International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Natural Polymers in Novel Drug Delivery System

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ABSTRACT:
Natural polymers have gained significant attention in the development of novel drug delivery systems due to their biocompatibility, biodegradability, and low toxicity. These polymers, derived from plant, animal, and microbial sources, offer a versatile platform for targeted and controlled drug release, minimizing side effects and enhancing therapeutic efficacy. Key examples include chitosan, alginate, gelatine, and cellulose derivatives, which are explored in diverse drug delivery formats like hydrogels, nanoparticles, and microcapsules. Their structural flexibility enables drug encapsulation, sustained release, and specific targeting to diseased tissues or organs. Moreover, natural polymers can be functionalized to respond to physiological triggers such as pH, temperature, and enzymes, optimizing drug bioavailability and patient compliance. the landscape of personalized medicine. This review underscores the benefits, challenges, and future prospects of natural polymers in creating effective, safe, and innovative drug delivery systems.

Keywords: Natural polymers, Drug delivery systems, Biocompatibility, Biodegradability, Controlled release, Targeted delivery, Chitosan, Alginate, Gelatin.

1. INTRODUCTION:

Natural polymers extracted from organic sources such as microorganisms, algae, plants, or animals have been widely used for decades in biomedical applications such as pharmaceuticals, tissue regenerations [1]. Polysaccharides, proteins, and polyesters derived from plant and animal kingdoms are part of the family of natural polymers. Several of these polymers comprise our diet and have been used in various human application. These polymers are recognized by the biological environment and directed into metabolic degradation [2]

Natural polymers are components of biological systems responsible for performing various essential functions [3]. For instance, specific natural polymers, such as cellulose and chitin, play a vital role in maintaining the structural integrity of cells in plants and animals. In contrast, others, such as lysozymes, offer biological protection against surrounding environments [4]. The diversity in their origin and composition provides these natural polymers with distinct physicochemical and biological properties and are of interest in various fields, e.g., in the manufacture of paper goods and textiles, as additives in food products, in the formulation of nutraceuticals and functional foods, and in the biomedical field (e.g., in cosmetic treatments and drug delivery) [5]. Their exploitation is favourable due to the natural abundance, renewability, and intrinsically low carbon footprint of polymers derived from renewable resources. Natural polymers are essential for supporting life and enabling organisms to adjust to their surroundings through vital biological processes like molecular identification and genetic information transfer [6].

Sodium alginate is a natural polymer extracted from marine algae that has a wide range of applications in the industrial field because of its unique and excellent structural and chemical properties, including the preparation of new materials for pharmaceutical preparations, the biomedical field, the food field, the cosmetics field and the environment field[7,8,9,10,11,12] .Natural reserves of are very abundant, and natural polymers are preferred over synthetic polymers due to their excellent biocompatibility and natural degradability, and they are considered sustainable and promising alternative to petroleum- derived polymer[13,14].With the development of nanotechnology, the preparation of nanostructured SA materials has gained in-depth research and made great progress [15]. Among them, nanofibers are considered one of the most promising nanotechnologies for overcoming the current challenges and shortcomings of modern drug delivery systems and achieving the desired release pattern [17,18,19] Sodium alginate nanofiber (SANF) membranes prepared based on electrostatic spinning technology have excellent properties, such as high specific surface area, high drug loading capacity, controlled drug delivery, and reduced drug side effect [16].

One of main causes of impairment world is bone loss brought on by non-healing fracture following trauma, disease like osteoporosis and which impact millions of individuals worldwide [20]. Despite their long history and widespread use, the materials currently used in clinics include metals ceramics and polymers [21]. Nanotechnology has made significant strides in recent years, with the use of nanomaterials in regenerative medicine as well as in bone tissue engineering. Osteoprogenitor cell migration and recruitment is the first step in the complicated and dynamic process of bone tissue engineering, followed by the cell's proliferation, differentiation, matrix formation and bone modelling [22] The structure and organization of the extracellular matrix (ECM) and cells that are hierarchal and span multiple orders of magnitude (nm to cm) greatly influence the characteristics of bone tissue. Therefore, novel approaches are taking into account the hierarchal assembly of tissue, from the nanoscale to macroscale, and are needed for the healing and restoration of bone defects [23]. Nan composites and nanomaterials are a potential platform for bone tissue engineering because they can resemble the structure of the natural extracellular matrix and ensure robust bone tissues by utilizing bone-shaped architecture. Which deal with the implementation of natural biopolymers that mimic the environment of the natural extracellular matrix (ECM). In bone tissue engineering, scaffolds are the substitute for the extracellular matrix. Scaffolds are composed of biodegradable biopolymers, which are porous in nature and can provide a bioactive environment in which the cells can adhere and proliferate. It also contains cells, some growth factors and certain biochemical signals, which can replace and repair the damaged tissues by creating a new environment that will allow the cells to build up their own native extracellular Matrix [24]. A morphogenetic signal, receptive host cells, an appropriate carrier of the signals that can send them to specific places and subsequently function as a scaffold for the emergence of the responsive host cells, and a healthy well-vascularized host bed are all required for the regeneration of bone. This also provides structural integrity and a supporting matrix for bone regeneration [25]. Scaffolding materials for bone tissue engineering can be stiff or injectable, with the latter requiring surgical implantation [26]. The optimum bone tissue scaffolds for bone tissue engineering must be osteoconductive and osteogenic. The requirement of osteo conductivity of these scaffolds is to promote the attachment, survival and migration of osteogenic cell [27]. Directing stem cells towards the osteoblastic lineage, osteo inductive scaffolds not only provide the physical strength but also assist in incorporating pharmacological action [27]. To establish functional bone tissue engineering. Sustained release of a hydrophilic drug from the hydrophobic polymer carrier might be difficult, and phase separation and splitting of the drug from the matrix may occur, causing sudden release of the active substance in a layered scaffold-drug delivery system the hydrophilic drug can be preserved in a hydrophilic polymer in a form of particles, and integrated into the hydrophobic scaffold allowing for a longer and more stable release. This system many advantages since it can provide physical bonds between biological parts such as cells and scaffolds due to drug and polymer scaffolds cell retention capacity [28].

Tetracycline (Tet) is an antibiotic used in the prophylaxis and treatment of both human and animal infections against microorganisms such as gram-positive and gram-negative bacteria, protozoa, parasites, and mycoplasmas. Tet, which has a versatile and changeable structure, has been used in the treatment of diseases for more than half a century now due to its chemical backbone that interact with the cellular target. Basically, in the working mechanism of Tet antibiotic interfere with bacterial proteins by binding to them at the site of biosynthesis through the 30S subunit of the bacterial ribosome. The mechanism of action of tetracyclines makes it impossible for bacteria to attach tRNA and in consequence the inhibition of the development of the bacterial cell occurs. Tet is used clinically for bacterial dysentery, trachoma, pertussis pneumonia purulent meningitis, skin infections and otitis media. In the study of swamy et al used PCL nano fibres enriched with Tet in different concentrations and tested the influence of the concentration of the drug on the speed of tissue regeneration.

The treatment of skin diseases through topical drug administration offers significant advantages compared to systemic routes. These advantages include targeted drug delivery, minimized systemic drug exposure (and, consequently, fewer systemic side-effects), and avoidance of hepatic first-pass effect Topical formulations are also easy and painless to administer (non-invasiveness), ensuring good patient compliance. They can be tailored to have controlled drug release, leading to therapeutic effects that last for a longer period of time studies.

2. NATURAL POLYMER:

Plant based polymers are naturally available and can be made into natural polymers. Natural gums are hydrophilic carbohydrate polymer of high molecular weight. As these plant elements are rich in carbohydrates most, they are insoluble in organic solvents. Gum either water soluble or absorb water and swell in cold water in order to provide viscous solution [29].

2.1CLASSIFICATION OF NATURAL POLMERS:

Natural polymers are classified in three main categories, such as.

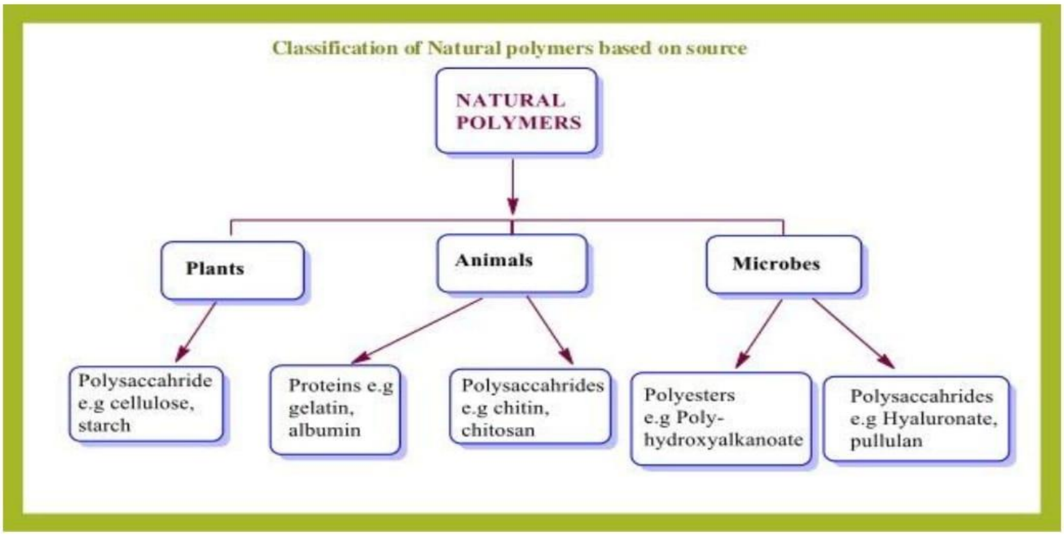

Fig No. 1: Classification of natural polymers.

