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TO STUDY THE BIODEGRADABLE POLYMER-BASED ON NANOCOMPOSITE HYDROGELS

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ABSTRACT

Hydrogels are commonly used in biological applications because they have qualities similar to genuine soft tissue and are programmable. Biodegradable hydrogels have the extra benefit of degrading in an aqueous environment, eliminating the requirement for disposal when the useful life has expired. In this study, we looked into biodegradable hydrogel systems made of poly (-amino ester) (PBAE). To begin, factors impacting macromer synthesis were investigated in order to improve the reproducibility of the hydrogels produced and develop novel strategies for modifying their properties. The hydrogel behaviour was then fine-tuned by varying the hydrophilic/hydrophobic balance of the chemicals utilised in the synthesis, resulting in systems with linear and two-phase breakdown profiles. The study's purpose was to learn more about how to manipulate hydrogel properties so that systems for a variety of biological applications may be developed.

Keywords: Hydrogels, biodegradable, macromer, hydrophobic, hydrophilic

INTRODUCTION

Polymeric hydrogels with a viscoelastic network and self-supporting, water-swollen three-dimensional (3D) structures. Due to the presence of hydrophilic functional groups (carboxyl, amide, amino, and hydroxyl) in their polymeric chains, these materials have the potential to imbibe water or biological fluids up to several thousand percent and swell rapidly without dissolving. Hydrogels have been around for almost 50 years, with one of the oldest descriptions in the literature being "by Wichterle and Lim" in 1954-1960, who described a flexible crosslinked structure of a poly-hydroxyethyl methacrylate (pHEMA) based hydrogel. Since then, hydrogel technology has broadened significantly, indicating a promising future for their use in biological sciences. In terms of structure, properties, and applications, the term hydrogel is self-explanatory. In terms of formulations and uses,

hydrogels have captivated materials scientists and biomedical researchers. Hydrogels have a higher thermodynamic affinity for solvents, which accounts for their swelling properties. Which can be changed as needed by introducing different crosslinkers via covalent bonds or physical interactions via intramolecular and intermolecular attractions. These hydrogels also have excellent capillary action, osmotic pressure, and water diffusion. Biopolymer-based hydrogels (such as chitosan, starch, guar gum, alginate, and others) have good biodegradability and biocompatibility. A. Vashist et al., for example, produced a biocompatible interpenetrating network for drug delivery utilising chitosan, methyl methacrylate (MMA), and oleo polyol. Later, they produced nanocomposite hydrogel films made of chitosan, acrylonitrile, oleo polyol, and MWCNT that have good mechanical strength, biodegradability, and biocompatibility. Clay dispersed poly (vinyl alcohol)-chitosan-honey based new nanocomposite hydrogels for wound dressing applications were reported by S. Noori et al. These hydrogels are both biocompatible and antimicrobial.

Temperature, pH, ionic concentration, light, magnetic fields, electrical fields, and chemicals are all examples of external stimuli that smart hydrogels respond to. These characteristics lead to a huge potential for their numerous advanced technological applications, such as regulated medication administration, which has been a hot topic of research. To meet the ever-increasing demands of the pharmaceutical industries, many new hydrogel-based delivery systems have been developed. Hydrogels are classified according to their ingredients, physical and chemical structures, polymeric forms (such as homo and co-polymers), blends, interpenetrating networks (IPNs), and composites. In subsequent units, their benefits, disadvantages, and applications are addressed in greater detail.

Advantages of Hydrogels

1. They have a high degree of flexibility, akin to real tissue, due to their high water holding capacity.
2. Maximum stiffness and toughness in the swelling media and during storage.
3. Drug or nutrition release on time.
4. Biocompatible, biodegradable, and mechanically strong, with the ability to be injected into the human body.
5. It's colourless, odourless, and completely non-toxic.
6. Their physical texture may alter in response to external stimuli (e.g., an electric signal, pH, temperature, and the presence of enzymes or other ionic species).
7. Excellent transport qualities and ease of modification.

