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Recent advancements in transdermal patches: Literature review

Sharma Chandan

University Institute of Pharma Sciences, Chandigarh University, Punjab, India
Correspondence author email: chand22g@gmail.com

Thakur Nishant

University Institute of Pharma Sciences, Chandigarh University, Punjab, India

Kaur Bhupinder

University Institute of Pharma Sciences, Chandigarh University, Punjab, India

Goswami Manish

Saraswati College of Pharmacy, Gharuan, Punjab, India

Abstract---Transdermal route of drug administration is novel as well as reliable means of sustained drug delivery. With more and more research being carried out in this field and increasing interest of researchers in this form of drug delivery, number of transdermal devices reaching the marketplace are expected to increase sharply. The aim of this review is to present latest explorations carried out in recent years utilizing possible drug candidates. Also, new polymer candidates along with novel penetration enhancers have been presented. For the purpose of study, various databases viz. Sciencedirect, Web of Knowledge, Pubmed, Google Scholar, etc. have been explored. After going through all the research work done by researchers in recent past it is appropriate to state that transdermal route is no longer reliant on few polymers and penetration enhancers but studies have now provided lot many more options for transdermal device formulation as evident from the data compilations. It can be concluded that most of the researchers have been utilizing HPMC as the preferred film forming polymer but recently use of Eudragit grades also has gained interest amongst scientists.

Keywords---Transdermal patches, topical delivery, sustained drug delivery.

Introduction

Oral route of drug delivery has remained the route of choice for drug delivery to systemic circulation from centuries back for therapeutic effectiveness due to well-known advantages of patient compliance and ease of self-administration.^{1,2} But conventional dosage forms suffer certain limitations like non specificity and inactivation while passing through gastrointestinal tract and inability provide sustained effect.³ Transdermal route of drug delivery, hence appears to be a good alternative approach instead of oral route as it eliminates chances of drug loss by hepatic metabolism and even provides better patient compliance as opposed to other routes like parenteral route.^{4,5}

Topical route is not new to human beings as it has been in constant use for cosmetics and topical medications but the word transdermal appeared in 1944 when Webster introduced it as a route of drug delivery.⁶ Transdermal patch is a self-contained dosage that is applied to intact skin and provides drug in a controlled manner.⁷

The aim of this article is to report research carried out in transdermal formulations. Various online databases viz. Sciencedirect, Web of knowledge and Pubmed were explored for literature compilation. Mishra *et al.* (2022), prepared and evaluated the transdermal patches of Simvastatin. Casting method was utilized by authors for formulating patches. Eudragit grade viz. RS100 and RL100 were explored for forming patches in proportion 4:6 and 2:8. DBP was utilized as plasticizer and DMSO was employed as penetration enhancer. Results of the various assesment parameters confirmed that patch comprising of Eudragit RS100: Eudragit RL100 in 2:8 and 40% DBP alongwith 0.5 % DMSO provided optimum results.⁸

Shivalingam *et al.* (2021), fabricated transdermal patches of Pantoprazole. Solvent casting technique was employed as manufacturing technique. PVP K30 and Eudragit L100 along wit HPMC E5 were explored as potential film forming polymers. Prepared patches were tested for folding endurance, thickness, content uniformity, weight uniformity, percent uptake moisture, surface pH, in vitro drug release profile and swelling index. It was concluded that patches with composition Eudragit L100: HPMC E5 (1:1) provided best results.⁹

Rasool *et al.* (2021), prepared dimenhydrinate transdermal patch utilizing various combination of polymers viz. Eudragit S100, Ethylcellulose, HPMC and PVP. Eucalyptus oil, oleic acid and polyethylene glycol were explored fore permeation enhancement effect with glycerol acting as plasticizer. Results of evaluation concluded that formulation with HPMC:EC in ratio 7:3 and eucalyptus oil 5% provided maximum flux.¹⁰ Rajesh *et al.* (2021), prepared and evaluated transdermal patches utilizing Prochlorperzine. Solvent evaporation technique was utilized to form the patches. Chitosan, HPMC and Ethylcellulose were utilized as formulating polymers for matrix of the patches along with combination of Chloroform and methanol as solvent. The results confirmed that the formulated patches had acceptable properties and therapeutic efficacy.¹¹

Suhaitamy *et al.* (2021), prepared Meloxicam transdermal patches using different combination of polymers including PVP and HPMC. Propylene glycol was used as permeation enhancer in different concentrations ranging from 10-30 % w/v. Solvent evaporation technique was used to fabricate the patches. The findings of research work shown that the optimized patches had acceptable characteristic features.¹²