2.2 C0MPOUND OF NATURAL POLYMERS:

1. POLYSACCHARIDES FROM PLANT ORIGIN:

Natural polysaccharides are complex carbohydrates composed of long chains of monosaccharide (sugar) units linked together by glycosidic bonds. These biopolymers are found in various natural sources, including plants, animals, and microorganisms. Natural polysaccharides serve a wide range of functions in biological systems and have numerous industrial and commercial applications. Natural polysaccharides are valued for their biodegradability, biocompatibility, and sustainable sourcing. They are widely utilized in the food industry, pharmaceuticals, cosmetics, agriculture, and other sectors, making them an essential class of biopolymers.

CELLULOSE: Cellulose is the most prevalent organic substance on Earth and a form of carbohydrate [30,31,32,33]. dressings have high absorption capacity, which helps in managing exudate, preventing. Cellulose -based wound dressings can help prevent biofilm formation on the wound surface. Biofilms are communities of bacteria that can impede the healing process and make wounds more susceptible to infection. Cellulose dressings can create a barrier that inhibits biofilm formation. Some cellulose-based biomaterials, particularly those with 3D structures, can provide a scaffold for the formation of granulation tissue. Granulation tissue is a critical part of the proliferative phase of wound healing and plays a role in wound closure and tissue repair. It's important to note that the effectiveness of cellulose-based wound dressings may vary depending on the specific product, wound type, and individual patient needs. Overall, cellulose-based biomaterials are part of the broader field of biomaterials used in wound care. It complex polysaccharide composed of repeating glucose molecules and is present in the cell walls of all plants and many algae. Cellulose provides structural rigidity and resilience to plants, and is essential for their growth and development. Additionally, it is an essential component of wood, cotton, and other natural fibers. There are numerous industrial applications for cellulose, including the production of paper, textiles, biofuels, and other renewable materials. In some culinary products, it is also used as a low-calorie thickener and stabilizer. Due to its capacity to promote tissue regeneration and lesion closure, cellulose has been used in Wound healing. Cellulose-based dressings, when placed to a wound, can provide a moist environment that helps hasten healing and inhibit the growth of germs. Additionally, cellulose dressings can absorb excess wound exudate, thereby reducing inflammation and preventing infections. Certain types of cellulose dressings, such as those manufactured from carboxymethyl cellulose (CMC), can form a gel-like barrier over the incision to promote healing and alleviate pain. Another form of cellulose-based Wound dressing is manufactured from bacterial cellulose, which is generated in a manner similar to 3D printing by certain bacteria. This form of dressing has a highly porous structure and can serve as a scaffold for the growth of new tissue and the healing of wounds. Burns, chronic ulcers, and surgical incisions are among the categories of lesions for which cellulose-based dressings have been shown to be safe and effective in both preclinical and clinical studies [34,35,36].

Cellulose-based biomaterials can play a beneficial role in skin Wound healing. These materials are used in various wound care products and dressings to support the healing process by providing a suitable environment for tissue regeneration. Cellulose-based wound dressings are often designed to maintain a moist environment around the wound. Proper moisture control helps create conditions that are conducive to cell migration, proliferation, and tissue repair. Moist wound healing can promote faster healing and reduce scarring. Wounds often produce exudate, which is a combination of blood, serum, and other fluids. Cellulose-based dressings have high absorption capacity, which helps in managing exudate, preventing dressings have high absorption capacity, which helps in managing exudate, preventing it from accumulating around the wound, and reducing the risk of infection [37]. Cellulose-based wound dressings can help prevent biofilm formation on the wound surface. Biofilms are communities of bacteria that can impede the healing process and make wounds more susceptible to infection. Cellulose dressings can create a barrier that inhibits biofilm formation. Some cellulose-based biomaterials, particularly those with 3D structures, can provide a scaffold for the formation of granulation tissue. Granulation tissue is a critical part of the proliferative phase of wound healing and plays a role in wound closure and tissue repair. It's important to note that the effectiveness of cellulose-based wound dressings may vary depending on the specific product, wound type, and individual patient needs. Overall, cellulose-based biomaterials are part of the broader field of biomaterials used in wound care, and they contribute to creating a favourable environment for the body's natural wound healing mechanisms to function optimally.

2. PROTEINS FROM ANIMAL ORIGIN:

Natural proteins are large, complex molecules that play vital roles in biological processes. They are one of the fundamental classes of biomolecules and are made up of long chains of amino acids. Proteins are essential for the structure, function, and regulation of various components of living organisms. Natural proteins are fundamental biological macromolecules with diverse functions, and they are crucial for the proper functioning of living organisms. They are extensively studied and have a wide range of applications in various fields, including medicine, biotechnology, and scientific research.

GELATIN: It derived from collagen obtained from animal tissues, has been explored for its potential applications in wound healing. Collagen is a major component of the extracellular matrix in connective tissues, and it plays a crucial role in tissue repair and regeneration. dressings or sponges can be used as wound dressings. These materials provide a moist environment, which is conducive to wound healing, and they can also serve as a barrier against microbial. these dressings may help promote cell proliferative and tissue repair. It can used to create hydrogels, which are water-containing gels that can provide hydration to the wound. Hydrogels are designed to maintain a moist environment, which supports cell migration, angiogenesis (the formation of new blood vessels), and other processes crucial for wound healing.

CHITOSAN: Chitosan is a naturally occurring polysaccharide derived from the exoskeletons of crustaceans, such as shrimp, crab, and lobster. Biodegradable, non-toxic, and biocompatible, chitosan is a Linear polymer composed of randomly distributed -(1–4)-linked d-glucosamine and *N*-acetyl-d-glucosamine units. Chitosan's capacity to adhere to and trap fats and cholesterol in the digestive tract has made it a popular weight loss and cholesterol-lowering dietary supplement] [38,39,40,41]. it is also used as a biodegradable packaging material and for wound healing and water remediation. Although chitosan has been studied for its potential antibacterial, antifungal, and antitumor properties, additional research is required in these areas. Chitosan's potential to promote wound healing has been investigated. Chitosan, when administered to a wound, can produce a protective film that prevents infection and promotes healing. It is believed that its wound-healing properties result from its ability to stimulate the production of growth factors and promote the formation of new blood vessels, both of which are necessary for the regeneration of damaged tissue [42]. Chitosan can also promote the formation of granulation tissue, a type of tissue that forms during the healing process and is composed of new blood vessels and connective tissue.

3. FROM MICROBE POLY ESTERS:

Now a day, Polyesters are one of the most economically important and widely used classes of polymers among the polycondensation polymers. The 'Polyesters' is a term used for polymeric material having ester groups in the polymeric main chain of macromolecules instead of ester groups in the side chain of macromolecules, as in the case of poly (vinyl acetate), poly (methyl methacrylate), Or Cellulose triacetate, etc. Since time immemorial, the use of natural polyester has been in vogue to mankind. The reports show that the shellac (Natural polyester) was used in the mummies embalming by esters of Egyptians and as a resin for phonographic records journey of synthesizing synthetic polyesters has been known since the late eighteenth century as a resinous form, the exact composition of which remained unknown. Earlier reports of these types of polyester resin show that Berzelius was the first scientist who synthesized first polyesters of polybasic acids and polyvalent alcohol by reacting tartaric acid and glycerol in 184741. Many other efforts had been made at the same time those from Berthelot, who obtained a resin by reacting glycerol and camphoric acid in 1853 who made glycerides of succinic acid and citric acid in 1856 first commercially important polyester was alkyd resins, developed for the coating, varnishes, and paints applications. Alkyd resins are essentially polyester of phthalic anhydride, glycerol, and monocarboxylic unsaturated fatty acids. Alkyd resin was first marketed in 1929 by the General Electric Company of the However, the modern history of polyesters began with the work of the Carothers in 1930s. He proved the macromolecular theory of Staudinger by experimental studies on the reaction between aliphatic dibasic acids and diols and recognized the relationship between the degree of polymerization.