NANOCOMPOSITE HYDROGELS (NCHS)

NCHs are cross-linked biopolymer networks that have expanded due to water absorption in the presence of nanoparticles or nanostructures (10-100 nm). When compared to typical hydrogels, they have superior qualities (greater elasticity and mechanical strength). The hard nanoparticles (segment) strengthen the soft organic (segment) polymer matrix, resulting in synergistic qualities in the final NCHs. According to the literature, the researchers used a variety of nanoparticles, including carbon-based, polymeric, ceramic, and metallic nanofillers, to greatly increase the biological properties of these hydrogels. Haraguchi et al. created NCHs with improved mechanical strength, swelling ability, ocular precision, and stimuli responsiveness utilising poly-N-isopropylacrylamide (PNIPAAm) and montmorillonite nanoclay. The current thesis describes the synthesis of unique NCHs films with star and dendrimer morphology, which have significantly improved swelling and mechanical properties and hence have potential applications in biomedical sciences.

OBJECTIVE OF THE STUDY

- Various nanocomposite hydrogels were develop and characterized.

RESULTS AND DISCUSSION

❖ BIOPOLYMER BASED NCHS

Researchers have been focusing on biopolymer-based materials in recent years due to their biocompatibility and wide range of applications in biomedical sciences, particularly in drug delivery, tissue engineering, and wound healing. Natural biocompatible polymers such as polysaccharides, carbohydrates, modified celluloses, and poly(- aminoacids) are utilised to make hydrogels with the goal of using them in the field of biomaterials. Based on their chemical structures, natural polymers are classified into the following primary groups: Polysaccharides I (chitosan, guar gum, agar, starch, gum tragacanth, aloevera gel, hyaluronic acid, alginate, and agarose) (ii) Polyamides (or Polypeptides-collagen, gelatin, fibroin, wheat, soya, and fibrin) and (iii) Polyesters (Polyamides-polyamides-polyamides-polyamides-polyamides-polyamides-polyamides-polyamides-polyamides-polyamides-poly (3-hydroxyalkanoate). Nanocomposite hydrogels with better characteristics were created using a variety of nanomaterials and biopolymers. Biopolymeric nanocomposite hydrogels with a variety of beneficial features and uses have been described by a number of researchers. Barkhordari et al., for example, used double layered hydroxides (LDH)–carboxymethyl cellulose to create a hydrogel nanocomposite for regulated administration

of ibuprofen (CMC). Tanpichai et al. created NCH films with better mechanical and thermal properties utilising Cellulose nanocrystal and poly(vinyl alcohol). Clay dispersed cellulose NCHs, according to Peng et al., have exceptional mechanical strength and superabsorbent characteristics for methylene blue.

