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Research Article

FORMULATION AND EVALUATION OF GLIMEPIRIDE PATCHES FOR TRANSDERMAL DRUG DELIVERY

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ABSTRACT

Transdermal drug delivery has been accepted as a potential non-invasive route of drug administration, with advantages of prolonged therapeutic action, less side effect, easy use and improved patient compliance. "Glimepiride is an anti-diabetic drug with a shorter half life of ~5 hours, low bioavailability and extensive first pass metabolism due to these limitations required to maintain the therapeutic level it has chosen as transdermal drug delivery system." The present study was to formulate and evaluate transdermal drug delivery system of Glimepiride using polymers such as HPMC & Eudragit RS100 by solvent casting technique. Central composite design (CCD) was applied by using design-expert to optimize composition of HPMC and ERS100 for Transdermal Drug Delivery. The prepared formulations were evaluated for different physicochemical characteristics like Weight Variation, Folding Endurance, Flatness, pH of patches, % Moisture Content, % Moisture uptake, % Elongation, % Drug Content & % Drug Release. The drug release characteristics of the formulation were studied *in-vitro* by using semi-permeable membrane. The *in-vitro* drug release plot **"showed "** that the drug release followed zero order kinetics & Higuchi model, which was evidenced from the regression values. Based on the drug release and physicochemical values obtained from the formulation F_3 is considered as an optimized formulation which shows higher percentage of drug release (97.33±0.26% at 24 hour) with diffusion mediated mechanism. Korsmeyer-Peppas exponential plots shows fairly linear add, it is well supported by their regression **coefficient** values & slope value (n) were **more than 1** which suggest that drug was released by Super Case-II transport.

Key words: Transdermal Patches, Transdermal Drug Delivery, Glimepiride, Solvent Casting Method, Central Composite Design & Anti- Diabetic Patches.

Introduction

Introduction starts from next sentence currently, --

Currently, transdermal drug delivery is one of the most prominent way for drug delivery to the systemic circulation via skin[1]. The transdermal route offers several advantages over conventional dosage forms such as tablets and injections, including avoidance of first-pass metabolism by the liver[2], minimization of pain, reduction of side effects, extended duration of activity, reduction in the fluctuations of drug concentrations in the blood, avoidance of gastro-intestinal incompatibility[3], reduced frequency of dosing with improved patient compliance and rapid termination of drug input by removal of the system from the skin[4, 5].

Diabetes mellitus continues to increase in terms of the number of affected and in significance worldwide, and is a growing burden with regard to public health. It is reported that there were 285 million people worldwide with diabetes in 2010, and this number is expected to increase 439 million by 2030[6]. It is a chronic metabolic disorder characterized by a high blood glucose concentration (hyperglycemia) caused by insulin deficiency, and it is often combined with insulin resistance[7].

Glimepiride a third-generation sulfonylurea drug, is effective for the treatment of Type 2 diabetes mellitus[8] and acts by stimulating pancreatic β-cells to produce more insulin and lower the blood glucose level (BGL). It has shown several advantages

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such as being highly protein bound, long acting and allowing for concomitant use with insulin. However, the drawback for the use of Glimepiride as oral dosage forms is attributable to its low aqueous solubility and slow dissolution rate, which lead to low oral bioavailability[9,10]. The molecular weight of glimepiride is 490.616 g/mol with an octanol/water partition coefficient of 3.5. It is completely absorbed after oral administration[11], short half-life of ~5 hours due to the extensive hepatic oxidative metabolism to its major metabolite, cyclohexylhydroxymethyl derivative (M1)[12,13]. Recently, a study has indicated that sustained delivery of Glimepiride through a transdermal route can helps to avoid toxicity due to a sudden high blood concentration.This study was undertaken to screen the potential of Glimepiride for transdermal delivery.

The purpose of the present work was to develop transdermal formulation of Glimepiride which increases the patient compliance and enhance the bioavailability by using polymers and permeation enhancers.

