

**EXPLOITING THE FEASIBILITY STUDY OF BIODEGRADABLE AND
BIOCOMPATIBLE NATURAL POLYMERS FOR DRUG DELIVERY SYSTEM**

Submitted in partial fulfillment of the requirements for the award of Bachelor of
Technology degree in Biomedical Engineering

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SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY

(DEEMED TO BE UNIVERSITY)

Accredited with Grade "A" by NAAC

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BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of **SAHEER ANAS (Reg. No. 38240029)**, **AFIF. A.S. (Reg. No. 38240002)** who carried out the project entitled **"EXPLOITING THE FEASIBILITY STUDY OF BIODEGRADABLE AND BIOCOMPATIBLE NATURAL POLYMERS FOR DRUG DELIVERY SYSTEM"** under our supervision from **September 2021 to March 2022**.

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Submitted for Viva-voce Examination held on **02.05.2022**

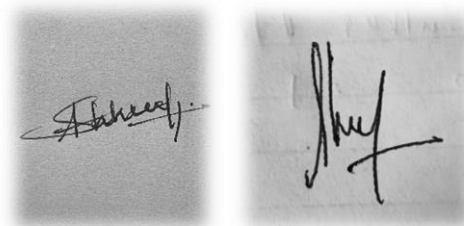
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DECLARATION

We **SAHEER ANAS (Reg. No. 38240029), AFIF. A.S. (Reg. No. 38240002)** hereby declare that the Project Report entitled “**EXPLOITING THE FEASIBILITY STUDY OF BIODEGRADABLE AND BIOCOMPATIBLE NATURAL POLYMERS FOR DRUG DELIVERY SYSTEM**” done by us under the guidance of **Dr. ANIMA NANDA, Department of Biomedical Engineering** is submitted in partial fulfillment of the requirements for the award of **Bachelor of Technology** degree in **Biomedical Engineering**.

Two handwritten signatures in black ink on a light background. The signature on the left is more cursive and includes a horizontal line at the end. The signature on the right is more stylized and vertical.

DATE: 23/04/2022

PLACE: CHENNAI

SIGNATURE OF THE CANDIDATE

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ABSTRACT

Since the decay, drug delivery system that are caused owing to various reasons that attracts researcher attention to find a practical way to treat. Drug delivery is the method or process of administering pharmaceutical compound achieve a therapeutic effect in humans or animals. For the treatment of human disease, nasal and pulmonary routes of drug delivery or gaining increasing importance. Many studies were conducted. Nanotechnology also suggested some ways and the newest one is called tissue engineering. Drug delivery system are used for targeted delivery of therapeutic agents. They use biodegradable and biocompatible polymer in order to make the pharmaceutical products. Bio-degradable and bio-compatible polymers are dominant in scaffolding materials in tissue engineering field. In this current research we are going to do a feasibility testing for different kind of bio-degradable and bio-compatible. Selecting different kind of functional polymers for testing. Testing for selected polymers like cytotoxicity, sensitization assays, irritation tests, Geno toxicity, implantation tests, haemo-compatibility. Biodegradable testing for selected functional polymers is done. Application of functional polymers in tissue engineering is explained.

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CHAPTER -1

INTRODUCTION

Materials that widely occur in nature and are extracted from plants and animals are known as natural polymers. It is very important to humans as our daily life human forms are based on the also water based. Polymer like vulcanized rubber and pectin is an example of natural polymers. It is widely used in biomedical applications like drug delivery, tissue regeneration scaffolds, and also in imaging agents. It is also widely used in wound care as dressing a acute chronic wounds. They can also be derived from microorganisms. They have the similarity with the extracellular matrix, high water holding capacity, mechanical tunability, and also for skin repair and regeneration process. A great challenge for researches is to modify and select the accurate sample or material for a scaffold that holds properties for the type of wound which is targeted. Polymer properties depend of their structure and they are divided into classes according to their physical basis. Many physical and chemical properties describe how a polymer behaves as a continuous macroscopic material. They are classified as bulk properties, or intensive properties according to thermodynamics. The bulk properties of a polymer are those most often of end-use interest. These are the properties that dictate how the polymer actually behaves on a macroscopic scale.

1.1 USES OF NATURAL POLYMERS IN BIOMEDICAL APPLICATIONS:

Natural polymers are used in biomedical fields such as tissue regeneration scaffolds, pharmaceuticals, imaging agents and drug delivery system. It can be derived from the sources like microorganisms, plants and animals. They are also used in skin repair and regeneration. They are also used in wound care as dressing for chronic acute wounds as regeneration templates. People used polymers in their life but they did not know until World War II. Relatively few materials were available for the manufacture of the article needed for a civilized life. Steel, wood, stone, and concrete for most of the construction and cotton, wood, and a few other agricultural products for clothing manufacture were used. The word polymer is derived from classical Greek poly meaning "many" and meres meaning "parts". The molecular weight of polymer is (between 10 000-1000 000 g /mol) and consists of several structural units usually bound together by covalent bonds.¹, 3 Polymers are obtained

through chemical reaction of monomers. Monomers has an ability to react with another molecule from another type or from the same type to form the polymer chain. This has resulted to the formation of natural polymers, while the synthetic polymers are man-made. These polymers has been around us in the natural world from the very beginning e.g., starch, and natural rubber. Polymeric materials have been studied from the middle of the nineteenth century. Today, the polymer industry has rapidly developed and is larger than the copper, steel, aluminum and some other industries combined.

1.2 HYDROGEL FORMATION:

Degradable polymeric network, in which cross-links plays important role in formation of structure and degradation are known as hydrogels. Cross-linking is a stabilization process in which chemistry of polymer lead to multi-dimensional extension of polymeric chains, and it also result in structures of networks. Hydrogels are formed into stable structure that vary from their raw materials. And this result is obtained through cross-linking. Synthetic or natural polymers are used to prepare hydrogels. Based on the type cross-linking, hydrogels can be differentiated into two groups: they are the chemically cross-linked and physically-crosslinked.

