International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 16s,2025
https://theaspd.com/index.php

Formulation And Characterization Of Hydrogel For Ophthalmic Sustained Delivery Of Docosahexaenoic Acid

Vivek Kanseri[1], Tarun Parashar[2], Shilpa Mamgain[3]
[1]Research Scholar, School of pharmacy and research, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, India-248007, vivekkanseri2@gmail.com
[2]Associate Professor, School of pharmacy and research, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, India-248007, Uttarakhand – 248007, parashar89tarun@gmail.com
[3]Assistant Professor, School of pharmacy and research, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, India-248007, mamgain.shilpa@gmail.com
*Corresponding author: Dr. Tarun Parashar,Email id: parashar89tarun@gmail.com
Orcid id: 0000-0002-8250-5859

Abstract:
Ocular disorders are a major global health concern due to their potential to significantly impair vision and reduce quality of life. Conventional eye drops formulations often fail to maintain therapeutic drug levels because of rapid tear turnover and ocular barriers like the blood-retina and blood-aqueous barriers. This study focusses to develop a hydrogel-based delivery system for the sustained ophthalmic release of Docosahexaenoic Acid (DHA), a polyunsaturated fatty acid with neuroprotective and anti-inflammatory effects on retinal tissues. Hydrogels were formulated using Carbopol 940 and polyvinyl alcohol, crosslinked with glutaraldehyde, and evaluated across eight formulations for parameters including appearance, pH, viscosity, spreadability, swelling, and drug release. The optimized formulation showed desirable physical properties, ocular compatibility, and a sustained drug release profile. These outcomes propose that the DHA-loaded hydrogel system could improve drug bioavailability, reduce dosing frequency, and improve therapeutic outcomes in the treatment of chronic ocular diseases such as diabetic retinopathy and age-related macular degeneration.
Keywords: *Docosahexaenoic acid, ocular drug delivery, hydrogel, crosslinking, bioavailability*

INTRODUCTION:

Ocular sicknesses are a major global health problem for the reason that they can drastically weaken vision and decrease overall quality of life. According to existing forecasts, over 2.2 billion people worldwide have distant or near vision impairment, with 43 million blind, the most common vision threatening conditions embrace cata racts, dry eye syndrome, glaucoma, age related macular degeneration, diabetic retinopathy, and retinal vein occlusion [1]. The eye is a highly intricate and confined organ in the body, which can be categorized into two main segments: the anterior and posterior segments. The anterior segments include the cornea, conjunctiva, aqueous humour, ciliary body, and crystalline lens. In contrast, the posterior segment comprises the sclera, choroid, and retinal pigment epithelium [2]. The cornea refracts and transmits light to the lens and retina while also protecting the eye from infection and structural damage to its deeper sections. The sclera forms a connective tissue layer that protects the eye from internal and external stresses while maintaining its shape [3]. The eye's function is affected by a variety of disorders, including inflammations and bacterial and viral infections. Most disorders affecting anterior eye tissues may be easily treated with large dosages of medication. Diseases affecting the posterior tissues of the eye are difficult to access and cure [4]. Drug delivery to the eye is a difficult to treat loaction,but has progress significantly in the recent years. With numbers of defence mechanism such as cornea, blood-retina barrier, blood-aqueous barrier, nasolacrimal drainage system, and blinking reflex prevent objects from entering the eye [5]. To overcome the limitations of conventional methods, there are critical need of sustained ocular drug delivery systems [6]. Topical eye drops has poor bioavailability (less than 5 %) due to rapid tear clearance and face high patient non- adherence [7]. For posterior segments disease frequent intravitreal injections impose substantial burdens and compromise treatment efficacy, necessitating sustained delivery systems which provides extended drug release to reduce dosing frequency and minimize risks [8]. The continuous development of innovative drug delivery methods such as hydrogels, is being used to increase the poor bioavailability of medication and to overcome the various barriers in the eye [9].

