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Innovative transitive development of Hydrogel by Copolymerisation and Grafting technology of polymer

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ABSTRACT: This review article composes a hydrogel-polymer chain multi-unit component system. There are swollen state characteristics and mechanisms involved in the process of gelations as their structured configuration are several based on polymer composition and features. Furthermore, there is an enumerating of the major sources of polymer which facilitate the preparation of hydrogel by using various techniques and especially emphases on the preparation of hydrogels by graft Technology for modification of polymers for better strength, stable, flexible rigid and compatible hydrogel formulation. This article represents the overview of the historical background of hydrogels and their origin based on generation, characteristic features, advantages, limitations, and various applications in a different area, its possible release mechanisms, and evaluation methods of the hydrogel. Moreover, especially mainly focus on the novel concept of copolymerization, grafting its type and their different techniques of grafting technology methods to create a newer synthesized molecule of hydrogel, its rationale, and various evaluation method of Grafting hydrogel with commercialized hydrogel formulation in the market, and patented hydrogel product. Conclusions: The Novel grafting technology imperatively modified the challenges associated with the existing technology of hydrogel preparations and cope with the new technology revolution in global science.

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INTRODUCTION:

Hydrogels term expressed as two- or multi-component systems consisting of a hydrogen-bonded self-assembled network of three-dimension polymer chains obtained from a class of synthetic and/or natural polymers which can absorb and retain water that fills the space between in the swollen state and the proportion of water is significantly higher than the proportion of polymer [1-2]. The latest new embarrassing technology grafting basically modification in the surface and it overcomes

the associated problem for improving the existence limitation associated with hydrogel by the natural or synthetic polymers. Hydrogel polymers may be derived from a natural source or synthetically. The synthetic hydrogel has replaced the existing natural origin hydrogel due to the relatively good absorption capacity of water, stability, and hydrophobic/ hydrophilic nature. Hydrogel preparation is actually initiated by immersing cross-linked polymers into aqueous or biological fluids and allowing the mixture to swell various examples [3] of the polymer containing hydrophilic groups like hydroxyl, carboxylic acid, amide, sulphonic acid, and amide either embedded in or grafted to their polymeric backbones. Natural hydrogels are principally physiological hydrogels, it consists of the Extracellular matrix in *vivo*, whereas synthetically derived are natural modified polymers [4]. The classification of the hydrogel is considered, as either amorphous or crystalline and may be either synthetic or biological. Synthetic hydrogels can be produced extensively from homo- or copolymers. The wide variety of hydrogels has various applications available in different forms like cationic, anionic, or neutral in nature. Biological hydrogels can be obtained from extracellular proteins examples are gelatin, collagen, silk, or peptides and polysaccharides derived examples are Agarose, alginate, cellulose, chitosan, dextran, and hyaluronic acid [5-7]. Stimuli-responsive hydrogels also termed intelligent hydrogels, which can undergo a reversible phase transition in response to greater external stimuli including temperature, light, pH with respective due to electric charge has attracted towards medical and biological applications [8]. Hydrogel has some desirable properties such as softness, elasticity, swelling, flexibility and their capacity to store water, mechanical strength, absorbent and biocompatible nature [9]. The terminology gel and hydrogel are widely used by scientists for food and biomaterials to describe the cross-link network structure of polymeric chains. Gelation followed by network formation linking of macromolecular molecules together which initially begin to lead to a progressively larger branch of the network. The term "sol" is expressed as a polydisperse soluble branched polymer of the finite mixture and gel is an infinite polymer, In addition, if the transition from finite branched polymer to infinite molecules is called sol-gel transition or gelation and the critical point where gel first appears is called the gel point [10]. Numerous types of gelation mechanisms are proposed by researchers. Generally they take place either by physical gelation or chemical gelation. The physical gel is categorized into strong physical gel and weak gel. Strong physical gel compared produce intact physical bond between polymers whereas, weak physical gels temporary association of chain of polymer in between polymer molecules. Chemical gelation undergoes covalent bond formation and forms a strong gel and the process will employ condensation, vulcanization, and polymerization, during this stage of gelation a wide variety of factors triggered gel formation i.e, change in pH, temperature, ionic strength, and thermally induced material [11]. Consequently, the hydrogel can be synthesized by polymerization, the process of parallel cross-linking natures, multifunctional monomers, and numerous steps involved in the synthesis of polymer molecules having reactive key component groups so that it facilitates cross linking of polymers by treating with suitable cross-linking agents. Polymerization technique can be adapted to form gels including bulk, solution, and suspension polymerization and it consists of monomer, initiator, and cross-linker as an integral part of a hydrogel. Preparation of hydrogel by bulk polymerization is not a strongly bonded structure hence to overcome this problem it could be grafted on a surface coated rigid support to improve the mechanical properties. This technique involves the generation of free radicals getting a strong support surface and polymerizing monomers directly onto it additionally, a chain of monomers is covalently bonded [12] to the compact support to increase the rationale properties of hydrogel and to enhance the wettability and compatibility of surface polymer. A variety of polymers have been used for the synthesis of the hydrogel by grafting technique [13].