Joshi (2021), developed matrix based transdermal patches of Flurbiprofen for treating rheumatoid arthritis with different proportion of lipophilic and hydrophilic polymers. Eudragit RL100 and HPMC K15M were investigated as possible candidates for matrix. Results revealed that patch containing Eudragit RL100: HPMC K15M (1:3) along with d-limonene as permeation enhancer in concentration 7.5 % w/w provided maximum flux of drug. Also the developed patches showed no oedema and erythema.¹³

Sahu *et al.* (2021), developed transdermal patches of Dexamethasone and Ondansetron comprising different ratio of hydrophobic and hydrophilic polymers. Solvent casting technique was employed with plasticizer in concentration 15 % w/v and penetration enhancer in concentration of 5 % w/v. The fabricated optimized patches were evaluated for various characteristic properties like drug content, thickness, folding endurance, tensile strength and in vitro dissolution. Results showed that EC patches were having best characteristics features as compared to other polymers.¹⁴

Yasemin and Emel (2021), prepared transdermal patches of Donepezil for treating Alzheimer's disease. Various combination of polymers were explored for making patches including gelatin/ sodium alginate/ hydroxyethyl cellulose and PVP. Plasticizer used in patches was Transcutol. Characterization was done with FT-IR. Drug release of formulated patches was done by Franz diffusion cell studies. Results provided enough evidence that sodium alginate containing PVP patches provided sustained drug release.¹⁵

Malvey *et al.* (2021), fabricated Ketorolac tromethamine transdermal patches. HPMC E5 was used as film forming polymers. PEG 400 was employed for the role of plasticiser. DMSO was the permeation enhancer in the formulation. Solvent casting method was used to prepare patches. The fabricated optimized patches were evaluated for various characteristic properties like drug content, thickness, folding endurance, tensile strength and in vitro dissolution. Patches with HPMC E15 and drug in quantity 200 mg each with 8 % DMSO was found to be optimized formulation.¹⁶

Patel *et al.* (2021), prepared transdermal patches of Apixaban. HPMC E50 LV and Eudragit RS100 were utilized as rate controlling polymers in the matrix. Glycerin and PEG 400 were employed as permeability enhancer and plasticizer respectively. FTIR study was done to ascertain any drug polymer interaction. Prepared batches of patches were examined for appearance and weight variation, percent elongation and folding endurance. Also optimized patches with combination of polymers shoed pH between 6.8 to 7.1.¹⁷

Trivedi & Goyal (2020), prepared patches using Dexketoprofen trometamol as model drug. Solvent casting technique was employed for fabrication of transdermal system. Different proportions of polymers were explored as possible matrix forming agents including HPMC, Eudragit RS 100 and EC. Various evaluations parameters were utilized to assess the patches. Results showed that transdermal patches consisting of EC: HPMC in proportion 1:4 provided highest release i.e 85.77 % after 24 hours. Resulting data was found to be best fitting in Higuchi model. ¹⁸

Shivalingam *et al.* (2020), fabricated transdermal patches of Pantoprazole. Solvent casting technique was employed as manufacturing technique. PVP K30 and Eudragit L100 along with HPMC E5 were explored as potential film forming polymers. DMSO was used as penetration enhancer. Prepared patches were tested for folding endurance, thickness, content uniformity, weight uniformity, percent uptake moisture, surface pH, in vitro drug release profile and swelling index. In vitro studies of drug release showed optimum release of 93.14 %. ¹⁹

Jajala, Sravya & Kanagala (2020), fabricated transdermal patches using Zidovudine for antiviral therapy. Solvent casting technique was utilized for formulation patches. PVP K30, Eudragit and HPMC were explored for film forming potential. T-anethole was used as penetration agent with PG as plasticizer. Various parameters of transdermal patches were evaluated including thickness, folding endurance, moisture content, weight uniformity and swelling characteristics. Optimized formulations consisted of HPMC 1% and 4% Eudragit RL 100. Maximum flux of 614 mcg/ cm²/hr. No skin irritation was observed in animals. ²⁰

Yanping *et al.* (2020), prepared medicament in adhesive transdermal patch for delivering Koumine. Dura-Tak 87-4287. Solvent casting technique was utilized as the method of preparation. Evaluation of transdermal patches comprising of azone in concentration 10 % proved to exhibit significant potential for improved drug flux. In vivo evaluation of patches in rats provided evidence that these formulations deliver Koumine at sustained rate. ²¹

