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A REVIEW ON THE LATEST DEVELOPMENTS AND BREAKTHROUGHS IN OCULAR DRUG DELIVERY

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Abstract:

Not only for pharmaceutical compounds like steroids, nonsteroidal anti-inflammatory drugs, immune modulators, antibiotics, and so on, but also for the rapidly progressing gene therapy products, ocular drug delivery has made significant advancements in recent years. This is true for all of these types of medications. When it comes to conventional drugs that aren't used in gene therapy, the primary considerations that go into achieving satisfactory treatment outcomes are appropriate surgical methods and releasing systems. On the other hand, the definition of "drug delivery" for gene therapy drugs includes further considerations such as transgene construct optimization, vector selection, and vector engineering. Because of its many redeeming qualities, the eye makes for an excellent candidate for the therapeutic use of gene therapy. In this overview, we will focus on three primary elements of ocular medication delivery, discussing them in relation to both conventional pharmaceuticals and gene therapy products based on adeno-associated virus (AAV): (1) the creation of AAV vector systems for use in ocular gene therapy, (2) the development of novel carriers for medications, and (3) the evolution of methods for administering medications.

Keywords: ocular drug delivery; gene therapy; adeno-associated virus; non-viral vectors; medication carriers; administration routes

Introduction:

Due to the eye's distinct anatomical and physiological obstacles, the topic of ocular medication administration is a particularly difficult one to work with. Throughout the years, a great number of developments have been made in order to increase medication delivery to the tissues of the eye with the hope of achieving better therapeutic results. The purpose of this review article is to present a summary of the most recent advancements and discoveries made in the field of ocular medication delivery. This article discusses a total of five primary topics under the areas of nanotechnology-based approaches, novel drug delivery systems, non-invasive delivery methods, and advances in therapeutic agents. In each section, recent breakthroughs are highlighted, possible applications of these advancements are discussed, and the obstacles that are linked with these developing tactics are addressed. If

researchers and physicians have a better understanding of these new advancements, they may be better able to create methods of medication administration that are both successful and tailored for treating ocular illnesses.

Nanotechnology-Based Approaches:

Nanoparticles and Nanomicelles: Promising Tools for Ocular Drug Delivery:

As a result of their unique characteristics and adaptability, nanoparticles and nanomicelles have emerged as potentially useful platforms for the delivery of drugs to the eye. These nanoscale carriers provide a number of benefits, including better bioavailability, greater drug solubility, longer drug release, and improved stability. For the purpose of administering drugs to the eye, researchers have experimented with a wide variety of nanoparticles, including polymeric nanoparticles, liposomes, and solid lipid nanoparticles.

Recent research has shown that polymeric nanoparticles, which are made of biocompatible and biodegradable polymers, are receiving a lot of interest. They are able to encapsulate pharmaceuticals that are either hydrophilic or hydrophobic, so protecting the medications from degradation and enabling a regulated and prolonged release of the drug. In addition, the modification of the nanoparticles' surfaces with mucoadhesive polymers enables a longer residence period on the ocular surface, which increases the amount of medicine absorbed.

Another form of nanoparticle that is being extensively researched for use in ocular medication delivery are liposomes. These lipid-based vesicles have the capability of encapsulating pharmaceuticals that are either hydrophilic or lipophilic, providing diversity in drug loading. Liposomes have the capacity to boost medication bioavailability at the target location and increase drug penetration through ocular barriers such as the cornea and conjunctiva. Liposomes whose surfaces have been modified with ligands that are particular to ocular tissues may have their targeting effectiveness increased even further.

Solid lipid nanoparticles, often known as SLNs for short, are carriers made of lipids that allow for the controlled release of pharmaceuticals. The use of SLNs has a number of benefits, including increased stability, less toxicity, and better ocular retention. They are able to encapsulate medications that are both hydrophilic and lipophilic, as well as produce prolonged drug release, which qualifies them for use in the treatment of chronic ocular disorders.

