ENHANCEMENT OF MECHANICAL PROPERTY OF POLYACRYLIC ACID HYDROGEL USING MAGNETIC NANOCOMPOSITE BASED CROSSLINKER

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Certification of Thesis

A thesis on

ENHANCEMENT OF MECHANICAL PROPERTY OF POLYACRYLIC ACID HYDROGEL USING MAGNETIC NANOCOMPOSITE BASED CROSSLINKER

Submitted by

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(Md. Sohanur Rahman)

DEDICATED TO

My Father- Md. Rejaul Karim

My Mother- Mst. Shahanara Begum

My Elder Brother- Md. Sohel Rana

My Reverent Mentor - Dr. Md. Mahbub Alam

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Md. Sohanur Rahman

Abstract

Derivatives of cellulose, particularly carboxy methyl cellulose (CMC) is one of the popular physical crosslinkers used to improve the mechanical toughness and self-healing capability of polymeric hydrogels. In addition to good mechanical properties and self-healing properties, hydrogels capable of responsive to magnetic field are promising materials for biomedical applications. In this study, along with CMC as the physical crosslinker, Ni-nanoparticle was used to synthesize polyacrylic acid (PAA)-Ni-Cellulose nanocomposite. Polymerization was carried out using the free radical polymerization (FRP) technique using potassium persulfate (KPS) as initiator under inert atmosphere. The successful incorporation of Ni nanoparticle was confirmed using FTIR spectra as well as FESEM images. The incorporation of Ni-nanoparticle to hydrogel not only improved the mechanical toughness, it also introduced magnetic field to the prepared hydrogel. The amount of Ni-nanoparticle was varied to study the effect of Ni-nanoparticle on the mechanical toughness and self-healing capability of PAA-Ni-Cellulose nanocomposite. It was found that with the increasing amount of Ni-nanoparticle, the tensile strength increases while elongation of the hydrogel decreases. The nanocomposite hydrogel also showed considerable self-healing capability due the ionic and coordination interaction of Ni-nanoparticle with numerous physical interaction sites CMC provides. The prepared nanocomposite hydrogel also demonstrated responsiveness to the magnetic field due to the presence of Ni-nanoparticle. Therefore, PAA-Ni-Cellulose composite hydrogel with excellent mechanical toughness, self-healing capability, and responsiveness to magnetic field possesses immense potential to be applied in biomedical applications, particularly in biosensor, remote-controlled drug delivery etc.

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List of Abbreviations

Full name	Abbreviate name
Polyacrylic acid	PAA
Polyethylene glycol	PEG
Polyacrylamide	PAAm
Polyvinyl alcohol	PVA
Polyvinyl pyrrolidone	PVP
Interpenetrating Network	IPN
N, *N*′-methylenebis(acrylamide)	MBA
Sodium carboxymethyl cellulose	CMC
Potassium persulfate	KPS
Ultraviolet	UV
Field emission scanning electron microscopy	FESEM
Fourier transform infrared	FTIR
Thermogravimetric analysis	TGA
Differential thermogravimetric analysis	DTGA

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CHAPTER-1

Introduction

1.1 INTRODUCTION

A three-dimensional network of hydrophilic cross-linked polymers known as hydrogels can swell in water and other organic solvents while maintaining their original structural integrity. Hydrogels do not dissolve in water or other organic solvents [1]. In general, a cross-linked polymer can retain at least 10–20% of its initial weight in water [2]. The high thermodynamic affinity of this family of materials for the solvent accounts for their water-absorbing properties. The hydrophilicity and degree of cross-linking of the polymer chains are two important characteristics that influence the properties of hydrogels [3]. Different functional groups like hydroxyl (–OH), carboxylic (–COOH), amidic (–CONH–), primary amidic ($–CONH_2$), and sulphonic ($–SO_3H$) are found within the polymer network of hydrogel [4]. The copolymerization and crosslinking of one or more functional monomers can be used to synthesize hydrogels. Generally, the initiator, monomer, and cross-linker are the main components of hydrogels. The characteristics of hydrogels can be regulated by changing the synthetic parameters such as initiator concentration, the concentration of monomer, temperature of the reaction, reaction vessel, reaction time, and the ratio of cross-linker and monomer.

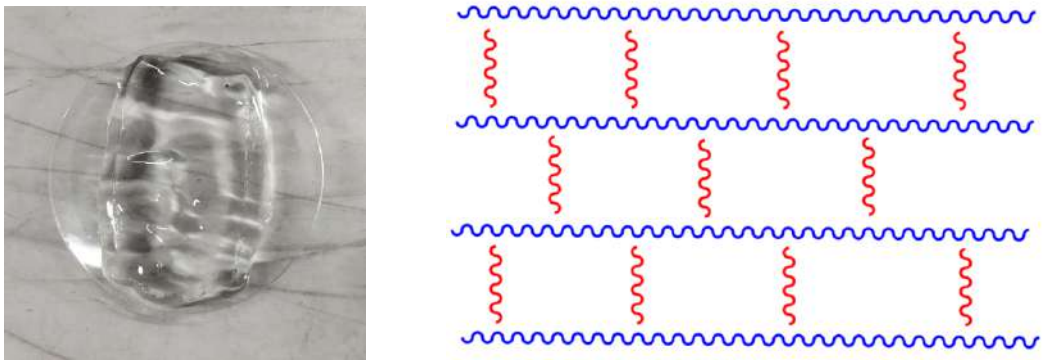

Fig. 1.1.1: Hydrogel – physical outlook (left), typical structure (right)

Along with swelling properties, they show excellent mechanical, optical, magnetic, and electrical properties based on their monomer units and preparation processing. Again, they contain hydrophobic and hydrophilic groups in their network, which is very important to express their different properties under different conditions. These properties are prerequisites for their specific application. For example, the contact lens often requires a combination of different desirable

properties, e.g., high optical transparency, good oxygen permeability, excellent biocompatibility, high water content, and strong mechanical properties. And hydrogel is an ideal candidate for combining these properties. Hydrogels are different based on source, cross-linking method, composition, charge, etc. According to the source, hydrogels can be divided into natural and synthetic polymers-based hydrogels. The hydrogels can be divided into chemical and physical gels based on the cross-linking method. Physical gels are formed by molecular self-assembly through ionic or hydrogen bonds, but chemical gels are formed by covalent bonds [5]. Hydrogels can be designed to exhibit significant volume changes in response to small changes in their environment such as pH, ionic strength, temperature, electric field, solvent, or magnetic field [6]. These types of hydrogels are called smart hydrogels. Micro- and nano-sized hydrogels are faster in responding to changes in their environment than their macroscopic or bulk counterparts. Although hydrogels were first reported by Wichterle and Lim in 1960 [7], which were based on poly (hydroxyethyl methacrylate) (PHEMA) and used in the biomaterial field. Hydrogel research has expanded dramatically in the last 10 years, primarily because hydrogels perform well for biomedical applications. Recently, scientists have devoted much energy to developing novel hydrogels for applications such as biodegradable materials for drug delivery [8], tissue engineering [9], sensors [10], contact lenses [11], water purification [12], etc. This is true for both synthetic and natural hydrogels. Synthetic polymer-based hydrogels have been reported such as those formed by cross-linking poly (ethylene glycol) (PEG) [13], poly (vinyl alcohol) [13], poly(amido-amine) [14], poly (N-isopropyl acrylamide) [15], poly(acrylamide) [16], and poly (acrylic acid) [17] and their copolymers [18]. Synthetic hydrogels like PEG-based hydrogels have advantages over natural hydrogels, such as the ability for photo-polymerization, adjustable mechanical properties, and easy control of scaffold architecture and chemical compositions, but PEG hydrogels alone cannot provide an ideal environment to support cell adhesion and tissue formation due to their bio-inert nature [19]. Several natural polymers have similar properties to PEG in terms of biocompatibility and low protein and cell adhesion, and they can be biodegraded into nontoxic products that are easily assimilated by the body [20]. Natural polymers including polynucleotides, polypeptides, and polysaccharides are derived from a variety of naturally occurring sources such as plants, animals, and humans, or are synthesized. Polymer collagen, for example, is obtained from cows, pigs, and humans, depending on the type of collagen required. Polypeptides can be synthesized by a protection/solid support scheme or through recombinant DNA techniques. Hydrogels of naturally

occurring polymers are prepared by the chemical or physical cross-linking of these polymers. The chemical crosslinking reaction of polysaccharides (alginate, chitin, chitosan, cellulose, oligopeptides, and hyaluronic acid) [21] and proteins (albumin, gelatin) leads to a variety of well-defined hydrogels [21]. Hydrogels prepared from these polymers exhibit excellent biocompatibility, primarily because they mimic the structural components of the body. In humans, glycosaminoglycans are hydrogels that exist in the connective tissue, such as skin, tendon, and bone [21].

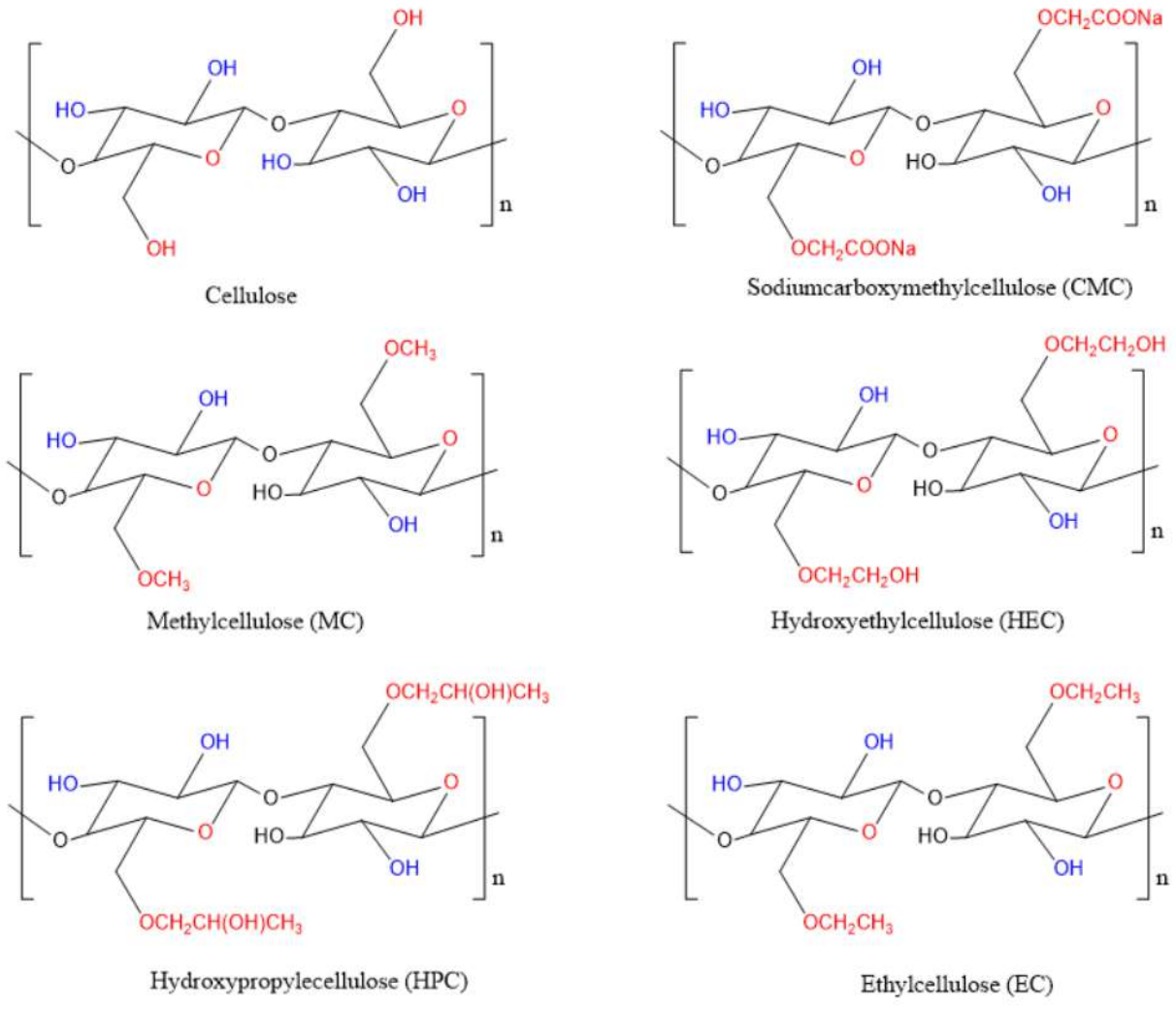

Fig. 1.1.2: Structure of cellulose and some cellulose derivatives

Among these natural polymers, cellulose is the most abundant naturally occurring glucose polymer found in plants and natural fibers such as cotton and linen [22]. Cellulose with abundant hydroxyl groups can easily prepare hydrogels with fascinating structures and properties [23]. Hydrogels based on natural cellulose can be prepared from a pure cellulose solution through physical cross-linking due to numerous hydroxyl groups, which can link polymer networks through hydrogen bonding [23]. Moreover, numerous new functional materials from cellulose are being developed over a broad range of applications because of the increasing demand for environmentally friendly and biocompatible products [24]. Most of the water-soluble cellulose derivatives are obtained by etherification of cellulose, where the active hydroxyl groups of cellulose react with organic species, such as methyl and ethyl units [25] to give MC, EC, HEMC, HPC, and Na-CMC [26]. Cellulose and its derivatives are blended with natural and biodegradable polymers or synthetic polymers [27] to achieve a new structural design and functional properties [28]. A special type of water-soluble hydrogel called polyelectrolyte complexes can be constructed by introducing other positively charged polyelectrolytes in the presence of CMC [29]. Another special type of hydrogel is Magnetic composite hydrogel. Magnetic composite hydrogel materials are also referred to as "soft matter" and "soft magnet" due to their low elastic modulus and void remnant magnetization in the absence of an applied field [30]. Recently, many research groups have studied a wide range of magnetic composite hydrogelto develop novel biomedical applications [30]. It is important to note that almost all high-water-content hydrogels possess poor mechanical properties. Again, due to the random nature of the crosslinking reactions during the polymerization, many polymer gels have poor mechanical properties [31]. This is a significant drawback of the hydrogels restricting their applications specifically where high stress is required [31]. Magneto-/ electro-responsive polymers (MERPs) are stimuli-responsive materials that are actuated when triggered by external magnetic/ electric fields. MERPs exhibit rapid, reversible, and safe multi-functional and dynamic properties, which can effectively be manipulated at different length scales. These features make MERPs very attractive, particularly in biomedical engineering (e.g., drug delivery systems and tissue engineering), soft matter engineering (e.g., soft robotics), and the structural design of smart materials with unprecedented properties [32]. To overcome the poor mechanical properties and incorporate the magnetic properties of these materials, it is necessary to copolymerize these "super absorbent" monomers with monomers that can improve the overall tear strength of the material. Incorporating different materials such as ceramics, metals, silicates, magnetics, and natural or

synthetic particles into the hydrogel matrix usually leads to improved properties, enhanced mechanical strength, magnetic properties, and structural stability.

Consequently, the present research aims to synthesize magnetic hydrogel based on acrylic acid (AA) monomer and Ni-Cellulose nanocomposite crosslinker through free radical polymerization (FRP).

The main objective of the present was:

I. To introduce a cellulose-coated Ni nanoparticle-based physical crosslinker
II. To develop a mechanically tough PAA-Ni-Cellulose composite hydrogel
III. To introduce magnetic properties in PAA-Ni-Cellulose composite hydrogel

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Chapter-2

Background

2.1 Hydrogels

We can define hydrogel as three-dimensional crosslinked polymers that have water uptake capacity but the word “hydrogel”, was first introduced in 1894 to explain a colloidal gel made with inorganic salts. The first water absorbent was synthesized in 1938 using a thermal polymerization process of acrylic acid and divinylbenzene. Later, in 1950, Otto Wichterle and Lim introduced hydrogel for contact lenses. But now, hydrogels are used in various sectors such as pharmaceuticals, agriculture, water purification, tissue engineering, and optoelectronics. That’s why hydrogels are pampered by scientific and commercial communities and huge amounts of hydrogels are produced around the world for their commercial application. These huge amounts of hydrogels can be classified from different aspects.

2.2 Classification of Hydrogels

In the present world, hydrogels are used in different fields. A huge number of hydrogels are produced around the world. We can classify these hydrogels into several categories based on origin, composition, ionic charge, physical structure, and cross-linking.

