PREPARATION OF CELLULOSE-BASED HYDROGELS AND ITS APPLICATIONS: ‘A REVIEW’

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CANDIDATE'S DECLARATION

I, Vipin (2K23/MSCCHE/70), student of M.Sc. Chemistry hereby certifies that the work which is being presented in the dissertation entitled Preparation of cellulose-based hydrogels and its Applications: 'A Review' In partial fulfilment of the requirements for the award of the Degree of Master of Science, submitted to the Department of Applied Chemistry, Delhi Technological University, is an authentic record of our work carried out under the supervision of Prof. Archna Rani.

We have not submitted the matter presented in the dissertation for the award of any other degree of this or any other Institute.

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CERTIFICATE

I hereby certify that the dissertation titled Preparation of cellulose-based hydrogels and its Applications: ‘A Review’, which is submitted by Vipin (2K23/MSCCHE/70) to the Department of Applied Chemistry, Delhi Technological University, Delhi, in partial fulfillment of the requirements for the award of Master of Science. This dissertation embodies results of original work, and studies are carried out by the student; the contents of this dissertation do not form the basis for the award of any other degree to the candidates or anybody else from this or any other University/Institution.

Place: Delhi **PROF. ARCHNA RANI**

Date: 30th May 2025 **SUPERVISOR**

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Table 1: Comparative Overview of Cellulose Derivatives

LIST OF ABBREVIATIONS

- MC: Methyl cellulose
- CMC: Carboxymethyl cellulose
- HEC: Hydroxyethyl cellulose
- HPC: Hydroxypropyl cellulose
- 3D: 3-Dimensional
- PVA: Polyvinyl Alcohol
- HEC/PANI-PPy: Hydroxyethyl Cellulose Grafted with Copolymer of Polyaniline and Poly-pyrrole
- DS: Degree of Substitution
- API: Active Pharmaceutical Ingredients
- FTIR: Fourier Transform Infrared Spectroscopy
- FIG: Figure
- LCST: Lower Critical Solution Temperature
- ECH: Epichlorohydrin
- SDG: Sustainable Development Goals

ABSTRACT

Cellulose-based hydrogels have become a crucial category of biopolymeric materials owing to their plentiful availability, compatibility with biological systems, and eco-friendly characteristics. This review presents an in-depth analysis of the synthesis, functionalization, and wide-ranging applications of hydrogels derived from cellulose and its primary derivatives—namely carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), and methylcellulose (MC). The article highlights important preparation methods, including both physical and chemical crosslinking, techniques for polymer dissolution, and smart gelation processes, emphasizing how these factors affect the mechanical, swelling, and responsive properties of the resulting hydrogels. It additionally examines their essential functions in various areas such as drug delivery, wound care, tissue engineering, environmental cleanup, agriculture, and food preservation. By incorporating recent developments in formulation methods and multifunctional composite systems, this review highlights the transformative capabilities of cellulose-based hydrogels in the creation of sustainable materials for the future. The aim is to connect materials science with biomedical engineering by investigating how natural polymers can be tailored for high-performance uses, while tackling the persistent issues of mechanical stability, scalability, and responsiveness to stimuli.

CHAPTER 1: INTRODUCTION AND LITERATURE SURVEY

Cellulose-based hydrogels are a significant category of biopolymeric materials that are increasingly being recognized for their renewable source, eco-friendliness, and exceptional compatibility with biological systems. These hydrogels are derived from cellulose, which is the most plentiful organic polymer found on Earth, and they exhibit several beneficial properties such as non-toxicity, biodegradability, and adjustable physicochemical attributes. Although cellulose is naturally insoluble in water, it can be chemically modified to produce derivatives like carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), and methylcellulose (MC), each of which provides distinct solubility and gel-forming characteristics.((Kabir et al., 2018)

This review highlights the various preparation methods for cellulose-based hydrogels, including physical crosslinking, chemical crosslinking, and polymer dissolution techniques. It further explains how these methods of preparation affect hydrogel properties such as swelling capacity, mechanical strength, and responsiveness to environmental triggers like pH and temperature. The intelligent behaviour of these materials—such as reversible gelation and targeted drug delivery—renders them suitable for a diverse array of applications.

Important application domains encompass biomedical areas, such as drug delivery mechanisms, wound dressing solutions, and tissue engineering, alongside environmental applications like the treatment of wastewater and agricultural practices for moisture retention and regulated agrochemical discharge. This review seeks to connect foundational material science with engineering applications by showcasing how cellulose-derived hydrogels can be tailored to meet particular societal and industrial needs.(Hu et al., 2021)

Over the last twenty years, significant research has focused on the development of cellulose- derived hydrogels for applications in biomedicine, agriculture, environmental cleanup, and food preservation. CMC, known for being anionic and highly soluble in water, has been extensively utilized in wound dressings, drug delivery systems, and 3D bio-printing, particularly because of its ability to swell in response to pH changes and its straightforward chemical modification. Investigations have shown that CMC hydrogels, particularly when combined with PVA or nanoparticles, demonstrate remarkable mechanical properties and therapeutic effectiveness.((Sabbagh et al., 2019)

In a similar vein, methylcellulose (MC) is well-regarded for its temperature-responsive sol-gel transition characteristics, making it suitable for injectable drug delivery formulations and tissue regeneration applications

Hydroxy-ethyl cellulose (HEC), characterised by its non-ionic properties and stable rheological behaviour across a broad pH spectrum, has found applications in wound healing, cosmetics, and bio-sensing. HEC-based hydrogels that incorporate Aloe vera and silver nanoparticles, for instance, have demonstrated significant antibacterial effects and facilitated wound healing.

Hydroxy-propyl cellulose (HPC) is notable for its amphiphilic composition, solubility in both water and organic solvents, and thermoplastic properties. Recent developments have enabled its application in 3D printing, environmental remediation, and neural tissue engineering, often in conjunction with graphene oxide or other nanomaterials.

Together, these studies underscore the adaptability and potential for engineering cellulose-based hydrogels. Nonetheless, challenges like low mechanical strength in purely physical gels, variability in natural source batches, and difficulties in scaling production persist. Future initiatives aim to develop multi-functional, stimuli-responsive, and composite hydrogel systems that can bridge the gap between laboratory research and practical applications.

2. CHAPTER 2: CELLULOSE AND ITS DERIVATIVES

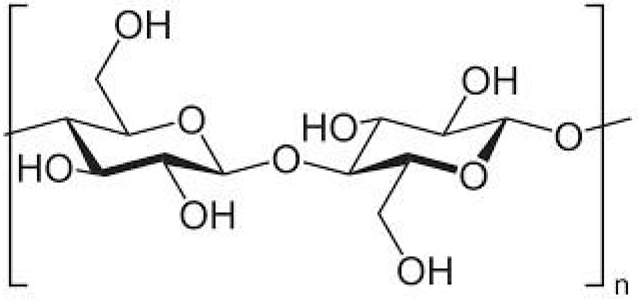
2.1 Cellulose:-

Cellulose is a linear polysaccharide with a high molecular weight, made up of β-Dglucopyranose units that are connected through β(1→4) glycosidic bonds. The native form of cellulose has a semi-crystalline structure, resulting from the intense hydrogen bonding between hydroxyl groups and the van der Waals forces between cellulose chains. This arrangement at the molecular level leads to its insolubility in water and most organic solvents, which limits its direct application in various uses, particularly in hydrogel formation**.(Fig.1)**Chemical modifications that focus on the plentiful hydroxyl groups in the cellulose structure facilitate the transformation of cellulose into polymers that are soluble in water or capable of swelling. These modified versions demonstrate changes in hydrogen bonding, crystallinity, and solubility, allowing them to create hydrogels via physical or chemical crosslinking methods.

Cellulose, the main component of plant cell walls, is a naturally occurring water-attracting polymer that contributes to the structural integrity of cells. Consequently, cellulose is arguably the most abundant organic material found on Earth. It has a high molecular weight, notable crystallinity, and is insoluble in water. The oil palm fronds (OPFs) consist of 58% cellulose, 24% hemicelluloses, 5% lignin, 8% extractives, and 5% ash. The cellulose content in OPF is greater than that in other byproducts (such as leaves and empty fruit bunches) of oil palm trees.[(Rasila et al., 2017)

The dissolution of cellulose is hindered by certain limitations. Water and most organic solvents are known to have minimal effectiveness in breaking down cellulose. Nevertheless, due to their accessibility and straightforward application, researchers often utilize various solvent solutions for dissolving cellulose, including ionic liquids (ILs), NaOH/urea, and NaOH/thiourea. Ionic liquids are intricate and can be difficult to handle. The NaOH/urea solvent system is the most commonly used, as it is simple to prepare, cost-effective, practical, and can enhance the rate of cellulose dissolution even at lower temperatures.[(Piltonen et al., 2016).