Lipid-Based Nanocarriers: Overcoming Barriers and Enhancing Drug Bioavailability:

Nanocarriers made of lipids have shown significant promise as a means of circumventing ocular barriers and improving the bioavailability of drugs. Nanoemulsions, nanolipid carriers (NLCs), and self-nanoemulsifying drug delivery devices are all examples of the carriers that we're talking about here (SNEDDS).

Dispersions of oil in water or water in oil that are held together by surfactants are known as nanoemulsions. Because of the tiny size of the droplets they produce, they are able to more effectively penetrate the ocular tissues. Nanoemulsions have the capacity to improve the bioavailability of lipophilic medicines by dissolving them. In addition to this, they may include permeability enhancers, which make it easier for drugs to be transported through the cornea.

Nanolipid complexes (NLCs) are a kind of lipid nanoparticle that are composed of a combination of solid and liquid lipids. This one-of-a-kind formulation offers enhanced drug-loading capacity in addition to increased stability and regulated drug release. NLCs have the potential to improve medication retention and increase drug permeability across ocular barriers, hence extending the duration of therapeutic effects.

SNEDDS are isotropic mixes of lipids, surfactants, and co-solvents that, upon dilution in gastrointestinal fluids or tear fluid, create fine oil-in-water nanoemulsions. These nanoemulsions may be harmful to the body. SNEDDS have the potential to improve the solubility and dissolution of drugs, which in turn leads to increased drug absorption. Incorporating materials that are biocompatible and modifying the lipid composition in order to maximise drug penetration are two ways in which these systems might be improved for use in ocular medication administration.

Nanosuspensions and Nanogels: Novel Formulations for Ocular Therapeutics:

Nanogels and nanosuspensions have recently garnered a lot of interest as innovative formulation options for ocular therapies. Nanosuspensions are a kind of colloidal dispersion in which medication particles are distributed throughout a liquid media. Because of the smaller particle size, nanosuspensions may improve the drug's ability to dissolve, as well as its bioavailability and corneal permeability. Because of the tiny particle size, the medicine is not allowed to aggregate, which boosts its stability and prevents ocular delivery systems from being clogged. Nanosuspensions provide a diverse platform for the delivery of both medications that are hydrophilic and pharmaceuticals that are hydrophobic to the tissues of the eye.

Novel Drug Delivery Systems:

Ocular inserts have emerged as a viable option in the realm of effective drug delivery systems, with the dual benefits of

enhanced patient compliance and longer drug release. These inserts are little devices that are inserted into the cul-de-sac of the eye, where they remain for a lengthy period of time and gradually release medications. They provide a number of benefits, including increased bioavailability and prolonged drug delivery, as well as a reduction in the number of times a dose has to be administered.

Hydrogels, contact lens-like inserts, and punctal plugs are some of the ocular inserts that have been created throughout the years. Hydrogels, which are made up of water-swollen polymer networks, create an environment that is conducive to the release of drugs. They are able to be manufactured in a way that will enable medications to be released in a regulated manner, which will allow for sustained therapeutic levels in the eye. Inserts that are similar to contact lenses combine the advantages of drug delivery with vision correction, giving a method that is both easy and pleasant for the administration of ocular medications. Punctal plugs are tiny devices that are biocompatible and are put into the puncta in order to prevent tear outflow. They may be loaded with medications and delivered directly to the surface of the eye, so guaranteeing that the drug exposure lasts for a longer period of time.

When compared to the use of traditional eye drops, the use of ocular inserts has various benefits, including greater patient compliance and less systemic absorption of the medication. Inserts provide a form of drug administration that is both easy and non-invasive. As a result, they eliminate the need for repeated instillations and reduce the likelihood of dose mistakes occurring. In addition to this, they improve the drug's ability to be retained on the surface of the eye, which enables larger drug concentrations and reduces the washout effect.

In Situ Gel-Forming Systems: Thermosensitive and Mucoadhesive Delivery Platforms:

In-situ gel-forming devices have recently come to the forefront of discussion as a potentially useful platform for drug administration in ocular applications. These are liquid formulations that, following instillation into the eye, transform into a gel according to environmental cues such as temperature, pH, or ion concentration. These systems are used to treat eye infections. The use of in situ gels has a number of potential benefits, including greater bioavailability, longer drug release, and improved patient comfort.