Samiullah *et al.* (2020), designed transdermal patches of Pseudoephedrine hydrochloride by solvent casting method using Eudragit RL 100 as polymer. Thymus oil, eucalyptus oil, castor oil and Tween 20 were explored as penetration enhancers. Formulated patches were evaluated for tensile strength, folding endurance, weight variation, physical appearance, stability, moisture content and thickness. Results proved that Tween 20 was best penetration enhancer amongst various options explored. The formulation containing 5 gm of Eudragit RL 100 and 5 gm of Tween 20 provided maximum drug release of 83 %. ²²

Kulkarni (2019), developed transdermal patches using Atomoxetine hydrochloride as model drug. Solvent casting technique was utilized to formulate the patches. Different combinations of polymers were utilized to fabricate patches using Polyox 303, HPMC and Eudragit RL100. Water: ethanol was employed as solvent system. FTIR was employed to examine for any possible drug-polymer interactions. Various parameters of transdermal patches were evaluated including thickness, folding endurance, moisture content, weight uniformity and swelling

characteristics. Results shown that folding endurance was found to be less than 500. Also it was established through evaluation of various properties that Eudragit and HPMC exhibited maximum release of drug.²³

Raj (2019), developed nanostructured lipid carrier loaded transdermal patches using various PVP, Poly vinyl alcohol. DMSO was utilized as penetration enhancer. Polyethylene glycol was used as plasticizer. Formulated patches were evaluated for tensile strength, folding endurance, weight variation, physical appearance, stability, moisture content and thickness. It was found from results that optimized patch showed acceptable bioavailability.²⁴

Mahajan *et al.* (2018), prepared Piroxicam transdermal patches utilizing various combinations of polymers like HPMC E15, PVP K30 and EC in different proportions and SLS as penetration enhancer along with PEG 400 (plasticizer). Various parameters of transdermal patches were evaluated including thickness, folding endurance, moisture content, weight uniformity and swelling characteristics. Results shown that formulation consisting of lipophilic and hydrophilic polymers in proportion (1:3) provided maximum release and penetration up to 12 hours.²⁵

Agubata *et al.* (2020), prepared Chlorpheniramine maleate transdermal patches utilizing various combinations of polymers viz cassava starch and HPMC in different proportions along with PEG 4000, Tween 80 and PG. Method used for fabrication was solvent casting. Various parameters of transdermal patches were evaluated including thickness, folding endurance, moisture content, weight uniformity and swelling characteristics. Results shown that formulation consisting of cassava starch: HPMC 466mg: 1866 mg was found to be patch with acceptable patch characteristics for efficient delivery of Chlorpheniramine maleate.²⁶

Suksaeree *et al.* (2018), fabricated transdermal patches of polyherbs comprising of leaves of Curcuma longa, Cymbopogon citratus stem, Acacia rugata leaves, leaves and rind of Citrus hystrix, leaves of Tamarindus indica and Zingiber cassumunar rhizomes. For patch forming, PVA and HPMC was dissolved in water after which glycerin was incorporated in mixture for plasticizer effect that was followed by drying in oven for five hours (70 °C). Prepared patches were tested for folding endurance, thickness, content uniformity, weight uniformity, percent uptake moisture, surface pH, in vitro drug release profile and swelling index. For period of six months, accelerated stability tests were performed utilizing ICH guidelines (40°C and 75% Relative Humidity). Patch containing 10 % PVA 15 gm exhibited acceptable mechanical strength and stable.²⁷

Furuishi *et al.* (2019), prepared and evaluated Transdermal patch of Eptozocine. Patches were formed using Eudragit E100 Isopropyl myristate and glyceryl monostearate were used as permeation enhancers. Addition of 5 % citric acid to polymer Eudragit resulted in three times flux increase of Eptozocine. It was concluded from results that patch consisting of 10 % Isopropyl myristate and 5 % glyceryl monocaprylate provided maximum value of flux.²⁸

Yadav & Urade *et al.* (2019), prepared and evaluated Transdermal patches of Lornoxicam. Chitosan was employed as rate controlling polymer. Permeation enhancer used was Tween 20. Solvent casting technique was used for preparing patches. Physicochemical characteristics evaluated like in vitro drug release, skin irritation tests. Drug polymer interaction was also investigated by FTIR. Patch containing high Tween 20 amount provided diffusion twelve our time. Korsmeyer-Peppas model was found to be applicable. It was show from results these patches could provide controlled release of Lornoxicam. ²⁹

