Papaya *(Carica Papaya)* Mucilage Based Hydrogel: Synthesis and Characterization

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Submitted by:

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DECLARATION

I Nishtha, 2K21/MSCCHE/31 student of M. Sc. Chemistry hereby announce that the work introduced in this significant undertaking report entitled "**Papaya *(Carica Papaya)* Mucilage Based Hydrogel: Synthesis and Characterization**" which is submitted by me to the Department of Applied Chemistry, Delhi Technological University, Delhi in partial fulfillment of the requirement for the award of the Master of Science in Chemistry is original and not copied from any source without proper citation. This work has not previously formed the basis for the award of any Degree, Diploma Associateship, Fellowship or other similar title or recognition.

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CERTIFICATE

This is to ensure that the work introduced in this significant task report entitled "**Papaya *(Carica Papaya)* Mucilage Based Hydrogel: Synthesis and Characterization**" which is submitted by **Nishtha (2K21/MSCCHE/31)** Department of Applied Chemistry, Delhi Technological University, Delhi in partial fulfillment of the requirement for the award of the degree **Masters of Science**, is a record of the project word carried out by student under my supervision. It is additionally confirmed that the work typified in this report has neither in part nor completely submitted to some other college or foundation for the honor of any degree or confirmation.

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DATE: MAY 2023 **(SUPERVISOR)**

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ABSTRACT

The aim of this study is to synthesize and characterize citric acid crosslinked *Carica papaya* seed mucilage-based hydrogel film. The mucilage and hydrogel film were characterized using Attenuated total reflectance- Fourier transform infrared spectroscopy (ATR-FTIR), thermogravimetric analysis (TGA), x-ray diffraction (XRD), scanning electron microscope (SEM), ^{1}H and ^{13}C- nuclear magnetic resonance (^{1}H and ^{13}C- NMR). The results of ATR-FTIR, TGA and solid state ^{13}C-NMR confirms the formation of ester crosslinking between the mucilage and citric acid.

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ABBREVIATIONS

Table 1. List of abbreviations used

Pm	Papaya seed mucilage
Pm-CAH	Papaya seed mucilage based citric acid hydrogel
CA	Citric acid
NMR	Nuclear Magnetic Resonance
TGA	Thermogravimetric Analysis
FTIR	Fourier-Transformed Infrared spectroscopy
SEM	Scanning Electron Microscopy
XRD	X-Ray Diffraction

1. INTRODUCTION

Hydrogels are referred as three-dimensional cross-linked polymeric networks, which tend to hold an enormous amount of water and swell because of their porous structure. These polymeric materials do not dissolve in water at physiological pH levels and temperatures, instead they remarkably swell in aqueous conditions [1]. Hydrophilic monomers and polymers along with multifunctional cross-linkers are often utilized in copolymerization/cross-linking free-radical polymerizations to create hydrogels [2]. The hydrogels made from natural bio-degradable polymers are preferred more over synthetic polymers due to their cost-effectiveness, bio-degradable and bio-compatible nature [3].

Hydrogels can absorb a significant amount of water, several thousand times their dry weight, to form chemically resistant or biodegradable gels. The properties of hydrogels, including their hydrophilic nature, polymer composition, network density, and structure, determine their absorbency. Hydrogels can be categorized based on factors such as polymer origin, manufacturing technique, ionic charge, size, and physical characteristics. They find applications in various fields, including soft robotics, electronic devices, tissue engineering, drug delivery, biomedical materials, sensors, and neutron shielding. Special hydrogels with unique properties, such as responsive, self-healing, injectable, adhesive, and superabsorbent hydrogels, are particularly noteworthy [4].

Mucilage, is a natural polysaccharide, that combine with water to forms a viscous solution. It is a common plant property with a variety of characteristics, often present around plant structures that come into contact with the environment and serves a variety of purposes, including adhesion and protection [5]. Mucilage is known as a polymeric polysaccharide complex which is mostly composed of carbohydrates with extremely branched structures, such as L-arabinose, D-xylose, D-galactose, galacturonic acid and L-rhamnose monomer units. Additionally, there are glycoproteins and several bioactive substances like tannins, alkaloids, and steroids. Mucilage is a water-soluble edible adhesive substance that contains

uranic acids units in addition to carbohydrates in a variety of plant parts like the mucous epidermis of the outer most layer of seeds, leaves, bark, roots, and buds. Most plant species create mucilage from their seed coat, a process known as myxospermy; however, certain plant species also make it from the fruit epicarp, a process known as myxocarpy. Among the families that make mucilage from seed coats are *Plantaginaceae, Acanthaceae, Linaceae,* and *Brassicaceae,* whereas *Poaceae, Asteraceae*, and *Lamiaceae* produce Myxocarpy i.e. from fruit mucilage[6]. It is a cost- effective, eco- friendly, edible polysaccharide which is mainly composed of carbohydrates having extensively branched structures. Mucilages are used for a variety of purposes, including gelling, film-forming, and texturing in food and nutraceuticals, disintegrants and binders for drug delivery systems in pharmaceuticals, and stabilizers in cosmetics [7].

Papaya (*Carica papaya)*, which belongs to *Caricaceae* family, is a highly commercialized tropical fruits [8]. It is one of the most significant tropical plant cultivated worldwide. The papaya plant has numerous edible and medicinal elements, including roots, leaves, peels, latex, flowers, fruits, and seeds. Despite having medicinal value, papaya seeds are typically thrown during the fruit processing. The seeds make up about 20% of a papaya's fresh mass. Protein, dietary fiber, phytochemicals, antioxidants, and minerals are present in both the seeds and the leaves. Regardless of cultivar, the seeds and leaves contain 16–32% protein. The seeds are nutritious alternative energy sources that could supplement the undernourished population since they include a considerable quantity of lipid (21-30%) and carbohydrate (8-58%) in the seeds and leaves [9].According to studies, a 100 g intake of papaya seeds may include 15%, 60%,120%, 35%, 80%, 80%, 130%, and 70% of the following elements, respectively: K, Cu, Mg, Fe, P, Zn, Mn, and Ca. Dietary fibres are abundant in papaya seeds and peels. Dietary fibres are well known for their ability to decrease cholesterol and eliminate toxins from the digestive system, among other health benefits. Phytochemicals are abundant in papaya seeds. They include beneficial phytochemicals such carotenoids, phytosterols, tocopherols, and phenolics. In general, phytochemicals have a variety of advantageous features, such as the ability to inhibit the growth of cancer cells and to protect against cellular oxidative damage. They also lower the risk of the occurrence of non-communicable diseases

[9]. Papaya seeds include phytochemicals that have nephroprotective, hypolipidemic, and hypoglycemic effects. One of the potential mechanisms responsible for these beneficial properties is the antioxidant action [10].

The hydrogels made from natural polymers can be synthesized through chemical or physical crosslinking. However, physically crosslinked hydrogels are mechanically fragile in nature and the cross-linked structure is susceptible to breakdown in response to variations in environmental variables such temperature, pH, or ionic strength [11]. Therefore, the preferred method for the synthesis of hydrogel is chemical crosslinking. Although, there have been allegations of unsafe crosslinking chemicals being used in the preparation of chemically crosslinked hydrogels, despite the fact that they are resilient. In order to overcome this safety concern, citric acid (CA) can be utilized as a cross-linker.

CA, a safe cross-linking agent for hydrogel synthesis, has gained attention recently. When exposed to high temperatures, CA undergoes a reaction that produces a cyclic anhydride, which then esterifies the hydroxyl groups present in nearby polymer chains. This process leads to the formation of crosslinks within the hydrogel structure. Notably, CA is derived from renewable resources and is primarily produced through the fermentation of carbohydrates, such as starch or glucose. It is also easily accessible and reasonably priced [12]. Moreover, as CA is a metabolic product of human body which is non-toxic in nature and used as a natural food additive in food industry [13].

In the present study, papaya seed mucilage (Pm) was extracted and papaya seed mucilage-based hydrogel films (Pm-CAH) with various formulations using CA as a cross-linking agent were synthesized. Extracted mucilage and Pm-CAH-3 hydrogel film were selected for various characterization like ATR-FTIR, TGA, XRD, SEM, ^{1}H and ^{13}C- NMR and evaluated for swelling study. According to our literature survey, Pm has not been used with CA in hydrogel film preparation to the best of our knowledge.

OBJECTIVES

- Extraction of papaya seed mucilage.
- Synthesize citric acid crosslinked hydrogel film based on extracted mucilage.
- Characterize the extracted mucilage and its hydrogel film.