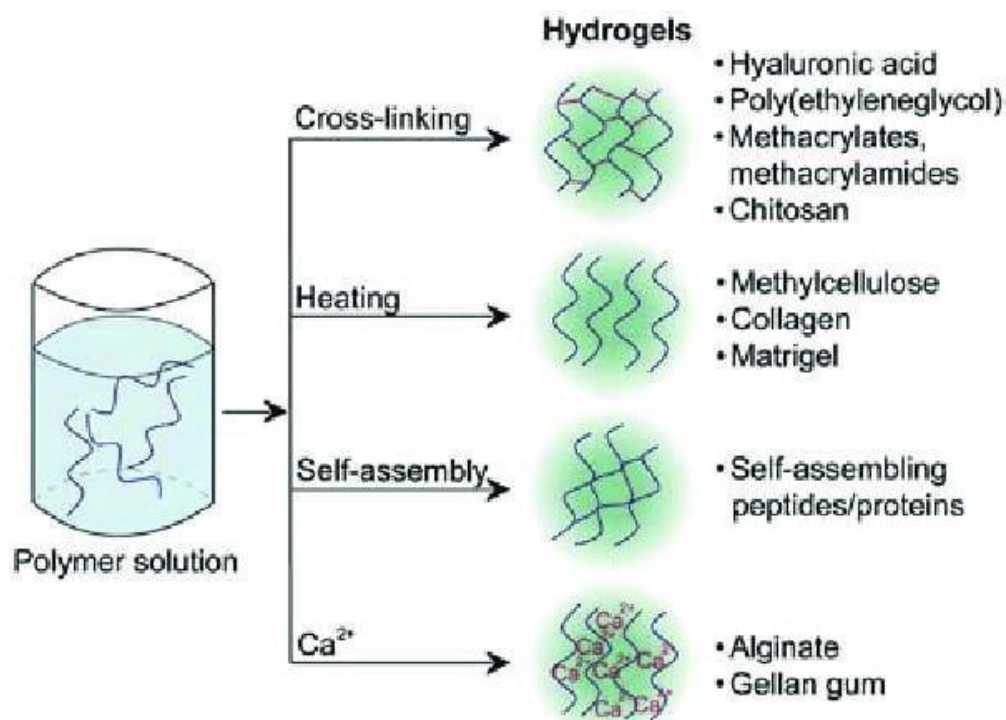


Fig 1.1. Formation of Hydrogel

1.3 BIODEGRADABLE TESTING:

This testing is done when the intension grew high for product claims related to biodegradability, it should incorporate several factors of the product actual performance. These products are combination and formulation of several product and components. As per the majority component biodegradability can mislead to when it is used as the assessment of entire complete product. Ester, amide, and ether linkages are common in biodegradable polymers. Based on their structure and production, biodegradable polymers can be divided into two categories. Agro- polymers, or those generated from biomass, are one of these groups. Bio polyesters, which are generated from microorganisms or synthesized from naturally or synthetic monomers, are the other type.

1.4 PROCEDURE OF BIODEGRADATION:

It measures the biochemical process that happens when the microorganism intake a given type of material. Although it is very complicated the results of the test measure the simple makers of the biodegradation process. Ability of the product to biodegrade depends on the amount of carbon available for microbial consumption. At the present time biodegradability claims need regulations which is based on the aerobic biodegradation, the aerobic biodegradation which is helpful to measure CO₂ production, oxygen consumption and the state of inorganic carbon intermediates. Selecting a Method Challenges with this testing include the complexity of the biochemical interactions, the composition of the materials tested, and the specific needs of each biodegradation test. Materials that are made up of components known to biodegrade sometimes don't pass and materials made of inorganic components don't necessarily fail the various assessments of biodegradability. Knowing which biodegradation test method to use for a specific material is key.

1.5 BIOCOMPATIBLE TESTING:

The suitability of a polymer to body and body fluids exposure is known as the term biocompatibility. This polymer improves the functions of the body without changing its normal functions and creating allergies and other side effects. The most often accurate evaluation of device compatibility is implant studies. On the living tissue the

Test material is placed directly. After some hours the implant site is recovered and the study will be undergone microscopically for tissue reaction.

Medical gadgets that come into contact with patients must undergo biocompatibility testing. ISO/IEC 10993 Most major national regulatory organizations, including the FDA and the CE mark, accept biological evaluation of medical devices as the gold standard for selecting the biological tests required to assess a medical device's safety. Manufacturers must identify which tests are required, which is dependent on how the medical device will be utilized. The antioxidant-stabilized UHMWPE material was evaluated using a complete biocompatibility test plan designed in line with the ISO draught guide on the Conduct of Biological Evaluation within a Risk Management Process (ISO/DTR 15499). Methods that addressed FDA guidance documents, specifically ISO 10993 parts 3–6, 10, and 11, were incorporated in the test plan. Other USP tests to describe leachable components were done in addition to the ISO 10993 testing. Bulk PBHP-stabilized GUR 1020 irradiated at 75 kGy, referred to as AOX, was used for biocompatibility testing. This section contains a summary of the various tests and their results.

1.6 DRUG DELIVERY SYSTEM:

In an integral role in the advancement of drug delivery technology polymers have played a main role providing controlled release of therapeutic agents in regular or constant doses over long periods, continuous dosage, and regulated release of both hydrophilic and hydrophobic drugs.

The main use of drug delivery system is to provide targeted delivery and controlled release of therapeutic agents. The methods of drug delivery had been changed widely in the past few years and even greater changes are been looking forward in the upcoming future. Biomedical engineers have been main role in understanding the barriers to efficient drug delivery, such as drug movement through cells and tissues, transport in the circulatory system; they have also contributed to the development of many new modes of drug delivery that have entered into medical and clinical practice. Temperature is the most effective factors to control the drug release compared with other stimuli. Pathophysiological conditions, such as inflammation and tumors, has higher temperatures than normal tissues. Considering the temperature difference between cancer tissues and normal tissues, functionalized nanoparticles could be triggered to enhance their drug release in

tumors. Another temperature- responsive strategy is that the tumor site could be heated by external triggers (US, magnetic field, etc.) to improve the drug release within the tumor vasculature microenvironment. Thermos - sensitive nanocarriers are designed to retain their payloads around the physiological temperature of 37°C, and release the payloads rapidly when temperature is increased higher than 40-45°C. Towards the thermo-responsive nanoplateforms, the current challenge is to maintain the safety of the platforms without sacrificing their sensitivity to slight temperature changes

CHAPTER -2

LITERATURE SURVEY

Fathemeh Asghari, et al. (2017) this topic explains the study of biodegradable and bio compatible polymers for tissue engineering application. Here the methodology used and explained is that bio degradable polymers in order to replace or damage the structures in tissue engineering to make it practical. And also the biodegradable polymers are dominant in scaffolding material in tissue engineering field, here in this survey they have mentioned about the biodegradable polymers and their application as scaffolds. The outcome of this survey is they have concluded by explaining that tissue engineering is to repair damaged tissue and also different methods are used to make scaffolds, such as solvent casting, gas forming, electro spinning. The most common method resulting in nano fibers in different sizes.

N Vijaya Kumar et al. (2021) feasibility studies on bio composites using PLA and epoxy for structural application. The methodology of this survey describes that this is used to reduce the dependence of synthetic polymer, and to reinforcing PLA in an epoxy matrix is used. The % of PLA is varied from 10 to 50% in a step of 10% using solution. The outcome of the survey mention that PLA composites with 20% PLA showed improved tensile strength & reduce flexural strength compared to 10 and 30%. The epoxy and PLA with 20% PLA improved composite material for chosed structural application.

Mihai R, et al. (2018) invitro biocompatibility testing for some synthetic polymers used for the achievement of nervous conduits, the survey of the method used explains that PVC, APV, PEG invitro biocompatibility was evaluated by fibro blast culture testing. The cytotoxic effect of polymeric material was measured by MTT test. The outcome explains that experiments were carried in a cell culture laboratory RENAR in accordance with SR standard requirements to determine the cytotoxicity of medical devices by quantitative and qualitative methods.

Bret D, et al. (2017) biomedical application of biodegradable polymers, the methodology of this survey explains that hydrolytically degradable polymers are materials that possess chemical bonds that can break down without secondary influence. The outcome of this survey explains that In addition the emergence of

combination polymer holds promise for the creation of novel materials that possess desired properties for high specific application.