Hydrogel Classification:

Hydrogels are called permanent or chemical gels when they are covalently cross-linked networks. Chemical hydrogels may assist cross linking of water-soluble polymers, or by transforming hydrophobic polymers into hydrophilic polymers where cross linking is not necessary. In some cases, due to the solvent composition, temperature, and solids concentration during gel formation.

The hydrogel product can be classified accordingly as based on [14-16];

***Source*:** Natural, synthetic and semisynthetic.

***Polymeric composition*:** Homopolymer, copolymer & multipolymer.

Table 1. Natural and Synthetic hydrogel preparation material examples.

Material	Examples
Natural	Collagen, fibrin, hyaluronic acid, matrigel, and derivatives of Natural materials such as chitosan, Alginate, skill fibers.
Synthetic	Acrylamide, acrylic acid, ε-caprolactone Ester, ethylene oxide, glycolic acid, hydroxyethyl methacrylate, lactic acid, *N*-isopropylamine

Table 2. Hydrogels, Cross linking agent and application [14].

Hydrogel	Cross-linking agent	Applications
Poly Vinyl Alcohol	Sodium borate/boric acid	Packaging
Poly Vinyl Alcohol	Glyoxal	Plastic Adhesives filmsused for packaging and water-soluble plastic bags for Binders Fuel-resistant hoses
Starch	Glyoxal	Paper industry
Guar gum	Epichlorohydrin	Biomedical application
Gellan gum	Endogen polyamine spermidine	Drug delivery
Glycol chitosan	Oxidized alginate	Drug delivery
Hydroximated alginates	Zinc	Drug delivery
Alginate bead	Zinc	Drug delivery
Scleroglucan	Borax	Drug delivery
Poly(acrylic-co-vinylsulfonic) acid	Ethyleneglycol dimethacrylate	Drug delivery
Polyacrylamide/guar gum graft copolymer	Glutaraldehyde	Water transport and drug release

Chemical and physical-based configuration structure: Amorphous, semicrystalline and crystalline,

***Electrical charge network-based*:** presence or absence of electrical charge located on the cross-linked chains and classified as nonionic, ionic, amphoteric, and zwitterionic.

***Physical appearance based*:** As polymerization technique adopted, polymers may be classified as matrix, film, or microsphere.

Based on the type of cross-linking: Chemically cross-linked networks produce permanent junctions And Physically cross-linked networks produce transient junctions.

***Based on responses to stimuli*:** Smart and Conventional.

Based on durability: Durable and degradable.

ORIGIN OF HYDROGEL:

The article was published in 1894, According to Lee, Kwon and Park expressed hydrogel is not a material that we have described today, it was indeed a colloidal gel prepared with several inorganic salts. Various researchers describe through their literature study and survey stated the first cross linked branched-chain network materials its typical properties e.g., polyhydroxyethylmethacrylate material having high affinity of water. However, in a study in 1960, the major goal of targets is using them in permanent contact applications with human tissues [17]. In fact, hydrogel is the first material developed for use inside patients, later the number of studies describing the application of hydrogel for biomedical purposes began to rise especially from the decades of the ’70s. The history of hydrogels can be categorized into three blocks. Hydrogels' first generation comprises extensively by cross linking procedures involving the chemical modifications of a monomer or polymer with an initiator. The general aim is to develop material with high swelling, good mechanical properties, and a relatively simple rationale. In the second generation, different concepts of hydrogel promote and material capable of specific stimuli such as changes in physical and physiochemical properties like temperature, pH, or the concentration of specific molecules in solution. These specific stimuli urge exploited to trigger likewise specific events, for example, the polymerization of the