2. LITERATURE REVIEW

2.1. PAPAYA SEEDS

Figure 2.1. Papaya Seed

Papaya (*Carica papaya*) is a tropical fruit that is available all year long. Around the world, papaya is widely renowned for its remarkable nutritional and therapeutic benefits. *Carica papaya* belongs to the family of *Caricace*ae [14]. The seeds are found to be embedded in the papaya. When the fruit is developing in its immature state, they are pale in color; when the fruit is fully grown, they get darker in color. It has a spherical form, a seed coat covered by an exterior layer known as the sarcotesta, and an inner endosperm. Protein is abundant in the seed pericarp, whereas oil and protein are abundant in the endosperm. Papaya seeds, particularly the sarcotesta, are a great source of amino acids [15]. Despite having therapeutic value, the mature papaya seeds are often discarded during fruit processing and are regarded as a by-product. They make up around 16% of the weight of the fresh fruit. The nutritionists have been urged to use this by-product as a protein-rich feed ingredient as well as a useful feed for poultry due to papaya seed's wide availability throughout the year and low economic worth [16]. There are various degrees of macro- and micronutrient richness in these papaya

sections. For instance, regardless of cultivar, the seeds and leaves contain 16-32% protein. The seeds are high amounts of fat (21-30%), carbohydrate (8-58%), and protein (8-58%), making them suitable as supplementary foods for people that are undernourished. A 100 g serving of papaya seeds may include 15%, 120%, 80%, 130%, 35%, 60%, 80%, and 70% of the following elements, respectively: K, Mg, Zn, Mn, Fe, Cu, P, and Ca, according to studies. Dietary fibers, which are well known for their ability to decrease cholesterol and eliminate toxins from the digestive system, among other health advantages are found in abundance in the papaya seeds and peels. Phytochemicals are abundant in papaya seeds. They include beneficial phytochemicals such carotenoids, phytosterols, tocopherols, and phenolics. In general, phytochemicals have a variety of advantageous features, such as having the ability to prevent cellular oxidative damage and restrain the development of cancer cells. They also lower the risk of the occurrence of non-communicable illnesses [9]. Papaya seeds include phytochemicals that have hypolipidemic and hypoglycemic, hypo-lipidemic, and nephroprotective effects. One of the underlying reasons for these protective benefits may be the papaya seeds' antioxidant activity [10].

2.2. MUCILAGE

Nearly all plants and a substantial number of protists, particularly phytoplankton and green algae, exude mucilage, a material that is sticky and mucus-like. Mostly polysaccharides, proteins, minerals, lipids, and uranic acid units make up this substance's primary components [17]. Because mucilage is naturally occurring, biocompatible, inexpensive, and readily accessible, it is preferable over semi-synthetic and synthetic excipients [18]. Mucilage is a cost-effective, environmentally beneficial, and edible polysaccharide that is mostly taken from living things including bacteria, fungus, plants, animals, and algae. Mucilage possesses exceptional viscosity, water and oil holding ability, and antibacterial action even at low concentrations. Mucilage is a promising component with potential uses as a fat replacement, gel forming, thickening, and emulsifier as a result of these exceptional functional qualities. Mucilage is made up of polysaccharide units of D-galactose, L-rhamnose, D-xylose, and L-arabinose and is a physiological byproduct of plant metabolites. A modest amount of proteins

and organic acids are also present. The source and the kinds of extraction and purification techniques have a significant impact on the physicochemical, functional, and chemical contents of mucilage [6]. In flowering plants, a variety of organs, including seeds, fruits, roots, leaves, and stems, may exude several types of mucilage with cell wall-like compositions, giving an astounding diversity of physical qualities [5]. The majority of plant species produce mucilage from the coating of seed through a process known as myxospermy. However, some species of plants also produce it from the fruit epicarp by a process called myxocarpy. Plants that produce mucilage from their seed coats are members of the *Plantaginaceae, Acanthaceae, Linaceae,* and *Brassicaceae* families, whereas those that produce myxocarpy (mucilage from fruit) are often found in the *Poaceae, Asteraceae,* and *Lamiaceae* families. The mucilage on the seed coat protects the plant against initial seedling development and the effects of drought during germination. Fruit's mucilage, which creates a jelly-like structure, holds onto moisture, prevents seeds from drying up completely, and provides both hydration and energy [6]. One of its outstanding qualities is its ability to thicken and structure (form a gel), which results from the high structure conformational diversity caused by the side groups of the polymer chain interacting with one another intramolecularly via hydrophobic interactions or hydrogen bridges [19].

2.3. HYDROGELS

Hydrogels are known as three-dimensional crosslinked hydrophilic polymer systems that may imbibe huge volumes of water or biological fluids to create aqueous semi-solid/solid gel networks. The hydrogel's polymer networks have an arbitrary lower limit of 10-20% and a maximum water absorption capacity of thousands of times their dry weight. Because hydrophilic groups like –CONH–, $–SO_3H$, $–CONH_2–$ and –OH are present in the polymers creating the hydrogel structures, these materials have a strong affinity for absorbing water. The hydration level of a polymer can vary depending on the properties of the aqueous environment and the composition of the polymer itself. This is influenced by the contributions of different groups and domains within the network. In some cases, the polymer can become hydrated to a significant degree, even exceeding 90% of its weight. In an aqueous

environment, hydrogels prefer to expand rather than dissolve because of the critical crosslinks that make up their structure [20].

The addition of molecules susceptible of creating inclusion complexes, such as cyclodextrins, or the integration of hydrophobic molecules in the hydrogel structure are two of the primary methods for increasing the compatible nature of hydrogels with hydrophobic substances. However, this is not the primary hydrogel type utilized for the delivery of drugs that are poorly water soluble. More complex systems, such as hydrogels having micelles or nanoparticles built into their structure, have been characterized [21].

Benefits of hydrogels [20]

- Biocompatible.
- Can be introduced into a live creature as a liquid that gels at its internal temperature.
- Shielding of cells.
- Timed release of a nutrient or drug
- the ease of customization.
- Good transport capabilities (such as delivering nutrients to cells or cell products from cells).
- Biosorption or biodegradation potential.

Limitations of hydrogel [20]

- Weak mechanical strength,
- high price,
- difficult to handle,
- difficult to load with medications or nutrition,
- possibly challenging to sterilize, and non-adherent.

2.4. CLASSIFICATION OF HYDROGELS

The classification of hydrogels in accordance with the various classification criteria is summarized briefly in **Figure 2.2.**

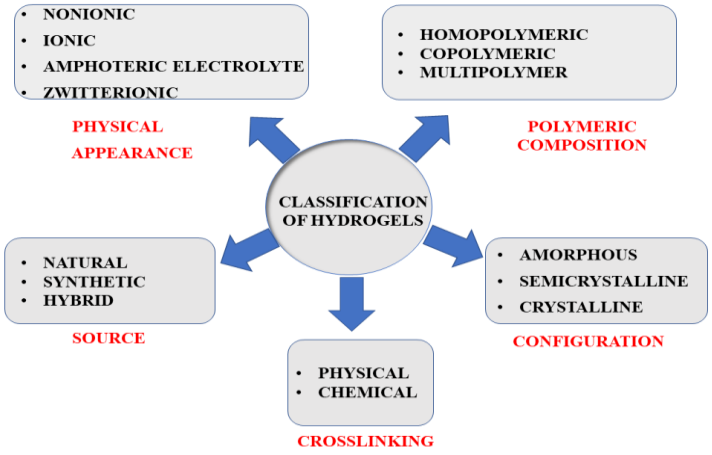

Figure 2.2. Classification of hydrogels.

2.4.1. CLASSIFICATION BASED ON SOURCE

Based on whether they are made of natural or artificial materials, hydrogels may be divided into two categories.

NATURAL HYDROGELS

Natural polymers, which are high molecular weight substances with repeating units that form a long, linear chain as their fundamental structure, are extensively found in plants, animals, and other species. Examples include polypeptide, protein, chitin, alginic acid, starch, agar, and so on [22].

Natural polymers including hyaluronic acid, chitosan, dextran, alginate, and proteins like collagen, gelatin, and fibrin are used to create hydrogels of natural origin. Biodegradable and

supportive of biological function are natural hydrogels. They may have advantages like high biocompatibility, cellular interactions that are natural, biodegradability, and low byproduct toxicity, but they may also have intrinsic disadvantages like insufficient mechanical strength and inflammatory immune responses. The batch-to-batch variability and potential for disease transmission from animal-derived materials are additional downsides of these natural hydrogels [23].

SYNTHETIC HYDROGELS

For the creation of hydrogels, synthetic polymers made from tiny organic monomers have been widely used. Although hydrogels made of synthetic polymers have excellent mechanical and water absorption properties, their low biodegradability and possible toxicity severely restrict their use in biomedicine [22].

Synthetic hydrogels are commonly used when there is a need for higher strength and durability, and they are produced through chemical polymerization techniques. Several components are typically employed in the synthesis of synthetic hydrogels, including polyacrylamide, polyethylene glycol, polyvinyl alcohol, and poly(2-hydroxyethyl methacrylate) [24].

HYBRID HYDROGELS

Hydrogels that are hybrid or nanocomposite mix several molecules from synthetic and organic components. Through better molecular structure and organization, this combination improves the hydrogel's physical, electrical, chemical, and biological characteristics [24].

2.4.2. CLASSIFICATION BASED ON POLYMERIC COMPOSITION

The method of synthesis results in the development of major kinds of hydrogels. These may be shown using the following:

HOMOPOLYMERIC HYDROGELS

Homopolymers are polymer networks that consist of only one type of monomer, serving as the fundamental building block for all polymer networks. The presence of a cross-linked framework in homopolymers depends on the characteristics of the monomer and the technique used for polymerization [3].

COPOLYMERIC HYDROGELS

These hydrogels consist of multiple monomer species, including at least one hydrophilic component, arranged in various patterns along the polymer chain network. These patterns can be block, alternating or random, depending on the specific composition of the hydrogel [25].