2.2.1 Classification Based on Origin

Natural Hydrogels

This hydrogel is naturally originated and is prepared using natural polymers such as proteins and polysaccharides like alginate, chitosan, and dextran [1].

Synthetic Hydrogels

Synthetic-originated polymeric substances that are formed from synthetic products or man-made products are called synthetic hydrogels and these types of hydrogels are synthesized via chemical polymerization. These hydrogels can be homopolymeric, co-polymeric, and multi-polymeric [2].

Hybrid Hydrogels

The hydrogels which are formed by a combination of natural polymers with synthetic polymers are called Hybrid Hydrogels. Wang et al. synthesized a protein cross-linked 2- hydroxypropyl meth acrylamide hybrid hydrogel [3].

2.2.2 Classification Based on Composition

Homopolymer Hydrogels

This type of hydrogel is a cross-linked polymer network derived from only one type of monomer. The structural framework of homopolymer hydrogels is dependent on the nature of the monomer, polymerization technique, and cross-linker [4].

Copolymer Hydrogels

Copolymer hydrogels are produced from two different types of monomers in which one monomer contains a hydrophilic group and is responsible for the swelling property of the hydrogel [5].

Multiplier Hydrogels

An example of multipolymer hydrogel is poly (acrylic acid-2-hydroxy ethyl methacrylate)/gelatin hydrogel [6]. These types of hydrogels are produced from three or more monomers using polymerization and cross-linking reactions.

Interpenetrating Network (IPN)

The hydrogels which are made up of two intertwined polymer networks without any chemical bond between the polymers are called interpenetrating networks. Although the network of the first polymer is linear, the second polymer has a cross-linked network. The linear network of the first polymer diffuses into the second polymer [7].

2.2.3 Classification Based on Ionic Charge

Hydrogels are classified into three groups based on the nature of an electric charge on cross-linked chains [8].

Neutral (Non-Ionic) Hydrogels

The hydrogels which have no charge on their backbone or side groups are called neutral hydrogels. Poly (Acrylamide) is used to prepare neutral hydrogel [9].

Ionic Hydrogels

Ionic hydrogels can be cationic or anionic. Cationic hydrogels containing positively charged groups (e.g., amines and sulphonic acid) exhibit an increase in the swelling at low pH, whereas anionic hydrogels containing negatively charged groups (carboxylic acid, sulphonic acid) and show an increase in swelling at high pH [10].

Ampholytic Hydrogels

Ampholytic hydrogels carry negative as well as positive charges on the same polymer chain, which balances at the isoelectric point. PAC is an ampholytic hydrogel that was prepared from acrylamide (AM) and 4 (2 ((carboxylatomethyl)dimethylammonio) ethoxy) −4-oxobut- 2-enoate (CMD) through free-radical polymerization by using ammonium persulfate (APS) as an initiator and methylenebisacrylamide (MBA) as a crosslinker.

2.2.4 Classification Based on Pore Size

Hydrogels are classified into three types based on porosity [11] namely:

a. nonporous

b. microporous and

c. super porous

2.2.5 Classification Based on Physical Appearance

Based on physical appearance, hydrogels can be a matrix, film, or microsphere, depending on the polymerization method [12].

2.2.6 Classification Based on Configuration

Depending on the physical structure and chemical composition, hydrogels can be classified as follows [12].

Amorphous (Non-Crystalline)

In amorphous hydrogels, the polymeric network contains randomly arranged macromolecular chains.

Semi-Crystalline

Semi-crystalline is a complex mixture of amorphous and crystalline phases and is characterized by dense regions of ordered macromolecular chains.

2.2.7 Classification Based on Cross-Linking

Based on the nature of cross-linking, hydrogels are of two types:

a. Physical hydrogels

b. Chemical hydrogels.

Physical hydrogels are cross-linked by various physical processes such as crystallization, hydrogen bonding, and hydrophobic interactions, whereas covalent cross-linking is used to prepare chemical hydrogels [13].

2.3 Monomers used in hydrogels

2.3.1. Synthetic Materials used in hydrogels

Synthetic polymers offer engineers highly versatile materials with physical and chemical properties that can be easily controlled and altered. One such property is degradability, which can be altered by creating copolymers or polymer blends. These polymers and blends are generally easier to process than natural polymers and have more predictable results. Conversely, synthetic polymers are less biocompatible than naturally derived polymers and not as bioactive.

2.3.1.1 Poly (acrylic acid) (PAA)

Synthetic polymers allow for a higher degree of swelling and impart superior mechanical properties and adhesion strength to the hydrogels as compared to those in the case of natural polymers. PAA is a hydrophilic and highly absorbent polymer that has been widely applied to biomaterials due to its high solubility and biodegradability [14]. PAA hydrogels have been widely used as drug carriers because of their good bio-adhesive properties and enhanced drug penetration.

2.3.1.2 Polyethylene glycol (PEG)

PEG is a water-soluble synthetic polymer [15]. PEG is used in hydrogels due to its biocompatible, nontoxic, and water-soluble properties. PEG-based hydrogels are called “smart polymers” or

“intelligent gels” because they are stimuli-based hydrogels. The stimuli may be physical (temperature, solvent, light, radiation, pressure) or chemical (PH, specific ions). These hydrogels are also used for the controlled release of drugs [16].

2.3.1.3. Poly(acrylamide) (PAAm)

Poly(acrylamide) (PAAm) is an important hydrophilic polymer for the preparation of hydrogels [17]. PAAm hydrogels and their derivatives are the subjects of many studies [18]. PAAm hydrogels have proven capability of water absorption and biocompatibility with physiologic body fluids. The application of PAAm hydrogels in the controlled release of agrochemicals and bioactive has been investigated.

2.3.1.4 Polyvinyl alcohol (PVA)

PVA is also another synthetic polymer that extensively is used to prepare hydrogel. Due to its water-retaining ability and biocompatibility, it is used as a scaffold for tissue cultures, contact lenses [15], cartilage reconstitution [15], and wound dressing [16]. PVA-based hydrogels are obtained by freezing and thawing process.

2.3.1.5 Polyvinyl pyrrolidone (PVP)

PVP is soluble in water and polar solvents [15]. PVP is used in wound dressing because of storing large quantities of water, low production cost, and good elasticity properties. PVP, combined with other polymers like CMC, is also used to enhance mechanical properties and biocompatibility. Retaining a high quantity of water PVP is also used in making contact lenses [16].

2.3.2. Natural Materials used in Hydrogels

Nature is a vast source of polymeric materials that can synthesize polymeric materials. Naturally derived scaffold materials such as alginate carrageenan, collagen, chitosan, gelatin, alginates, hyaluronic acid, etc. have been processed from nature and possess good biocompatibility properties with low cytotoxicity. Due to their biocompatibility and biodegradability, these naturally derived polymers synthesize hydrogel which has been vastly used in different sectors, especially in biomedical applications. Here some of them are illustrated.

2.3.2.1 Alginate

Alginate is a linear polysaccharide extracted from brown, seaweed, and algae [19]. Alginate is made up of (1,4)-linked β-D-mannuronate (M) and α-L-guluronate [19]. In the presence of ions, they undergo a complexation reaction due to the carboxylic group [20]. Gelling property of alginate is due to the presence of the G block [20]. Hydrogels containing famotidine for stomach targeting are formed by incorporating sodium alginate and polyacrylamide through grafting [19].

2.3.2.2 Chitosan

Chitosan is a natural polymer obtained from shrimp, crab, and lobster shells [20]. It is a cationic polysaccharide [20]. Mostly chitosan is obtained by deacetylation of chitin [21]. Chitosan is made up of glucosamine and N-acetyl glucosamine units [21]. A thermo and P^H-sensitive-based hydrogel of chitosan was prepared to contain doxorubicin hydrochloride as a model drug.

2.3.2.3 Hyaluronic acid

Hyaluronic acid is also called hyaluronan and hyaluronate (HA) or sodium hyaluronate [21]. It is an N-acetyl-D- glucosamine and beta-gluconic acid [20]. HA is a naturally occurring polymer found in tissues of higher animals [21], in the vitreous of the eye and synovial fluid [21]. HA-based hydrogels are used for the delivery of therapeutic agents for tissue repair.

2.3.2.4 Gelatin

Gelatin is a water-soluble natural polymer [21]. Gelatin is produced by the hydrolysis of collagen obtained from connective tissues and bones of animals [20]. Hydrogel-based wound dressings consisting of sodium alginate and gelatin were prepared by crosslinking sodium chloride/glutaraldehyde.

2.3.2.5 Dextran

Dextran is a natural polymer synthesized from sucrose. Due to its water solubility, biocompatibility, and unique properties, it is used for sustaining the effects of proteins, interleukin-2, and other drugs. Paclitaxel an anti-cancer drug is used to make dextran-based hydrogels. These hydrogels are pH sensitive and are utilized for colon targeting.

2.3.2.6 Xanthan gum

Xanthan gum is produced by the fermentation of carbohydrates with Xanthomonas campestris. It is a cream-colored powder soluble in hot as well as cold water. Xanthan gum is stable over pH 4-10 [22]. Super porous hydrogels were prepared by using xanthan gum, acrylic acid, and 2-hydroxyethyl methacrylate (HEMA) by graft copolymerization technique.

2.3.2.7 Starch

Starch is synthesized and stored by all plants for energy purposes. Available in small granules ranging in size from 1-100 micrometers. Starch is a biodegradable polymer that has pharmaceutical applications [22]. pH-sensitive hydrogels were prepared using starch and methacrylic acid by copolymer method loaded with ketoprofen as a model drug.

2.3.2.8 Cellulose

Cellulose is the most abundant natural biopolymer available on the earth and it is a structural constituent of the cell wall of various plants. It is important not only for plant growth and development but also for industrial use. Apart from plants, cellulose is also present in various living species, such as algae, fungi, bacteria, and even in some sea animals, such as tunicates [23]. Cellulose is a fibrous, tough, and water-insoluble polymer. The chemical structure of cellulose is shown in Figure 2.1.

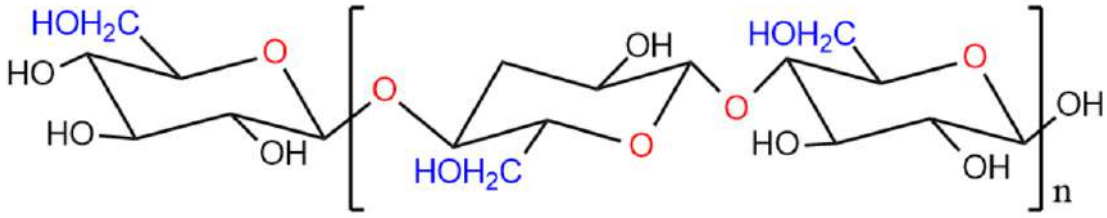

Fig. 2.3.2.8.1 Typical structure of cellulose

It contains three different parts-a reducing end group with a free hemiacetal at the C1 position, a non-reducing end group with a free hydroxyl group at the C4 position, and an internal anhydroglucopyranose rings joined at the C1 and the C4 positions through β 1-4 glycosidic bonds.

The internal anhydroglucopyranose units are predominant due to the long chain lengths and contain three hydroxyl groups. The hydroxyl group at the C6 position is a primary alcohol, while the hydroxyl groups at the C2 and C3 positions are secondary alcohols, and these are corkscrewed at 180° with respect to its neighbors [24]. Due to the linear and quite regular structure of cellulose and having many hydroxyl groups, cellulose polymers can form ordered crystalline structures. These crystalline regions give important mechanical properties to the cellulose fibers. The hydroxyl groups in the cellulose polymer can form hydrogen bonds between different cellulose polymers (intermolecular hydrogen bonds) or within the polymer itself (intramolecular hydrogen bonds). The intramolecular hydrogen bonds give stiffness to the polymer chain, while the intermolecular bonds allow the linear polymers to form sheet structures. With the van der Waal forces, hydrogen bond helps to aggregate polymer chains together side-by-side and promotes parallel stacking of cellulose microfibrils into crystalline cellulose [25]. The high crystallinity and the many hydrogen bonds in the cellulose fibers make cellulose insoluble in water and in most conventional organic solvents.

2.4. Magnetic Hydrogels

2.4.1 Magnetic Nanomaterials

In recent years, magnetic nanomaterials have been incorporated into tissue engineering hydrogels to make them responsive to magnetic fields and thus easier to control from outside the body using externally applied electromagnetic fields [26-28]. This interaction between magnetic nanomaterials and tissue engineering hydrogels can, in the long run, yield stimuli-responsive hydrogels that can actuate and heal on command within the human body. The working principle behind these systems relies on reversible links between the magnetic nanomaterial and the hydrogel backbone. However, such intelligent tissue engineering systems are still in their infancy, with only a few published studies. Most of these studies have focused on incorporating iron nanoparticles into hydrogels and have utilized catechol–iron coordination bonds to endow self-healing properties to these systems. For instance, a mixture of magnetic iron nanoparticles and a four-arm terminated polyethylene glycol (PEG) polymer enabled spontaneous hydrogel cross-linking through metal coordination interactions between the polymer chains and iron nanoparticles

[27]. This hydrogel was magnetic, self-healable, biocompatible, and stretchable. Despite the many interesting properties of the iron-4cPEG system, its magnetic properties were not fully utilized. It would be interesting to examine the self-healing time and its efficiency as a function of an externally applied magnetic field. Another hydrogel with self-healing and magnetic properties was recently manufactured from the combination of chitosan and negatively charged iron-coated graphene oxide (FeGO) nanomaterials [28]. These films demonstrated self-healing ability due to electrostatic interactions between positive amine groups on chitosan and the negatively charged FeGO nanomaterials. Specifically, the incorporation of FeGO into chitosan had a direct effect on the hydrophobicity of the resulting hydrogel, as well as its mechanical and magnetic properties.

Interestingly, the FeGo–chitosan system also displayed some remarkable antibacterial properties, which could be utilized to develop hydrogels that can regenerate chronic wounds, while at the same time reducing the probability of wound infection and possible foreign body responses. However, in our opinion, the authors of this study did not fully tap into the exciting magnetic properties of their system. Indeed, the area of magnetic and self-healable tissue engineering hydrogels presents a host of yet unexplored scientific possibilities, which, once fully harnessed, might push the field of tissue engineering to exciting new highs [29].

2.4.2 Magnetic Nanocomposite Hydrogels

Most human body tissues are characterized by highly anisotropic physical properties and biological organization. Hydrogels have been proposed as scaffolding materials to construct artificial tissues due to their water-rich composition, biocompatibility, and tunable properties. However, unmodified hydrogels are typically composed of randomly oriented polymer networks, resulting in homogeneous structures with isotropic properties different from those observed in biological systems. Magnetic materials have been proposed as potential agents to provide hydrogels with the anisotropy required for their use in tissue engineering [30].

2.5. Cellulose-Based Hydrogels

Manufacture of hydrogels from cellulose and its derivatives generally is accomplished in two steps [31], (i) dissolving of cellulose fibers or powder and (ii) cross-linking (chemical and/or physical) of the chains, to obtain a three-dimensional network of hydrophilic polymer chains, which can absorb and retain a significant amount of water.

Additional natural and/or synthetic polymers might be combined with cellulose to obtain composite hydrogels with specific properties. These properties can be changed under different environmental conditions. This hydrogel is known as stimuli-sensitive hydrogel. Cellulose 18 and its derivatives can be used to prepare stimuli-sensitive hydrogels. Some common cellulose derivatives with their common applications are given below, which are used to prepare stimuli-sensitive hydrogel.

Table-2.5.1: List of cellulose derivatives and their applications

Cellulose derivatives	**Applications**	**Ref.**
Carboxymethylcellulose	Biomedical and agriculture	[32]
Methylcellulose	Releasing fertilizers	[33]
Hydroxy ethyl cellulose	Smart materials	[34]
Hydroxypropyl methylcellulose	Controlled release	[35]
Cellulose acetate	Drug carrier system	[36]

However, still very limited works are performed by using native cellulose for the preparation of hydrogels. This is due to the difficulty of the dissoluble properties of cellulose in several solvents for the regeneration process [37]. Although cellulose derivatives are somewhat soluble in water and other liquids, their applications are limited due to lower mechanical properties. The present study will describe the fabrication of such cellulose-based hydrogel, which is biocompatible and less cytotoxic for a new type of environmentally friendly with enhanced mechanical properties.