Hydrogels are three-dimensional, crosslinked polymeric networks characterized by their high water content. They are designed through the linking of monomers or polymer chains using moreover co-valent bond or physical interactions such as hydrogen bonding or ionic forces [10]. Hydrogels retain their water absorbing capacity for the reason that of the occurrence of hydrophilic functional groups along the polymer backbone. At the same time, crosslinking of polymer chains offers structural stability, keeping the hydrogel from disintegrating in aqueous surroundings. Hydrogels finished from natural polymers are emerging as pleasing biodegradable and renewable soft materials [11]. Docosahexaenoic acid (DHA) plays crucial roles in photoreceptor cells in acquisition of visual function. Dietary DHA modulates the maturation and survival of photoreceptor cells, and animal grownup with the polyunsaturated fatty acid free diets grow with irregular electroretinopathy (ERG) with decreased retinal DHA contents suggesting that dietary DHA is crucial for visual function [12]. DHA is a dominant fatty acid of retinal phospholipids and affects rhodopsin content at discs, as well as photoresponses. DHA is known to possess anti-inflammatory properties and plays a crucial role in maintaining retinal structure and function [13]. DHA supplementation with high dose can improve macular function, improve antioxidant capacity, and reduce inflammation in conditions like diabetic retinopathy, reduce oxidative stress and performs preventative role in age- related macular degeneration [14].

MATERIAL AND METHOD:

Materials

Docosahexaenoic acid (DHA). Carbopol 940 (carboxy vinyl polymer 940 extra pure) obtained from SISCO CHEM Maharashtra, india. Poly vinyl alcohol (PVA cold) obtained from Paskem Finechemical Industries, Gaziabad U.P., India. Propylene glycol (Propane- 1,2 diol) obtained from NICE chemicals, Kerala, India. Tween 80 obtained from Central Drug House (P) Ltd, Delhi, India. Potassium Dihydrogen Phosphate (KH_2PO_4) obtained from Avarice Industries, Ghaziabad, India. Benzalkonium Chloride obtained from Central Drug House, Delhi, India. Glutaraldehyde Soln. 25% obtained from Central Drug House (P) Ltd. Delhi, India. Sodium hydroxide (NaOH =40) obtained from NICE chemicals, Kerala, India. Sodium Chloride (Nacl= 58.44 extra pure) obtained from Avarice Industries, U.P. India.

Preformulation Studies:

1) Organolaptic Properties of drug:

Take drug in small amount & place it on butter paper & examine under proper lighting condition [15].

S. No.	Drug	Observation			
		Color	**Odor**	**Appearance**	**Taste**
1	Docosahexaenoic acid	White or light yellow	Mild, marine or fatty scent	Homogeneous, free flowing powder	Mild and fatty
2	Carbopol 940	White	Odoless	Fine, fluffy, loose powder	Tasteless
3	Polyvinyl alcohol	White	Odoless	Granular or powdery solid	Tasteless

Table 1: Organolaptic Properties of drugs

2) Melting point:

The capillary tube method is commonly used to check the melting point of a drug. In this, the drug is filled in the capillary tube and then the capillary tube is sealed, then it will be placed in the melting point apparatus and heating will be started, after that the sample is closely observed and temperature recorded [16].

S. no.	Drug	Observation
1	Docosahexaenoic acid	60 – 62°C
2	Carbopol 940	70 – 75°C
3	Polyvinyl alcohol	180 – 230°C

Table 2: Melting point of drugs

3) Solubility:

Accurately weigh a small amount of the drug and place it in a clean test tube or vessel. Add a measured volume of selected solvent to the drug, mix the contents throughly than visually inspect the mixture.

S. no.	Solvent	Solubility
1	Ethanol	High
2	Methanol	High
3	Propylene glycol	High
4	Distilled water	Very low

Table 3: Solubility of drugs

4) Fourier Transform Infrared Spectroscopy:

FTIR is an analytical technique used to obtain infrared spectrum from solid, liquid or gas [17].