MULTIPOLYMER

Interpenetrating polymeric hydrogels (IPN) are a significant class of hydrogels consisting of two different polymer components that are independently cross-linked and constrained within a network structure. One of the components in an IPN hydrogel is a crosslinked polymer, while the other component is a non-crosslinked polymer [25].

2.4.3. CLASSIFICATION BASED ON CONFIGURATION

The following examples show how hydrogels can be categorized based on their physical and chemical composition:

- Crystalline
- Amorphous
- Semicrystalline (A complicated admixture of crystalline and amorphous phases)

2.4.4. CLASSIFICATION BASED ON CROSSLINKING

CHEMICALLY CROSS-LINKED HYDROGELS

Chemically cross-linked hydrogels utilize covalent bonds to connect multiple polymer chains, resulting in a stable network that cannot be dissolved in solvents without breaking the covalent cross-links. This chemical cross-linking imparts a high mechanical strength to the hydrogel and can significantly prolong its degradation process. The degradation duration depends on the specific chemical connections between the constituent components and the cross-links, allowing for control over the degradation rate [26].

PHYSICALLY CROSS-LINKED HYDROGELS

Physically cross-linked hydrogels, also called reversible gels, have gained popularity due to their straightforward manufacturing process and the absence of cross-linking chemicals during synthesis. These gels are held together by physical interactions between polymer strands, ensuring their stability. However, the design flexibility of physically cross-linked hydrogels is somewhat restricted, as it is challenging to precisely control parameters like gelation length, chemical functionalization, internal network pore size, and degradation time [26].

2.4.5. CLASSIFICATION BASED ON PHYSICAL APPEARANCE

A hydrogel's appearance can be described as a matrix, microsphere, or film, depending on the polymerization method utilized during the formation process. Depending on whether or not the crosslinked chains contain an electrical charge, hydrogels may be divided into four types.

(a) Nonionic (don't have any electrical charge).

(b) Ionic, which can be either anionic or cationic.

(c) Amphoteric electrolyte (having both basic and acidic groups).

(d) Zwitterionic (each structurally repeating monomer or unit contains both cationic and anionic groups)

2.5. PROPERTIES OF HYDROGELS

2.5.1. MECHANICAL PROPERTIES

For usage in pharmaceutical and biological applications, hydrogels must have a high mechanical strength. For a variety of reasons, including biomedical applications, tissue engineering, tendon and ligament healing, wound dressing, cartilage replacement, and drug delivery matrix, it is crucial to assess the mechanical strength of hydrogels. The hydrogel must hold onto its physical texture for a predetermined period of time while transporting therapeutic agents.

The mechanical properties of hydrogels can be optimized by adjusting their crosslinking characteristics. Increasing the degree of crosslinking leads to stronger hydrogels, but it also makes them more brittle and less extensible. Therefore, the ideal level of crosslinking is typically chosen to achieve a hydrogel that is moderately elastic and strong [27]. The degree

of crosslinking is a theoretical factor that influences the mechanical properties of hydrogels [28].

2.5.2. BIOCOMPATIBILITY

When developing new materials for medical applications, particularly for internal use, several factors need to be considered. One of the most important characteristics is the biocompatibility of the materials. Biocompatibility refers to the ability of a medical material to coexist in the body without causing any adverse effects. This means that the material should not activate the immune system, harm surrounding tissues or cells, and should remain inert. Hydrogels, due to their structure, consistency and highwater content, often exhibit good biocompatibility with living tissues. To enhance the biocompatibility of hydrogels, it is important to remove any residual harmful ingredients that may be present from the production process.

Biocompatible hydrogels find extensive use in various fields such as regenerative medicine, tissue engineering, wound care, parenteral medication delivery, and the development of cell growth environments. Biomimetics is a closely related concept to biocompatible materials, particularly hydrogels. Biomimetics involves designing and producing devices that mimic the structure of biological entities. In the context of pharmaceutical biomimetics, the goal is to create a drug carrier material that closely resembles a component of the human body. Understanding the intricacies of bodily functions, particularly immunological responses, which heavily influence the future use of pharmacological substances like drug carriers, is of utmost importance [29].

2.5.3. BIODEGRADABILITY

In the biomedical sector, using biodegradable hydrogels is vital. The word "biodegradability" describes how quickly hydrogels may decompose into harmless metabolites. The systems' moieties and the manufacturing process have an impact on how biodegradable hydrogels are. Degradation mechanisms for the biological components of hydrogels include hydrolysis and solubilization in final products. Through bio-absorption and bio-erosion, the hydrogels may break down and leave the body. Biodegradable polymers include several hydrophilic natural and manmade polymers. Polymers with the capability to absorb water undergo a swelling process through diffusion, leading to substantial expansion. As they absorb more water, these polymers can eventually disintegrate. The degradation of such polymers is influenced by multiple factors, including their hydrophilicity, interactions with water, and molecular weight. Environmental conditions such as pH and temperature can also impact the degradation process by affecting the solubility of the polymers. It is important to note that these factors collectively govern the degradation behavior of these polymers [30]. However, it should be noted that the number of biodegradable polymers within this particular class is relatively restricted [31].

2.5.4. SWELLING BEHAVIOR OF HYDROGEL

Hydrogels are versatile materials that can swell in various environments, including aqueous solutions with different pH levels and ionic strengths. They exhibit responsive behavior to factors such as solvent composition, electric fields, light exposure, and temperature changes in both biological and environmental settings. Several variables impact the swelling kinetics and equilibrium of hydrogels, including the crosslinking ratio, polymer composition, ionic environment, and synthesis conditions. The extent of swelling is commonly measured using the swelling ratio, which compares the weight of the swollen hydrogel to its dry weight. The crosslinking density of the hydrogel affects the swelling ratio, with highly crosslinked structures exhibiting lower swelling ratios and vice versa. Furthermore, the chemical structure of the hydrogel plays a significant role in its swelling properties. The presence of hydrophilic and hydrophobic groups along the polymer chains influences the degree of swelling, with hydrogels containing more hydrophilic groups generally swelling more than

those with hydrophobic groups. Temperature and pH also have notable effects on hydrogel swelling. pH-sensitive hydrogels, for instance, undergo swelling due to the ionization of hydrophilic groups in response to pH changes. This ionization causes electrostatic repulsion between like charges on the polymer chains, disrupting secondary bonding and promoting swelling. The swelling process of hydrogels involves three steps: water diffusion into the hydrogel network, loosening of polymer chains, and expansion of the hydrogel network. When a hydrogel is dehydrated, it is in a glassy state, whereas when it is swollen, it is in a rubbery state [31].

2.6. SYNTHESIS OF HYDROGELS

Hydrogels are commonly produced by using hydrophilic monomers that enable the formation of a crosslinked network capable of absorbing water. The transition from a sol state to a gel state, known as the sol-gel transition, is a critical step in hydrogel formation [30].

Chemical hydrogels can be crosslinked through methods like grafting, radical polymerization, enzymatic reactions, click chemistry, thermo-gelation, and radiation crosslinking. Adding ions like Ca^{2+}, Mg^{2+}, and Zn^{2+} to hydrogel precursors can induce gelation through ionic bonds, particularly in polymers like alginate that have anionic groups. Naturally derived hydrogels primarily self-assemble through physical crosslinking processes involving ionic crosslinking, hydrophobic interactions, and hydrogen bonding. Gelation can be achieved by adjusting precursor temperature (37 °C or -20/-80 °C).

Various parameters can be adjusted or controlled during gelation to achieve desired hydrogel structure. Combining chemical and physical crosslinking methods can create hydrogels with specific properties. [30].

2.7. APPLICATIONS OF HYDROGELS

2.7.1. BIOMEDICAL APPLICATIONS

Hydrogels possess the remarkable ability to mimic the behavior of human organs by responding to changes in environmental conditions such as pH, temperature, enzymes, and electric fields. This unique characteristic has led to a wide range of applications in various fields. In the medical field, hydrogels are utilized in the development of medical implants, prosthetic muscles or organs, and robotic grippers. These hydrogel-based devices can replicate the functionalities of human organs and tissues, allowing for improved treatment and patient care. Diagnostic devices incorporating hydrogels enable the detection and monitoring of specific biomarkers or analytes. By responding to changes in the surrounding environment, hydrogels can provide valuable information for medical diagnosis and personalized medicine. Hydrogels also play a crucial role in the stabilization of bone implants. They can provide mechanical support, promote tissue integration, and enhance the healing process at the implant site. In the context of urinary catheters, hydrogels are used to prevent bacterial colonization on the catheter's surface. By creating a smooth and slippery surface, hydrogels improve biocompatibility and reduce the risk of infection. Furthermore, hydrogels have demonstrated the ability to convert electrochemical stimuli into mechanical work, as reported by Park et al. This unique property allows hydrogels to exhibit reversible contraction and relaxation, similar to human muscles. Such electrically driven muscle-like actuators hold promise for the development of advanced artificial muscles and tissue engineering applications. Overall, the versatile nature of hydrogels and their ability to respond to environmental stimuli make them valuable tools in medical applications, diagnostics, tissue engineering, and other fields where biomimetic properties are desired [32].