2.6. Synthesis of Hydrogels

Hydrogels are polymer networks prepared from natural or synthetic polymers using various polymerization techniques such as bulk, solution, and suspension by physical and chemical cross-linking routes [12]. Physical cross-linking involves hydrogen bonds, stereo complexation, and soft assembly, whereas chemical cross-linking involves cross-linking in the presence of different cross-linkers. There are other methods to synthesize hydrogel, including physical and chemical methods.

- Physical method
- Chemical method
- High energy irradiation
- Using enzymes

Of all the above-mentioned cross-linking methods, chemical methods and physical methods are the most widely used.

2.6.1. Physical method

In this method, hydrogels are crosslinked via non-covalent bonding or various physical interactions, including hydrogen bonding, hydrophobic interaction, aggregation, association, complexation, crystallization, and ionic interactions [38]. Hydrogels may be grouped into weak or strong physical hydrogels based on this method. In addition, they are reversible in nature due to conformational changes. Structures of a few strong physical hydrogels and weak physical hydrogels are shown in Figures 2.6.1.1 (A) and 2.2(B).

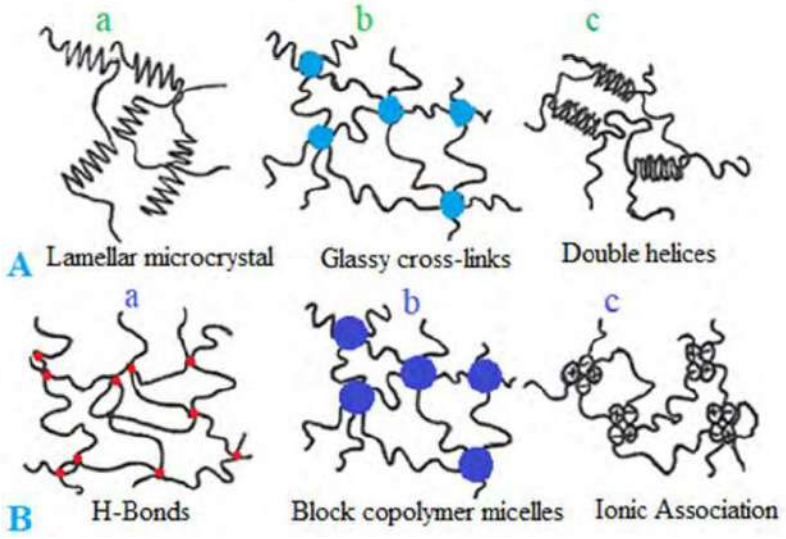

Fig. 2.6.1.1: (A) strong physical hydrogels and (B) weak physical hydrogels

[Figure reference: M. Akram, R. Hussain, Nanohydrogels: History, Development, and Applications in Drug Delivery. In Nanocellulose and Nanohydrogel Matrices, 2017, Doi: 10.1002/9783527803835.ch11]

A list of a few well-known physical hydrogels and their applications is presented in Table 2.6.1.1.1

Table- 2.6.1.1.1: List of physical hydrogels and their applications

S.N.	Name	Application	Ref.
1	Polyelectrolyte complex hydrogel	Tissue engineering matrices	**39**
2	Blend hydrogels	Drug delivery, wound dressing	**40**
3	Block copolymer gels	Drug delivery	**41**
4	Thermally-induced hydrogel	Drug and gene delivery	**42**
5	Counter ion-induced hydrogel	Dentistry and drug delivery	**43**

6	Interpenetrating polymer hydrogels or network (IPNS)	Drug delivery and tissue scaffold	**44**

2.6.2. Chemical method

In contrast to physical network-based hydrogels, chemical cross-linking-based hydrogels involve chemical covalent cross-linking in their formation. Monomers with vinyl groups like acrylic acid, AAm, hydroxyl ethyl methacrylate, and so on, or some macromolecules modified with vinyl groups such as albumin, dextrin, starch, and so on can be polymerized through chemical initiation to prepare chemical gels. Similarly, photoionization or gamma irradiation processes may be utilized to synthesize chemical hydrogels. Chemical hydrogel synthesis occurs in molecules with divinyl groups, which act as covalent cross-linkers [38]. Polymers having other functional groups can also be cross-linked to produce chemical hydrogels. Gelatin and albumin form intermolecular Cross-link through the dialdehyde group; cysteine, and polypeptides through cross-linking of cysteine bonds are good examples of chemical hydrogels [45]. Chemical hydrogels may be formed with a degradable polymer backbone or degradable cross-linking agent prepared using chemical cross-linking [38]. This type of hydrogel is considered irreversible or permanent due to the involvement of configurational changes.

2.6.3. Radical cross-linking method

The chemical hydrogel can convincingly form by Irradiation method, including irradiation of solid polymer, monomer (in bulk or in solution), or polymer aqueous solution [46]. The advantage of radical cross-linking is that cross-linkers are not required in the fabrication process here, which limits hydrogel applications in the food, drug, and pharmaceutical industries due to their toxicity. The concentrated aqueous solutions of cellulose derivatives, such as CMC, HPC, and MC, can be cross-linked under ionizing radiation to prepare cellulose-based hydrogels [47]. Bin et al. have found that carboxymethyl cellulose with a high degree of substitution (DS) and high concentration can be effectively cross-linked to form CMC hydrogels through irradiation [47]. The effects of the

aging time, concentration, and dose rate on the cross-linking of CMC in aqueous solutions under ionizing radiation are also examined.

2.6.4. Ionic Interaction method

The ionic interaction method can be employed to prepare hydrogel using alginate (a polysaccharide with mannuronic and glucuronic acid residues) is a well-known polymer that can be cross-linked with calcium ions [48]. This type of cross-linking can be done under ambient conditions of temperature and physiological pH; hence, these hydrogels are commonly employed as templates for encapsulating living cells and releasing proteins [49]. Similarly, a synthetic polymer, poly-di(carboxylatophenoxy) phosphazene (PCPP), can also be cross-linked with Ca ions like alginate ions. Such hydrogels are called ionotropic and can degrade under physiological conditions.

2.7. Properties of Hydrogels

2.7.1 Swelling properties of hydrogel

A crosslinked polymer hydrogel swells but does not dissolve when water or a solvent enters it. The imbibed liquid serves as a selective filter to allow free diffusion of some solute molecules, but the polymer network serves as a matrix to hold the liquid together. Hydrogels may absorb from 10-20% (an arbitrary lower limit) up to thousands of times their dry weight in water [50].

The swelling properties depend on many factors, such as network density, solvent nature, and polymer-solvent interaction parameter. Water acts as a plasticizer in a hydrophilic polymer network system. The swelling process of the hydrogel can be considered under a rubbery state and can be described by the free energy of mixing ΔG_{mix} from the polymer and solvent interaction and the elastic free energy $\Delta G_{elastic}$ from the crosslinked network:

$$\Delta G_{system} = \Delta G_{mix} + \Delta G_{elastic} \quad (2.1)$$

At the beginning of swelling, the $\Delta G_{mix} << 0$, $\Delta G_{elastic} > 0$, $\Delta G_{mix} + \Delta G_{elastic} < 0$, so the swelling is favored, and the solvent diffuses into the network. During the processing of swelling, the ΔG_{mix}

and $\Delta G_{elastic}$ both increased until $|\Delta G_{mix}| = |\Delta G_{elastic}|$ and $\Delta G_{system} = \Delta G_{mix} + \Delta G_{elastic} = 0$ so that the driving force for swelling is gone: equilibrium swelling is reached and swelling stops.

When a dry hydrogel begins to absorb water, the first water molecules entering the matrix will hydrate the most polar, hydrophilic groups, leading to primary-bound water. As the polar groups are hydrated, the network swells and exposes hydrophobic groups that interact with water molecules, leading to hydrophobically-bound water, or secondary-bound water. Primary and secondary bound water are often combined and called total bound water. After the polar and hydrophobic sites have interacted with and bound water molecules, the network will imbibe additional water, due to the osmotic driving force of the network chains towards infinite dilution.

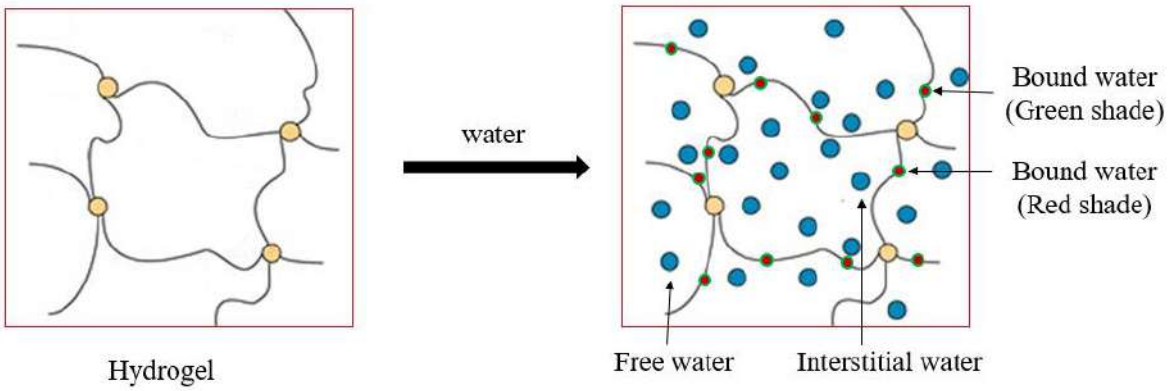

Fig. 2.7.1.1.1.1: Water swelling process by hydrogel.

This additional swelling is opposed by the covalent or physical crosslink, leading to an elastic network retraction force. Thus, the hydrogel will reach an equilibrium swelling level. The additional swelling water that is imbibed after the ionic, polar, and hydrophobic groups become saturated with bound water is called free water or bulk water and is assumed to fill the space between the network chains, and/or the center of larger pores, macropores or voids.

As the network swells, if the network chains or crosslink are degradable, the gel will begin to disintegrate and dissolve at a rate depending on its composition.

2.7.1.1 Swelling ratio measurement

2.7.1.1.1. Free-absorbency Capacity

Generally, when we have used the terms swelling or absorbency without specifying its conditions; it implies the uptake of distilled water without any load put on the testing sample. On the basis of sample viz. the amount of the available sample, the sample absorbency level, and the method's precision and accuracy there are several simple methods for free absorbency testing.

2.7.1.1.2. Tea-bag Method

The tea bag method is fast and more suitable among all the conventional methods for limited amounts of samples (W_0= 0.1-0.3 g) [51]. In this method, the sample is placed into a tea bag (acrylic/polyester gauze with fine meshes). The bag is dipped in excess water or saline solution for a definite time to reach the equilibrium swelling. Then the excess solution is removed by hanging the bag until no liquid is dropped off. The tea bag is weighed (W1) and the swelling capacity is calculated by equation (2.2). The method's precision has been determined to be around ±3.5%.

$$Se = (W_1-W_0)/W_0 \quad (2.2)$$

2.7.1.1.3. Centrifuge Method

The centrifugal data are more reliable than the tea bag method and are occasionally reported in patents and data sheets [52]. Thus, 0.2 g (W_1) of the sample is kept in a bag (60×60 mm) made of non-woven fabric. At room temperature, this bag is dipped in 100 mL of saline solution for half an hour. Then the bag is taken out and the excess solution is removed with a centrifugal separator (3 min at 250 g). After that, the weight of the bag (W_2) is measured. This experiment is repeated without a sample and the weight of the empty bag (W_0) is measured. The swelling capacity is calculated by equation (2.3).

$$Se = (W_2-W_0-W_1)/W_1 \quad (2.3)$$

Since the inter-particle liquid is noticeably removed by this method, the measured values are often more accurate and lower than those obtained from the tea-bag method values.

2.7.2. Mechanical properties

The mechanical properties can vary and be tuned depending on the purpose of the material. It is possible to obtain a gel with higher stiffness increasing the crosslinking degree or lowering it by heating the material. Different causes and variables are responsible for changing the mechanical properties of polymeric materials. That's why different analyses must be made according to the material, the conditions, and the aim of the study. For example, if we want to know the elasticity of a hydrogel, we can use a UTM machine, but if we want to know viscoelastic properties, then we should use a Dynamic Mechanical Analysis (DMA) device or a rheometer. It's important to note that in a hydrogel, the Young Modulus is the result of the union between water and gel matrix. If we have to seed osteoblast cells, we will need a stiffer material than if we culture adipocytes, the same rationale is valid for developing a heterogeneous prosthetic device, for example, a substitute for the intervertebral disc.

2.7.2.1. Measurement of mechanical properties of hydrogels.

Common methods for measuring the mechanical properties of hydrogels include tensile and compression testing methods. Most tensile tests are run at constant extension rates with varying loads until the sample reaches ultimate failure. One obtains information about several sample properties from tensile testing at various loads. The most used method to determine the mechanical properties of hydrogels is tensile testing. These methods have been extensively used to study the mechanical behavior of various hydrogels [53]. For most uniaxial tensile testing, dumbbell-shaped samples of the polymer are placed between two clamps, and one end of the material is pulled away from the other at varying loads and rates of extension. Dies are available to cut samples to the appropriate shape. A dumbbell shape is desirable because it prevents samples from breaking at the clamps where the stress concentration would be high in a uniform strip. A dumbbell-shaped sample should exhibit ultimate fracture in materials without structural defects at the centre of the sample. The technique involves applying a tensile force to strips of material held between two grips (Figure 2.7.2.1.1a). Alternatively, the force can be applied to a ring instead of a single strip (Figure 2.7.2.1.1b). Applied force and the elongation of the material are used to obtain a stress-strain chart. This chart can derive several mechanical properties of the hydrogel including Young's modulus, yield strength, and ultimate tensile strength. This method can also examine the viscoelastic

characteristics of a hydrogel material by elongating the material strip to a particular length and examining the stress relaxation response over time at a constant strain. Figure 2.7.2.1.2 shows the typical mechanical behavior in a uniaxial tensile test.

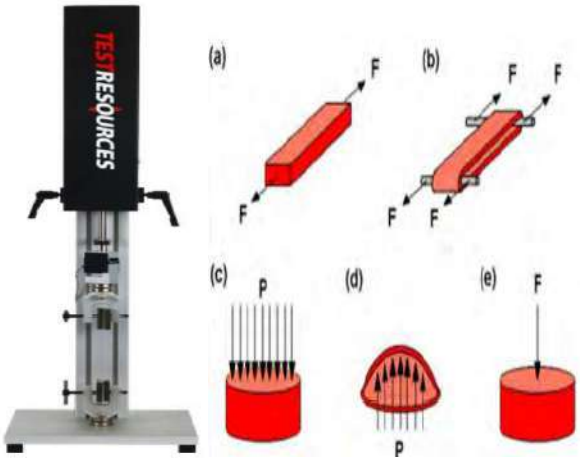

Fig. 2.7.2.1.1: Determination of mechanical properties by UTM machine

The compression test is another technique that has previously been used to examine the mechanical properties of several different types of hydrogels [54]. This technique involves placing the material between two plates and compressing it (Figure 2.7.2.1.1c). The pressure applied to the surface of the hydrogel and the distance the hydrogel is compressed can be used to calculate the mechanical properties of the hydrogels using a theoretical model. One of the advantages of the compression test over the extensometer is that it does not limit the hydrogel geometry to strips or rings, although it does require a flat surface. This approach has several limitations, including bulging the hydrogel under compression and difficulty applying pressure evenly. Bulging can be overcome by confining the hydrogel around its outer edge although this changes the nature of the measurements. Several studies have used the compression test to examine the mechanical properties of cell-seeded hydrogels.

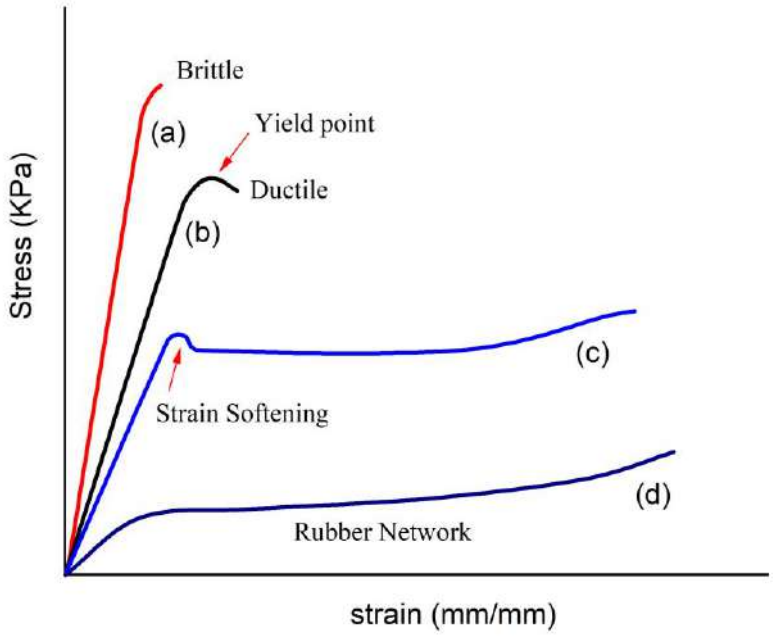

Fig. 2.7.2.1.2: Typical stress-strain curves of polymers: curves (a)-(c) represent glassy polymers. The curve (d) corresponds to the rubber state. The ends of the curves indicate the points of material failure: (a) brittle and (b)-(d) ductile.