Methods

Procedure for hydrogel preparation by Aldehyde based chemical crosslinking method [18]:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
DHA	05	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Carbopol 940	0.8	0.4	0.6	0.8	0.4	0.4	0.8	0.6
Polyvinyl Alcohol	0.4	0.6	0.8	0.4	0.8	0.8	0.6	0.4
Glutaraldehyde	0.8	0.8	0.6	0.4	0.4	0.6	0.4	0.8
Sodium Phosphate	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Potassium Dihydrogen Phosphate	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Propylene Glycol	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Tween 80	1	1	1	1	1	1	1	1
Sodium Chloride	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Benzalkonium Chloride	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Sodium Hydroxide	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Distilled Water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table 4 : Formulation Table (8 Formulations)

1) Phosphate Buffer solution:

To prepare a phosphate buffer solution of pH 7.4, dissolve required amount of Sodium Phosphate and Potassium Dihydrogen Phosphate in distilled water.

2) Dispersion of Carbopol 940:

Add 20 ml of distilled water in a 100 ml beaker. Weigh the required amount of carbopol 940 and disperse in distilled water with continuous stirring in a magnetic stirrer at 500 rpm for 2 hours. Than allow hydration for the carbopol 940 & distilled water mixture for 24 hours at room temperature.

3) Preparation of Polyvinyl alcohol solution:

Add 20 ml of distilled water in a 100 ml beaker. Heat the distilled water to 60°C in a water bath. Weigh the required amount of polyvinyl alcohol (PVA) and add it to the distilled water while continuously stirring with a magnetic stirrer at 500 rpm and maintaining the temperature at 60°C until it is fully dissolved. Now cool this solution to room temperature.

4) Preparation of DHA solution:

Add required amount of Propylene glycol and Tween 80 in a 50 ml beaker. Dissolve required amount of DHA in Tween 80 & Propylene glycol under mild stirring.

5) Combining components:

Mix PVA solution with carbopol 940 dispersion in a 250 ml beaker while continuously stirring at 500 rpm for 15 minutes. Add 5 ml of buffer solution and stir. Add DHA- Propylene glycol-Tween 80 mixture and stir for 30 minutes. Add NaCL to adjust tonicity and BKC as a preservative and stir.

6) Chemical crosslinking:

Dilute 25% Glutaraldehyde with 2ml of distilled water and add dropwise in prepared combined solution while stirring at 250 rpm for 1 hour. Adjust pH using 0.1N NaOH solution.

7) Homogenization and Storage:

Homogenize the final hydrogel at 5000 rpm for 10 minutes. And store at 4°C to maintain stability.

Characterization of Docosahexaenoic acid Hydrogel [19, 20]

1. Physical appearance: The prepared hydrogel is visually inspected for its colour, transparency, homogeneity, consistency and phase separation.

2. pH evaluation: The pH of each prepared hydrogel formulation was measured using pH paper and a digital pH meter by dipping the pH electrode directly into the hydrogel than wait for the reading and record the pH value displayed on the digital meter.

3. Spreadability: A specific amount of the hydrogel (0.5 or 1.0 g) placed between two glass plates, then applying standard weight on the upper plate and allow it to rest for 5 minutes, the diameter of spread hydrogel is measured in centimeters.

It is calculated by using the formula S= M.L/T

Where S= spreadability, M= weight tide to upper slide, L= length of glass slide, T= time taken to separate the slides completely.

4. Viscosity: Viscosity of the prepared hydrogel formulations was determined by Brookfield viscometer at 25°C. The hydrogel samples are placed into the viscometer and spindle 52 immersed in the gel. The instrument measures viscosity values.

5. Rheological Studies: Assessed to determine flow behavior, which affects gelation and drug release.

6. Swelling index: It is determined by taking 1gm of hydrogel in a porous aluminum foil and mixed with 0.1N NaOH kept in a beaker. Then samples are withdrawn at different time intervals and kept for drying and it is reweighed.

7. Gelation Test: Evaluates the ability of the formulation to transition from solution to gel upon exposure to physiological conditions (tear fluid pH or temperature).

8. Sterility testing: Safeguards the absence of microbial contamination, which is critical for ocular safety.

9: Skin irritation: Skin irritation test was performed on healthy human volunteers which included both male and female candidates. For this, about 0.5g of DHA hydrogel was taken and applied on the skin area and then left in open for 1 hour and after this, observe the skin for any type of irritation or redness.