material, drug delivery, or an *in situ* pore formation. Finally, the third generation of hydrogels majorly focuses on the investigation and terminal progressive development of stereo complexed materials e.g. PEG-PLA interaction hydrogels cross-linked by other physical interactions e.g. cyclodextrin. This emerging development in hydrogel science is rapidly raising leads to enhance the development of hydrogel so-called "smart hydrogels", the pioneering work was done by Wichterle and Linn in 1960 on cross linked hydrogels due to their hydrophilic character and potential biocompatibility i.e., polymeric matrixes which have imperial tunable wide spectrum properties and trigger stimuli. Similarly, In 1980 Linn and Sunn expressed in their research the influential work application of calcium alginate microcapsules for cell application. Later 1980s, Yannas and co-workers in his research used collagen and shark cartilage as natural polymers and the ultimate preparation is hydrogel in artificial burn dressings. It was found that the natural and synthetic polymers being an interest of researchers for encapsulation and especially innovative and attractive to the new area of tissue engineering and lead to increase trend for repairing and regeneration of tissue and organs in different forms.

The Characteristic Features of the Hydrogel [18]:

The highest absorption capacity i.e, maximum equilibrium swelling in saline and desired required rate of absorption is depends on particle size, porosity, and applicant requirement.

- Absorbency under load must be highest (AUL).
- Minimum soluble content and residual monomer.
- Cheap rate price.
- Durability and stability must be maximum in the swelling environment and inappropriate storage conditions.
- The degree of biodegradability is highest without the formation of toxic species.
- pH- neutrality check after swelling in water.
- Colorless, odorless, and absolutely non-toxic.
- Photostability.

Re-wetting capability, if required the hydrogel must be imbibed in solution and to be maintained as per requirement e.g., in agricultural or hygienic applications. The general following benefits and limitations of the hydrogel are given below:

- Its biocompatibility.
- It can be injected *in vivo* in a whole, living organism as a liquid that then gels at body temperature.
- Protect cells.
- Well transport system properties of nutrients or cell product
- The time-release of medicines or nutrients.
- Easy to modify.
- It can be biodegradable or bio-absorbable.

APPLICATIONS OF HYDROGEL [20]:

Hydrogels are extensively used in various fields such as tissue engineering, proteomic, bio-separations, electrophoresis, chromatography, foods, medicines, diapers as absorbent, water purification as a filtration, in a controlled drug release system. Some of the applications of hydrogels are explained below:

a) Domestic application: The water adsorption nature of hydrogels is used in diapers that hold water, also used in creams and perfume.

b) Environmental application: Enhance capacity to retain water with oil-pollutant molecules

c) Bacteria culture: Bacteria can be cultured inside the matrix of hydrogels. Agar is the important ingredient for bacterial culture in biotechnological application

d) Biosensor: Application of hydrogels we can prepare biosensor, act as supports for immobilization of enzymes e.g. Polycarbamoylsulphonate is used for immobilization of the D-fructose dehydrogenase enzyme.

e) Sealant and adhesive: Hydrogels can act as adhesive to various materials such as plastics also due to hydrophobic interactions their application as a sealant for vessels containing corrosive acids.

f) Contact lenses: Some polymers have a wide supplication like soft contact lenses e.g., poly (2-hydroxyethyl methacrylate)-based hydrogels are used due to their extensive property.

g) Biomedical application: Hydrogels have an enormous application in biomedical such as, Immunotherapy, Vaccines, Plastic surgery, Wound healing, Electrophoresis, Proteomic, Tissue engineering (Bone regeneration, Cardiac, Dental), Drug Delivery, Wound dressing and so on. e.g., pre polymerized powders of polymethyl methacrylate and liquid methyl methacrylate monomer with two aqueous dispersions of tricalcium phosphate grains and calcium-deficient hydroxyapatite powders. The final composites appeared to be porous and acted as microsponges.

h) Miscellaneous: It is found some important roles of hydrogels are also in food, agriculture, industry, cosmetics, medicine, medical treatments, etc.

RELEASE MECHANISMS OF HYDROGELS [21]:

Diffusion-controlled release in which porosity is greater than drug molecules size diffused from a hydrogel. Drug diffusion from hydrogel related to porosity and tortuosity nature of hydrogels. it may act as a reservoir or matrix system. In a reservoir system, drug molecules could be encapsulated and coated by polymeric network hydrogels and therefore drug release mostly follows the order first law of diffusion whereas in a matrix system drug molecules disperse homogeneously in a polymeric network of hydrogel and drug release follows the second law of diffusion.

