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Review Article

A Review Article On: Polymers Are Used in TDDS

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ABSTRACT

Transdermal drug delivery systems may be absorbed directly into the systemic circulation and do not require liver metabolism before working, they have emerged as one of the most effective controlled drug release systems in topical formulation. To improve the transdermal drug delivery system's efficacy in regulating drug release, polymers are incorporated into the formulation. The TDDS's use of polymers has slowed the drug's controlled release rate from the patch. Combining polymers has increased the medication release's effectiveness. A thorough explanation of the application of polymers in the transdermal medication delivery system is provided in this article. Additionally, polymers aid in the medicine's skin-sticking properties and encourage a greater degree of drug release from the dosage form. Recent advances have led to a rise in the quantity and kind of polymers utilised in TDDS. The usage of synthetic, semisynthetic, and natural polymers in TDDS is discussed in this article. Natural polymers have been found to have a greater influence on TDDS and to have fewer side effects, such as allergy and irritation. As a result, patient compliance has increased and medication release has been more effectively achieved. Artificial and semisynthetic order to effectively manage the release of the medication from the patches, polymers have been created and used extensively in TDDS patches. A transdermal patch is a medicated adhesive patch that is applied above the skin to release a predetermined amount of medication into the bloodstream at a predetermined rate through the skin.

INTRODUCTION

A polymer is a big molecule or macromolecule made up of repeating building blocks, or monomers, joined together in a lengthy chain. In a pharmaceutical formulation, these are the foundation. “Poly,” the word for polymer, comes from the Greek “poly” meaning many pieces. Because they are composed of units that repeat (monomers) along their chain, polymers have relatively large molecular weights (1). Transdermal patches are rate-controlled drug delivery devices intended to provide a therapeutically relevant dosage of medication into the bloodstream. Polymers are essential for

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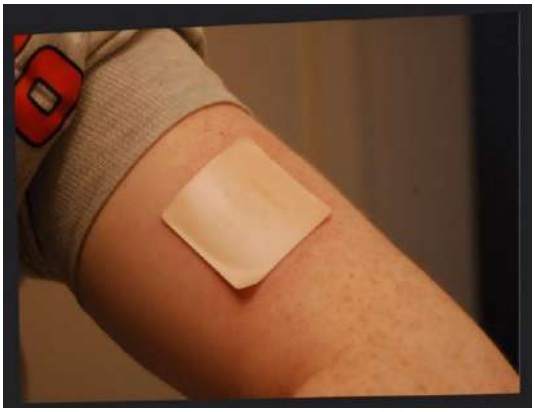
regulating the release of medication from transdermal patches. The core of TDDS is polymers.TDDS are multilayered polymeric laminates with a drug source or matrix sandwiched between the layers; the outside polymer keeps the drug from being lost, while the inner polymer sticks to the skin's membranes. Patches with a higher hydrophilic polymer content release a larger percentage of medication more quickly. Drugs can be delivered through the skin using transdermal delivery systems at a controlled rate, avoiding the liver's first-pass effect. Transdermal drug administration improves upon the drawbacks of oral drug delivery techniques. This allows the medication to be released under regulated conditions into the bloodstream and reach the intended organs via the skin. This article compiles extensive data regarding the applicability of different kinds of polymers.

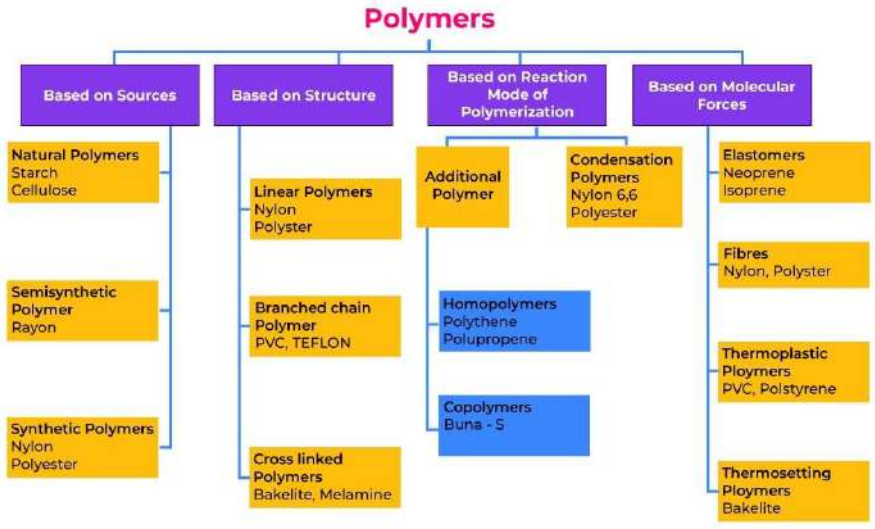
Some common polymers in life are:

Disaccharides and polysaccharides like maltose, sucrose, and glycogen. All protein made from amino acid. Nucleic acid, like DNA and RNA made from a nucleotide. The pharmaceutical applications of polymers are due to its longevity and self-transforming quality. Polymers have, for decades, performed a valuable function as excipients in tablet and capsule formulations and flow controlling agents in liquids, suspensions and emulsions.



Transdermal patch

Classification of Polymers:



1. Classification based on the source of origin which is classified in three types:

a) Natural polymers: Natural polymers are derived from either plants or animals. We refer to them as animal and plant polymers. Examples include: cellulose, jute, leather, silk, wool, R&A, DNA, and natural rubber.

b) Semisynthetic polymers: These are polymers made from natural fibres that are generated through a straightforward chemical process to enhance their physical characteristics, such as tensile strength and lastrus nature.

For example, viscous rayon, cupra ammonium silk, and acetate rayon.

c) Synthetic fibres: In a lab, synthetic fibres are created by polymerising basic chemical molecules. For example, nylon, terylene, polyethene, polystyrene, nylon, PVC, backlite, Teflon, Orion, and synthetic rubber.

2. The classifications based on the structure are three types of polymers as follows:-

a) Linear polymers: These polymers consist of a long, straight chain formed by the links between the monomers. There are no side chains in these chains. Their molecules have a high melting temperature, tensile strength, and density due to their close packing.

For example, polyesters, Nylons, PVC, and polyethene.

b) Branched polymers: They have a straight long chain with different side chains. Their molecules are irregularly packed hence they have low density, tensile strength and melting point.

Ex. Polypropylene (side chain -CH3), amylopectin and glycogen

c) Network or crosslinked polymers: In these monomeric units are linked together to constitute a three dimensional network. The links involved are called cross links. They are hard, rigid and brittle due to their network structure.

Ex. Bakelite, Maia mine, formaldehyde resins, vulcanized rubber etc.

3. The classifications based on polymerization process are two types as follows:-

a) Addition polymers: These are polymers created by continuously adding monomers without removing the byproducts in between. These polymers are integral multiples of the monomer unit because they contain all of the monomer atoms.

Examples include PVC, Teflon, polyethene, and polypropylene. Typically, alkenes and their derivatives serve as the monomeric units.

b) Condensation polymers: These are created when two monomers are combined and tiny molecules like NH3, alcohol, or water are removed. Their molecules are linked by amide and ester bonds. They do not have an integral multiple of monomer units in their molecular mass.

Ex: Polyesters, polyurethanes, and polyamides (Nylons)

4. The classification based on molecular forces:-

a) Elastomers: These are polymers in which the weakest attractive forces maintain the integrity of the polymer chains. They consist of sparsely cross-linked, randomly coiled molecular chains. The polymer stretches when the stain is applied, then returns to its original place when the force is released. These polymers, often known as elastomers, are elastic.

For example, vulcanised rubber and neoprene

a) Fibers: They have high intermolecular attractive force like H-bonding. They have high tensile strength and used in textile industries.

Ex. Nylon-6, Nylon-66, and Terylene

c) Thermoplastic polymers: These are the polymers having intermolecular forces between elastomers and fibers. They are easily molded in desired shapes by heating and subsequent cooling at room temperature. They may be linear or branched chain polymers. They are soft in hot and hard on coding.

Ex. Polythene, Polystyrene, PVC

d) Thermosetting polymers: When heated, these polymers become rigid and infusible. These do not remould when heated under pressure and do not become pliable. These polymers are cross-linked and are not reusable.

For example, Bakelite

5. The classification based on the homogeneity of Polymers: Pectin homopolymers and copolymers.

a) Homopolymers consists of only one type of repeating unit.

b) Copolymers are polymers consisting of more than one type of repeating unit.