Four commonly utilized cellulose derivatives for creating hydrogels are carboxymethyl cellulose (CMC), hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), and hydroxyethyl cellulose (HEC). Each derivative has a distinct substitution pattern and functional groups that affect its physicochemical properties, swelling behaviour, gelation attributes, and interactions with other components of the hydrogel.



Structure of cellulose (**Fig.1)**(Nishiyama et al., 2002)

2.2 Cellulose Derivatives:-

While cellulose is an excellent raw material, its applications are limited due to the challenges associated with its decomposition. Another approach to expand its uses is by transforming it into various derivatives through chemical reactions. Cellulose's unique ability to form hydrogen bonds allows hydrogels to retain their integrity when crosslinking agents are applied.

The four derivatives of cellulose are:--

1. Methylcellulose (MC)

2. Hydroxyethyl cellulose (HEC)

3. Carboxymethyl cellulose (CMC)

4. Hydroxypropyl cellulose (HPC)

2.2.1 Methylcellulose (MC) :-

Methylcellulose (MC) is a cellulose derivative that has been extensively researched and has gained significant interest in hydrogel development due to its distinctive physicochemical and biological characteristics. It is created through the methylation of cellulose, during which the hydroxyl groups (-OH) on the anhydro glucose units are replaced with methoxy groups (OCH_3). This alteration confers water solubility and thermo-responsive properties on the polymer, distinguishing it from both native cellulose and other cellulose ethers. The degree of substitution (DS), generally ranging from 1.3 to 2.6, is crucial in influencing the solubility, gelation, and rheological properties of MC. Higher DS values correlate with increased hydrophobicity and enhanced gel-forming ability in aqueous media (Klemm et al., 2005).

This gelation process that can be reversed is beneficial for biomedical uses, especially in injectable formats, as the substance can be delivered in liquid form and then transition to a gel in the body at normal temperature. (Boateng et al., 2008)

The rheological properties of MC are essential for its role in hydrogel systems. MC displays shear-thinning behaviour, meaning its viscosity reduces as shear rate increases. This pseudoplastic behaviour enhances its ability to be injected and used in formulations that necessitate delivery through narrow-gauge needles.(Pakulska et al., 2015)

In the field of drug delivery, hydrogels based on MC have shown remarkable potential. These hydrogels are capable of encapsulating various therapeutic agents and releasing them in a time-controlled manner. For instance,(Kuo et al., 2025) Created a thermos-responsive hydrogel by combining MC with hyaluronic acid (HA) to deliver mesalamine for ulcerative colitis treatment. This formulation exhibited excellent mucoadhesive characteristics and provided prolonged drug release, which led to improved therapeutic results in preclinical research. In a similar vein,(Pakulska et al., 2015)developed hybrid crosslinked MC hydrogels for targeted protein delivery. Their approach utilized a combination of physical and chemical crosslinking to improve mechanical strength and regulate the release rates of embedded proteins, including growth factors and enzymes.

On the other hand, chemical crosslinking involves the formation of covalent bonds—often facilitated by agents like glutaraldehyde—resulting in hydrogels that possess greater mechanical strength but may have decreased biocompatibility (Bonetti et al., 2023). In contrast, hybrid crosslinking merges the advantages of both methods, achieving a balance between injectability and mechanical strength. These dual crosslinked MC systems have demonstrated predictable swelling, enhanced durability, and adjustable drug release profiles (Pakulska et al., 2015).

To sum up, methylcellulose is a biocompatible, thermo-responsive cellulose derivative with significant potential for use in biomedical hydrogels. Its distinctive physicochemical characteristics, such as the sol-gel transition occurring at physiological temperatures, shear-thinning viscosity, and chemical adaptability, render it applicable to a wide range of uses, including drug delivery, tissue engineering, and wound healing. Ongoing advancements in crosslinking methods and composite formulations are anticipated to further expand the applications and usefulness of MC-based hydrogels in clinical environments.

2.2.2. Carboxymethyl cellulose (CMC):-

Carboxymethylcellulose (CMC) is a well-known anionic derivative of cellulose that has attracted considerable interest in the biomedical sector due to its remarkable biocompatibility, biodegradability, hydrophilicity, and potential for chemical modification.**(Fig.3)** CMC is produced through a carboxymethylation process in which cellulose reacts with monochloroacetic acid in an alkaline environment, usually involving sodium hydroxide, resulting in the replacement of hydroxyl groups in cellulose with carboxymethyl groups (–CH_2–COOH).**(Fig.2)** This alteration significantly improves the water solubility of cellulose, a characteristic that native cellulose naturally lacks because of its high crystallinity and strong intra- and inter-molecular hydrogen bonds (W. ; Zhang et al., 2022). The degree of substitution (DS), which is defined as the average quantity of substituted hydroxyl groups for each anhydroglucose unit, is crucial in influencing the physicochemical and functional characteristics of CMC. A higher DS typically leads to greater water solubility, viscosity, and reactivity, which enhances its versatility in the formulation of hydrogels.

The molecular architecture of CMC gives it amphiphilic characteristics, with the hydrophilic carboxymethyl groups providing solubility in water, while the hydrophobic cellulose backbone contributes to its mechanical strength and stability. The interplay of these interactions is essential for generating hydrogels with adjustable properties. Additionally, the viscosity and gelation characteristics of CMC are significantly affected by its molecular weight and degree of substitution (DS), with higher molecular weights and appropriate substitution levels resulting in more robust and elastic hydrogels (Capanema et al., 2018). Furthermore, CMC demonstrates pH-sensitive properties due to its ionizable carboxyl groups, which expand in alkaline conditions and contract in acidic environments. This pH-responsive swelling behaviour is especially beneficial for drug delivery systems that require targeted release at specific sites.

Hydrogels made from carboxymethyl cellulose (CMC) can be produced through either physical or chemical crosslinking techniques. Physical crosslinking generally relies on ionic interactions, hydrogen bonds, or thermal gelation, resulting in hydrogels that are often reversible and biocompatible. However, CMC hydrogels created through physical crosslinking frequently fall short in mechanical strength for load-bearing biomedical purposes. As a result, chemical crosslinking is frequently utilized to enhance the mechanical properties, stability, and functional adaptability of CMC hydrogels**.(Fig.2)** Various crosslinking agents, such as citric acid, glutaraldehyde, genipin, and polyethylene glycol diglycidyl ether (PEGDGE), have been extensively applied to establish durable three-dimensional polymer networks (Zhang et al., 2022).

For instance, (Capanema et al., 2018) developed CMC–PEG hydrogels using citric acid as an eco-friendly and biocompatible crosslinker, yielding hydrogels characterized by outstanding water retention, mechanical strength, and cytocompatibility, which make them suitable for wound dressing applications.

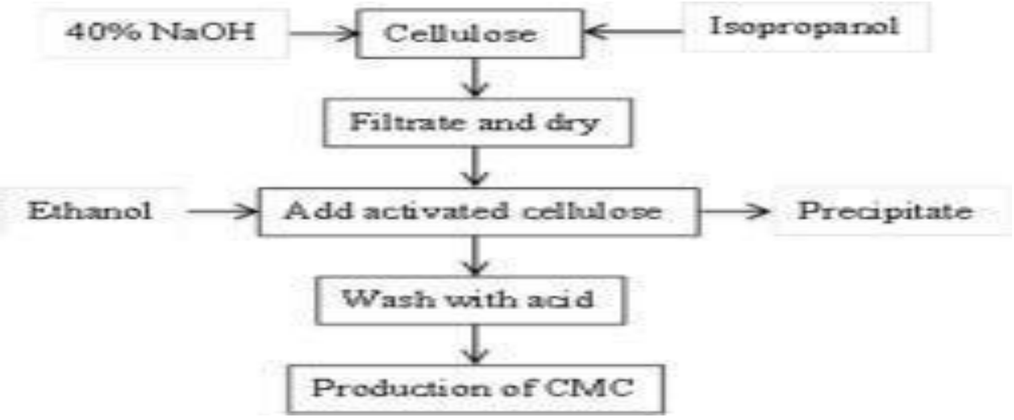
One of the most thoroughly researched uses of CMC-based hydrogels is in the field of wound healing. Chronic wounds, including diabetic ulcers, burns, and surgical incisions, necessitate dressings that preserve a moist environment, enable gas exchange, and absorb excess exudate while remaining non-toxic and encouraging tissue regeneration. CMC-based hydrogels meet all these requirements and provide additional advantages such as ease of application, self-healing capabilities, and compatibility with bioactive substances like antibiotics and growth factors. In a recent study by (Mansur et al., 2023)A bio-adhesion-enhanced hybrid hydrogel composed of CMC and polyvinyl alcohol (PVA) was developed, which was functionalized with boronic acid. This hydrogel exhibited remarkable adhesion, strong mechanical properties, and improved healing in models of chronic wounds, showcasing the versatility and effectiveness of CMC composites in regenerative medicine. The inclusion of boronic acid groups allowed for reversible covalent interactions with diol-containing biomolecules on tissue surfaces, significantly improving the strength of adhesion while maintaining biocompatibility.