Iqbal, et al. (2017) recent concepts in biodegradable polymers for tissue engineering paradigms. In this survey the methodology explains that Vascularize trachea by utilizing bioresorbable PLGA and PCL scaffold. To retain long-term survival, the reconstructed trachea was reinforced by external stenting on either side of trachea. The outcome describes that Stimulus responsive materials having ability to tailor their properties to specific requirements are the most beside biomaterials for tissue engineering.

R.C Thomson, et al.(2019), biodegradable polymer scaffolds to regenerate organs. The methodology used and describes is The technique used to manufacture scaffolds for organ regeneration is dependent on the properties of the polymer and its intended application. The outcome proven that PLLA, PLGA co polymers and PGA are biocompatible, biodegradable polymers which are proven to be suitable substrate for many cell types.

GUO baolin et al. (2020), synthetic biodegradable functional polymers for tissue engineering. The extracellular matrix (ECM) consists of variety of proteins that are assembled into organised network. PLA, PGA, PGLA are commonly synthesized by ring opening polymerisation of the monomers, this is the methodology used and explained in this survey. The out describes or conclude that this is a functionalized 3D scaffolds are no longer available just physical templates for cell growth and tissue formation the functional polymers are helpful in tissue engineering.

Jing sun, et al. (2018), synthesis and characterization of biocompatible nano particles. This describes us the different methodology used here they are initial treatment on reactants, preparation of nano particles, after the preparation of nano particles the X-ray diffraction method is undergone, after the diffraction the particle size is analysed using TEM. These methods and treatment is undergone to obtain the outcome and the outcome is obtained as Nanoparticles prepared by previous method can be promising as a potentially good magnetic support to be employed in magnetic carrier technology with good economic aspects, good biocompatibility,

good magnetic quality.

Joseph jagur-grodzinski, et al. (2017), methods used in this survey is Polyisobutylene based thermoplastic elastomers are considered to be prospective implant materials for replacement of soft tissue. Intracortical neural implants, with embedded microfluidic channels were fabricated on the basis of poly(benzocyclobutane)(BUB). The outcome is optimistic that Very optimistic assessments of benefits that such discoveries for example self-assembly of certain biomolecules. A very enthusiastic response to the introduction of the DESs seems also to be a bit premature.

Rober J, et al. (2020), biodegradable polymers in tissue engineering, three methods are used in this survey report they are auto crafting with bone, regeneration of cell, finally the crystallinity, these three methods are used in the bone tissue engineering. The outcome evolves that computational modelling will be helpful in selecting the appropriate polymers out of thousands of candidates stored in their property during manufacturing and their behavior after implantation process over the degradation process.

CHAPTER-3

AIM AND SCOPE

3.1 AIM and OBJECTIVES:

- To study the feasibility of biodegradable nature of polymer.
- To study the biocompatibility of natural polymer for drug delivery system.
- To study the adhesion of scaffolding materials.

3.2 SCOPE:

- It is essential that selected polymers should have biodegradable properties like nontoxic, which is capable of maintaining good mechanical integrity until degraded and it is capable of controlled rates of degradation.
- Natural Polymers are biocompatible, biodegradable, low cost and easy to prepare the biomaterials for human welfare.
- The proposed study would be a reference against the physically and chemically synthesized polymers, which are toxic or immunological response when exposed to the body or polymers should have cytotoxicity, mutagenicity, carcinogenicity and immunogenicity.

CHAPETR - 4

MATERIALS AND METHODS

4.1 MATERIALS:

4.1.1 ALGINATE:

This polymer is naturally occurring polymer. It is also an ionic polymer which is obtained from a seaweed called brown seaweed. It has been investigated extensively and also used for many applications of biomedical due to its low toxicity, affordable cost, biocompatibility, mild gelation by adding the divalent cation such as Ca^{2+} . This is made up of two copolymers named guluronic acid and mannuronic acid. This copolymer provides flexibility and strength to alginate. This has some unique features such as gelling properties, high viscosity, and high stability. It also has numerous numbers of applications such as formation of gel one of the main applications which we have used in our research. And it is also had the application of localizing drug delivery. The use of hydrogel alginate for tissue drug delivery is widely used in nowadays. Gaviscon Liquid (GL), which contains sodium alginate, CaCO_3 , NaHCO_3 , and flourishes a powerful floating raft in the bitter region of the belly, also has raftforming capabilities (Yousaf et al., 2019). Alginate-based hydrogels are routinely combined with other medicines, like as antacids, to boost the efficacy of raft compositions (Mandel et al., 2000). Alginate protects bacteria and improves their adhesion to solid surfaces, which causes alginate-based bio-synthetic genes to migrate and boost alginate production. As a result, alginate biofilms are being produced to help bacteria survive and proliferate. These biofilms have a low molecular weight (50–2000 kDa) and exhibit strong water absorption and low viscosity emulsification. In the pharmaceuticals business, alginate plays a significant role in the long-term release of drug delivery solutions. The regulated drug delivery method of alginate or its derivatives is illustrated in several therapeutic aspects in this review.

APPLICATION OF ALGINATE:

- It is used in the form of hydrogel in biomedicine field, including drug delivery and wound healing, and tissue engineering applications. They are

cross-linked in the three-dimensional networks made of hydrophilic polymers with high water content.

- Iron and calcium which is present in the blood from stomach wall bleeding reacts with the alginate to form a soft gel. This formed soft gel reduces or controls the stomach's acid-induced attack present in the wall. It also prevents pain and it also helps in healing. Sodium alginate is also present in oral drug.
- The most used form of an alginate is hydrogel formation in biomedicine field, drug delivery, wound healing and tissue engineering applications.
- The alginate available commercially is typically extracted from brown algae (Phaeophyceae), including *Laminaria hyperborea*, *Laminaria digitata*, *Laminaria japonica*, *Ascophyllum nodosum*, and *Macrocystis pyrifera* by treatment with aqueous alkali solutions, typically with NaOH. The extract is filtered, and either sodium or calcium chloride is added to the filtrate in order to precipitate alginate. This alginate salt can be transformed into alginic acid by treatment with dilute HCl. After further purification and conversion, water-soluble sodium alginate powder is produced. On a dry weight basis, the alginate contents are 22–30% for *Ascophyllum nodosum* and 25–44% for *Laminaria digitata*.
- The molecular weight of sodium alginates range between 32,000 and 400,000 g/mol.

4.1.2 GELATIN:

Gelatin is a natural polymer which is soluble in water. The absorption rate of the gelatin is 5-10 times the equivalent weight of water. The dissolution speed can be accelerated to certain degree when the temperature is increased. From the collagen a protein product will be derived. It has a combination of amino acids which is its unique characteristics which helps in the important health benefits. It plays a main role in brain function, joint health, and also helps to improve the appearance of hair and skin. Mainly gelatin is made from hides of the animals which are decayed, crushed bones which are boiled and the connective tissues of pigs and cattle. These skins, animal bones, and tissues are obtained from slaughter house. The amino acid sequence in gelatin is unique. It's made by hydrolyzing collagen, which is a major component of connective tissues like skin, tendons, and bones, among others. Collagen is made up

of protein chains that are linked together. Collagen's tertiary structure is broken up by hydrolysis, resulting in gelatin, which shares a primary structure with up to 20 distinct amino acids in varying amounts. The amino acid content and sequence in gelatin varies depending on the source, but it always includes non-polar and polar amino acids. Pigskin gelatin and bone gelatin, for example, do not contain cysteine, which is contained in fish scale and bone, and have a lower amount of glycine (Gly) than mammalian sources (Zhang et al. 2011).