6. The classification based on growth polymerization, implies two types:

a) Chain growth polymerisation: In this type of polymerisation, molecules are added across the double bond at the reactive end of the expanding chain. Growth chain polymerisation is a common process for alkenes and their derivatives. For example, polyethene

b) Step growth polymerisation: This kind of polymerisation uses a sequence of independent reactions to cause step-wise intermolecular condensation. Losses of simple molecules like NH3, H2O, and HCl occur during this process. When a monomer has many functional groups, it is feasible. It continues by forming trimmers, tetramers, dimers, etc. For example, Dacron.

7. The classification based on bio-stability:

a) Biodegradable: Once the active agent has been released, the biodegradable polymer breaks down naturally in the body through biological processes, without the need to remove a drug delivery system. The majority of biodegradable polymers are made to hydrolyse into increasingly smaller, physiologically acceptable molecules when the polymer chains break down. Additionally WO ss He Water cannot dissolve biodegradable polymers because they are hydrophobic. On the other hand, they experience hydrolysis and fragment into smaller pieces. Despite not being soluble in water, they can be broken down by the body. The degradation products are commonly employed in controlled medication delivery because they are biocompatible. For example, polyanhydrides, polyorthoesters, polylactides (PLA), polyglycolides (PGA), and poly(lactide-co-glycolides) (PLGA).

a) Non-biodegradable: Since these polymers don't erode or break down, they must be cleared out of the system as soon as the medicine has completely released from them. Example: Polymethacrylates

HISTORY

• Pharmaceutical and medical product compositions frequently include polymers. Polymers have long been used in the medical industry. For decades, natural polymers and synthetic polymers have been utilised in herbal medicines; nonetheless, the issue is complex. The initial research in the 1960s focused on the use of polymers as wound dressings, injectable or implanted deporters, and blood plasma expanders. In 1975, Helmut Ringsdorf presented the first design for polymers with pharmacological effects.

• The first polymer-drug conjugation to treat cancer was tested in a clinical setting in 1994. It was a Doxorubicin copolymer, or HPMA (N 2-hydroxy propyl meth) acrylamide).

• Five years after the first therapeutic nanoparticles were approved as a treatment for metastatic breast cancer, two polymer-protein conjugates were introduced to the market: PEG-GCSF and PEG-interferon-u, an antiviral medication used to treat chronic hepatitis C and hepatitis B (3).

• **Advantage**:

1.Controlled medication release: The release rate of pharmaceuticals may be precisely regulated thanks to polymers, which produces therapeutic benefits that are both maintained and controlled while lowering the frequency of dosage requirements.

2.Enhanced solubility and stability of poorly soluble drugs can be achieved using polymers, hence improving their bioavailability and efficacy.

3. Tailored delivery: polymers allow for the administration of drugs to particular cells, tissues, or organs in a tailored manner, reducing adverse effects and optimising therapeutic results

4.Lessened toxicity: some medications' toxicity can be decreased by encasing them in polymers. Enhancing their security profile.

5.Minimisation of dosage frequency: The development of an extended-release polymer can lessen the frequency of management, enhancing adherence of patients

6.Benefits of the transdermal method include the avoidance of gastrointestinal absorption issues and

hepatic pass effect, dosage reduction, and dosage interval.

7. Increases patience compliance and lengthens the activity's duration.

8. Prompt removal from the skin

9. Using topical patches is a non-invasive, painless technique to send drugs straight to the body.

10. These systems enable self-administration.

11. Systemic medication interactions are decreased.

12. It provides a longer action duration.

• Disadvantages:

1.High cost: creating a polymer-based simulation can be expensive, particularly when working with new polymers or intricate delivery networks.

2. Complex formulation: Creating drug delivery systems based on polymers can be difficult and call for specific expertise in material science and polymer chemistry.

3.Difficulties with regulations Obtaining regulatory approval for innovative polymer-based drug delivery systems can present difficulties because of worries about long-term impacts, safety, and biocompatibility.

4. Potential innsnogenicity: Certain polymers, particularly those obtained from natural sources, may cause immunological reactions in certain people.

5. Variable release profiles: It might be difficult to achieve constant and predictable medication release rates from polymer matrixes because of things like polymer breakdown and physiological state fluctuation.

•Physiology of skin:

The human skin is the largest and most accessible organ in the body. It has been utilised as a location for pharmaceutical drug administration.