CMC serves as an excellent basis for creating drug delivery systems due to its significant water content, adjustable porosity, and pH-responsive swelling properties. These hydrogels can trap a range of drug molecules, including small antibiotics and larger biologics, facilitating their release in a steady and controlled fashion. This is especially beneficial for localized treatments where extended drug action is essential. The addition of nanoparticles into CMC hydrogels has enhanced their capabilities even further. For instance, Capanema et al., 2019) developed a hybrid hydrogel system that combined CMC, silver nanoparticles, and the anticancer agent doxorubicin. This multifunctional hydrogel demonstrated strong antibacterial and anticancer effects against melanoma skin cancer cells. The presence of silver nanoparticles provided bactericidal effects, while the hydrogel matrix enabled a prolonged release of doxorubicin, showcasing the potential of CMC hydrogels for dual-function therapeutic applications.

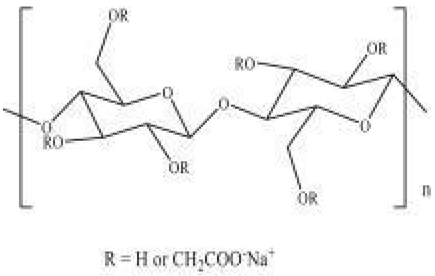
Despite its many benefits, some shortcomings of CMC-based hydrogels must be addressed. Although their mechanical strength is sufficient for applications involving soft tissues, it falls short for load-bearing uses like bone regeneration. Additionally, CMC is susceptible to hydrolytic degradation when exposed to extreme pH levels, which can jeopardize its stability in specific environments. To tackle these issues, approaches such as integrating reinforcing agents like nanocellulose, carbon nanotubes, or graphene oxide have been investigated. These additives not only improve the mechanical properties but also provide extra functionalities, including electrical conductivity, antibacterial properties, and enhanced cell interaction (W. ; Zhang et al., 2022)

Looking ahead, the creation of stimuli-responsive CMC hydrogels is an increasingly notable field of research. These hydrogels can adapt to various environmental factors such as temperature, pH, ionic strength, and light, allowing for dynamic manipulation of their physical properties and drug release mechanisms. Intelligent CMC hydrogels offer potential uses in on-demand medication delivery, adaptable wound dressings, and diagnostic applications. For instance, a pH-sensitive CMC hydrogel containing insulin has been suggested for oral administration, where it safeguards the drug in the acidic environment of the stomach and releases it at the neutral pH level of the intestine(Tudoroiu et al., 2021). Such advancements present exciting possibilities for the creation of personalized and responsive therapeutic systems.

In summary, carboxymethylcellulose is distinguished among cellulose derivatives due to its remarkable water solubility, chemical properties, and compatibility with biological systems. These characteristics position it as a prime choice for forming hydrogels in various fields, such as wound care, drug delivery systems, tissue engineering, environmental cleanup, agricultural practices, and food preservation. By modifying their chemical composition, altering crosslinking methods, and developing composite formulations, CMC-based hydrogels can be tailored to demonstrate specific mechanical, biological, and responsive properties suited for different applications. Future studies should aim to improve its mechanical strength, investigate innovative crosslinking techniques, and create multifunctional hybrid systems to maximize the potential of CMC in advancements in biomedical and industrial sectors.



Production of carboxymethyl cellulose (**Fig.2)**(Zainal et al., 2021)



Structure of carboxymethyl cellulose (**Fig.3)**(Zainal et al., 2021)

2.2.3 Hydroxyethyl cellulose (HEC):-

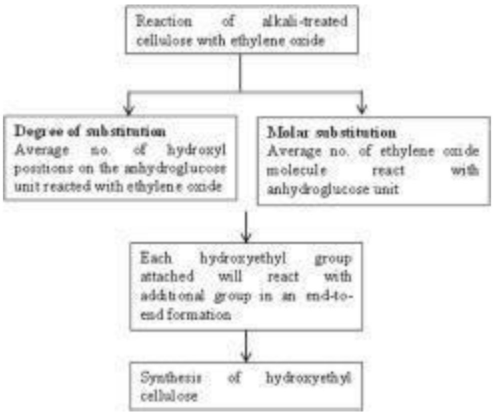
Hydroxyethylcellulose (HEC) is a non-ionic cellulose derivative that is soluble in water, playing a crucial role in the creation of modern hydrogel systems due to its outstanding physicochemical and rheological characteristics. HEC is derived from cellulose through the introduction of hydroxyethyl groups ($-CH_2CH_2OH$) into the anhydroglucose units of the cellulose backbone by reacting with ethylene oxide in alkaline conditions. This etherification process leads to a significant decrease in the crystallinity of native cellulose, enhancing its solubility in water and flexibility while maintaining its biocompatibility and biodegradability

(Alven & Aderibigbe, 2020).**(Fig.5)** Because of these benefits, HEC is widely used in pharmaceutical, cosmetic, food, and industrial sectors, with a growing interest in its application within hydrogel systems for biomedical purposes.

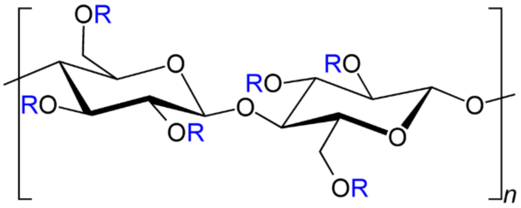
Chemically Modified HEC for Enhanced Muco-adhesion. The synthesis and properties of this are that the mucoadhesive qualities of native HEC are weak. By grafting unsaturated groups, such as methacryloyl, maleimide, acryloyl, and divinyl sulfone, onto its polymeric backbone, HEC can be chemically modified to overcome this restriction and allow for extended contact with mucosal surfaces. In ambient settings, this derivatisation frequently occurs using a simple one-pot synthesis approach, which makes the process scalable and effective**.(Fig.4)** Reactive sites for interaction with biological tissues are provided by the unsaturated groups that have been introduced and have properties. These compounds' main improved characteristic is noticeably better mucoadhesion. This is accomplished by a Michael addition reaction that creates covalent connections between the modified polymer's electronegative unsaturated end groups and the less electronegative components of mucin glycoproteins, especially cysteine residues. The derivatives mostly preserve the inherent water solubility and non-ionic character of native HEC in spite of these changes, which is essential for preserving compatibility with a variety of active pharmaceutical ingredients (APIs), including charged drug molecules.(CentAUR, n.d.)

Hydroxyethyl Cellulose-Acrylamide Graft Polymer-Bentonite Nanocomposites, A hydroxyethyl cellulose-acrylamide graft polymer is created for this derivative, usually via a microwave-assisted grafting polymerisation process. Following that, this graft polymer is added to bentonite clay composites. The polymer effectively intercalates between the layers and sticks to the bentonite surface, creating a stable nanocomposite, according to characterisation investigations using FTIR, X-ray diffraction (XRD), and scanning electron microscopy (SEM) and its having properties is In comparison to unmodified HEC, the grafting of acrylamide onto HEC greatly lengthens the polymer's molecular chain, improving its thermal stability and resilience to high temperatures. The application limits of native HEC alone are normally approximately 110 °C, but these graft polymers show better temperature tolerance. Additionally, the nanocomposites show excellent rheological characteristics and the ability to reduce fluid loss. For example, the composite can meet key characteristics for drilling fluids, such as a yield point/plastic viscosity ratio greater than 0.6 and a minimal fluid loss of only 9.3 mL. (Liao et al., 2022)

Hydroxyethyl Cellulose Grafted with Copolymer of Polyaniline and Poly-pyrrole Bio-composite (HEC/PANI-PPy), Grafting a copolymer of polyaniline (PANI) and poly-pyrrole (PPy) onto the HEC polymer creates this bio-composite. An oxidant, such as ammonium persulfate (APS) solution, is gradually added while the HEC solution is mixed with a monomer solution (aniline and pyrrole) and stirred continuously for several hours at room temperature. After that, the HEC/PANI-PPy bio-composite is separated, cleaned, and allowed to dry and its properties is Excellent water solubility, biodegradability, and chemical stability are displayed by the HEC/PANI-PPy bio-composite. Crucially, it exhibits extremely effective adsorption properties for hazardous organic pigments. Its efficacy in eliminating these prevalent textile contaminants is demonstrated by experiments that have documented adsorption capabilities of 30.06 mg/g for Rhodamine B (RhB) and 29.3 mg/g for Methyl Orange (MO). Techniques including FTIR spectroscopy, scanning electron microscopy (SEM) for morphology, X-ray diffraction (XRD) for crystalline structure, and Brunauer-Emmett-Teller (BET) analysis for surface area are used to demonstrate the effective grafting and material properties.(Bajaber et al., 2022)