2.7.2.2. Control of mechanical properties

Once the mechanical characteristics of the material have been determined, it is often necessary to improve them in some manner to make the material suitable for the desired application. In this section, we will explore three different ways of controlling the mechanical properties:

altering the co-monomer composition, increasing or decreasing the cross-linking density, and changing the conditions under which the polymer is formed. We will also address the relationship between the hydrogel's mechanical properties and its degree of swelling. It must be remembered that these changes in the polymer will affect not only the mechanical properties but also other material behavior.

2.7.2.2.1. Effects of comonomer composition

One of the first and simplest changes that can be performed is altering the composition of the comonomers used in preparing the hydrogel. If the hydrogel is not a homopolymer, then increasing the relative amount of physically stronger components will lead to an increase in the mechanical strength of the final product. Such a change may alter the mechanical strength by increasing the stiffness of the backbone polymer or it may alter the hydrophilicity of the polymer. Additional changes to the comonomer composition can include varying the amount and type of cross-linking agent. For example, the addition of NVP to the HEMA copolymer [55], reduced Young's modulus, a direct measure of the material's strength of the swollen polymer by an order of magnitude as the NVP content was increased from 5 to 60%. These results are expected since NVP is an extremely hydrophilic moiety that significantly increases swelling compared to HEMA. Increasing the relative content of more hydrophilic monomers will lead to increased swelling for the resulting hydrogel. This, in turn, will lead to a decrease in the mechanical strength of the polymer.

2.7.2.2.2. Effects of cross-linking density

The mechanical strength of a hydrogel is often derived almost entirely from the cross-links in the system. The strength of the material increases dramatically with increasing cross-linking density. The addition of a larger amount of cross-linking agent can easily increase the cross-linking density. But a larger number of cross-linking agents create heterogeneities in polymer networks. Generally, these highly cross-linked heterogeneities exist when more than 5% cross-linking agent is present during the radical polymerization. A wide range of studies on the dependence of mechanical properties on the concentration of cross-linking agents has been performed on hydrogels [56]. Poly (acrylic acid) (PAA) based copolymers hydrogel have been shown to have small-scale heterogeneities [57], which were found to increase as the amount of cross-linking agent was increased. Though the material strength increases as the amount of cross-linking agent increases in these polymerizations, the heterogeneities do result in a reduction in the number of cross-links that are formed. Within these heterogeneities, the cross-linking agent forms a large number of cycles that do not contribute significantly to the mechanical strength of the polymer. Different studies have demonstrated that it is possible to significantly enhance material strength with increases in cross-linking agent concentration [58]. However, when the crosslinking density is

altered, changes to properties other than the strength are likely to occur. Diffusivities, and hence release and swelling rates, are likely to be reduced, and the maximum degree of swelling is also likely to decrease. These changes would likely affect the desired properties of the material and should be re-examined as the cross-link density is changed.

2.7.2.2.3. Effects of polymerization conditions

The reaction conditions will dramatically affect the final polymer product that is formed. Considerations with regard to the polymerization reaction are the reaction time, temperature, and amount and type of solvent. The type and amount of solvent used during the polymerization are of particular importance. If a large amount of solvent is used during the polymerization, the cross-linking agent will tend to form cycles rather than cross-links. This change will reduce the effective cross-link density, thus lowering the material strength. When the type of solvent or the nature of the solvent (e.g., pH or ionic strength of aqueous solutions) is altered, the copolymer structure may be changed. Since ionic strength and pH affect the reactivity of monomers differently. It is possible that changes in these conditions would convert the copolymer from random to block or cause significant copolymer compositional changes. In general, monomers will be more reactive in their unionized state or when the high solution ionic strength shields ion-ion interactions. Recent studies on the copolymerization of HEMA and 2- dimethylaminoethylmethacrylate have clearly shown that the relationships between the polymerization conditions and the hydrogel properties exist [59]. The structure and nature of the polymer formed in the presence of a large amount of solvent significantly differ from the polymer formed in bulk polymerization. Other reaction conditions which can be varied include the reaction time and temperature. In the case of photopolymerizations, the light intensity can be varied as well. With all of these parameters, the functional group conversion can be controlled. Increased double-bond conversion lowers the amount of residual soluble fraction and may increase the cross-link density. If hydrogels are to be used without any post-reaction treatments, increasing the double bond conversion can lead to greatly enhanced mechanical strength [59]. Post-reaction treatments can also be quite effective in changing the network structure and material strength. One method of altering the polymer structure is to add a compound that complexes with the monomer/polymer [60]. Another way to alter the structure is to cycle the polymer thermally [61]. This technique involves the successive freezing

and thawing of the polymer. By cycling the polymer in this manner, Young's modulus of the polymer is significantly increased [62], while many of the other properties of the gel remain relatively unchanged.

2.8 References

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CHAPTER-3

Experimental

3.1. MATERIALS & INSTRUMENTS

Chemicals and reagents

The main chemicals and materials for the synthesis of Ni-Cellulose cross-linked PAA hydrogels are listed below with the name of origin:

- Nickel chloride hexahydrate (Sigma Aldrich Chemical Co. Germany)
- Hydrazine hydrate (Merck, Germany)
- Sodium hydroxide (Merck, Germany)
- Sodium Carboxymethyl cellulose (Merck, Germany)
- Acrylic acid (Sigma Aldrich Chemical Co. Germany)
- Potassium persulfate (BDH, Turkey)
- Ethanol (Merck, Germany)
- *N, N'*-Methylene bis(acrylamide) (MBA) (Sigma Aldrich Chemical Co. Germany)

Instruments

Synthesis, characterization, and data analysis were performed by using the following instruments:

- Fourier transform infrared spectrophotometer (Shimadzu FTIR-8400)
- Field emission scanning electron microscope (JSM-7600F, Tokyo, Japan)
- Energy-dispersive X-ray spectroscope (JSM-7600F, Tokyo, Japan)
- Thermo-gravimetric analyzer (Netzsch, 449F3)
- Universal testing machine (Testresourses, 100P250-12 System)
- Centrifuge machine (Hettich, Universal 16A)
- Freeze dryer (Heto FD3)
- Drying Oven (Lab Tech, LDO-030E)
- Vacuum drying oven (HYSC, VO-27)
- Ultrasonicator (Powersonic 603)
- Digital Balance (AB 265/S/SACT METTLER, Toleto, Switzerland)
- Hot plate & magnetic stirrer (Snidjers, 34532)
- Gauss meter (Lakeshore 421)

3.2. Preparation of Ni nanoparticle

$NiCl_2.6H_2O$ was the source materials. The reaction solution was prepared by dissolving $NiCl_2.6H_2O$ in distilled water. With vigorous stirring, 80% $N_2H_4.H_2O$ was added into the solution instantaneously, which resulted in a pale violet precipitate. The precipitate on the wall was washed with additional distilled water. The solution temperature was increased to 80°C. A Ni complex was formed between $NiCl_2$ and N_2H_4. After the complex formation 50 wt%, NaOH solution was added. The complex was turned into a black precipitate of Ni nanoparticles. The black Ni precipitate was washed six times with distilled water and dried at room temperature for 16h under constant ventilation [1,2].

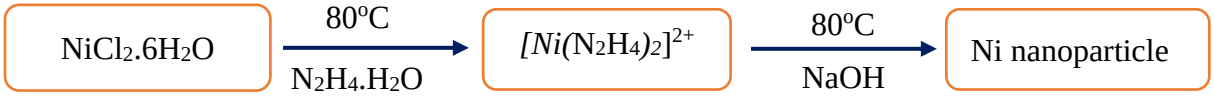

Fig. 3.2.2: Schematic diagram of the preparation of Ni nanoparticle

3.3. Preparation Ni-Cellulose nanocomposite

Firstly, Urea and 50% NaOH Solution will be mixed, and Ni nanoparticles will be dissolved. This solution will be stirred for 15 mins and kept in freeze at -12°C for 1 hour. After that CMC will be added and stirred again for 15mins, then kept in a freeze at -12°C for 1 hour. Ni-Cellulose will be synthesized [3,4].

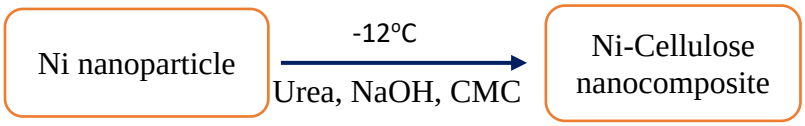

Fig. 3.3.1: Schematic diagram of the preparation of Ni-Cellulose nanocomposite

3.4. Preparation of poly PAA-Ni- hydrogels

The cross-linked PAA composite hydrogels were prepared using initial solutions consisting of monomer, AA); cross-linker, Ni; initiator, KPS. 2 mL of AA monomer (density = 1.008 g mL^{-1}) was taken in a test tube. A previously specified amount of Ni was mixed with it and left stirring for about 30 min [5,6]. During stirring, a specific weight of KPS was added in 1 mL of DI water in another test tube and sonicated for 30 min. The initiator was transferred to AA-Ni solution under vigorous stirring. After nitrogen gas bubbling, the total solution mixture was poured into a glass mold consisting of two parallel glass plates separated by 2 mm silicone spacers. The sample was heated at 56 °C for 8 h for polymerization. After the polymerization, prepared hydrogels were taken off the glass plates and stored for further studies of mechanical properties and swelling behavior. The whole process is illustrated below:

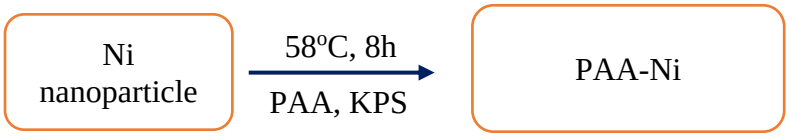

Fig. 3.4.1: Schematic Diagram of preparation of PAA-Ni hydrogel

3.5. Preparation of PAA-Ni-Cellulose Hydrogel

The Ni-Cellulose cross-linked PAA composite hydrogels are prepared using several steps. The Ni-Cellulose cross-linker was prepared from Ni nanoparticles and CMC and then incorporated into the PAA hydrogel matrix. The whole process is illustrated below:

Fig. 3.5.1: Schematic diagram of preparation of PAA-Ni-Cellulose hydrogel

Table 3.5.1.1**:** Compositions of prepared Hydrogels

Types of hydrogels	Concentration of monomer (M)	Amount of cross-linker (mass% with respect to AA)
PAA-Ni	6	0.20
PAA-Ni	6	0.30
PAA-Ni	6	0.35
PAA-Ni	6	0.40
PAA-Ni	6	0.50
PAA-Ni-Cellulose	6	0.20
PAA-Ni-Cellulose	6	0.30
PAA-Ni-Cellulose	6	0.35
PAA-Ni-Cellulose	6	0.40
PAA-Ni-Cellulose	6	0.50

3.6. Study of swelling kinetics of PAA-Ni hydrogels

Specific sized of hydrogel was placed in a 250 mL beaker and 150 mL of distilled water was added. The swollen sample was removed from water and weighed after blotting off the remaining water on the sample surface with filter paper. The swelling ratio was defined as the weight ratio of the net liquid uptake to the dried hydrogel. The swelling ratio was determined by the following equation [7,8]:

$$\text{Swelling ratio} = \frac{m_s - m_d}{m_d} \times 100$$

Where, m_s is the mass of swollen hydrogel in equilibrium at a given temperature and m_d is the mass of dry sample.

3.7. Mechanical properties analysis PAA-Ni-Cellulose hydrogels

All hydrogels were prepared in rectangle shapes with 10mm × 5mm × 2mm ($l \times w \times t$) before the tensile measurement was conducted. The tensile measurement was performed on a UTM at ambient temperature, with a crosshead speed of 100 $mmmin^{-1}$. The stress and strain were recorded. The stress (σ) was calculated according to the equation [9],

$$\sigma = F/A$$

Where F is the recorded load and A is the original area of the specimen.
The strain (ε) was calculated from the change of the fracture length (l) to the initial gauge length (l_0) of the measured sample, and was calculated by the equation [10],

$$\varepsilon = l / l_0$$

The initial modulus was calculated as the initial slope of the stress-strain curve. The fracture toughness was calculated by integrating the area underneath the stress-strain curve of each sample.

3.8. References

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CHAPTER-4

Results and Discussion

4.1. Preparation and characterization of Ni nanoparticle

The nickel nano particles were characterized by Fourier transform infrared spectrophotometer FTIR (Shimadzu FTIR-8400). The particle size and morphology were tested with a Field emission scanning electron microscope (JSM-7600F, Tokyo, Japan). The magnetic properties were measured by Gaussmeter (Lakeshore 421).

4.1.1. FTIR Analysis of Ni nanoparticle

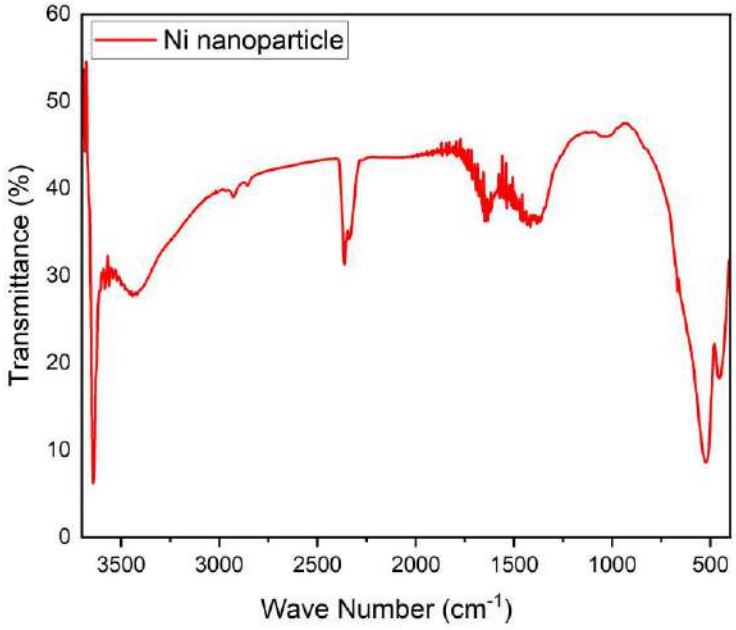


Fig. 4.1.1.1: FTIR of Ni nanoparticle

FTIR spectroscopy is used to study the interaction chemical composition of the mixture. The figure shows the IR spectra of Ni nanoparticles recorded in the range of 400-4000 cm^{-1}. The IR spectrum of Ni nanoparticles covers an absorption band at 3600 cm^{-1}, 3300 cm^{-1}, 2275 cm^{-1}, 1633 cm^{-1}, 1403 cm^{-1}, 1076 cm^{-1}, and 465 cm^{-1} which refers to N-H stretching, O-H stretching, cross-linked C=O asymmetric stretching, stretching vibration of CHO group, C-H bending, C-O stretching, and Ni-O stretching, respectively [1].