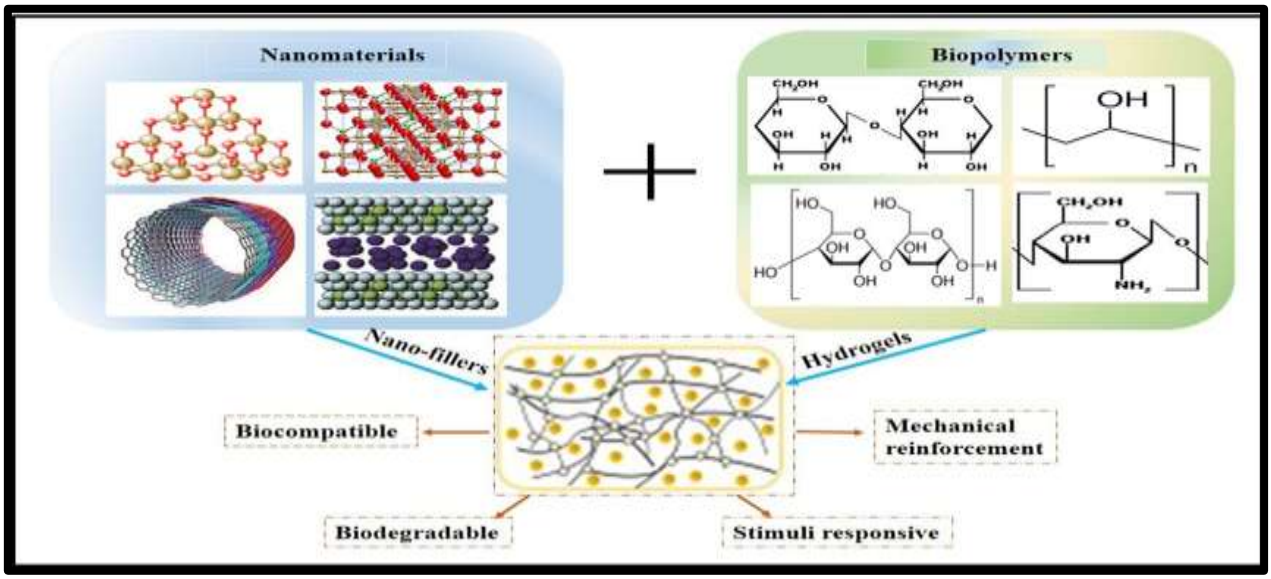

FIGURE-1: THE CHARACTERISTICS OF NANOMATERIALS AND BIOPOLYMER-BASED NANOCOMPOSITE HYDROGELS

❖ CHITOSAN BASED NANOCOMPOSITE HYDROGELS

Chitosan is a linear polysaccharide made up of glucosamine and N-acetyl glucose amine units linked by b (1-4) glycosides bonds and formed when chitin is deacetylated in an acidic environment. To increase chitosan's solubility in water or organic solvents, the reactive polar groups (amino and hydroxyl) can be changed. Due to the protonation of amino groups in an acidic environment, it can be soluble in glacial acetic acid. Chitosan's diverse biological and physicochemical features make it a promising material for a wide range of biomedical applications. Despite these impressive characteristics, chitosan hydrogels have a low mechanical strength. Various nanofillers have been placed in chitosan to address this limitation, considerably improving mechanical, thermal, and electrical characteristics. Tushar et al., for example, used an ionic liquid to create hybrid materials and nanocomposite ionogels utilising agarose-chitosan via dissolution, regeneration, and sol-gel transition. The homogeneous dispersion of silver nanoparticles into a chitosan-based polymeric matrix resulted in a nanocomposite with good thermal and mechanical properties that might be used in actuators, sensors, food packaging, wound treatment, and drug delivery systems.

