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REVIEW ARTICLE

CELLULOSIC ON TRANSDERMAL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Transdermal patch is a medicated adhesive patch that is placed on the skin to deliver the drug through the skin in order to achieve systemic absorption of drug at a predetermined rate over a prolonged period of time. The amalgamation of polymer and pharmaceutical sciences led to the introduction of polymer in the design and development of drug delivery systems. Polymeric delivery systems are mainly intended to achieve controlled or sustained drug delivery. Polysaccharides fabricated into hydrophilic matrices remain popular biomaterials for controlled-release dosage forms and the most abundant naturally occurring biopolymer is cellulose; thus, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), microcrystalline cellulose (MCC) and ethyl cellulose (EC) can be used for production of controlled transdermal drug delivery systems (TDDS). This paper assembles the current knowledge on the structure and chemistry of cellulose, and in the development of innovative cellulose esters and ethers for controlled release TDDS. In addition, bacterial cellulose applications through chemical modification as a new TDDS will be discussed.

Key words: Cellulosic, Transdermal Drug Delivery System, Bacterial Cellulose, Adhesive Patch

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INTRODUCTION

Transdermal drug delivery (TDD) represents an attractive alternative to oral delivery of drugs and is poised to provide an alternative to hypodermic injection too.[1] TDD is defined as self-contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin at controlled rate to the systemic circulation.[2,3]

Advances in transdermal delivery systems can be categorized as undergoing three generations of development from the first generation of systems that produced many of today's patches by judicious selection of drugs that can cross the skin at therapeutic rates with little or no enhancement; through the second generation that has yielded additional advances for small molecule delivery by increasing skin permeability and driving forces for transdermal transport; to the third generation that will enable transdermal delivery of small molecule drugs, macromolecules (including proteins and DNA) and virus based/other vaccines through targeted permeabilization of the skin's stratum corneum.[1]

The amalgamation of polymer and pharmaceutical sciences led to the introduction of polymer in the design and development of drug delivery systems.[2] Polymeric delivery systems are mainly intended to achieve controlled or sustained drug delivery. Polysaccharides fabricated into hydrophilic matrices remain popular biomaterials for controlled-release dosage forms and the most abundant naturally occurring biopolymer is cellulose; thus, HPMC, HPC, MCC and EC can be used for production of controlled TDDS.

For the development of film forming polymeric solutions as TDDS the choice of a suitable polymer for the formulation is very important. The film former does not only influence the mechanical properties of the formed film such as flexibility or abrasion resistance, the adhesion to the skin (in cooperation with the plasticizer) or the appearance of the film (transparency, smoothness, gloss) but affects also the drug permeation from the film into the skin. Depending on their chemical properties, polymers and drugs can interact in different ways, for example by ionic forces, hydrogen bonding or through the degree of solubilization of the drug in the polymer. An important factor with impact on the drug permeation can be the ability of the polymer to influence the physical state of the drug in the matrix by acting as crystallization inhibitor. When the

formulation is applied to the skin the drug is completely dissolved. With the evaporation of the solvent the drug concentration within the formulation rises which increases the thermodynamic activity of the drug in the formulation and with it the drug flux.[4,5]

BACTERIAL CELLULOSE ON TDDS

Silva et al. (2014) explored bacterial cellulose (BC) membranes as novel nanostructured transdermal delivery systems for diclofenac sodium salt.[6] Wei et al. (2011) obtained BC dry films after immersion in benzalkonium chloride and observed the drug effects lasting for at least 24 h against contaminated wound flora such as *Staphylococcus aureus* and *Bacillus subtilis*.[7]

BC fibres with silver nanoparticles have successfully produced up to 99.99% antibacterial activity against *Escherichia coli* and *S. aureus*.[8] The use of silver nanocomposites with BC has been endorsed as a promising strategy in which antibacterial properties are required.[9]

The *S*-enantiomer of propranolol has been released from a composite layer of BC membrane with methacrylate, and applied to transdermal application where primary control of drug release came from the parent BC membrane.[10] These encouraging results indicated that BC, which acts as a base for molecular imprinting networks, are amendable to treatments like reactive pore filling that make BC suitable for chiral applications.

