International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 13s,2025
https://theaspd.com/index.php

Docosahexaenoic Acid Hydrogels: Advancements And Applications In Ophthalmic Therapeutics

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's: Dr. Tarun Parashar, Email: parashar89tarun@gmail.com

Abstract:
Docosahexaenoic acid (DHA) hydrogels represent a novel innovation in modern ophthalmic treatment for illnesses including dry eye disease (DED) and postoperative complications associated with ocular surgery. Tear Film instability and ocular surface inflammation, associated with discomfort and visual impairment, are the key components of DED. Most often, what is offered as a traditional treatment include tear substitutes, which in many cases do not work at treating the underlying inflammation or provide long term relief. Omega 3 fatty acid DHA, has been found to have anti Inflammatory properties and is essential for ocular health. DHA has been shown in recent studies to have the ability to maintain tear film stability, protect epithelial cell health and thus can be a very supportive and valuable ingredient for adding to hydrogel formulations. In addition to lubrication, these hydrogels deliver DHA directly to the ocular surface to produce the therapeutic effect. Additionally, antioxidant activity of DHA is important to reduce oxidative stress in retinal cells, a situation which could help prevent both age-related macular degeneration and diabetic retinopathy. Using DHA hydrogels for the treatment of DED has been shown to have potential for using this system to decrease postoperative fibrosis after glaucoma filtration surgery. Topical application of DHA has been shown to maintain lower intraocular pressure and foster larger bleb areas than control groups, and this may be one means to increase success with surgical outcomes. Taken as a whole, DHA hydrogels represent a wide spectrum of approaches to improve ocular surface health, and treat various ophthalmic conditions employing their specialized properties.
Keywords: *Anti-inflammatory, Docosahexaenoic acid, postoperative complications, postoperative fibrosis, visual impairment.*

1. INTRODUCTION

The eye is an extremely difficult and restricted organ in the body, which can be considered into two main sections: the anterior and posterior sections. The anterior section includes the cornea, conjunctiva, aqueous humour, iris, ciliary body and crystalline lens. In disparity, the posterior section comprises the sclera, choroid and retinal pigment epithelium [1]. Dry eye disease is a complex eye surface illness characterised by a decrease in tear film homeostasis, which includes hyper-osmolarity and tear film instability. In increment to inflammation and harm to the eye surface, neuro-sensory disfunctions can assistance to ocular distress, grittiness, pain, foreign body sensation and impaired vision [2]. The expanding global prevalence of eye sickness has necessitated the expansion of novel therapeutic techniques to expand treatment efficacy and patient acquiescence. Outdated ophthalmic rehabilitations, characteristically in the form of eye drops, recurrently have inadequate bioavailability and speedy exclusion from the ocular surface, resulting in suboptimal therapeutic properties [3]. This difficulty is especially acute for disorders affecting the eye's posterior region, like age-related macular degeneration and diabetic retinopathy which demands long-term drug delivery systems to obtain successful treatment outcomes [4]. Drug delivery to the, a difficult to treat area, has increased dramatically in recent years. With a number of defences and mechanisms in place to prevent objects from entering, the eye is relative to an isolated organ in the body [5]. These consist of the cornea, blood aqueous barrier, blood- retina barrier, nasolacrimal drainage system, and blinking reflex. It is more challenging to deliver medication to the anterior and posterior regions of the eye when these systems are combined [6]. The continuous development of innovative drug delivery methods, such as hydrogels, is being used to overpower the poor bioavailability of various traditional ophthalmic preparations [7].