10. Drug release profile: The hydrogel system makes the delivery of DHA sustained, with in vitro studies demonstrating a prolonged release profile compared to conventional eye drops. The release rate is influenced by polymer type, crosslinking density and environmental pH/temperature [21].

RESULT AND DISCUSSION

Physical characteristics:

Formulation	Appearance	Homogeneity	Phase separation	Consistency
1	White	Excellent	None	Excellent
2	White	Good	None	Good
3	Light yellow	Good	None	Good
4	Light yellow	Average	None	Average
5	White	Good	None	Good
6	White	Good	None	Good
7	Light yellow	Good	None	Good
8	Light yellow	excellent	None	Excellent

Table 5: Physical characteristics of hydrogel formulations

(a) **(b)** **(c)**

Fig 1: A: hydrogel in glass vials; B & C: texture of hydrogel

pH evaluation:

Formulation	pH
1	7.2
2	7.0
3	7.5
4	7.3
5	7.6
6	7.2
7	7.0
8	6.7

Table 6: pH evaluation of hydrogel formulations

Viscosity evaluation:

Formulation	Viscosity	Remarks
1	7400	High Carbopol& crosslinker
2	5100	Moderate viscosity, Low Carbopol
3	6100	Balanced
4	6800	Lower glutaraldehyde
5	4900	Low viscosity, Low Carbopol,
6	5300	Moderate crosslinking
7	7200	High viscosity, High Carbopol
8	6900	Good consistency

Table 7: Viscosity evaluation of hydrogel formulation

Fourier Transform Infrared Spectroscopy:

1) Fourier Transform Infrared Spectroscopy for DHA:

The FTIR spectrum of docosahexaenoic acid was recorded using a Nicolet Summit LITE spectrometer equipped with a KBr beamsplitter and LiTaO3 detector. The sample was analysed in the range of 4000-400 CM^{-1}, and spectra were collected with 16 scans for both sample and background.

Wavelength (cm^{-1})	Intensity	Assignment
2920-2850	High	C-H stretching (aliphatic)
1740	High	C=O stretching (carboxylic)
1460-1370	Moderate	CH_2/CH_3 bending
1200-1000	Variable	C-0 stretching

Table 8: FTIR peaks table for DHA

Fig 2: Shows FTIR spectra of DHA

2) Fourier Transform Infrared Spectroscopy for DHA + Carbopol 940:

The physical mixture of DHA and Carbopol 940 was analyzed using FTIR spectroscopy (Nicolet Summit LITE, $LiTaO_3$ detector, KBr beamsplitter). The spectra were recorded in the range of 4000-400 cm^{-1} with 16 scans per sample. The FTIR spectrum of the DHA + Carbopol 940 mixture displayed characteristic absorption bonds corresponding to both components.

S. no.		Wave number (cm^{-1})	Intensity	Assignment	component
1		3436	24.613	O-H stretching (broad)	DHA/ Carbopol (hydroxyl)
2		3266, 3309	13.112, 14.012	O-H stretching (H bond)	Carbopol/ DHA
3		2906 – 2977	10.911-8.258	C-H stretching (alkyl)	DHA (fatty acid chain)
4		1719	10.053	C=O stretching (carboxylic acid)	DHA/ Carbopol
5		1640	10.041	C=O stretching (amide/ carboxyl)	Carbopol
6		1456 – 1580	28.576-23.727	COO^- asymmetric stretching	Carbopol
7		1199 – 1256	15.119-18.827	C-O stretching	DHA/ Carbopol
8		1046 – 1144	6.312-10.545	C-O stretching	DHA/ Carbopol
9		3802 – 3991	55.442-54.292	O-H Overtone/ combination bands	Moisture/ Carbopol