APPLICATION OF GELATIN:

- Depends on their origin and sources it has unique characteristics.
- Bright future in biodegradable films can be seen due to nanomaterials incorporation and antioxidant films.
- It also has been incorporated with other ingredients with the aim to develop their mechanical and physical properties.
- In food industry, gelatin is used to provide stabilization, gelation, texturization and dairy, beverages, and emulsification of bakery. And it is also used in cosmetic, photographic industry.
- Gelatin is nearly tasteless and odorless with a colorless or slightly yellow appearance. It is transparent and brittle, and it can come as sheets, flakes, or as a powder. Polar solvents like hot water, glycerol, and acetic acid can dissolve gelatin, but it is insoluble in organic solvents like alcohol.[3] Gelatin absorbs 5–10 times its weight in water to form a gel. The gel formed by gelatin can be melted by reheating, and it has an increasing viscosity under stress (thixotropic). The upper melting point of gelatin is below human body temperature, a factor that is important for mouthfeel of foods produced with gelatin. The viscosity of the gelatin-water mixture is greatest when the gelatin concentration is high and the mixture is kept cool at about 4 °C (39 °F).
- Commercial gelatin will have a gel strength of around 90 to 300 grams Bloom using the Bloom test of gel strength. Gelatin's strength (but not viscosity) declines if it is subjected to temperatures above 100 °C (212°F), or if it is held at temperatures near 100 °C for an extended period of time.
- Gelatins have diverse melting points and gelation temperatures, depending on the source. For example, gelatin derived from fish has a lower melting and gelation point than gelatin derived from beef or pork.

4.1.3 PECTIN:

Pectin is a polymer which polysaccharide based in which the backbone consists of rhamnose and galacturonic acid with side chains made up of galactose, xylose, fucose, arabinose. It can be seen in the primary cell walls and in the ground plants of intercellular spaces. The report had clearly mentioned that it has properties of hypocholesterolemia due to its high capacity of gelling. And it cannot be incorporated in products of food at high concentration as its sensory characteristics affect the products negatively. The polysaccharide cell wall of pectin allows the primary cell wall extension and growth of plant. It is broken down by pectinase enzymes and pectin esterase and this breakage is done in fruit ripening. In this process the fruit becomes more softer the middle layer breakdown and the cells of the fruit become separated from each other.

Citrus peel or apple pomace are both used to make commercial pectin. An aqueous extraction under gently acidic conditions extracts the pectin from these materials, which is then precipitated and ground up to a powder with standardised characteristics. The majority of commercial pectin is made up of polymerized galacturonic acid that has been partially esterified with methanol. The fraction of galacturonic acid subunits that are methyl esterified has a significant impact on the pectin's functional characteristics. Low-ester pectins and high-ester pectins are the two types of commercial pectins. When the water activity of many fruit systems is lowered by adding enough sugar, high-ester pectins can form gels at low pH levels. Pectins, on the other hand, can form gels in the presence of water. Calcium is absorbed through a fundamentally different method, which is exclusively used with low-ester pectins in practise.

Many fruit materials have been known for ages to create gels when heated with sugar. The natural pectin content of the fruit was used to make this traditional jam. Commercial jam production accounts for the majority of pectin production today, although other uses, such as the stability of acidified milk products, are gaining traction.

APPLICATION OF PECTIN:

- Pectin is used to reduce blood cholesterol levels and gastrointestinal

disorders. The other uses of pectin include edible films, paper substitute, foams and plasticizers, etc.,

- Pectin is also used in food as a stabilizer and gelling agent. It has gained a big interest in its important use as a source of dietary fiber, lipid, cholesterol, serum glucose, and lowering level of Insulin effect, and delay emptying.
- Pectin is widely used in thickener, emulsifier, gelling agent, stabilizer, and in low calorie food in replacement of fat or sugar.
- The food sector lies in its ability to form gel in the presence of Ca^{2+} ions or a solute at low pH. The exact mechanism of gel formation is not clear, significant progress has been made in this direction. Based on the pectin, coordinate bonding with Ca^{2+} ions and hydrophobic interactions are involved in gel formation. In low-methoxyl pectin, gelation results from ionic linkage via calcium bridges between two carboxyl groups belonging to two different chains in close contact with each other. And also in high-methoxyl pectin, the cross- linking of pectin molecules involves a combination of hydrogen bonds and hydrophobic interactions between the molecules.
- The presence of other solutes, molecular size, degree of methoxylation, the arrangement of side chains, and charge density on the molecule--influence the gelation of pectin. It is used in jams, jellies, frozen foods, and more recently in low-calorie foods as a fat and/or sugar replacer in food industry. It is used to reduce blood cholesterol levels and gastrointestinal disorders in the pharmaceutical industry.
- Pectin include use in edible films, paper substitute, foams and plasticizers, etc. pectin are susceptible to heat degradation during processing, and the nature of the ions and salts present in the system is influenced to degradation. Although present in the cell walls of most plants apple pomace and orange peel are the two major sources of commercial pectin due to the poor gelling behavior of pectin from other sources. This paper briefly describes the structure, chemistry of gelation, interactions, and industrial applications soft pectin.

4.1.4 POLYVINYLPYRROLIDONE:

Polyvinylpyrrolidone, also known as povidone or PVP, is used in the pharmaceutical industry as a synthetic polymer vehicle for dispersing and suspending drugs. The polyvinylpyrrolidone is a water-soluble polymerization is obtained by polymer of

monomer N-vinylpyrrolidone. It is an inert, non-toxic, temperature-resistant, pH- stable, biocompatible, biodegradable polymer that helps to encapsulate and cater both hydrophilic and lipophilic drugs. PVP is soluble in water and other polar solvents. It is soluble in various alcohols, such as methanol and ethanol, as well more exotic solvents like the deep eutectic solvent formed by choline chloride and urea. When dry it is a light flaky hygroscopic powder, readily absorbing up to 40% of its weight in atmospheric water. In solution, it has excellent wetting properties and readily forms films. This makes it good as a coating or an additive to coatings.

PVP, often known as povidone, is an amorphous, hygroscopic synthetic polymer made composed of linear 1-vinyl-2-pyrrolidinone groups. PVP is used as a binder in concentrations ranging from 0.5 percent to 5% by weight. PVP polymerization levels varied, resulting in polymers with varying molecular weights. It's defined by its viscosity in aqueous solution compared to water, which is represented as a K value in the 10– 120 range. Povidones with K-values less than 30 are sprayed and dried as spheres, whereas those with higher K-values are drum dried and dried as plates (Chakraborty, Ghosh, & Chakraborty, 2015). Wet granulation with povidone K25/30/90 produces tougher granules with superior flow qualities than other binders with higher binding strength and lower friability. Furthermore, povidone aids in the breakdown of APIs.