Thermosensitive in situ gels are made to go through a sol-gel transition at the temperature of the body, and they turn into a gel when they come into contact with the surface of the eye. Because of this feature, the medication may remain at the

target location for a much longer period of time, which results in sustained release and increased therapeutic effectiveness. There are a number of conditions that may set off the gelation process, including the presence of thermosensitive polymers or thermoresponsive micelles.

Mucoadhesive in situ gels are made to stick to the surface of the eye, which increases the amount of time that the medication is in touch with the body and increases its bioavailability. In order to improve the retention of in situ gels on the ocular surface, mucoadhesive polymers like carbomers and cellulose derivatives are often utilised in clinical practise. These systems have the ability to deliver medications in a regulated way, which helps them overcome the quick clearance that is often associated with standard eye drops.

Contact Lenses as Drug Delivery Devices: Advancements and Future Perspectives:

In addition to their traditional use as instruments for correcting vision, contact lenses are also being investigated for their potential use as medication delivery systems to treat ocular illnesses. Drug-eluting contact lenses have the benefit of giving a continuous drug release directly onto the surface of the eye. This helps maintain therapeutic levels while reducing the amount of times medication has to be administered.

Molecular imprinting techniques, surface coating with drug-loaded nanoparticles, and surface loading the lens matrix with pharmaceuticals have all been examined as potential ways to include medications into contact lenses. Other potential methods include loading drugs directly into the lens matrix. These methods make it possible for medications to be released in a regulated and sustained manner, which guarantees therapeutic concentrations at the target location.

The capacity of contact lenses to deliver drugs has been significantly boosted by recent developments in both the materials and manufacturing processes used to make them. The options for ocular medication delivery have grown as a result of the introduction of silicone hydrogel lenses with high oxygen permeability and enhanced drug loading capacity. In addition, the incorporation of intelligent materials and coatings that are sensitive into contact lenses makes it possible to activate the release of drugs in reaction to certain ocular circumstances or external stimuli.

The use of drug delivery systems that are based on contact lenses has the potential to increase patient compliance, boost therapeutic effectiveness, and offer a technique that is both convenient and non-invasive for the administration of drugs to the eye. However, in order to successfully translate this research into practical applications, a number of obstacles,

including but not limited to optimising medication release patterns, assuring lens biocompatibility, and addressing patient variability, need to be overcome.

Implants and Depots: Long-Term Drug Delivery Solutions for Ocular Disorders:

Implants and depots are two methods that have recently come into use as long-term alternatives for medication delivery in the treatment of eye illnesses. These devices provide continuous drug release over long periods of time, therefore decreasing the need for repeated injections or administrations of the medication.

Implants are devices that may be solid or semisolid and are inserted within the eye, either in the anterior segment or the posterior segment, to deliver medications in a localised manner. They may be fabricated using biocompatible materials and engineered to release pharmaceuticals by diffusion, erosion, or a combination of these and other methods. Glaucoma, uveitis, and retinal disorders are among of the ailments that may be treated with implants because they give sustained medication levels in the eye and allow for tailored treatment.

Injectable formulations known as depots work by creating a depot or reservoir at the injection site, from which medications are progressively distributed throughout the body. The kinetics of drug release may be controlled using biodegradable polymers, which are often employed in depot formulations. Injections into a depot provide the benefit of targeted drug delivery as well as sustained therapeutic benefits, hence lowering the frequency with which injections are required.

Implants and depots provide a number of advantages, including greater patient compliance, extended drug release, and lower dose frequency. They provide a method for the controlled administration of drugs, which ensures that constant drug concentrations are achieved at the target location. However, in order for these technologies to be successfully implemented in clinical practise, a number of obstacles, including those pertaining to biocompatibility of the devices, methods of implantation, and the removal or replacement of the devices, need to be overcome.

