Polymers used in the transdermal drug delivery system of carvedilol: Review

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ABSTRACT*: The current review article focuses on polymers in Transdermal drug delivery system. Polymers are the backbone of transdermal drug delivery system as they control the release of the drug from the device. As they can be broken down into non-toxic monomers and, more importantly, because they can be used to build controlled release devices, biodegradable polymers are suitable for application. Polymers' primary function is to protect drugs from their physiological environment and prolong their release to increase their stability. Diffusion, degradation, and swelling release the drug from the polymer. This review highlights the role of different polymers in the transdermal drug delivery system of carvedilol drug. Carvedilol is the antihypertensive drug used in the hypertension and cardiac heart failure (CHF). This also gives information about polymers classification. The collected data provides knowledge about polymers which is further useful for the researchers for transdermal drug delivery system of carvedilol.

INDEX TERMS: Polymers, transdermal drug delivery system, controlled release, carvedilol.

INTRODUCTION:

POLYMERS:

Polymers have played a pivotal role in the development of topical formulations. Polymers are huge molecules made up of repeated structural components, or monomers that are linked together by chemical bonds. These substances are used to make natural products such as paper and amber, biological products such as proteins and nucleic acid, and synthetic products such as plastics and polyethylene materials. Synthetic polymers are now used in almost every industry, and their adaptability has led to technological developments in the pharmaceutical business that meet a wide range of medical demands [1].

Polymer Matrix: Polymer is an essential and crucial component of the transdermal drug delivery system. To accomplish rate-controlled transdermal administration, various polymeric materials have been employed. The mechanism of drug release is determined by the drug's physicochemical properties as well as the polymer employed in the device's manufacturing [2].

The following criteria should be satisfied for a polymer used in the transdermal drug delivery system:

a) The polymer's molecular weight and chemical functionality should be such that the specific medicine diffuses and is released properly through it.
b) The polymer should be stable.
c) The polymer must not be harmful.
d) The polymer should be easily of manufactured
e) The polymer should be affordable.
f) The polymer and its degradation product must not be poisonous or hostile to the host organism.
g) It contains large quantities of the active ingredient [3].

The polymers used in transdermal drug delivery system can be classified as,

TYPES OF POLYMERS:

a) Natural polymers: Cellulose derivative, Gelatine, Waxes, Proteins. Gum, Shellac, Natural rubber, starch. rubber, Nitrile, Acrylonitrile, Neoprene.
b) Synthetic elastomers: Hydrin rubber, Polybutadiene, polyisobutylene, silicon rubber, nitrile, butyl rubber etc.
c) Synthetic polymers: Polyvinyl alcohol, polyvinyl chloride, polyethylene, polypropylene, polyamide, polyurea, epoxy [4].

To change the polymer characteristics and consequently the release rates, many approaches have been used:

Polymers with Cross-Linking

The more crosslinking there is, the denser the polymer becomes and the slower drug molecules diffuse through the matrix.

Polymer Blends

Different ratios of polymers have been blended to combine the benefits of distinct polymers. Polymer blends offer a number of benefits, including simplicity of device manufacturing, drug loading adjustment, and other device features like hydration, degradation rate, and mechanical strength.

Plasticizers

Plasticizers have been found to improve the drug's diffusion characteristics by reducing the stiffness of the polymer backbone. Plasticizers such as polyethylene glycol, polypropylene glycol, glycerol, and dibutyl phthalate are widely used [2].

POLYMERS IN TDDS:

A transdermal medication delivery system's backbone is polymers. Multi layered polymeric laminates for transdermal delivery are made up of a drug reservoir or a drug–polymer matrix sandwiched between two polymeric layers: an outer impervious backing layer that prevents drug loss through the backing surface and an inner polymeric layer that acts as an adhesive and/or rate-controlling membrane [5].

Transdermal drug delivery systems are commonly classified into the following three types.