4.1.5 MAGNETIC STIRRER:

A magnetic stirrer is a device widely used in laboratories and consists of a rotating magnet or a stationary electromagnet that creates a rotating magnetic field. This magnetic stirrer device is used to make a stir bar, immerse in a liquid, quickly spin, or stirring or mixing a solution, for example. The current magnetic stirrers rotate the magnets by means of an electric motor. This equipment is one of the simplest to prepare mixtures. This type of device is silent and provide the possibility of stirring closed systems without the need for isolation, as in the case with mechanical agitators.

In case of its size, stir bars can be cleaned and sterilized more easily than other devices such as stirring rods. Because of its limited size of the stir bars enables using this system only for volumes less than 4 liters. viscous liquid or dense solutions are barely mixed using this method. Particular kind of mechanical stirring is

commonly used.

A stir bar consists of a magnetic bar used to agitate a liquid mixture or solution (Figure 6.6). magnetic field does not affect significantly because of the glass, and most of the chemical reactions are undergone in glass vials or beakers, stirring bars function adequately in glassware commonly used in laboratories. Typically, stirring bars are coated with Teflon® or glass, so they are chemically inert and do not contaminate or react with the system in which they are immersed. Increase in size efficiency during stirring vary their size, because of this their size varies from a few millimeters to a few centimeters.



Fig 4.1. Agitation of liquid mixture on Magnetic stirrer

4.2 METHODOLOGY:

GELATION PROCESS:

Gelation has been described by Glicksman (1982) as cross-linking of long polymer chains to form a three-dimensional continuous network which immobilizes the liquid within it to form a rigid structure that is resistant to flow, under pressure. The process mainly involves polymerization of monomers to form a 3D hydrogel, and other reactions including cross-linking and catalysis. It can proceed in both non aqueous and aqueous solvents. It is a process that is of importance to a wide range of applications in food, pharmaceutical and material sciences. It is a general way to convert a fluid to a solid and has been used since antiquity to produce a variety of foods with distinctive textures. When gelation occurs, a dilute or more viscous polymer is converted into a system of infinite viscosity, i.e. a gel. The process Gelation is promoted by gelling agents. This process can be done by physical linking or by chemical crosslinking. While the physical gels involve physical bonds, chemical gelation involves covalent bond. This process mainly involves polymerization of monomers to form 3D hydrogel, as well as other reactions including cross-linking and catalysis. Gelation process results in both nonaqueous and aqueous solvents. The Nonaqueous solvent usually refers to some organic

solvents, such as dibutyl phthalate, dibasic ester, petroleum solvents, pyrrolidones, and long-chain ethanol. The Various monomers, as well as other organic binders, they should dissolve in nonaqueous solvents. To eliminate all of the binders and solvents, the firing process can take several steps. Furthermore, increased polymer exhaust from nonaqueous solvents may result in environmental issues. In contrast, aqueous gel-casting is frequently preferred and employed in both laboratories and industry. The aqueous slurry's viscosity is low enough for casting. Furthermore, because water is used as the solvent, the gel-casting process is not dissimilar to other wet-forming techniques, and similar colloidal effects and drying processes could be used in gel-casting.

One of the most distinguishing characteristics of gel-casting is the monomer, which comes in two types: monofunctional and difunctional. Monofunctional monomers have a single bond and polymerize to produce a linear chain. A cross-linked polymer network is formed by difunctional monomers with at least two double bonds. As a

result, cross-linkers are also known as difunctional monomers. The polymerization process can be accomplished in two ways, depending on the monomer's functions. The first is an acrylate-based system. Nonfunctional monomers hydroxyethylmethacrylate (HEMA), methyl acrylate (MA), and N-vinylpyrrolidone (NVP) are extensively employed, as are difunctional monomers ethyleneglycol dimethacrylate (EDMA) and diethylene glycol diacrylate (DEGDA) (cross-linkers). Because the two types of monomers are not miscible in water at the same time, a cosolvent like NMP is frequently required.

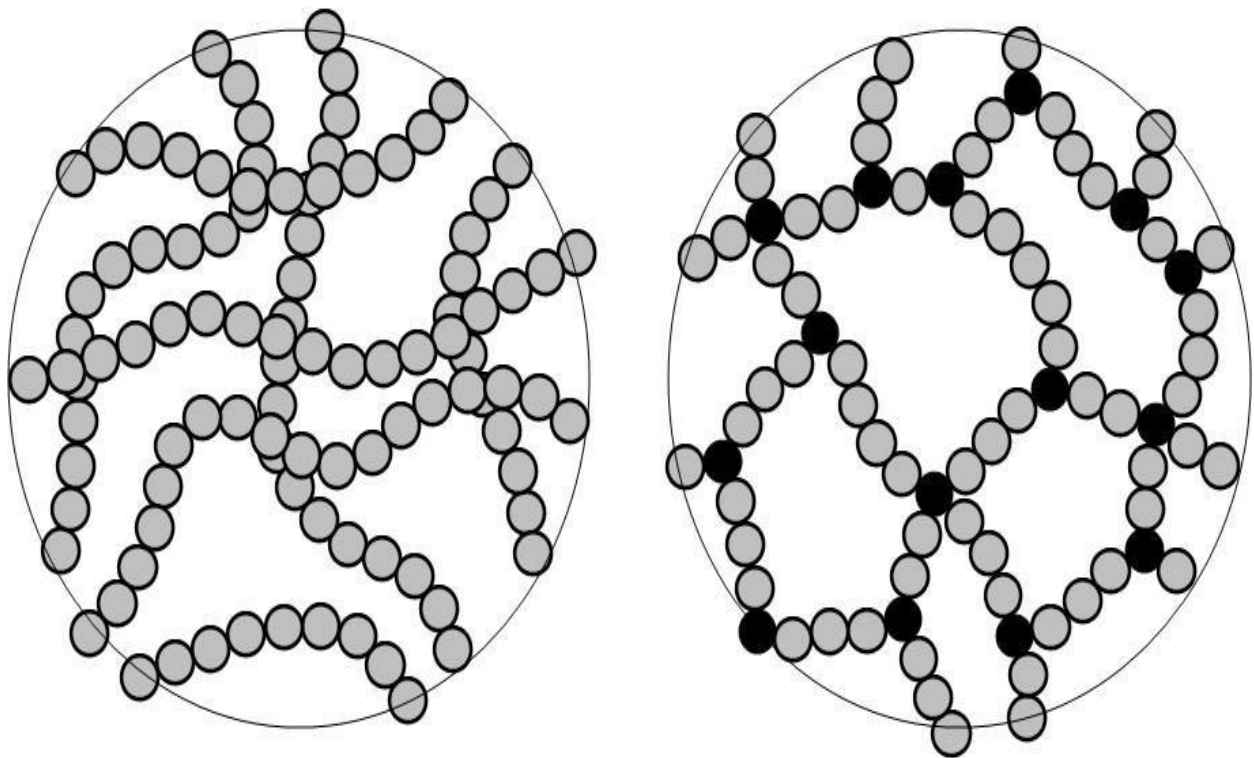


Fig 4.2. Gel-casting process of two monomers.

4.2.1 ALGINATE GEL FORMATION:

For this process we are taking 0.2g of alginate and 0.5g of gelatin with 40ml of distilled water. And heating it until it mixed well, after heating we should let it to be cool at room temperature. Also, we adding 0.2g of CaCl_2 into the 20ml of distilled water, and stirred it well. Whenthe alginate mix is cooled, we pouring CaCl_2 into it. And we should leave it for 15mins to get the gel formation.



