151-P192.

[65] Yang, C., Yang, J., Lu, A., Gong, J., Yang, Y., Lin, X., ... & Xu, H. (2022). Nanoparticles in ocular applications and their potential toxicity. *Frontiers in Molecular Biosciences*, *9*, 931759.

[66] Kulkarni, M. B., Velmurugan, K., Prasanth, E., Amreen, K., Nirmal, J., & Goel, S. (2021). Smartphone enabled miniaturized temperature controller platform to synthesize nio/cuo nanoparticles for electrochemical sensing and nanomicelles for ocular drug delivery applications. *Biomedical Microdevices*, *23*, 1-13.

[67] Taka, E., Karavasili, C., Bouropoulos, N., Moschakis, T., Andreadis, D. D., Zacharis, C. K., & Fatouros, D. G. (2020). Ocular co-delivery of timolol and brimonidine from a self-assembling peptide hydrogel for the treatment of glaucoma: In vitro and ex vivo evaluation. *Pharmaceuticals*, *13*(6), 126.

[68] Gedde, S. J., Lind, J. T., Wright, M. M., Chen, P. P., Muir, K. W., Vinod, K., ... & Mansberger, S. L. (2021). Primary open-angle glaucoma suspect preferred practice pattern®. *Ophthalmology*, *128*(1), P151-P192.

[69] Shah, S., Bhanderi, B., Soniwala, M., & Chavda, J. (2021). Lutein-Loaded solid lipid nanoparticles for ocular delivery: Statistical optimization and ex vivo evaluation. *Journal of Pharmaceutical Innovation*, 1-15.

[70] Gugleva, V., & Andonova, V. (2023). Recent Progress of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers as Ocular Drug Delivery Platforms. *Pharmaceuticals*, *16*(3), 474.

[71] Umama, Y., Venkatajah, G., Shourabh, R., Kumar, R., Verma, A., Kumar, A., & Gayoor, M. K. (2019). Topic-The scenario of pharmaceuticals and development of microwave as; sisted extraction technique. *World J Pharm Pharm Sci*, *8*(7), 1260-1271.

[72] Nyarko, R. O., Roopini, R., Raviteja, V., Awuchi, C. G., Kumar, R., Faller, E. M., ... & Saha, P. (2022). Novel Sars-CoV-2 Variants & Therapeutic Effects. *Journal for Research in Applied Sciences and Biotechnology*, *1*(2), 25-34.

[73] Sultana, A., Singh, M., Kumar, A., Kumar, R., Saha, P., Kumar, R. S., & Kumar, D. (2022). To identify drug-drug interaction in cardiac patients in tertiary care hospitals. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 146-152.

[74] Nyarko, R. O., Awuchi, C. G., Kumar, R., Boateng, E., Kahwa, I., Boateng, P. O., ... & Saha, P. (2022). Evaluation of cafeteria diet in experimental animal with plant extract of calotropis procera for obesity parameter. *Journal for Research in Applied Sciences and Biotechnology*, *1*(3), 107-113.

[75] Prajapati, A. K., Sagar, S., & Kumar, R. (2022). Past and Current Prospectives of Herbal Product for Skin Care. *Journal for Research in Applied Sciences and Biotechnology*, *1*(5), 145-160.

[76] Awuchi, C. G., Saha, P., Amle, V. S., Nyarko, R. O., Kumar, R., Boateng, E. A., ... & Asum, C. (2023). A Study of Various Medicinal Plants used in Ulcer Treatment: A Review. *Journal for Research in Applied Sciences and Biotechnology*, *2*(1), 234-246.

[77] Gedde, S. J., Lind, J. T., Wright, M. M., Chen, P. P., Muir, K. W., Vinod, K., ... & Mansberger, S. L. (2021). Primary open-angle glaucoma suspect preferred practice pattern®. *Ophthalmology*, *128*(1), P151-P192.

[78] World Health Organization. *World Report on Vision*; World Health Organization: Geneva, Switzerland, 2019; ISBN 9789241516570.