MATERIALS & METHODS

Materials

Glimepiride was obtained as a gift sample from USV Limited(Khed, Ratnagiri, Maharashtra, India), HPMC K100M from Colorcon Asia Pvt. Ltd., (Goa, India). Eudragit RS100(ERS100) from Evonik India Pvt. Ltd(Mumbai, India), Propylene Glycol & Polyethylene Glycol(PEG)-400 from Nulife Pharmaceutical, (Pune, India), Dimethylsulfoxide(Suresh Traders-LaBin, Pune), Double Distilled water was used throughout the study & all other chemicals and solvents were analytical reagent grade and purchased from commercial suppliers. The results obtained were analyzed for various pharmacokinetic parameters using pk functions of Microsoft excel & GraphPad Prism (Version 5.00 GraphPad Software Inc. San Diego, California, USA).

Methods

Drug–Polymer Interaction Studies

To search the possible interaction between Glimepiride and polymeric materials of the patches, infrared (IR) spectra of pure substances and their formulation (F_7) were recorded using IR Spectrophotometer (FTIR-4100 JASCO- Japan) by KBr pellet method[14,15].

Preparation of Transdermal Patches

Glimepiride loaded transdermal patches containing different ratios of HPMC K100M and Eudragit RS100 were prepared by solvent casting method. The requisite ratios of polymers were weight and were allowed to swell for 6 h in Methanol–Dichloromethane (1:1) solvent mixture. Plasticizer such as PEG-400 was incorporated at 30% w/w of dry polymer weight. & Permeation enhancer such as Propylene glycol & Dimethylsulfoxide (DMSO) was incorporated at 40% (1:1) w/w of polymer dry weight. Calculated amount of Glimepiride was mixed with homogenous polymer solution and poured into aluminum foil wrapped glass ring as mold (28.26 cm^2). A funnel was placed over the mould in inverted position to control the rate of evaporation. The casting solvent mixture was allowed to evaporate overnight at room temperature. The dried patches were cut into required size (3.14 cm^2) and wrapped in aluminum foil. Then, these Patches were kept in desiccator containing saturated solution of $CaCl_2$ as desiccant, at room temperature prior to use[16, 17].

Experimental Design:

A response surface type Central Composite Design was employed using Design-Expert Software (Version 7.0.0 Stat-Ease Inc., Minneapolis, USA). Independent factors are HPMC K100M (X_1) and Eudragit RS100(X_2) concentrations at three levels[18,19]. % Moisture Content (Y_1), % Moisture uptake(Y_2), % Elongation(Y_3), & % Drug Release after 24 hours(Y_4) were kept as dependent variables[18,19]. The different formulations of Glimepiride Transdermal Patches is as shown in Table-I.

Table 1: Different formulation batches are as follows.

Code	Drug	Polymer		Plasticizers	Enhancers	Name of Solvents	Quantity
	Glimepiride	HPMC K100M	Eudragit RS100	PEG-400	PG:DMSO (1:1)	DCM: Methanol	
F_1	90.00 mg	250.00 mg	300.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_2	90.00 mg	150.00 mg	600.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_3	90.00 mg	200.00 mg	237.87 mg	30 % w/w	40 % w/w	1:1	15 ml
F_4	90.00 mg	200.00 mg	662.13 mg	30 % w/w	40 % w/w	1:1	15 ml
F_5	90.00 mg	129.29 mg	450.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_6	90.00 mg	270.71 mg	450.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_7	90.00 mg	200.00 mg	450.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_8	90.00 mg	250.00 mg	600.00 mg	30 % w/w	40 % w/w	1:1	15 ml
F_9	90.00 mg	150.00 mg	300.00 mg	30 % w/w	40 % w/w	1:1	15 ml

Note: 3.14 CM^2 Patch Contains 10 mg Glimepiride. DCM: Dichloromethane, PG: Propylene Glycol

EVALUATION OF TRANSDERMAL PATCHES

Weight Variation

Prepared patches were cut into 3.14 cm^2 pieces and weight of each patch was determined by using digital balance. The average weight of each patch and standard deviations were calculated[20, 21].

Folding Endurance

A strip of Patch of specific surface area (2 cm^2) was cut and folded repeatedly at one place till it broke. The number of times the patch was folded before breaking at the same place represented folding endurance[22, 23].