HYALURONIC ACID: The body naturally produces hyaluronic acid (HA), which is present in many tissues including the skin, joints, and eyes. It is a glycosaminoglycan , a kind of molecule composed of units of sugar molecules that repeat repeatedly. Hyaluronic acid is crucial for the skin's ability to retain moisture, elasticity, and plumpness. It can store 1000 times its weight in water, preventing dryness and wrinkles while preserving the skin's hydration levels. Dermal fillers, which plump up the skin and minimize the appearance of wrinkles and fine lines, are only one example of how hyaluronic acid is employed in a variety of medicinal and cosmetic purpose [43,44,45,46,47]. it is used in certain joint injections to lessen discomfort and inflammation in arthritis sufferers. The healing of wounds benefits greatly from hyaluronic acid (HA). The body reacts to a skin injury by creating a blood clot to halt the bleeding , and then it begins to restore the tissue. In this healing process, hyaluronic acid plays various roles. Hyaluronic acid generates a gel-like matrix after an injury that gives new cells a framework to develop into. This matrix aids in the creation of a scaffold for the generation of new tissue. This matrix may aid in preventing scarring by directing the creation of new tissue. Hyaluronic acid promotes cell migration and proliferation by attracting and activating immune cells and other cells vital to the healing of wounds. Additionally, it promotes the growth of fibroblasts, which are cells that create the proteins required for tissue repair, including collagen. Inflammation is a normal component of the healing process for wounds, however excessive inflammation may slow down healing and cause scarring. Hyaluronic acid aids in reducing inflammation. By preventing the synthesis of pro-inflammatory molecules, hyaluronic acid aids in the reduction of inflammation.

3.0 NATURAL POLYMERS FOR BIO MEDICAL USE:

3.1. Antibacterial:

Antimicrobial medication coatings, antimicrobial gauze or dressings, and medical tapes containing antimicrobial agents are a few examples of antimicrobial wound healing techniques. Chi et al. created a patch called the biomass-energetic chitosan microneedle array (CSMNA) to aid in healing wound [48]. Due to its exceptional qualities and inherent antibacterial capabilities, chitosan is often utilized for wound healing [49] The microneedle’s microstructure also helps to prevent excessive skin and patch adherence while delivering the drug-carrying agent to the target location. Meanwhile, a temperature-sensitive hydrogel wraps vascular endothelial growth factor (VEGF) in the CSMNA micropore [48]. As a consequence, the temperature rise brought on by the inflammatory response of the wound may be exploited to regulate the release of smart drugs. Biomass CSMNA patches have been proven in studies to support tissue regeneration, angiogenesis, collagen synthesis, and inflammatory control during wound healing Therefore, this multifunctional CSMNA patch may be helpful in clinical applications such as wound healing [50].

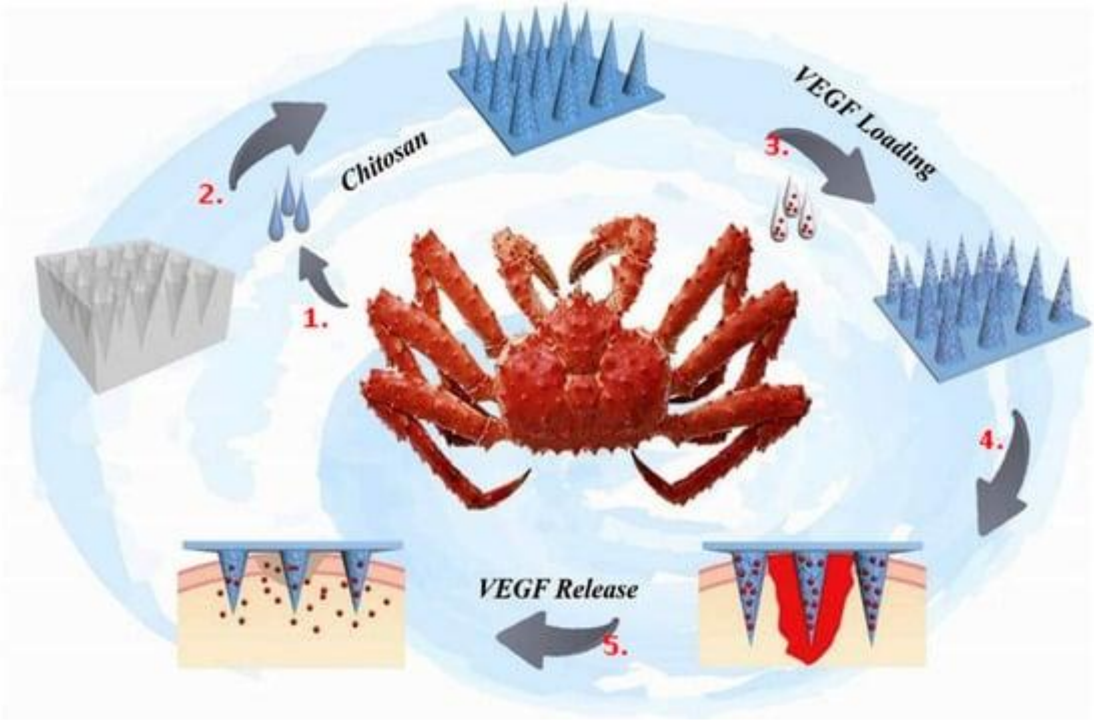

Fig no:2 Antibacterial agents

3.2. Hydrogel Preparation and Application

Hydrogels prepared from natural polymers have attracted extensive attention in many due to their excellent biocompatibility, degradability, and flexibility [59]. Hydrogels are three-dimensional networks formed by hydrophilic polymers through chemical cross-linking (covalent or ionic bonds) or physical cross-linking (hydrogen bonds, van der Waals forces, and physical entanglement) swollen in water [51,52]
Hydrogels based on natural polymers such as alginate, starch, cellulose derivatives, chitosan, collagen, hyaluronic acid, pectin, and so on show good degradability, biocompatibility, nontoxic degradation products, good flexibility similar to natural tissue, and have natural abundance, which endows them with widespread applications in medicinal fields, for instance, as drug carriers, wound dressing for wound healing, substrates for cell culture, cell delivery systems, scaffolds for tissue regeneration[53,54].
Hydrogels based on natural polymers have emerged as promising alternatives for the ECM in biomedical applications due to their unique integration of biodegradability, biocompatibility, mechanical property tunability, biomimicry, and responsiveness, which could provide microenvironments with the preservation of cellular functions, promotion of cell health, and encouragement of tissue formation [55,56].
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3.3. Drug Delivery

Extensive research has been conducted on the use of natural polymers as carriers for drugs and other bioactive substances, which has garnered a great deal of interest. Natural polymers have inherent advantages such as biocompatibility, controlled enzyme degradation, specific interactions with some biomolecules and easy modification, which make them versatile for drug delivery applications. In this context, drug delivery systems (DDSs) constructed using representative natural polymers such as polysaccharides (chitosan and hyaluronic acid) and proteins (silk fibroin and collagen) are generally summarized. These DDS systems are used to deliver payloads, which mainly include low molecular weight drugs, proteins, and DNA, and are employed for various applications such as tissue engineering, wound healing, or anticancer therapy. Moreover, a DDS constructed by modified biopolymers has also been presented, focusing on the chemical and morphological modifications, the additions of smart stimuli-triggered or targeted motifs, and so on, which promoted delivery and therapy efficiency.

Polysaccharides and protein-based materials show more similarities to the extracellular matrix, thus endowing natural polymer-based drug carriers with minimally invasive properties Moreover, polymer chains are abundant in some groups with accessibility to modification, including amino groups, carboxyl groups, hydroxyl groups [58]

***3.4. Wound Healing**:*

Natural polymers play significant roles in different skin wound healing processes, contributing to the overall effectiveness of wound management and tissue repair. Natural polymers such as chitosan and hyaluronic acid can help reduce inflammation in the early inflammation phase of wound healing. With its anti-inflammatory properties, chitosan can minimize the inflammatory response, while hyaluronic acid contributes to a balanced immune response, potentially reducing excessive inflammation [59].

Natural polymers like collagen, chitosan, and keratin provide a scaffold for cell migration and proliferation. Collagen-based dressings act as a structural framework for cells to move into the wound area and stimulate cell division, promoting granulation tissue formation As a primary component of the extracellular matrix, collagen facilitates the formation of this supportive network. It guides fibroblasts to synthesize new collagen, helping reestablish tissue integrity. Hyaluronic acid and alginate maintain a moist wound environment conducive to cell proliferation and migration. This wet environment also helps prevent the formation of scabs, promoting faster healing. Specific natural polymers, such as keratin, have been found to minimize scarring and promote a more natural appearance of healed tissue This is particularly valuable in aesthetic areas or where scar formation could impair function. Chitosan has inherent antimicrobial properties, helping prevent infections in the wound area. Chitosan dressings can inhibit the growth of bacteria, making them suitable for wounds at risk of infection. Alginate dressings, composed of seaweed-derived alginic acid, absorb excess exudate from the wound. This maintains a moist environment and helps prevent bacterial proliferation in overly damp condition.