Swelling-controlled drug release may occur in which the rate of drug diffusion is higher than the rate of swelling hydrogel. The kinetic model mostly follows for a purely swelling controlled system fit to the zero-order model. In hydrogels swelling induced transition phase causes comparatively faster drug diffusion and release from the polymeric network chain. Hence more than the optimum rate of swelling and drug release from the hydrogel. On the other hand, the considering factor ability of hydrogels is water absorption and thickness of polymeric gel in swelling of drug release when the rate of drug diffusion is faster than the rate of hydrogel swelling.

Chemically controlled drug release mechanism the reaction takes place within the hydrogel matrix in this reaction generally enzymatic or hydrolytic cleavage of the polymeric network is responsible for drug release. The cleavage of polymeric chain most occurs through bulk or surface erosion.

The entrap or disperse form of the drug would be released from a hydrogel. The rate-limiting step in this process is polymer chain cleavage.

The concept of specialty polymer emerged because most of the polymers were unable to perform under high temperature and pressure specified conditions. The study describes the surface morphology of polymers as the choice of interest, valuable and commercial products modification carried out due to reactive sites. These reactive sites are used for the incorporation and improvement of properties like hydrophilicity, hydrophobicity, and resistance towards acid-base attack along with higher thermal stability.

CHARACTRIZATION OF HYDROGEL [22,23]:

Morphology: The morphology study was characterized and analyzed by an equipment stereomicroscope. Similarly, the texture of these biomaterials is analyzed by using a Scanning electron microscope.

Rheology: Viscosity study of hydrogels are evaluated under the constant temperature of 4°C by using a Cone Plate type viscometer and is highly specific for the evaluation of viscosity.

X-ray diffraction: Crystalline or amorphous characteristics are estimated by Diffraction analysis basically it is used to determine broad holes and patterns of the arrangement where the hydrogels are distributed.

Light scattering: Coupling of Gel permeation chromatography with multi-laser light scattering is a widely used technique to find out the molecular distribution and various parameters of a polymer system and more preferably used in quantifying hydrogels of several hydrocolloids. e.g., gelatin, pullalin.

Fourier Transform Infrared Spectroscopy: FTIR Technique is reliable to use to identify the presence of the functional group in molecules, collection of absorption bands to confirm the identity of purity of compounds, and detect the presence of any kind of impurities.

Scanning Electron Microscopy: SEM The technique is mostly applicable to characterize the network structure in the hydrogel. It is also used to provide information on the molecular surface topography, composition, and electric conductivity properties.

Swelling measurement: The swelling studies can be performed by immersing xerogel into 250 ml of distilled water. The samples of the imbibed hydrogel are weighed after removal of surface water by using filter paper at a particular frequency of interval time. The result is calculated given below by equation;

$Q=W_s/W_d$……..(1)

Where Ws is the mass of the hydrogel in the swollen state, Wd is the mass of the hydrogel in the dried state and Q is the equilibrium swelling ratio.

In-Vitro dissolution: *In-vitro* dissolution studies are carried out to determine the release profile of hydrogel and bioequivalence studies to estimate the release of dosage forms.

Water Vapour Transmission Rate: The quantity of water vapor passes across the unit area surface of film material in a predetermined fixed time under ideal specified temperature and humidity conditions. Water vapor transmission rate is measured in grams per square meter.

***BiocompatibilityTest*:** Hydrogels are biocompatible and nonirritant in nature. The biocompatibility is determined by placing the material in close contact with the relevant host environment and incubated for a

specific period of time at 37°C and in another method; the materials are placed in a physiological solution and incubated for 37°C to determine leaching from the material.

COPOLYMERISATION:

The copolymer is known as polymer when repeating units are of two different monomers are attached. the sequence in which monomer attaches depends upon their relative reactivates [24-25]. Copolymers can be random, alternate, block, and graft copolymers. In the random copolymer, case monomer units are not specified placed similarly in the case of the alternate copolymer, monomers are present in an ordered form, and in Block copolymer involves the segments of different monomers attached together at terminals. Copolymerisation is used to improve the properties and the utility of a system in various applications such as modification symmetry of the polymer chain and intermolecular forces, glass transition temperature, crystallinity, solubility, elasticity, permeability, and chemical reactivity can be tuned within wide limits [26-27]. Graft copolymer acts as a backbone in which polymeric chains are attached at different sites. The graft copolymerization involving a single monomer usually occurs in a primary step. Subsequently, graft copolymerization in the presence of vinyl monomers binary mixtures may occur with the secondary or tertiary sequential addition of monomers. When two monomers are added side by side, it is called mosaic grafting. The presence of functional groups on the backbone is the basic essential requirement for the synthesis of graft copolymers molecule. The graft polymerization process can be carried out by identifying the solubility of the component and the nature of the solvent used for the reaction i.e., homogenous and heterogeneous system.