Synthesis of hydroxyethyl cellulose (Fig.4)(Zainal et al., 2021)



Structure of hydroxyethyl cellulose (Fig.5)(File:Hydroxyethyl Cellulose)

2.2.4 Hydroxypropyl cellulose (HPC):-

Hydroxypropylcellulose (HPC) is a non-ionic ether of cellulose that has attracted significant interest in recent years due to its solubility in water, thermoplastic properties, ability to form films, and compatibility with biological systems.**(Fig.7)** It is produced by partially replacing the hydroxyl groups in cellulose with hydroxypropyl groups through etherification with propylene oxide in an alkaline environment.**(Fig.6)** This modification creates both hydrophilic and hydrophobic segments within the cellulose chain, which markedly changes the solubility and thermal behaviour of the polymer (Chen et al., 2017)HPC sets itself apart from other cellulose derivatives, like carboxymethylcellulose (CMC) and hydroxyethylcellulose (HEC), because it is soluble in both water and select organic solvents. This dual solubility renders HPC an important excipient in pharmaceuticals and a functional element in hydrogel formulations for a wide array of biomedical and non-biomedical uses(Rowe, R. C., Sheskey(2009).) .

Unlike ionic cellulose derivatives, HPC is not prone to degradation from pH changes and remains stable across a wide range of pH levels (pH 3–10), which makes it suitable for biomedical applications that require maintenance of physiological pH. Additionally, HPC’s thermal gelation properties—where the polymer experiences a reversible sol–gel transition at body temperature—have driven investigations into injectable, in situ-forming hydrogels for drug delivery and tissue engineering (Gong et al., 2024).

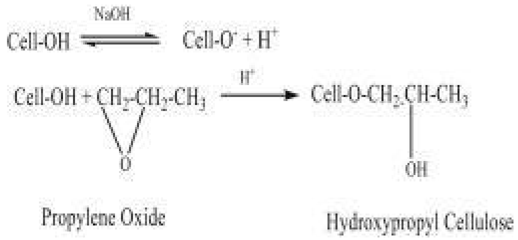
Hydrogels that utilize HPC can be produced through either physical or chemical crosslinking techniques. Physical hydrogels depend on mechanisms such as hydrogen bonding, hydrophobic interactions, or gelation induced by temperature variations. For instance, an aqueous HPC solution can generate a reversible gel when the temperature exceeds its lower critical solution temperature (LCST) because of enhanced hydrophobic interactions among the polymer chains. This thermos-responsive characteristic has been applied in developing hydrogels that respond to temperature changes for localized and prolonged drug release (Filho et al., 2023).

Propylene oxide serves as an alternative for cellulose by forming ether connections with the three reactive hydroxyl groups found in the cellulose monomer unit. The production of hydrogel from hydroxypropyl cellulose (HPC) using γ-radiation has enhanced both the white sensitivity and turbidity.(Ogawa et al., 2014)

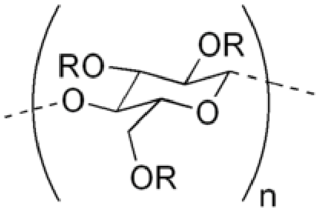
Beyond the biomedical sector, HPC-based hydrogels find widespread applications in the food and pharmaceutical industries. Within pharmaceuticals, HPC acts as a binder, a film-coating agent, and a matrix creator in formulations designed for controlled release. Its capacity to absorb water and create thick barriers in gastrointestinal fluids makes it a favoured excipient for (P. Chen et al., 2017b)prolonged drug release. In the food sector, HPC is utilized as a thickening agent, emulsifier, and stabilizing agent in sauces, dairy products, and beverages because of its solubility in cold water and its resistance to degradation in acidic conditions (Rowe, R. C., Sheskey(2009).). Furthermore, its GRAS (Generally Recognized As Safe) designation by the FDA highlights its safety for use in consumable products.

A study indicates that the reaction involving alkynyl-HPC leads to significant water absorption and results in thicker pore walls, while incorporating metals with HPC has proven effective in dye removal from aqueous solutions. The alkynyl group, characterized by a carbon–carbon triple bond, is easily decomposed and can form additional hydrogen bonds with HPC, which helps preserve the network structure of hydrogels. HPC has been researched as a promising candidate for retaining sufficient moisture for wound healing and could serve as an innovative dressing material in medical uses. Conversely, because of its viscous characteristics, HPC is commonly utilized as a thickening agent, emulsifier, and binder in solid pharmaceutical formulations (Miao et al., 2016; Yamashita et al., 2014). The attributes exhibited by HPC hydrogels indicate that this cellulose derivative is simple to formulate into hydrogels. By incorporating crosslinking agents and other substances such as polymers or through radiation methods, the properties of HPC hydrogels can be enhanced to make them more suitable and exceptional for medical and pharmaceutical uses.

In conclusion, Hydroxypropylcellulose (HPC) is a versatile cellulose derivative that offers a unique combination of thermoresponsiveness, solubility, biocompatibility, and film-forming ability, making it a compelling candidate for hydrogel development. Its applications span wound healing, drug delivery, tissue engineering, 3D bioprinting, pharmaceuticals, food, and environmental remediation. Ongoing advancements in composite materials, smart hydrogel design, and bio-fabrication are poised to unlock the full potential of HPC in biomedical science and industrial technologies. As the demand for sustainable, responsive, and patient-specific materials grows, HPC-based hydrogels are expected to play an increasingly central role in the next-generation therapeutic platform.



Reaction of hydroxypropyl cellulose (**Fig.6)**(Zainal et al., 2021)



$R = H$ or $CH_2CH(OH)CH_3$

Structure of hydroxypropyl cellulose (**Fig.7)**(Barty-King et al., 2021)

2.3 Comparative Overview of Cellulose Derivatives:-

Each cellulose derivative exhibits distinct physicochemical properties influenced by its functional groups and substitution patterns. These differences affect solubility, rheological behaviour, gelling mechanism, and suitability for specific applications.

Table No. 1:- Comparative Overview of Cellulose Derivatives(Y. Zhang et al., 2025)

Property	**CMC**	**HPMC**	**MC**	**HEC**
Ionic Character	Anionic	Non ionic	Non ionic	Non ionic
Solubility	Cold & hot water	Cold water only	Cold water only	Cold & hot water
Gelation Mechanism	Ionic/covalent	Thermal	Thermal	Physical entanglement
Main Functional Groups	$–CH_2COOH$	$–OCH_3$, $–CH_2CHOHCH_3$	$–OCH_3$	$–CH_2CH_2OH$
Common Applications	Drug delivery , wound healing, environmental	Ophthalmic delivery, oral drugs, tissue scaffolds	Injectable gels, bioprinting	Topicals, agriculture, cosmetics

CHAPTER 3: PREPARATION OF HYDROGEL

3.1 PREPARATION TECHNIQUES USED FOR THE PREPARATION OF HYDROGEL

Cellulose derivative-based hydrogels have attracted considerable interest in both research and industry because of their compatibility with biological systems, safety, and adjustable physical and chemical characteristics. For optimal functionality in uses such as drug delivery and tissue engineering, it is essential to comprehend and meticulously manage the processes involved in the creation and analysis of these hydrogels. This chapter presents different methods for preparing these materials for cellulose derivative-based hydrogels, with a focus on carboxymethylcellulose (CMC), hydroxyethylcellulose (HEC), and hydroxypropylcellulose (HPC).

3.2 POLYMER DISSOLUTION TECHNIQUE:-

The dissolution of polymers is a crucial step in creating hydrogels, especially those made from cellulose and its derivatives. This process lays the groundwork for the necessary crosslinking, molding, and shaping steps that follow. The behaviour of cellulose derivatives, including carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), and hydroxypropyl cellulose (HPC), is pivotal in determining the homogeneity, rheology, and overall performance of the resulting hydrogel network. Therefore, comprehending the mechanisms and factors that affect the dissolution of these polymers is vital for customizing hydrogel systems for use in biomedical, pharmaceutical, agricultural, and industrial fields.