Transdermal delivery is the process of delivering a medication via healthy skin to the systemic circulation.

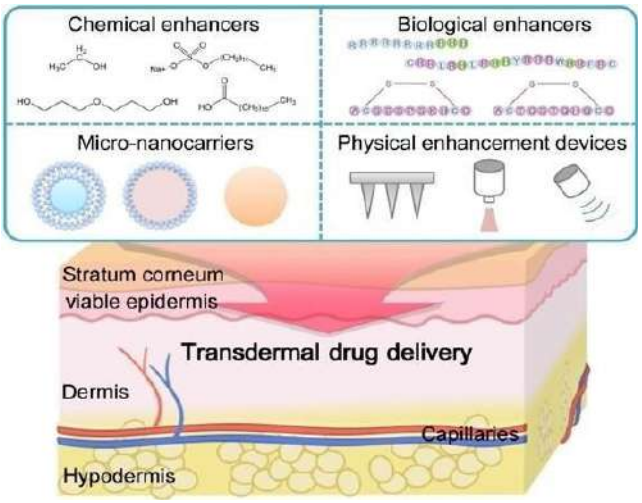


Fig: Structure and layers of the skin

● Pathways for transdermal drug delivery systems:

Drug penetration into the skin can happen in a variety of ways when it is administered to the skin's surface.

》 Membrane penetration controlled system.

》 Matrix diffusion controlled systems.

》 Adhesive dispersion type system.

》 Micro reservoir type diffusion system.

Drugs may enter through the appendages or the stratum corneum.

There are two potential pathways for penetration into the stratum corneum:

1. Penetration through corneocytes and Transcellular route.

2. Permeation through the gaps between the cells.

The Transdermal Drug Delivery System (TDDS) uses the following polymers:

Natural Polymers for Transdermal Medication Administration: Predefined drug delivery rates can be attained by the use of natural polymers. Since natural polymers are hanically polysaccharides, they have low toxicity, are biodegradable, and are highly friendly with humans. For example: Chitosan, Sodium CMC, Xanthan Gum, and Sodium Alginate. Natural rubber.

1. Xanthan Gum:

The fermentation of Xanthomonas campetrix, which is present in the plant's leaves and other green sections, produces xanthan gum.

° It is a polymer with a high molecular weight that contains sugars such as d-glucose and d-mammose.

° XG has high stability in both acidic and alkaline medium.

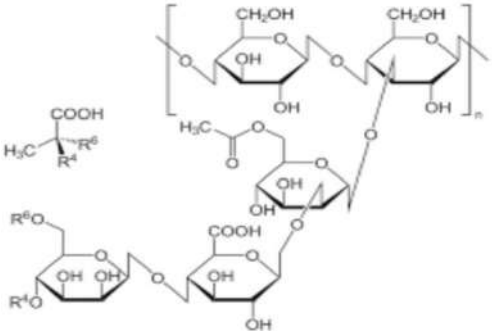
° The rate of release of drug can be controlled by changing the pH of the release medium.

° The regulated release of medications in TDDS is enhanced and increased when XG is combined with other polysaccharides.

° XG possesses excellent muco adhesive properties, which are crucial for formulations like TDDS.

° Extended drug release of 98.f65% over a 12-hour period is demonstrated with XG-based patches.

° Utilising clove oil, PEG-400, and tween 80 in the formulation of the Topical nanoemalgel, XG has employed it.



Structure of xanthan gum

Xanthan Gum

1) Sodium alginate:

Sodium alginate consists of sodium salt of Alginic acid which is a mixed of polychromic acid and composed of residues of D-mannmuronic acid and L-glucoronic acid.

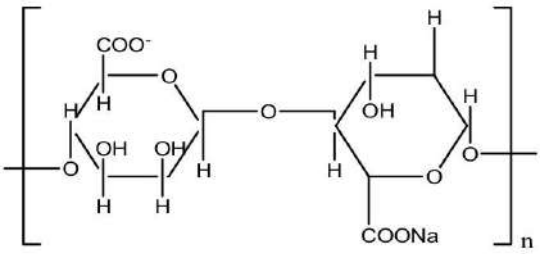
° The sodium alginate is a versatile functional biomaterial. For increasing of viscosity, stahility, and also used as matrising (adhesive) agent in transdermal drug delivery system.