GRAFTING:

Grafting leads to polymerization, where the Activation of polymer chains under specified conditions by the action of suitable chemical reagents, or high-energy radiation treatment. The hybridize technique is used for synthetic and natural polymers which assists in the fundamental investigation of the structure-property relationships. Properties like melting point, solubility, permeability glass transition temperature, elasticity, and chemical reactivity can be modified through graft copolymerization as per the specific requirements. Activation of macroradicals due to the growth of functional monomer leads to branching and further to cross-linking. During the last decades, several methods have been introduced for the preparation of graft copolymers by conventional techniques like chemical, radiation, crosslinking, aqueous state radiation, etc [24].

Grafting methods:

Chemical induced grafting:

Radical polymerizations are one of the useful methods for the polymerization of a different variety of vinyl monomers and can be plagued by a lack of control over the mechanism; radical polymerizations have many different reactions occurring simultaneously namely initiation, propagation, and termination by coupling, disproportionate or chain transfer. Synthesization is a crucial step in the creation of an active site on the backbone of the existing polymer to develop a highly appreciate polymer for binding. The active site may be either free radicals or chemical group may get avail and involved in anionic polymerization (anionic or cationic) or in a condensation process

Free radical techniques can be subdivided into two general categories, the first involves the polymerization of an olefinic monomer in the presence of a preformed polymer bearing labile hydrogen, e.g., grafting of styrene onto polybutadiene. Initiation is achieved with peroxides, irradiation, or thermal methods. The second category features initiation of the monomer by hydroperoxide or functional groups already on the preformed backbone. Examples of these techniques are the initiation of styrene polymerization by hydroperoxides of polypropylene and the ceric ion redox initiated grafting of methyl methacrylate onto cellulosic or polyvinyl alcohol. The general trend for free radical initiated by initiation. In this process, the initiator produces a free radical and transfers it to the substrate polymer to initiate the reaction with the monomer. The monomer is linked directly to the backbone surface of the polymer and then converted into a free radical. Following initiation, the next unit of monomer molecule gets strike and bind to the monomer-free-radical which is previously attached to the polymeric backbone and is converted into free radical. This process is continuous and the chain length of grafted polymer propagates. Various examples of imitators such as ferrous ammonium sulfate, Ceric ammonium nitrate, Potassium diperiodatocuprate, Potassium persulfate, Thiocarbonation potassium bromated, and ammonium persulfate. In propagation finally, chain-propagation

occurs to the terminal end by coupling between two propagating polymeric free radicals and single monomeric free radicals or propagating polymeric free radical and propagating homopolymeric (composed with only grafting monomer molecules) free radical resulting grafted copolymer. Homopolymer formation results from the coupling between two propagating homopolymeric free radicals. Ionic polymerization has to be carried out in presence of an anhydrous medium and/or in presence of a considerable quantity of alkali metal hydroxide example sodium methoxide or alkali metal salt alkyl aluminum. The limitation of ionic grafting is that low weight graft copolymers are obtained while in the example of free radicals grafting high molecular weight grafting polymers can be prepared. Graft copolymer technology has been discussed in various studies literature [25].

Anionic grafting:

Hossein Hosseinzadeh in his research used a modified polysaccharide, sodium hyaluronate by graft copolymer reaction of acrylic acid. This grafting process is initiated by using anionic initiator ammonium persulfate. Researchers studied that an increase in the molecular mass of sodium hyaluronate after extraction of homopolymer is considered as the endpoint of grafting, and also the prime basis to determine grafting parameters. In this study, the effect of concentration of acrylic acid, sodium hyaluronate, and ammonium persulfate as well as grafting temperature on the grafting process was evaluated [24].