3.2.1 BASIC PRINCIPLES OF POLYMER DISSOLUTION:-

The process of polymer dissolution is a complex physico-chemical phenomenon that entails the breakdown of the solid polymer structure into solvated polymer chains distributed within a solvent. Unlike small molecular-weight solutes, polymers do not dissolve right away. Typically, this process can be categorized into three stages: solvent infiltration into the polymer matrix, swelling of the polymer, and the disentanglement or diffusion of polymer chains into the solvent (Flory, 1953). These stages are influenced by a mix of polymer-solvent interactions, temperature, the molecular weight of the polymer, and the degree of substitution (DS) for cellulose derivatives.

The interactions between solvents and polymers play a significant role in whether a polymer can dissolve. An effective solvent should have a solubility parameter that is similar to that of the polymer, which ensures favourable thermodynamic compatibility. For hydrophilic cellulose derivatives, water is typically the preferred solvent due to the numerous hydroxyl, carboxymethyl, or hydroxyethyl groups that facilitate hydrogen bonding and ionic interactions (Sannino et al., 2009a). The strength and concentration of these interactions dictate if the polymer will swell or fully dissolve.

3.2.2 DISSOLUTION OF SPECIFIC CELLULOSE DERIVATIVES:-

1) Carboxymethyl Cellulose (CMC):-

CMC is a carboxymethylated cellulose derivative that is anionic and soluble in water, featuring carboxymethyl groups ($-CH_2-COOH$) distributed along its cellulose structure. The degree of substitution (typically ranging from 0.4 to 1.2) plays a crucial role in influencing its solubility and gelation characteristics. Increased DS values elevate the number of hydrophilic sites, thereby improving water solubility and absorption(Kulkarni & Sa, 2008). CMC easily dissolves in water at room temperature, creating solutions that are clear to slightly cloudy and viscous. The dissolution process begins with the rapid hydration of the carboxymethyl groups, followed by the widening and separation of polymer chains due to electrostatic repulsion among the negatively charged carboxylate ions (Zhao et al., 2015).

The process of dissolution can be improved by stirring and adjusting the pH. CMC shows the best solubility in neutral to slightly alkaline conditions because the carboxyl groups become deprotonated, enhancing electrostatic repulsion and the mobility of the chains (Peppas et al., 2000). Conversely, in very acidic conditions, protonation can decrease solubility and result in aggregation or gel formation.

2)Hydroxyethyl Cellulose (HEC):-

HEC is a cellulose ether that is non-ionic, distinguished by its hydroxyethyl groups (CH_2CH_2OH) which improve its solubility in both cold and hot water. At lower concentrations, it creates colloidal dispersions, while at higher concentrations, it forms very viscous gels. The process of dissolving HEC consists of several stages, including water penetration, chain hydration, and molecular dispersion (Thakur et al., 2014).

HEC necessitates specific dissolution conditions to prevent the formation of lumps, as its high surface activity and quick hydration of the outer layer can lead to issues. The suggested method is to mix HEC in cold water while stirring at high speeds, and then gradually heat the mixture to ensure it fully dissolves. This strategy helps to avoid early gel formation that could entrap undissolved particles(Nguyen & Lee, 2010).

3)Hydroxypropyl Cellulose (HPC):-

HPC is a non-ionic cellulose ether distinguished by its hydroxypropyl groups ($CH_2CHOHCH_3$) and is known for its unique thermoresponsive characteristics. This compound is soluble in cold water and has a lower critical solution temperature (LCST) around 40–45 °C, where it begins to precipitate from the solution. Below the LCST, the HPC molecules are well-solvated due to interactions like hydrogen bonding and hydrophilicity. When the temperature rises, dehydration of the hydroxypropyl groups occurs, along with enhanced hydrophobic interactions among the polymer chains, leading to gel formation or precipitation.

The solubility of HPC is affected by its molecular weight and the extent of hydroxypropyl substitution. An increased substitution enhances solubility but reduces the LCST, an important factor for uses that require temperature-sensitive properties, such as injectable hydrogels (Jiang et al., 2019). Generally, HPC is mixed with water while stirring at room temperature and allowed to hydrate overnight for consistent dissolution.

3.2.3 FACTORS AFFECTING POLYMER DISSOLUTION:-

- **Molecular Weight:-**

  Polymer molecular weight significantly impacts the dissolution rate and final viscosity of the solution. Higher molecular weight polymers exhibit slower dissolution due to increased entanglement and slower chain diffusion, but they form stronger, more cohesive hydrogels (Hoffman, 2012). For instance, high-viscosity grades of HEC may require extended stirring or heating to dissolve fully.

- **pH and Ionic Strength:-**

  The solubility of polyelectrolytic cellulose derivatives, such as CMC, is influenced by pH levels. Higher alkaline pH levels promote the ionization of carboxyl groups, enhancing chain repulsion and facilitating dissolution. Conversely, the presence of divalent and trivalent cations (like Ca^{2+} and Al^{3+}) can lead to ionic crosslinking, causing precipitation, particularly in CMC-based systems(Sannino et al., 2009b). Consequently, dissolution is typically performed in deionized water to minimize ionic interference.

3.2.4 PRACTICAL CONSIDERATIONS IN POLYMER DISSOLUTION:-

When preparing solutions of cellulose derivatives for hydrogel synthesis, several practical recommendations are adhered to. Initially, the polymer is usually pre-dispersed in a nonsolvent, such as ethanol, to avoid clumping, followed by a gradual incorporation into water. Alternatively, the dry powder can be incrementally added to water that is being stirred vigorously at room temperature. After all the polymer has been included, the solution is stirred continuously for a duration of 1 to 4 hours, which depends on the viscosity and solubility of the mixture. Certain formulations may necessitate overnight hydration at temperatures between 4 and 8 °C to ensure complete dissolution.

In the case of cross-linkable hydrogel systems, the polymer solution commonly serves as the medium for the introduction of the crosslinker. Therefore, it is essential to ensure complete dissolution before crosslinking, as any undissolved particles can introduce defects or cause inhomogeneities in the final gel (Nguyen & Lee, 2010)

3.3 PHYSICAL CROSSLINKING:-

Physical crosslinking refers to a process that does not involve chemical crosslinkers, relying instead on thermodynamic or interactive forces to reinforce the polymer network. These interactions tend to be reversible, enabling the material to display self-healing, stimuli-responsive, and biodegradable characteristics(Peppas et al., 2000). The reversibility of these physical interactions is beneficial for uses such as injectable hydrogels, wound dressings, and drug delivery systems, where in situ gelation or biodegradability is preferred.

In hydrogels made from cellulose derivatives, physical crosslinking occurs due to the plentiful functional groups (–OH, –COOH, $–CH_2CH_2OH$, etc.) present on CMC, HEC, HPC, and other derivatives' chains. These functional groups engage in hydrogen bonding and electrostatic interactions that are crucial for the formation of the network (Sannino et al., 2009a)

3.3.1 FREEZE–THAW CYCLE:

- **Mechanism:-**

  The freeze–thaw method is a well-known technique for physically crosslinking hydrophilic polymers, such as cellulose derivatives. This approach entails subjecting a polymer solution to repeated cycles of freezing and thawing to trigger phase separation and create crystalline regions that serve as physical crosslinking sites (Hennink & Van Nostrum, 2002). When the solution freezes, water forms ice crystals, which compress polymer chains into dense areas where they develop microcrystalline structures. After thawing, water is reabsorbed, but the microcrystals persist, resulting in a gel that is physically crosslinked (S. C. Lee et al., 2013). With each cycle of freeze–thaw, both the quantity and size of crystalline regions grow, which improves the mechanical properties, gelation, and elasticity of the hydrogel. The ideal number of cycles, the freezing temperature, and the time required vary according to the specific polymer used, its concentration, and the intended characteristics of the final hydrogel.

- **Advantages and Limitations:-**
  - Advantages:-
    - No chemical crosslinkers required, reducing cytotoxicity
    - Simple and cost-effective process
    - Enhances crystallinity and mechanical strength
    - Suitable for biomedical and pharmaceutical applications

  - Limitations:-
    - Limited to polymers capable of phase separation or crystallization
    - Requires multiple cycles and extended processing time
    - Hydrogel properties depend heavily on freeze–thaw parameters

3.3.2 Ionic Crosslinking:-

Mechanism:-

Ionic crosslinking refers to the interaction of ionizable functional groups present on polymers with ions that hold an opposite charge. In cellulose derivatives, such as carboxymethyl cellulose (CMC), the $–COO^-$ groups can bond with divalent or trivalent cations like Ca^{2+}, Fe^{3+}, or Al^{3+} to create ionic bridges, which help reinforce the hydrogel structure (Peppas & Narasimhan, 2014)Typically, these crosslinks are reversible and can be disrupted by chelating agents or variations in pH.

The method involves simply combining the polymer solution with the crosslinking ions under normal or mild conditions, making it particularly appealing for applications involving sensitive bioactive materials or cell encapsulation.