Fig: 4.3. Formation of alginate-gelatin gelation.

4.2.2 PECTIN GEL FORMATION:

In this process we taking 1g of pectin and 0.5g of alginate with 50 ml of distilled water. We are adding 50 ml of PVP solution with continuous stirring to get a homogenous mixture. And also, we are adding glutaraldehyde reagent (0.2 ml HCL + 1 ml GA) into the homogenous mixture. Stirrer continuously at room temperature for half an hour. Later we keep the hydrogel to dry at room temperature for 72. Wash it with distilled water to remove excess HCL and GA.



Fig: 4.4. Formation Pectin-Alginate gelation

CHAPTER - 5

RESULTS AND DISCUSSION

5.1. SAMPLE PREPARATION:

ALGINATE GEL FORMATION:

During the alginate gel formation process 0.2g of alginate and 0.5g of gelation was mixed with 40ml of distilled water and heated until it gets mixed well. The mixture was then followed to be cool at room temperature. Further 0.2g of CaCl_2 were added into the 20ml of distilled water and stirred it well to get the proper mixture. When the alginate mix is cooled, then the CaCl_2 was added into it and left for 15mins to get the formation of gel.

PECTIN GEL FORMATION:

The pectin gel formation process was carried out with 1g of pectin and 0.5g of alginate added with 50 ml of distilled water. Then to get a homogenous mixture the process was followed with 50 ml of PVP solution with continuous stirring. During the preparation of homogenous mixture, the glutaraldehyde reagent (0.2 ml HCL + 1 ml GA) was added and stirred it continuously at room temperature for half an hour to form a hydrogel. Further the hydrogel has to dry at room temperature up to 72h and followed by a wash with distilled water to remove excess HCL and GA.

5.2. FTIR RESULT:

FTIR - Fourier transform infrared spectroscopy (FTIR) is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high-resolution spectral data over a wide spectral range. The tendency of the functional groups of sodium alginate chains to create complex structures with calcium ions is due to carboxylate groups. 1500 cm^{-1} and 1400 cm^{-1} were attributed to asymmetric and symmetric stretching vibrations of the COO^- groups, respectively, and are specific to the ionic binding C.R. BADITA et, al, 2019. The peak of C–C stretching (1028.4 cm^{-1}) shows a higher intensity, suggesting either a stronger O–H binding vibration or a stronger binding of the Ca^{2+} to the guluronic acids from sodium alginate. Moreover, the stretching vibration bands observed at approximately of 945 cm^{-1} , 887 cm^{-1} and 816 cm^{-1} are specifics to

the guluronic and mannuronic acids. Also, the small shifts of carboxyl groups indicate an ionic binding between Ca_2^+ and sodium alginate chains C.R. BADITA et. al, 2019. The peak corresponding to the bending mode of O-P-O bonds falls on 550cm^{-1} . The absorption bands of amide I and amide II related to pectin group observed in the spectra of the drug delivery cage. Giada catteian et al., 2013, observed that the IR spectral study of pectin band peaked at 1800cm^{-1} C=O stretch corresponding to amide I group. In the present study the absorption band of the amide I and amide II related to pectin can observed in the FTIR spectra of the drug delivery cage.

Wavelength	Chemical Bond	Functional Group
4000-3500	O–H stretch, free hydroxyl	alcohols, phenols
3400-3200	N–H stretch, O–H stretch, free hydroxyl	1°, 2° amines, amides, alcohols, phenols
2500-2000	$\text{C}\equiv\text{N}$ stretch, $\text{--C}\equiv\text{C--}$ stretch	Nitriles, alkynes
1800-1500	C=O stretch, C=O stretch	carboxylic acids, esters, saturated aliphatic
1500-1000	C–C stretch (in–ring), C–H bend	Aromatics, alkanes
750-450	$\text{--C}\equiv\text{C--H}$: C–H bend	alkynes

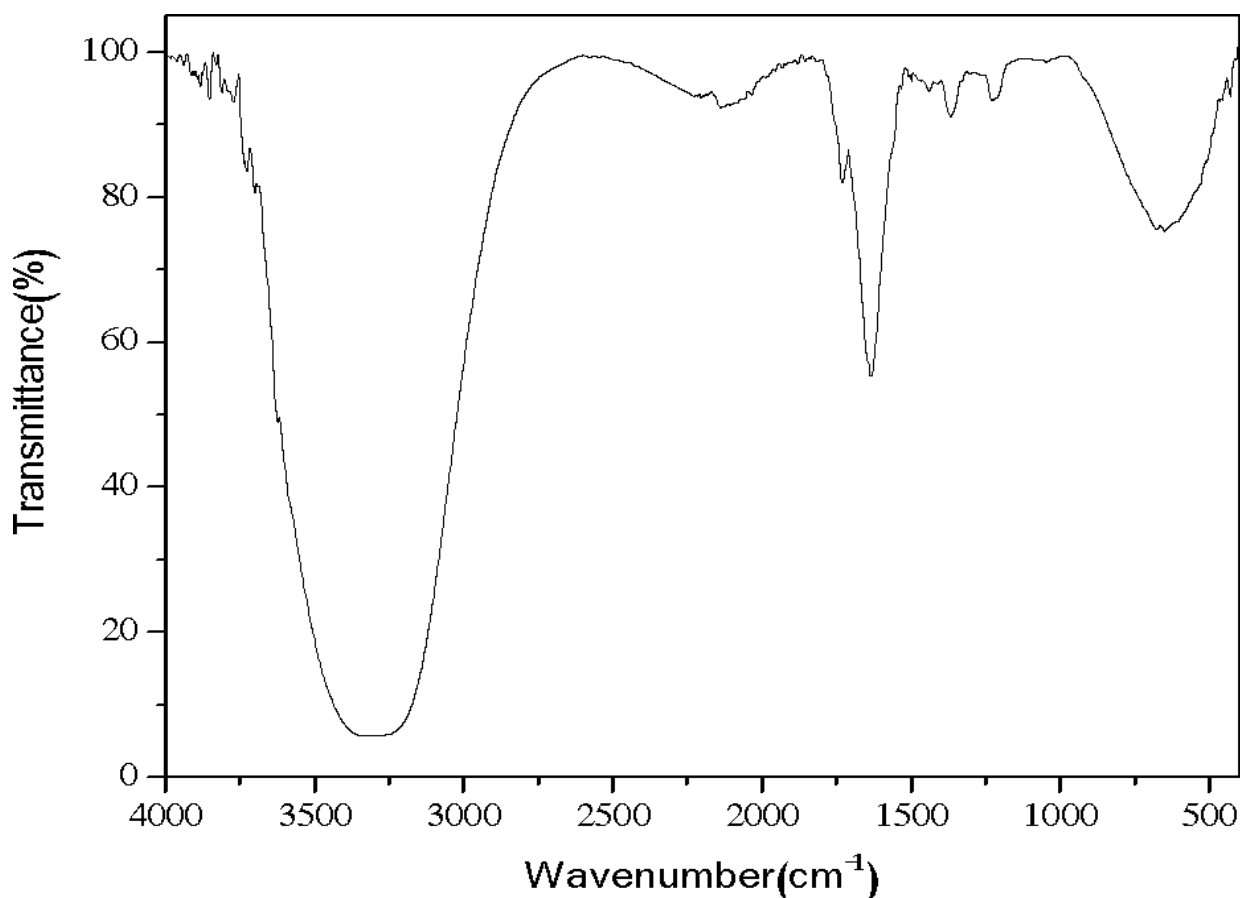


Fig 5.1. FTIR graph

5.3 SEM RESULT:

SEM -A Scanning Electron Microscope (SEM) is a type of electron microscope that obtains images by scanning the surface of a sample with a concentrated stream of electrons. When electrons collide with atoms in a sample, they emit a variety of signals that reveal the surface topography and composition of the sample.