[79] Usgaonkar, U.; Shet Parkar, S.R.; Shetty, A. Impact of the use of digital devices on eyes during the lockdown period of COVID-19 pandemic. *Ind. J. Ophthalmol.* 2021, *69*, 1901–1906. [

[80] Shalini, S.; Ipsita, P.; Abhay, P.; Pandey, A.K. Life style disorders in ophthalmology and their management. *Environ. Conserv. J.* 2019, *20*, 67–72.

[81] García-Marqués, J.V.; Talens-Estarelles, C.; García-Lázaro, S.; Wolffsohn, J.S.; Cerviño, A. Systemic, environmental and lifestyle risk factors for dry eye disease in a mediterranean caucasian population. *Cont. Lens Anterior Eye.* 2022, *45*, 101539.

[82] Bourne, R.R.A.; Steinmetz, J.D.; Flaxman, S.; Briant, P.S.; Taylor, H.R.; Resnikoff, S.; Casson, R.J.; Abdoli, A.; Gharbieh, E.A.; Afshin, A.; et al. Trends in prevalence of blindness and distance and near vision impairment over 30 years: An analysis for the Global Burden of Disease Study. *Lancet Glob. Health.* 2021, *9*, e130–e143.

[83] Gote, V.; Sikder, S.; Sicotte, J.; Pal, D. Ocular Drug Delivery: Present Innovations and Future Challenges. *J. Pharmacol. Exp. Ther.* 2019, *370*, 602–624.

[84] Patel, A.; Cholkar, K.; Agrahari, V.; Mitra, A.K. Ocular drug delivery systems: An overview. *World J. Pharmacol.* 2013, *2*, 47–64.

[85] Nayak, K.; Misra, M. A review on recent drug delivery systems for posterior segment of eye. *Biomed. Pharmacother.* 2018, *107*, 1564–1582.

[86] Bachu, R.D.; Chowdhury, P.; Al-Saedi, Z.H.F.; Karla, P.K.; Boddu, S.H.S. Ocular Drug Delivery Barriers-Role of Nanocarriers in the Treatment of Anterior Segment Ocular Diseases. *Pharmaceutics* 2018, *10*, 28.

[87] Wilson, C.G. Ophthalmic Formulation. In *Specialized Pharmaceutical Formulation: The Science and Technology of Dosage Forms*, 1st ed.; Tovey, G.D., Ed.; Royal Society of Chemistry: London, UK, 2022; pp. 1–44.

[88] Kuno, N.; Fujii, S. Recent Advances in Ocular Drug Delivery Systems. *Polymers* 2011, *3*, 193–221.

[89] Jünemann, A.G.M.; Chorągiewicz, T.; Ozimek, M.; Grieb, P.; Rejdak, R. Drug bioavailability from

ISSN: 2583-4053

Volume-2 Issue-3 || June 2023 || PP. 238-249

https://doi.org/10.55544/jrasb.2.3.32

topically applied ocular drops. Does drop size matter? *Ophthalmol. J.* 2016, *1*, 29–35.

[90] Taghe, S.; Mirzaeei, S. Preparation and characterization of novel, mucoadhesive ofloxacin nanoparticles for ocular drug delivery. *Braz. J. Pharm. Sci.* 2019, *55*, e17105.

[91] Gaudana, R.; Ananthula, H.K.; Parenky, A.; Mitra, A.K. Ocular drug delivery. *AAPS J.* 2010, *12*, 348–360.

[92] Baranowski, P.; Karolewicz, B.; Gajda, M.; Pluta, J. Ophthalmic drug dosage forms: Characterisation and research methods. *Sci. World J.* 2014, *2014*, 861904.

[93] Wu, Y.; Liu, Y.; Li, X.; Kebebe, D.; Zhang, B.; Ren, J.; Lu, J.; Li, J.; Du, S.; Liu, Z. Research progress of in-situ gelling ophthalmic drug delivery system. *Asian J. Pharm. Sci.* 2019, *14*, 1–15.