Cationic grafting:

Yoshikawa et al. in their experimental research grafted chitosan with cationic living polymers such as poly (isobutyl vinyl ether) and poly(2-methyl-2- oxazoline). In this study, analysis of the effect of molecular weight of living polymer reaction on the mole number of the grafted polymer processed researcher found that as increase the grafting process, the viscosity of the resulting polymer is found to increase with the increasing percentage of grafting. This grafted polymer is also found to be soluble in water [25].

Grafting by living polymerization:

Living polymer" is "that it retains its ability to propagate the chain and tendency grows to a desired expected maximum size and their degree of termination or chain transfer is very short. it provides living polymers with regulated molecular weights and low polydispersities [28].

Photochemical grafting:

Photochemical radiations generally are used for initiation grafting and cause dissociation of the chromophore to reactive free radicals with or without sensitizer. There is a generation of free radicals on the backbone by using without sensitizer and grafted polymer with sensitizer. the mechanism involved with sensitizer forms free radicals, which can undergo diffusion so that they abstract hydrogen atoms from the base polymer, producing the radical sites required for grafting.

Enzymatic grafting:

Enzymes can cause chemical/electrochemical grafting reactions. Utilization of green approach offers by the application of enzymes so as to eliminate the use of reactive reagents or chemicals in grafting techniques with respect to safety, efficacy, and economy. Enzymes specificity may offer the potential for precisely tailoring macromolecular properties to desired ones.

Radiation grafting:

Exposure of high-energy radiation over the polymeric backbone to form active sites. it serves as a site where grafting for propagation and ultimately to form side chain grafts and it gets easily react with appropriate functional monomers to form a covalent bond and consequently, there has been increasing the growth of macromolecular chains which are used as the chemical initiators [29].

RESEARCH ON GRAFTING:

Grafting by Acrylic Acid:

Banyal, *et al.* reported in their research that mulberry silk fiber was graft copolymerized with binary mixtures of acrylic acid, methyl acrylate, and acrylonitrile with methyl methacrylate as the principal monomer units in an aqueous medium by using CAN as a redox initiator. Graft copolymerization is carried out by using binary vinyl monomers using appropriate conditions and reaction time. Grafting optimum concentration of MMA and CAN report earlier on the backbone and it was characterized in acidic and alkaline medium using FTIR, SEM, swelling studies, moisture absorption, and chemical resistance also estimate dye uptake gentian violet on graft copolymers at 420 nm by using photo-calorimetrically.

It was shown that the dying capability of the graft copolymers is higher than the reference graft copolymer of methyl methacrylate [30,31], butyl methacrylate (BMC), and acrylic acid (AA) onto carboxymethylcellulose

(CMC) under argon atmosphere in a homogeneous aqueous medium [32]. Similarly, Kaith, *et al.*, reported experimentally psyllium mucilage which is obtained from Plantago ovate, and modification has been carried out through graft copolymerization and network formation using acrylic acid (AA) as the monomer, potassium persulphate (KPS) as an initiator, and hexamethylenetetramine (HMTA) as a cross-linker respectively [33].

Grafting by Acrylo-Nitrile:

Anionic natural polysaccharide is the source obtained from the seeds of *Plantago psyllium* and its mucilage consists of constituent's pentosan and uronic acid grafted in presence of acrylonitrile (AN) and initiated by ceric ion-initiated solution polymerization technique and are characterized by instrumentally FT-IR spectroscopy, scanning electron microscopy and differential scanning calorimetric.

Vandna, *et al.* 2003 prepared the grafting of polyacrylonitrile (PAN) onto guar gum in water, without using any radical initiator or catalyst within a very short reaction time through microwave (MW) irradiation. Polyacrylonitrile grafted agar/ sodium alginate has been synthesized in an aqueous medium under reflux conditions in the presence of potassium persulfate as a free radical initiator [34].

Grafting by Acryl Amide:

Vandna, *et al.* (2005) carry out a synthesization reaction and reported her study in absence of a radical initiator using Chitosan-graft-polyacrylamide (Ch-g-PAM) or catalyst by using microwave (MW) irradiation. Under optimal conditions, 169 % grafting is observed at 80 % MW power in 1. 16 min [35].

Polymermethylmethaacrylate grafting:

The graft copolymerization of methyl methacrylate into chitosan is investigated using ceric ammonium nitrate as the initiator. The effect of initiator concentration, monomer concentration, time, and temperature on % G and % GE are studied. The antibacterial activity of chitosan, as well as the grafted samples, is investigated using some gram-positive and gram-negative bacteria. Grafted products of polymer show some improvable properties of antibacterial activity [36].