Flatness

Longitudinal strips were cut out from the prepared patch, the length of each strip was measured, and then variation in the length due to the non-uniformity in flatness was measured. Flatness was calculated by measuring constriction of strips, and a 0% constriction was considered to be 100% flatness[24, 25].

Constriction (%) = $L_1 - L_2 / L_1 \times 100$

Where, L_1 = Initial length of each strips and L_2 = Final length of each strips.

Surface pH

For the determination of surface pH three patches of each formulation were allowed to swell for 2 hrs in a petridish containing 5 ml of phosphate buffer pH 7.4[26]. The surface pH was measured by pH paper placed on the surface of patches and allowed to equilibrate for 1 min. The average of the three readings was recorded[27].

Percentage of Moisture Content

The prepared patches were weighed and kept in desiccator containing activated silica at room temperature for 24 h**.** The individual patches were weighed on every alternate day until a constant weight was achieved. The percentage of moisture content was calculated by determining the difference between initial and final weight with respect to final weight[28-30].

Moisture Content (%) = $W_1 - W_2 / W_2 \times 100$

Where, W_1 = Initial weight of each patch and W_2 = Final weight of each patch

Moisture Uptake

Glimepiride Transdermal patches were weighed and placed in desiccators containing a saturated solution of sodium chloride at 74% relative humidity (RH). After first week, the patches were taken out and weighed. The percentage of Water Absorptive Capacity (Moisture Uptake) was calculated as the difference between the final and initial weight with respect to the initial weight[31, 32].

Moisture Uptake (%) = $W_2 - W_1 / W_1 \times 100$

Where, W_1 = Initial weight of each patch and W_2 = Final weight of each patch

Percentage of Elongation

Elongation of the Patches was determined by Texture Analyzer (Brookfield-CT3-10KG). Rectangular strips of 40mm×30mm were fixed in such a way that the length of patch between the jaws. The percentage elongation was determined by noting the length just before the break point and substituted in the following Equation[33, 34].

Elongation (%) = $L_1 - L_2 / L_2 \times 100$

Where, L_1 = Final length of each strips and **L_2** = Initial length of each strips.

Determination of Drug Content

Formulated drug-loaded Patches were evaluated for uniformity of drug content. Strips of 3.14 cm^2 from each formulation were randomly selected and transferred into a 100 ml volumetric flask containing pH 7.4 phosphate buffer and Methanol. The flask was stirred for 4 h on magnetic stirrer[35]. A blank was similarly prepared using a drug-free Patch. The obtained solutions were filtered through a 0.45 µm membrane. The drug content was then determined after proper dilution by UV spectrophotometer at 231 nm (JASCO V-630, Japan)[36].

In Vitro Drug Release Study

Drug release studies were performed with freshly prepared patches in Franz diffusion cells with volume of 27 ml and a diffusion area of 4.90 cm^2. The receptor compartment contained pH 7.4 Phosphate Buffer containing 30 % v/v PEG-400 as solubilizer[37], at 37°C by a circulating water bath (corresponding to 32 ^{0}C at the release interface) and was stirred at 50 rpm with a magnetic stirrer. Circular patches (diameter: 2.00 cm, patch thickness: approximately 0.35 mm to 0.51 mm) were centrally attached to circular piece of cellulose acetate membrane with a diameter of 2.5 cm. The cellulose acetate membrane was mounted between the donor and receptor compartment of the diffusion cell. The 1 ml samples were withdrawn at different time intervals and an equal amount of phosphate buffer, pH 7.4 was replaced each time. Absorbance of the samples were measured spectrophotometrically at 231 nm taking phosphate buffer solution, pH 7.4, as blank The experiment was performed in triplicates and the mean values were calculated[38-41].

RESULT AND DISCUSSION

Drug–Polymer Interaction Studies

The incompatibility between the Drug Excipients were studied by FTIR spectroscopy. The spectral data of pure Glimepiride, HPMC K100M, ERS100 and Glimepiride Transdermal Patch (F_3) are presented in Fig.01-04. The results indicate that there was no chemical incompatibility between drug and excipients used in formulation.

