Biological Forum – An International Journal **15(5): 520-524(2023)**

ISSN No. (Print): 0975-1130
ISSN No. (Online): 2249-3239

An Education on the Previous Successful Attempts at Transdermal Delivery Patches

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(Received: 01 March 2023; Revised: 14 April 2023; Accepted: 18 April 2023; Published: 20 May 2023)
(Published by Research Trend)

ABSTRACT: The objective of the study was to use a factorial design to gather data on prior attempts at transdermal medication delivery devices. Systems for transdermal drug delivery provide the medication for a protracted length of time (days). The authors conducted a thorough Internet search for relevant literature, consulted national and international peer-reviewed publications, and gathered and summarized data from earlier studies on transdermal patches using factorial analysis. The use of QbD is becoming more prevalent compared to conventional trial-and-error techniques. The medicine was released when the transdermal patches, which were of the matrix and membrane types, were externally attached to the skin. Because they decrease the frequency of treatment and improve patient compliance, the study finds that transdermal drug delivery systems are superior formulations for treating chronic illnesses.

Keywords: Drug delivery, Literature, Patch, Permeation, Polymers, Transdermal.

INTRODUCTION

Although the oral route is the most widely used method of drug delivery, it has certain drawbacks, including first-pass metabolism and drug degradation due to enzymes, pH, etc. in the gastrointestinal tract (Bala *et al*., 2013). A unique drug delivery mechanism was created to solve these issues. The transdermal delivery system (TDDS) was used (Ahad *et al.*, 2010; Shravani *et al.*, Swetha *et al.*, 2010). When applied to the skin, these medicated adhesive patches spread the medication across the skin. They come in a variety of sizes and include multiple ingredients. They penetrate skin barriers to transfer active compounds into systemic circulation once applied to intact skin (Jyothika *et al*., 2022). A transdermal patch is applied to the skin and left there for a long time, allowing a high dose of medication to diffuse into the bloodstream (Hindustan *et al*., 2011).

Components of the TDDS. The main components in the TDDS are as follows (Monton *et al.*, 2022; Sailaja *et al.*, 2022):

- Polymer matrix/drug reservoir
- Drug
- Permeation enhancers
- Adhesive
- Backing layer
- Release liner
- Plasticizers
- Solvents

Merits of TDDS. The main outcomes of TDDS are as follows (Dinh *et al*., 2022; Sabbagh & Kim 2022):

- Drug first-pass metabolisms are prevented.
- Digestive incompatibilities are prevented.
- Self-treatment is an option.
- The action's duration lengthens and becomes predictable.
- Negative side effects are reduced.
- The plasma drug concentration remains stable.
- The number of dosages is reduced, which improves patient compliance.
- By eliminating issues with medications, including decreased absorption, GI discomfort, and breakdown owing to hepatic first-pass metabolism, many pharmaceuticals' therapeutic efficacy is boosted.

Demerits of TDDS. The pitfalls of TDDS are as described here (Choudhury *et al.*, 2021):

- Possibilities of allergic reactions such as itching, rashes, local oedema, etc. at the application site.
- Drugs with molecular weights above 1000 have trouble being absorbed.
- On the same or different people, the barrier function of the skin varies from site to site.
- Drugs with hydrophilic properties have lower permeability than drugs with lipophilic properties, making them less suitable.

The past literature on transdermal patches is shown in Table 1.

Table 1: Drugs, and polymers used in the making of transdermal patches using factorial design.