Kharia *et al.* (2019), prepared and characterized Transdermal patches of quercetin for the purpose of treatment of inflammation. Solvent casting technique was used for preparation. Ethyl cellulose and Hydroxy propyl methyl cellulose were used as polymers Polyethylene Glycol was employed as plasticizer. Physicochemical characteristics and drug release, Draize test for the formed patches were evaluated. Results shown that optimized formulation provided good release of drug.³⁰

Morise *et al.* (2019), prepared and characterized Transdermal patches of Scopolamine. Drug was incorporated directly into natural rubber latex membrane. Various evaluation parameters employed were wettability, SEM, FTIR and assays for hemolysis. Results confirmed that there was no drug- membrane interaction. No hemolysis was seen and other tests also proved that this system could be a good drug delivery option in case of scopolamine. ³¹

Ruan *et al.* (2019), investigated the effect of penetration enhancers on permeation of Zolmitriptan “Transdermal” patch. Isopropyl myristate was used in various concentrations as chemical penetration enhancer. Isopropyl myristate was used in concentration of 2, 5, 10, 12 and 15 %. Maximum drug release was achieved using 10 % concentration of isopropyl myristate. It was observed that linear relationship exists in range 0-10 % whereas no change was seen in rage of 10-15 %. From results it was concluded that isopropyl myristate increased fluidity of pressure sensitive adhesives. ³²

Shabbir *et al.* (2018), fabricated and evaluated Transdermal patches of tizanidine hydrochloride and also studied effect of penetration enhancers on drug release . HPMC and Eudragit L-100 were used in combination as film forming polymers. Span 20 and DMSO were used as penetration enhancer. From results it was found that Eudragit and HPMC in ration 7:3 and Span 20 (15 % w/w) provided highest flux. Zero order release was obtained. ³³

Likhitha *et al.* (2018), developed Transdermal patches of Galantamine. Eudragit L100, HPMC-K4M and HPMC-K15M were the polymers used in combination. Solvent casting technique was employed for patch preparation. PG and Tween 80 were the used penetration enhancers. All patches were evaluated for in vitro drug release by dialysis membrane. Pappas mechanism for drug diffusion was applicable . FTIR studies were conducted for drug excipient interaction and it was found that no interaction occurred in polymer and drug. ³⁴

Harsanyova *et al.* (2018), prepared and evaluated Transdermal patches loaded with Rhodiola rosea. Various combinations of polymers were tested. After testing

the patches for patch adhesion and dissolution of drug, various mixes, gelatin with chitosan or pectin with polyethylene glycol was found to show suitable properties.³⁵

Floriano *et al.* (2018), fabricated and evaluated drug in adhesive loaded Transdermal system. Ketoprofen was loaded in Natural rubber latex. The drug and polymer were tested for any possible interaction via FTIR study. Results shown that there was no interaction between drug and polymer and the Transdermal system provided drug release fifty hours. As per Scanning Electron Microscopy, some amount of Ketoprofen was present on rubber latex also.³⁶

Shehata *et al.* (2018), prepared and evaluated Transdermal patches of atorvastatin using different polymers. Solvent evaporation method was used for fabrication. Various combinations used for preparation were hydroxyl propyl methyl cellulose with either eudragit RS 100 or Polyvinyl pyrrolidone in different ratios using PEG 400 as plasticizer. Results shown that combination of HPMC with Polyvinyl pyrrolidone in the ratio 3:1 had most appropriate physicochemical characteristics.³⁷

Regenthal *et al.* (2018), prepared and characterized Anastrozole “Transdermal” systems which were drug-in-adhesive type “Transdermal” patches. Various physicochemical tests were performed to evaluate the patch. Franz diffusion cell was employed to study in vitro release profile of drug. Beagle dogs were used for in vivo study from formulation. The formulation provided 65 % release of drug in 48 hours.³⁸

Anirudhan *et al.* (2018), prepared and evaluated “Transdermal” patches of Diltiazem hydrochloride. Polyethylene glycol coated vinyl trimethoxy silane-g-chitosan were used as polymer matrix. Diltiazem hydrochloride encapsulated copolymer was dispersed in sodium alginate, carboxy methyl cellulose and poly vinyl alcohol. Poly vinyl alcohol “Transdermal” patches provided optimum results. Animal studies carried out on rat skin which indicated that there were no histological changes on skin.³⁹