BC could also be used in conjunction with a conducting polymer, such as polyaniline, which has been reported to have electro-conductivity, and thus, has the potential to act as electrically stimulated drug delivery device. The product was formed by polymerisation of aniline on single side of the BC membrane and this composite acted as super capacitor.[11]

This property could therefore be combined with biocompatibility, biodegradability and improved mechanical properties of BC, although the hydrophobicity of the conducting polymers needs to be modified for successful protein entrapment. Considering this, iontophoresis (drug delivery by electric potential) can be applied to expand the application of BC. In this view, BC was combined with multi walled carbon nanotubes and electro-conductivity was increased up to 1.4×10^{-1} S/cm.[12, 13]

HYDROXYPROPYL METHYLCELLULOSE (HPMC)

The controlling regime for HPMC and drug release from a swollen matrix includes both the gelled matrix and the gelled matrix-bulk solution interface. The transport hindrance within the gelled matrix is dictated by the structure and composition of the gelled matrix. On the other hand, release kinetics at the gelled matrix-bulk solution interface plays a significant role as well.[14]

HPMC, a hydrophilic swellable polymer widely used in oral controlled drug delivery, also has been explored as a matrix former in the design of patches of propranolol hydrochloride. HPMC has been shown to yield clear films because of the adequate solubility of the drug in the polymer. Matrices of HPMC without rate-controlling membranes exhibited a burst effect during dissolution testing because the polymer was hydrated easily and swelled, leading to the fast release of the drug.[15]

Garala et al. (2009) designed to formulate a transdermal therapeutic system of tramadol HCl using a polymeric (HPMC) matrix film. Several diffusion pathways created due to the blend of the polymers to generate overall desired steady and sustained drug release from the patches. The manner by which drug release in most of the controlled/sustained release devices including transdermal patches is governed by diffusion. Diffusion is naturally a probabilistic process described by the random walk of molecules. The polymer matrix has a strong influence on the diffusivity as the motion of a small molecule is restricted by the three dimensional network of polymer chains.[14,16]

When this matrix patch comes into contact with an *in-vitro* study fluid, the fluid is absorbed into the polymer matrix and this initiates HPMC chain dissolution process in the matrix. HPMC chain dissolution from the matrix surface involves two distinguishable steps. The first step involves changes in entanglement of individual drug molecules at the matrix surface, which depends on the rate of hydration. The second step involves the shift of this molecule from the surface across the diffusion membrane initially to the surface and then to the bulk of the *in vitro* study fluid. It is well known that the addition of hydrophilic component to an insoluble film former leads to enhance its release rate constant. This may be due to dissolution of the aqueous soluble fraction of the film, which leads to creation of pores and decrease of mean diffusion path length of the drug molecule to be released.[14, 17]

Monolithic matrix transdermal systems containing tramadol HCl were prepared by Garala et al. (2009) using various ratios of the polymer blends of HPMC and Eudragit S (ES) 100 with triethylcitrate as a plasticizer. The moisture content of the prepared transdermal film was low, which could help the formulations remain stable and from being a completely dried and reduce brittleness during storage. It was observed that initially there was rapid release of drug from the patch. This rapid drug release (burst effect) from the prepared transdermal patch might be due to rapid dissolution of the surface drug. The burst release can be useful for dermal penetration of drugs. When the drug is released from the matrix in such a way that the rate of release of the drug remains constant, the release kinetics of the drug are believed to follow a zero-order kinetics. The release profile of the dissolved drug can generally be described by the Fick's law and predicted that the cumulative mass released is proportional to the square root of time.[16]

Orally Clopidogrel bisulfate has a short elimination half-life (7-8 hrs), low oral bioavailability (50%) undergoes extensive first pass metabolism (85%) and

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frequent high doses (75 mg) are required to maintain the therapeutic level as a result, dose development toxic effect. TDDS of Clopidogrel bisulfate formulated and evaluated by using various polymers such as HPMC, PVP and EC by solvent evaporation technique for improvement of bioavailability of drug and reducing toxic effects. The result of diffusion study showed that formulation, F2 (HPMC and PVP) showed maximum release of 90.06 % in 24 h. Based on the drug release and physicochemical values obtained the formulation F2 is considered an optimized formulation which showed higher percentage of drug release of 90.06 % in 24 h. The developed transdermal patches increase the therapeutic efficacy and reduced toxic effect of Clopidogrel bisulfate.[18]

The matrix type TDDS of LRDP (Lercanidipine Hydrochloride) were prepared by solvent evaporation technique. Formulations were composed of HPMC and Eudragit RL100 (ERL). All the six formulations carried 10 mg of LRDP/patch area, 8 % v/w of d-limonene as a penetration enhancer, 20 % v/w of propylene glycol as plasticizer in methanol and dichloromethane as solvent system. All the formulations exhibited satisfactory physicochemical characteristics. By fitting the data into zero order, first order and Higuchi model, it was concluded that drug release from matrix films followed Higuchi model and the mechanism of the drug release was diffusion mediated. The patches were seemingly free of potentially hazardous skin irritation. The patches composed of ERL, HPMC (1.5:8.5) with 8 % v/w limonene as penetration enhancer may be selected for the development of TDDS of LRDP for potential therapeutic use by using a suitable adhesive layer and backing membrane.[19]