4.1.2. FESEM of Ni nanoparticle

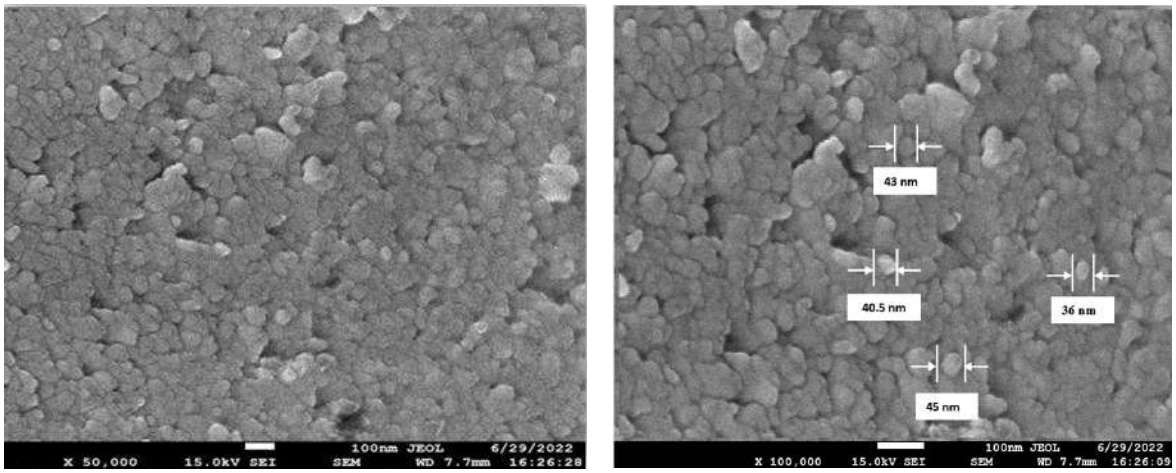


Fig. 4.1.2.1: Field emission scanning electron microscopy of Ni nanoparticle

Field emission scanning electron microscopy (FESEM) was used to analyze the morphology and surface microstructure of Ni nanoparticle. Surface morphology of Ni nanoparticle shows that the shape of particles is spherical and average diameter is 48 nm [2].

4.2. Preparation and characterization of Ni-Cellulose nanocomposite

The Ni-cellulose nano composite were characterized by Fourier transform infrared spectrophotometer FTIR. The particle size and morphology were tested with Field emission scanning electron microscope. The magnetic properties were measured by Gaussmeter.

4.2.1. FESEM of Nickel-cellulose nanocomposite

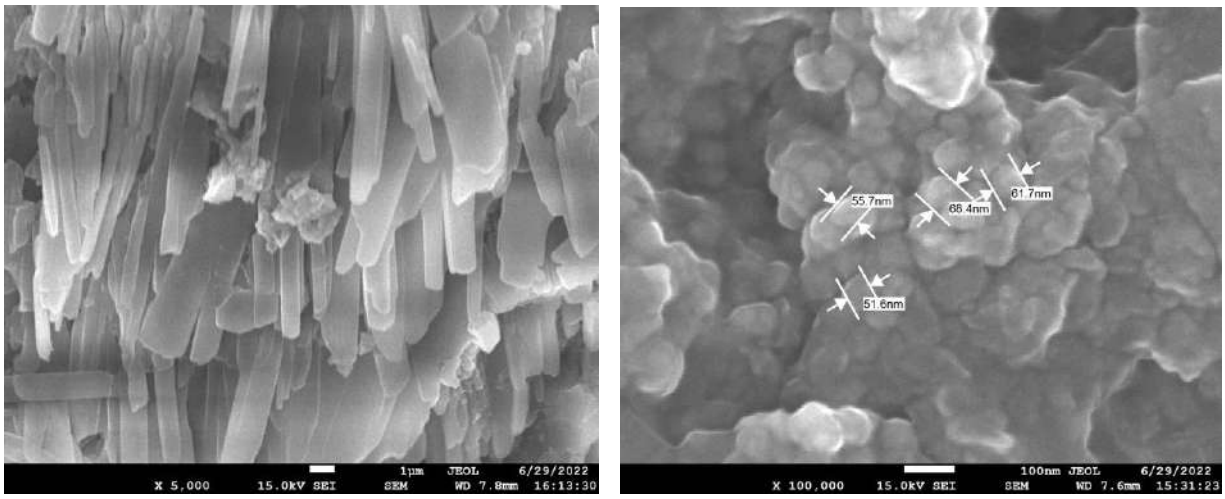


Fig. 4.2.1.1: Field emission scanning electron microscopy of Ni-Cellulose nanocomposite

Field emission scanning electron microscopy (FESEM) was used to analyze the morphology and surface microstructure of Ni-Cellulose nanocomposite. Surface morphology of Ni-Cellulose nanocomposite shows that the average diameter of Ni-cellulose nanocomposite 60 nm. The size of Ni-cellulose nanocomposite is larger than Ni nanoparticle. This indicates that the Cellulose particles are coated on Ni nanoparticle surface [3].

4.2.2. FTIR spectral analysis of Ni-Cellulose nanocomposite

The Ni-Cellulose cross-linker was prepared from Nickel nanoparticle and Carboxymethylcellulose. Figure 4.4 displays the FT-IR spectra of Ni-cellulose nanocomposite and carboxymethylcellulose.

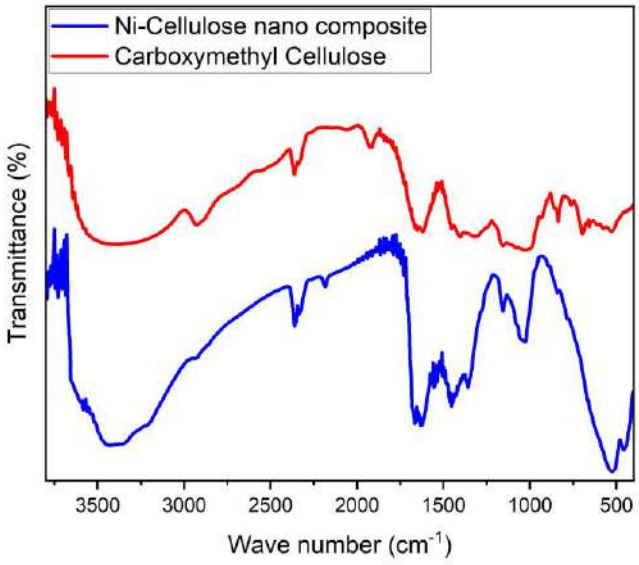


Fig. 4.2.2.1: Comparison of FT-IR spectra Ni-Cellulose nanocomposite and carboxymethylcellulose

Pure carboxymethylcellulose and Ni-Cellulose nanocomposite molecules were comparatively illustrated. The wide band at about 3369 cm^{-1} is related to OH stretching in pure carboxymethylcellulose compounds. This broad band was shifted to a less broad band at 3334 cm^{-1} in the case of the nickel nanoparticle attached with carboxymethylcellulose owing to the formation of a chemical bond on the nickel nanoparticle interface. Furthermore, peaks at 2897, 1650 and 1033 cm^{-1} were attributed to C-H stretching, COO^- (asymmetric) and C–O symmetric stretching, respectively. However, compared with the pure Ni-cellulose nanocomposite powder absorption peaks changed to 2871, 1605 and 1006 $cm^{-1,}$ respectively. These findings confirm that the adsorption of CMC and CMC/Ni NP composites could take place among the free COO- group in the ring of CMC. The O-heteroatoms in CMC has an electron lone pair that may be transmitted to the unoccupied d-orbital of Nickel (chemical adsorption). In addition to the physisorption, chemical adsorption should occur due to the coordinate bonds that may be formed between functional groups in CMC molecules and empty d-orbitals of Ni nanoparticle. FT-IR spectroscopy is very useful for obtaining information about the chemical changes after chemical treatments. A huge difference can be found in the FTIR spectra of CMC after the formation of Ni-cellulose

nanocomposites with Ni nano particle. The peak is related to OH more board in CMC, but it becomes low in intensity in Ni-cellulose nanocomposite. In addition, the characteristic peaks for Ni-Cellulose nanocomposite at 457.21 cm^{-1} have been assigned to Ni–O vibrations [3].

4.2.3. Thermogravimetric Analysis of CMC and Ni-Cellulose nanocomposite

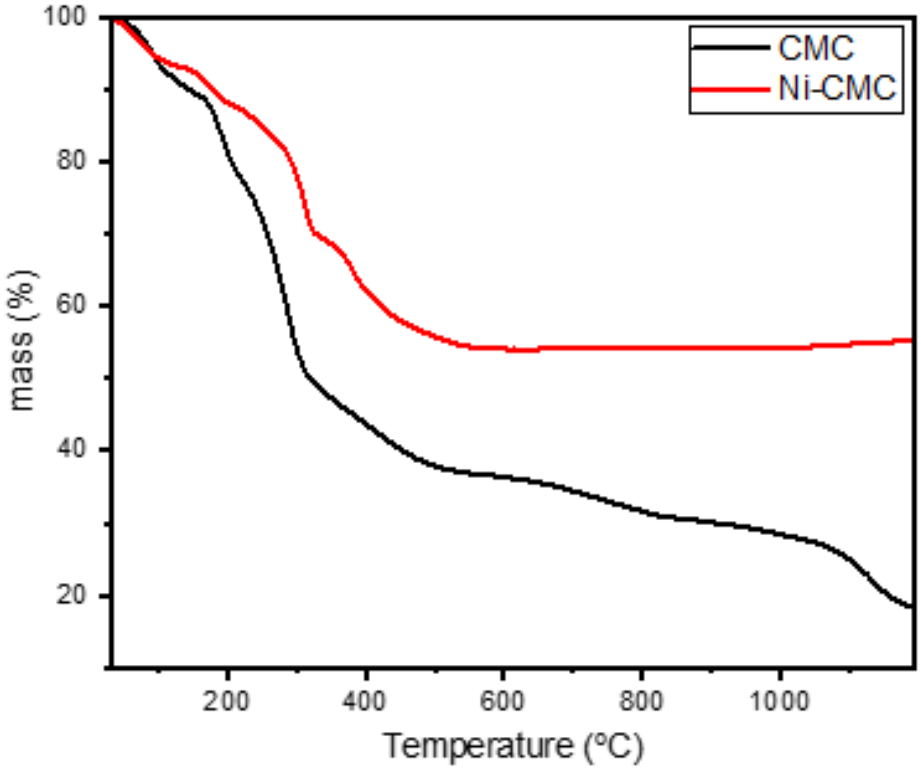


Fig. 4.2.3.1: TGA Curve of CMC and Ni-Cellulose nanocomposite

Carboxymethylcellulose losses its 81% initial mass within 1200°C and Ni- cellulose nanocomposite losses it's only 46% initial mass within 1200°C that indicates Ni-Cellulose nanocomposite is thermally more stable than carboxymethyl cellulose.

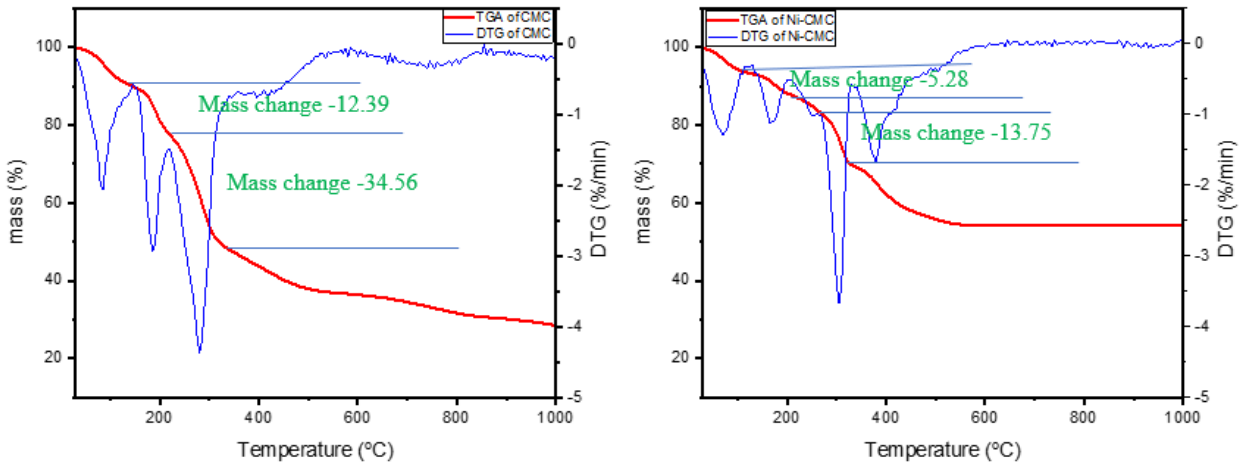


Fig. 4.2.3.2: TGA & DTGA Curve of CMC and Ni-Cellulose nanocomposite

DTGA curve refers that the major weight loss points of carboxymethylcellulose is three. First one is at 90°C for moisture and H_2O removal second one is at 200°C due to CO_2 removal from $-COO^-$ of carboxymethylcellulose, and the third one is at 300°C due to C-O-C breakdown from carboxymethylcellulose.[4] On the other hand, Ni-Cellulose nanocomposite has five major weight loss point. First one is at 90°C for moisture and H_2O removal second one is at 200°C due to CO_2 removal from $-COO^-$, the third one is at 250°C for most probably breakdown of electrostatic interactions between Ni^{2+} and COO^-, the Fourth one is at 300°C due to C-O-C breakdown and the fifth one is at 400°C for most probably Ni-O coordination interaction breakdown. Carboxy methyl cellulose losses its 12.39% mass at 200°C temperature due to CO_2 removal from $-COO^-$ group but Ni-Cellulose losses only 5.28% of its initial mass at 200°C due to CO_2 Removal from $-COO^-$ group that indicates a large amount of COO^- are already involved electrostatic interactions with Ni^{2+}. Carboxy methyl cellulose losses its 34.56% mass at 300°C temperature due to C-O-C breakdown but Ni-Cellulose losses only 13.75% of its initial mass at 300°C due to C-O-C breakdown that indicates a large amount of O atoms of C-O-C are already involve Coordination bonding interactions with Ni^{2+}. According to provided data, it can be confirmed that Ni is attached to carboxymethylcellulose and we have successfully synthesize Ni-Cellulose nano-composite.

4.2.4. Magnetic properties of Ni nanoparticle and Ni-Cellulose nanocomposite

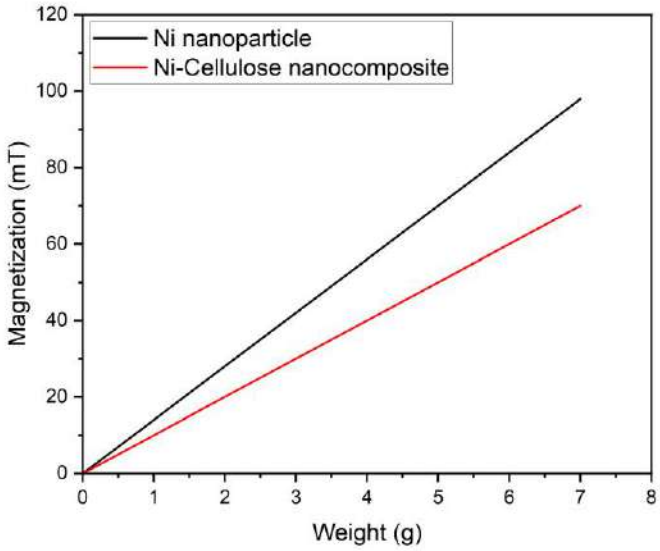


Fig. 4.2.4.1: Comparison of Magnetization of Ni-Cellulose nanocomposite and carboxymethylcellulose

Magnetic properties were measured with a gaussmeter named lakeshore gaussmeter 421. The magnetization of Ni nanoparticle and Ni-cellulose nanocomposite is $14mTg^{-1}$ and $10mTg^{-1}$ respectively. Ni-Cellulose nanocomposite shows less magnetization than Ni nanoparticle due to coordination bond between Ni and O atom of Cellulose. After formation of coordination bond, number of lone pair election decrease from the d-orbital of Ni and decrease the magnetic moment. The comparative magnetization curve indicates that cellulose is attached to Ni nanoparticles [5].

4.3. Mechanical properties of PAA-Ni and PAA-Ni-Cellulose hydrogels

Tensile measurements were conducted systematically to investigate the influence of the simultaneous presence of Ni nanoparticle and Ni-Cellulose nanocomposite cross-linker on the mechanical behavior of PAA hydrogels. The tensile stress-strain curves of PAA-Ni hydrogels at different concentrations of Ni nanoparticles are compared in Figure 4.3.1.1.