1. Reservoir systems
   The drug reservoir is sandwiched between an impermeable backing layer and a rate-controlling membrane in this device. Only the rate-controlling membrane, which might be microporous or nonporous, allows the medicine to be released. The drug can be in the form of a solution, suspension, gel, or dispersed in a solid polymer matrix in the drug reservoir compartment. A small layer of drug-compatible, hypoallergenic adhesive polymer can be placed to the polymeric membranes outside surface [6].
2. Matrix systems
   I. Drug-in-adhesive system
      The medication reservoir is created by dispersing the drug in an adhesive polymer and then spreading the medicated polymer adhesive onto an impervious backing layer by solvent casting or melting the adhesive (in the case of hot-melt adhesives). Layers of unmedicated sticky polymer are put on top of the reservoir.
   II. Matrix-dispersion system
      In a hydrophilic or lipophilic polymer matrix, the medication is spread uniformly. After that, the drug-containing polymer disc is fixed to an occlusive base plate in a compartment made of a drug-impermeable backing layer. Instead of applying adhesive to the front of the drug reservoir, a strip of adhesive rim is formed around the circumference [7].
3. Microreservoir systems
   The reservoir and matrix-dispersion systems are combined in this drug delivery device. The drug reservoir is created by suspending the drug in an aqueous solution of a water-soluble polymer and then homogeneously spreading the solution in a lipophilic polymer to generate thousands of unleachable, microscopic drug reservoir spheres. By cross-linking the polymer in situ, the thermodynamically unstable dispersion is soon stabilised.
   One of the most rapidly developing fields of innovative drug delivery is transdermal drug delivery technology. Developments in the field of polymer science have aided this expansion. This article focuses on the physicochemical and mechanical features of polymeric materials used in transdermal delivery systems, with the goal of assisting formulators in the selection of polymers. Polymers are used in transdermal delivery systems in various ways, including as
   - matrix formers
   - rate-controlling membranes
   - pressure-sensitive adhesives (PSAs)
   - backing layers
   - release liners [6].

POLYMERS USED IN TRANSDERMAL DRUG DELIVERY SYSTEM OF CARVEDILOL:

1. HPMC:
   HPMC, a hydrophilic swellable polymer widely employed in the delivery of oral controlled drugs, has also been investigated as a matrix formed in the development of propranolol hydrochloride patches. HPMC has been shown to produce transparent films due to the drug's acceptable solubility in the polymer. During dissolution testing, HPMC matrices without rate-controlling membranes displayed a burst effect because the polymer was rapidly hydrated and swollen, resulting in rapid drug release. [5;8].
2. Eudragit RL-100:
   It's a quaternary ammonium copolymer made up of ethyl acrylate, methyl methacrylate, and a little amount of methacrylic acid ester. Ammonium groups exist as salts in the polymers, making them permeable.
   Product Form- Granules Targeted Drug Release Area- Time controlled release, pH independent.
   Characteristics
   Insoluble
   High permeability

pH independent swelling
Customized release profile by combination of RL and RS grades in different ratios.
Suitable for matrix structures [9].

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4. Ethyl cellulose:
Some of the hydroxy groups on the repeating glucose units are changed to ethyl ether groups in EC, which is a cellulose derivative. Depending on the manufacturer, the quantity of ethyl groups can vary.
EC is a polymer that is insoluble in water and is utilised in controlled-release dose formulations. Because release kinetics would be heavily influenced by the porosity of the hydrophobic compact in the absence of polymer swelling ability, EC compatibility becomes a critical issue in such systems. EC, despite its insoluble nature, may absorb water. Because of the polarity difference, it has the ability to form hydrogen bonds with water.
When an in vitro research fluid that is thermodynamically compatible with the polymer comes into contact with the matrix patch containing EC, the fluid is absorbed into the polymer matrix, causing the polymer chain dissolution process to begin [5;10].
5. Polyvinyl pyrrolidone (PVP):
PVP, commonly known as polyvidone or povidone, is a biodegradable and water-soluble polymer formed from the monomer N-vinylpyrrolidone. PVP is a hydrophilic polymer with great solubility in a variety of polarity solvents and outstanding binding characteristics. PVP is a non-toxic and biocompatible polymer [11].
PVP has a number of distinct physical and chemical properties, including being chemically inert, colourless, temperature-resistant, and pH-stable. The various molecular weight PVPs are distinguished by different K-values, e.g., K12 (3100–5700 Daltons), K17 (7900–10,800 Daltons), K25 (23,000–32,000 Daltons), K30 (35,000–51,000), and K90 (900,000–1,300,000 Daltons). PVP has been used to produce several drug delivery systems in the pharmaceutical and biomedical areas, including oral, topical, transdermal, and ocular administration.
The influence of the polymer's molecular weight on formulation preparation and drug dissolution kinetics was investigated using different molecular weights of PVP (PVP K15, K30, and K90). PVP is a polymer with a lot of potential for making pharmaceutical formulations because of its versatility and distinctive features. PVP has good film-forming properties, and PVP-based films were primarily made by solution casting and solvent evaporation. Because of the water absorption, PVP film is more flexible [12].
6. Polyvinyl alcohol (PVA):
PVA is a synthetic, biocompatible, and toxicologically safe polymer that can be utilised as a matrix forming for sustained release hydrogel drug delivery systems. It is suitable for a wide range of pharmaceutical formulations, including solid, liquid, and semi-solid formulations. Poly vinyl alcohol (PVA) is a granular powder with a cream colour that is made from polyvinyl acetates. PVA comes in a variety of grades, and its viscosity is related to its molecular weight. It thickens and adheres to surfaces. PVA solution can be gelled without the use of an external crosslinking agent by freezing and thawing it repeatedly, giving highly strong, ultrapure, biocompatible hydrogels that have been utilised for vascular stents, cartilages, contact lenses, and other applications. The dry PVA films with xanthan gum and plasticizers had their mechanical performance tested as well. When compared to polyvinyl alcohol film alone, polyvinyl alcohol xanthan gum mixes demonstrated a high rate of drug release. Skin is unaffected by PVA, which is incompatible with inorganic salts [13].
7. Sodium CMC:
Sodium carboxymethyl cellulose (CMC) is one of the most important products of cellulose ethers, which are cellulose derivates with an ether structure generated through natural cellulose modification. Because the acid form of CMC has a low water solubility, it is normally maintained as sodium carboxymethylcellulose, which is widely utilised in many industries and is commonly referred to as monosodium glutamate. CMC can be used as a flocculant, chelator, emulsifier, thickener, water-retaining agent, sizing agent, and film-forming material, among other things [14].