FTIR spectra of Glimepiride

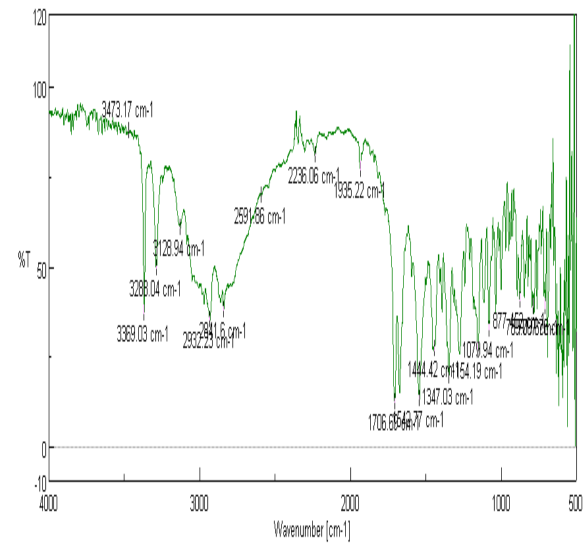

Fig: 01: FTIR spectra of Glimepiride

FTIR spectra of HPMC K100M

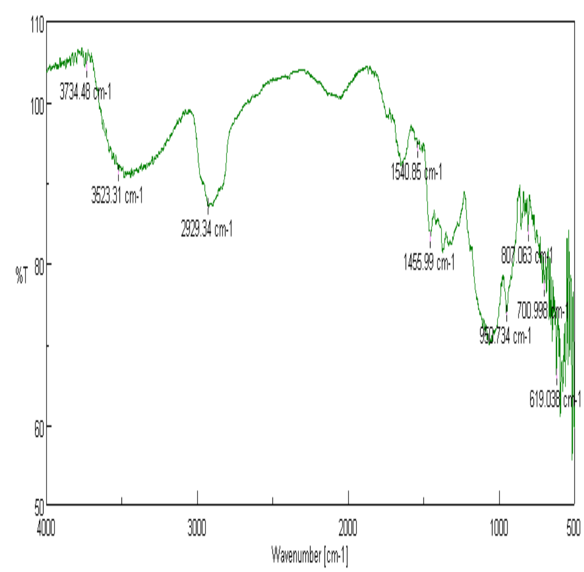

Fig: 02: FTIR spectra of HPMC K100M

FTIR spectra of Eudragit RS100

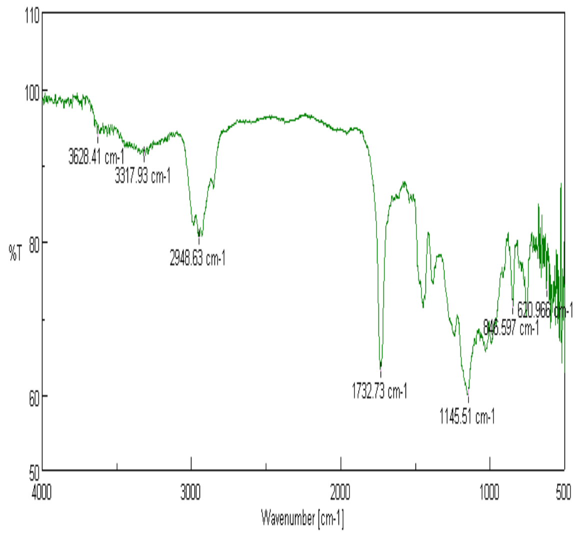

Fig: 03: FTIR spectra of Eudragit RS100

FTIR spectra of Glimepiride Transdermal Patch (F_3)