3.3.3 Hydrogen Bonding and Entanglement:-

Mechanism:-

Hydrogen bonding occurs when electronegative atoms like oxygen or nitrogen attract hydrogen atoms covalently bonded to other electronegative atoms. In cellulose derivatives, hydroxyl, carboxyl, and ether groups can form extensive hydrogen bonding networks both intra- and inter-molecularly. Physical entanglement, meanwhile, arises when long polymer chains become intertwined, further stabilizing the hydrogel matrix.

These interactions can be enhanced by thermal annealing, solvent casting, or evaporation-induced assembly, leading to the formation of gels without the need for chemical crosslinkers.

3.3.4 Thermoresponsive Gelation:-

Certain cellulose derivatives, such as HPC and MC, demonstrate thermoresponsive characteristics, creating physical gels at higher temperatures due to hydrophobic interactions. These polymers are soluble at cooler temperatures but begin to aggregate as temperatures rise, resulting in reversible gel formation (Li et al., 2024).

For instance, cellulose has a lower critical solution temperature (LCST) that ranges from 40 to 45°C, making it ideal for injectable hydrogels that solidify at body temperature. This attribute is utilized in minimally invasive drug delivery systems and applications in tissue engineering (Ee & Yau Li, 2021).

3.4 CHEMICAL CROSSLINKING:-

Chemical crosslinking is a widely utilized method in the synthesis of hydrogels. It entails creating covalent bonds between polymer chains, which leads to the formation of a stable three-dimensional network capable of holding large quantities of water while preserving its structural integrity. This technique provides improved mechanical strength, adjustable degradation rates, and lasting stability, making it suitable for various biomedical and industrial purposes (Caló & Khutoryanskiy, 2015)

In cellulose derivatives like carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), and hydroxypropyl cellulose (HPC), chemical crosslinking is frequently used to address the drawbacks of physical hydrogels, such as their low mechanical strength and vulnerability to fast dissolution. This chapter offers a comprehensive exploration of chemical crosslinking techniques for hydrogels based on cellulose derivatives, including the most commonly used crosslinking agents, the mechanisms behind gelation, the conditions required for processing, and their applications, along with references to recent scientific research.

3.4.1 Principles of Chemical Crosslinking:-

Chemical crosslinking is a process that utilizes bifunctional or multifunctional agents to create covalent bonds between polymer chains, either via condensation reactions or addition reactions. These crosslinkers can be composed of organic compounds, enzymes, or reactive polymers, all of which can selectively interact with specific functional groups present in the polymer backbone.

In cellulose derivatives, common reactive sites include:

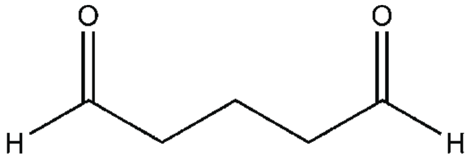
- **Hydroxyl groups** (–OH)
- **Carboxyl groups** (–COOH)
- **Amino groups** (if grafted)

3.4.2 Common Crosslinking Agents Used for Cellulose Derivatives:-

1) Glutaraldehyde (GA):-

Glutaraldehyde is one of the most widely used crosslinkers for cellulose-based hydrogels. It reacts with hydroxyl and amino groups through **Schiff base formation**, producing stable acetal or imine linkages (J. Chen & Park, 2000)The crosslinking process typically occurs under acidic or mildly basic conditions and is influenced by temperature and polymer concentration.**(Fig.8)**

Glutaraldehyde can also be employed as a ligand modification to remove metals instead of hydrogels. As a crosslinking agent, glutaraldehyde is used with chitosan to change the efficiency of ligands, eliminate metal ions, and improve the water absorption of the film.(Igberase et al., 2017) However, residual glutaraldehyde can be cytotoxic, requiring extensive washing or detoxification.

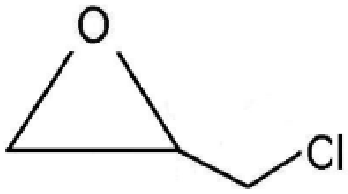


Structure of Glutaraldehyde (Fig.8)(Sehmi et al., 2016)

2) Epichlorohydrin (ECH):-

Epichlorohydrin serves as a popular crosslinking agent for polymers that are rich in hydroxyl groups, such as cellulose derivatives. Hydrogels crosslinked with ECH are commonly utilized in environmental applications, including water treatment and the adsorption of heavy metal ions**.(Fig. 9)** When ECH is added as a crosslinker, the hydrogel network's ability to hold water increases due to the hydrogel's enhanced pore size and formation. Conversely, the use of ECH in the hydrogel production of chitosan improves the capacity for metal sorption and inhibits chitosan dissolution during metal sorption in acidic environments. Consequently, ECH increases the water-uptake capacity of hydrogel by causing phase separation and the creation of a heterogeneous network.(Emami Meybodi et al., 2013)

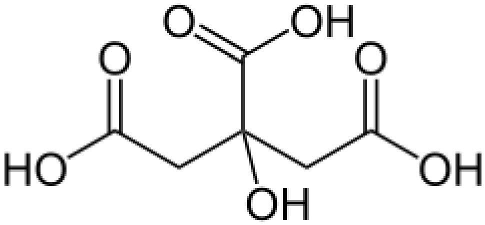
For instance, CMC-ECH hydrogels have shown excellent ion exchange capacity and resistance to chemicals, making them appropriate for use in challenging environments (K. Y. Lee & Mooney, 2012)



Structure of Epichlorohydrin (Fig. 9)(Analysis of Epichlorohydrin)

3)Citric Acid (CA):-

Citric acid, a naturally occurring tricarboxylic acid, functions as a biodegradable crosslinker that interacts with hydroxyl groups through esterification when subjected to heat (Thakur et al., 2013). Its non-toxic characteristics make it well-suited for applications in food packaging and biomedicine. Because it's cheap, nontoxic, hydrophilic, and a naturally occurring organic compound with 3-OH groups that may form a network in the majority of hydrogel preparations, citric acid (CA) has been utilised as a crosslinking agent**.(Fig.10)** It has been demonstrated that Citric acid strengthens hydrogen bonds to increase heat stability and water swelling. Additionally, it contains more binding sites and hydrogen bonds and aids in balancing hydrophilicity.(Gyawali et al., 2010)

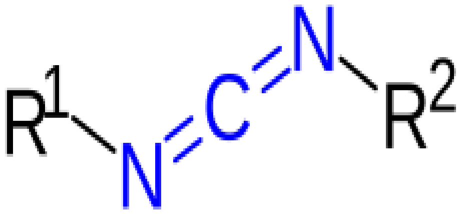


Structure of citric acid (Fig.10)(Favre & Powell, 2014)

4)Carbodiimide (EDC/NHS):-

EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) is a zero-length crosslinker commonly used in conjunction with **NHS (N-Hydroxysuccinimide)** to form **amide bonds** between carboxyl and amine groups**.(Fig.11)** Though cellulose itself lacks amino groups, modification with chitosan or gelatin allows the formation of chemically crosslinked networks (K. Y. Lee & Mooney, 2012).EDC/NHS is particularly useful for creating **bio-**

functional hydrogels for drug delivery and tissue engineering, as the reaction conditions are mild and aqueous.



Structure of Carbodiimide(Fig.11)(McGuire et al., 2012)

CHAPTER 4: APPLICATIONS OF CELLULOSE-BASED HYDROGELS

Hydrogels derived from cellulose derivatives have garnered significant attention in both research and industrial sectors due to their compatibility with biological systems, water-attracting properties, safety, and eco-friendliness. These hydrogels—primarily obtained from cellulose derivatives such as carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcellulose (HPMC), and methylcellulose (MC)—have been extensively studied across various fields, including biomedical, pharmaceutical, agricultural, environmental, and food industries (Cervin et al., 2012; Thakur et al., 2018). This section explores these main areas of application, supported by relevant literature and examples.