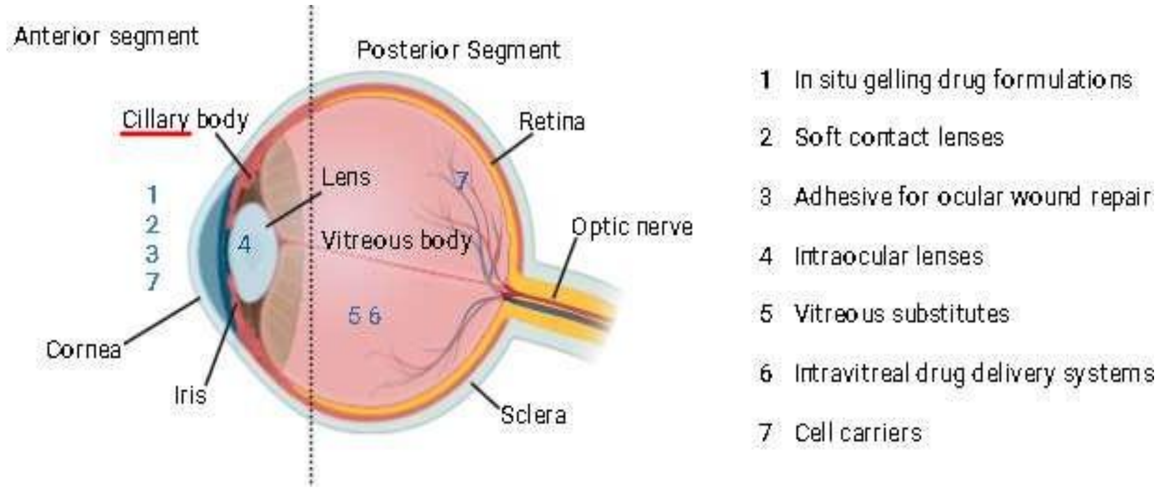

Figure 1 - Emphasizing the potential use of hydrogels in ocular medication delivery

1.2 hydrogel

Hydrogels are three-dimensional polymer networks that can hold substantial amounts of water, making them excellent candidates for ophthalmic applications due to their biocompatibility, controlled drug release, and potential to improve drug stability [8].They can hold a lot of water and have a soft rubbery texture, comparable to biological tissues. This styles them an admirable material for an extensive range of applications. Hydrogels with suitable utility, reversibility, sterilisation, and biocompatibility gratify equally both material and biological parameters for mending or swapping tissue and organs, reinstating live tissue purpose, and interacting with the biological system [9]. Hydrogel technology has numerous limitations, counting low solubility, high crystallinity, non-biodegradability, deprived mechanical and thermal physical characteristics, unreacted monomers, and the usage of hazardous crosslinkers. Novel characteristics can be developed by mixing natural and synthetic polymers through predefined attributes, such as biodegradation, solubility, crystallinity, and biological activities [10]. Hydrogels' crosslinked nature prevents them from dissolving when swollen. Crosslinking can take place in two different settings: in vivo (in-situ), following application to a particular area of the body, or in vitro, during the hydrogel's production. Mix a polymer in the reaction mixture with a low molecular weight crosslinking agent to initiate chemical crosslinking [11]. Intended for the purpose that the hydrophilic linear polymer chains and water are thermodynamically companionable, they dissolve in water in the nonappearance of crosslinking sites. Nevertheless, at what time the crosslinking points are present, the retractive force of the network's crosslinking points' flexibility balances solubility. Swelling approaches equilibrium as these pressures balance out [12].