ETHYLCELLULOSE (EC)

EC is a water-insoluble polymer used in controlled-release dosage forms. In the absence of polymer swelling ability, EC compatibility becomes a key factor in such systems, because release kinetics would depend largely on the porosity of the hydrophobic compact. Although EC is considered insoluble, it can take up water. This is because of its hydrogen bonding capability with water due to the polarity difference between the oxygen atom and the ethyl group of the polymer.[20]

When the active agent (drug) is released from the matrix in such a way that the rate of release of the drug remains constant, the release kinetics of the drug are believed to follow a zero-order kinetics. The formulation studied by Mukherjee et al (2005) appeared to follow similar patterns of drug release profiles, i.e. initially apparent zero-order and then first order release kinetics. Initially for first few hours the drug release, kinetic patterns followed zero-order drug release profiles and with the enhancement of time the release profiles gradually changed into the concentration dependent first order release kinetics. The drug polymer matrix initially ensured constant concentration of drug in *in vitro* study fluid, but afterwards, concentration dependent release kinetic made the reaction towards the first order kinetic.[21]

Drug release from a porous, hydrophobic polymeric drug delivery system occurs when the drug comes into contact with the release media, subsequently dissolves and diffuses through media filled pores. Thus, the geometry and structure of the pore network are important in this process. The Higuchi model has been reported to fail at drug loading levels below the percolation threshold. Below the percolation threshold, incomplete drug release is observed presumably due to limited accessibility of many drug particles to the dissolution medium since they are encapsulated by water insoluble polymeric materials.[22]

When the matrix patch which contains EC comes into contact with an *in vitro* study fluid, thermodynamically compatible with the polymer, the fluid is absorbed into the polymer matrix and this initiates polymer chain dissolution process in the matrix. Polymer chain dissolution from the matrix surface involves two distinguishable steps. The first step involves changes in entanglement of individual drug molecules at the matrix surface, which depends on the rate of hydration. The second step involves the transport of this molecule from the surface across the skin, adjacent to the matrix patch, initially to the surface and then to the bulk of the *in vitro* study fluid. Molecular diffusion through polymers is an effective, simple and reliable means of attaining sustained/controlled release of a variety of active agents.[21]

Gupta and Mukherjee (2003) select a suitable formulation for the development of TDDS of diltiazem hydrochloride. Transdermal patches of the drug, employing different ratios of polymers, EC, and PVP were developed and evaluated for the potential drug delivery using depilated freshly excised abdominal mouse skin. The cumulative amount of drug was found to be proportional to the square root of time, i.e., Higuchi kinetics. From this study, it was concluded that the films composed of PVP: EC (1:2) should be selected for the development of transdermal drug-delivery system of diltiazem hydrochloride, using a suitable adhesive layer and backing membrane, for potential therapeutic use.[23]

EC and PVP matrix films with 30% dibutyl phthalate as a plasticizer have been fabricated to deliver diltiazem hydrochloride and indomethacin. The addition of hydrophilic components such as PVP to an insoluble film former such as ethyl cellulose tends to enhance its release-rate constants. This outcome can be attributed to the leaching of the soluble component, which leads to the formation of pores and thus a decrease in the mean diffusion path length of drug molecules to release into the dissolution medium. The result is higher dissolution rates. Substances such as PVP act as antinucleating agents that retard the crystallization of a drug. Thus they play a significant role in improving the solubility of a drug in the matrix by sustaining the drug in an amorphous form so that it undergoes rapid solubilization by penetration of the dissolution medium.[24]

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Mukherjee et al. (2005) developed a suitable matrix type TDDS of dexamethasone using blends of two different polymeric combinations, PVP and EC and Eudragit with PVP. All the formulations were found to be suitable for formulating in terms of physicochemical characteristics and there was no significant interaction noticed between the drug and polymers used. *In vitro* dissolution studies showed that the drug distribution in the matrix was homogeneous and the SEM photographs further demonstrated this. The formulations of PVP: EC provided slower and more sustained release of drug than the PVP:Eudragit formulations during skin permeation studies and the formulation PVP:EC (1:5) was found to provide the slowest release of drug. Based on the above observations, it can be reasonably concluded that PVP-EC polymers are better suited than PVP-Eudragit polymers for the development of TDDS of dexamethasone.[21]