Table 9: FTIR peaks of DHA + Carbopol 940 mixture

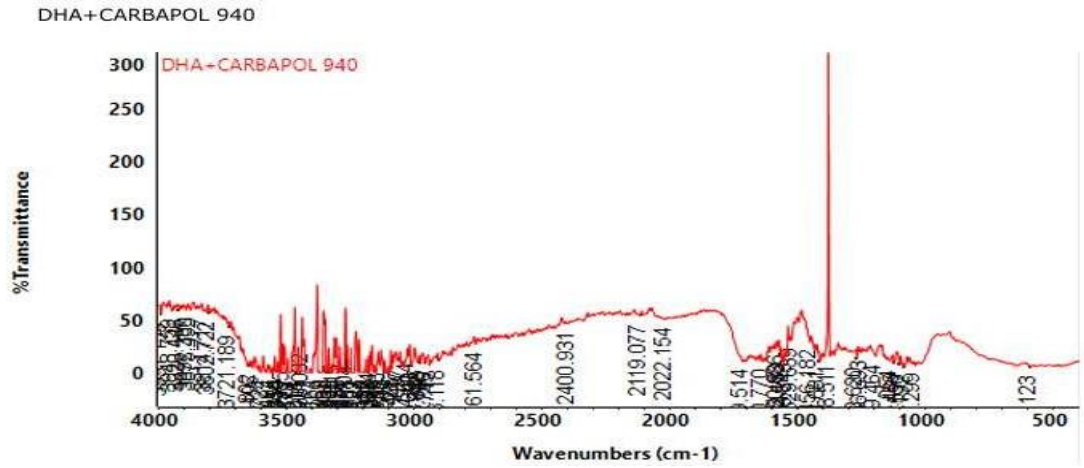

Fig 3: Shows FTIR spectra of DHA + Carbopol 940

3) Fourier Transform Infrared Spectroscopy for DHA + Polyvinyl alcohol:

The physical mixture of DHA and PVA was analyzed using FTIR spectroscopy (Nicolet Summit LITE, KBr beamsplitter). Spectra were recorded from 4000 to 400 cm^{-1} with 16 scans per sample. The resulting spectra were analyzed for characteristics peaks and shifts to assess possible interactions between components.

S. no.	Wavenumber	Intensity	Assignment	component
1	929 – 1153	3.9 – 24.9	C-O stretching, C-C stretching	PVA, DHA
2	1204 – 1227	65.2 – 70.1	C-O stretching (alcohol/ ester)	PVA, DHA
3	1357 – 1417	50.2 – 73.8	CH_2 bending, COH bending	PVA
4	1504 – 1582	40.8 – 146.8	COO^- asymmetric stretch, C=C	PVA, DHA

5	1640	58.9	C=O stretching (amide/carboxyl)	DHA
6	1743	123.6	C=O stretching (carboxylic acid)	DHA
7	2856 – 3054	57.8 – 104.5	C-H stretching (alkyl)	DHA, PVA
8	3331 – 3541	7.9 – 18.5	O-H stretching (broad)	PVA, DHA
9	3646 – 3969	45.1 – 131.9	O-H stretching	PVA, MOISTURE