Yamsani *et al.* (2017), prepared and evaluated “Transdermal” patches consisting of Cinnarizine. Various proportions of polymers like HPMC and Eudragit RL100 were used to prepare patches. Solvent evaporation technique was used for patch preparation. Polyethylene glycol 400 was used in form of plasticizer. Drug-excipient compatibility was checked by FT-IR testing. Skin irritation tests were also performed. It was shown by results that flux of 8527.5 gm/cm²/ hr was obtained. It was concluded that polymer Hydroxy propyl methyl cellulose and Eudragit RL100 in combination in ratio 19:1 provided optimum results.⁴⁰

Malipeddi *et al.* (2017), prepared matrix “Transdermal” patches. Metoprolol tartarate was used as drug in the matrix “Transdermal” patches. Blends of Polyvinyl pyrrolidone and Polyvinyl alcohol were employed to prepare “Transdermal” patches. Various physicochemical tests were carried out to evaluate patches. FTIR analysis was done ensure drug excipient compatibility. Optimized patches were tough, non-sticky with better tensile strength. In vitro

drug release studies of patches across skin showed 58 % release and followed zero order kinetics for 24 hours. ⁴¹

Zaman *et al.* (2017), prepared “Transdermal” patches containing Repaglinide and Ramipril. Hydroxypropyl methyl cellulose K4M and ethyl cellulose were used in different proportions were used as film forming polymers. Solvent casting method was used for preparing patches. Penetration enhancers used were oleic acid and propylene glycol. Polyethylene glycol 400 was plasticizer. FTIR studies confirmed any absence of drug-polymer interaction. The prepared patches possessed acceptable mechanical strength. It was observed that drug release pattern was through Korsmeyer-Peppas model. Results shown that there good amount of drug was released from patches in a sustained way. ⁴²

Budhathoki *et al.* (2016), fabricated and evaluated “Transdermal” patches of atenolol. Hydroxy propyl methyl cellulose K4M and Polyvinyl pyrrolidone were used in different proportions as film forming polymers . Solvent casting method was used for preparing patches. 3% propylene glycol was employed as plasticizer. 6 % Tween 80 was used as permeation enhancer. Various physicochemical tests were performed. In-vitro drug release characteristics were studied using Franz diffusion cell . From results it was concluded that patch consisting of 265 mg Hydroxypropyl methylcellulose and 770 gm Polyvinyl pyrrolidone was the best formulation. ⁴³

Niharika *et al.* (2016), prepared and evaluated drug in adhesive type patches of metoprolol succinate. Duro-Tak387-2052, Duro-Tak 387-2051, Duro-Tak 87-2677 were various adhesives used for formulating the patches. Various physical properties of the patches were evaluated. In vitro and ex-vivo drug release studies were also carried out. Albino rats were employed for skin irritation studies. Different concentrations of l-menthol were employed to evaluate effect of penetration enhancers on permeation of drug. From results it was concluded that Duro-Tak 87-2677 containing patches were sufficiently promising in delivering the drug in a sustained manner with good physical patch characteristics. ⁴⁴

Singh & Bali (2016), prepared and evaluated duloxetine hydrochloride “Transdermal” patches. Solvent evaporation method was used method of preparing patches. Hydroxypropyl methyl cellulose and polyethylene glycol-400 as plasticizer was used to form patches. Drug release and skin irritation tests were also performed. No skin hypersensitivity was visible upon application of patch. Results shown that drug was first released after 2 hours of administration and 94 % release was obtained after 24 hours. ⁴⁵

Saleem & Idrees *et al.* (2016), prepared and evaluated “Transdermal” patches of Unani ingredients for antiemetic activity. Solvent evaporation method was used for preparing patches. Physicochemical tests like thickness, weight uniformity, folding endurance, moisture content, drug content and acceptability were analyzed”. Franz diffusion cell was used for in-vitro drug release characteristic study . “Cumulative drug was found to be 77.38 % in 24 hours . ⁴⁶

Bhattacharya & Banerjee *et al.* (2015), prepared and evaluated matrix type “Transdermal” patches of buflomedil hydrochloride. Solvent casting method was used to formulate “Transdermal” patches. Solvent casting method was used to prepare the patches. Physicochemical parameters like thickness, weight variation, moisture content and content uniformity were evaluated. FTIR was used to find out any possible drug-polymer interaction. Results shown that formulated “Transdermal” patches provided good sustained release of drug.⁴⁷

Zhan *et al.* (2015), prepared and evaluated reservoir “Transdermal” patches of isosorbide dinitrate. Patch comprised of five layers a liner, an adhesive, reservoir and backing. The prepared patches were compared with marketed formulations. Cumulative release ratio of commercial patch in 48 hours was up to 89.8 % but prepared patch was 34 %. This meant sustained release time was longer than commercial patch.⁴⁸

