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AS A REVIEW ON HYDROGEL IN PHARMACEUTICAL SCIENCES

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ABSTRACT

Hydrogels are hydrophilic, three-dimensional networks, which are able to imbibe large amounts of water or biological fluids, and thus resemble, to a large extent, a biological tissue. Softness, smartness, and the capacity to store water make hydrogels unique They are insoluble due to the presence of chemical (tie-points, junctions) and/or physical crosslinks such as entanglements and crystallites. Hydrogels that are responsive to specific molecules, such as glucose or antigens, can be used as biosensors as well as drug delivery systems. These materials can be synthesized to respond to a number of physiological stimuli present in the body, such as pH, ionic strength and temperature. The main aim of the current article is to describe about all the information of Hydrogels.

KEYWORDS: Hydrophilic, biosensors, Hydrogels.

INTRODUCTION

The research on hydrogel is more than four decades old there has been a tremendous growth in the recent past because of their unique bulk and surface properties. Hydro gel's have been extensively explored for their potential in the development of controlled drug delivery system.[2] They form the basis of many novel drug delivery system. Hydrogel have been used in the preparation of molecularly recognizable synthetic membranes for biosensors, which are a critical component of single responsive drug delivery system. Hydrogel can be made to respond to the environment and the extent of response can be controlled. The environment condition to which a hydrogel can be made responsive can be ph, temperature, electric field, ionic strength, salt type solvent light or combinations of these. It is because of these unique properties that these classes of polymer based system embrace numerous pharmaceutical application.[1]

Hydrogel are cross linked, three dimensional macromolecular polymer network that are insoluble but are able to swell rapidly in water. In the process they can retain large volume of water in their swollen three dimensional network. Drying of the hydrogel causes evaporation of the water from the gel and the surface tension causes collapse of gel body. The dried hydrogel are called as Xerogel. If the water is removed without disturbing the polymer network either by freeze-drying or by organic solvent extraction then the remaining material is extremely light with excellent porosity. Such dehydrated hydrogel is called an Aero gel.[2]

Topical application of drug at the affected site offers potential advantage of delivering the drug directly to the site of action. Hydrogel contain liquid such as water, glycerin. In case of hydrogel water is principle liquid their will be chances of bacterial growth in it. Gel's better potential as a vehicle to administer drug topically in comparison to ointment. They are non sticky requires low energy during formulation & are stable. Local infection can best be treated by application of product that form transparent water vapour and air permeable film over the skin surface from which the drug releases continuously to the application site. In these we study about through which parameter does the hydrogel will be pass during the formulation and after the formulation.

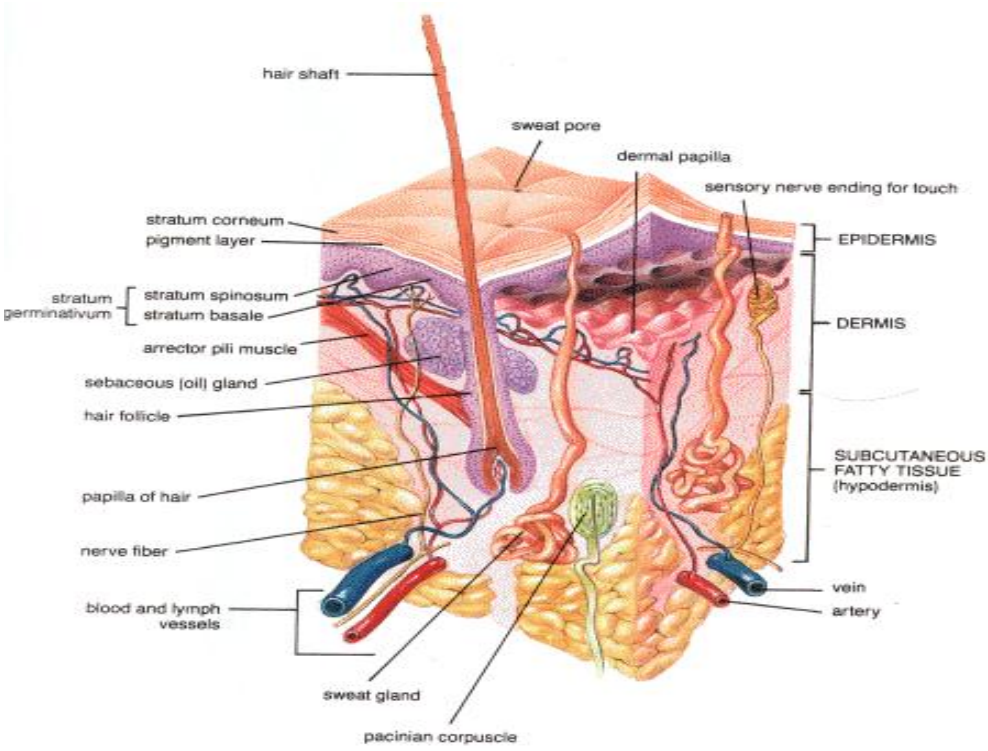
Now a days hydrogel can be used for various purposes such as ocular drug delivery, wound dressing, bone reconstruction, ocular drug delivery.

SKIN

Skin it is a largest organ of body playing role as barrier and a regulating influence between the outside world and the inside body.