Drug	Permeability Enhancers	Design name	Independent variables	Dependent variables	Reference
Glimepiride and Duloxetine	Ethanol	3^2 Full factorial design (FFD)	Phospholipid (X_1)	entrapment efficiency (EE) (Y_1) particle size (PS) (Y_2)	(Patra, 2022)
Simvastatin	dimethyl sulphoxide (DMSO)	2^3 FFD	Eudragit (X_1) polymer 100 (X_2) ERS100 (X_3)	Flux (Y_1), amount of drug permeated (DP) (Y_2)	(Mishra *et al.*, 2022)
Lercanidipine HCl	linseed oil, jojoba oil, and pumpkin seed oil	3^2 FFD	HPMC K15M (X_1)	Flux (Y_1)	(Upadhye *et al.*, 2022)
Chlorpheniramine maleate	PEG-1000, span-60, and span-80	2^3 FFD	Cholesterol (X_1), span-60 (X_2) and span-80 (X_3)	% yield (Y_1), drug content (Y_2), EE (Y_3), and PS (Y_4)	(Afreen *et al.*, 2022)
Curcumin	DMSO	2^2 FFD	HPMC (X_1), and PVP K30 (X_2)	DP(Y_1), moisture content (Y_2), and folding endurance (Y_3)	(Naik & Mathews 2021)
Ibuprofen	PEG 400, PEG-400, and ethanol	2^2 FFD	PVP (X_1), and HPMC (X_2)	Weight uniformity (Y_1) Thickness (Y_2) and swelling index (Y_3)	(Pratiwi *et al.*, 2020)
Aceclofenac	Propyleneglycol (PG), glycerine, ethanol and oleic acid	3^2 FFD	HPMC (X_1), Methylcellulose (MC) (X_2)	DR (Y_1)	(Sravanthi *et al.*, 2020)
Hesperidin	Dibutyl phthalate (DBP), and glycerin	3^2 FFD	HPMC E5 (X_1), and Eudragit S-100	Weight uniformity (Y_1) Thickness (Y_2) and swelling index (Y_3)	(Bhalerao *et al.*, 2019)
Zinc Oxide	PEG	2^3 FFD	HPMC E5 (X_1), and PEG-400	Weight uniformity (Y_1) Thickness (Y_2) and swelling index (Y_3)	(Kothawade *et al.*, 2019)
Ketoprofen	PG, and Tween 80	3^2 FFD	HPMC E5 (X_1)	Weight uniformity (Y_1) Thickness (Y_2) and swelling index (Y_3)	(Rao *et al.*, 2019)
Valsartan	PG, and PEG-400, DBP, and glycerin	3^2 FFD	HPMCK15M (X_1), and Eudragit RL100 (X_2)	Weight uniformity (Y_1) Thickness (Y_2) and swelling index (Y_3)	(Jani *et al.*, 2019)
Simvastatin	DMSO, and PG	3^3 FFD	Homogenization speed (X_1), and span 80 (X_2)	PS (Y_1), zeta potential (Y_2), and entrapment efficiency (Y_3)	(Brito Raj *et al.*, 2019)
Selegiline HCl and Nicotine	PG	3^2 FFD	Ethyl Cellulose (X_1), and PVP (X_2)	Flexibility (Y_1), drug content (Y_2) and permeation (Y_3)	(Jagtap & Wagh 2018)
5-fluorouracil	PG, and ethanol	2^{5-2} Fractional Factorial Design	Phospholipon®90H (X_1), and Sonication time (X_2)	vesicle size(X_1) and %EE (Y_2)	(Paradkar & Patel 2018)
Atorvastatin	PG	FFD	EudragitE100 (X_1), and PVP K30 (X_2)	Drug content (Y_1) and thickness (Y_2)	(Castañeda *et al.*, 2017)
Ropinirole HCl	PEG 400	3^2 FFD	PEG-400 (X_1), and HPMC K4M (X_2)	DR (Y_1)	(Nannaware & Chemate 2017)
Dexibuprofen	Ethanol	3^2 FFD	HPMC (X_1), and PVP K30 (X_2)	Weight uniformity (Y_1), Folding endurance (Y_2), tensile strength (Y_3), % Flatness (Y_4), moisture content (Y_5) and moisture absorption (Y_6)	(El-Houssieny *et al.*, 2016)
Atenolol	Tween 80	2^3 FFD	PVP(X_1) HPMC K4M(X_2)	DR at 2 h (Y_1), DR at 4h (Y_2), DR at 6h (Y_3) and DR at 8h (Y_4)	(Budhathoki *et al.*, 2016)
Ormeloxifene	PG, and PEG-400	3^2 FFD	Polydimethyl siloxane (X_1), and EC(X_2)	Flux (Y_1), Permeability coefficient (Y_1), DP at 32 h (Y_3)	
Diltiazem HCl	PG, and tween-80	3^2 FFD	weight ratio (X_1) concentration of pumpkin seed oil (X_2)	Tensile strength (Y_1) DR at 1 h (Y_2) and DR at 16 h (Y_3)	(Gupta *et al.*, 2016)
Rivastigmine tartarate	Tween 80	3^2 FFD	Eudragit RS100 (X_1) Eudragit RL100 (X_2)	Folding Endurance (Y_1) and DR (Y_2)	(Patel & Jani 2016)
Buflomedil HCl	PG	3^2 FFD	Span 40 (X_1), Span 60 (X_2), and Span 80	DR at 10 h (Y_1)	(Kesharwani *et al.*, 2016)
Heparin sodium	PEG 400	3^2 FFD	isopropyl myristate (X_1) and oleic acid (X_2)	DR at 24h (Y_1)	(Akhtar *et al.*, 2015)