Researchers have investigated the combination of hydrogels with other materials to develop composite wound dressings suitable for various types of wounds. Shah et al. proposed a composite material consisting of a fibrous substrate (e.g., cotton gauze) impregnated with a thermoplastic hydrogel-forming polymer. The hydrogel-forming polymers used in their study included A-B-A block copolymers, multiblock copolymers, graft copolymers, and polymer

blends. These polymers incorporated both hydrophilic components like polyethylene oxide or poly(hydroxyalkyl methacrylate), and hydrophobic components such as polystyrene, poly(methyl methacrylate), or polyesters. The resulting hydrogel exhibited microphase separation, wherein the hydrophobic portion of the polymer became water-insoluble while still retaining its ability to absorb water. This unique property allowed the composite dressing to absorb wound exudate, leading to a slimy consistency that prevented adherence to the wound surface and reduced the risk of further trauma. Consequently, the dressing could be changed less frequently, providing convenience and potentially improving wound healing outcomes. This unique property allowed the composite dressing to effectively absorb wound exudate, resulting in a slimy consistency that prevented the dressing from adhering to the wound surface, thereby reducing the risk of further trauma. As a result, the dressing could be changed less frequently, providing convenience and potentially improving wound healing outcomes [33].

2.7.2. DRUG DELIVERY

Various strategies have been developed to create effective medication delivery systems, and hydrogels have emerged as promising candidates for targeted therapeutic agent delivery, bio-adhesive devices, and controlled release devices [34].

Because they can absorb and hold a lot of water, hydrogels are hydrophilic materials that may be used to create drug delivery systems that can regulate the release of solutes over certain time periods. Various biomaterials have been studied for controlled release applications, employing two primary mechanisms. Firstly, by altering the crosslinker concentration and the ratio of hydrophilic to hydrophobic monomers, regulated release may be obtained. Secondly, hydrogel carriers can exploit the weak interaction between hydrogels and active molecules like proteins and peptides, enabling the release of these molecules. These mechanisms offer strategies for achieving controlled and targeted release of active substances

from hydrogels. Employing regulated and targeted medication delivery strategies has the dual objectives of reducing undesirable side effects while increasing therapeutic efficacy [34].

Drug release from hydrogels has been described via a number of methods, including diffusion, release, swelling, and chemical control in may lead to environmental factors. The role of matrix devices in diffusion-controlled release systems is significant. The medicine may be contained within a hydrogel membrane within the empty chambers of matrix systems, such as capsules, cylinders, or spheres. Due to the high drug concentration in the system's center, this configuration guarantees continuous drug release. Another kind of matrix system includes the medication being evenly distributed or dissolving across the hydrogel's three-dimensional structure. This structure allows for regulated and prolonged release of the therapeutic agent [27] since drug release happens through the hydrogel's macromolecular pores.

Swelling-controlled release devices operate by loading the drug into a glassy polymer, which remains in a compact state initially. When the device comes into contact with a bio-fluid, such as body fluids or tissue moisture, the hydrogel begins to swell. As the hydrogel swells, it expands beyond its original boundaries, creating space for the drug to diffuse out. The hydrogel's polymeric chains relax throughout the diffusion process, allowing the medicine to be released gradually over time. Because it controls the diffusion channel and the amount of medicine that is available for release, the hydrogel's swelling is a key factor in regulating the release rate. The release of the medication may be precisely controlled to provide the desired therapeutic effect by carefully planning the hydrogel's composition and structure[27].

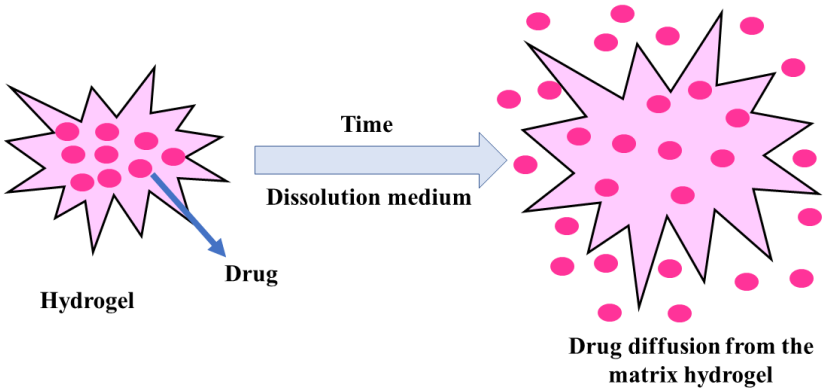

Figure 2.3. Schematic representation of drug release from hydrogel matrix.

2.7.3. AGRICULTURAL AND HORTICULTURAL

Due to their capacity to absorb significant volumes of water, superabsorbent polymers are widely utilized in horticulture and agriculture. These hydrophilic polymer cross-linked networks have various advantageous impacts on the soil. They increase the infiltration rate, density, texture, and permeability of the soil. They also lessen soil erosion while improving soil aeration, microbial activity, and water retention capacity. Pectin, chitosan, and carboxymethyl cellulose are examples of polysaccharide-based hydrogels that are frequently employed as fertilizers to improve the characteristics of soil [35].

Clay-loaded hydrogels have attracted more attention lately since they have special qualities and a variety of uses. By adding clay nanoparticles, scientists have created hydrogels with nanocomposite bases that allow for gradual and controlled release of macro and micronutrients in a variety of systems. Through hydrolysis treatment, these nanocomposites display improved physicochemical characteristics and a greatly increased water absorption capacity, up to 5000 times their original weight. The inclusion of clay nanoparticles in the

hydrogel structure leads to a substantial improvement in swelling capacity. Notably, hydrogels containing high levels of calcium montmorillonite (MMt), a type of clay, have shown promising results in agricultural applications. These hydrogels can act as carriers for nutrient release, providing a controlled and sustained supply of essential nutrients to plants. The utilization of clay-loaded hydrogels in agriculture holds great potential for improving nutrient management, enhancing crop growth, and promoting sustainable agricultural practices [27].

The environmental issue of polyphenols and organic content in olive mill effluent has also been addressed with the use of hydrogels. Hydrogels assist in immobilizing wastewater so that it may be utilized as plant fertilizer. In addition to being stable against UV radiation, oxygen, ozone, acidic rain, temperature change, microbes, and soil composition, agricultural hydrogels should absorb ion-containing aqueous solutions. Maintaining the hydrogels' stability in the agricultural and horticultural areas under challenging and protracted environmental conditions is a significant problem. The swelling capabilities of hydrogels can be degraded by ions and UV light by complexing or destroying the crosslinks [36].

2.8. CITRIC ACID AS A CROSSLINKER

Citric acid (CA) has emerged as a safe and environmentally friendly cross-linking agent for hydrogel synthesis. This naturally occurring organic acid is derived from renewable resources and can be produced through the fermentation of citrus fruits or carbohydrates such as starch or glucose. CA's low cost, availability, and non-toxic properties set it apart from other chemical cross-linking agents including carbodiimide, divinyl sulphone, glutaraldehyde, epichlorohydrin, genipin, and sulphuric acid. CA has been recognized as a "green cross-linker" due to these favorable attributes [37].CA has recently come to light as a safe cross-linking agent for the synthesis of hydrogels.CA creates a cyclic anhydride at high enough temperatures, which esterifies the hydroxyl groups on nearby polymer chains. Crosslinks start to form as a result. It is primarily derived from renewable resources and is

mainly produced through the fermentation of carbohydrates such as starch or glucose. It is also easily accessible and reasonably priced [12]. Moreover, as CA is a metabolic product of human body which is non-toxic in nature and used as a natural food additive in food industry [13].

According to the literature, CA is a multifunctional and ready-to-use monomer with diverse pharmaceutical applications. It is appropriate for investigation in the pharmaceutical and biomedical industries due to its adjustable mechanical characteristics, biocompatibility, and appealing in vitro and in vivo qualities. CA finds broad application in various industries, including food, nutraceuticals, beverages, pharmaceuticals, and cosmetics. It has also been successfully used for cross-linking ultrafine protein fibers in biomedical applications. Overall, CA's favorable physical-chemical properties and environmentally friendly nature have contributed to its rapid utilization in different industries, with its potential in pharmaceutical and biomedical fields being actively explored [38].

3. EXPERIMENTAL WORK

3.1. MATERIALS REQUIRED

3.1.1. SPECIFICATION AND SOURCES OF RAW MATERIALS

Table 3.1. Sources of raw materials

S. No.	Chemical	Source
1	Papaya seeds	local market, New Delhi, India.
2	Anhydrous citric acid	CA, CDH, New Delhi, India.
3	Distilled water	Innovation laboratory, Delhi Technological University, New Delhi, India

3.1.2. APPARATUS

- Beaker
- Glass rod
- Petri dish
- Magnetic stirrer
- Forceps

3.2. EXTRACTION OF MUCILAGE

Mucilage of *Carica papaya* was extracted using a previously described method, with some modifications[39]. Briefly, the mucilage was removed from the papaya seeds with the help of forceps. The mucilage was washed with acetone to remove the impurities. Then, the mucilage was left to dry in hot air oven at 50° C for 24 hours. The dried and finely powdered mucilage was stored in an air tight container. The obtained mucilage was confirmed by

various identification tests like Ruthenium Red test (mucilage), Ferric chloride test (tannins), Wagner's test (alkaloids), and Ninhydrin test (proteins) [40].