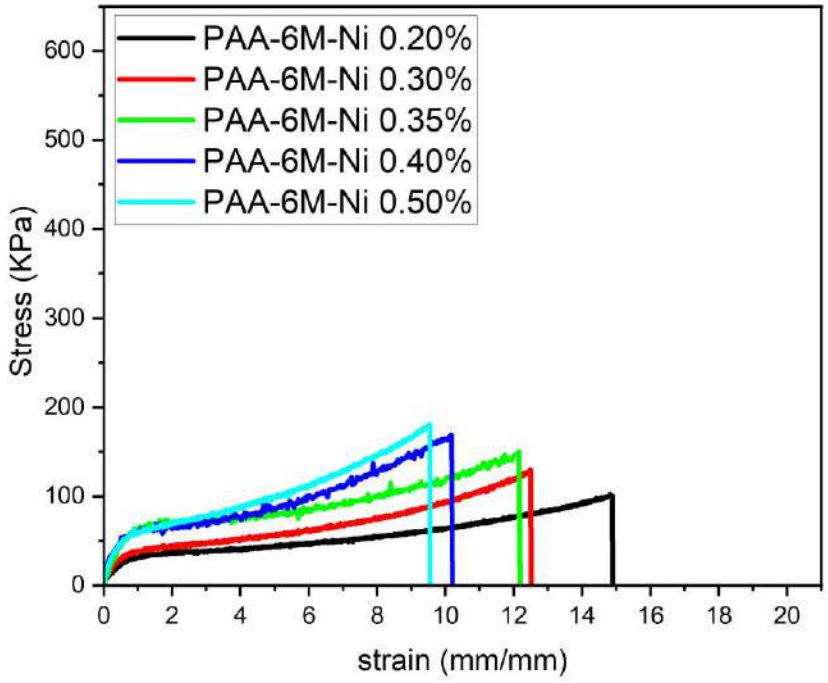


Fig. 4.3.1.1: Stress-strain curves of PAA-Ni hydrogels with different concentrations

Incorporation of Ni nanoparticle to the PAA hydrogels improved the mechanical toughness significantly till 0.35% of Ni nanoparticle. Further increase in Ni nanoparticle decreased mechanical toughness. PAA-Ni hydrogel show 833kJmole^{-1}, 854 kJmole^{-1}, 1104 kJmole^{-1}, 973 kJmole^{-1}, and 971 kJmole^{-1} for incorporation of Ni nanoparticle 0.20%,0.30%,0.35%, 0.40%, 0.50% respectively.

Table: 4.3.1.2.1: Mechanical characteristic data of as-prepared composite hydrogel

% Of Crosslinker	Properties							
	Tensile strength (kPa)		**Elongation at break (%)**		**Mechanical Toughness ($kJmole^{-1}$)**		**Young's modulus (kPa)**	
Hydrogels	PAA-Ni (6M)	PAA-Ni-CE (6M)	PAA-Ni (6M)	PAA-Ni-CE (6M)	PAA-Ni (6M)	PAA-Ni-CE (6M)	PAA-Ni (6M)	PAA-Ni-CE (6M)
0.20%	102	165	1488	1745	833	1780	37	42
0.30%	130	175	1250	1496	854	1960	47	68
0.35%	150	315	1215	1291	1104	2297	61	107
0.40%	169	350	1017	664	973	1680	89	155
0.50%	180	425	954	492	971	1666	108	194

The tensile stress-strain curves of PAA-Ni-Cellulose composite hydrogels at different concentrations of Ni-Cellulose nanocomposite are compared in Figure 4.3.1.2. Incorporation of Ni-Cellulose nanocomposite into the PAA hydrogels improved the mechanical toughness significantly till 0.35% of Ni nanocomposite. Further increase in Ni-Cellulose nanocomposite decreased mechanical toughness. PAA-Ni-cellulose hydrogel show 1780$kJmole^{-1}$, 1960 $kJmole^{-1}$, 2297 $kJmole^{-1}$, 1680 $kJmole^{-1}$, and 1666 $kJmole^{-1}$ for incorporation of Ni-cellulose nanocomposite 0.20%,0.30%,0.35%, 0.40%, 0.50% respectively.

Ni nanoparticle and Ni-Cellulose nanocomposite incorporated hydrogel follow the same trend of change in mechanical toughness. Ni-Cellulose nanocomposite increases toughness significantly higher than increasing same amounts of Ni nanoparticle.

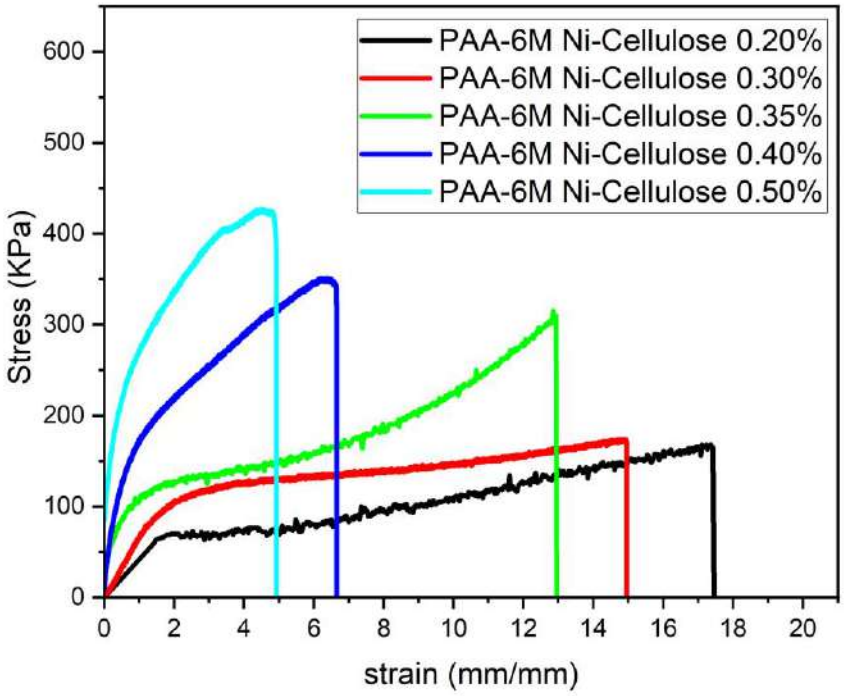


Fig. 4.3.1.2: Stress-strain curves of PAA-Ni-Cellulose hydrogels with different concentrations

The Young's modulus, tensile strength, and toughness of the hydrogels were evaluated from the stress-strain curves. Incorporation of Ni nanoparticle to the PAA hydrogels exhibited higher Young's modulus and tensile strength, by increasing the amount of Ni nanoparticles. While using Ni-cellulose nanocomposite as a crosslinker in PAA hydrogel, Young's modulus and tensile strength increased significantly. Incorporation of more crosslinker increase bond density in polymer chain that is responsible for increasing Young's modulus and tensile strength.

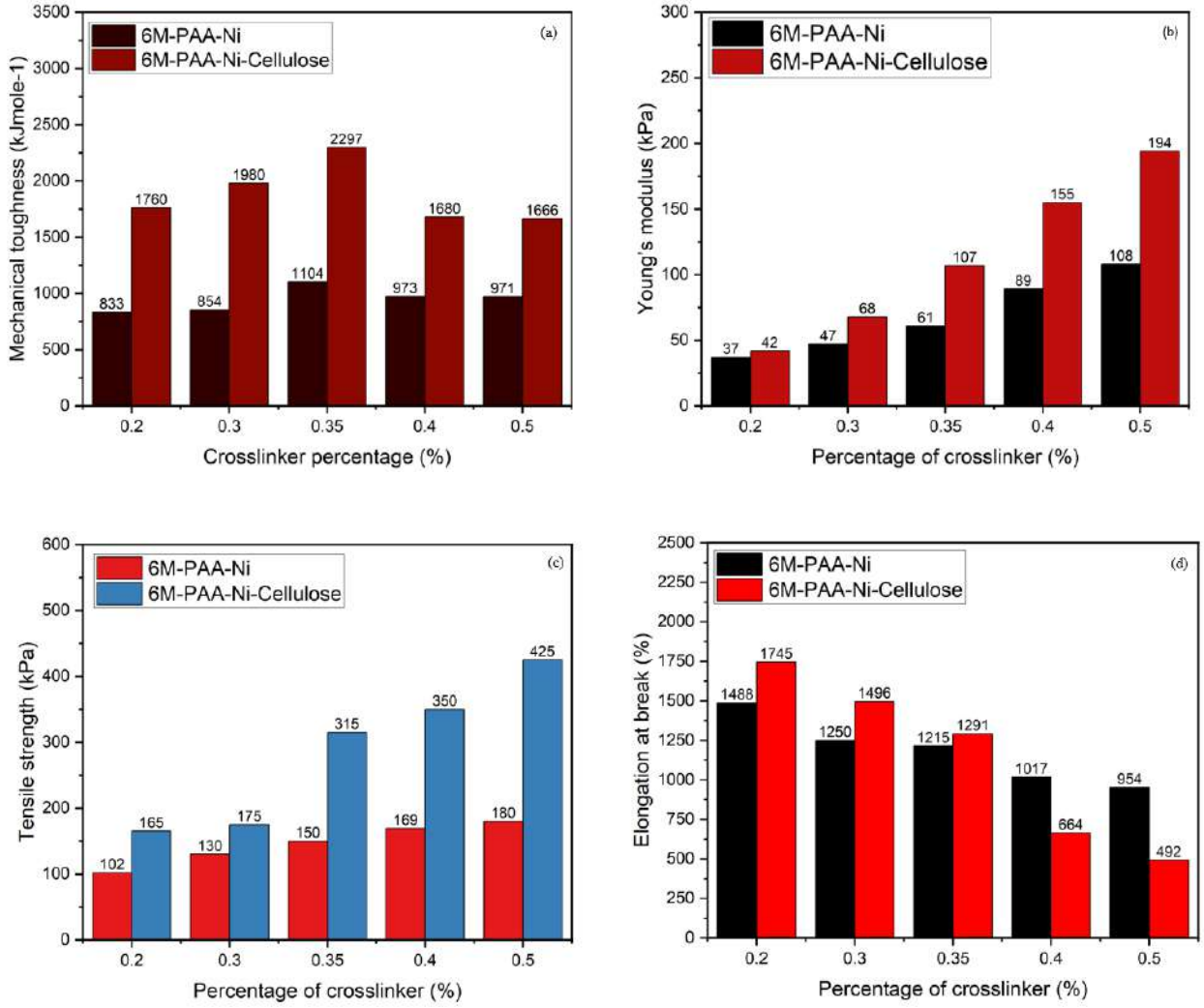


Fig. 4.3.1.3: Comparison of different properties of PAA-Ni and PAA-Ni-Cellulose hydrogel (a)mechanical toughness (b) Young's modulus (c) Tensile strength and (d) Elongation at break

Both Ni nanoparticle and Ni-Cellulose nanocomposite incorporated hydrogel follow same type of decreasing trend of elongation of hydrogel at breaking point. Incorporation of more crosslinker increase bond density in polymer chain that is responsible for make hydrogel more tough and decrease the elongation.

The presence of Ni-Cellulose nanocomposite moderately improved the toughness of PAA hydrogels till 0.35% crosslinker.

4.3.1. Comparison of mechanical properties between Ni-Cellulose and other Crosslinker

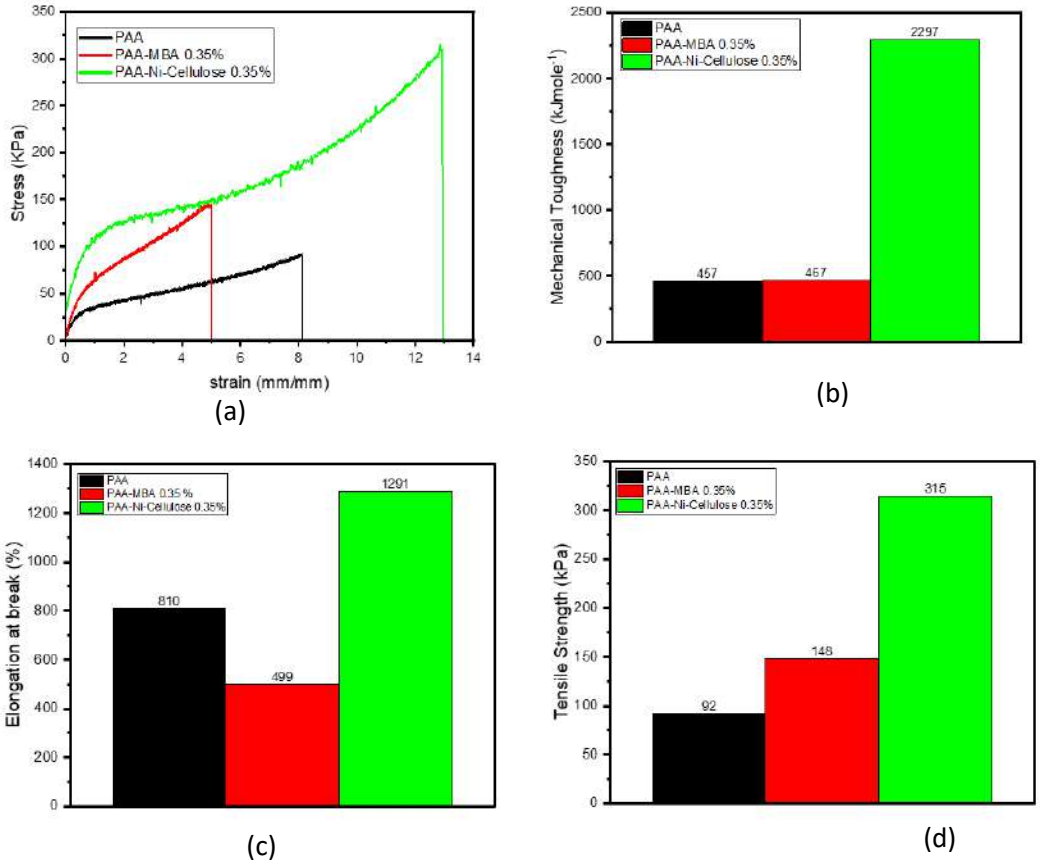


Fig. 4.3.1.4: Comparison of mechanical properties with another Crosslinker

The incorporation of synthetic crosslinkers like MBA for the formation of an integrated polymer network by making numerous covalent crosslinking points is a general trend to improve the mechanical properties of hydrogels [6]. Ni-Cellulose crosslinker showed better mechanical property than *MBA*. Incorporation of MBA showed good improvement in stress and Young's modulus but cannot enhance toughness similarly because of lower elongation. Ni-Cellulose show significant improvement in mechanical properties. Enhancement of mechanical properties of various kinds of hydrogels through the incorporation of Ni-cellulose nanocomposite will certainly improve the biodegradability and biocompatibility of the material and expand the practical applications of hydrogels in biomedical engineering, especially for the development of artificial tissues and organs.

4.4. Magnetic properties

4.4.1. Magnetic properties of Ni nanoparticle and Ni-cellulose nanocomposite

Magnetic properties were measured with a gaussmeter named lakeshore gaussmeter 421. The magnetization of Ni nanoparticle and Ni-cellulose nanocomposite is $14mTg^{-1}$ and $10mTg^{-1}$ respectively.