Propranolol	DMSO, butyl-oleate (BUOL), and ethyl-oleate (ET-OL)	2^4 FFD	matrix thickness (X_1) matrix type(X_2), drug concentration (X_3), and skin penetration enhancer concentration (X_4)	Flux (Y_1) and DR at 24 h (Y_2)	(Patel *et al.*, 2014)
Carvedilol	DBP, and Tween 80	2^3 FFD	PMMA (X_1), and DMSO (X_2)	DR at 1h (Y_1), DR at 4h (Y_2), DR at 8h (Y_3) and DR at 20h (Y_4)	(Cilurzo *et al.*, 2014)
Verapamil HCl	DBP, and ethanol	2^3 FFD	Eudragit RL 100 (X_1), Eudragit RS 100 (X_2), HPMC (X_3) and EC (X_4)	DR at 24 h (Y_1)	(Oza *et al*., 2013)
Acyclovir	PEG-400, tween 80, DBP and glycerin	3^2 FFD	Jackfruit mucilage (X_1), and Tween 80 (X_2)	Folding endurance (Y_1), and DR (Y_2)	(Aparna *et al.*, 2013)
Pioglitazone HCl	DMSO	3^2 FFD	Eudragit NE 30D (X_1), and DMSO (X_2)	DR at 10h (Y_1), DR at 24 h(Y_2)	(Kusum Devi *et al.*, 2003)
Glipizide	triethyl citrate	3^2 FFD	HPMC (X_1), and EC(X_2)	DR (Y_1)	(Bhoyar *et al.*, 2015)
Amlodipine Besylate	Glycerine	3^2 FFD	sodium alginate (X_1), and sodium starch glycolate (X_2)	DR at 6h (Y_1),	
Felodipine	Tween-80, methanol, and PG	3^2 FFD	Ethanol(X_1), and lecithin (X_2)	EE (Y_1), DR at 24h (Y_2)	
Ondansetron HCl	PG	2^2 FFD	HPMC (X_1) and Eudragit RL 100 (X_2)	DR at 12 h (Y_1)	(Shelke *et al*., 2012)
Desloratadine	PG	3^2 FFD	HPMC 6 cps (X_1), and PG (X_2)	DR at 24h (Y_1)	(Mishra *et al*., 2012)
Repaglinide	PEG400, and PG	3^2 FFD	HPMC (X_1), and PVP K30 (X_2)	DR at 1h (Y_1), DR at 9h (Y_2)	(Denge *et al*., 2012)
Ketorolac tromethamine	Ethanol	3^2 FFD	PVP (X_1) and EC (X_2)	Permeation flux (Y_1), DR at 8 h (Y_2)	(Trivedi *et al.*, 2011)
Gliclazide	PG	3^2FFD	HPMC (X_1), Eudragit RL 100 (X_2), and Chitosan (X_3)	DR at 12 h (Y_1)	(Prajapati *et al*., 2011)
Polymethylmethacrylate	PEG-400, and glycerin	2^4 FFD	PEG 400 (X_1), Glycerin (X_2), and sorbitol (X_3)	Tack (Y_1), holding power (Y_2), *in vivo* skin contact duration (Y_3)	(De *et al.*, 2011)
Propranolol HCl	PEG-400	3^2 FFD	Eudragit L-100 (X_1), and PVP K30 (X_2)	DR (Y_1)	*(Shinde et al.*, 2010)
Aceclofenac	Oleic acid and glycerol	3^2 FFD	Oleic acid (X_1) and Isopropyl myristate (X_2)	DR at 8h (Y_1)	(Cilurzo *et al.*, 2010)
Tramadol HCl	triethyl citrate	3^2 FFD	HPMC (X_1), and Eudragit S 100 (X_2)	DR at 12 h (Y_1)	(Patel *et al.*, 2007)

CONCLUSIONS

Transdermal technology (TDDS) was widely acknowledged as the creation of a mass delivery methodology, making it the preferred drug injection modality for transdermal delivery across skin types while avoiding first-pass metabolism and other sensitivities linked to various alternative drug administration routes. Drugs may be distributed uniformly at predetermined and controlled rates with TDDS since it is non-invasive, not allergenic, and has a predetermined duration and dose delivery technique. In the pharmaceutical industry, TDDS technology is expanding quickly and has been successful in seizing significant market value as a formulation technique that can enhance drug administration via topical channels.

FUTURE SCOPE

To improve the patients' health in the future, these efforts should be expanded to other hospitals as well.

Conflicts of Interest. None.

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How to cite this article: Bariki Rajasekhar and Haranath Chinthaginjala (2023). An Education on the Previous Successful Attempts at Transdermal Delivery Patches. *Biological Forum – An International Journal, 15*(5): 520-524.