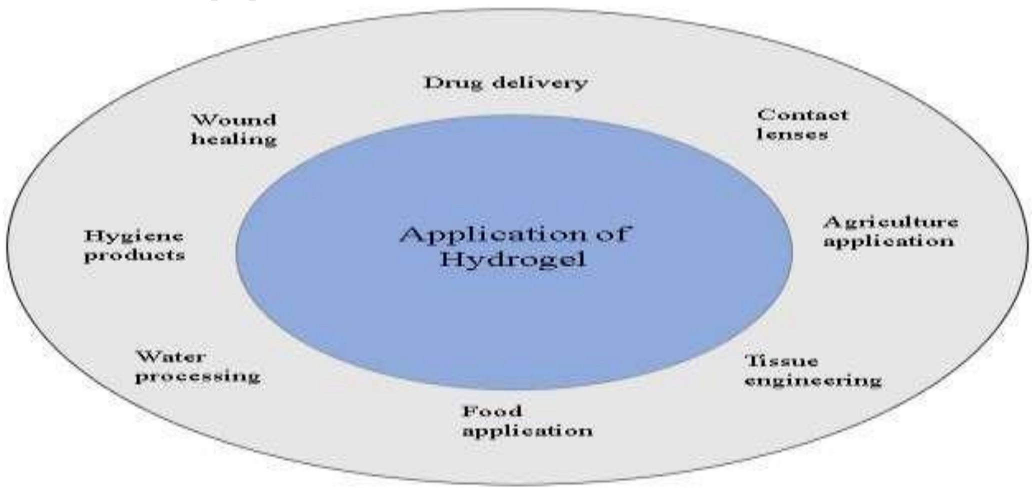

Figure 2: Applications of Hydrogel

1.3 CLASSIFICATION OF HYDROGEL

Hydrogels are multipurpose materials distinguished by their measurements to hold significant volumes of water inside their networks of three-dimensional polymers. They can be categorised conferring to a number of characteristics, together with as their structure, origin, reaction to environmental stimuli, and crosslinking procedures. The consequential provides a comprehensive categorisation of hydrogels [13]. Hydrogels are multipurpose materials acknowledged for their ability to hold massive amounts of water inside their three-dimensional polymer networks. They can be constructed based on a variation of criteria, composed with their structure, origin, reactivity to environmental stimuli, and crosslinking procedures. The resultant is a comprehensive classification of hydrogels [13].

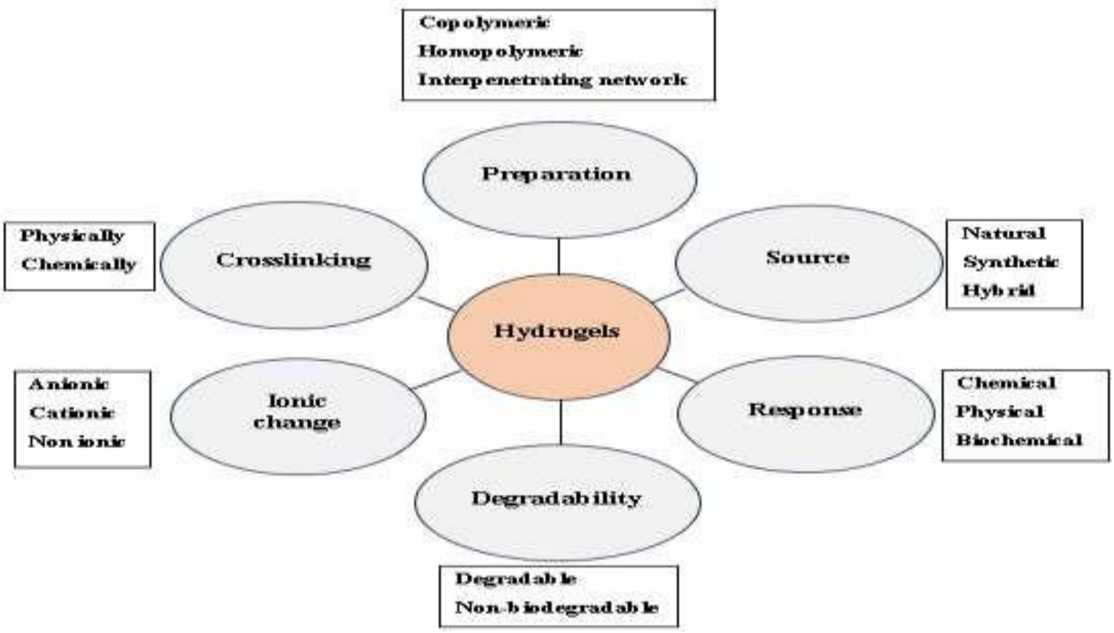

Figure 3: Classification of Hydrogel

(a) Origin-Based:

Natural hydrogels: Natural hydrogels are constructed from polysaccharides such as alginate, chitosan, hyaluronic acid (HA), and agarose. These materials are extensively recognised for their biodegradability and biocompatibility. Collagen and gelatin are two proteins that are extensively used in biomedical applications and have great biocompatibility [14].

Synthetic hydrogels: These hydrogels are made from synthetic polymers and can be tailored for specific applications. PEG or polyethylene glycol is well-known for being compatible and hydrophilic. Polyvinyl alcohol (PVA) is used in a range of therapeutic applications due to its beneficial properties [15].

(b) Structure- based: Homogeneous hydrogels have consistent features due to their uniform structure [15]. Composite hydrogels improve performance by combining the advantages of two or more different materials (for example- natural and synthetic polymers) [16].

(c) based on Smart (Stimuli-Responsive) to Environmental Stimuli:

When exposed to external stimuli like light, pH, or temperature, these hydrogels can alter chemically or physically. For example: Hydrogels that react to heat: Adapt to changes in temperature to change their condition. pH- responsive hydrogels change their swelling behavior when the pH level changes [17]. Non-smart hydrogels These have permanent properties that are independent of the environment and do not respond to change [18].