3.3. SYNTHESIS OF HYDROGEL FILM

Using the procedure previously described, Pm was reacted with CA to create the hydrogel films [41]. The hydrogel films were synthesized by reacting Pm with CA using the following method. A 1% w/v aqueous solution of Pm was prepared by stirring it with deionized water for 2 hours at ambient temperature. Then, a 0.2% w/v CA solution was added to the homogenized Pm solution and stirred for an additional hour. The resulting solution was casted into a petri dish and cured for 5 minutes at 140°C. The cured hydrogel film was washed with deionized water to remove any unreacted CA, dried in a hot air oven at 50°C for 24 hours, and stored in a desiccator for further use. Different formulations were prepared to study the effect of cross-linker concentration (CA) on the properties of Pm-CAH hydrogel films, as summarized in **Table 3.2.**

Table 3.2. Composition of Pm-CAH hydrogel films

S. No.	**Formulations**	**Parameters**	
		Pm (% w/v)	**CA (% w/v)**
1.	Pm-CAH-1	1	0.05
2.	Pm-CAH-2	1	0.1
3.	Pm-CAH-3	1	0.2
4.	Pm-CAH-4	1	0.3
5.	Pm-CAH-5	1	0.4

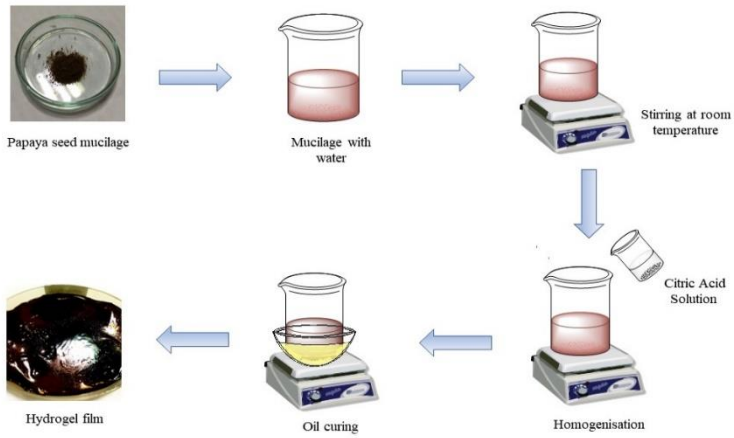

Figure 3.1. Pictorial representation of complete process.

3.4. SWELLING STUDIES

A 50 ml stoppered measuring cylinder was filled with a precise half gram of papaya seed mucilage powder. The measuring cylinder's initial powder volume was recorded. The volume was filled with distilled water to a capacity of 50 ml. The cylinder was sealed, lightly shook, and left alone for 24 hours. After 24 hours, the mucilage's volume was measured. As a percentage, swelling index (SI) is computed using the calculation shown below. Where X_t represents the height occupied by inflated mucilage after 24 hours, and X_0 represents the original height of the powder in the graduated cylinder. A muslin cloth was used to filter the contents of the measuring cylinder from the previous test, and water was then allowed to completely drain into a dry, 50 ml graduated cylinder. The collected water volume was recorded, and the discrepancy between the initial mucilage volume and the drained volume was considered as the water retained by the sample, known as water retention capacity or water absorption capacity [42].

$$\textbf{Swelling Index (SI)} = (X_t\text{-}X_0/X_0)\ \textbf{X}\ 100$$

The swelling index of the synthesized hydrogel was evaluated in a distilled water system. Initially, 500 mg of the hydrogel was immersed in an excess amount of distilled water, and

the weight of the drained hydrogel was measured at specific time intervals for up to 24 hours. The swelling index of the hydrogel was calculated using the formula:

$$\textbf{Swelling index} = (W_s - W_d)/ W_d$$

where Ws represents the weight of the swollen hydrogel and Wd represents the dry weight of the hydrogel [43] .

3.5. CHARACTERIZATION TECHNIQUES

The mucilage and Pm-CAH-3 hydrogel film were characterized by ATR-FTIR, XRD, SEM, TGA and ^{1}H and ^{13}C- NMR. The swelling index (SI) of extracted mucilage and Pm-CAH-3 hydrogel was also investigated. Further details of characterization methods and swelling index are available in the supplementary information.

3.5.1. Fourier-Transformed Infrared spectroscopy

Figure 3.2. FTIR Instrument

3.5.2. Scanning Electron Microscope

Figure 3.3. SEM Instrument

3.5.3. Thermal Analysis

Figure 3.4. TGA Instrument

2.5.4. X-Ray Diffraction

Figure 3.5: XRD Instrument

4. RESULTS AND DISCUSSIONS

We have successfully extracted the mucilage from papaya seeds, which was brown in appearance and had a rough fracture. The qualitative identification test, shown in **Table 4.1.,** confirms the presence of mucilage and absence of impurities like tannins, alkaloids, and proteins.

The good quality of hydrogel film was successfully developed with a minimum CA concentration of 0.2 %w/v. The creation of hard hydrogel films was observed when the CA concentration was over 0.3%w/v, whereas the formation of soft hydrogel films occurred when the CA concentration was below 0.2%w/v. The formation of crosslinks between CA and Pm is attributed to the esterification reaction. When CA is heated at higher temperatures, an intermediate cyclic anhydride is formed. This cyclic anhydride intermediate reacts with the -OH group of mucilage through esterification, leading to the formation of a new carboxylic acid unit. This unit has the ability to create new intra-molecular anhydride moieties with neighboring carboxylic acid units. [44].

4.1. PHYTOCHEMICAL IDENTIFICATION

The qualitative identification test, shown in **Table 4.1**, confirms the presence of mucilage and absence of impurities like tannins, alkaloids, and proteins.

Table 4.1. Phytochemical identification of the extracted mucilage

S. No.	**Identification Test**	**Active constituent**	**Observation**
			Pm
1.	Ruthenium Red test	Mucilage	+
2.	Ninhydrin test	Protein	-
3.	Ferric chloride test	Tannin	-
4.	Wagner's test	Alkaloids	-
+ = Present, - = Absent			

4.2. SWELLING STUDIES

SI of Pm and Pm-CAH-3 is shown in **Table 4.2.** From the obtained result it was found that the SI of mucilage was lower than that of the synthesized hydrogel. Therefore, the hydrogel has greater capability to absorb and retain huge amount of water compared to its precursor. Thus, the hydrogel is showing greater swelling capability than the mucilage alone.

Table 4.2. Swelling index of mucilage and hydrogel film.

S. No.	Sample	Swelling Index (%)
1.	Pm	180
2.	Pm-CAH-3	1025

4.3. FOURIER TRANSFORM INFRARED SPECTROSCOPY

ATR-FTIR spectra of CA, Pm and Pm-CAH-3 are shown in **Figure 4.1.** In the ATR-FTIR analysis, the CA spectrum displayed distinct peaks indicating specific molecular vibrations. The stretching vibration of the -OH group was assigned to a broad peak at 3217 cm^{-1}, while the C-H asymmetric vibration resulted in a peak at 2986 cm^{-1}. Additionally, a sharp peak at 1695 cm^{-1} was observed, which was attributed to the hydrogen-bonded C=O stretching vibration [41]. Similarly, the ATR-FTIR spectrum of Pm showed characteristic features. The -OH stretching vibration produced a broad band around 3280 cm^{-1}, and the asymmetric vibration of the C-H group resulted in a peak at 2912 cm^{-1} [45]. The stretching vibration of the carbonyl (C=O) group caused an absorption peak at 1634 cm^{-1}. Moreover, the sharp peak at 1025 cm^{-1} indicated the presence of C-O-C and C-O-H stretching vibrations in the glycosidic bond of the polysaccharide[40]. The ATR-FTIR spectrum of the hydrogel film (Pm-CAH-3) exhibited an additional peak at 1734 cm^{-1}. This peak was assigned to the carbonyl band (C=O) of an ester formed during the crosslinking of the polymer. The presence

of this peak confirmed the cross-linking of CA with the mucilage, indicating the formation of ester bonds [46].

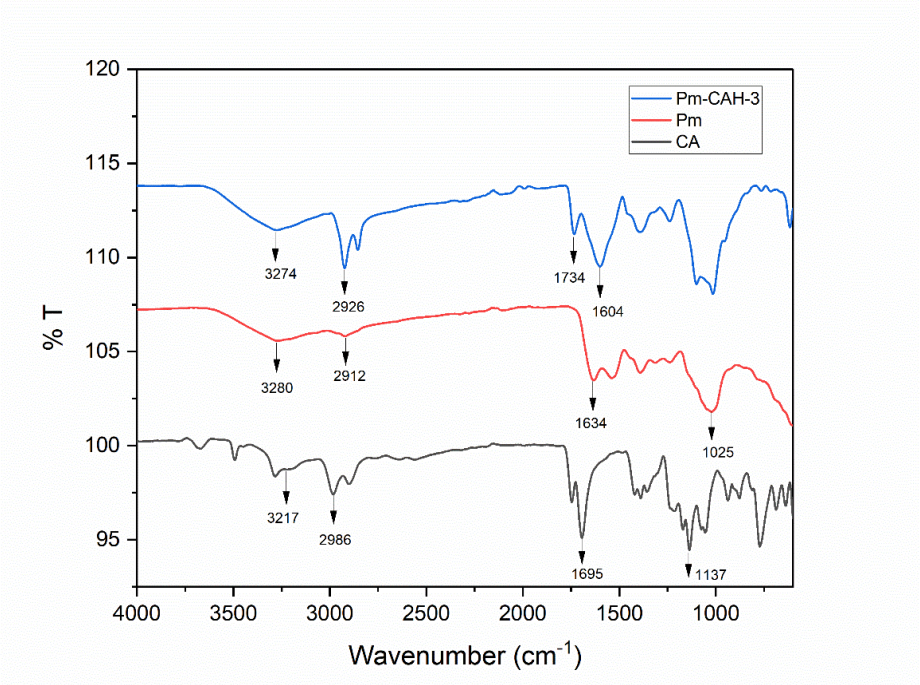

Figure 4.1. FTIR spectra of CA, Pm and Pm-CAH-3

4.4. X-RAY DIFFRACTION

XRD is usually carried out for the analysis of crystalline, amorphous and semi-crystalline nature of the material. **Figure 4.2.** shows the XRD pattern of Pm and Pm-CAH-3. In the XRD diffractogram of Pm, there was no sharp peaks and there was a broad diffraction peak around 15°- 28°, which indicates the amorphous nature of the mucilage. In case of hydrogel film, due to the crosslinking of the mucilage with CA, it showed some degree of crystallinity. Thus, it can be concluded that there may be showed transformation from amorphous to semi-crystalline nature [47].