Wang *et al.* (2015), prepared and evaluated “Transdermal” patches using aceclofenac. Span-20 and limonene were used as penetration enhancers. Solvent evaporation method was used for preparation. “Transdermal” patches shown high drug content in range 94.9 to 98.2. Flat surface was obtained with good folding endurance i.e 120-182. Enhanced drug release 61.02 to 93.4 % was obtained. “Transdermal” patches had no irritant effect on skin on wistar rats. It was concluded from study that d-limonene provided greater permeation rate of drug as compared to Span 20.³²

Mirza & Lohani *et al.* (2015), prepared and characterized drug within adhesive type “Transdermal” patches. Buflomedil hydrochloride was employed as model drug. Solvent evaporation method was used for fabrication. Duro-Tak 387-2052 was used as adhesive. Isopropyl myristate and oleic acid were employed as permeation enhancers. 3M-Scotchpak-TM-9723 was used as backing membrane. Patch was characterized for weight variation, thickness, moisture uptake, surface pH, folding endurance and bioadhesivity. Patch shown good physicochemical characteristics upon evaluation. It was concluded from result that patch with 95 % adhesive and 10 % isopropyl myristate provided good in vitro drug release. “Transdermal” patches released drug by zero order.⁴⁹

Idrees *et al.* (2014), prepared and characterized matrix type “Transdermal” patches. Flurbiprofen was incorporated in the “Transdermal” patches. Ethyl cellulose was used as film forming polymer. Plate casting method was employed for preparing the patches. Propylene glycol and dibutyl phthalate were used as plasticizers. Span 20, Tween 20, sodium lauryl sulphate, isopropyl myristate and ethanol were investigated as permeation enhancers. It was concluded from results that patches with ethanol and ethylcellulose provided uniform physical characteristics. Higuchi and Korsmeyer -peppas model was applicable through patch.⁵⁰

Solanki *et al.* (2012), prepared and evaluated “Transdermal” system using granisetron hydrochloride. Solvent evaporation technique was used for preparing patches. Eudragit RL100 and Eudragit RS100 were used to form polymer film. Tween 80 and Span 80 were employed as permeation enhancers. Patches formed were found to exhibit good physical characters. Tensile strength, thickness,

content uniformity and folding endurance of the formed patches were satisfactory. In vitro permeation tests were done using Franz diffusion cell. From results it was concluded that, Span 80 shown better permeation as compared to Tween 80.⁵¹

Rajabalaya *et al.* (2012), prepared and evaluated "Transdermal" drug delivery system. Matrix type patches using Ondansetron hydrochloride drug was developed. Eudragit RS100 and polyvinyl pyrrolidone were used to form matrix of patch. Eugenol, castor oil along with triethyl citrate and dibutyl sebacate were employed as plasticizer. It was concluded from evaluation that increasing amount of PVP in the patch led to increased percent of drug release. Dibutyl sebacate containing patches were found to show greater drug release than with triethyl citrate. The optimized patches were shown to be effective in enhancing duration of drug delivery with no first pass metabolism.⁵²

Kshirsagar *et al.* (2012), prepared and evaluated "Transdermal" patches of carvedilol. Solvent casting method was used for preparing patches. Various combinations of polyvinyl pyrrolidone and ethyl cellulose were used to prepare patches. Optimized formulation with ratio 4:1 of polyvinyl pyrrolidone and ethyl cellulose was best for sustained release of drug. Maximum flux of 30 mcg/ cm² was achieved over a period of 24 hours.⁵³

Bhatia *et al.* (2012), prepared and characterized "Transdermal" patches of Pregabalin. Solvent evaporation method was employed. Various polymers and combinations of Hydroxy propyl methyl cellulose, Polyvinyl pyrrolidone, Polyvinyl alcohol, Eudragit RL-100 and Eudragit RS-100 and Ethyl cellulose in different ratios. Dimethyl sulphoxide was employed in form of penetration enhancer. PG was incorporated as plasticizer. Patch was characterized for thickness, weight variation, flatness, tensile strength, folding endurance, moisture content and moisture uptake. In-vitro test and ex-vivo skin penetration were performed. Patch consisting of Hydroxy propyl methyl cellulose and Polyvinylpyrrolidone in combination 3:1 was considered optimum. PG in concentration 5 % w/v was used. Dimethyl sulphoxide in concentration 6% w/v was used in optimized formulation. It was confirmed from results that the optimized formulation could be a good potential for drug delivery.⁵⁴