(d) Crosslinking method- based:

Chemically crosslinked hydrogels: are made by utilizing crosslinking chemicals to form covalent bonds between polymer strands. Hydrogels created with this approach are typically stable and long-lasting [19].

Physical crosslinked hydrogels: are formed by ionic or hydrogen bonding, which are both non-covalent interactions. In some cases, these hydrogels may dissolve [20].

(e) According to Water Content:

Less than 30% water makes up low water content hydrogels, which are frequently employed in applications that need for mechanical strength [21].

More than 30% water makes up high water content hydrogels, which give them a pliable, soft structure that is appropriate for biological applications [22].

(f) Degradation Mechanism based:
Biodegradable hydrogels are ideal for tissue engineering and medication delivery because they are made to decompose naturally through hydrolysis or enzymatic activity [23].
Non-biodegradable hydrogels are frequently utilised in applications requiring long-term stability because they maintain their stability in biological settings [24].

1.4 Drug - Docosahexaenoic Acid (Dha)

Docosahexaenoic acid (DHA), an omega-3 fatty acid originate abundantly in fish oil and algae, has garnered consideration for its beneficial effects on ocular health [25]. DHA is accredited to possess anti-inflammatory properties and plays a significant role in maintaining retinal structure and function [26]. Its incorporation into hydrogel formulations presents an opportunity to leverage these benefits while addressing the limitations of traditional drug delivery methods [27]. Docosahexaenoic acid accumulated significantly in brain tissue. Polyunsaturated fatty acids have been shown to be beneficial to human health and nutrition via clinical and epidemiological studies [28]. DHA is nearly entirely found in a large proportion in different seafood (fish, shellfish, micro and macroalgae, and even certain mammals) [29].

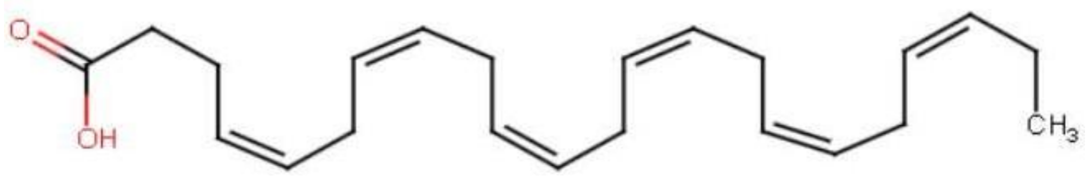

Figure 4: Chemical structure of Docosahexaenoic acid ($C_{22}H_{32}O_2$)

Table 1 - Docosahexaenoic Acid Profile: 26

Drug Name	Docosahexaenoic Acid
Mol. Formula	$C_{22}H_{32}O_2$
Mol. Weight	328.488 g/mol
Drug Class	Omega 3 polyunsaturated Fatty acid [24]
Category	Nutritional supplement, lipid-modifying agent [26]
Appearance	Dry, White or light yellow
Trade Name	Lovaza, Vayarin, Vayacog
Dosage	200-500 mg/day
Half-Life	Approximately 20 hours