1.1 ROLE

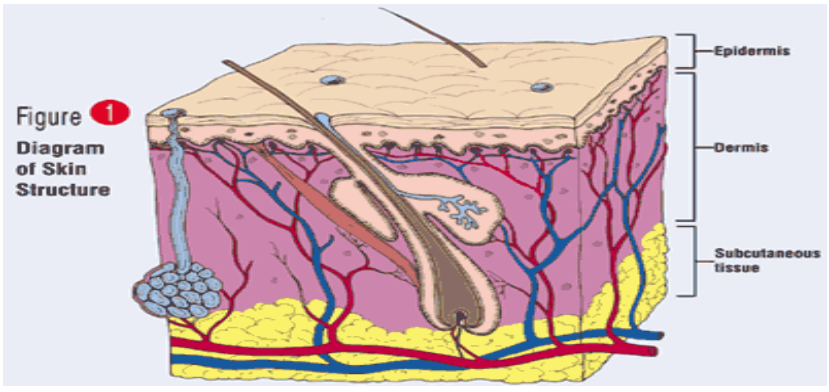
1. Internal body temperature is controlled trough several process generally by sweat production.
2. Physical toughness of the skin prevent the ingress of harmful chemical and bacteria.
3. Vitamin D, which is essential for growth and maintenance of our boneis Produc in skin.[3]



2. DESPOSITION OF DRUG VIA SKIN

1 Routes of Traditional Transdermal Drug Penetration

There are two main pathways by which drugs can cross the skin and reach the systemic circulation. The more direct route is known as **the Tran cellular pathway.** By this route, drugs cross the skin by directly passing through both the phospholipids membranes and the cytoplasm of the dead keratinocytes that constitute the stratum corneum. Although this is the path of shortest distance, the drugs encounter significant resistance to permeation. This is because the drugs must cross the lipophilic membrane of each cell, then the hydrophilic cellular contents containing keratin, and then the phospholipid bilayer of the cell one more time. This series of steps is repeated numerous times to traverse the full thickness of the stratum corneum.[4]



The more common pathway through the skin is via **the intercellular route**. Drugs crossing the skin by this route must pass through the small spaces between the cells of the skin. Although the thickness of the stratum corneum is only about 20 µm, the actual diffusional path of most molecules crossing the skin is on the order of 400 µm. The 20-fold increase in the actual path of permeating molecules greatly reduces The rate of drug penetration.

A less important pathway of drug penetration is **the follicular route**. Hair follicles penetrate through the stratum corneum, allowing more direct access to the dermal microcirculation. However, hair follicles occupy only 1/1,000 of the entire skin surface area. Consequently, very little drug actually crosses the skin via the follicular route.[5]

2.2 Factors Influencing Percutanous Absorption

Thickness of stratum corneum

Trauma

- ✓ **Hydration**
- ✓ **Age**
- ✓ **Humidity and temprature**
- ✓ **Hair follicale**

2.3 Types of Topical Apllied Preparation

Semisolid: 1.ointment, 2. Cream, 3. Paste, 4.gel.

Liquid: 1.lotion, 2.liniment.

Solid Dosage Form: Powder

New drug delivery system

Transdermal implant

Transdermal implants are a form of body modification used both in a medical and aesthetic context. In either case, they consist of an object placed partially below and partially above the skin, thus *trans*dermal. The skin around it generally heals as if it were a piercing. Medically, transdermal implants are used to create "ports. In the body piercing community, these types of modification are generally called fairly "heavy" due to the complexity of the procedure and the social implications**.**

The skin is lifted and the implant is passed through. Then, a hole is opened at the site for it to pass through, and it is moved so that the top part fills the hole. In any case, the part of the

implant which passes under the skin generally is somewhat large and has holes. The skin will grow into them, making it more permanent.[6]

2.4 ADVANTAGES

1. Percutanous drug delivery system avoid the first pass effect.
2. Percutaneous drug delivery system avoid the pain associated with injection.
3. Continuous sustained release of drug with infrequent dosing.
4. They impart both, local as well as systemic effects.

1.5 Disadvantage

1. Disadvantages to transdermal drug delivery is the possibility that a local irritation will develop at the site of application. Erythema, itching, and local edema can be caused by the drug, the adhesive, or other excipients in the patch formulation. For most patients, site rotation can minimize irritation.
2. Disadvantage of transdermal drug delivery is that the skin's low permeability limits the number of drugs that can be delivered in this manner. Because the skin serves a protective functions it inhibits compounds from crossing it. Many drugs with a hydrophilic structure permeate the skin too slowly to be of therapeutic benefit. Drugs with a lipophilic character, however, are better suited for transdermal delivery. Many of the recent developments in transdermal drug delivery target the more hydrophilic compounds that were previously undeliverable via this method.[7]

HYDROGEL

3.1 What is Hydrogel?

Hydrogel is hydrophilic polymer capable of containing large amounts of water. Water absorbed by hydrogel should not be released under ordinary pressure. Konjak-mannan, a jelly-like food made from the starch of devil's tongue (seaweed), and agar are examples of hydrogel that are familiar to us. Hydrophilic groups such as hydroxyl (OH) and carboxy (COOH) in principal and their side chains absorb and store water.

Konjak-mannan and agar exist in nature and are called natural polymers. We have developed hydrogel from hydrophilic polymers chemically synthesized as a part of research on new functional materials using radiation.

As feed materials for hydrophilic polymers, water-soluble substances such as polyvinyl alcohol, polyethylene oxide, polyvinyl pyrrolidine, etc. are used, and irradiating them produces a network of chemical bonding between molecular chains, called a "cross linkage reaction". This process enables highly polymerized materials to confine water in their molecular chains by raising their bonding force. This then is hydrogel as resulting from irradiation; its solubility decreases remarkably, it can withstand boiling at 100^0 C and sterilizing by autoclave at 121^0C.

As an example of hydrogel use, take sanitary goods like disposable paper diapers, which are already on the market. Dried hydrogel is used for absorbing and trapping urine in their molecular structure. Soft contact lenses are another instance of hydrogel use. We produced highly purified hydrogel only from water and hydrophilic polymers using radiation and applied it as for medical dressing purposes.[8]

3.2 What, exactly, is this material?

Applied to wounds, burns or surgical incisions, this material covers the injured parts of skin (wounds) and promotes healing and skin growth. There are two ways of curing; under dry or wet conditions. In the former gauze is applied to the skin, the latter calls for the use of hydrogel. Since many agree that wounds heal faster in a wet environment, hydrocolloid type materials mixed with gelatin, hydrophobic polymers and water have been developed and already see practical use. However, these materials are mechanically weak and require periodic change, and the residue must be removed by washing with physiological salt solution, a process which sometimes exfoliates new skin and delays healing. Too, removing the dressing induces pain. Thus the need to develop a new wound dressing material to resolve such problems and simplify treatment.