3.5. Skin Tissue Engineering

Due to their excellent biocompatibility, biodegradability, and low cytotoxicity, as compared to synthetic polymers, natural polymers find extensive application in skin tissue engineering Polysaccharides and protein-based materials are the two primary categories of natural polymers employed in hydrogels for this purpose. Dermal substitutes comprising collagen or hyaluronic acid serve as scaffolds for cellular growth. On the other hand, epidermal substitutes, consisting of keratinocytes and fibroblasts, replace the outermost layer of skin Natural polymers, including alginates, collagens, hyaluronic acid, and, are commonly used in bone tissue engineering. These polymers are employed in three primary forms: nanofibrous scaffolds, hydrogels, and microspheres. have also been developed for bone tissue engineering by combining natural polymers with hydroxyapatite. Bone scaffolds serve as a crucial application of natural polymers and provide a supportive structure for cellular. Osteogenic differentiation, involving transforming mesenchymal stem cells into bone-forming osteoblasts, is another essential aspect of natural polymer utilization. Additionally, natural polymers are used in bone regeneration strategies, acting as scaffolds or carriers for growth factors to promote the restoration of damaged or lost bone tissue [60]

3.6. Cartilage Tissue Engineering

Cartilage is composed of thick proteoglycans and collagen. This thick and lubricated structure presents particular challenges for adhesives and bonding strategies. Furthermore, cartilage defects lack a regenerative capacity, as they lack blood vessels/neural tubes. Natural polymers, such as collagen, chitosan, alginate, silk fibroin, and hyaluronan, have extensive applications in cartilage tissue. serve as primary natural polymers in cartilage tissue engineering, providing a supportive structure for cellular growth. Various materials can fabricate these scaffolds, including chitosan, collagen, alginate, silk fibroin, hyaluronan, and. Chondrogenic differentiation is another significant application of natural polymers involving transforming mesenchymal stem cells into chondrocytes, contributing to cartilage formation. Furthermore, natural polymers are being investigated for repair and regeneration techniques to promote the restoration of damaged or lost cartilage tissue. These techniques often employ natural polymers as scaffolds or carriers for growth factors [61]

3.7 Heart Valve Tissue Engineering:

Polysaccharides are the most abundant biomaterials in nature and meet several criteria for eligibility for tissue engineering, which include biocompatibility, biodegradation, and the ability to support cell development. Due to their biological properties and structural and functional similarities to ECM, it is reasonable to use them in tissue engineering Polysaccharides become essential to promote heart valve tissue regeneration in combination with appropriate cells or bioactive molecules. Their applications for heart valve tissue engineering are vast and varied, and approximately 70% of all studies in this field focus on chitosan, alginate, hyaluronic acid, and cellulose, respectively [62]

3.8 Cell Encapsulation:

Cell encapsulation instead of therapeutic product encapsulation leads to longer delivery times, as cells continuously release encapsulated products. Moreover, cell encapsulation allows for the transplantation of non-human cells, which may be considered an alternative to the limited supply of donor tissues. In addition, genetically modified cells could also be immobilized to express any desired protein in vivo without host genome modifications Cell immobilization displays a significant advantage compared to protein encapsulation, allowing for the sustained and controlled delivery of de novo-produced therapeutic products at constant rates, leading to physiological concentrations. The versatility of this approach has adapted its use in treating diabetes, cancer, central nervous system diseases, heart diseases, and endocrinological disorders, among others. Hydrogels are among the most promising biomaterials for recreating native extracellular matrix (ECM) properties due to their high-water content, biological compatibility, and moldability [63].

4] Natural Polymers for Environmental Use

4.1. Food Packaging:

Various natural polymers from renewable sources have been used to develop biobased food packaging. The primary natural sources used for packaging are derived from polysaccharides, lipids, proteins, or

blends of these polymers. The utilization of these natural materials is linked to their biodegradability and renewability However, other advantages are expected when used for food packaging. For example, these materials can act as carriers of functional substances, add well-being benefits, incorporate flavourings and colourings, enhance organoleptic characteristics, improve mechanical and barrier resistance, etc.
Polysaccharides possess suitable oxygen barriers and have sites for hydrogen bonding formation, which can be used to incorporate functional substances, e.g., colouring, flavouring, and antioxidant agents. In contrast, these materials do not exhibit an excellent barrier to water vapor, which can be overcome by blending with other hydrophobic substances, such as lipids. Polysaccharides have been used to develop natural-based packaging [64,65]

4.2.NanoFertilizersandMicronutrients:

Biopolymers such as alginate, cellulose, chitin, chitosan, hemicellulose, lignin, polypeptides, and polyesters, used as nanocarriers to encapsulate nutrients and avoid dissolution and oxidation, are an eco-friendly option due to their natural origins and are biodegradable when compared to bulk synthetic. Chitosan is the most accepted biopolymer for agriculture due to its innocuous origin and ability to protect plant cells. It is also an easy-to-manipulate matrix to program the adsorption and slow release of the target active ingredient. The cover of nano fertilizers is designed to be porous for the slow release of the nutrient content [66,67].

4.3. Nanocarriers of Insecticides

Polymer-based materials have also been found to be effective insecticide carriers, mainly by increasing their solubility in water. Microspheres composed of chitosan and cashew tree gum were developed and loaded with the essential oil of active against larvae of *Aedes aegypti*, to use as a bioinsecticide to control larvae proliferation. These chitosan-based capsules showed a prolonged larvicidal effect. Similarly, microcapsules of alginate and chitosan were found to be suitable matrices to carry nano imidacloprid bioinsecticide [68]

5. NATURAL POLMER APPOACH IN SUSTAINED RELEASE DRUG DELIVERY SYSTEM:

The use of natural polymers and their semi-synthetic derivative in drug delivery continues to be an area of active research. Drug release retarding polymers are the key performer in matrix systems. Various polymers have been investigated as drug retarding agents, each presenting a different approach to the matrix system. Based on the features of the retarding polymer, matrix systems are usually classified into three main groups: hydrophilic, hydrophobic and plastic. Hydrophilic polymers are the most suitable for retarding drug release and there is growing interest in using these polymers in sustained drug delivery. There are various numbers of natural polymers which have been investigated as sustained release agent.

5.1. ALOE MUCILAGE:

The inner part of the leaves of Aloe vera (L.) many compounds with diverse structures have been isolated from both the central parenchyma tissue of Aloe vera leaves and the exudates arising from the cells adjacent to the vascular bundles. The bitter yellow exudates contain 1, 8 dihydroxyanthraquinone derivatives and their glycosides [69,70]. The aloe parenchyma tissue or pulp has been shown to contain proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and small organic compounds in addition to the different carbohydrates. These matrix systems showed good swelling properties that increased with an increase of aloe gel concentration in the formulation. The directly compressed matrix type tablets also showed modified release Behaviour with 35.45% and 30.70% of the dose released during the first hour and the remaining of the dose was released over a 6 hours period for those formulations containing the lower ratios of gel to drug, namely 1:0.5 and 1:1. The formulation that contained the highest ratio of gel to drug, namely 1:2 exhibited only a 23.25% drug release during the first hour with the remaining of the dose being released over an 8 hour period. The dried A. vera gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained- release matrix type tablets. In another investigation matrix tablets of Glimepiride with Aloe miller leaves mucilage and Povidone was formulated and studied its functionality as a matrix forming agent for sustained release tablet formulation. They found to have better satisfactory physicochemical properties with low SD values[71,72].

Fig no:3 Aloe mucilage

5.2. FENUGREEK MUCILAGE:

Trigonella commonly known as Fenugreek, is plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids [73]. husk from the seeds is isolated by first reducing the size, and then separated by suspending the size reduced seeds in chloroform for some time and then decanting. Successive extraction with chloroform removes the oily portion which is then air dried [74]. A different extraction procedure is also reported to isolate the mucilage from the husk. The powdered seeds are extracted with hexane then boiled in ethanol. The treated powder is then soaked in water and mechanically stirred and filtered. Filtrate is then centrifuged, concentrated in vacuum and mixed with 96% ethanol. a study the mucilage derived from the seeds of fenugreek, was investigated for use in matrix formulations containing propranolol hydrochloride.K4M was used as a standard controlled release polymer for comparison purposes. A reduction in the release rate of propranolol hydrochloride was observed with increase in concentration of the mucilage in comparison to that observed with matrices. The rate of release of propranolol hydrochloride from fenugreek mucilage matrices was controlled by the drug: mucilage ratio.

Fenugreek mucilage at a concentration of about 66.\. W\W was found to be better release retardant compared to Hypromellose at equivalent content [75].

Fig no:4 Fenugreek mucilage

5.3. GUAR GUM;

Guar gum comes from the endosperm of the seed of the legume plant Cyamopsis tetragonolobus. Guar gum is prepared by first drying the pods in sunlight, then manually separating from the seeds. The gum is commercially extracted from the seeds essentially by a mechanical process of roasting, differential attrition, sieving and polishing. The seeds are broken and the germ is separated from the endosperm. Two halves of the endosperm are obtained from each seed and are known as Guar Splits. Refined guar Splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing. The refined Guar Splits are then treated and finished into powders by a variety of routes and processing techniques depending upon the end product desired [76]. Chemical, guar gum is a polysaccharide composed of the Sugars galactose and mannose. The backbone is a linear chain of 1, 4- linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side- branches [77]. Guar gum is more soluble than locust bean gum and is a better emulsifier as it has more galactose branch points. It degrades at extremes of pH and temperature (e.g. pH 3 at 50°C) [78]. stable in solution over pH range 5-7. Strong acids cause hydrolysis and loss of viscosity, and in strong concentration also tend to reduce viscosity. It is insoluble in most hydrocarbon solvents. Guar gum is used and investigated Guar gum is used and investigated as a thickener in cosmetics, sauces, as an agent in ice cream that prevents ice crystals from forming and as a fat substitute that adds the "mouth feel" of fat and binder or as disintegrator in tablets. The I.R spectral analysis studies confirmed no interaction between phenytoin with used natural gums.