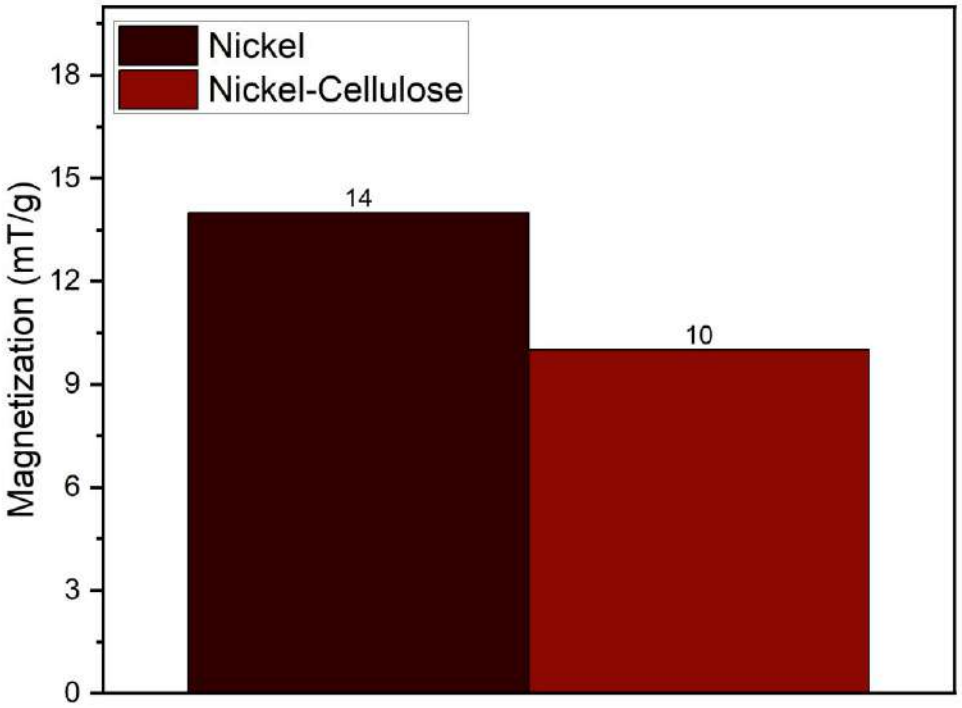
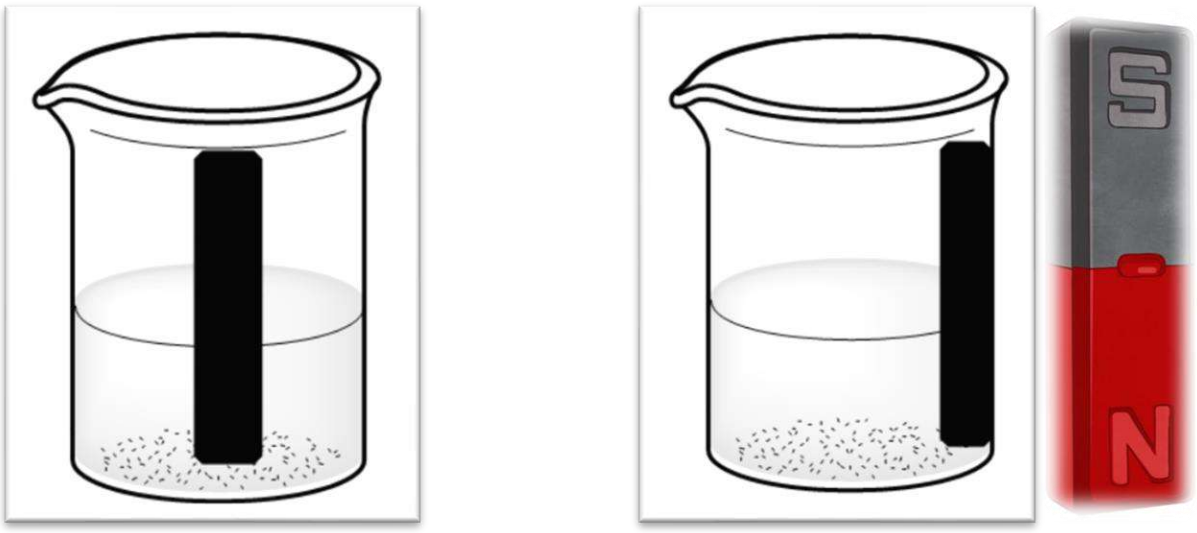


Fig. 4.4.1.1: Comparison of Magnetization of Ni nanoparticle and Ni-Cellulose nanocomposite

Ni-Cellulose nanocomposite shows less magnetization than Ni nanoparticle due to coordination bond between Ni and O atom of Cellulose. After the formation of coordination bond, number of lone pair election decrease from d-orbital of Ni and decrease the magnetic moment. The comparative magnetization curve indicates that Cellulose is attached with Ni nanoparticle [5].

4.4.2. Magnetic properties of PAA-Ni and PAA-Ni-cellulose composite hydrogel



In absence of an external magnet In presence of an external magnet

Fig. 4.4.2.1: Magnetic behavior of PAA-Ni and PAA-Ni-Cellulose Hydrogel

Both PAA-Ni and PAA-Ni-cellulose hydrogels attracted toward an external magnet.

Magnetic properties were measured with a gaussmeter named lakeshore gaussmeter 421. The magnetization of PAA-Ni hydrogel and PAA-Ni-cellulose composite hydrogel is $60Tm^{-3}$ and $40Tm^{-3,}$ respectively.

PAA-Ni-Cellulose nanocomposite shows less magnetization than PAA-Ni nanoparticle due to coordination bond between Ni and O atom of Cellulose. After formation of coordination bond, number of lone pair election decrease from d-orbital of Ni and decrease the magnetic moment. The comparative magnetization curve indicates that Cellulose is attached with Ni nanoparticle [5].

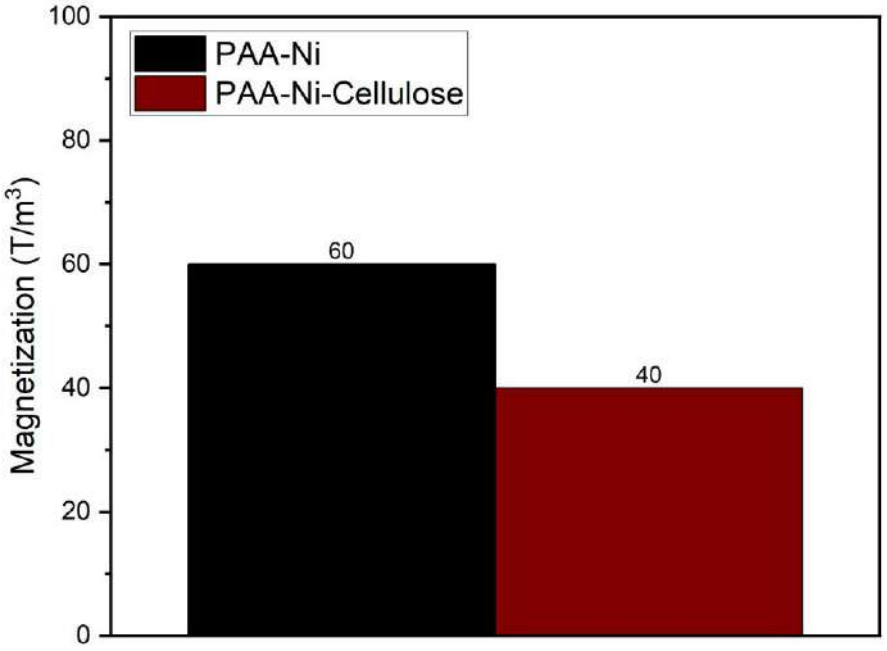


Fig. 4.4.2.2: Comparison of Magnetization of Ni nanoparticle and Ni-Cellulose nanocomposite

4.5. Swelling properties of PAA-Ni and of PAA-Ni-Cellulose composite hydrogels

The cross-linking ability of ferric ions in PAA-GOBC hydrogels was investigated by studying swelling behavior. The swelling kinetics of the PAA nanocomposite hydrogels with different ferric ion concentrations has been shown in **Fig. 4.5.1**.

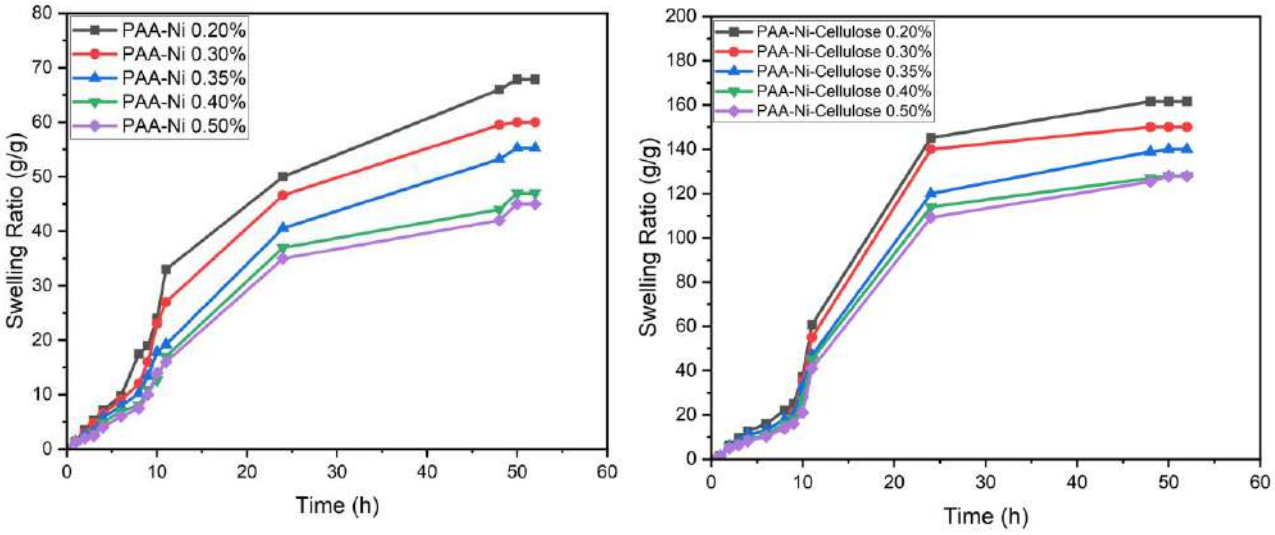


Fig. 4.5.1: Comparison of swelling behavior of as prepared (a) PAA-Ni hydrogels with different concentrations of Ni nanoparticle (b) PAA-Ni hydrogels with different concentrations of Ni-cellulose nanocomposite

The nature of cross-linking and cross-linking density of the hydrogel network plays an important role in the swelling ratio. It has been observed that the PAA hydrogel with Ni nanoparticle absorbs a large amount of water over time. The swelling capacity increased significantly after till 48h. The PAA hydrogels with Ni nanoparticle showed less swelling kinetics. However, when the Ni-cellulose nanocomposite was incorporated into the PAA composite hydrogels, the swelling capacity was found to be increased and swelling ratio was stable after 48h. The addition of Ni-cellulose nanocomposite increased the swelling capacity of PAA hydrogel. Cellulose has great water retention capacity, responsible for increased swelling behavior of all PAA-Ni-cellulose hydrogels.

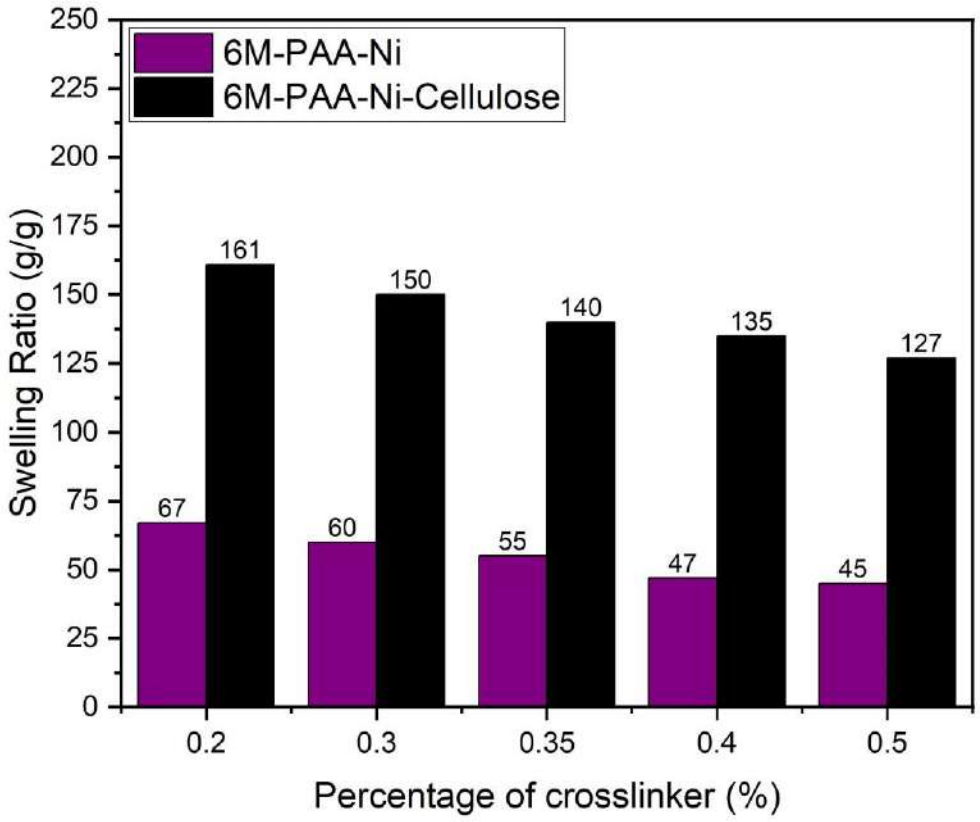


Fig. 4.5.2: Comparison of swelling behavior of PAA-Ni hydrogels with different concentrations of Ni nanoparticle and PAA-Ni-cellulose hydrogels with different concentrations of Ni-cellulose nanocomposite

4.6 Self-healing properties

Using a hybrid network constructed by a combination of reversible physical cross-linking, we have shown that it is possible to significantly enhance the mechanical characteristics of hydrogels while still exhibiting limited self-healing capability. However, generally covalently cross-linked PAA hydrogels cannot repair themselves. The prepared PAA-Ni-Cellulose composite hydrogels have high mechanical properties and exhibit excellent self-healing ability under room temperature conditions. The self-healing ability of the prepared hydrogels was investigated by cutting the

materials into two parts and rejoining them. The joints were kept in contact for a particular time at room temperature. Then, tensile tests were performed to evaluate the healing efficiency. **Figure** 4.6.1 shows the images of original, cut and joined samples (after 24 h).

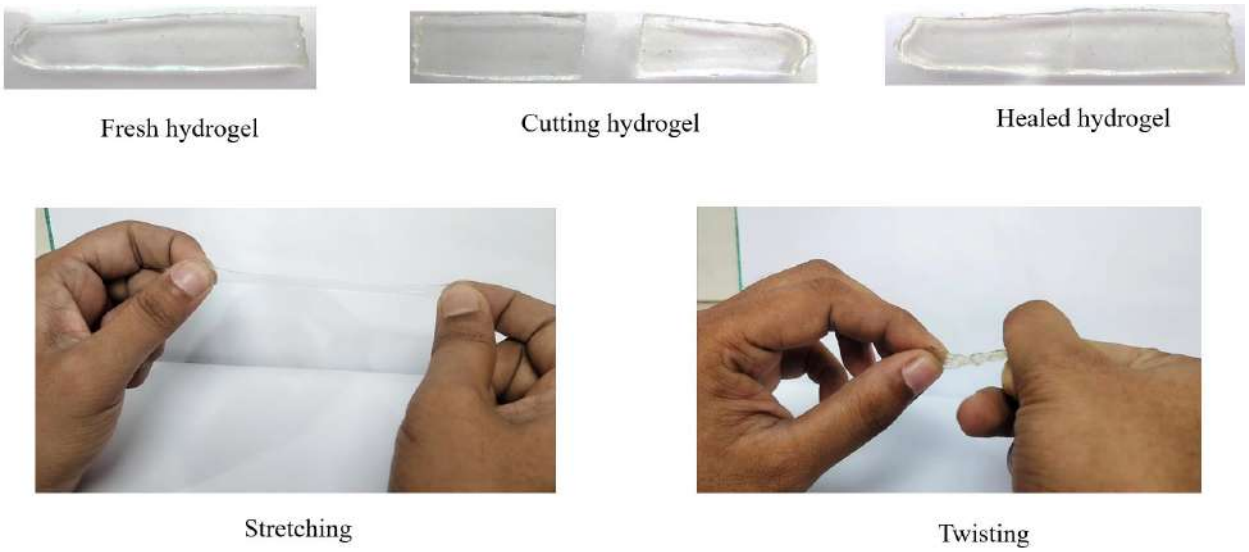


Fig. 4.6.1: Real-time images of PAA-Ni-Cellulose hydrogel's self-healing

It can be observed that the fractured surface is almost unnoticeable in a joined hydrogel. The joined sample is stretchable to a great extent without fracture. The fracture marks almost disappeared at the interfaces between the two adjacent hydrogel sections, and the healed hydrogel could be bent winding and even stretched without breakage**,** exhibiting its excellent self-healing ability. It was also observed that the stretched gel could be kept for a long time without breakage. The comparison of the stress-strain curves of PAA hydrogels with different cross-linker is presented in **Fig.** 4.6.2. The PAA hydrogels containing Ni-Cellulose healed significantly. The mechanical stress, and strain were recovered with time. The level of recovery depends on the amount of Ni-Cellulose present in the hydrogels.