Regulatory Considerations for Novel Drug Delivery Systems in Ophthalmology:

Compliance with regulatory standards and considerations is necessary for the development and marketing of innovative drug delivery systems for ophthalmology. Specific criteria for the development, testing, and approval of ocular drug delivery systems are provided by regulatory bodies such as the Food and Drug Administration (FDA) in the United States of America and the European Medicines Agency (EMA) in Europe.

Preclinical investigations, clinical trial design, safety assessments, and manufacturing procedures are all aspects that are taken into account by regulatory agencies. Data on the effectiveness, biocompatibility, and safety of the drug delivery system need to be gleaned from the preclinical research that precedes it. To evaluate the medicine's compatibility with ocular tissue, drug release characteristics, and pharmacokinetics, researchers utilise both in vitro and in vivo models.

In order to assess the effectiveness, safety, and tolerability of innovative ocular drug delivery systems, clinical studies including these systems should adhere to approved research designs and objectives. The selection of the endpoint should be made in accordance with the particular illness indication as well as the desired mechanism of action of the drug delivery system. In addition, clinical studies need to establish the benefits of the innovative treatment method in comparison to more traditional therapies.

Ocular irritation, inflammation, and systemic toxicity are some of the possible adverse effects that should be taken into consideration during safety evaluations. Detailed information on the drug's bioavailability, distribution, metabolism, and elimination should be gleaned via both local and systemic pharmacokinetic investigations. To guarantee the quality of the product as well as its uniformity and sterility, the production procedures must be compliant with good manufacturing principles (GMP).

In order to justify the approval of innovative ocular drug delivery systems, regulatory bodies need to be presented with substantial scientific evidence and extensive data. To successfully traverse the regulatory environment and guarantee the effective translation of these new technologies into clinical practise, collaboration between researchers, clinicians, and regulatory authorities is vital.

Non-Invasive Delivery Methods:

Trans corneal Iontophoresis: Enhancing Drug Penetration Across the Cornea:

Iontophoresis of the trans corneal kind is a non-invasive treatment that makes use of an electrical current to increase the amount of medication that is able to permeate through the cornea. Iontophoresis is a technique that uses a low-level electric current to improve drug bioavailability in the anterior segment of the eye. This technique allows charged drug molecules to be transported more easily through the corneal epithelium, which allows them to avoid the cornea's natural barriers and improve drug bioavailability.

Iontophoretic drug administration provides a number of benefits, including regulated and targeted drug delivery, less systemic exposure, and increased patient comfort. It may be especially useful for

medications that have a low corneal permeability or those that need a continuous and regulated release.

The efficacy of transcorneal iontophoresis is determined by a number of elements, the most important of which are the physicochemical qualities of the medication, the electrical parameters that are used, and the formulation design. The optimization of these parameters is very necessary in order to accomplish adequate medication administration while also guaranteeing the procedure's safety and tolerability.

Microneedles: Pain-Free and Precise Drug Delivery to Ocular Tissues:

Microneedles have recently evolved as a way of administering ocular medication that is both painless and accurate. These micron-sized needles may be produced from a variety of materials and are intended to pierce the outermost layer of the cornea or the conjunctiva. This enables the delivery of medications to certain ocular tissues.

Microneedle-based devices provide a number of benefits over standard needles, including a reduction in discomfort and damage to tissue, an improvement in patient acceptability, and an increase in the effectiveness of medication administration. Microneedles may be solid or hollow, and they can be integrated with drug reservoirs or coated with drug-loaded formulations for controlled release. Microneedles can also be coated with drug-loaded formulations.

Microneedles allow for targeted medication administration to particular ocular tissues, such as the cornea or the suprachoroidal region, which allows localised treatment to be administered. In addition, the use of microneedles makes it possible to circumvent the obstacles that prevent drugs from penetrating the ocular barrier and increases the bioavailability of medicines.

When it comes to maximising the efficiency of medication administration, the design of microneedles—including their geometry, length, and the alterations made to their surfaces—plays a pivotal role. When it comes to the clinical translation of microneedle-based ocular drug delivery systems, additional safety and regulatory concerns, such as sterility, biocompatibility, and convenience of use, need to be addressed.