Hydrogel microstructure morphologies are one of the most significant aspects to consider. Scanning electron microscopy was used to examine the surface morphology of the samples. Figure shows an SEM micrograph of alginate- pectin and alginate-gelatine hydrogels obtained from the surface of the drug delivery cage. It is supposed that these pores are the regions of water permeation and interaction sites of external stimuli with the hydrophilic groups of the graft copolymers B. KAZEMZADEH1, etc., al, 2013. The hydrogel sample contain pores to enhance the interaction between drug molecules to cell, which facilitate the adherence of the drug into the interpenetrating network of the hydrogel.

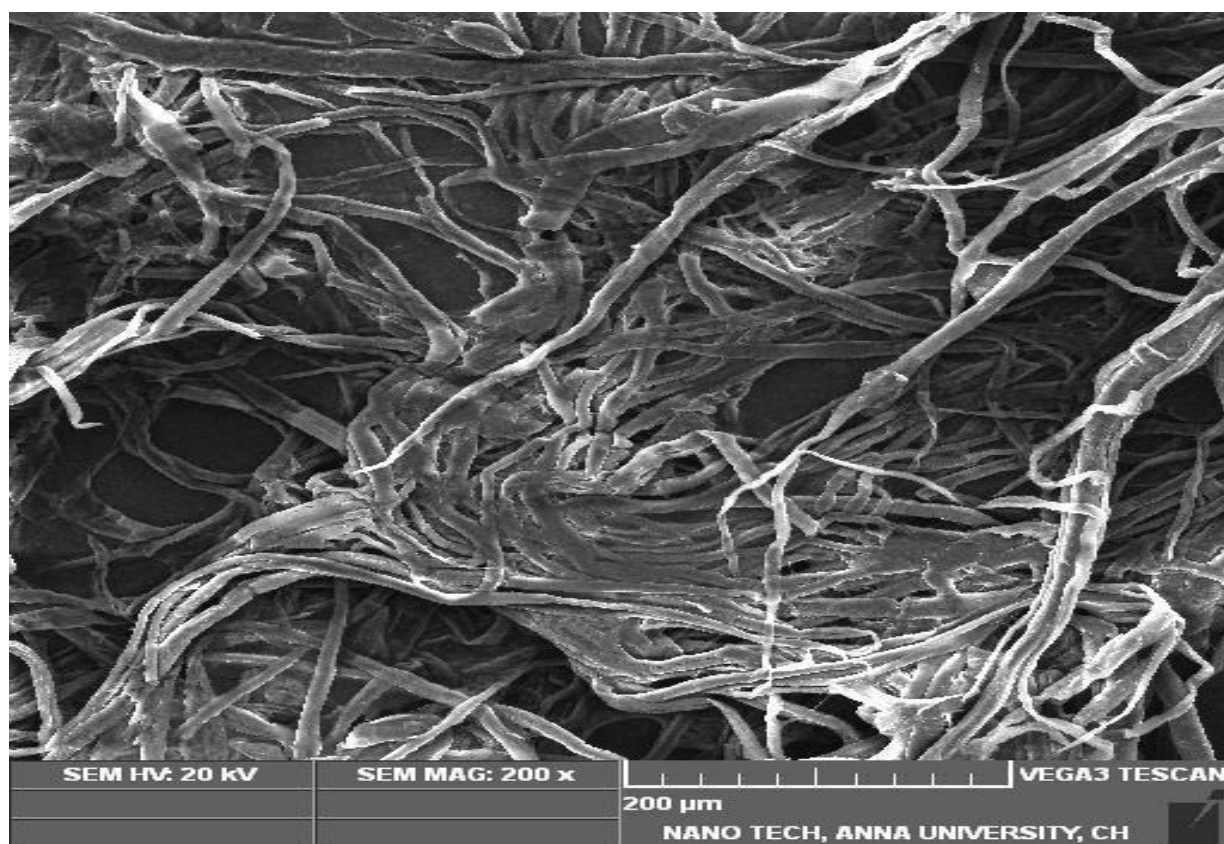
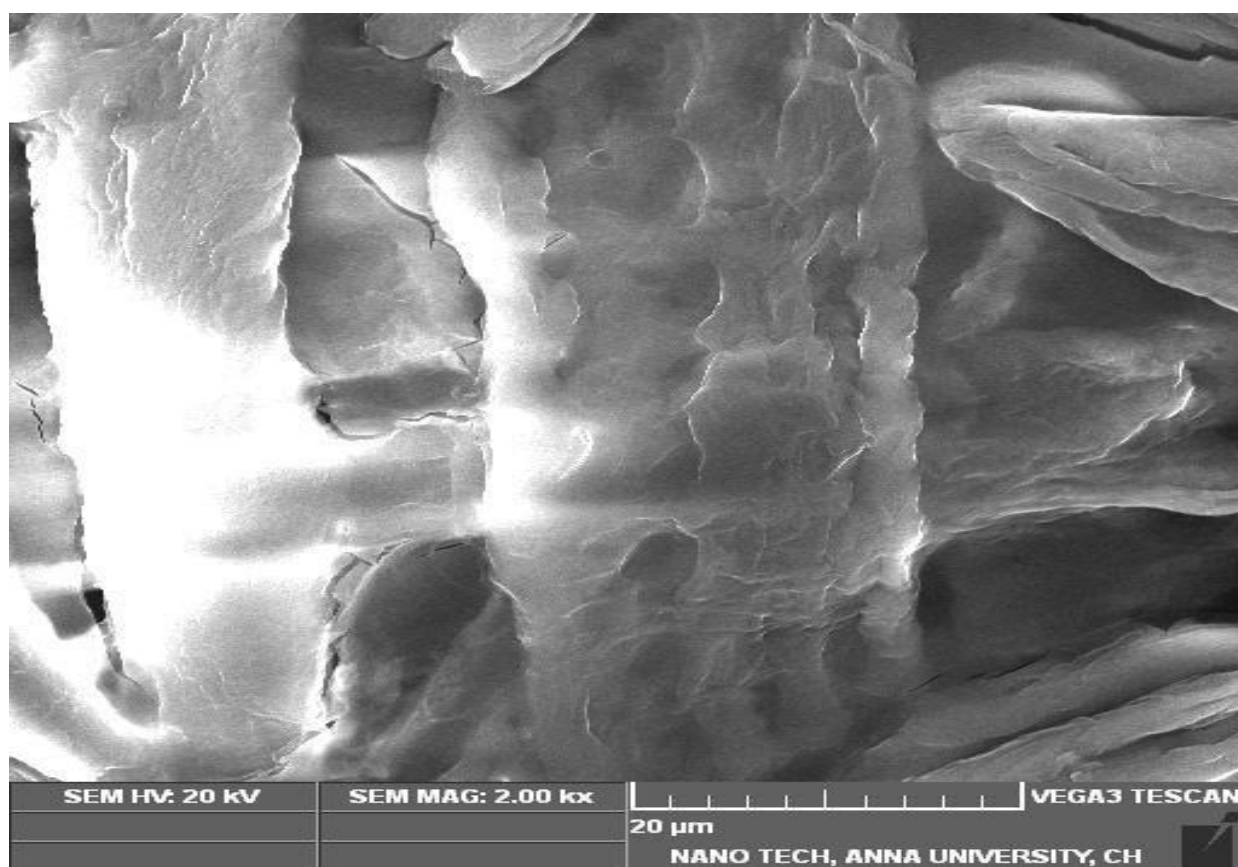