HPMC WITH EC

EC blended with HPMC are frequently used in drug delivery systems. By using polymer combinations, formulators may be able to develop sustained-release drug dosage forms with better performance than is shown by the individual polymer components. Various polymer blends have been studied in order to achieve the desired release kinetics. The presence of more than one polymer in a formulation may result in a spatial configuration, but it is also possible that a polymer additive may become part of the gel network. The externally adsorbed water in the insoluble polymers (EC) can assist in the formation of liquid bridges between the particles. Any soluble component in the formulation could dissolve in these liquid bridges and thus assist in the formation of solid bridges between the particles on drying, which would sustain the granule integrity and alter the physicochemical properties of the matrixing agent. These polymers can be expected to experience an aqueous environment in production and *in vivo*. The water-polymer and polymer-polymer interactions and their distribution and/or configuration within a formulation are critical to their applications in wet massing techniques.[20] Transdermal patches control the delivery of drugs at controlled rates by employing an appropriate combination of hydrophilic and lipophilic polymers.[25]

The mechanical properties of free films prepared from various ratios of HPMC and EC with and without plasticizer were characterized. The film made from HPMC alone without plasticizer was very hard and brittle, expressed by the very high Young's modulus value. Plasticization of hydrophilic polymers like HPMC with hydrophobic plasticizer provided the higher strength but lower elongation film as compared to those of the hydrophilic polymer film plasticized with hydrophilic plasticizer. Addition of EC into the HPMC film resulted in the lower ultimate tensile strength, percent elongation at break and Young's modulus. The molecular structure of EC contains long chain of AGU linked together with acetal linkage. This kind of structure is hydrophobic in nature. Therefore, the presence of EC might have been responsible for the lower strength and elongation when compared to HPMC alone.[26]

The matrix TDDS bearing naproxen was fabricated using various concentration ratios of EC and HPMC. The drug was uniformly distributed in the polymer films and drug content was found to be 98.6% to 99.0% per cm^2 in the TDDS. Films of lipophilic-hydrophilic polymers in various proportions were studied. The combination of EC and HPMC in a ratio of 2:8 and 4:6 showed highest cumulative drug release. Increasing the proportion of HPMC concentration increases the cumulative amount release. From the release studies it was observed that by increasing the proportion of HPMC tend to increase the cumulative amount of drug release. This increased release rate may be due to higher hydrophilic nature of HPMC. Due to its high hydrophilicity it absorbs water and swells resulting in the more release of drug from the patches. The decrease in drug release rate from films containing more lipophilic polymer combination may be attributed to the relatively hydrophobic nature of polymer which has less affinity for water, this result in decrease in thermodynamic activity of the drug in the film and decreased drug release.[27]

Limpongsa and Umprayn (2008) prepared the suitable polymeric films for the development of diltiazem hydrochloride TDDS. HPMC and EC used as hydrophilic and hydrophobic film formers, respectively. The films composed of 8:2 HPMC/EC, 30% dibutyl phthalate (DBP) and 10% Isopropyl myristate (IPM), Isopropyl palmitate (IPP) or tween 80 loaded with 25% diltiazem HCL selected for manufacturing transdermal patch by using a suitable adhesive layer and backing membrane.[26]

Transdermal patches of Promethazine hydrochloride and Ondensetron hydrochloride with HPMC and EC was prepared by solvent evaporation technique. The patch was found to be efficacious, safe, stable and nonirritant to skin. The establishment of steady state levels *in vitro* for 48h showed the clear advantage of transdermal patches over current modes of administration. Drugs like promethazine Hydrochloride and Ondensetron Hydrochloride were formulated into matrix type patches in an attempt to solve the problems associated with oral administration. The drug release was found to be linear and follow the Higuchi diffusion equation. The release kinetics of Promethazine Hydrochloride and Ondensetron Hydrochloride formulations follows zero order and first order kinetics. Hixon Crowell equation also found to be linear, these indicating that the release from the patches was by both diffusion and erosion methods.[28]

HPMC and EC films were prepared using DBP as plasticizer with eighteen different combinations of these three polymers by solvent evaporation technique. Polyvinyl alcohol was used to prepare the backing membrane. Formulations containing higher proportion of hydrophilic polymers blended with lower proportions of hydrophobic polymer were found less consistent in comparison to the patches comprised of higher proportion of hydrophobic polymer. Skin irritation