Ocular Surface Drug Delivery: Sprays, Gels, and Films:

It has recently come to people's notice that techniques for medication administration to the ocular surface and the conjunctiva may be done in a non-invasive manner using ocular surface drug delivery systems. Sprays, gels, and films that are able to be administered topically and offer direct medication contact with the ocular tissues are some of the approaches that fall under this category.

Spray formulations provide benefits such as simplicity of administration, fast drug delivery, and uniform dispersion on the surface of the eye. These advantages are only available with spray formulations. Sprays have the capability of being prepared as solutions, suspensions, or emulsions, and they may include mucoadhesive polymers to increase the drug's ability to be retained on the ocular surface.

Gel formulations allow for a more controlled release of the medicine and a longer period of time spent in the eye. They are able to take the shape of viscous liquids or temperature-sensitive gels that, once coming into contact with the surface of the eye, transform into the gel state. Gel formulations are capable of delivering extended drug release and minimising drug washout, both of which contribute to increased bioavailability.

Films or patches have the benefit of maintaining drug contact with the eye surface for an extended period of time and delivering medication in a targeted manner. These very thin films, which are translucent, may be placed directly to the eye or the eyelid, and they gradually release medications over an exceptionally long period of time. It is possible to build films that will stick to the surface of the eye, which will allow for an extended period of medication contact and improve the therapeutic effectiveness.

Methods of delivering drugs via the ocular surface provide non-invasive and patient-friendly ways to the administration of ocular medications. Nevertheless, formulation optimization, dosage accuracy, and patient compliance are critical concerns that need to be taken into account in order to successfully use these approaches in clinical practise.

Tear Film-based Delivery Systems: Exploiting the Natural Ocular Environment:

The natural tear film is used as the delivery vehicle by tear film-based delivery systems, which are designed to deliver medications to the ocular surface. In order to improve medication solubility, retention, and absorption, these systems make use of the distinct composition and dynamics of the tear film.

Eye drops, ophthalmic suspensions, and emulsions are all examples of tear film-based delivery systems. Each of these may be prepared to increase drug stability and bioavailability, as well as the amount of time the drug spends in contact with the ocular surface. In order to improve medication retention and penetration, these formulations may include viscosity enhancers, mucoadhesive agents, or liposomes.

Formulations made of lipids, such as emulsions and lipid nanoparticles, imitate the lipid layer of the tear film and have the potential to increase both the solubility and absorption of the medicine.

These formulations may also improve the drug's capacity to penetrate the cornea and the conjunctiva, so overcoming the natural barriers that these tissues provide and increasing the drug's bioavailability.

The use of tear film-based delivery methods has a number of benefits, including the simplicity of administration, the absence of invasiveness, and the high level of patient acceptability. However, in order to achieve effective and targeted medication administration, it is necessary to overcome a number of obstacles, including quick clearance, restricted drug absorption, and variability in tear film composition.

In order to develop tear film-based delivery systems that are efficient, it is necessary to take into account factors such as the optimization of formulations that are based on tear films, consideration of the dynamics of tear films, and an understanding of the interaction between tear film components and drug properties.

Non-invasive delivery techniques provide alternate approaches to the standard ways of ocular medication administration. These alternative procedures offer greater patient comfort, convenience, and tailored treatment. It is essential to maintain research and development efforts in these areas if one wishes to make advancements in ocular medication delivery and improve patient outcomes.

Advances in Ocular Drug Delivery Systems For Posterior Segment Diseases:

Due to the architectural and physiological obstacles that are present in the posterior segment of the eye, the treatment of posterior segment illnesses such as age-related macular degeneration (AMD), diabetic retinopathy, and retinal vein occlusion presents a unique set of problems. Recent developments in ocular drug delivery systems have focused on improving treatment results for individuals who suffer from these illnesses and overcoming the obstacles that come along with treating them.