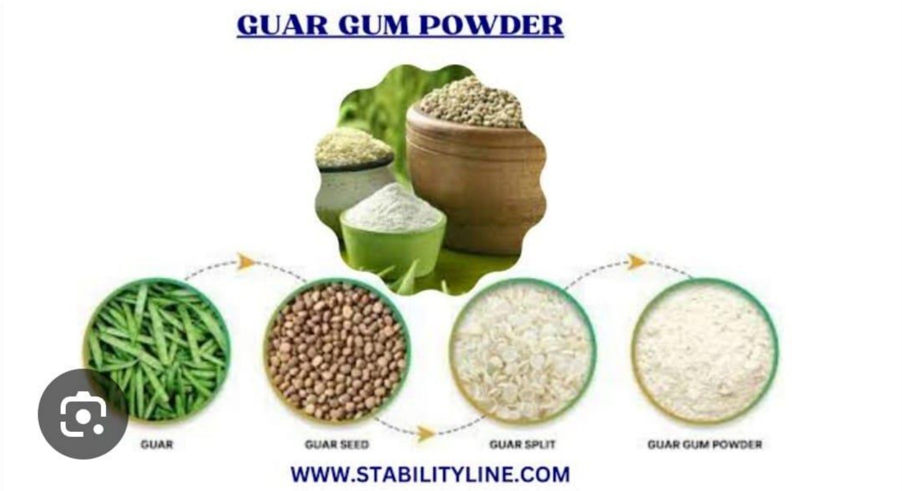

Fig no: 5 Guar gum

5.4 TAMARIND GUM:

Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, Tamarindus indica, a member of the evergreen family. Tamarind Gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds. The seeds are processed in to gum by seed selection, seed coat removal, separation, hammer milling, grinding and sieving. Tamarind gum is a polysaccharide composed of glucosyl: xylose: galactosyl in the ratio of 3:2:1. Xyloglucan is a major structural polysaccharide in the primary cell walls of higher plants. Tamarind xyloglucan has a (1 4)-! -D-glucan backbone that is partially substituted at the O-6 position of its glucopyranosyl residues with "-Dxylopyranose. Some of the xylose residues are! -D-glycosylated at O-2 .It is insoluble in organic solvents and dispersible in hot water to form a highly viscous gel such as a mucilaginous solution with a broad pH tolerance and adhesivity. Tamarind gum is nonnewtonian and yield higher viscosities than most starches at equivalent concentrations] [79,80]

Polymer Drug Release Mechanism: Different methods allow the therapeutic chemicals linked to the polymers to be released from the polymeric matrix at a regulated place. Polymer characteristics are used to distribute a medication to tissues over a predetermined period. For instance, polymers that release drugs only when the PH or temperature changes are known as stimuli sensitive polymer [81].

Degradation: natural physiological and biological processes breakdown some biodegradable polymer. Additionally, they may be engineering to break down when hydrolysed resulting in shorter more controlled chain with negative consequence

Diffusion: Often, a reservoir device is Utilised to store the medication, which is housed in the tablets core or polymeric network and protected by a shell. The drugs rate of diffusion from the core will be controlled by the polymer used in the shell water diffuses into the centre of the device dissolving the mediation which is subsequence released Depending on the polymer the shell may be swell or degrade Diffusion system may be divided into two categories:

1. only the dissolved substance in the centre is used there is a reduction in drug load overtime as the central
2. The initial concentration of the mediation in the core is greater than the concentration of aqueous solubility drug load remain stable for a longer length of time as the dissolved substance diffuses outwards more rapidly

Swelling: distribution is swelling as it fills up, the matrix former may regulate the place at which the mediation is released. As a result of increased polymer swelling diffusion paths becomes longer, decreasing the gradient of drug concentration .so the medication is released in to the bloodstream over the longer period of time. swelling of the polymer on the other hand, may speed up the release by increasing molecular mobility Diffusion **Another** governing factor in mediation – controlled system and drug release formulation triggered by solvents have made enormous development overall. With the use of hydrogels and other polymeric carrier systems, therapeutic drugs may be delivered safely and more effectively to difficult-to-reach physiological areas such as the brain and liver The polymer-conjugated therapeutics have demonstrated better drug release kinetics by avoiding carrier buildup, according to the research[82]

6. APPLICATION OF NATURAL POLYMERS IN DRUG DELIVERY SYSTEM:

6.1. Gelling agents

Study was carried out to find the gelling potential of gum exudates from the stem of moringa oleifera. Diclofenac sodium gels were formulated with concentration of mucilage ranging from 5.5 to 8.5 W/W Better gel characteristics were observed at the concentration of 8 percent W/W. As the PH Of the gum is below 5.77 and the viscosity of the formulation [83]

6.2. SUSPENINGAGENTS

comparative Study of gums of moringa oleifera and tragacanth was reported. Zinc oxide suspensions were prepared with gum of Moringa oleifera and tragacanth. Their sedimentation profile, degree of flocculation and rheological behaviour were compared. The results revealed that the suspending properties of Moringa oleifera gum are comparable with that of gum tragacanth [84].

6.3 Surfactants:

A Study on interfacial properties and fluorescence of a coagulating protein extracted from Moringa seeds and its interaction with sodium dodecyl sulphate [SDS] was carried out. The study reported.[85]

6.4. Film forming property:

Study of reported that gum of M. oleifera has enormous potential for use in the preparation of polymeric films as drug delivery the films as prepared using gum of M. oleifera using gum of M. oleifera parts of 10 percent W/W of mucilage of gum of M. oleifera with different proportion of plasticizers. There were evaluated for parameters like water uptake tensile strength, folding endurance and water vapour transmission rate [86]

6.5.AS Stabilizer:

Plant phenolics have gained considerable interest in recent years for their potential effects against food related microorganisms. Phenolic extract obtained from the leaves of M. oleifera & Morainic showed stabilizing activity. In the present study effect of addition of phenolic extract from leaves of M. oleifera and M. indica on the shelf life of pineapple juice stored at 4 0 C was investigated by monitoring the changes in titration acidity and sensory parameters for 8 weeks. Results observed that the extracts of natural phenolics can be used to improve the quality and safety of foods [87]

6.6. Cosmetics use:

Various parts of Moringa oleifera have cosmetic value. Cognisa Laboratories Aerobiologist team developed Puri care TM and Puri soft TM, two active ingredients based on botanical peptides from the seeds of Moringa oleifera tree that purify hair and skin and offer protection against the effects of pollution. Moringa seed oil, known as Behen oil is widely used as a carrier oil in cosmetic preparations. The healing properties of Moringa oil were documented by ancient cultures. Moringa oil possesses exceptional oxidative stability which may explain why the Egyptians placed vases of Moringa oil in their tombs. It can be used in body and hair care as a moisturizer and skin conditioner. Other uses include soap making and for use in cosmetic preparations such as lip balm and creams [88]

6.7 water purification:

Moringa has the ability to remove hazardous materials from water. After oil extraction of Moringa seeds the left press cake contains water soluble proteins that act as effective coagulants for water purification. The charged protein molecules can serve as nontoxic natural polypeptides to settle mineral particles and organics in the purification of drinking water, vegetable oil, depositing juice and beer. Moringa seeds showed similar coagulation effects to alum. It is also reported that a recombinant protein in the seed is able to flocculate gram positive and gram-negative bacterial cells. Moringa seeds could be used as a bio absorbent for the removal of cadmium from aqueous media. Thus, water purifying attributes of Moringa seeds are as coagulant, microbial elimination and as a biosorbent [89].

ADVANTAGES OF NATURAL POLYMERS IN DRUG DELIVERY SYSTEM:

1. Naturally occurring polymers produced by living organisms hence they are biodegradable and biocompatible.

2. They show no adverse effect on the environment or human being.
3. Carbohydrates in nature and composed of repeating monosaccharide units. Hence, they are non-toxic.
4. Economic and Easy availability.
5. Safe and devoid of side effect They are from a natural source and hence, safe and Without side effects.