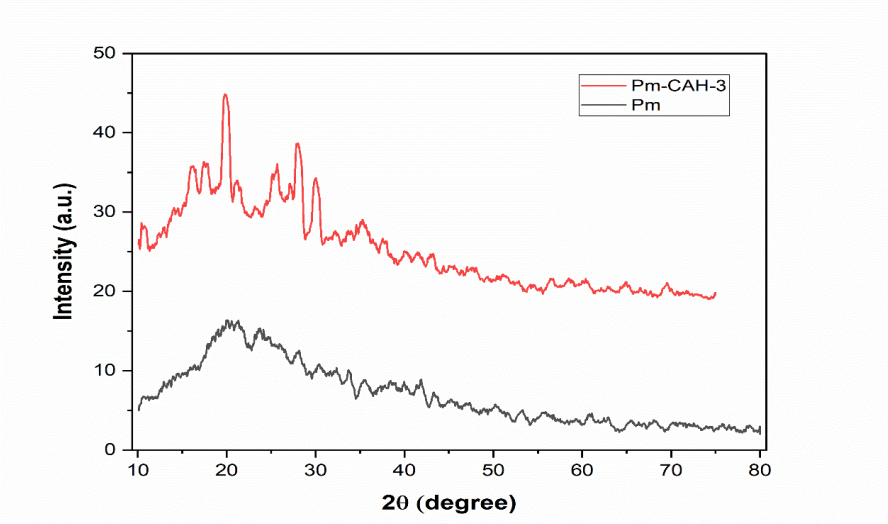

Figure 4.2. XRD of Pm and Pm-CAH-3

4.5. SCANNING ELECTRON MICROSCOPY

Figure 4.3. shows the SEM images of Pm and Pm-CAH-3 at 500 magnification. As shown in the figure, the mucilage is having high degree of irregularity in shape and dimension. It has a rough and uneven surface. In case of hydrogel film, it has smooth and homogeneous surface with small pores which suggests the homogeneous crosslinking [12].

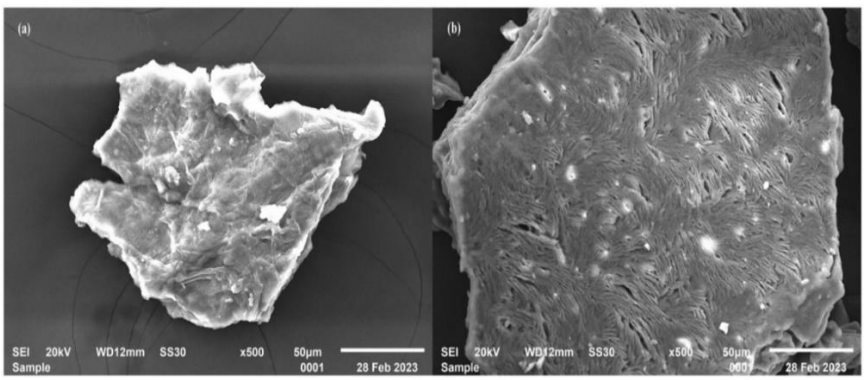

Figure 4.3. SEM of (a) Pm and (b) Pm-CAH-3

4.6. THERMO-GRAVIMETRIC ANALYSIS

The TGA thermograms of Pm and Pm-CAH-3 are presented in **Figure 4.4.** The thermal decomposition of Pm exhibited three weight loss events. The first stage, occurring between 30°C and 190°C, resulted in an initial weight loss of approximately 4.11%. This weight loss was attributed to the desorption of free and bound water from the mucilage. The second stage, spanning from 190°C to 420°C, showed a weight loss of 56.50%. This weight loss was due to the decomposition of the mucilage, leading to the breaking of the polysaccharide branches. The final stage, ranging from 500°C to 800°C, involved the degradation of the polysaccharide backbone [48]. In the case of the hydrogel film (Pm-CAH-3), the thermal decomposition also occurred in three stages. The first stage, from 30°C to 200°C, resulted in a weight loss of 3.92%. This weight loss was primarily due to the loss of moisture. The second stage, spanning from 200°C to 460°C, exhibited a weight loss of 51.82%. This weight loss was attributed to the decomposition of the crosslinked Pm mucilage hydrogel. The third stage, ranging from 460°C to 800°C, showed a weight loss of 17.86%. This weight loss was associated with the breakdown of the main polymeric backbone[49]. The residual weights at 800°C were 3.38% for Pm and 20.55% for Pm-CAH-3. The higher residual weight of the hydrogel film indicated that the crosslinked Pm-CAH-3 underwent less decomposition compared to Pm. This suggests that the crosslinking of the mucilage with CA in the hydrogel film improved the thermal stability of the mucilage.

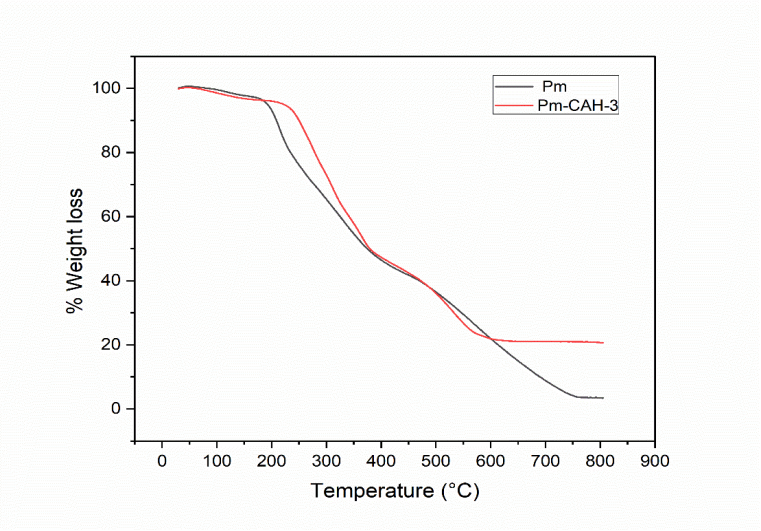

Figure 4.4. TGA of Pm and Pm-CAH-3

4.7. NUCLEAR MAGNETIC RESONANCE

The liquid state ^{1}H-NMR of mucilage and solid state ^{13}C cross-polarization-magic angle spinning (^{13}C CP-MAS) NMR spectra of hydrogel film is shown in **Figure 4.5.** In ^{1}H-NMR of mucilage, the peak around δ 1.2 ppm is attributed to methyl groups. The spectrum shows a crowded region near δ 3.1- 3.8 ppm, which specifies the polysaccharide region and indicates the presence of different sugar units in the mucilage. The peak in between δ 3- 4.3 ppm is assigned to non-anomeric protons [50],[51].

Solid state ^{13}C-NMR of Pm-CAH-3 shows three distinct peaks. The peak at δ 74 ppm is due to carbon atom connected to hydroxyl group (-OH), δ 63 ppm is assigned to C6 carbon atom of CH_2OH group, and δ 105 ppm is assigned to the anomeric carbon (C1) of the polysaccharide. The broad resonance peak in the range of δ 172- 180 ppm confirms the formation of ester crosslinks in the hydrogel film [52].