° Brown algae are rich in alginic acids and their salt (Pheophyta).

° It is hacmo compatible and does not accumulate in any organ and as it is biodegradable, there is no need for surgical removal after the drug is completed.

° Aqueous solutions of sodium alginate with concentrations ranging from (0.5%m 2.5%) can be employed for the treatment of smooth skin.

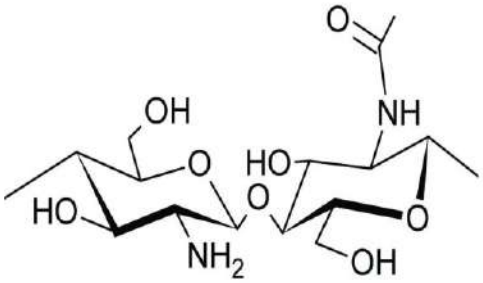
° It is used to increase blood volume and maintain blood pressure conditions in conditions like burns, blood loss and circulatory system stability.



Structure of sodium alginate.

Sodium alginate.

2) Chitosan: Chitosan is one of the most important naturally occurring polymer, which is chemically (1.4)-2-amino-2-deoxy beta D-glycan.



Structure of Chitosan

Chitosan

° It is produced from chitin by alkaline deacetylation of chitin from the shells of crab, shrimp.

° Chitosan is widely used in transdermal drug delivery due to its variety of properties like non cytotoxicity, biocompatibility, and non-allergic behavior.

° Chitosan greatly enhances the transport of polar drugs across epithelial surface.

° The increase in water content of the stratum corneum increases the drug permeation in chitosan, well as in another derivative of monoclonal acetyl chitosan (MCC) This increuses cell membrane fluidity and decreases cell membrane potentials.

° Chitosan, and its derivatives, have a hygroscopic and three-dimensional network structure that allows water to seep into the stratospheric corneum in a short amount of time and soak into the skin for an extended period.

° Cix 1. 4-polyisoprene, the major polymer from Natural Rubber Latex (NRL), obtained from *Hevea brasiliens* has interesting properties such as biocompatibility, high mechanical resistance capability to form a film.

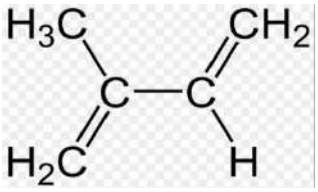
° The NRL from *Hevea brasiliens* has low cost and has high mechanical strength resistance. It is biocompatible material which can stimulate natural Angiogenesis and capable of adhering cell on its surface.

° Natural rubber latex is a colloidal dispersion of polymer particles in a liquid. It is harvested from rubber trees by a tapping process.

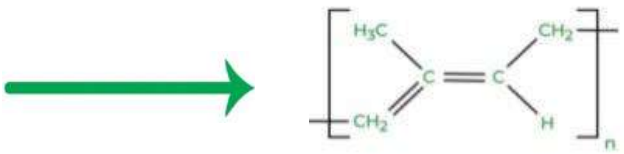
° Reservoir type nicotine transdermal patches (NTP) were manufactured by heat-sealing. The nicotine solution is embedded between the backing layer and the controlling layer mendwane. The goal of this study was to develop a new controlling layer membrane made from deproteinised natural rubber latex.

3) Natural Rubber:

Isopren



Polyisoprene



Structure of natural rubber

4) Sodium methyl cellulose:

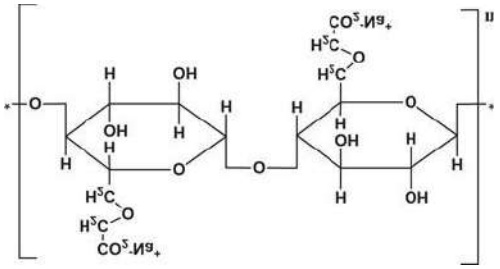
° One of the most significant byproducts of cellulose ethers is sodium carboxy methyl cellulose. Derivatives of cellulose. Since the acid form of CMC is less soluble in water, it is highly lipophilic and can pierce lipid layers.

° CMC binds to the surface of corneal epithelial cells via its glucopyranose subunits binding to

glucose receptors and show the action of controlled drug delivery system as in transdermal drug delivery system.

° Since the acid form of CMC is less soluble in water, it is highly lipophilic and can pierce lipid layers.