8. DISADVANTAGES OF NATURAL POLYMERS IN DRUG DRLIVERY SYSTEM:

1. Microbial contamination during production they are exposed to external environment and hence, there are chances of microbial contamination.
2. Batch to batch variation – manufacturing is controlling procedure with fixed quantities of ingredients While production of natural polymer dependent on environment and various physical factors
3. The uncontrolled rate of hydration-Due to differences in the collection of natural materials at different times, as well as difference in region, species and climate conditions the percentage of chemical constituents present in a given material may vary.
4. Heavy metal contamination-There are chances of heavy metal contamination often associated with herbal excipients

9. LIMITIONS OF NATURAL POLYMERS IN DRUG DELIVERY SYSTEM:

Natural polymers have limitations in drug delivery system include;

1. Poor aqueous solubility, low bioavailability, and drug in viscosity upon storage
2. They also have uncontrolled hydration limited thermal stability, and in ability to perform under high temperature and pressure.
3. These drawbacks restrict their applications in drug delivery systems. However, grafting of natural polymers can improve their properties and characteristics, such as gel strength, and drug release profile.
4. Graft co polymers have gained important in the development of drug delivery systems.
5. In addition, natural polymers like alginates have limitations in the development of modified- release dosage forms and formulations with adequate mechanical strength.
6. Blending alginates with other natural polymers such as chitosan, pectin and carrageenan can overcome these limitations and improve drug carriers.
7. Overall, natural polymers have limitations in drug delivery, but grafting and blending with other polymers offer potential solutions.

10. CONCLUSION

In this review, we have highlighted the enormous potential and diverse importance of polyphenolic substances in tissue engineering and drug delivery. These natural compounds have unique features, such as antioxidant, anti-inflammatory, and anticancer activities, that offer great opportunities for improving current medical practices. The potential of polyphenols can be further improved by producing various biomaterials. Polyphenolic substances can provide significant benefits.

Effective treatment of obesity has always been a major clinical problem, as traditional drug therapy makes it difficult to achieve the desired therapeutic effect and is always accompanied by side effects. Therefore, this has led to the development of innovative DDSs that use safe and degradable polymers as carriers to deliver therapeutic agents to the appropriate target cells. Although there are still significant challenges, there are already a large number of important results from preclinical.

ACKNOWLEDGEME

The task of preparing the dissertation has been an overwhelming experience, an achievement in itself, like the birth of a river in the mountain cascading through the slope to the plains and meeting the sea and even as we rejoice in post completion euphoria, it affords us an immense pleasure to acknowledge with gratitude; the help and guidance renders to us by a host of people of whom we owe a substantial measure in the completion of my review article. I remain debted to them for the fresh lease of life, new dimensions to our life, which remains a lot for me and which has blended the past and the present and opened the doors for the future. Many thanks to Almighty God, for it he who began this work in me and carried to completion. It is He who has blessed us with the people whose names I feel privileged to mention here.

I am deeply indebted to Dr. B. V. RAMANA M. Pharm Ph. D, for inspiring and valuable guidance throughout my work. I would like to thank him for all the advices, encouragement, help and everything that we learnt from him. He showed us different ways to approach the completion of this review article. His profound knowledge in Pharmaceutics and his dedication to advancing this field have inspired and motivated me throughout the process. His keen insights and constructive suggestions helped shape this work and allowed me to gain a deeper understanding of the nuances and complexities involved.

REFERENCE:

1. Puertas-Bartolomé, M.; Mora-Boza, A.; García-Fernández, L. Emerging Bio fabrication Techniques: A Review on Natural Polymers for Biomedical Applications. *Polymers* 2021, *13*, 1209. [Google Scholar] [Crossruff]
2. Aaradhana.; Ramos, D.M.; Nada, A.A.; Kumbar, S.G. Chapter 4—Natural Polymers: Polysaccharides and Their Derivatives for Biomedical Applications. In *Natural and Synthetic Biomedical Polymers*; Elsevier: Amsterdam, The Netherlands, 2014; pp. 67–89.Availableonline: **https://www.sciencedirect.com/science/article/abs/pii/B9780123969835000041** (accessed on 15 March 2024).
3. Schultz, B.; Snow, E.S.; Walker, S. Mechanism of D-Alanine Transfer to Teichoic Acids Shows How Bacteria Acylate Cell Envelope Polymers. *Nat. Microbial.* **2023**, *8*, 1318–1329. [**Google Scholar**] [Crossruff] [**PubMed**]
4. Caillou, S. Special Issue "Natural Polymers and Biopolymers II". *Molecules* **2020**, *26*, 112. [**Google Scholar**] [crossruff]
5. Rajeswari, S. Natural Polymers: A Recent Review. *World J. Pharm. Pharm. Sci.* **2017**, *6*, 472–494. [**Google Scholar**] [Crossruff]
6. Silva, A.C.Q.; Silvestre, A.J.D.; Vilela, C.; Freire, C.S.R. Natural Polymers-Based Materials: A Contribution to a Greener Future. *Molecules* **2022**, *27*, 94. [**Google Scholar**] [**CrossRef**]
7. Pawar, S.N.; Edgar, K.J. Alginate Derivatization: A Review of Chemistry, Properties and Applications. *Biomaterials* **2012**, *33*, 3279–3305. [**Google Scholar**] [Crossruff] [**PubMed**]
8. Priya, S.; Batra, U.; Samhita, R.S.; Sharma, S.; Chaurasiya, A.; Singhvi, G. Polysaccharide-Based Nanofibers for Pharmaceutical and Biomedical Applications: A Review. *Int. J. Biol. Macrogol.* **2022**, *218*, 209–224. [**Google Scholar**] [crossruff] [**PubMed**]
9. Hinderer, S.; Layland, S.L.; Schenke-Layland, K. ECM and ECM-like Materials—Biomaterials for Applications in Regenerative Medicine and Cancer Therapy. *Adv. Drug Deliv. Rev.* **2016**, *97*, 260–269. [**Google Scholar**] [crossruff]

10. Rezaei, S.; Viipuri, A.; Hosseini Radande, S.A.; Kouhei, M.; Ghasemi MO Barakeh, L. Fabrication, Characterization, and Drug Release Study of Vitamin C–Loaded Alginate/Polyethylene Oxide Nanofibers for the Treatment of a Skin Disorder. *Polymer. Adv. Technol.* **2019**, *30*, 2447–2457. [Google Scholar] [crossruff]
11. Mokena, T.C.; Machine, M.J.; Mite, A.; John, M.J.; Sadiku, E.R.; Safadi, J.S. Electro spun Alginate Nanofibers Toward Various Applications: A Review. *Materials* **2020**, *13*, 934. [Google Scholar] [CrossRef]
12. Healy, L.E.; Zhu, X.; Pejic, M.; Sullivan, C.; Tiwari, U.; Curtin, J.; Tiwari, B.K. Biomolecules from Macroalgae—Nutritional Profile and Bioactive for Novel Food Product Development. *Biomolecules* **2023**, *13*, 386. [Google Scholar] [CrossRef]
13. Safi, S.; Morshed, M.; Hosseini Radande, S.A.; Ghaibi, M. Study of Electrospinning of Sodium Alginate, Blended Solutions of Sodium Alginate/Poly (Vinyl Alcohol) and Sodium Alginate/Poly(Ethylene Oxide). *J. Appl. Polymer. Sci.* **2007**, *104*, 3245–3255. [Google Scholar] [CrossRef]
14. Song, R.; Murphy, M.; Li, C.; Ting, K.; Soo, C.; Zheng, Z. Current Development of Biodegradable Polymeric Materials for Biomedical Applications. *Dove Med. Press* **2018**, *12*, 3117–3145. [Google Scholar] [CrossRef]
15. Taemeh, M.A.; Shravani, A.; Kareem, M.A.; Demi, H. Fabrication Challenges and Trends in Biomedical Applications of Alginate Electro spun Nanofibers. *Carbohydras. Polymer.* **2020**, *228*, 115419. [Google Scholar] [CrossRef]
16. Dodero, A.; Alberti, S.; Gaggero, G.; Ferretti, M.; Botter, R.; Vicini, S.; Castellano, M. An Up-to-Date Review on Alginate Nanoparticles and Nanofibers for Biomedical and Pharmaceutical Applications. *Adv. Mater. Interfaces* **2021**, *8*, 2100809. [Google Scholar] [CrossRef]
17. Kajdič, S.; Planinšek, O.; Galperin, M.; Kocbek, P. Electro spun Nanofibers for Customized Drug-Delivery Systems. *J. Drug Deliv. Sci. Technol.* **2019**, *51*, 672–681. [Google Scholar] [CrossRef]
18. Yu, D.-G.; Gong, W.; Zhou, J.; Liu, Y.; Zhu, Y.; Lu, X. Engineered Shapes Using Electrohydrodynamic Atomization for an Improved Drug Delivery. *WIREs Nanomed.Nanobiotechnol.* **2024**, *16*, e1964. [Google Scholar] [CrossRef] [PubMed]
19. Xie, D.; Zhou, X.; Xiao, B.; Duan, L.; Zhu, Z. Mucus-Penetrating Silk Fibroin-Based Nanotherapeutics for Efficient Treatment of Ulcerative Colitis. *Biomolecules* **2022**, *12*, 1263. [Google Scholar] [CrossRef] [PubMed]
20. Aibar-Almazán, A.; Votes-Martínez, A.; Castello-Caballero, Y.; Afanador-Restrepo, D.F.; Carcelén-Fraile, M.d.C.; López-Ruiz, E. Current status of the diagnosis and management of osteoporosis. *Int. J. Mol. Sci.* **2022**, *23*, 9465. [Google Scholar] [CrossRef]
21. Shen, Z.-S.; Cui, X.; Hou, R.-X.; Li, Q.; Deng, H.-X.; Fu, J. Tough biodegradable chitosan–gelation hydrogels via in situ precipitation for potential cartilage tissue engineering. *Rsc Adv.* **2015**, *5*, 55640–55647. [Google Scholar] [CrossRef]
22. Tosi, S.; Behaving, J. Osteogenesis and bone remodelling: A focus on growth factors and bioactive peptides. *Bio factors* **2020**, *46*, 326–340. [Google Scholar] [CrossRef]
23. Koons, G.L.; Dibba, M.; Mikos, A.G. Materials design for bone-tissue engineering. *Nat. Rev. Mater.* **2020**, *5*, 584–603. [Google Scholar][cross Ref]
24. Joshi, M.; Nazarenko, M.; Prabhakar, B. Albumin nanocarriers for pulmonary drug delivery: An attractive approach. *J. Drug Deliv. Sci. Technol.* **2020**, *56*, 101529. [Google Scholar] [CrossRef]