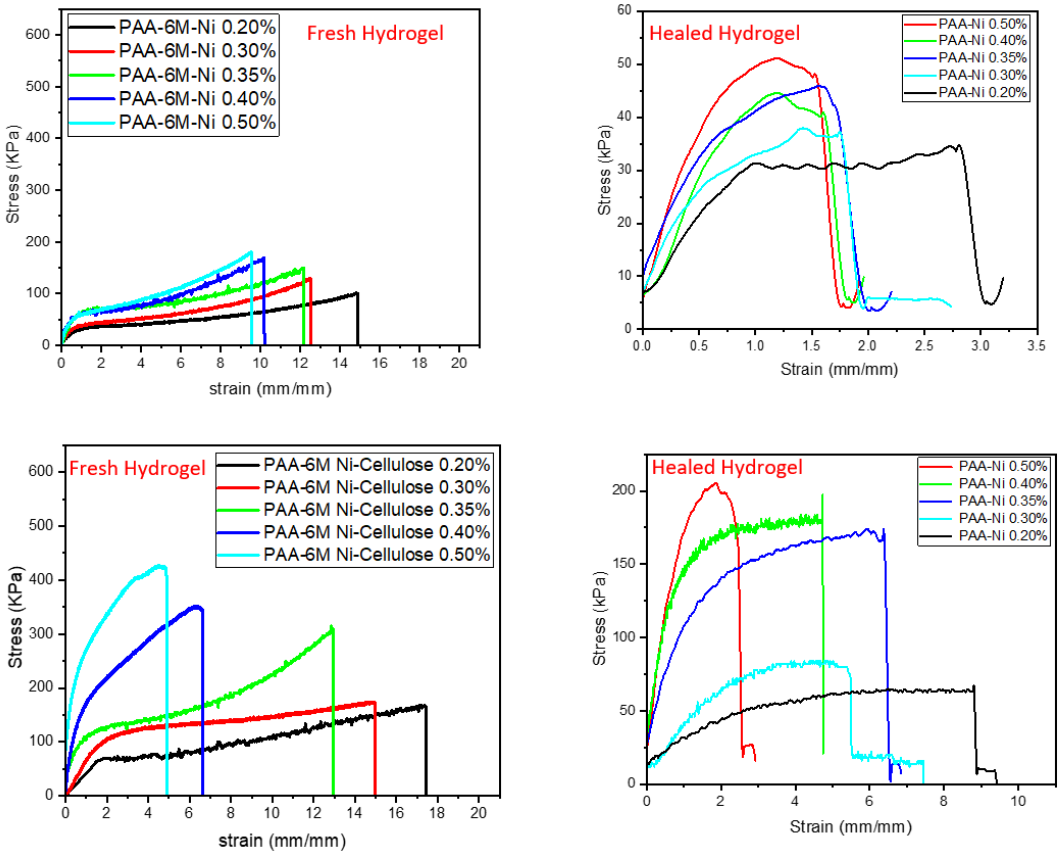


Fig. 4.6.2: Comparison of self-healing efficiency of PAA-Ni and PAA-Ni-Cellulose Composite Hydrogel

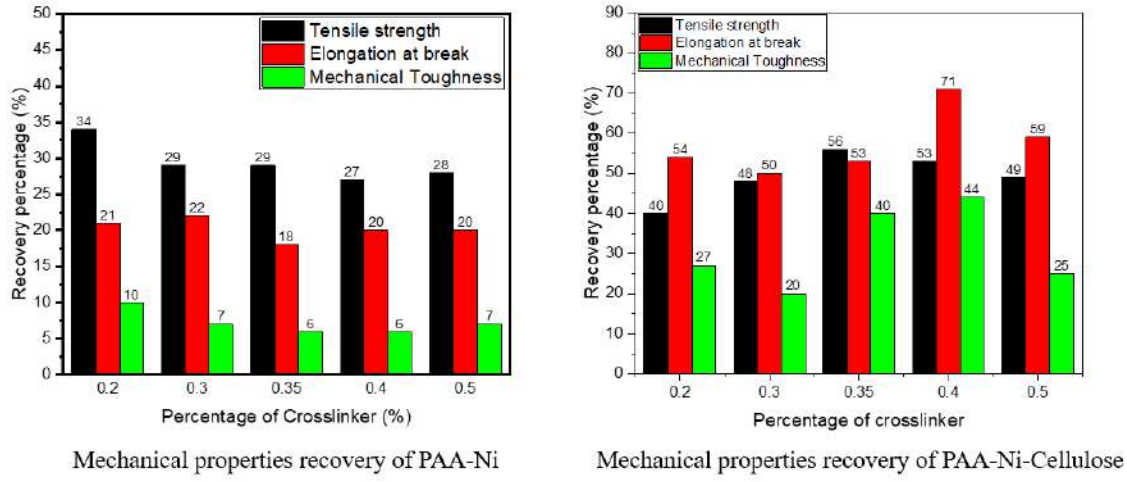


Fig. 4.6.3: Mechanical Properties recovery of Hydrogel with different amounts of crosslinkers

The PAA-Ni-Cellulose 0.35% hydrogels recovered about 56% of its strength within 24 h. It is the highest recovery in 24h among all compositions. The highest recovery of Elongation at break within 24h is 71% that is for 0.4% of Ni-Cellulose. PAA-Ni-cellulose hydrogel show 40, 48, 56, 53 and 49 percent of its strength recovery for 0.20, 0.30, 0.35, 0.40 and 0.50 percent of Ni-Cellulose crosslinker. PAA-Ni-cellulose hydrogel show 54, 50, 53, 71 and 59 percent of its elongation at break recovery for 0.20, 0.30, 0.35, 0.40 and 0.50 percent of Ni-Cellulose crosslinker. The highest recovery of mechanical toughness within 24h is 44% that is for 0.4% of Ni-Cellulose. PAA-Ni-cellulose hydrogel show 27, 20, 40, 44 and 25 percent of its strength recovery for 0.20, 0.30, 0.35, 0.40 and 0.50 percent of Ni-Cellulose crosslinker.

Table: 4.3.1.3.2: Self-healing data of PAA-Ni hydrogel

6M-PAA-Ni	Tensile Strength (kPa)			Elongation at Break (%)			Mechanical Toughness(kJmole^{-1})		
	Fresh	Healed	Recovered percentage	Fresh	Healed	Recovered percentage	Fresh	Healed	Recovered percentage
0.20%	102	35	34%	1488	320	21%	833	83	10%
0.30%	130	38	29%	1250	270	22%	854	59	07%
0.35%	150	44	29%	1215	220	18%	1104	68	06%
0.40%	169	46	27%	1017	200	20%	973	58	6%
0.50%	180	51	28%	954	190	20%	971	67	07%

On the other hand, the highest recovery percentage of tensile strength, elongation at break and toughness are 34, 22 and 10 percent for Ni nanoparticle crosslinker.

Table: 4.3.1.4.3: Self-healing data of PAA-Ni-Cellulose hydrogel

6M-PAA-Ni-Cellulose	Tensile Strength (kPa)			Elongation at Break (%)			Mechanical Toughness(kJmole^{-1})		
	Fresh	Healed	Recovered percentage	Fresh	Healed	Recovered percentage	Fresh	Healed	Recovered percentage
0.20%	165	66	40%	1745	939	54%	1780	472	27%
0.30%	175	84	48%	1496	741	50%	1960	384	20%
0.35%	315	176	56%	1291	683	53%	2297	923	40%
0.40%	350	184	53%	664	471	71%	1680	747	44%
0.50%	425	208	49%	492	292	59%	1666	410	25%

However, the PAA-Ni hydrogel recovered only its ionic interaction or coordination bonds. The recovery of huge amount of hydrogen bonds, coordination bonds, ionic interactions and vender waals interactions enhances the healing capability of PAA-Ni-Cellulose. PAA-Ni composite hydrogel has nominal number of hydrogen bonding sides as a result it exhibited exiguous poor self-healing behavior. This is because Ni nanoparticles are not able to form hydrogen bonds. Ni nanoparticles can make only electrostatic interactions for their surface charge. As a result, it is tough to improve self-healing behavior. The self-healing properties of PAA-Ni-Cellulose hydrogels are mainly attributed to reversible noncovalent bonds in the 3D networks (i.e., hydrogen bonds in the Ni-Cellulose and PAA network and coordination interactions in the PAA and Ni-Cellulose network).

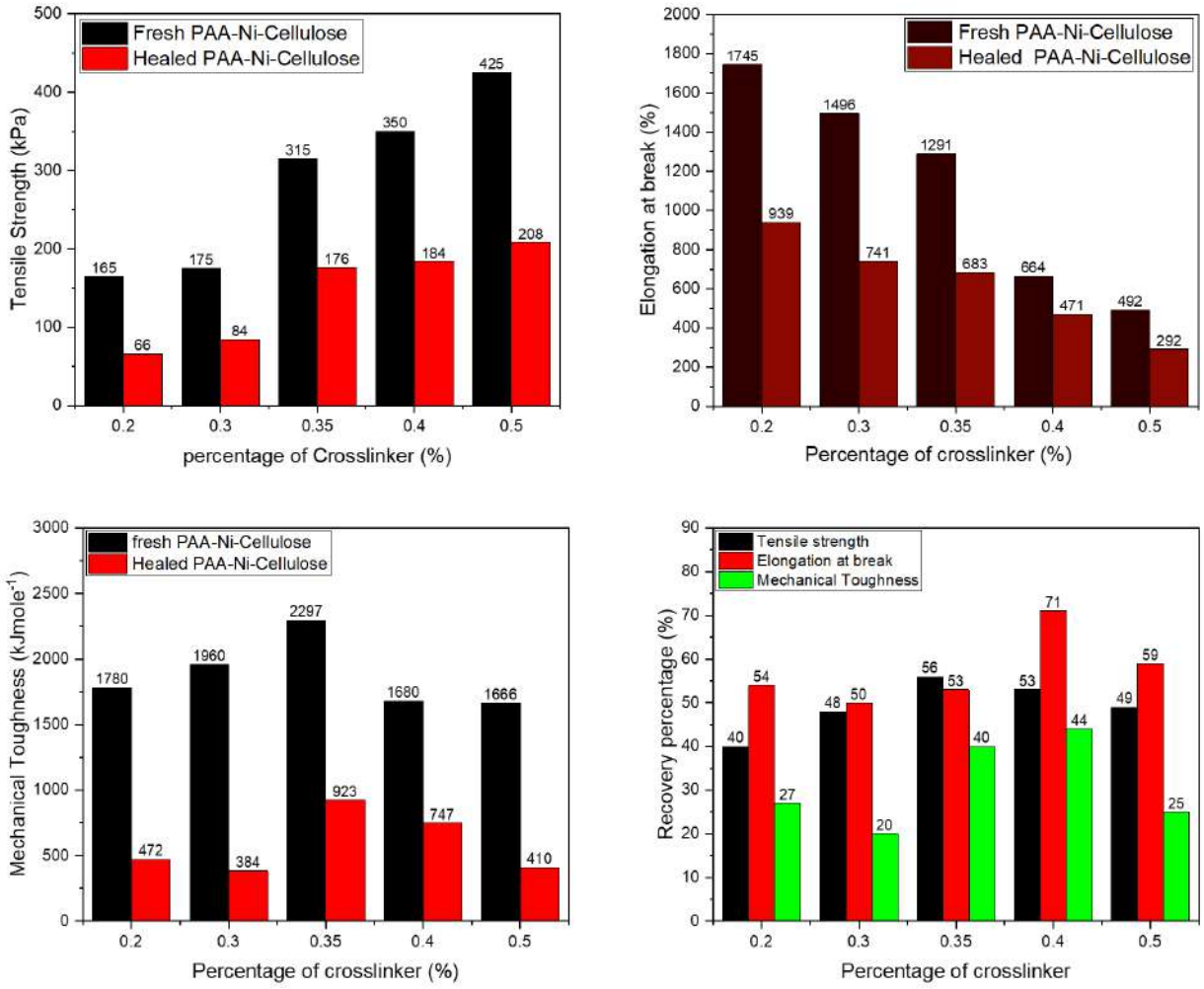


Fig. 4.6.4: Comparison of Tensile strength, Elongation at break and mechanical toughness of Fresh and Healed PAA-Ni-Cellulose Composite Hydrogel and recovery percentage of PAA-Ni-Cellulose composite hydrogels.

The results showed that PAA-Ni-Cellulose hydrogels had better self-healing capability than conventional hydrogels.

A possible mechanism is proposed to explain the self-healing ability of these hydrogels, which is demonstrated in **Fig.** 4.6.4. The self-healing performance of hydrogels mainly depended on the amount of ionic interaction formed between the Nickel ions and PAA chains. The ionic interaction formed is strong and reversible in nature.

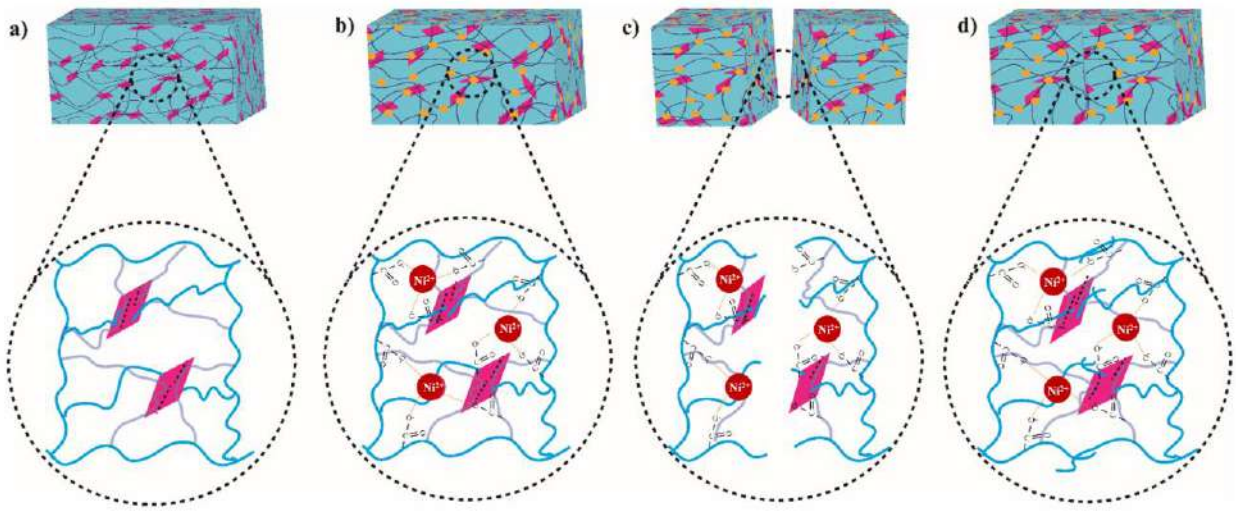


Fig. 4.6.5: Illustration of a possible mechanism of the self-healing process

When the hydrogels are separated by cutting and the damaged regions are put in contact, the nickel ions and COO^{-} groups of PAA are attracted to each other by ionic interaction and forming coordination bonds, contributing to the healing of the fracture. Here it has been observed that the presence of Ni-Cellulose significantly influences the self-healing capability. It can be considered that Ni-Cellulose concentrates the nickel ions over its surface to form strong ionic interactions. Additionally, the Ni-Cellulose provided covalent and hydrogen bonds to regain the original mechanical performance. The hydrogen bonds might also take part in the self-healing process. But due to the few hydrogen bonds, PAA-Ni weakly perform the self-healing. Adding Ni-Cellulose in the polymer matrix of PAA remarkably improved the self-healing performance for the considerable coordination interactions between nickel ion and COO^{-} groups and hydrogen bonds provided by both PAA and Ni-Cellulose nano composite.

4.7. References

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CHAPTER-5

Conclusions

Conclusions

We have successfully developed Ni-Cellulose nanocomposite crosslinker where Ni-nanoparticles contribute to improve mechanical toughness of the hydrogel as well as imparts magnetism into the prepared composite hydrogel. The incorporation of Ni-nanoparticle into cellulose was confirmed using FESEM by comparing the nanoparticle size, and FTIR also showed characteristic peaks for Ni-cellulose nanoparticles. PAA-Ni-cellulose composite hydrogel was prepared using free radical polymerization KPS as the initiator. The effect of the hydrogel's mechanical toughness and self-healing capability was studied by varying the composition of Ni-nanoparticle in the hydrogel. It was found that the hydrogel with lower percentage of Ni-nanoparticle showed better elongation than hydrogels with higher percentage of Ni-nanoparticle. As the percentage of Ni-nanoparticle increases, elongation of the hydrogel decreases while tensile strength increases. The prepared hydrogel also showed significant self-healing capability due to the physical bonding sites offered by the cellulose network. PAA-Ni-cellulose hydrogel showed almost 60% recovery of tensile strength, while the recovery in elongation was more than 70%. Most importantly, the prepared hydrogel showed responsiveness to magnetic field as characterized by Gaussmeter. This responsive nature of the hydrogel and excellent mechanical toughness and self-healing capability, PAA-Ni-cellulose composite hydrogel exhibits the potential to be applicable in several applications, particularly in biosensor, remote controlled drug delivery etc.