Table 10: FTIR peaks of DHA + Polyvinyl alcohol

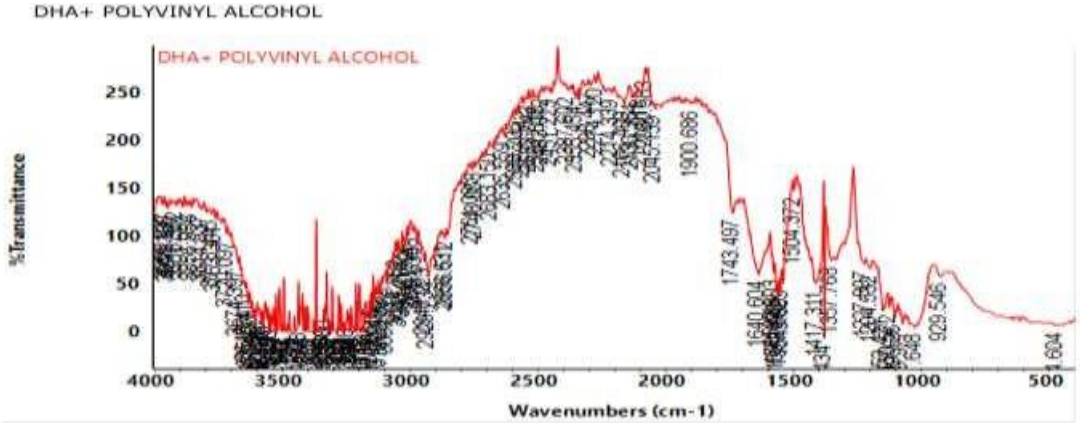

Fig 4: Shows FTIR spectra of DHA + Polyvinyl alcohol

DISCUSSION

The results showed that all eight hydrogel formulations displayed acceptable physical appearance, most of which were white or light yellow, homogeneous, and free from phase separation, which indicate effective mixing and stability. The pH value of the formulation ranged from 6.7 to 7.6, which is within the physiologically acceptable range for ophthalmic applications, which ensures ophthalmic compatibility and minimizes the risk of irritation. Viscosity measurements showed that formulations with higher concentrations of Carbopol 940, such as F1 (7400 cPs) and F7 (7200 cPs), had higher viscosity. which contributed to better retention on the ocular surface, while formulations with lower Carbopol 940 or crosslinker content, such as F5 (4900 cPs), had lower viscosity and may thus provide better spreadability but may potentially provide lower retention. FTIR analysis confirmed the successful incorporation of DHA into the hydrogel matrix and the presence of specific functional groups from both the drug and the polymer, which did not have any significant changes or new peaks indicating chemical incompatibility, thus supporting the physical entrapment of DHA within the hydrogel network. Of the eight formulations, F1 and F8 displayed the most desirable combination of properties, including optimal viscosity, consistency, and pH, making them most suitable for continuous ophthalmic delivery. These formulations maintained a balance between viscosity (ensuring prolonged ocular residence time) and dispersibility (facilitating easy application), while their pH values closely matched that of physiological tear fluid, which minimized the possibility of irritation. The overall results suggest that these optimized hydrogel systems can provide a sustained release of docosahexaenoic acid, this could potentially increase drug bioavailability, reduce dosing frequency, and improve therapeutic outcomes in chronic eye diseases.

CONCLUSION

The research validates that hydrogel-based systems are extremely effective for the sustained ophthalmic delivery of Docosahexaenoic acid (DHA). Hydrogels offer several advantages over conventional ocular drug delivery approaches, counting prolonged retention time, controlled and sustained drug release, increase bioavailability, and reduced dosing frequency. These properties help overcome the physiological barriers of the eye, which characteristically limit drug absorption and retention and therefore improve the therapeutic effectiveness of DHA for ocular diseases.The biocompatibility and tunable physicochemical properties of hydrogels allow for safe administration and customization according to exact therapeutic needs. The capability to encapsulate and gradually release DHA from the hydrogel

matrix safeguards that effective drug concentrations are maintained at the target site for extended periods, which is crucial for treating chronic or progressive ocular situations. Furthermore, hydrogels can be engineered for minimally invasive delivery, increasing patient comfort and adherence to therapy.Though, challenges continue in optimizing the stability of DHA within the hydrogel, ensuring consistent drug release under physiological conditions, and translating these systems into large scale clinical use. Continued research is needed to address these limitations and to further refine hydrogel formulations for personalized and effective ocular therapies.In conclusion, hydrogel-based ophthalmic delivery platforms represent a promising and versatile approach for the sustained release of DHA with the potential to significantly improve outcomes in the management of various vision-related disorders.