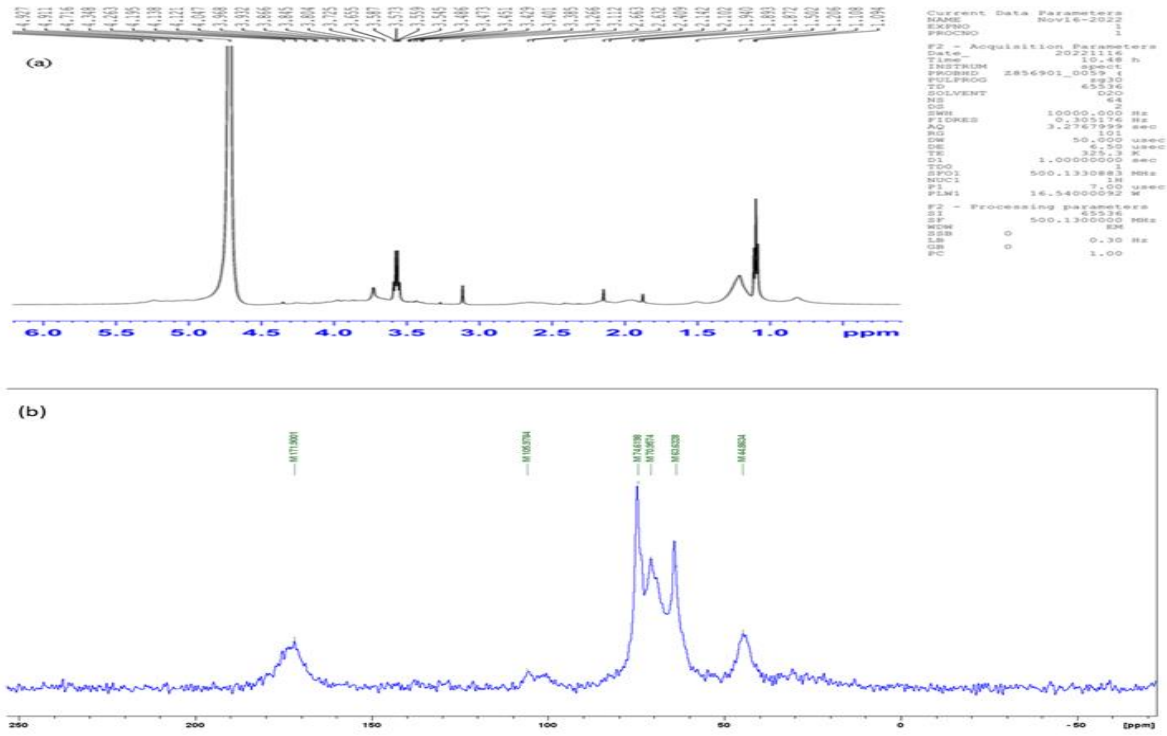

Figure 4.5. (a) ^{1}H-NMR of Pm (b) Solid state ^{13}C-NMR of Pm-CAH-3

5. CONCLUSION

This study demonstrates the utilization of mucilage derived from *Carica papaya* seeds for the development of CA crosslinked Pm-CAH hydrogel films. It is the first time that *Carica papaya* seeds mucilage has been explored as a hydrogelling agent, and CA has been used as a crosslinker for Pm. ATR-FTIR and solid-state ^{13}C-NMR analysis confirmed the formation of ester linkages between Pm and CA. TGA analysis revealed that the synthesized hydrogel film exhibited greater thermal stability compared to the mucilage alone. The swelling index of the mucilage was enhanced by crosslinking it with CA to form the hydrogel. Therefore, it can be concluded that Pm has the ability to form hydrogel films using CA as a crosslinking agent. The study suggests that further investigations on Pm-based hydrogels could be conducted for potential applications in pharmaceutical, food, and cosmetic industries.

6. REFERENCES

[1] M. P. Kusuma and M. N. S. Mogili, "Formulation and Development of β-glucan Hydrogel using Design of Experiments (DOE)," *International Journal of Drug Delivery Technology*, vol. 12, no. 3, pp. 1266–1274, Jul. 2022, doi: 10.25258/ijddt.12.3.56.

[2] X. Shen, J. L. Shamshina, P. Berton, G. Gurau, and R. D. Rogers, "Hydrogels based on cellulose and chitin: Fabrication, properties, and applications," *Green Chemistry*, vol. 18, no. 1. Royal Society of Chemistry, pp. 53–75, Nov. 16, 2015. doi: 10.1039/c5gc02396c.

[3] E. M. Ahmed, "Hydrogel: Preparation, characterization, and applications: A review," *Journal of Advanced Research*, vol. 6, no. 2. Elsevier B.V., pp. 105–121, 2015. doi: 10.1016/j.jare.2013.07.006.

[4] J. Li, X. Jia, and L. Yin, "Hydrogel: Diversity of Structures and Applications in Food Science," *Food Reviews International*, vol. 37, no. 3. Bellwether Publishing, Ltd., pp. 313–372, 2021. doi: 10.1080/87559129.2020.1858313.

[5] S. Viudes, V. Burlat, and C. Dunand, "Seed mucilage evolution: Diverse molecular mechanisms generate versatile ecological functions for particular environments," in *Plant Cell and Environment*, Blackwell Publishing Ltd, Dec. 2020, pp. 2857–2870. doi: 10.1111/pce.13827.

[6] M. M. Tosif *et al.*, "A comprehensive review on plant-derived mucilage: Characterization, functional properties, applications, and its utilization for nanocarrier fabrication," *Polymers*, vol. 13, no. 7. MDPI AG, Apr. 01, 2021. doi: 10.3390/polym13071066.

[7] G. Archana *et al.*, "Preparation and characterization of mucilage polysaccharide for biomedical applications," *Carbohydr Polym*, vol. 98, no. 1, pp. 89–94, 2013, doi: 10.1016/j.carbpol.2013.04.062.

[8] M. S. A. Sani, J. Bakar, A. Azid, and M. J. Iqbal, "Chemometrics-based evaluation on the effect of sonication, contact time and solid-to-solvent ratio on total phenolics and flavonoids, free fatty acids and antibacterial potency of Carica papaya seed against S. enteritidis, B. cereus, V. vulnificus and P. mirabilis," *Food Chemistry Advances*, vol. 1, Oct. 2022, doi: 10.1016/j.focha.2022.100033.

[9] J. M. Dotto and S. A. Abihudi, "Nutraceutical value of Carica papaya: A review," *Scientific African*, vol. 13. Elsevier B.V., Sep. 01, 2021. doi: 10.1016/j.sciaf.2021.e00933.

[10] S. Salla, R. Sunkara, S. Ogutu, L. T. Walker, and M. Verghese, "Antioxidant activity of papaya seed extracts against H2O2 induced oxidative stress in HepG2 cells," *LWT*, vol. 66, pp. 293–297, Mar. 2016, doi: 10.1016/j.lwt.2015.09.008.

[11] R. T. Malatani *et al.*, “Development of Tofacitinib Loaded pH-Responsive Chitosan/Mucin Based Hydrogel Microparticles: In-Vitro Characterization and Toxicological Screening,” *Gels*, vol. 9, no. 3, p. 187, Feb. 2023, doi: 10.3390/gels9030187.

[12] D. S. Franklin and S. Guhanathan, “Synthesis and characterization of citric acid-based pH-sensitive biopolymeric hydrogels,” *Polymer Bulletin*, vol. 71, no. 1, pp. 93–110, Jan. 2014, doi: 10.1007/s00289-013-1047-4.

[13] V. Coma, I. Sebti, P. Pardon, F. H. Pichavant, and A. Deschamps, “Film properties from crosslinking of cellulosic derivatives with a polyfunctional carboxylic acid.” [Online]. Available: www.elsevier.com/locate/carbpol

[14] Y. D. Nakhate, K. S. Talekar, S. V Giri, R. D. Vasekar, H. C. Mankar, and P. R. Tiwari, “PHARMACOLOGICAL AND CHEMICAL COMPOSITION OF CARICA PAPAYA: ON OVERVIEW,” *Nakhate et al. World Journal of Pharmaceutical Research*, vol. 8, p. 811, 2019, doi: 10.20959/wjpr20195-14650.

[15] O. Kadiri, B. Olawoye, O. S. Fawale, and O. A. Adalumo, “Nutraceutical and Antioxidant Properties of the Seeds, Leaves and Fruits of Carica papaya: Potential Relevance to Humans Diet, the Food Industry and the Pharmaceutical Industry-A Review,” 2016. [Online]. Available: www.agrifoodscience.com,

[16] S. Sugiharto, “Papaya (Carica papaya L.) seed as a potent functional feedstuff for poultry - A review,” *Veterinary World*, vol. 13, no. 8. Veterinary World, pp. 1613–1619, Aug. 01, 2020. doi: 10.14202/vetworld.2020.1613-1619.

[17] G. Goksen *et al.*, “Mucilage polysaccharide as a plant secretion: Potential trends in food and biomedical applications,” *Int J Biol Macromol*, vol. 230, Mar. 2023, doi: 10.1016/j.ijbiomac.2023.123146.

[18] “Review on natural gums and mucilage and their application as excipient,” *Journal of Applied Pharmaceutical Research*, vol. 5, no. 4, pp. 13–21, Dec. 2017, doi: 10.18231/2348-0335.2017.0010.

[19] C. Soukoulis, C. Gaiani, and L. Hoffmann, “Plant seed mucilage as emerging biopolymer in food industry applications,” *Current Opinion in Food Science*, vol. 22. Elsevier Ltd, pp. 28–42, Aug. 01, 2018. doi: 10.1016/j.cofs.2018.01.004.

[20] S. Priya Nagam, A. Naga Jyothi, J. Poojitha, S. Aruna, and R. Rao Nadendla, “A Comprehensive review on hydrogels,” 2016. [Online]. Available: https://www.researchgate.net/publication/316887977

[21] E. Larrañeta, S. Stewart, M. Ervine, R. Al-Kasasbeh, and R. F. Donnelly, “Hydrogels for hydrophobic drug delivery. Classification, synthesis and applications,” *Journal of Functional Biomaterials*, vol. 9, no. 1. MDPI AG, Jan. 24, 2018. doi: 10.3390/jfb9010013.