4.1 Biomedical Applications: -

Cellulose-derived hydrogels, particularly those altered from carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), and methyl cellulose (MC), are excellent materials for applications such as wound dressings, scaffolds in tissue engineering, and matrices for drug delivery. These hydrogels create a humid environment that promotes healing, shield the wound area from microbial infections, and enhance the exchange of oxygen and nutrients.(Boateng et al., 2008),

It is also used in tissue Engineering and Regenerative Medicine because of its high-water content and three-dimensional polymeric network mimics the extracellular matrix seen in nature, creating an ideal milieu for tissue regeneration, cell proliferation, and differentiation. They serve as scaffolds for a variety of tissues, such as cartilage, bone, and skin.(Tamo, 2024)

It is used for 3D bioprinting because of their printability and biocompatibility. cellulose-based hydrogels—especially nanocellulose-based ones—are being utilised more and more in 3D bioprinting to produce intricate tissue structures and organs.(Wang et al., 2021)

4.2 Agricultural Applications: -

Hydrogels made of cellulose are used in agriculture to increase crop output and conserve water

- **Controlled-release fertilizers and pesticides**

  They can encapsulate and release pesticides and fertilisers gradually, minimising pollution in the environment, enhancing plant uptake of nutrients, and decreasing nutrient loss.(Ahmad et al., 2023)

- **Soil water retention**

  Because hydrogels absorb a lot of water and release it gradually to plant roots, they can greatly enhance soil water retention, particularly in arid or semi-arid locations. This encourages sustainable farming and aids in water conservation.(Tofanica et al., 2024)

- **Soilless culture**

  They can serve as a medium for soilless farming, giving plants the nutrients and moisture they need to grow.(Tofanica et al., 2024)

4.3 Food Industry Applications

Cellulose-based hydrogels are gaining traction in the food industry for various functionalities.

- **Food Packaging**

  Because of their antimicrobial qualities, they are employed in smart food packaging, frequently in conjunction with natural colourants, to monitor food freshness (e.g., pH changes indicating decomposition) and prevent bacterial development. They provide an eco-friendly, non-toxic, and natural substitute for synthetic packaging materials.(Yang et al., 2024)

- **Functional Foods**

  By serving as carriers, they can enhance the stability and bioavailability of active food ingredients and allow for controlled release inside the digestive tract(Nath et al., 2023).

- **Thickeners and Stabilizers:**

  The thickening, gelling, and stabilising properties of cellulose derivatives, which are frequently utilised in hydrogel form, improve the texture and shelf life of a variety of food products.(Nath et al., 2023)

CHAPTER 5: CONCLUSION

The development of hydrogels based on cellulose derivatives has progressed notably in recent years due to the growing global need for sustainable, biocompatible, and multifunctional materials. This thesis has thoroughly examined the structural characteristics, synthesis methods, and extensive applications of hydrogels obtained from cellulose derivatives, including carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropyl methylcellulose (HPMC), and methylcellulose (MC). These hydrogels have shown impressive capabilities across a variety of fields, such as biomedical, pharmaceutical, agricultural, environmental, and food industries.

A key advantage of hydrogels based on cellulose derivatives lies in their availability, renewability, and environmental friendliness. Unlike synthetic polymers sourced from petroleum, cellulose derivatives are derived from natural materials and are naturally biodegradable and non-toxic. Their molecular architecture, which includes functional groups such as hydroxyl, carboxyl, and ether linkages, allows for straightforward modification, chemical crosslinking, and physical gelation, rendering them highly versatile for different design applications.

This thesis investigated a range of hydrogel preparation methods, including polymer dissolution, physical crosslinking (e.g., freeze–thaw cycles, ionic interactions), and chemical crosslinking (e.g., utilizing glutaraldehyde, citric acid, or carbodiimides). Each technique presents distinct advantages and drawbacks concerning mechanical strength, swelling behaviour, and biocompatibility. Physical methods tend to maintain the hydrogel's biological safety and degradability, while chemical crosslinking provides improved stability and customizable properties. The interplay between the method of preparation and the requirements of applications remains an essential focus of ongoing research.

Regarding applications, cellulose derivative-based hydrogels have been widely utilized in wound healing, tissue scaffolding, and drug delivery systems, driven by their high water content, adaptability, and responsiveness to stimuli. In environmental contexts, these hydrogels have demonstrated efficacy in eliminating heavy metals, organic dyes, and oil pollutants from aquatic environments. Their role in agriculture—particularly concerning water retention and slow-release fertilizers—underscores their significance in sustainable farming practices. Furthermore, the food industry benefits from their application as edible coatings and stabilizers, aiding in both preservation and sustainability.

Notwithstanding these benefits, various challenges remain. The mechanical properties of cellulose hydrogels, particularly those produced through physical crosslinking, may be insufficient for load-bearing biomedical applications. Additionally, variability in the natural cellulose sources can influence reproducibility from batch to batch. Future investigations should concentrate on creating multifunctional hybrid hydrogels that combine cellulose derivatives with other biopolymers, nanoparticles, or synthetic polymers to modify their properties for specific uses.

Furthermore, new studies are delving into intelligent and stimuli-responsive cellulose hydrogels capable of reacting to pH, temperature, magnetic fields, or enzymes. These advancements hold significant potential for applications in targeted drug delivery, biosensing, and advanced wound care. The integration of nanotechnology, 3D printing,

Mapping of Cellulose Derivative-Based Hydrogels to SDGs

- **SDG 3 – Good Health and Well-being:-**Hydrogels are extensively employed in tissue engineering, drug delivery, and wound healing, all of which improve healthcare outcomes.
- **SDG 6 – Clean Water and Sanitation:-** Hydrogels based on cellulose have been used in wastewater treatment and water purification, helping to eliminate colours and heavy metals.
- **SDG 9 – Industry, Innovation, and Infrastructure:-** The creation of intelligent and biodegradable hydrogels promotes sustainable industrial innovation in packaging, agriculture, and pharmaceuticals.
- **SDG 12 – Responsible Consumption and Production:-** Reducing reliance on synthetic polymers and promoting ecologically friendly products are two benefits of using renewable cellulose resources.
- **SDG 13 – Climate Action:-**Biodegradable hydrogels contribute to climate-friendly technologies and reduce plastic pollution.
- **SDG 14 – Life Below Water:-**Marine environments indirectly benefit from eco-friendly hydrogels' reduction of microplastic contamination.
- **SDG 15 – Life on Land:-**Hydrogels based on biopolymers are used in agriculture to help retain soil moisture, which promotes soil health and sustainable agricultural methods.

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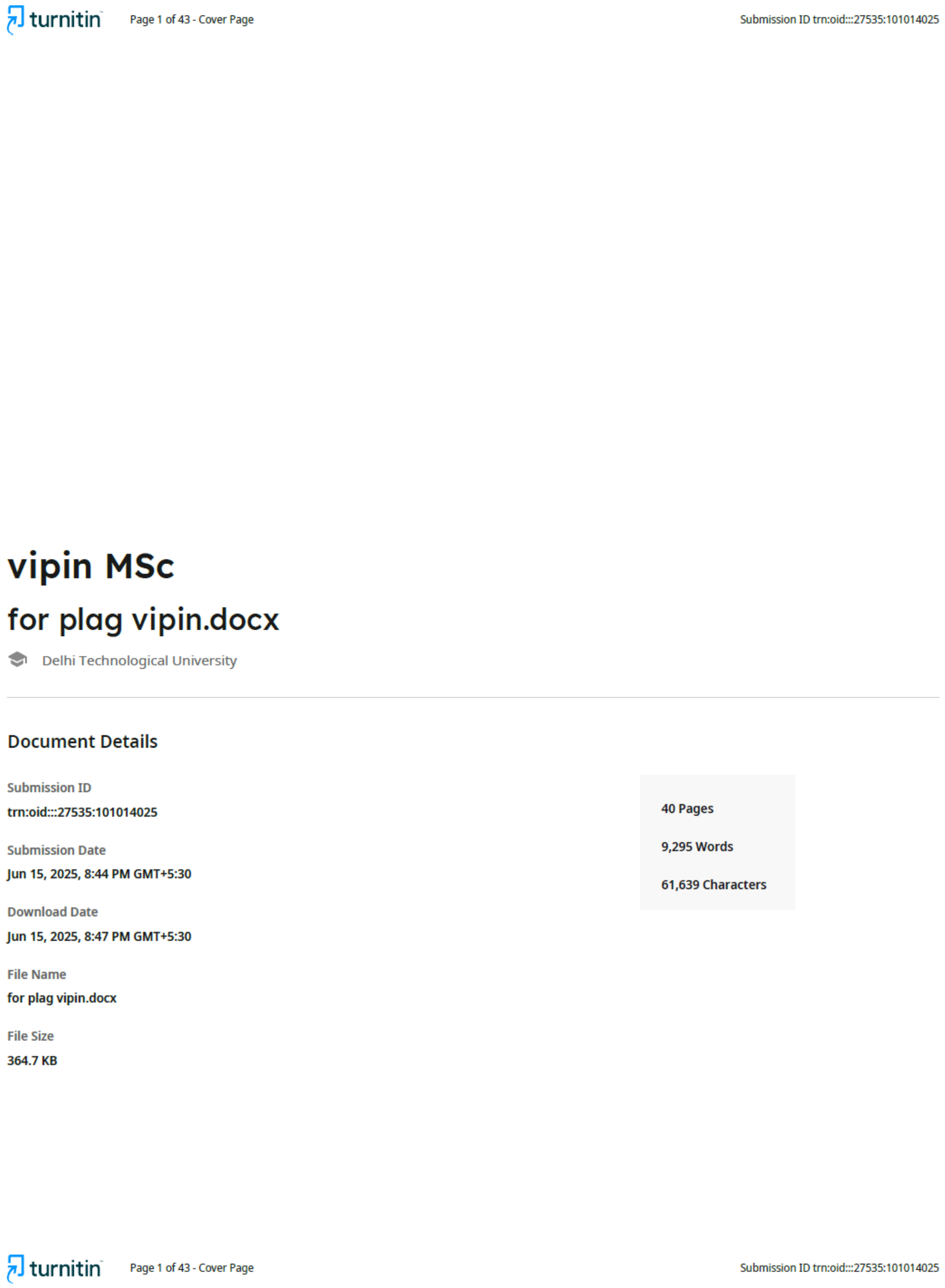