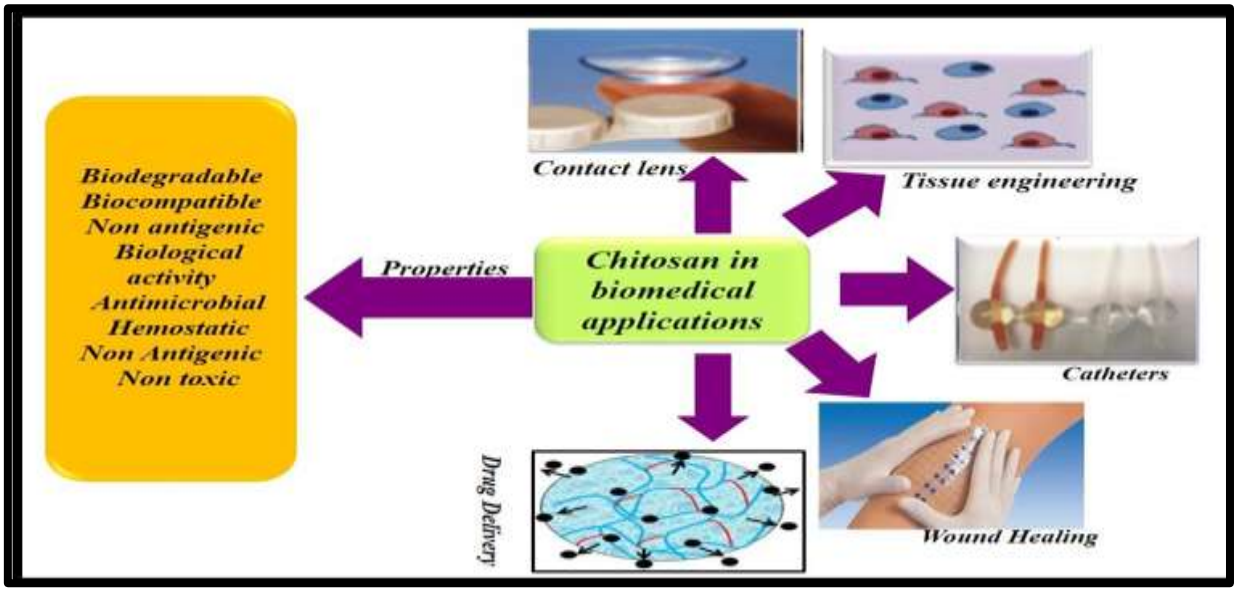

FIGURE-2: CHITOSAN'S PROPERTIES AND BIOLOGICAL APPLICATIONS

❖ STARCH BASED NANOCOMPOSITE HYDROGELS

Alpha glucose produces starch, which is a polymer made up mostly of linear amylase and highly branched Amylopectin. Plants produce it enzymatically, and it can be extracted from tubers, seeds, roots, and stems. Several starch-based hydrogels have been created for biomedical purposes in recent years. Weak processability, high brittleness, low water content, poor mechanical strength, and oxygen barrier qualities are some of the drawbacks of starch. In this case, several nanofillers (hydroxyapatite, MWCNT, nanoclays, metal oxides, and so on) have been incorporated into a starch-based polymer matrix to generate nanocomposite hydrogels.

The inclusion of nanofillers has a significant impact on the physicochemical and physicomechanical properties of the material. Spagnol et al., for example, used starch-g-poly (sodium acrylate) and nanowhiskers (CNW) to create superabsorbent hydrogel nanocomposites. The dispersion of CNWs in polymeric matrices up to 10% would improve their swelling ability and mechanical strength. Fama et al. produced nanocomposite hydrogels with starch as a matrix and extremely small concentrations of multiwalled carbon nanotubes (MWCNTs), which had a high elastic modulus (about 100 percent) but a 43 percent lower water vapour permeability than plain starch hydrogels.

❖ CELLULOSE BASED NANOCOMPOSITE HYDROGELS

Cellulose is one of the most abundant, natural, and renewable biopolymer resources on the planet, and it may be found in a variety of biomasses, including trees, plants, tunicates, and

bacteria. The molecule of cellulose is made up of 1, 4-D-linked glucose chains, with the chemical formula (C6H10O5) n (n range from 10,000 to 15,000). Acetyl oxygen covalently bonds the C1 of one glucose ring to the C4 of the next ring. Because of their biocompatibility and hydrophilicity, cellulose-based hydrogels are ideal candidates for food packaging, medicine, and wound healing, among other applications. Chemical interactions inside the structure, such as H-bonding and Vander Waals forces, prevent total dissolution in the aqueous media. As a result, chemical changes have been made to address this constraint. Hydrogels based on cellulose derivatives such as methyl cellulose (MC), hydroxyl propyl cellulose (HPC), hydroxylpropylmethyl cellulose (HPMC), and carboxymethyl cellulose (CMC) have been used for chemical alterations, according to the literature. For example, using bacterium cellulose (BC) and gelatin, researchers generated cellulose-based nanocomposites hydrogels with high mechanical strength, swelling capacity, and crystallinity. However, due to its high cost, BC production is highly limited, which limits its applications. As a result, cellulose nanocrystals (CNC) were generated from plants with lower costs than BC, and CNC are highly soluble in water, suggesting that they could be used in the development of nanocomposite hydrogels. For example, employing CNC and poly (acrylamide-co-acrylate) (PAM-AA) via a free radical copolymerization process, researchers created pH responsive superabsorbent nanocomposite hydrogels. Later, A.C. Babu et al. used a free radical polymerization approach to make nanocomposite hydrogels with CMC, poly(acrylamide-co-2-acrylamido-2-ethylpropanesulfonicacid), and silver nanoparticles for antibacterial purposes. Zhang et al., on the other hand, created a graphene oxide distributed CMC-Polyacrylamide nanocomposite hydrogel. These hydrogels outperform pristine hydrogels in terms of swelling ratios and mechanical strength, making them ideal for tissue engineering and drug delivery.