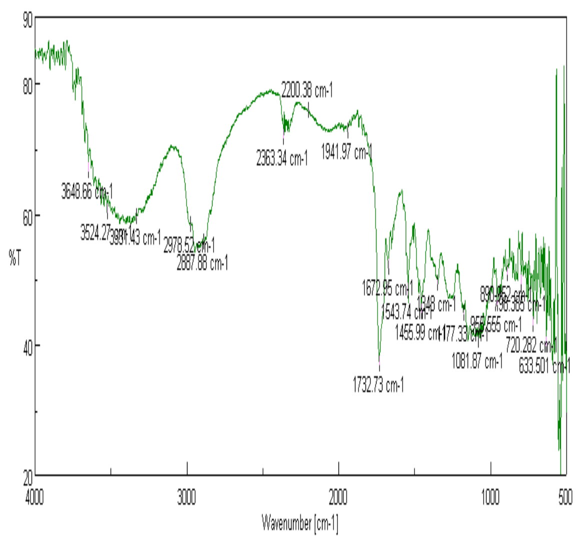

Fig: 04: FTIR spectra of Glimepiride Transdermal Patch (F_3)

Weight Variation

The weight of patches ranged between 70.66±1.15 mg and 105.66±0.57 mg, which indicates that different batches patch weights, were relatively similar. The individual weights of patches within the same formulation varied only slightly as shown by the low standard deviations. The average weight of the Patches increased with increased concentration of the polymers used in producing the Patches as shown in Table –II [42].

Folding Endurance

The values of folding endurance were found to vary from 257±4.04 to 289±4.50 which indicates good strength and elasticity. The folding endurance test results (Table-II) showed that the Patches prepared from all formulations were more flexible and durable. These results demonstrates the sturdiness of the patches in maintaining their integrity with general skin folding when applied.

Flatness

Flatness (%) of these patch formulations were found satisfactory, which ranged between 99.75±0.66 and 100.16±0.38 % (Table-II). The results of the flatness study showed that the formulation Patches have a negligible change in the length along the longitudinally cut edges, indicating a near 100% flatness. The patches from all tested formulations appeared to have a smooth, flat surface and that smooth surface could be maintained when the patch was applied to the skin without any visible signs of constriction[43].

Surface pH

For a dermatological preparation to be safe and nonirritant its pH must be between 4 and 7[44]. Surface pH Determination was mainly done to know whether the patch is acidic or basic. Irritation will persist if the Patch is more acidic or basic. Surface pH of the transdermal patches was in between 5.33±0.57 and 6.66±0.57 (Table-II) which match to the pH of the skin, infers that the patch is nonirritant & desirable property45.

Table 2: Physicochemical Properties of Glimepiride Transdermal Patches.

Formulation	Weight Variation (mg)	Folding Endurance	Flatness (%)	Surface pH	MC (%)	MU (%)	Elongation (%)	Drug Content (%)
F_1	75.66±1.52	263±2.08	99.83±0.38	6.00±1.00	4.11±0.05	7.34±0.04	23.33±1.44	99.67±0.11
F_2	95.00±1.00	281±3.05	99.91±0.38	6.33±0.57	2.75±0.10	4.90±0.20	35.83±3.81	99.61±0.19
F_3	70.66±1.15	257±4.04	100.16±0.14	5.66±0.57	3.07±0.13	5.59±0.23	21.66±1.44	99.74±0.11
F_4	105.66±0.57	289±4.50	99.83±0.14	6.66±0.57	3.43±0.00	6.38±0.21	40.83±1.44	99.48±0.22
F_5	79.33±1.52	265±1.52	99.91±2.50	5.66±1.15	2.30±0.06	3.94±0.23	32.50±2.50	98.95±0.40
F_6	92.33±0.57	274±3.05	99.75±0.66	6.33±0.57	4.73±0.08	9.76±0.27	27.50±2.50	99.21±0.39
F_7	85.66±1.15	269±4.16	100.16±0.38	5.66±1.15	3.25±0.05	6.14±0.17	29.16±1.44	98.62±0.19
F_8	102.33±1.15	283±5.50	99.91±0.14	5.66±0.57	4.49±0.12	8.04±0.06	34.16±1.44	98.76±0.22
F_9	72.66±1.52	259±5.13	100.16±0.38	5.33±0.57	2.58±0.00	4.70±0.28	25.83±1.44	99.28±0.30

*All values are expressed as mean ± SD (n = 3). MC: Moisture content & MU: Moisture uptake

Experimental Design, Regression Analysis and Model Building

The central composite design was selected for optimization because central composite design require 5 levels of each factor -α, -1, 0, 1, and +α. One of the commendable attributes of the central composite design is that its structure lends itself to sequential experimentation. A statistical model incorporating interactive and polynomial terms were used to evaluate the responses.