° CMC is a penetration enhancer polymer used to enhance the penetration of drugs into the skin. The polymer plays a vital role in the drug delivery system of transdermal drugs. CMC plays a critical rule in the drug release propensity of the drug from the drug delivery system. CMC is also known as non-eractive, non-toxic. Biocompatible and biodegradable. Structure of sodium cmc polymer. Sodium CMC polymer.

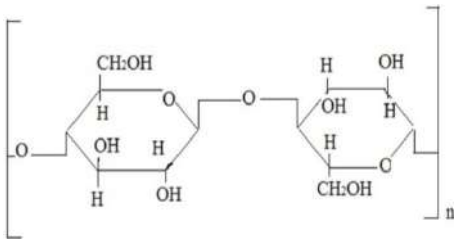


2. Semi-synthetic polymers used transdermal drug delivery system:

1. HPMC (Hydroxy Propyl Methyl Cellulose):

HPMC is semi-synthetic polymer belonging to the category of hydrophilic and swelling polymer. HPMC has also been explored to fabricate a matrix type of transdermal patches. It has an extensive application in oral controlled drug delivery system. HPMC has the potential to yield clear film due to adequate solubility of polar drugs in the polymer. HPMC chain dissolution from the matrix surface involves two main steps the first step involves change in the entanglement of individual polymer chain at the matrix, surface which depends on the rate of hydration. The second step, involve the diffusion of drugs molecule from the surface of the polymeric matrix structure of the bulk of medium. Organogels and some nonionic surfactants such as sorbitane monosterate, lecithin, and Tween) tend to associate into reverse micelles. These surfactants in an organic solvent. Upon the addition of water undergo association reorientation to form a gel. These organogels can be used as a matris for the Transdermal delivery of drug with greater influx. Organogels can cause slight disorganization of the skin outcome that is attributing to the organic solvent that is used to make the gel. Thus organogels can enhance the permeation. Of various substances.

Guyotelal (2000) formulated an adhesive matris for transdermal delivery of propanol by employing two different polymers via HPMC and poly isobutylene. Uceryl polymer. an acryline polymer was employed as an outer tale controlling membrane Propylene glycol is used as a plasticizer was found to have a positive effect on the release rate of drug more than 70% of the initial drug load was released within the first hour whervas release from the coated matrices become nuove regular and slow.

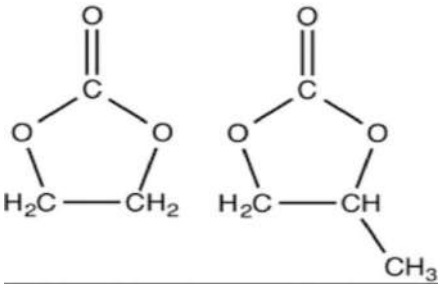


Stucture of HPMC **HPMC**

2. Ethyl cellulose:

EC is a water insoluble polymer used in controlled release drug forms. As it can't undergo swelling EC compatibility becomes a key factor in such systems, as release kinetics would depends largely on the porosity of the hydrophobic compound. Although EC is considered insoluble, it can take up water. This is because of its hydrogen bonding capacity with water. Idress etal (2014) attempted to formulate a mairis patch of flubiprofen by employing EC as matrix former. Propylene glycol or di-butyl phthalate [DBP) was used as plasticizer and span 20. Tween 20, Sodium lauryl sulphate, iso propyl myristate (IPM) ethanol were employed as permeation enhancer's the drug release from patches followed the HIGUCHI model where masinum drug permeations from the patch containing EC as matrix forming polymer, DBP plasticizer and IPM as penetration enhancer was found to be 903 micrograms in 48 hrs.

Mukherjer el al (2005) developed a suitable matrix type TDDS of dexamethasone using blends of polymeric combinations PVP and EC and Eudrgit with respectively. Therefore both the polymer combinations containing suitable plasticiner could be used for developing matrix type. TDDS exhibits controlled drug release.