[94] Bastawrous, A.; Burgess, P.I.; Mahdi, A.M.; Kyari, F.; Burton, M.J.; Kuper, H. Posterior segment eye disease in sub-Saharan Africa: Review of recent population-based studies. *Trop. Med. Int. Health.* 2014, *19*, 600–609

[95] Tóth, G.; Szabó, D.; Sándor, G.L.; Nagy, Z.Z.; Limburg, H.; Németh, J. Hátsószegmens-betegségek okozta látásromlás és vakság Magyarországon az 50 évnél idosebb korú lakosság körében [Visual impairment and blindness caused by posterior segment diseases in Hungary in people aged 50 years and older]. *Orv. Hetil.* 2022, *163*, 624–630.

[96] Varela-Fernández, R.; Díaz-Tomé, V.; Luaces-Rodríguez, A.; Conde-Penedo, A.; García-Otero, X.; Luzardo-Álvarez, A.; Fernández-Ferreiro, A.; Otero-Espinar, F.J. Drug Delivery to the Posterior Segment of the Eye: Biopharmaceutic and Pharmacokinetic Considerations. *Pharmaceutics* 2020, *12*, 269.

[97] Otero-Espinar, F.J.; Fernández-Ferreiro, A.; González-Barcia, M.; Blanco-Méndez, J.; Luzardo, A. Stimuli sensitive ocular drug delivery systems. In *Drug Targeting and Stimuli Sensitive Drug Delivery Systems*, 1st ed.; Grumezescu, A., Ed.; Elsevier: Amsterdam, The Netherlands, 2018; pp. 211–270.

[98] Sánchez-López, E.; Espina, M.; Doktorovova, S.; Souto, E.B.; García, M.L. Lipid nanoparticles (SLN, NLC): Overcoming the anatomical and physiological barriers of the eye—Part I—Barriers and determining factors in ocular delivery. *Eur. J. Pharm. Biopharm.* 2017, *110*, 70–75.

[99] Sun, L.; Zhang, M.; Shi, Y.; Fang, L.; Cao, F. Rational design of mixed nanomicelle eye drops with structural integrity investigation. *Acta Biomater.* 2022, *141*, 164–177.

[100] Xu, X.; Sun, L.; Zhou, L.; Cheng, Y.; Cao, F. Functional chitosan oligosaccharide nanomicelles for topical ocular drug delivery of dexamethasone. *Carbohydr. Polym.* 2020, *227*, 115356

[101] Nayak, K.; Misra, M. PEGylated microemulsion for dexamethasone delivery to posterior segment of eye. *J. Biomater. Sci. Polym. Ed.* 2020, *31*, 1071–1090.

[102] Bachu, R.D.; Stepanski, M.; Alzhrani, R.M.; Jung, R.; Boddu, S.H.S. Development and Evaluation of a Novel Microemulsion of Dexamethasone and Tobramycin for Topical Ocular Administration. *J. Ocul. Pharmacol. Ther.* 2018, *34*, 312–324.

[103] Bravo-Osuna, I.; Vicario-de-la-Torre, M.; Andrés-Guerrero, V.; Sánchez-Nieves, J.; Guzmán-Navarro, M.; de la Mata, F.J.; Gómez, R.; de Las Heras, B.; Argüeso, P.; Ponchel, G.; et al. Novel Water-Soluble Mucoadhesive Carbosilane Dendrimers for Ocular Administration. *Mol. Pharm.* 2016, *13*, 2966–2976.

[104] Ghasemiyeh, P.; Mohammadi-Samani, S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: Applications, advantages and disadvantages. *Res. Pharm. Sci.* 2018, *13*, 288–303.

[105] Costa, C.P.; Barreiro, S.; Moreira, J.N.; Silva, R.; Almeida, H.; Sousa Lobo, J.M.; Silva, A.C. In Vitro Studies on Nasal Formulations of Nanostructured Lipid Carriers (NLC) and Solid Lipid Nanoparticles (SLN). *Pharmaceuticals* 2021, *14*, 711.