Fig 5.2. Scanning Electron Microscope Images of Pectin.

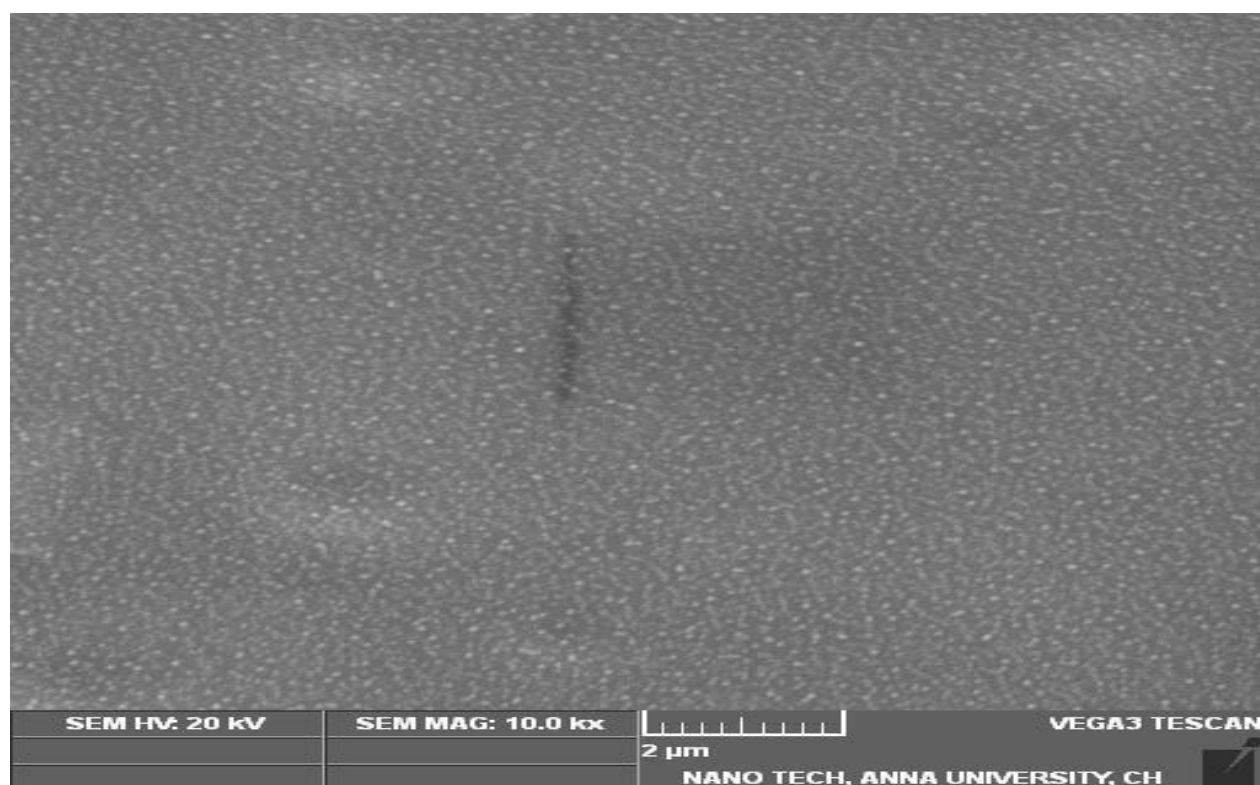


Fig 5.3. Scanning Electron Microscope Images Of Alginate.

5.4 BIO-DEGRADATION ANALYSIS:

Drug delivery are not considered as a permanent solution. Drug delivery cage should be reabsorbed with an appropriate degradation rate and also colonizing the adjacent cells to deliver the appropriate drug. The choice of a biodegradable biomaterial is thus of great importance with regard to tissue engineering (Iudovica Parisi et al 2018). Degradability of the drug delivery cage material is a concerned property for route, biomaterials because it's a crucial for targeted drug delivery, conduction as well as metabolic reaction. The degradation study was performed according to the ISO 10993-14 "Biological evaluation of medical device-Part 14". Table shows the swelling ratio of drug delivery cage in phosphate buffer saline in different time intervals. Here the samples were subjected in phosphate buffer saline with pH of 7.3 in different time interval.

S.NO	Alginate-Gelatin Cage	Alginate-Pectin Cage
H1	1.79g	1.90g
H2	1.49g	1.79g
H3	1.30g	1.70g
H4	1.10g	1.602g
H5	1.03g	1.49g

Table 5.3.1. Degradation study

The neutral pH of sample treated with phosphate buffer saline. The present study shows that the degradation of the drug delivery cage is pH dependent. However, the degradation rate of the drug delivery was slowed in alginate-pectin sample in 48h than compare to alginate-gelatin sample. Gelatin is denaturable protein derived by the partial hydrolysis of collagen. The amount of collagen renovation into the gelatin is most influenced with temperature, pH and time of hydrolysis process. Pectin and gelatin-based drug delivery cage is biodegradable and biocompatible biomaterials both in-vitro and in-vivo condition.

CHAPTER - 6

SUMMARY AND CONCLUSION

Polymers generally have cytotoxicity, genotoxicity, mutagenicity, carcinogenicity, and immunogenicity. In comparison to alginate-gelatin, the rate of drug delivery degradation was delayed in the alginate-pectin sample after 48 hours. When the biological synthesized polymers were exposed to the body, they did not create a toxic or immunological reaction. Gelatin is a denaturable protein made from collagen that has been partially hydrolyzed. Temperature, pH, and length of hydrolysis process have the most impact on the amount of collagen renovation into gelatin. *In vitro* and *In vivo*, pectin and gelatin-based drug delivery cages are biodegradable and biocompatible biomaterials. In the FTIR spectra of the drug delivery cage, the absorption band of the amide I and amide II associated to pectin can be seen. SEM micrograph of alginate-pectin and alginate-gelatin hydrogels obtained from the surface of the drug delivery cage. The hydrogel sample contain pores to enhance the interaction between drug molecules to cell, which facilitate the adherence of the drug into the interpenetrating network of the hydrogel. The selected polymers have biodegradable properties and non-toxic, capable of maintaining good mechanical integrity until degraded and capable of controlled rates of degradation.

CHAPTER – 7

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