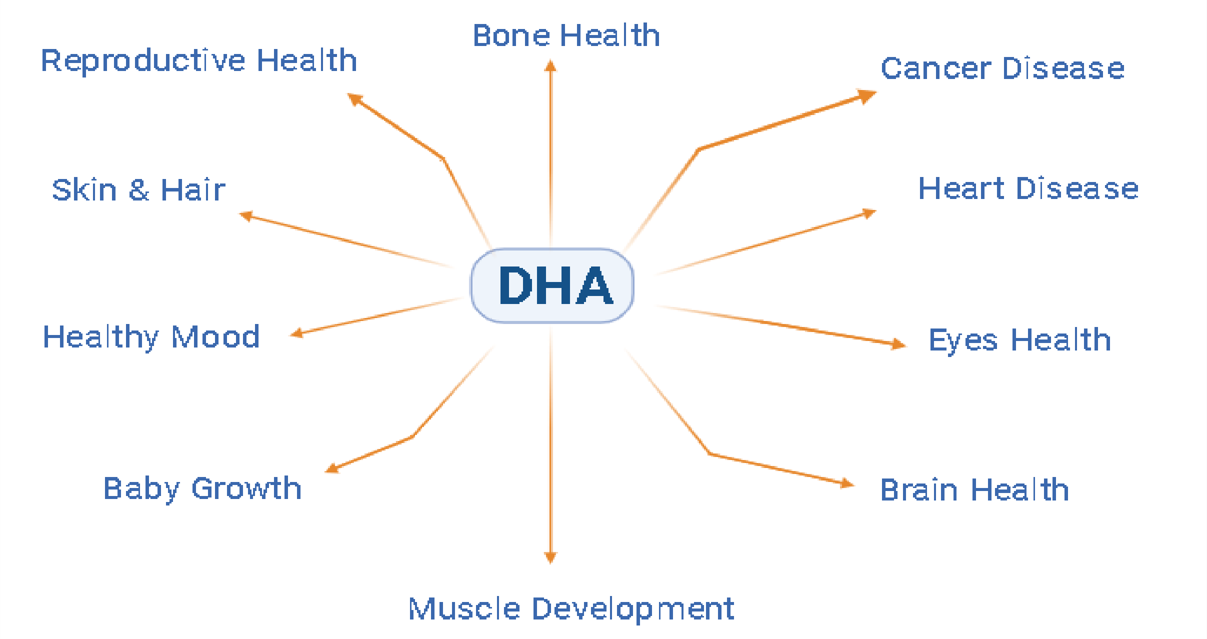

Figure 5: Applications of DHA

2. Advancements In Hydrogel Technology

The eye is a complicated organ with numerous obstacles that prevent efficient medication delivery. The cornea, conjunctiva, and nasolacrimal drainage system all contribute to the reckless clearance of topically administered medicines [30]. As a outcome, traditional eye drops frequently provide unsatisfactory therapeutic concentrations at the target region. This problem is worsened when treating posterior segment illnesses, when intravitreal injections are frequently necessary due to incomplete medication penetration into ocular tissues [31].

Hydrogels have various benefits over standard dosing forms.

- Hydrogels can deliver therapeutic substances in a regulated manner over time [32].
- Hydrogels increase medication absorption by extending residence duration on the ocular surface [33].
- Reduced dose frequency improves patient adherence to treatment regimens [34].

These properties make hydrogels an attractive substrate for the development of improved ocular medication delivery systems. And these attributes make hydrogels a promising platform for developing advanced ocular drug delivery systems.

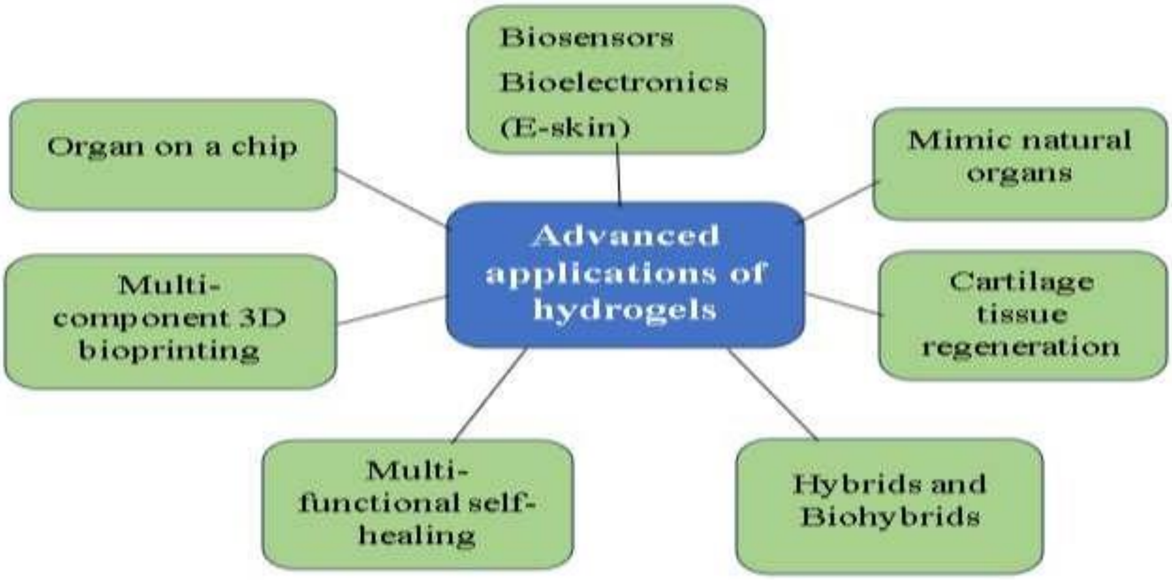

Figure 5: Advanced application of Hydrogels

3. Future Prospects

Better Drug Delivery: The development of innovative hydrogel systems that increase the bioavailability and long-term release of pharmaceuticals.