Mechanisms involved Reactive group grafting on Backbone Structure:

Although, in recent years, modification of chemical and physical properties of natural polymers and their derivatives through graft copolymerization has attracted much attention. There improving the wettability, biocompatibility, mechanical properties, etc. The two mechanisms of grafting polymer are grafting from and grafting to (Table 3). Grafting results show comparatively desire retentive properties of the base polymer and implicit favourable conditions in the grafted polymer. Polysaccharides polymer have an advantage over the modified synthetic polymers because of their Non-toxicity Less cost, Biodegradability, environment-friendly, efficiency, and ease of avail as a substrate. Polysaccharides appear as a very appealing alternative to substitution because they are renewable raw materials.

Table 3. Mechanisms involved reactive group grafting on backbone structure.

Mechanism	Reactive site
Radical	Allylic H
Radical	Hydroperoxide
Radical	Redox
Cationic	PVC Allylic & tertiary Cl
Anionic	Metallated PBD
Anionic	Ester group

POLYSACCHARIDE [37,38]:

Hydrogel source formally divided into two main classes artificial and natural and it can be subdivided into two subclasses such as polysaccharides and polypeptides. The natural-based hydrogel is prepared by the addition of synthetic parts over natural substrates e.g., graft polymerization of vinyl monomer on polysaccharide. Natural polysaccharides are used as pharmaceutical excipients and it's classified on the basis of charge. Non-ionic seed gums such as guar gum, locust bean, tamarind, xanthan, amylose, arabinans, cellulose, and galactomannans and anionic gums Arabic, karaya, agar, gellan, algin, tragacanth, carrageenans, pectic acid.

Classification of polysaccharides on the basis of the source. Marine origin/algal (seaweed) gums: agar, carrageenans, alginic acid, laminarin. The significance of synthetic polymer is chemical resistance, water repellency, rigidness, thermal stability and possesses better rein forming and compatibility materials.

Plant origin:

1. Shrubs/tree exudates: gum arabica, gum ghatti, gum karaya, gum tragacanth, khaya and albizia gums.
2. Seed gums: guar gum, locust bean gum, starch, amylose, cellulose.

Table 4. Commercialized Hydrogel formulation [19].

Name of the Hydrogel Drug	Application
Aquatrix II (Skin adhesive hydrogel)	Wound, Burn, Adhesive
Medicell	Medicated foam for burns
Hydromer	Antithrombic DNA immobilisation
Aquamere(Coating hydrogel)	Cosmetics
Dermaseal	Super absorbent
Suprasorb® G	Dry wounds, Lower leg ulcer, pressure ulcer, first and second-degree burns, scalds
AquaDerm™	Pressure ulcers, Minor burns and radiation tissue damage
DermaGauze	Acute or chronic partial and full thickness wounds
Neoheal® Hydrogel	Ulcers, abrasions, burns, bed sores and other chronic wounds
Simpurity™ Hydrogel	Dry wounds, skin burns and dry scabs
Restore Hydrogel	Partial and full thickness wound
ActivHeal®	Pressure ulcers, leg ulcers, diabetic foot ulcers, cavity wounds
DermaSyn®	Acute or chronic partial and full thickness wounds
NU-GEL™	Chronic wound, diabetic foot ulcers, venous leg ulcers and pressure ulcers
Purilon®	Leg ulcers, pressure ulcers, non-infected diabetic foot ulcers and First and second degree burns
INTRASITE Gel	Pressure ulcers, Diabetic foot ulcers Surgical incisions Venous ulcers
SOLOSITE Gel	Minor burns, cuts, abrasions, skin tears, Venous ulcers, Surgical incisions, Diabetic foot ulcers, Pressure ulcers,
Woun'Dres®	Dry wounds

Table 5. Recently filed patents in area of polymer grafting [43-46].