In response, research on hydrogel began eight years ago. Having succeeded, we evaluated the performance of this new wound dressing by experimenting with animals. We compared the healing rates of wounds covered with gauze and those using hydrogel, and the results are indicated in Figure 1. Wounds dressed with a hydrogel healed almost completely within 14 days, while those using gauze were only half-healed within that time.[9]

Based on the excellent results shown by hydrogel, the Japan Science and Technology Corporation contracted Nichiban, Inc., to launch research on this amazing substance. R&D for its commercial manufacture have been completed. The next stage is clinical tests to

confirm the safety and effects of the product, which will be conducted at two large university hospitals. If satisfactory results are obtained, these new wound dressings will join the market pursuant to authorization by the Ministry of Welfare.

Gelling agent used in it?

Gelling agent are also required during the manufacturing it can help in the formulation to prepare non-deformable structure .gel is formed due to interaction of two macromolecule at the restricted site. Restricted site formed by site of particle remain untreated with aqueous phase.

Due to environmental condition such as ph, ionic strength, solvent, salt type, temperature, external stress, light due to all that the hydrogel made responsible.

3.3 Advantages of Hydrogel

1. Exhibit good biocompatibility low degradation and processing ease.
2. Low interfacial tension with surrounding body fluid and tissue that minimizes the driving force for protein and absorption and cell adhesion.
3. It can stimulate some hydrodynamic properties of natural biological gel's cell and tissue many ways.
4. It can minimizes frictional and mechanical irritation to the surrounding tissue.
5. RELEASE of drug from a hydrogel is depend on it's composition swelling capacity and cross linked density and the release can thus be regulated by controlling water swelling density.[10]

3.4 Disadvantage

1. Their low mechanical strength and poor toughness after swelling.[1]

3.5 CLASSIFICATION

Classification of the hydrogel

1. BASED ON TYPE OF MONOMER

1. Homopolymer

Hydrogel contain only one type of monomer.

2. Copolymer

They are made with two type of monomer out of which at least one is hydrophilic.

3. **MULTIPOLYMER**

Made up from more than three types of Monomer.

2. Based On Structure

1. Amorphous hydrogel
2. Semicrystaline hydrogel:
3. Hydrogen bonded hydrogel;

3. BASED ON MECHANISUM

1. Diffusion Controlled Release

2 Swelling Controlled Release

3. Chemical Controlled Release

4. Enviorment Controlled Release

5. BASED ON IONIC CHARGES AND P^H DEPENDENT

1. Anionic hydrogel
2. Cationic hydrogel
3. Neutral hydrogel[1]

BASED ON IONIC CHARGES & P^H SENSITIVITY

Change in swelling properties is due to change in P^H

1. Anionic Hydrogel

Contain negatively charge contain moieties. Anionic polymer network contain carboxylic or sulphonic acid group ionization take place as the ph of external swelling medium rise above the pk^a of that ionizable moiety anionic hydrogel can be used in design of intelligent controlled release device for site specific drug delivery of therapeutic protein to large intestine where the biological activity of protein is prolonged. Anionic hydrogel are used to deliver protons to the colon where activity of proteolytic enzyme is comparatively lower.

EXAMPLE: methyl methacrylate & 2-hydroxyethyl methacrylate by bulk polymerization using ethylene glycol dimethacrylate as cross linked agent.

2. CATIONIC HYDROGEL

Tionic network contain positively charged moieties. Cationic hydrogel show swelling at ph values below pka of cationic group. The amino group protonated at ph lower than pka &become hydrophilic protonated & absorb water.

Cationic hydrogel are used in the preparation of self regulated insulin delivery system self regulated insulin delivery system utilizes glucose oxidase as glucose sensor & cationic hydrogel as the insulin release controller in such system glucose is oxidized to gluconic acid & catalyzed by GOD.

GLUCOSE + OXYGEON + WATER gives GLUCONIC ACID + HYDROGEN PEROXISIED

Formation of gluconioc acid inside. It ph inside it is decrease with increase glucose concentration.

3. Neutral or Ionic Hydrogel

Neutral network contain both positively & negatively charged moieties. in neutral hydrogel the driving force for swelling arise from the water polymer thermodynamic mixing contribution & elastic polymer contribution. In neutral hydrogel the swelling is due to previous two contribution. As well as ionic interaction between charged polymer & free ion.

Preparation of hydrogels. & hydrogel formulation aspect

4.1 Pre Paration of Hydrogel

Several techniques have been reported for the synthesis of hydrogels. The first approach involves copolymerizatoin/crosslinking of co-monomers using multifunctional co-monomer, which acts as cross linking agent. The polymerization reaction is initiated by chemical initiator. The polymerization reaction can be carried out in bulk, in solution, or in suspension. The Second method involves cross linking of linear polymers by irradiation, or by chemical compounds. The monomers used in the preparation of the ionic polymer network contain an ionizable group, a group that can be ionized, or a group that can undergo a substitution reaction after the polymerization is completed. As a result, hydrogels synthesized contain weakly acidic group like substituted amines, or a strong acidic and basic group like sulfonic acids, and quatemary ammonium compounds. Some of the commonly used cross linking agents include N. N. methylene bisacrylamide. Divinyl benzene, and ethylene glycol dimethacrylate. The monomers and the cross linking agents used in the preparation of hydrogels are given in Table 2.[11]

Table No: 1 Structure of monomer used in preparation of hydrogel.