25. Lee, P.; Manoukian, O.S.; Zhou, G.; Wang, Y.; Chang, W.; Yu, X.; Kumbar, S.G. Osteochondral scaffold combined with aligned nanofibrous scaffolds for cartilage regeneration. *RSC Adv.* **2016**, *6*, 72246–72255. [Google Scholar] [CrossRef]
26. Perez-Pulana, V.; Jiménez-Rosado, M.; Romero, A.; Guerrero, A. Polymer-based scaffolds for soft-tissue engineering. *Polymers* **2020**, *12*, 1566. [Google Scholar] [CrossRef] [PubMed]
27. Joshi, M.; Anjarlekar, M.; Prabhakar, B. Albumin nanocarriers for pulmonary drug delivery: An attractive approach. *J. Drug Deliv. Sci. Technol.* **2020**, *56*, 101529. [Google Scholar] [CrossRef]
28. Charbel, N.B.; Tambuwal, M.; Pollakiuria, S.S.; Worker, A.; Hromić-Jahjefendić, A.; Bakshi, H.; Zaccone, F.; Mishra, V.; Khadse, S.; Aljabali, A.A. Biomedical applications of three-dimensional bioprinter craniofacial tissue engineering. *Boeing. Transl. Med.* **2023**, *8*, e10333. [Google Scholar] [CrossRef] [PubMed]
29. Zubeidi SS, Mohammed S. Floating tablets and its polymers. Journals of Drug Delivery and Therapeutics2018Oct15;8[5-s]:16-24
30. Y. Long, M. Bai, X. Liu, W. Lu, C. Zhong, S. Tian, S. Xu, Y. Ma, Y. Tian, H. Zhang, L. Zhang, J. Yanga zwitterionic cellulose-based skin sensor for the real-time Polymer., 297 (2022) monitoring and antibacterial sensing wound dressing Carbohydrate. Google Scholar
31. W. Huang, Y. Wang, Z. Huang, X. Wang, L. Chen, Y. Zhang, L. Zhang On-demand dissolvable self-healing hydrogel based on carboxymethyl chitosan and cellulose nanocrystal for deep partial thickness burn wound healing Acs Appl Mater Inter, 10 (48) (2018), pp. 41076-41088View at publisher Cross ref View in Scopus Google Scholar
32. Y.-m. Cao, M.-y. Liu, Z.-w. Xue, Y. Qiu, J. Li, Y. Wang, Q.-k. Wu Surface-structured bacterial cellulose loaded with husk's accelerate skin wound healing by promoting angiogenesis in rats Biochemical. Biopsy's. Res. Common., 516 (4) (2019), pp. 1167-1174View PDFView article View in Scopus Google Scholar
33. J.D. Pedrosa de Amorim, C.J. Galdino da Silva Junior, A.D.L. Maia de Medeiros, H.A. do Nascimento, M. Sarabu, T.P. Maia de Medeiros, A.F. de Santana Costa, L.A. Sarabu Bacterial cellulose as a versatile biomaterial for wound dressing application Molecules, 27 (17) (2022) Google Scholar
34. A. Khalid, R. Khan, M. Ulf-Islam, T. Khan, F. Wahid Bacterial cellulose-zinc oxide nanocomposites as a novel dressing system for burn wounds Carbohydras. Polymer., 164 (2017), pp. 214-221 View PDFView article View in Scopus Google Scholar [72]
35. L.G. Silva, A.V. Albuquerque, F.C. Pinto, R.S. Ferraz-Carvalho, J.L. Aguiar, E.M. Lins Bacterial cellulose an effective material in the treatment of chronic venous ulcers of the lower limbs J. Mater. Sci. Mater. Med., 32 (7) (2021), p. 79 Google Scholar
36. G. Franceschini, G. Visconti, A.M. Sanchez, A. Di Leone, M. Saltarello, R. MasettiOxidized regenerated cellulose in breast surgery: experimental model. Surg. Res., 198 (1) (2015), pp. 237-244View PDFView article View in Scopus Google Scholar [74]
37. S. Gustative, J. Kazlauskas, J. Boogaloo, S. Parni, V. Dutch, J. Lie Siene, P. Prokopovich Characterization of cellulose based sponges for wound dressings Colloids Surf., A, 480 (2015), pp. 336-342View PDF View article View in Scopus Google Scholar
38. M.A. Metica, F.L. Aachmann, A. Todderick, H. Sletta, V. Mostafa Chitosan as a wound dressing starting material: antimicrobial properties and mode of action Int. J. Mol. Sci., 20 (23) (2019) Google Scholar
39. A. Mohini, P. Pedram, P. Makani, M. Malinconico, G.G. d'AyalaWound healing and antimicrobial

effect of active secondary metabolites in chitosan-based wound dressings: a review Carbohydrates. Polymers., 233 (2020) Google Scholar
40. J. Wang, S. Zhuang Chitosan-based materials: preparation, modification and application J. Clean. Prod., 355 (2022) Google Scholar
41. W. Wang, Q. Meng, Q. Li, J. Liu, M. Zhou, Z. Jin, K. Zhao Chitosan derivatives and their application in biomedicine Int. J. Mol. Sci., 21 (2) (2020) Google Scholar
42. C. Deng, F. Li, M. Griffith, M. Ruel, E.J. Suuronen Application of Chitosan-based biomaterials for blood vessel regeneration macrogol. Symp., 297 (1) (2010), pp. 138-146 View at publisher Cross review in Scopus Google Scholar
43. S. Zhang, J. Hou, Q. Yuan, P. Xin, H. Cheng, Z. Gu, J. Wu Arginine derivatives assist dopamine-hyaluronic acid hybrid hydrogels to have enhanced antioxidant activity for wound healing Chem. Eng. J., 392 (2020) Google Scholar
44. B. Hu, M. Gao, K.O. Boakye-Yiadom, W. Ho, W. Yu, X. Xu, X.-Q. Zhang An intrinsically bioactive hydrogel with on-demand drug release behaviours for diabetic wound healing Bioaction. Mater., 6 (12) (2021), pp. 4592-4606 View PDF View article View in Scopus Google Scholar
45. P. Zhai, X. Peng, B. Li, Y. Liu, H. Sun, X. Li The application of hyaluronic acid in bone regeneration Int. J. Biol. macrogol., 151 (2020), pp. 1224-1239 View PDF View article View in Scopus Google Scholar
46. F. Jabbari, V. Behaviour, S. Sharkie Comprehensive review on biosynthesis of hyaluronic acid with different molecular weights and its biomedical applications Int. J. Biol. Macrogol., 240 (2023) Google Scholar
47. M.F.P. Graca, S.P. Miguel, C.S.D. Cabral, I.J. Correia Hyaluronic acid-Based wound dressings: a review Carbohydrate. Polymer., 241 (2020) Google Scholar
48. Chi, J.; Zhang, X.; Chen, C.; Shao, C.; Zhao, Y.; Wang, Y. Antibacterial and Angiogenic Chitosan Microneedle Array Patch for Promoting Wound Healing. Bio act. Mater. 2020, 5, 253–259. [Google Scholar] [crossruff] [PubMed]
49. García, M.A.; Hensler, G.; Al-Gousei's, J.; Eisenhower, J.; Wagner, M.; Lanners, H.; Langguth, P. Novel Food Drug Interaction Mechanism Involving Acyclovir, Chitosan and Endogenous Mucus. Drug Meta. Pharmacokinetic. 2023, 49, 100491. [Google Scholar] [crossruff] [PubMed]
50. Zhao, L.; Zhou, Y.; Zhang, J.; Liang, H.; Chen, X.; Tan, H. Natural Polymer-Based Hydrogels: From Polymer to Biomedical Applications. Pharmaceutics 2023, 15, 2514. [Google Scholar] [crossruff] [PubMed]
51. tickborne, J.; Czech, C.; Medina-Montano, C.; Stein, L.; Xu, L.; Scherger, M.; Schild, H.; Grabbe, S.; Nuhn, L. Peptide-Decorated Degradable Polycarbonate Nanogels for Eliciting Antigen-Specific Immune Responses. Int. J. Mol. Sci. 2023, 24, 15417. [Google Scholar] [crossruff] [PubMed]
52. T.-C.; Chang, C.-C.; Chan, H.-P.; Chung, T.-W.; Shu, C.-W.; Chuang, K.-P.; Duh, T.-H.; Yang, M.-H.; Tyan, Y.-C. Hydrogels: Properties and Applications in Biomedicine. Molecules 2022, 27, 2902. [Google Scholar] [crossruff] [PubMed]
53. S.; Xie, C.; Lu, X. Natural Polymer-Based Adhesive Hydrogel for Biomedical Applications. BiosurfaceBiotribology 2022, 8, 69–94. [Google Scholar] [Crossruff]
54. Kamen ova, K.; Gracheva, A.; Stoyanova, S.; Radeta, L.; Tibi, I.P.-E.; Yocheved, K.; Kravtsov, M.A.; Marinova, M.K.; Simeonov, S.P.; Mitzva, S.; et al. Functional Hydrogels for Delivery of the Proteolytic Enzyme Serrati peptidase. Gels 2024, 10, 156. [Google Scholar] [Crossruff]