REFERENCES

1. Thrimawithana TR, Rupenthal ID, Räsch SS, Lim JC, Morton JD, Bunt CR. Drug delivery to the lens for the management of cataracts. Advanced drug delivery reviews. 2018 Feb 15; 126:185-94.
2. Fang G, Yang X, Wang Q, Zhang A, Tang B. Hydrogels-based ophthalmic drug delivery systems for treatment of ocular diseases. Materials Science and Engineering: C. 2021 Aug 1; 127:112212.
3. Willoughby CE, Ponzin D, Ferrari S, Lobo A, Landau K, Omidi Y. Anatomy and physiology of the human eye: effects of mucopolysaccharidoses disease on structure and function–a review. Clinical & Experimental Ophthalmology. 2010 Aug; 38:2-11.
4. Cholkar K, Dasari SR, Pal D, Mitra AK. Eye: anatomy, physiology and barriers to drug delivery. InOcular transporters and receptors 2013 Jan 1 (pp. 1-36). Woodhead publishing.
5. Kesharwani P, Bisht A, Alexander A, Dave V, Sharma S. Biomedical applications of hydrogels in drug delivery system: An update. Journal of Drug Delivery Science and Technology. 2021 Dec 1; 66:102914.
6. Williams R, Cauldbeck H, Kearns V. Sustained-release drug delivery systems. Eye. 2024 May 17:1-9.
7. Reddy A. Sustained drug delivery in ophthalmology. 2022 January 05.
8. Qiu G. New frontiers of retinal therapeutic innovation & strategic insights. EC Ophthalmology. 2015;2(2):81-91.
9. Akbari E, Imani R, Shokrollahi P, Jarchizadeh R. Hydrogel-based formulations for drug delivery to the anterior segment of the eye. Journal of Drug Delivery Science and Technology. 2023 Mar 1; 81:104250.
10. Zhang Q, Yan K, Zheng X, Liu Q, Han Y, Liu Z. Research progress of photo-crosslink hydrogels in ophthalmology: A comprehensive review focus on the applications. Materials Today Bio. 2024 May 6:101082.
11. Sole I, Vilchez S, Miras J, Montanyà N, García-Celma MJ, Esquena J. DHA and L-carnitine loaded chitosan hydrogels as delivery systems for topical applications. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2017 Jul 20; 525:85-92.
12. Shindou H, Koso H, Sasaki J, Nakanishi H, Sagara H, Nakagawa KM, Takahashi Y, Hishikawa D, Iizuka-Hishikawa Y, Tokumasu F, Noguchi H. Docosahexaenoic acid preserves visual function by maintaining correct disc morphology in retinal photoreceptor cells. Journal of Biological Chemistry. 2017 Jul 21;292(29):12054-64.
13. Rodriguez Gonzalez-Herrero ME, Ruiz M, López Román FJ, Marin Sanchez JM, Domingo JC. Supplementation with a highly concentrated docosahexaenoic acid plus xanthophyll carotenoid multivitamin in nonproliferative diabetic retinopathy: Prospective controlled study of macular function by fundus microperimetry. Clinical ophthalmology. 2018 May 29:1011-20.
14. Lafuente M, Rodríguez González-Herrero ME, Romeo Villadóniga S, Domingo JC. Antioxidant activity and neuroprotective role of docosahexaenoic acid (DHA) supplementation in eye diseases that can lead to blindness: A narrative review. Antioxidants. 2021 Mar 5;10(3):386.
15. Chaurasia G. A review on pharmaceutical preformulation studies in formulation and development of new drug molecules. Int J Pharm Sci Res. 2016 Jun 1;7(6):2313-20.
16. Tetko IV, Sushko Y, Novotarskyi S, Patiny L, Kondratov I, Petrenko AE, Charochkina L, Asiri AM. How accurately can we predict the melting points of drug-like compounds? Journal of chemical information and modeling. 2014 Dec 22;54(12):3320-9.
17. Mohamed MA, Jaafar J, Ismail AF, Othman MH, Rahman MA. Fourier transform infrared (FTIR) spectroscopy. InMembrane characterization 2017 Jan 1 (pp. 3-29). elsevier.
18. Echalier C, Valot L, Martinez J, Mehdi A, Subra G. Chemical cross-linking methods for cell encapsulation in hydrogels. Materials Today Communications. 2019 Sep 1; 20:100536.
19. Hu X, Qiu J, Tan H, Li D, Ma X. Synthesis and characterization of cyclodextrin-containing hydrogel for ophthalmic drugs delivery. Journal of Macromolecular Science, Part A. 2013 Jan 1;50(9):983-90.
20. Oelker AM, Grinstaff MW. Synthesis, characterization, and in vitro evaluation of a hydrogel-based corneal onlay. Ieee transactions on nanobioscience. 2011 Sep 8;11(1):37-45.
Gulsen D, Chauhan A. Dispersion of microemulsion drops in HEMA hydrogel: a potential ophthalmic drug delivery vehicle. International journal of pharmaceutics. 2005 Mar 23;292(1-2):95-117.