Anionic acidic monomers 1.acrylic acid - CH2=CH-COOH
2.methacrylic acid CH2=C-COOH
Cationic basic monomers 1.vinyl pyridine - CH2=CH
2.2-methacryloyloxy-trimethylammonium chloride
Neutral monomer for hydrogel synthesis 1.acrylamide - CH2=CH
2.2-hydroxyethyl methacrylate
Polyfunctional crosslinking monomer for hydrogel synthesis 1.n n methylenebisacrylamide
2.ethylene glycol dimethacrylate

4.1.1 Solution Polymerization/Crosslinking

In solution co-polymerization. cross linking reactions, and ionic or neutral monomers are mixed with the multifunctional cross linking agent. The polymerization is initiated thermally, by UV-light, or by redox initiator system. The presence of solvent serves as heat sink, and minimizes temperature control problems. The prepared hydrogels need to be washed with distilled water to remove the unreacted monomers, cross linking agent, and the initiator. The best example is preparation of poly(2- hydroxyethyl methacrylate) hydrogels from hydroxyethlmethacrylate, using ethylene glycol dimethacrylate as cross linking agent. Using the above method, a great variety of hydrogels have been synthesized. The hydrogels can be made pH-sensitive or temperature-sensitive, by incorporating methacrylic acid, or N-isopropylacrylamide, as monomers.

4.1.2 Suspension Polymerization

This method is employed to prepare spherical hydrogel microparticles with size range of 1mm to 1mm. In suspension polymerization, the monomer solution is dispersed in the non-solvent forming fine droplets, which are stabilized by the addition of stabilizer. The polymerization is initiated by thermal decomposition of free radicals. The prepared microparticles then washed to remove unreacted monomers, cross linking agent, and initiator. Hydrogel microparticles of poly (vinyl alcohol) and poly (hydroxy ethyl methacrylate) have been prepared by this method.[12]

4.1.3 Polymerization By Irradiation

High energy radiation like gamma and electron beam, have been used to prepare the hydrogels of unsaturated compounds. The irradiation of aqueous polymer solution results in

the formation of radicals on the polymer chains. Also, radiolysis of water molecules results in the formation hydroxyl radicals, which also attack the polymer chains, resulting in the formation of macro radicals. Recombination of the macro radicals on different chains results in the formation of covalent bonds, and finally a cross linked structure is formed. During radiation, polymerization macro radicals can interact with oxygen, and as a result, radiation is performed in an inert atmosphere using nitrogen or argon gas. Examples of polymers cross linked by radiation method include poly (vinyl alcohol) poly (ethylene glycol). Poly (acrylic acid). The major advantage over chemical initiation as the production relatively pure, residue-free hydrogels.[13]

4.1.4 Chemically Crosslinked Hydrogels

Polymers containing functional groups like-OHL, - COOH, - H - NH_2 are soluble in water. The presence of these functional groups on the polymer chain, can be used to prepare hydrogels by forming covalent linkages between the polymer chains and complementary reactivity, such as amine-carboxylic acid, isocyanate-OH/NH_2 or by Schiff base formation.

Gluteraldehyde can be used as a cross linking agent to prepare hydrogels of polymers containing - OH groups like poly (vinyl alcohol). Also, polymers containing amine groups (albumin, gelatin, polysaccharides), can be cross linked using gluteraldehyde.

Polymers that are water soluble, can be converted to hydrogels, using bias or higher functional cross linking agents like divinylsulphonate, and 1.6-hexanedibromide.

The cross linking agents react with the functional groups, present on the polymer, via-addition reaction. These cross linking agents are highly toxic, and hence unreacted agents have to be extracted. Moreover the reaction has to be carried out in organic solvent, as water can react with the cross linking agent. The drugs have to be loaded after the hydrogels are formed, as a result the release will be typically first order.

Cross linking between polymers through hydrogen bond formation occur as in the case of poly (ethylene glycol) The hydrogen bond formation takes place between the oxygen of poly (ethylene glycol) and carboxylic acid group of poly methacrylic acid) Carriers consisting of networks of poly (methacrylic acid-gethylene glycol) showed pH dependent swelling due to the reversible formation of interpolymer complex, stabilized by hydrogen bonding between

the etheric groups of the grafted poly (ethylene glycol), and the carboxylic acid protons of the poly (methacrylic acid).[14]

4.1.5 Physically Crosslinked Hydrogles

Most of the covalent cross linking agents are known to be toxic, even in small traces. A method to overcome this problem and to avoid a purification step, is to prepare hydrogels by reversible ionic cross linking. Chitosan, a polycationic polymer can react with positively charged components, either ions or molecules, forming a network through ionic bridges between the polymeric chains. Among anionic molecules, phosphate bearing groups, particularly sodium, tripolyphosphate is widely studied. Ionic cross linking is a simple and mild procedure. In contrast to covalent cross linking no auxiliary molecules such as catalysts are required. Chitosan is also known to form polyelectrolyte complex with poly(acrylic acid). The polyelectrolyte complex undergoes slow erosion, which gives a more biodegradable material than covalently cross linked hydrogels.[15]

4.2 Formulation Aspect

4.2.1 Type of Polymers

Polymers have been broadly classified as

A) Natural polymers

These include nucleic acids, proteins polysaccharides and complexes of proteins and polysaccharides.

B) Synthetic Polymers

These include polyesters, polyurethane, polyamides, polycarbonates, polysiloxanes, Polyolefins, polyvinyl compounds and acrylics.

4.2.1.1 Polymers can also be classified on the basis of their interaction with water

a) Non-biodegradable hydrophobic polymers

b) Hydrogels

c) Soluble polymers

d) Biodegradable polymers.