Subedi *et al.* (2011), prepared and evaluated pressure sensitive adhesive type "Transdermal" patches. Acrylic adhesives were employed as adhesives. Zolmitriptan was used as model drug. Limonene and cineole were the penetration enhancers employed in the patch. It was found from results that acrylic adhesives with hydroxyl functional groups provided excellent adhesion force and good flux.⁵⁵

Rasool *et al.* (2011), prepared and evaluated "Transdermal" patches of Propranolol hydrochloride. Chitosan was used as film forming agent. Evaluation parameters used were drug concentration uniformity, thickness, moisture uptake capacity and skin bio adhesion. Various permeation enhancers were employed and tested for optimum drug release. Skin sensitivity test was also performed. Results confirmed that "Transdermal" patches formed provided good patch characteristics.⁵⁶

Amgaokar *et al.* (2011), prepared and evaluated “Transdermal” patches of Budesonide. Eudragit RL100, Eudragit RS, ethylcellulose and polyvinyl pyrrolidone were employed as film forming agent. Mercury substrate method was used for preparing films. Polyethylene-400 was used as plasticizer. Urea and dimethyl sulphoxide were the two agents test for permeation characteristics. Patches formed were found to possess thickness and drug release characteristics. Upon stability testing, films containing polyvinyl alcohol and Eudragit RL100 provided best opposition to water vapor. It was concluded from the results that this patch upon application to skin of animals provided good drug permeation.⁵⁷

Cho *et al.* (2011), formulated and evaluated “Transdermal” patches containing torasemide. Ethylene vinyl acetate was used to form patch matrix. Various derivatives of propylene glycol, fatty acids, glycerides and pyrrolidones and non-ionic surfactants were used to enhance permeation characteristics of torasemide. Citrate and phthalates were employed for plasticizer action. In vitro drug release studies were studied in a Franz diffusion cell. Highest permeation was achieved using polyoxyrthylene-2-oleyl ether. Optimum plasticity characteristics were achieved using diethyl phthalate.⁵⁸

Hu *et al.* (2011), prepared drug in adhesive “Transdermal” patches. α -asarone was used as model drug. Eudragit E100 was used as film forming polymer. Oleic acid in combination with isopropyl myristate. Various in vitro and in vivo tests were carried out. It was found that a patch of size 4cm² and drug about 3 mg/cm² provided noticeable treatment of asthmatics comparable to dexamethasone.⁵⁹

Prajapati *et al.* (2011), formulated Repaglinide “Transdermal” using various combinations of patch employing HPMC with Polyvinyl pyrrolidone K30. Solvent casting method was employed for fabrication. Optimized batch containing HPMC K100 and PVP K30 was found to give best results among various tried combinations.⁶⁰

Latha *et al.* (2011), used Eudragit RL and Eudragit RS as polymers for preparing matrix type “Transdermal” patches. Domeperidone was used as drug. Various physicochemical properties of the patches were studied. “Transdermal” patch consisting of Eudragit RL and Eudragit RS when used in ratio 8:2 shown optimum concentration. Optimized patch was also tested for any possible hypersensitivity. From the results it could be concluded that the formulated patches could serve as good alternative for providing prolonged effect.⁶¹

Patel, Patel & Baria (2011), prepared and evaluated matrix type “Transdermal” systems incorporating aceclofenac using different proportions of ethyl cellulose (hydrophobic) and hydroxyl propyl cellulose (hydrophillic) as polymers by solvent evaporation technique employing 15 % w/w dibutyl phthalate as plasticizer. Oleic acid and isopropyl myristate were incorporated as penetration enhancers. Various physicochemical tests were performed on the prepare patches. It was confirmed from the results that formulation with oleic acid 15% along with isopropyl myristate showed better penetration of the drug across the skin of rat.⁶²

Mamatha *et al.* (2010), developed “Transdermal” patches of Lercanidipine hydrochloride. Hydroxy propyl methyl cellulose and Eudragit RL100 was employed in different ratios for formulating “Transdermal” patches. Propylene

glycol in concentration 20 % w/v plasticizer. 8 % v/w d-limonene was employed as penetration enhancer. Various evaluation tests were performed on the “Transdermal” patches. Results shown that all the patches had satisfactory physicochemical characters. It was concluded that Eudragit RL100 and Hydroxy propyl methyl cellulose in ratio 1.5: 8.5 along 8 % d-limonene is optimum for “Transdermal” patches. ⁶³