Subject /Title of patent	Patent Number	Material
Fast dissolving films for oral administration of drugs.	US 20040208931 A1	a polyvinyl alcohol-polyethylene glycol graft copolymer
Process for producing solid dosage forms.	US 7419685 B2	water-swellable graft copolymer or a mixture of graft copolymers employed binder
Fast dissolving films for oral administration of drugs.	WO 2004060298 A2	PVA-PEG and PVA-PEG
Solid dispersion of poorly soluble drugs in graft copolymers.	WO 2007115381 A2	using PVA-PEG copolymer, such as Kollicoat IR.
Cannabinoids-Ionic complex self-nanoemulsifying concentrate and method for preparation thereof.	P-202100132	Ionic Complex, water and optionally other excipients and stabilizers
Method for production of modified polyolefin.	JPH07173229A	inoculation with non-saturated carboxylic acid or anhydride of non-saturated carboxylic acid on polyolefin
Retro Diels Alder assisted polymer grafting process.	US4739017A	grafting process in which a Diels Alder adduct is mixed with a polyolefin or polyvinyl polymer substrate and thermally decomposed to form an ethylenically unsaturated monomer

3. Extract: pectin, larch gum.
4. Tuber and roots: potato starch.
5. Animal origin: Chitin and chitosan, chondroitin sulfate, hyaluronic acid.
6. Microbial origin (bacterial and fungal): xanthan, dextran, curdian, pullulan, zanflo, emulsan, Baker'syeast glycan, schizophyllan, lentinan, krestin, scleroglucan.

Semisynthetic:

1. Starch derivatives: hetastarch, starch acetate, starch phosphates.
2. Cellulose derivatives: carboxymethylcellulose (CMC), hydroxyethylcellulose, hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), microcrystalline cellulose (MCC) Techniques of grafting through monomers into natural polysaccharide backbone [39].

EVALUATION OF GRAFTING HYDROGEL [40-42]:

Grafting percentage and grafting efficiency (GE):

The grafting percentage (GP) indicates the increase in weight of original cellulose subjected to grafting with a monomer and is calculated by this equation:

GP (%) = [(Wt-Wo)/Wo]×100……(1)

GP – Grafting percentage, Wt-Wo - Weight of polymer grafted, Wo is the initial weight of backbone. Where Wt and Wo are the weights of the cellulose graft copolymer and the original cellulose, respectively. (GP) % defined above known as apparent graft yield. GP is a weight ratio of grafted polymer to original cellulose.

GE (%) = Weight of polymer grafted/Weight of polymer grafted + weight of homopolymer ×100

= (Wt-Wo)/ (Wt-Wo+W2) × 100…….(2)

FTIR spectroscopy:

FT-IR spectra are recorded by a Nicolet IS-10 spectrometer (Thermo Fisher, America) working in attenuated total reflectance mode, the resolution being 2 cm^{-1}, in the range 4000 to 600 cm^{-1} with 32 scans per sample cycle.

X-ray diffraction (XRD):

XRD profiles of the hydrogel samples are detected by using a DMAX-2200 diffractometer (40 kV and 40 mA) equipped with a Cu Ka radiation (0.154 nm) over the range of 10 to 60 °C.

Thermogravimetric analysis (TGA):

TGA study of hydrogel assay can be carried out by using TA Q-600 thermal analyzer. The sample is required to heat 600 °C at 20 °C/min in a nitrogen atmosphere.

Morphology observation:

The cross-section surface morphology of hydrogels can be studied by using a scanning electron microscope. In this prepared hydrogels are required to first freeze-dry and fracture in liquid nitrogen. Then, the hydrogels are pasted onto a mica sheet and vacuum coated with gold. The average pore size is evaluated from the SEM.

Mechanical properties:

Mechanical performance characteristics of the hydrogels are studied by using a Physica MCR 101 rheometer (Anton Paar) with a parallel plate of 40 mm diameter.

CONCLUSIONS:

Hydrogel is a multi-component system and is composed of natural or synthetic polymer to incorporate useful properties of the substrate. Synthetic polymer showing advantages improvable property of hydrogel and their method of preparation based on polymer nature and polymerization techniques examples are biological and stimuli hydrogel.

Various researchers were prepared hydrogel by a different method using polymer and peptides and have a wide application in various fields. The Novel advanced emerging copolymerization grafting is a newer concept that has shown a rationale in polymerization and imperative techniques for modification in the properties of the polymer and their modification by the natural and synthetic derivatives of polysaccharide and polypeptide. This modification is to overcome the challenges associated and provides compatible, flexible, rigid, and more stable synthesized or modified polymer for loading the drug.

Presently a number of patents are filed in the area of polymer grafting also industry also shows much interest due to attractive and applicable techniques in the field of polymer grafting. In the future, polymer grafting has a huge scope in the development of dosage form.

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