4.2.2.2 CHARACTERISTICS OF IDEAL POLYMER SYSTEM

1. It should be chemically inert and free from leach able impurities.
2. It should have good mechanical strength.

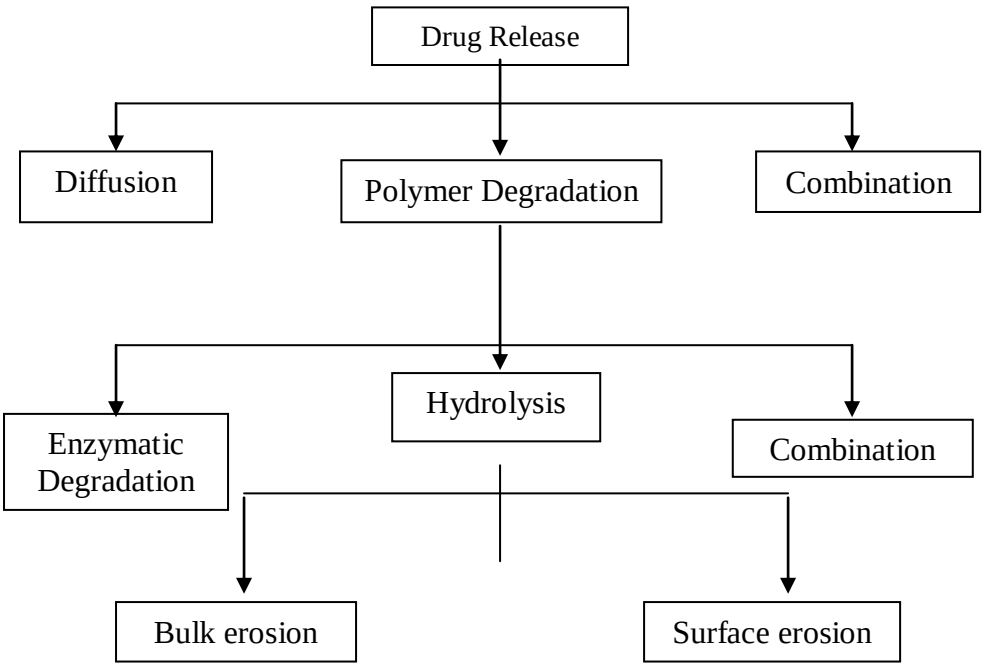
3. It should be non-toxic and compatible with the environment.
4. It should be easy and inexpensive to fabricate
5. It should be easily sterilized.
6. It should demonstrate acceptable shelf life.

In addition to carrier systems containing single polymeric systems, researchers are working on carrier systems containing block copolymers. These are the polymers formed through polymerization of two or more monomers. These networks when composed of hydrophilic and hydrophobic monomers are called polymer micelle. These micelles are suitable for enclosing individual drug molecules. Their hydrophilic outer shells help to protect the cores and their contents from chemical attack by the aqueous medium. Most micelle based systems are formed from poly(ethylene oxide)-b-polypropylene-b-poly(ethylene oxide) triblock network. In one of the studies carried out, micelles were used as a means of delivering doxorubicin, a hydrophobic anticancer agent. Results revealed that when dosed intravenously the system could withstand the body's normal blood circulation and effectively deliver the medication to a solid cancerous tumor.[16]

4.3 Drud Release Mechanisms For Polymeric Drug Delivery

Two broad categories of polymer systems have been studied. The reservoir device involves the encapsulation of a drug within a polymer shell, while the matrix device describes a system in which a drug is physically entrapped within a polymer network.

Table No:2 Possible drug release mechanisms for polymeric drug delivery.



As shown in figure I the drug will be released over time either by diffusion out of the polymer matrix or by erosion (due to degradation) of the polymer or by a combination of two mechanisms. Reviews have been presented on the mechanisms and the mathematical aspects of release of drug from polymer matrices.

Figure 2: Drug delivery from (a) bulk eroding and (b) surface eroding biodegradable system.

FACTORS GOVERNING THE DRUG RELEASE

For a given drug the release kinetics from the polymer matrix are governed predominantly by the following factors, viz, the polymer morphology and excipients present in the system.

POLYMER MORPHOLOGY

The polymer matrix could be formulated as either macro or nanospheres, gel film or an extruded shape (cylinder, rod, etc). Also the shape of the extruded polymer can be important to the drug release kinetics. It has been shown that zero order drug release can be achieved using a hemispherical polymer for. Polymer microspheres are the most popular form due to manufacturing advantages as well as ease of administration. The techniques, affects factors such as porosity, size distribution and surface morphology of the polymers.[17]

Table 3: List of polymers and their application.

POLYMER	APPLICATION
NATURAL POLYMERS	
Proteins and protein-based polymers	Absorbable, biocompatible, nontoxic, naturally avail able, typically elastic materials used as implants and in tissue engineering
Collagen	Absorbable sutures, sponge would dressing, drug del delivery microspheres.
Albumin	Used in cell and drug micro encapsulation.
Poly (Amino acids)	Nontoxic, no antigenic and biocompatible. Used as deoligomeric drug carriers.
Polysaccharides and derivatives	
From vegetable sources	
Carboxymethyl cellulose	Cell immobilization via a combination of ion otropi gelation and polyelectrolyte complex formation (e.g. with chitosan), in drug-delivery systems and dialysis membranes.
Cellulose sulphate	Component of polyelectrolyte complex's for Immunoisolation.
Agarose	Largely used as supporting materials in clinical analysis and as an immobilization matrix.
Alginate (marine sources, algae)	Excellent gel-formation properties, biocompatible, microstructure and viscosity are