55. M.; Brocchini, S. Synthetic Approaches to Uniform Polymers. Adv. Drug Deliv. Rev. 2006, 58, 1671–1687. [Google Scholar] [Crossruff] [PubMed]
56. Alleva, N.; Eigen, K.; Ng, D.Y.; Weil, T. A Versatile and Efficient Method to Isolate DNA–Polymer Conjugates. ACS Macro Lett. 2023, 12, 1257–1263. [Google Scholar] [Crossruff]
57. Jao, D.; Xue, Y.; Medina, J.; Hu, X. Protein-Based Drug-Delivery Materials. Materials 2017, 10, 517. [Google Scholar] [Crossruff] [PubMed]
58. Zhang, H.; Lin, X.; Cao, X.; Wang, Y.; Wang, J.; Zhao, Y. Developing Natural Polymers for Skin Wound Healing. Bio act. Mater. 2024, 33, 355–376. [Google Scholar] [Crossruff] [PubMed]
59. Horst, B.; Molimen, N.S.; Grover, L.M. Natural Polymers. In Biomaterials for Skin Repair and Regeneration; Woodhead Publishing: Cambridge, UK, 2019; pp. 151–192. [Google Scholar] [Crossruff]
60. Mantha, S.; Pillai, S.; Chambishi, P.; Upadhyay, A.; Zhang, Y.; Tao, O.; Pham, H.M.; Tran, S.D. Smart Hydrogels in Tissue Engineering and Regenerative Medicine. Materials 2019, 12, 3323. [Google Scholar] [Crossruff]
61. Ciolacu, D.E.; Nico, R.; Ciolacu, F. Natural Polymers in Heart Valve Tissue Engineering: Strategies, Advances and Challenges. Biomedicines 2022, 10, 1095. [Google Scholar] [Crossruff]
62. Cardoso, L.C.D.; Barreto, T.; Gama, J.F.G.; Alves, L.A. Natural Biopolymers as Additional Tools for Cell Microencapsulation Applied to Cellular Therapy. Polymers 2022, 14, 2641. [Google Scholar] [Crossruff]
63. Siracusa, V.; Broccoli, P.; Romani, S.; Rosa, M.D. Biodegradable Polymers for Food Packaging: A Review. Trends Food Sci. Technol. 2008, 19
64. González-López, M.E.S.; Gradilla-Hernández, M.S.; Barajas-Álvarez, P. Current Trends in Biopolymers for Food Packaging: A Review. Front. Sustain. Food Syst. 2023, 7, 1225371. [Google Scholar] [Crossruff]
65. Scelsi, E.; Angelini, A.; Pastore, C. Deep Eutectic Solvents for the Valorisation of Lignocellulosic Biomasses towards Fine Chemicals. Biomass 2021, 1, 29–59. [Google Scholar] [Crossruff]
66. Weepie, M.; Trzcińska-Wencel, J.; Golińska, P.; Avila-Quezada, G.D.; Ingle, A.P.; Rai, M. The Strategic Applications of Natural Polymer Nanocomposites in Food Packaging and Agriculture: Chances, Challenges, and Consumers' Perception. Front. Chem. 2023, 10, 1106230. [Google Scholar] [Crossruff] [PubMed]
67. Hussein, H.S.; Shaarawy, H.H.; Hussien, N.H.; Hawash, S.I. Preparation of Nano-Fertilizer Blend from Banana Peels. Bull. Natl. Res. Cent. 2019, 43, 26. [Google Scholar] [Crossruff]
68. Ross IA. Medicinal Plants of the World—Chemical Constituents, Traditional and Modern Medicine Uses. Totowa: Humana Press; 1999; 155-63.
69. Jani GK, Shah DP. Assessing Hibiscus rosa-sinensis Linn as an Excipient in Sustained Release Tablets. Drug Develop Ind Pharm 2008; 34(8):807–16.
70. Vazquez B, Avila G, Segura D, Escalante B. Anti-inflammatory activity of extracts from Aloe vera gel. J Ethnopharmacology 1996; 55:69-75.
71. Choi S, Chung MH. A review on the relationship between Aloe vera components and their Biologic effects. Semin Integer Med 2003; 1:53-62
72. Petropoulos GA. Fenugreek: The genus Trigonella. In: Petropoulos GA, (Ed.), Botany. London: Taylor and Francis 2002;9-17
73. Avachat AM, Gujar KN, Kotwal VB, Patil S. Isolation and evaluation of fenugreek husk as granulating

agent. Indian J Pharm Sci 2007; 69(5):667-79]
74. Ali N, Hossein N, Afagh K, Tariffed S, Hadi V, Ford JL. An In Vitro Evaluation of Fenugreek Mucilage as a Potential Excipient for Oral Controlled-Release Matrix Tablet. Drug Dev Ind Pharm 2008; 34:323–29.
75. Guar Gum Manufacturing Process [Online]. 2009 [cited 2009June 16] From: URL: http://www.guargum.biz/guargum_manufacturing_process.htm
76. URL: http://en.wikipedia.org/wiki/Guar_gum [cited 2009june 18]
77. Martin Chaplin. Water Structure and Behaviour: Guar Gum. London South Bank University April 2006
78. R. Eswaran, Sindhu Abraham, Bharath, B.V. Basavaraj, Sharon Furtado, Madhavan. Design and Characterization of Diclofenac sodium tablets containing Tamarind seed polysaccharide as Release retardant, International Journal of Pharm Tech Research CODEN. April-June 2009;1(2): 191-19]
79. Bharath Srinivasan, Anusha Ganta, Eswaran Rajamanickam, Basavaraj Dasappa Veerbhadra, Madhavan Varadharajan. Evaluation of tamarind seed polysaccharide as a drug release retardant International Journal of Pharmaceutical Sciences Review and Research, 2011; -31.
80. Kaur A, Kaur A, Kaur VP, Kaur M, Murthy RS (2014) Polymeric drug delivery approaches for colon targeting: a review. Drug Delivery Letters 4(1): 38-48.
81. Alonso-Sande M, Teijeiro-Osorio D, Remain-López C, Alonso M (2009) Glucomannan, a promising polysaccharide for biopharmaceutical purposes. European Journal of Pharmaceutics and Bio-pharmaceutics 72(2): 453-462.
82. Panda D. S., Swain S. S., Kanungo K. S. and Gupta R., Preparation and evaluation of gels from gum of Moringa oleifera, Indian J. Pharm. Sci., 2006, 68(6), 777-780.
83. Panda D.S., Choudhary N. S. K., Medukonduru M., Si S., Gupta R., Studies on a natural gum for its application as a suspending agent, available from priory.com/ pharmacy/suspension _ gum _ suspendingagent.html.
84. Maiko Kera R. and Kamba H. M., Interfacial properties and fluorescence of a coagulating protein extracted from Moringa oleifera seeds and its interaction with sodium dodecyl sulphate, News Rx., 2007, 55(2), 173-178.
85. Panda D.S., Choudhary N. S. K., Medukonduru M., Si S., Gupta R., Evaluation of film forming potential of natural gum, Asian J. Pharm., 2008, 2 (1), 50-52
86. Delouse S. A. and Urooj A., Application of phenolic extracts from selected plants in fruit juice, Int. J. of Food Properties., 2007, 10(3), 479-488.
87. Stassi I., Bioscan V., Pauly G. and McCauley J., Moringa oleifera: an interesting source of active ingredients for skin and hair care, SOFW journal. 2003, 129(9), 45-52
88. Available from www.bikudo.com/product
89. 43. Subramanium Kodeeswaran, Vikash Nand, Maata Matakite, Koshy Anayatha., Moringa oleifera and other local seeds in water purification in developing countries, Research Journal of Chemistry and Environment,2011, 15 (2), 135-138.