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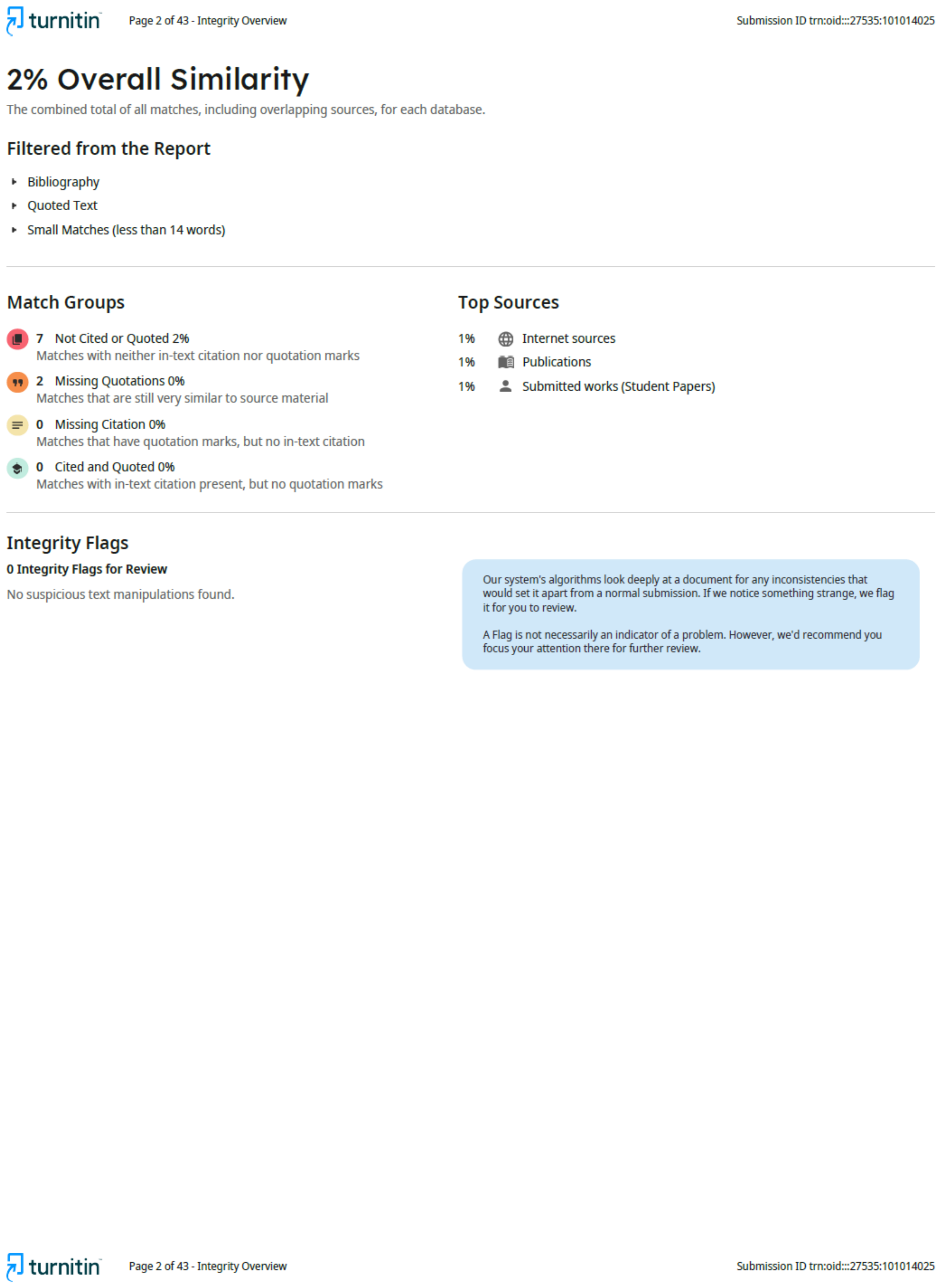

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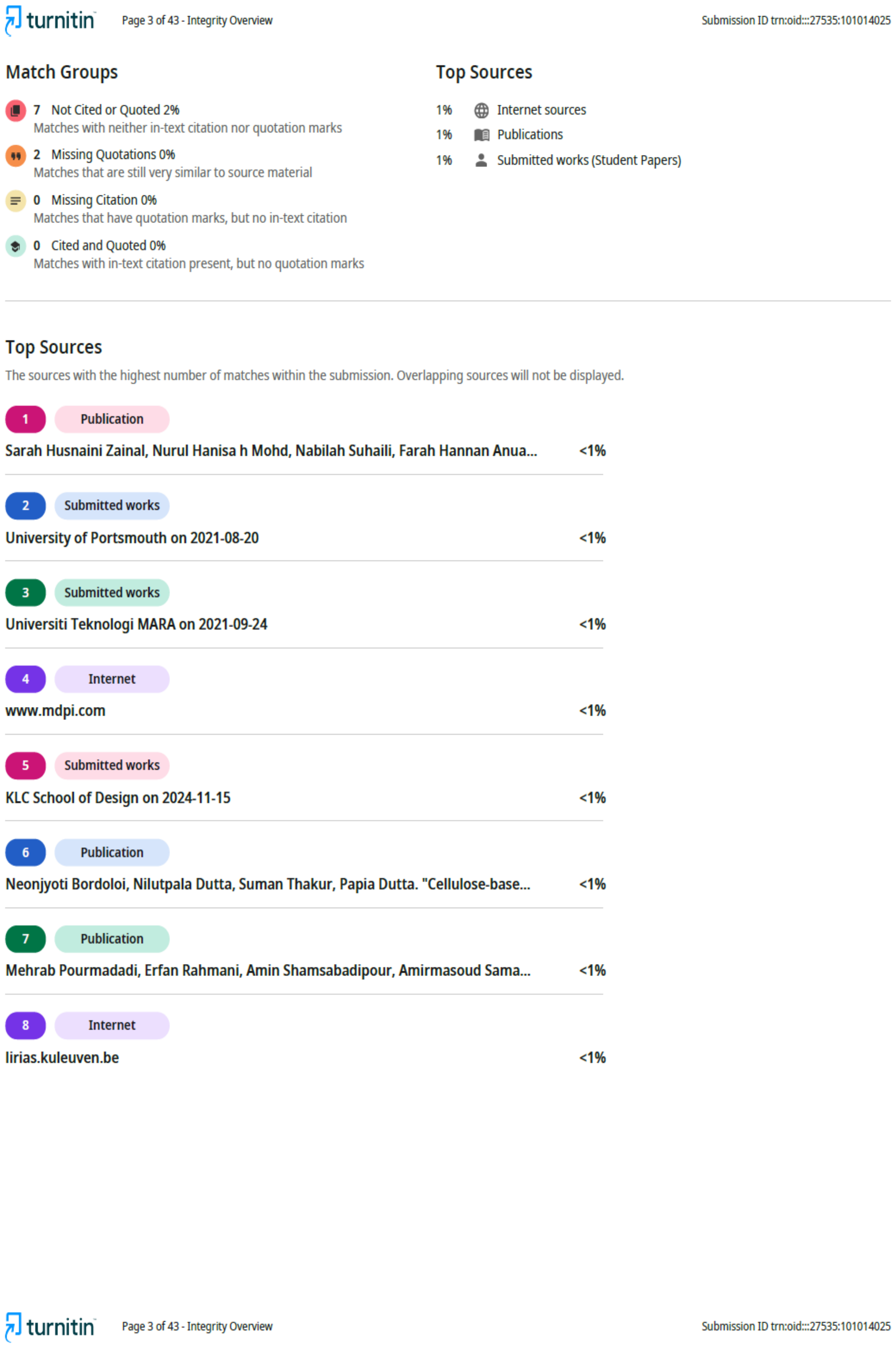

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