	dependent on the chemical composition (batch-to-batchvariations). Used as immobilization matrices for cells and enzymes, controlled release of bioactive substances, injectable microcapsules for treating neurodegenerative and hormone-deficiency diseases.
Carrageen an	Excellent thermo reversible properties Used for micro encapsulation.
f or human and animal sources	
Hyaluronic acid	Excellent lubricant, potential, therapeutic agent
Heparin and heparin-like Antithorombotic and anticoagulant proper properties.	Extensively used in glycosaminoglycans surgery. Some are candidates for ion tropic gelation and capsule formation.
Microbial polysaccharides	
Dextran and its derivatives	Excellent rheological properties, plasma expander, widely used as a drug carrier.
Chitosan and its derivatives	Biocompatible, nont0oxic, excellent gel-and d film-forming ability, natural polycation., Widely used in controlled-delivery systems (e.g. gels, membranes, microspheres)
SYNTHETIC POLYMERS	
Aliphatic polyesters	
Poly (lactic acid,) poly (glycolic acid) and their copolymers	Used in sutures, drug-delivery systems and in tissue engineering. Biodegradable, often co polymerized to regulate degradation time.
0 Polya amides (Nylons)	Sutures, dressing, haemofiltration membranes.
Polynydrides	Biodegradable, useful in tissue engineering and for the release of the bioactive molecules.
Poly (ortho esters)	Surface-droding polymers. Application In sustained drug delivery, ophthalmology.
Poly (cyano acrylates)	Biodegradable, depending on the length of the alkyl chain. Used as surgical adhesives and gues, , potentially used in drug delivery.
Polyphosphazenes	Can be tailored with versatile side-chain functionality. Made into films and hydrogels. . Applications in drug delivery.
Thermoplastic polyurethane's	Good elastomeric proprites. Can be tailored by varying the startling materials. Used in permanently implanted medical devices (prostheses, vascular grafts) catheters and drug g delivery systems . . Initial candidates for the artificial heart.
Polyethylene (low density)	Sutures, catheters, membranes, in surgery.
Poly (vinyl alcohol)	Gels and blended membranes are used in drug delivery and cell immunoisolation.
Poly (ethylene oxide)	Highly biocompatibic. Different polymer derivatives and copolymers have been utilized in a variety of biomedical application.
Poly (hydroxyethyl methacrylate)	Hydrogels have been utilized in a variety of biomedical application
Poly (methyl methacrylate	This and its copolymers are used as dental

	implants and in bone replacement.
Poly (tetrafluoroethylene) (Teflon)	Vascular grafts, clips and sutures, coatings.
Polydimethylsiloxanes	A silicone, implants in plastic surgery, orthopedics, blood bags and pacemakers.
Environmentally responsive. Synthetic polymers	
Poly (theylene oxide-b-propylene oxide)	Surfactants with amphiphilic properties used in protein delivery. Skin treatments.
Poly (Vinyl methyl ether)	Nomtoxic, temperature- sensitive polymer, excellent shape-memory properties.
Poly (N-alkyulacrylamides)	Temperature-sensitive gels whose lower critical l solution temperature can be adjusted via co-monomer incorporation.

Microspheres, which eventually affects the performance of the drug delivery product.

Excipients

The main objective of incorporating excipients in the polymer matrix is to modulate the drug release or to stabilize the drug or to modulate polymer degradation kinetics. Studies carried out have shown that by incorporating basic salts as excipients in polymeric micro sphere, the stability of the incorporated protein can be improved. These basic salts also slows down the degradation of the polymer. Similarly hydrophilic excipients can accelerate the release of drugs although they may also increase the initial burst effect.[18]

Factors Accelerating Polymer Degradation

1. More hydrophilic backbone.
2. More hydrophilic end groups.
3. More reactive hydrolytic groups in the backbone follows as anhydride.>esters> amides.
4. Less crystallinity.
5. More porosity.
6. Smaller device size.
7. Processing conditions.
8. Site of implantation.
9. Sterilization process.[13]

EVALUATION OF HYDROGEL

5.1 Determination of P^h

5.2 Drug Content Uniformity

5.3 Spredability

Spredability can be determined by an apparatus suggested by multimer et al which can be suitably modified in the laboratory and used for the study.

Spredability: S = ml/t

S=spredability, m = weight tied to the upper glass slide , l = length of the glass slide , t = time taken in second.

5.4 Extrudability

The apparatus used for extrudability can be suitably fabricated in the laboratory. It consist of a wooden block inclined at an angle of 45 degree fitted with a thin, long metal strip at one end, while the other end hold free . The Aluminium tube containing gel can be placed on free end of the aluminium strip just touched. The quantity of gel extruded from each tube was noted.[19]

5.5 Activity

5.6 Invitro Diffusion Study

The in vtro study was done by using an apparatus consist of a cylindrical glass tube which was opened at both the ends. 1gm of gel formulation equivalent to 10mg of hydrogel was spread uniformly on the surface of a cellophane membrane and was fixed to one end of the tube such that the preparation occupies inner circumference of the tube. The whole assembly was fixed in such a way that the lower end of the tube containing the gel just touched the surface of diffusion medium, The cellophane membrane acts as a barrier between the gel phase and the phosphate buffer. The content were stirred using magnetic stirrer at given rpm. sample withdraw from medium fluid at different time intervals. the released drug was estimated by using shimadzu uv/visible spectrophotometer at 290 nm and 1ml phosphate buffer was replaced each time. The data obtained was subjected to computerized regress ional analysis for higuchi"s and first order rate equation by using "PRO DISSO" softwere.[20]

APPLICATION OF HYDROGEL IN NEW RESERCH FIELD

6.1 Hydrogel Healling for Wound Care

Hydrogel dressings for healing of any kind of burn or other hard-to-heal wounds. The essence of an achievement is an **original technology** of production of hydrogel slides and application

of this material for routine healing of different kinds of **wounds**, mainly burn wounds, topical ulcerations, bedsores, etc.