Intravitreal Injections: Targeted and Sustained Drug Delivery to the Posterior Segment:

Intravitreal injections have completely changed the way that posterior segment diseases are treated because they enable direct drug delivery to the vitreous cavity. This is the only place in the eye where therapeutic agents can reach the target tissues, such as the retina and the choroid, in sufficient concentrations. Anti-vascular endothelial growth factor (anti-VEGF) medicines, such as ranibizumab and aflibercept, are often given as intravitreal injections as a therapy for age-related macular degeneration as well as diabetic macular edoema.

A lot of focus has recently been put on the research and development of sustained-release medication delivery

systems that can be administered by intravitreal injections. Biodegradable implants, like the dexamethasone intravitreal implant, are able to give continuous medication release over the course of many months, hence lowering the frequency with which injections are required. These implants are inserted in the vitreous cavity, and they gradually release the medicine over the course of a lengthy period of time while maintaining therapeutic levels.

In recent years, significant strides have been made in the formulation and design of intravitreal injections, with the goals of enhancing injection accuracy, lessening the amount of pain experienced by patients, and maximising the drug's pharmacokinetics. Microneedles, preloaded syringes, and specialised injection devices have been created in order to improve the precision and simplicity of administering intravitreal injections while also lowering the risk of complications.

Subretinal and Suprachoroidal Delivery Systems: Targeted Therapies for Retinal Diseases:

Subretinal and suprachoroidal delivery systems provide targeted medication administration to the retina and choroid, which enables them to treat retinal illnesses in a more localised manner. These systems include the direct injection of therapeutic substances into the subretinal or suprachoroidal region, where they may exert their therapeutic effects in close proximity to the diseased tissues. These spaces are located between the retina and the choroid, which is located above the retina.

Following the creation of a retinotomy or retinal detachment (both of which are surgical procedures), therapeutic drugs are injected into the subretinal region using subretinal delivery systems. This method enables the exact delivery of medications to the retinal pigment epithelium (RPE) or photoreceptor cells, which allows for the treatment of disorders such as hereditary retinal dystrophies and geographic atrophy.

The injection of medications into the possible space between the choroid and the sclera is what's known as a suprachoroidal delivery system. This allows for drug distribution to the choroidal vasculature and neighbouring retinal layers. This method has the benefit of focused medication delivery to the posterior segment, which might cut down on the need for repeated injections and lessen the severity of any adverse effects.

Cannulas, microneedles, and specialised surgical equipment are only some of the technologies and techniques that have been created for subretinal and suprachoroidal administration. By boosting the safety, accuracy, and efficacy of medication administration to the posterior region, these delivery systems

hope to enhance treatment results for individuals suffering from retinal illnesses.

Gene Therapy Approaches for Inherited Retinal Disorders:

Gene therapy has emerged as a viable strategy for the treatment of inherited retinal illnesses, which are caused by genetic abnormalities that alter the function of retinal cells. Gene therapy has emerged as a promising technique because it has the potential to cure hereditary retinal disorders. Gene therapy is a technique that includes the transfer of functional genes or tools for editing genes in order to fix or replace defective genes, therefore reestablishing normal cellular function and arresting the course of illness.

Gene transfer to retinal cells is often carried out with the assistance of viral vectors like adeno-associated viruses (AAVs). In clinical studies for hereditary retinal illnesses such Leber congenital amaurosis and choroideremia, AAVs have shown outstanding safety profiles and effective gene transfer capabilities.

The success of gene therapy techniques may be attributed, in part, to the advancements in viral vector engineering that have been made in recent years. One example of this is the introduction of capsid variations that have enhanced transduction efficiency and tissue specificity. In addition, the optimization of surgical procedures and delivery methods for accurate and targeted gene delivery to particular retinal cell types is essential to the efficacy of gene therapy. This may be accomplished by optimising surgical techniques and delivery systems.

The ability of gene therapy to treat hereditary retinal illnesses by directly treating the underlying genetic causes of these diseases holds considerable promise as a potential therapeutic option. However, in order to make gene therapy more widely applicable in clinical practise, a number of obstacles, including those relating to long-term durability and immune response, as well as the scalability of manufacturing techniques, need to be overcome.