$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_{12} + b_{22}X_{22}$ ------- (1)

One way ANOVA (analysis of variance) was used for statistical analysis of targeted response at 5% significant level and the significance of model, factors were determined using Design- Expert. In above equation, b_0 is the intercept representing the arithmetic averages of all 9 runs and b_1, b_2, b_{12}, b_{11} and b_{22} are the coefficients computed from the observed experimental values of responses Y_1 , Y_2, Y_3 & Y_4 and X_1 and X_2 stand for main response of independent variables. The terms X_1X_2, X_{11} and X_{22} represent interaction and quadratic terms of independent variables respectively[18, 19].

The factor effects involved in CCD model and associated p-values (table-III) for the responses Y_1, Y_2 & Y_3 are given. The model F- value of 58.60.36 for Y_1 implies the model is significant and there is only 0.01% chance that a "Model F-Value" this large could occur due to noise. Values of Prob > F less than 0.0500 indicate model terms are significant. In this case X_1, X_2 & X_1^2 are significant model terms. The Model F-value of 358.57 for Y_2 implies the model was significant. In this case X_1 & X_1^2 were significant model terms. The Model F-value of 44.77 for Y_3 implies the model was significant. In this case X_1 & X_1^2 were significant model terms. The Model F-value of 71.84 for Y_4 implies the model was significant. In this case X_2 were significant model terms. After eliminating insignificant terms the final equation of the responses (2-5) are as follows

$Y_1= +2.81-0.011 X_1-1.441 X_2+6.598 X_1X_2+6.212 X_1^2+1.121 X_2^2$ ---------(2)

$Y_2= +3.76-0.022 X_1+3.159 X_2+1.635 X_1X_2+1.245X_1^2-5.278 X_2^2$ -----------(3)

$Y_3=+30.14-0.073X_1+1.061X_2+2.777X_1X_2+8.332X_1^2+3.703X_2^2$ ------------(4)

$Y_4= +103.14+0.053 X_1-0.043 X_2-1.35-004 X_1X_2-2.700 X_1^2+1.177 X_2^2$ ---(5)

Positive sign in front of the factors indicates synergistic effect and negative sign indicates antagonistic effect of the factors on responses Y_1, Y_2, Y_3 & Y_4.

Table 3: Effect of each factor and its p-value.

Factor	Response parameters							
	Y_1		Y_2		Y_3		Y_4	
	Factor effect	*p* -value	Factor effect	*p* -value	Factor effect	*p* -value	Factor effect	*p* -value
X_1	+0.84	< 0.0001	+1.75	< 0.0001	-1.40	0.0061	-0.94	0.0899
X_2	+0.13	0.0003	+0.25	0.0746	+5.99	< 0.0001	-8.99	< 0.0001
X_1X_2	+0.049	0.1289	+0.12	0.4945	+0.21	0.6966	-1.02	0.1764
X_1^2	+0.16	0.0002	+0.31	0.0466	+0.21	0.6087	-0.067	0.8990
X_2^2	+0.025	0.2850	-0.11	0.3882	+0.83	0.0693	+0.27	0.6215
R^2	0.9933		0.9480		0.9600		0.9672	

Moisture Content & Moisture uptake

Moisture content and Moisture uptake studies provide information regarding stability of the formulation[46]. The % moisture content in the patches ranged from 2.30±0.06 to 4.73±0.08. The % moisture uptake in the formulations were in the range of 3.94±0.23 to 9.76±0.27 (Table-II). The results revealed that the Moisture Content (Y_1) & Moisture Uptake (Y_2), factor X_1 was found to be significant (< 0.05) i.e., as the concentration of HPMC increased, the Moisture Content (Y_1) & Moisture Uptake of the patches also increased. But, opposite effect was observed by increasing the amount of ERS100. Further, the interaction between factors X_1 and X_2 can be elucidated by using response surface plot as illustrated in Figure 5 & 6[47]. The low level of moisture content in the formulation helps to remain stable and from being a completely dried and brittle films and low moisture uptake protects the material from microbial contamination and bulkiness of the patches[48].