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study indicated that the prepared patches were having no effect of irritation upon administration and is safe for topical application. The scanning electron microscopic photographs showing formation of pores onto the surface of the film after skin permeation study was due to the exhaustion of the contained drug. It is evident that higher proportions of hydrophilic polymers (HPMC) in formulations resulted in an enhanced permeation of the contained drug. Whereas permeation of the contained drug was opposed when there was least concentration of hydrophilic polymers blended with highest concentration of hydrophobic polymer (EC).[29]

HYDROXYPROPYLCELLULOSE (HPC)

Repka and McGinity (2001) investigated the *in vivo* bioadhesive properties of HPC films containing seven polymer additives on the epidermis of 12 human subjects, including two ethnic sub-groups. HPC films containing polyethylene glycol (PEG 3350) alone, Vitamin E TPGS (TPGS) 5%, sodium starch glycolate 5%, Eudragit E-100 5%, carbomer 974P and 971P 5%, and polycarbophil 5%, all with and without plasticizer, were prepared by hot-melt extrusion utilizing a Randcastle Microtruder (Model [RCP-0750). *In vivo*, the TPGS-incorporated film exhibited a two-fold increase in FA when compared to the control film containing the PEG 3350 5%. The carbomer 971P and polycarbophil containing films were determined to have the highest FA and EAF, and the lowest MA of all films tested. The film containing carbomer 971P had a higher FA than the film containing 974P. In addition, films in one ethnic sub-group exhibited higher FA and EAF than the other. Force–deflection profiles obtained from these experiments indicate that the force of adhesion, elongation at adhesive failure and modulus of adhesion are a function of the polymer additive in the HPC extruded films. The incorporation of carbomer 971P and a polycarbophil into HPC films increased bioadhesion significantly when compared to the film containing HPC and PEG 3350. Differences in FA and EAF were discovered between two ethnic sub-groups tested.[25]

Schroeder et al. (2007) evaluated the potential of these systems for TDDS the permeation of ethinylestradiol from four formulations with different polymers was tested across heat separated human epidermis. The film forming solution showed a higher ethinylestradiol permeation through heat separated human epidermis than the commercial EVRA® patch *in vitro* and achieved measurable plasma concentrations of ethinylestradiol *in vivo* in pigs. The polymers used in the tested formulations were HPC, ammonio methacrylate copolymer type A (Eudragit® RL PO), polyurethane-14 and AMP-acrylates copolymer (DynamX®) and silicon gum (SGM 36).[30]

CELLULOSE ACETATE (CA)

When CA is used as a rate controlling membrane material for TDDS, generally requires plasticizers to improve its mechanical property. A plasticizer is supposed to weaken the intermolecular forces between the polymer chains, resulting in a softened and flexible polymer matrix. Thus, drug permeability through the membranes may also be affected by the addition of a plasticizer. The weight loss of membranes versus temperature is no detectable degradation below 200^{o}C. PEG is a non-solvent for cellulose acetate and can facilitate the phase inversion of the polymer solution. Faster phase inversion induced by the addition of PEG leads to more porous membrane structures. The morphology difference between the top surface and bottom surface may also arise from the difficulty in solvent transferring during the membrane formation.[31]

The plasticizer will interpose itself between the polymer chains and interact with the forces held together by extending and softening the polymer matrix. These are incorporated into the films for various reasons such as to reduce brittleness, impart flexibility, increase strength and also to improve adhesiveness of the film with other surfaces or membranes. Plasticizer shifts the glass transition temperature to lower temperature and is an important formulation factor. PEG 400, DBP and PG at a concentration of 40 % w/w of polymer were used as a plasticizer. Preliminary experiments indicated lower concentrations were found to give rigid and brittle patches whereas higher concentrations gave soft patches. So plasticizers at a concentration of 40 % was found to give good flexible patches and easily removed from the mercury surface without any rupture.[32]

Transdermal patches composed of highest proportion of hydrophobic polymer (CA) blended with lowest proportion of hydrophilic polymer (PVP and HPMC) were found to have low moisture content. This helps them to remain stable and prevent from being a completely dried and brittle film. Similarly, a low moisture uptake protects the material from microbial contamination and limits the bulkiness of the patches.[29]