The main **medical properties** of such dressings are as follows:

- Sooth pain
- Give pleasant cooling sensation protect against excessive loss of body fluids
- Are sterile form efficient antiseptic and particle barrier
- Absorb wound excreta
- Not sticky to a wound and removable/replaceable without any damage to new epidermis
- Gel transparency allows instant monitoring of healing process
- Not antigenic, Not allergenic, Easy in storing and usage
- Other features: Gels are environmentally friendly. The product is biodegradable, during production there is no waste or fumes, and all raw materials are of medical grade due to Pharmacopoeia.[21]

6.2 Nanogel and Microgel Formation

Nanogels are **cross linked** particles of sub-micrometer size made of **hydrophilic polymers**. They are soluble in water, but have properties different from linear macromolecules of similar molecular weight. Such structures, along with their bigger analogues - micro gels - have a number of practical applications, mostly in **medicine** (for example in stomatology) and **pharmacy** (stimuli-sensitive drug delivery systems). They are also being used as Nano catalysts and water purification systems.

6.3 Hydrogel Phantom for Radiation Domistery

The implementation of complex radiotherapy dose delivery techniques such as brachytherapy or conformal therapy necessitates the improvement in the field of dosimetry techniques by development of the three-dimensional, high-resolution dose calculation methods. Since 80-ties the gel dosimetry has been developing as potential method for determining the 3D dose distribution in the irradiated tissue. The beginning of the gel dosimetry is dated on 1984 when Gore et al. proposed that the radiation induced changes in the Fricke solution could be assessed by means of Nuclear Magnetic Resonance relaxation measurements. It was shown that the NMR spin-lattice and spin-spin relaxation rates (1/T1 and 1/T2, respectively) of the dosimeter were closely related to the amount of the Fe (III) ions produced in the Fricke solution by the absorbed dose. Due to this advantage it was also possible to observe the radiation-induced changes in the Fricke solution by Magnetic Resonance Imaging. Thus, it

was assumed that there was a possibility for 3D dosimetry based on MRI and ferrous sulphate.[22]

The high molecular weight of the compounds produced by the absorbed dose caused no their diffusion in the matrix being observed over the long period of time, so that, the spatial information on the absorbed dose had been greatly improved.

Plenty of advantages, among them the high sensitivity to irradiation, the major disadvantage to be overcome seems to be the toxicity of the monomers, as acrylamide, used for these gels preparation.

In this specific application i.e. phantom gels used in radiotherapy there is a necessity of fast polymerized and cross linked system to be worked out. Thus in our approach, the PEGDA (poly(ethylene glycol) di acrylate) was chosen as main constituent of the gel dosimeter. This cross linker is very sensitive to the small changes of radiation dose. Some features of the PEGDA while irradiated in aqueous solution has been assessed by means of pulse radiolysis study (Kozicki et al. 2001) The gels based on PEGDA, Bis (N,N'-methylenebisacrylamide) and gelatin had been prepared and subsequently irradiated in the dose range of up to 25 Gy. The irradiated gels were studied by means of NMR relaxation measurements using NMR minispectrometer, 20 MHz. The correlation between the absorbed dose and relaxation rates (R2=1/T2) was achieved.[23]

Currently, the research concerning the improvement of the dose response of the PEGDA gels by modification of its composition as well as detailed study on chemical-physical changes of the irradiated gel and particularly its basic acrylic constituent are being performed.

6.4 Drug Delivery System For Active Component

The hydrogel rod-shaped device for healing of endometrium cancer by precise drug delivery. In December, 1999 the preliminary clinical tests with over 70 patients has been completed with extremely good results. Retraction of cancer tissue after a few days from insertion of the device into the women's womb has been undoubtedly documented, Hydrogel device in form of thin rod for induction of childbirth as well as reduction of delivery pain. Device can be also used for removing of dead foetus and abortion. It has been clinically tested in a few clinics indicated by Ministry of Health, Poland and passed all these examination with excellent results.[24]

6.5 Hydrogel Intervertebral Disc Implant

The **spine** is a non-homogeneous complex-shape construction of 24 **vertebrae**, separated by **intervertebral discs** with numerous muscles and ligaments attached to them. Intervertebral discs act as a kind of **cushion** to soften the impacts caused by the movement of body. The intervertebral discs make up about one fourth of entire length of the vertebral column. The discs **absorb** the stress and strain transmitted to the vertebral column. The intervertebral disc is a structure composed of the annulus fibrosus, the nucleus pulpous and the end plates.

The spinal disc may be **displaced** or **damaged** due to trauma or a disease process. A **disc herniation** occurs when annulus fibers are weakened or thorn and the inner tissue of the nucleus becomes permanently bulged, distended or extruded out of its normal, internal annular confines. The mass of the herniated or "slipped" nucleus can **compress a spinal nerve** resulting in **pain**, **loss of muscle control** or even **paralysis**. Alternatively, with discal degeneration, the nucleus loses its water binding ability and deflates, as though the air had been let out of a tire. Subsequently, the height of the nucleus decreases causing the annulus to buckle in areas where the laminated plies are loosely bonded. As these overlapping laminated plies of the annulus begin to buckle and separate, either circumferential or radial annular **leaks** may occur, potentially resulting in persistent and disabling back pain.[25]

Whenever the nuclear tissue is herniated or removed by surgery, the disc space will narrow and may lose much of its normal stability. In many cases, to alleviate pain from degenerated or herniated discs, the nucleus or the disc as a whole is **removed** and the two adjacent vertebrae surgically fused together. While this treatment alleviates the pain, all discal motion is lost in the fused segment. Ultimately, this procedure places **greater stresses** on the discs adjacent to fused segment as they compensate for lack of motion, perhaps leading to premature **degeneration** of those adjacent discs.

A more desirable solution would involve replacing in part or as a hole the damaged disc with a suitable **prosthesis** having the ability to complement the height and motion of a disc. Therefore a substantial need exists for an easily implantable, prosthetic spinal disc of loading bearing ability and **pumping action** simulating the natural disc physiology. **Hydrophilic polymer systems** exhibiting a **water swelling** ability, called **hydrogels**, seem to satisfy the major demands made on such an implant and thus the possibility of use of hydrogels in the spinal disc prosthesis construction has been investigated for a couple of years.[26]

Our efforts have aimed at the development of such a material out of the range of synthetic polymers well know for their excellent biocompatibility, such as poly(vinyl pyrrolidone), poly(vinyl alcohol), poly(2-hydroxyethyl methacrylate), poly(methyl methacrylate) and others. To achieve best results various synthetic methods, post-synthesis treatment (chemical, thermal and with use of ionizing radiation) and mechanical testing procedures have been successfully employed.