CONCLUSION:

This article provides valuable information regarding the transdermal drug delivery system. To optimize this drug delivery system understanding of the different mechanisms of biological interactions and polymer are required. The synthetic polymers can be made as per requirement of the formulation by changing polymer characteristics and on the other hand natural pharmaceutical excipients are biocompatible, non-toxic, eco-friendly and economical. TDDS a realistic practical application as the next generation of drug delivery system.

REFERENCES:

1. Imran K. Tadwee, Sourabh Gore, Prashant Giradkar, "Advances in topical drug delivery system: a review", International Journal of Pharmaceutical Research & Allied Sciences, Vol. 1 (1), pp. 14-23, 2011.
2. Anchal Sharma, Rajeev Garg,,L. Raju and Sachin Goyal, "Transdermal drug delivery system: a review", World Journal of Pharmaceutical Research. Vol. 7 (7), pp. 260-288.
3. Audumbar Digambar Mali, Ritesh Bathe and Manojkumar Patil, "An updated review on transdermal drug delivery systems", International Journal of Advances in Scientific Research, pp. 2395-3616.
4. Bhairam Monika, Roy Amit, Bahadur Sanjib, Banafar Alisha, Patel Mihir, Turkane Dhanushram, "Transdermal drug delivery system with formulation and evaluation aspects: overview", Research Journal Pharmacy and Technology, Vol. 5(9), 2012.
5. Sateesh Kandavilli, Vinod Nair and Ramesh Panchagnula, "Polymers in transdermal drug delivery systems. Pharmaceutical Technology" 2002.
6. Nikhil Sharma, Geta Agarwal, A. C. Rana, Zulfiqar Ali Bhat, Dinesh Kumar, "A review: Transdermal drug delivery system: A tool for novel drug delivery system", International Journal of Drug Development & Research, Vol. 3(3), pp. 70-84, 2011.
7. Kumar Sahoo, B. (n.d.), "Novel Drug Delivery Systems", Unit-III BP 704T.
8. Daniel Esuendale and Tesfaye Gabriel, "Cellulosic on transdermal drug delivery system: a review", Journal of Drug Delivery and Therapeutics, Vol. 6(5), 2016.
9. Sonje A., & Chandra A., "Comprehensive review on eudragit polymers", International Research Journal of Pharmacy, Vol. 4(5), pp. 71–74, 2016.
10. Wasilewska K, Winnicka K, "Ethylcellulose-a pharmaceutical excipient with multidirectional application in drug dosage forms development" Materials (Basel), Vol. 12(20), 2019.
11. Kurakula M, Rao GSNK, "Pharmaceutical assessment of polyvinylpyrrolidone (PVP): As excipient from conventional to controlled delivery systems with a spotlight on COVID-19 inhibition", Journal of Drug Delivery Science Technology, Vol. 10(2), 2020.
12. Franco P., & de Marco I., "The use of poly(N-vinyl pyrrolidone) in the delivery of drugs: A review", In Polymers, Vol. 12(5), 2020.
13. Kasselkus, A., Weiskircher-Hildebrandt, E., Schornick, E., Bauer, F., & Zheng, M. (n.d.), "The life science business of Merck operates as milliporesigma in the Polyvinyl alcohol: Revival of a long lost polymer".
14. Heinze, Thomas & Koschella, Andreas, "Carboxymethyl Ethers of Cellulose and Starch – A Review", Macromolecular Symposia, Vol. 223, pp.13 – 40, 2005.
15. T. M. Pramod kumar, H. M. Umesh, H. G. Shivakumar, Valluru Ravi & Siddaramaiah, "Feasibility of polyvinyl alcohol as a transdermal drug delivery system for terbutaline sulphate", Journal of Macromolecular Science, Part A, Vol. 44(6), 2007.
16. S.S. Davis and L. Illum, "Drug delivery systems for challenging molecules", International Journal of Pharmacy, Vol. 176, pp. 1–8, 1998.