Structure of ethyl cellulose

Ethyl cellulose

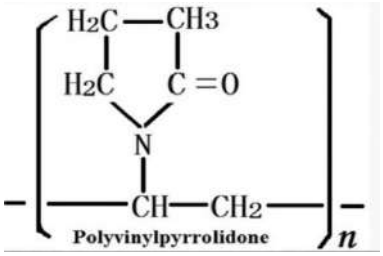
3. Synthetic polymers in TDDS:

1. Poly Vinyl Pyrrolidone (PVP):

PVP is hasically a water soluble polymer it is obtained by the polymerization reaction of monomer namely N-vinyl pyrrolidone. It is water soluble, inert, non-toxic, biocompatible and biodegradable polymer. PVP is also found to be used in transdermal patches due to its inherent film forming characteristics. However the challenges associated with the use of PVP include its inherent hydrophilicity and hygroscopicity issues. This hygroscopic nature of PVP films exhibit high water vapors absorption which in turn leads to nucmhial contamination to overcome this issue and in improve the properties and performance PVP was blended. With EC It has played a pivotal role in the development of topical formulation.

The procedure uses a laver to perform photosensitive vaporization of the prostate The PVP in EC filma drug release rate increases by increasing the concentration of hydrophilic and the PVP, EC in the ratio of 2:1 the highest cumulative of drug release of 88.35% lasting drugs.

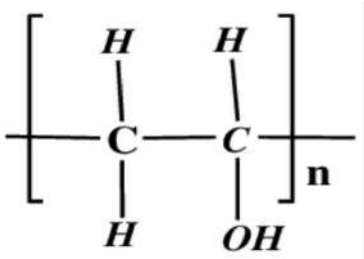
Structure of PVP



Poly Vinyl Pyrrolidone

2.Polyvinyl alcohol (PVA):

PVA is a colour less water soluble synthetic resin employed principally in the treating of textiles and paper and the PVA solution can be gelled through repeated freezing thawing yielding highly strong. The PVA is used in a variety of medical applications. Because of its biocompatibility low tendency for protein PVA based polymers are used widely in additive manufacturing for example 3D printed oral dosage forms demonstrate. Skin is unaffected by PVA which is incompatible with inorganic salts it hased on multi responsive hydrogel was prepared by introducing the dynamic and reversible supra molecular complexation.



Structure of PVA

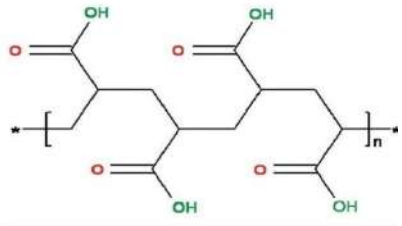
3. Carbopol:

Carbopol is synthetic polymer which is widely used in TDDS and gels to enhance drug delivery efficiency. Carbopol also known as polyacrylic acid is a cross linked polymer that forms a gel like consistency when dispersed in water. One of the primary functions of Carbopol in TDDS is to act as gelling agent when incorporated into the formulation; it can increase the viscosity of the drug release. The gel forming ability of Carbopol ensures that the drug is evenly distributed within the matrix, reducing the risk of dose damping where a large amount of drug released once. Carbopol are acrylic acid cross-linked polymers that are either polyethylene glycol (PEG) or polyvinyl ether (PV), Carbopol have a hydrophilic structure, which makes them suitable for topical use as a gel- type formulation.

Polyvinyl Alcohol (PVA) is a synthetic polymer that is bio- compatible, biodegradable, and non-toxic. It can be used as a matrix Form for sustained release drug delivery systems hased on hydrogel formulations. PVA is used in a variety of pharmaceutical applications, including solid, liquid or semi- solid formulation.

The PVA films with xantham gum and plasticizers had their mechanical performance tested well when compared to polyvinyl alcohol films alone. Polyvinyl alcohol xantham gum mixes demonstrated a high rate of drugs release. Skin is unaffected by PVA which is incompatible with organic salts.

Polyvinyl alcohol



Structure of carbopol

CONCLUSIONS

Polymers are generally most important excipients in the pharmaceutical formulations Polymers used to increase the release time and reserve time of drug in the body in transdermal drug delivery systems. The above review article gives a quality of information of different polymer used in TDDS and their effectiveness in the drug release in TDDS system. Polymer significantly shown more effectiveness in TDDS when they are used in combined with other polymers. Use of polymer in TDDS has not shown any decrease in activity and also no side effects with the drug. TDDS are the system which comes under the category of

controlled drug delivery system, use of the polymer combination gives m effectiveness for the controlled release. Polymers also used as plasticizers, blends, cross linking agents in the TDDS and pharmaceutical formulation. Thus the above review article can be used as base information for the study of polymers in TDDS.

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