Smart hydrogel: Mentions to the creation of responsive hydrogels that have the capability to modify drug release rates in response to environmental indications such as pH, temperature, or light.

Personalized Medicine: Customising hydrogel formulations to encounter the requirements of individual patients in demand to maximise the effectiveness of treatment for definite circumstances.

Regenerative Medicine: To encourage the regeneration of damaged tissues, hydrogels are utilised in tissue engineering and wound healing in regenerative medicine.

Combination Therapies: By using hydrogels as carriers, multiple drugs can be delivered simultaneously to enhance therapeutic outcomes.

Enhancements in Biocompatibility: Studies are being conducted to increase the stability and biocompatibility of hydrogels by the use of crosslinking and Chemical changes.

Applications in Clinical Practice Expansion: Hydrogels are being used more and more in specialities other than ophthalmology, such as dermatology, orthopaedics, and oncology. One way to combine nanotechnology with integration is to improve drug encapsulation and release qualities by adding liposomes or nanoparticles to hydrogel systems.

4. CONCLUSION

The purpose of this study is to look at improvements in DHA hydrogels, namely their characteristics, production, and uses in ophthalmic therapies. Recent advances in hydrogel technology have resulted in the creation of DHA-based hydrogels that not only allow for continuous medication release, but also increase patient comfort by lowering the frequency of administration. These hydrogels may be programmed to respond to physiological cues, allowing for on-demand medication delivery tailored to patient demands. Furthermore, hydrogels' viscoelastic qualities allow them to endure tear flushing and remain on the ocular surface for longer periods of time, increasing bioavailability as compared to traditional formulations.

REFERENCES:

1) 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.
2) Hyon JY, Han SB. The protective effect of polyunsaturated fatty acids against dry eye disease: a literature review. Applied Sciences. 2021 May 15;11(10):4519.
3) Lynch CR, Kondiah PP, Choonara YE, Du Toit LC, Ally N, Pillay V. Hydrogel biomaterials for application in ocular drug delivery. Frontiers in bioengineering and biotechnology. 2020 Mar 20; 8:228.
4) A Miles E, C Calder P. Omega-6 and omega-3 polyunsaturated fatty acids and allergic diseases in infancy and childhood. Current pharmaceutical design. 2014 Feb 1;20(6):946-53.
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) Widjaja LK, Bora M, Chan PN, Lipik V, Wong TT, Venkatraman SS. Hyaluronic acid-based nanocomposite hydrogels for ocular drug delivery applications. Journal of Biomedical Materials Research Part A. 2015 Jun;103(6):2201-.
7) 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.
8) Giri BR, Jakka D, Sandoval MA, Kulkarni VR, Bao Q. Advancements in Ocular Therapy: A Review of Emerging Drug Delivery Approaches and Pharmaceutical Technologies. Pharmaceutics. 2024 Oct 12;16(10):1325.
9) Tavakoli S, Klar AS. Advanced hydrogels as wound dressings. Biomolecules. 2020 Aug 11;10(8):1169.
10) Tanigo T, Takaoka R, Tabata Y. Sustained release of water-insoluble simvastatin from biodegradable hydrogel augments bone regeneration. Journal of Controlled Release. 2010 Apr 19;143(2):201-6.
11) Hennink WE, van Nostrum CF. Novel crosslinking methods to design hydrogels. Advanced drug delivery reviews. 2012 Dec 1; 64:223-36.
12) Maitra J, Shukla VK. Cross-linking in hydrogels-a review. Am. J. Polym. Sci. 2014 Jan;4(2):25-31.
13) Khandan A, Jazayeri H, Fahmy MD, Razavi M. Hydrogels: Types, structure, properties, and applications. Biomat Tiss Eng. 2017 Oct 3;4(27):143-69.
14) Garg S, Garg A, Vishwavidyalaya RD. Hydrogel: Classification, properties, preparation and technical features. Asian J. Biomater. Res. 2016;2(6):163-70.
15) Bruck SD. Aspects of three types of hydrogels for biomedical applications. Journal of biomedical materials research. 1973 Sep;7(5):387-404.
16) Faheem Ullah, Muhammad Bisyrul Hafi Othman, Fatima Javed, Zulkifli Ahmad, Hazizan Md. Akil, Classification, processing and application of hydrogels: A review, Materials Science and Engineering: C, Volume 57, 2015, Pages 414-433.
17) Sikdar P, Uddin MM, Dip TM, Islam S, Hoque MS, Dhar AK, Wu S. Recent advances in the synthesis of smart hydrogels. Materials Advances. 2021;2(14):4532-73.
18) Zhou H, Dong G, Gao G, Du R, Tang X, Ma Y, Li J. Hydrogel-based stimuli-responsive micromotors for biomedicine. Cyborg and Bionic Systems. 2022 Oct 7.
19) Parhi R. Cross-linked hydrogel for pharmaceutical applications: a review. Advanced pharmaceutical bulletin. 2017 Oct 1;7(4):515-30.
20) Singhal R, Gupta K. A review: tailor-made hydrogel structures (classifications and synthesis parameters). Polymer-Plastics Technology and Engineering. 2016 Jan 2;55(1):54-70.
21) Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. Journal of advanced research. 2015 Mar 1;6(2):105-21.
22) Sahu N, Gupta D, Nautiyal U. Hydrogel: preparation, characterization and applications. Asian Pacific Journal of Nursing and Health Sciences. 2020 Jun 30;3(1):1-1.
23) Liu Y, Wang J, Chen H, Cheng D. Environmentally friendly hydrogel: A review of classification, preparation and application in agriculture. Science of the Total Environment. 2022 Nov 10; 846:157303.
24) Stoy VA. New type of hydrogel for controlled drug delivery. Journal of biomaterials applications. 1988 Oct;3(4):552-604.
25) Horrocks LA, Yeo YK. Health benefits of docosahexaenoic acid (DHA). Pharmacological research. 1999 Sep 1;40(3):211-25.
26) Mittal C. The Role of DHA (Docosahexaenoic acid) in Ophthalmic Microemulsion Formulations: A Comprehensive Review. Trends in Pharmaceuticals and Nanotechnology (e-ISSN: 2582-4457). 2024 May 29:29-40.
27) Yuan M, Zhang Y, Hua T, Liu XL, Liu T, Yuan RY, Li GP, Zhu Y, Zhang X. Omega-3 polyunsaturated fatty acid supplementation improves lipid metabolism and endothelial function by providing a beneficial eicosanoid-pattern in patients with acute myocardial infarction: A randomized, controlled trial. Clinical Nutrition. 2021 Feb 1;40(2):445-59.
28) Wolff AC, Donehower RC, Carducci MK, Carducci MA, Brahmer JR, Zabelina Y, Bradley MO, Anthony FH, Swindell CS, Witman PA, Webb NL. Phase I study of docosahexaenoic acid-paclitaxel: a taxane-fatty acid conjugate with a unique pharmacology and toxicity profile. Clinical cancer research. 2003 Sep 1;9(10):3589-97.

29) Liu Y, Cao K, Li T, Mu D, Zhang N, Wang Y, Wu R, Wu J. Encapsulation of docosahexaenoic acid (DHA) using self-assembling food-derived proteins for efficient biological functions. Food Science and Human Wellness. 2023 Sep 1;12(5):1861-71.
30) Koehler J, Brandl FP, Goepferich AM. Hydrogel wound dressings for bioactive treatment of acute and chronic wounds. European Polymer Journal. 2018 Mar 1; 100:1-1.
31) Popescu I, Turtoi M, Suflet DM, Dinu MV, Darie-Nita RN, Anghelache M, Calin M, Constantin M. Alginate/poloxamer hydrogel obtained by thiol-acrylate photopolymerization for the alleviation of the inflammatory response of human keratinocytes. International Journal of Biological Macromolecules. 2021 Jun 1; 180:418-31.
32) Adelnia H, Ensandoost R, Moonshi SS, Gavgani JN, Vasafi EI, Ta HT. Freeze/thawed polyvinyl alcohol hydrogels: Present, past and future. European Polymer Journal. 2022 Feb 5; 164:110974.
33) Lv W, Xu D. Docosahexaenoic acid delivery systems, bioavailability, functionality, and applications: A review. Foods. 2022 Sep 2;11(17):2685.
34) Hashimoto M, Hossain S, Al Mamun A, Matsuzaki K, Arai H. Docosahexaenoic acid: one molecule diverse functions. Critical reviews in biotechnology. 2017 Jul 4;37(5):579-97.