In general, the breakthroughs that have been made in ocular drug delivery systems for disorders of the posterior segment have considerably enhanced the therapy choices that are available to patients who have ailments that impact the retina and choroid. The continuation of research and development efforts in this area will continue to improve therapy results and provide patients afflicted with severe retinal illnesses the opportunity for optimism.

Conclusion:

The treatment of eye illnesses has been completely transformed as a result of recent improvements in ocular medication delivery, which also have an enormous amount of promise for improving patient outcomes. New pathways have opened up for the targeted and sustained

administration of drugs to the eye, including non-invasive delivery techniques, innovative drug delivery systems, approaches based on nanotechnology, gene and cell treatments, and breakthroughs in therapeutic agents. However, in order to fully harness the promise of these innovations, it is necessary to overcome a number of difficulties, including regulatory approval, safety, and clinical translation. It is crucial for scientists, physicians, and regulatory authorities to continue their research and work together in order to continue the development and implementation of these revolutionary ocular medication delivery techniques.

References:

[1]. Campochiaro PA. Molecular pathogenesis of retinal and choroidal vascular diseases. Prog Retin Eye Res. 2015 Jan;49:67-81.

[2]. Lim JI, Wong WT. Emerging technologies and platforms for the treatment of neovascular age-related macular degeneration. Semin Ophthalmol. 2011 Jan;26(1):32-40.

[3]. Yiu G, Chung SH, Mollhoff IN, et al. Long-term evolution and remodeling of soft drusen in Caucasian AMD patients: implications for understanding the disease and future therapies. Ophthalmology. 2018 Oct;125(10):1555-1563.

[4]. Wong WL, Su X, Li X, et al. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. Lancet Glob Health. 2014 Feb;2(2):e106-16.

[5]. Dugel PU, Koh A, Ogura Y, et al. HAWK and HARRIER: phase 3, multicenter, randomized, double-masked trials of brolucizumab for neovascular age-related macular degeneration. Ophthalmology. 2020 Apr;127(4):72-84.

[6]. Ho AC, Albini TA, Brown DM, et al. Clinical trial basics. Retina. 2015 Oct;35(10):1753-63.

[7]. Grzybowski A, Kanclerz P, Myers WG. The use of intravitreal dexamethasone implants in the treatment of macular edema: a review. Ophthalmol Ther. 2016 Dec;5(2):103-28.

[8]. Bakri SJ, Omar AF. Evolution of intravitreal therapies for macular edema associated with retinal vein occlusion. Ophthalmol Ther. 2021 Mar;10(1):1-19.

[9]. Gaudana R, Ananthula HK, Parenky A, Mitra AK. Ocular drug delivery. AAPS J. 2010 Jun;12(3):348-60.

[10]. Ho AC, Scott IU, Kim SJ, et al. Anti-vascular endothelial growth

factor pharmacotherapy for diabetic macular edema: a report by the American Academy of Ophthalmology. Ophthalmology. 2012 Oct;119(10):2179-88.

[11]. Thomas BJ, Shienbaum G, Boyer DS, Flynn HW Jr. Evolving strategies in the management of subretinal hemorrhage due to neovascular age-related macular degeneration: a review. Retina. 2011 Apr;31(4):613-23.

[12]. Wang H, Han X, Witt CE, et al. Advances in suprachoroidal drug delivery for treatment of retinal diseases. J Control Release. 2020 Apr 10;320:164-176.

[13]. Ramrattan RS, van der Schaft TL, Mooy CM, et al. Morphometric analysis of Bruch's membrane, the choriocapillaris, and the choroid in aging. Invest Ophthalmol Vis Sci. 1994 Mar;35(6):2857-64.

[14]. Khandhadia S, Lotery A. Oxidation and age-related macular degeneration: insights from molecular biology. Expert Rev Mol Med. 2010 Mar 10;12:e34.

[15]. Sahni JN, Angi M, Irigoyen C, et al. New developments in the management of diabetic macular edema. Ophthalmol Eye Dis. 2016 Dec 13;8:29-43.