Results we have been getting so far look interesting and render our new synthetic pathways very promising for future development of a fully functional, hydrogel based prosthetic intervertebral disc.[27]

6.6 SUPERPOROUS HYDROGEL

While the slow swelling property is the one made hydrogel usrful in controlled drug delivery, many application require fast swelling of dried hydrogel. fast swelling is usually done by making very small particle of dried hydrogel.

Super porous hydrogels can be made to possess high mechanical strength even after swelling. The mechanical strength can be improved substantially by adding composite materials, e.g., Ac-Di-Sol, which is a hollow microparticles of a hydrophilic polymer.[3] The presence of hollow microparticles results in physical entanglements of polymer chains around the microparticles.

Recently, super porous hydrogels with an elastic property were prepared. The elastic property is useful in making mechanically strong super porous hydrogels more resilient to compression and elongation. Figure 5 demonstrates the elastic property of super porous hydrogels. The swollen hydrogel can be stretched to almost twice the original length without breaking. No previous hydrogels have shown such an elastic property. One way of making elastic superporous hydrogels is to form interpenetrating networks.[28]

6.6.1 DEVELOPMENT OF GASTRIC RETENTION DEVICES

Super porous hydrogels were initially developed to make gastric retention devices. The idea was to make an oral formulation to swell fast to a size large enough to prevent them from passing through the pylorus. To avoid emptying into the intestine by the housekeeper waves of the stomach that occur about every 2 hours, the oral formulation has to swell as fast as possible. This is because it is difficult to know when the next housekeeper wave will come

following administration of a super porous hydrogel formulation. The initial goal of fast swelling was to reach maximum swelling in about 20 minutes because water is known to remain in the stomach for about 30 minutes.

The animal experiments using polyvinylpyrrolidone (PVP) hydrogels showed that the hydrogels could stay in the stomach for more than 24 hours. The study, however, was done with the PVP hydrogels that were swollen in water for 2 hours before administration to dogs. Without preswelling for a few hours, the PVP hydrogels would empty quickly into the intestine. To avoid having to swell hydrogel formulations before administration, development of fast swelling hydrogels was necessary, and the result was the preparation of super porous hydrogels. The elastic property makes the oral formulations more resilient to the continuous contractions in the stomach. A clinical study is planned with the oral formulation under development.[29]

6.6.2 Development of Fast-Dissolving Tablets

For more than a decade, fast-dissolving (also called fast-melting) tablet technologies have been used to develop a large number of successful commercial products. The main advantage of the fast-dissolving tablet technologies is that the dosage forms can be administered easily in the absence of water and without the need of swallowing. This feature is especially beneficial to children and the elderly. The initial success of the first fast-dissolving tablet technology led to the development of many different technologies. There are basically three different technologies: freeze-drying, sublimation or heat molding, and direct compression.[10] Freeze-drying technology produces tablets that can dissolve in less than 5 seconds, while the sublimation and molding technology allow tablets to dissolve in less than 15 seconds. The two technologies, however, are expensive, and the prepared tablets are not mechanically strong. For this reason, direct compression technologies, which afford low cost of production and good physical resistance, are preferred.[30]

OTHER APPLICATIONS

Superporous hydrogels can be applied for the development of various non-pharmaceutical and non-biomedical products. As shown in Figure 4, superporous hydrogels swell extremely fast, and superporous hydrogels in many interesting shapes can be prepared. Superporous hydrogels can also be used as a tool in a science project for children. Children can enjoy the immediate swelling of superporous hydrogels in various shapes.[31]

6.7 Ocular Drug Delivery

Types of Contact Lenses

- Soft Contact Lenses
- Rigid Gas Permeable (RGP) Contact Lenses
- Extended Wear Contact Lenses
- Disposable (Replacement Schedule) Contact Lenses
- Lens Comparison
- Specialized Uses of Contact Lenses
  - Orthokeratology (Ortho-K)
  - Decorative (Plano) Contact Lenses

A major issue in ocular drug delivery is the maintenance of an adequate concentration of drug in the precorneal area. About 90% of eye medication are applied in the form of drop's. hydro gel are ideal for drug delivery application because they are nontoxic and their three-dimensional structure and degree of cross –linking can control drug release –the higher the degree of cross –linking the slower the release. compared to the numerous application of eye drops necessary for therapeutic regime the one time application of a drug laden lens has a simplicity that may lead to higher patient compliance. to enhance the ability of hydrogel to carry medication, the drug may first be dissolved into a particle which is in turn incorporate d into the hydrogel matrix. liposome are one such particle.[32]

Drug laden liposome place inside a hydrogel contact lens may fulfill the need for an ophthalmic drug delivery device that is convenient and at the same time will localize and maintain drug delivery at the site of application.[33]

CONCLUSION

Recent development in the field of polymer science and technology has led to the development of various stimuli sensitive hydrogel like ph, temperature, which are targeted delivery of proteins to colon, and chemotherapeutic agent to tumors. Some environmental variable such as low ph and elevated temperature are found in the body for this reason either ph sensitive and temperature sensitive hydrogel can be used for site specific controlled drug delivery. Hydrogel that are responsive to specific molecule such as glucose or antigen can be used as biosensor as well as drug delivery system. New synthetic methods have been used to prepare homo and co polymeric and protein delivery application. random copolymer with

balanced hydrophobicity can offer desirable release rates and dissolution profiles for the development of oral controlled drug delivery.

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