Rao and Diwan (1997) studied CA free films casted from chloroform solution containing different plasticizers to develop a suitable rate controlling membrane for transdermal use. DBP, PEG and PG were used as plasticizers at a concentration of 40% w/w of dry polymer weight. Water vapor transmission and drug diffusion through the free films followed zero order kinetics and decreased with increasing the film thickness. The films plasticized with PEG showed higher permeability for both drugs compared with other films. The order of decrease of permeability of plasticized films with plasticizers is PEG > PG > DBP. Diffusion of drugs through the free films of CA was extended over a longer period of time at a controlled rate and thus, these can be used as rate controlling membranes for the development of a transdermal drug delivery system.[33]

Wang (2002) studied on CA membrane used as controlled release in TDDS of scopolamine. In this study, the CA membranes were cast with acetone as a solvent at 22 and 40 C. PEG was used as a pore-forming agent. It was observed that the drug permeation through the CA membranes was obviously affected by the incorporated PEG content and formed membrane

morphology. There was no drug flux from the CA membranes prepared without PEG. An increased PEG content resulted in a faster scopolamine release due to a more porous structure created. Both the membrane fabrication temperature and the PEG content can affect the thermal, mechanical and morphological properties of the resultant membranes. With the optimized fabrication conditions, linear *in vitro* release profiles of scopolamine over 3 days were achieved. The membranes developed would be useful for transdermal delivery of drugs.[31]

HPMC: PVP polymer combination with DBP as plasticizer has maximum folding endurance while CA: PEG4000 with PEG400 showed least folding endurance. The tensile strength of the patches was found to vary with the nature of polymer and plasticizer. A soft and weak polymer is characterized by low tensile strength and low elongation, a hard and brittle polymer is defined by a moderate tensile strength and low elongation, and a soft and tough polymer is characterized by moderate tensile strength and high elongation, whereas a hard and tough polymer is characterized by high tensile strength and high elongation. Polymer combination CA: PVP plasticized with DBP possessed high tensile strength while polymers plasticized with Eudragit RL100: EudragitRS100 plasticized with PEG possessed low tensile strength. Among the plasticizers the tensile strength of the patches decreased in the following order DBP>PG>PEG400. Patches require certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The hardness of the patch varied from 132 g to 307 g, Surface pH varied 5.1 to 6.0 indicating that no irritation will occur on the skin after applications of the patches.[32] Table 1 also shows the review of cellulose derivatives used in TDDS.

Table.1 Cellulose derivatives used in TDDS

Polymer	**Types of Formulations**	**Drug**
CA	film	Drug free[33]
HPC HPC: Eudragit E 100 HPC: Carbopol 971P HPC: Polycarbophil	Matrix	Vitamin E[25]
CA	Membrane	Scopolamine[31]
EC: PVP	Matrix	Propranolol
EC: PVP; Eudragit: PVP	Matrix	Dexamethasone[21]
EC: PVP	Matrix	Propranolol
HPC Eudragit RL PO Silicon Gum Acrylate copolymer	Film forming polymeric solution	Ethinylestradiol[30]
HPMC: EC	Matrix	Diltiazem HCl[26]
EC:PVP EC:HPMC	Matrix	Losartan[29]
CA: HPMC PVP: PEG 4000 Eudragit RL 100-RS 100	Matrix	Drug Free Patch[32]
HPMC: Eudragit RS 100 HPMC: Eudragit RL 100	Matrix	Venlafaxine
HPMC: Eudragit RL 100	Bilayer Matrix	Domperidone
HPMC: Eudragit RL 100	Matrix	Lercanidipine[19]
HPMC, Eudragit RL 100, Chitosan	Matrix	Gliclazine
HPMC, PVP, Eudragit RS100	Matrix	Valsartan
EC: HPMC	Matrix	Naproxen[27]

FUTURE PERSPECTIVES

Transdermal route has vied with oral treatment as the most successful innovative research area in drug delivery. Since cellulose exhibits several unique properties, well established history in drug delivery and in food industry, its use in human is safe. So it is a good candidate in the formulation and developing a TDDS.

Cellulose and its derivatives have been used to fabricate different drug delivery systems including TDD. In order to utilize the full potential of Cellulose and its derivatives in the broad area of drug delivery, it is necessary to understand their fundamental physical, chemical and biological properties.

Bacterial cellulose has a great potential in TDDS due to its high purity and special chemical properties. But it

has not enough yields industrially and not economical. In order to meet the growing demand of BC, a robust and feasible industrial production and supply is crucial. Despite of the relatively simple fermentation process, new engineering processes are needed to produce desired BC with specific material properties. Moreover, genetic and biochemical investigations are also necessary to enhance BC production at molecular biological level and commercial purposes.

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