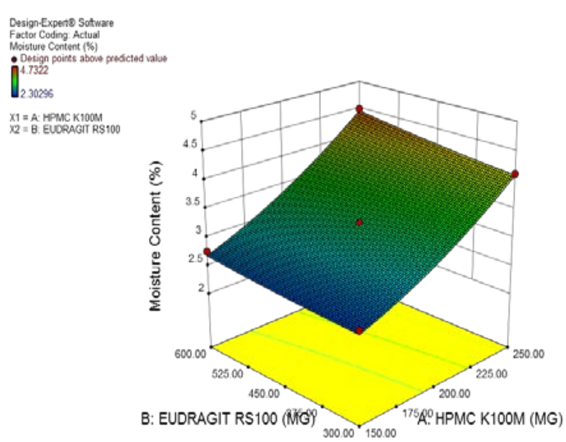

Figure: 05: Response surface for Moisture Content

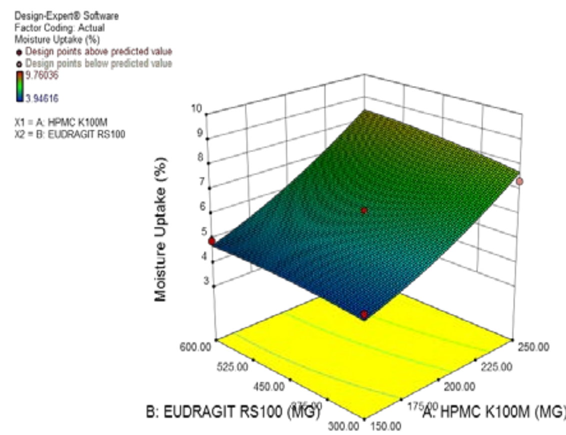

Figure: 06: Response surface for Moisture Uptake

Percentage of Elongation

Percentage Elongation at break of the formulations prepared from combination HPMC K100M & ERS100 at different ratios which ranged between 21.66±1.44 % to 40.83±1.44 % (Table-II). The prepared patches were also found to be strong enough & provide good mechanical properties. In the case of % elongation (Y_3), factor X_1 was found to be significant (< 0.05) i.e., as the concentration of HPMC increased, the % elongation of the patches also decreased. But, opposite effect was observed by increasing the amount of ERS100. Further, the interaction between factors X_1 and X_2 can be elucidated by using response surface plot as illustrated in Figure 7.It was also observed that the percentage elongation at break values increased with increasing concentration of ERS100 polymer[33, 49].

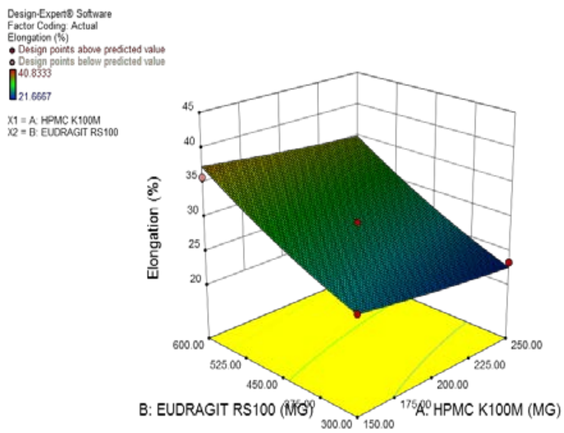

Figure: 07: Response surface for % of Elongation

Drug Content

The drug content (%) in all prepared formulations varied between the range 98.62±0.19 % to 99.74±0.11 %. This indicates that the uniform reproducible drug release from the patch [36] Uniformity of drug distribution throughout the patch was proved by the low value of SD (Table-II).