❖ POLYVINYL ALCOHOL (PVA) BASED NANOCOMPOSITE HYDROGELS

PVA is a linear synthetic polymer created by partially or fully hydroxylating polyvinyl acetate. PVA is insoluble in water due to its high degree of hydroxylation and polymerization. By utilising PVA as a physical or chemical cross-linker, PVA-based hydrogels give structural stability in water or any other physiological media. Because of their high hydrophilicity, biocompatibility, and film forming capabilities, they are extensively utilised in medical devices, paper products, and the food industry. Their mechanical strength, on the other hand, limits their biomedical applications. The addition

of nanofillers to these hydrogels in order to make them nanocomposite is a common technique for achieving diverse characteristics.

DRUG DELIVERY

The creation of smart nanocomposite hydrogels for drug delivery systems, which include micro- or nanoparticles embedded in hydrogels, is a promising strategy. The incorporation of pharmaceuticals in particles, followed by the loading of particles in the hydrogel network, has been employed to enable sustained drug delivery of hydrophobic medications. The rate of drug release from nanocomposite hydrogels is determined by the swelling behaviour, particle size, and dispersion coefficient of nanoparticles. The medication can be placed into a hydrogel, and then released using a variety of processes, including diffusion control, swelling control, chemical control, and environmental responsive release. Environment-responsive nanocomposite hydrogels have a good ability in drug delivery systems, allowing drugs to be released intelligently in response to external stimuli such as electric field, magnetic field, temperature, and pH. Different biocompatible nanocomposite hydrogels for prolonged drug administration without causing any side effects were recently reported by researchers. W. Zhu et al., for example, used poly(ethylene glycol)-b-poly(acrylic acid) (PEG-b-PAA) block copolymer nanoparticles to construct an injectable supramolecular hydrogel for prolonged delivery of cisplatin in cancer therapy. In vitro cytotoxicity testing indicated that cisplatin-loaded hydrogels kill EJ cells from human bladder cancer. A carboxybetain injectable hydrogel was produced by Chien et al. The MTT assay is used to determine the cytotoxicity of monomers such as MMA, HEMA, and PEGMA in vitro. The hydrogels' potential as a cell encapsulation scaffold material was demonstrated by percent cell viability testing of the produced hydrogels.

CONCLUSION

The ability to control drug release remotely was proven, indicating that this unique method could be employed in vivo to provide external control of an implanted drug delivery device. There are various ways to boost the AMF's effectiveness even more. Longer dosage times, as well as raising the intensity and strength of the field, can be employed to boost the effect. Extended field dosing periods can keep the system's temperature up for longer periods of time, exacerbating deterioration. A higher powerful field source could be utilised, causing the particles to heat up more and thereby raising the gel temperature. This option, however, would be limited in in vivo applications due to the need to regulate the

temperature of the gels as well as the body's exposure to the AMF. Other options include working with the polymer itself. The same quantity of heating would have a far bigger impact on systems with greater temperature dependent deterioration, and the degradation rate would increase. The degradation rate and time duration of the system are also influenced by the polymer chemistry. For this investigation, a very fast deteriorating system was chosen for testing feasibility. However, because of the rapid breakdown timeline, this device would not be suitable for in vivo deployment. Longer degrading systems that may respond to the AMF differently and exhibit better control over drug release would be required.

This study reveals the possibility of external control over an implantable biomaterial that degrades (e.g., drug delivery device). The process involves heating tiny magnetic particles remotely to improve the rate of disintegration of a degradable hydrogel and, as a result, the rate of drug release from the system. Though this hydrogel system disintegrated quickly and could not be used in vivo, this approach may also be used to manage slower-degrading systems.

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