[22] Z. Bao, C. Xian, Q. Yuan, G. Liu, and J. Wu, “Natural Polymer-Based Hydrogels with Enhanced Mechanical Performances: Preparation, Structure, and Property,” *Advanced Healthcare Materials*, vol. 8, no. 17. Wiley-VCH Verlag, Sep. 01, 2019. doi: 10.1002/adhm.201900670.

[23] R. Singhal and K. Gupta, “A Review: Tailor-made Hydrogel Structures (Classifications and Synthesis Parameters),” *Polymer - Plastics Technology and Engineering*, vol. 55, no. 1, pp. 54–70, Jan. 2016, doi: 10.1080/03602559.2015.1050520.

[24] M. M. Khansari *et al.*, “Classification of Hydrogels Based on Their Source: A Review and Application in Stem Cell Regulation,” *JOM*, vol. 69, no. 8. Minerals, Metals and Materials Society, pp. 1340–1347, Aug. 01, 2017. doi: 10.1007/s11837-017-2412-9.

[25] S. Garg, A. Garg, and R. Durgavati Vishwavidyalaya, “Hydrogel: Classification, Properties, Preparation and Technical Features Phytochemical analysis and investigation of antineoplastic activity View project Formulation and Evaluation of Herbal Effervescent Granules Incorporated with Calliandra Haematocephala Leaves Extract View project.” [Online]. Available: www.ajbr.in

[26] K. Varaprasad, G. M. Raghavendra, T. Jayaramudu, M. M. Yallapu, and R. Sadiku, “A mini review on hydrogels classification and recent developments in miscellaneous applications,” *Materials Science and Engineering C*, vol. 79. Elsevier Ltd, pp. 958–971, Oct. 01, 2017. doi: 10.1016/j.msec.2017.05.096.

[27] S. Mishra, P. Rani, G. Sen, and K. P. Dey, “Preparation, Properties and Application of Hydrogels: A Review,” 2018, pp. 145–173. doi: 10.1007/978-981-10-6077-9_6.

[28] H. Kamata, X. Li, U. Il Chung, and T. Sakai, “Design of Hydrogels for Biomedical Applications,” *Adv Healthc Mater*, vol. 4, no. 16, pp. 2360–2374, Nov. 2015, doi: 10.1002/adhm.201500076.

[29] A. Chyzy and M. E. Plonska-Brzezinska, “Hydrogel Properties and Their Impact on Regenerative Medicine and Tissue Engineering,” *Molecules*, vol. 25, no. 24. MDPI AG, Dec. 01, 2020. doi: 10.3390/molecules25245795.

[30] M. C. Catoira, L. Fusaro, D. Di Francesco, M. Ramella, and F. Boccafoschi, “Overview of natural hydrogels for regenerative medicine applications,” *J Mater Sci Mater Med*, vol. 30, no. 10, Oct. 2019, doi: 10.1007/s10856-019-6318-7.

[31] S. Bashir *et al.*, “Fundamental Concepts of Hydrogels: Synthesis, Properties, and Their Applications,” *Polymers (Basel)*, vol. 12, no. 11, p. 2702, Nov. 2020, doi: 10.3390/polym12112702.

[32] F. Ullah, M. B. H. Othman, F. Javed, Z. Ahmad, and H. M. Akil, “Classification, processing and application of hydrogels: A review,” *Materials Science and*

Engineering C, vol. 57. Elsevier Ltd, pp. 414–433, Dec. 01, 2015. doi: 10.1016/j.msec.2015.07.053.

[33] E. Caló and V. V. Khutoryanskiy, "Biomedical applications of hydrogels: A review of patents and commercial products," *European Polymer Journal*, vol. 65. Elsevier Ltd, pp. 252–267, 2015. doi: 10.1016/j.eurpolymj.2014.11.024.

[34] N. A. Peppas, P. Bures, W. Leobandung, and H. Ichikawa, "Hydrogels in pharmaceutical formulations." [Online]. Available: www.elsevier.com/locate/ejphabio

[35] S. Thakur, V. K. Thakur, and O. A. Arotiba, "History, Classification, Properties and Application of Hydrogels: An Overview," 2018, pp. 29–50. doi: 10.1007/978-981-10-6077-9_2.

[36] H. Omidian and K. Park, "Introduction to Hydrogels," in *Biomedical Applications of Hydrogels Handbook*, Springer New York, 2010, pp. 1–16. doi: 10.1007/978-1-4419-5919-5_1.

[37] R. Salihu *et al.*, "Citric acid: A green cross-linker of biomaterials for biomedical applications," *European Polymer Journal*, vol. 146. Elsevier Ltd, Mar. 05, 2021. doi: 10.1016/j.eurpolymj.2021.110271.

[38] S. Nangare, Y. Vispute, R. Tade, S. Dugam, and P. Patil, "Pharmaceutical applications of citric acid," *Futur J Pharm Sci*, vol. 7, no. 1, Feb. 2021, doi: 10.1186/s43094-021-00203-9.

[39] L. P. Yalavarthi, P. K. Jonnadula, M. V. Manthina, and A. Addagalla, "CUBOSOMES: A NOVEL DRUG DELIVERY SYSTEM OVERVIEW," *Int J Res Ayurveda Pharm*, vol. 11, no. 5, pp. 198–204, Oct. 2020, doi: 10.7897/2277-4343.1105169.

[40] U. V. Deore and H. S. Mahajan, "Isolation and structural characterization of mucilaginous polysaccharides obtained from the seeds of Cassia uniflora for industrial application," *Food Chem*, vol. 351, Jul. 2021, doi: 10.1016/j.foodchem.2021.129262.

[41] K. K. Mali, S. C. Dhawale, and R. J. Dias, "Synthesis and characterization of hydrogel films of carboxymethyl tamarind gum using citric acid," *Int J Biol Macromol*, vol. 105, pp. 463–470, Dec. 2017, doi: 10.1016/j.ijbiomac.2017.07.058.

[42] U. A. Sanker, F. Stanley, and C. Author, "Isolation and Characterization of Mucilage Obtained from Abroma augustum Leaf," *International Journal of Research and Review (ijrrjournal.com)*, vol. 7, no. 5, p. 5, 2020.

[43] N. Thombare, S. Mishra, R. Shinde, M. Z. Siddiqui, and U. Jha, "Guar gum based hydrogel as controlled micronutrient delivery system: Mechanism and kinetics of

boron release for agricultural applications," *Biopolymers*, vol. 112, no. 3, Mar. 2021, doi: 10.1002/bip.23418.

[44] C. Demitri *et al.*, "Novel superabsorbent cellulose-based hydrogels crosslinked with citric acid," *J Appl Polym Sci*, vol. 110, no. 4, pp. 2453–2460, Nov. 2008, doi: 10.1002/app.28660.

[45] S. M. Jose and M. Anilkumar, "Anti-inflammatory, antioxidant, and dye removal properties of mucilage isolated from Litsea quinqueflora (Dennst.) Suresh," *Chemical Papers*, vol. 75, no. 12, pp. 6531–6543, Dec. 2021, doi: 10.1007/s11696-021-01821-6.

[46] N. Reddy and Y. Yang, "Citric acid cross-linking of starch films," *Food Chem*, vol. 118, no. 3, pp. 702–711, Feb. 2010, doi: 10.1016/j.foodchem.2009.05.050.

[47] M. E. L. Fernandez and N. Miskolczi, "Production of Cellulose Nano-Fibers and Its Application in Poly-Lactic-Acid: Property Improvement by New Types of Coupling Agents," *Polymers (Basel)*, vol. 14, no. 9, May 2022, doi: 10.3390/polym14091887.

[48] M. de A. Lucena *et al.*, "Biopolymer from Water Kefir as a Potential Clean-Label Ingredient for Health Applications: Evaluation of New Properties," *Molecules*, vol. 27, no. 12, Jun. 2022, doi: 10.3390/molecules27123895.

[49] K. Dharmalingam and R. Anandalakshmi, "Fabrication, characterization and drug loading efficiency of citric acid crosslinked NaCMC-HPMC hydrogel films for wound healing drug delivery applications," *Int J Biol Macromol*, vol. 134, pp. 815–829, Aug. 2019, doi: 10.1016/j.ijbiomac.2019.05.027.

[50] S. Singh and S. Bothara, "Morphological, physico-chemical and structural characterization of mucilage isolated from the seeds of Buchanania lanzan Spreng," *International Journal of Health & Allied Sciences*, vol. 3, no. 1, p. 33, 2014, doi: 10.4103/2278-344x.130609.

[51] U. V. Deore and H. S. Mahajan, "Isolation and characterization of natural polysaccharide from Cassia Obtustifolia seed mucilage as film forming material for drug delivery," *Int J Biol Macromol*, vol. 115, pp. 1071–1078, Aug. 2018, doi: 10.1016/j.ijbiomac.2018.04.174.

[52] V. S. Ghorpade, A. V. Yadav, and R. J. Dias, "Citric acid crosslinked β-cyclodextrin/carboxymethylcellulose hydrogel films for controlled delivery of poorly soluble drugs," *Carbohydr Polym*, vol. 164, pp. 339–348, May 2017, doi: 10.1016/j.carbpol.2017.02.005.

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