Chauhan & Bajpai *et al.* (2010), prepared and tested patches of Raloxifene hydrochloride. Different combinations of Eudragit RL100, Poly vinyl Pyrrolidone K30, Hydroxy propyl methyl cellulose, Cellulose acetate phthalate and Polyethylene glycol 6000 were employed to prepare matrix. It was inferred from results that patches containing Eudragit RL100 and Polyvinyl pyrrolidone in ratio 6:4 provided good characteristics. ⁶⁴

Bhatt *et al.* (2008), prepared and evaluated matrix “Transdermal” patches of Metoprolol tartarate. Mercury substrate technique was employed for formulation of the patches. Ethyl cellulose and Polyvinyl pyrrolidone was used as forming polymers. Dibutyl phthalate was used as plasticizer. Based on parameter of evaluation results, it was concluded that Higuchi model was applicable. Ethylcellulose and Polyvinyl pyrrolidone in ratio 3:2 produced optimum formulation. Results shown that optimized formulation provide flux of 163.25 mcg/ cm². ⁶⁵

Mukherjee *et al.* (2005), prepared and evaluated “Transdermal” patches consisting of Dexamethasone drug in the patches. Various ratios of Povidone, Eudragit and Ethylcellulose were used for preparing patches. Patches were evaluated for moisture content, moisture uptake. Flatness study was also performed. FTIR studies were carried to identify any possible drug-polymer interaction. Franz diffusion cell was employed to study penetration patterns. As per results it was confirmed that patches consisting of Polyvinyl pyrrolidone and ethylcellulose polymeric blends provided more sustained release as compared to patches with Polyvinyl pyrrolidone and Eudragit polymeric blends. ⁶⁶

Devi *et al.* (2003), prepared and evaluated “Transdermal” patches of verapamil hydrochloride using four different polymers (individual and combination): Eudragit RL100 (ERL100), Eudragit RS100 (ERS100), hydroxypropyl methylcellulose 15cps (HPMC), and ethyl cellulose (EC). Results shown that ERL100 and HPMC in the ratio 8:2 can serve as good prospective combination of polymers”. ⁶⁷ Table 1 summarizes various permeation enhancers that have been explored for transdermal devices.

Table 1
Penetration enhancers used in recent times for transdermal formulations

| Penetration enhancers employed in study | Reference |
|---|-----------|
| d-limonene and oleic acid | 68 |
| 4% tween, 20% propylene glycol, 20% polyethylene glycol, 4% sodium lauryl sulfate | 69 |
| 10% Azone, isopropyl myristate (10,15 & 20%), and 10% menthol | 70 |
| tween 80 (1, 2.5 & 5%), N-methyl pyrrolidone (5,10 & 20%), | 71 |

| | |
|---|----|
| laurocapram (Azone®)(1, 2.5 & 5%), transcutol P (5,10 & 20%), terpineol (2.5, 5 & 10%),and cineole (1,2 & 5%) | |
| capsaicin, dimethyl sulfoxide (DMSO), and N-methyl pyrrolidone (NMP), 1-8-cineole (all 50 mg each) | 72 |
| 5% dill oil, 5% coriander oil, 5% lemon oil | 73 |
| span-60 (0.5 mL), dimethyl sulfoxide (DMSO) (0.5 mL), glycerine(0.5 mL) | 74 |
| turpentine oil, dimethyl formamide (DMF), menthol, dimethyl sulfoxide (DMSO), pine oil, and 2-pyrrolidone | 75 |
| propylene glycol, polyethylene glycol 400, oleic acid, isopropyl myristate | 76 |
| oleic acid, propylene glycol, lemon oil and aloe vera (2 mL each) | 77 |
| Span 20 and DMSO | 78 |

Conclusion & Future Perspective

Transdermal delivery of drugs may be the future of painless injections. It is being investigated as alternative for nano vaccine delivery. Various transdermal devices have already successfully reached market with numerous others in line of launch. This review has briefly reported the research carried by the researchers in this arena recently. Various methods employed have been reported in the paper along with polymers employed for the same.

Although most of the researchers have been utilizing HPMC as the preferred film forming polymer but recently use of Eudragit grades also has gained interest amongst scientists. Keeping in view the future requirements for transforming into laboratory scale patches to be more robust in production on large scale, specifications must be brought up by regulatory bodies. Thus, it can be concluded that this technology of transdermals is aptly being looked as alternate for sustained delivery of medicaments.

Conflict of Interest:

Authors declare no conflict of interest.

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