In Vitro Drug Release

The *in vitro* drug release pattern of Glimepiride from formulated transdermal patches are shown in Fig. : 09-12. All these transdermal patches slowly released the drug, incorporated and sustained over a period of 24 h. The drug release from transdermal patches varied with respect to the polymer composition and nature. In the case of *In vitro* drug release at 24 h (Y_4), factor X_1 was found to be significant (< 0.05) which shows increase in drug release from the transdermal patches was found with increasing concentration of polymers that are more hydrophilic in nature. But, opposite effect was observed by increasing the amount of ERS100. Further, the interaction between factors X_1 and X_2 can be elucidated by using response surface plot as illustrated in Figure 8[42,50]. Among all formulations, the maximum *in vitro* drug release (97.33±0.26%) over a period of 24 h was observed in the case of formulation No. F_3, while the minimum i*n vitro* drug release (70.99±0.20%) was found in the case of formulation No. F_4 which shows that the Increased concentration of Eudragit RS100 decreases the drug release. The *in vitro* Glimepiride release data from transdermal patches were evaluated kinetically using various mathematical models like zero-order, first order, Higuchi, and Koresmeyer–Peppas. The results of curve fitting into these above mentioned models (Figure: 09-12) indicates the drug release behavior from these formulated transdermal patches of Glimepiride at 24 h (Table-IV). When the release rate of Glimepiride and their respective correlation coefficients were compared, it was found to follow zero-order kinetic (R^2=0.997 to 0.999), First Order (0.809 to 0.970) and Higuchi models (R^2=0.997 to 0.999) (Table-IV). In order to understand the mechanism of drug release, *in vitro* release data were treated to kinetic models and linearity was observed with respect to zero-order kinetic & Higuchi equation. As indicated by higher values R^2, the drug release from all the formulations follows Zero-order drug release and Higuchi model. Therefore it was confirmed as zero-order kinetic & Higuchi model and the mechanism was found to be sustained release diffusion mediated. The above formulations treated for Korsmeyer-Peppas exponential plots (fig.12) were found to be fairly linear & it is well supported by their regression coefficient values (0.946 to 0.964) (Table IV). The slope values (n) was also calculated & they are >1(Table IV) which suggest that drug was released by Super Case-II transport.

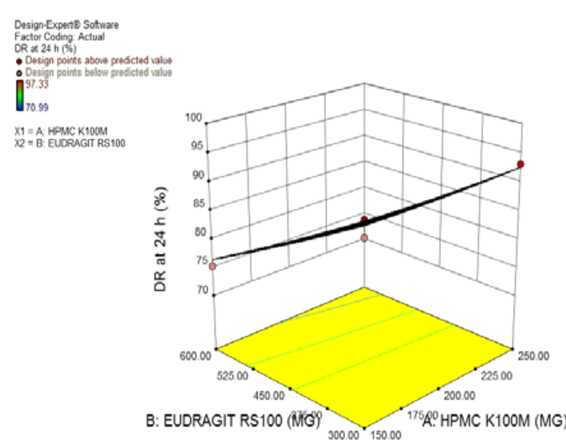

Figure: 08: Response surface for *In Vitro* release

Table 4: *In Vitro* drug Release of Glimepiride Transdermal Patches

Formulation	% Drug Release after 24 hrs*	Zero Order	First Order	Higuchi's	Korsmeyer-Peppa's	
		R^2			R^2	n
F_1	93.13±0.20	0.998	0.873	0.998	0.946	1.120
F_2	75.32±0.13	0.999	0.970	0.999	0.962	1.117
F_3	97.33±0.26	0.999	0.809	0.999	0.948	1.137
F_4	70.99±0.20	0.997	0.956	0.997	0.964	1.089
F_5	86.50±0.20	0.998	0.919	0.998	0.956	1.125
F_6	80.49±0.26	0.999	0.954	0.999	0.957	1.115
F_7	83.32±0.59	0.999	0.944	0.999	0.958	1.126
F_8	73.77±0.27	0.999	0.970	0.999	0.963	1.112
F_9	90.61±0.33	0.999	0.910	0.999	0.951	1.128

*All values are expressed as mean ± SD (n = 3).

- **Zero order plots for Prepared Glimepiride Transdermal Patches(F_1-F_9)**

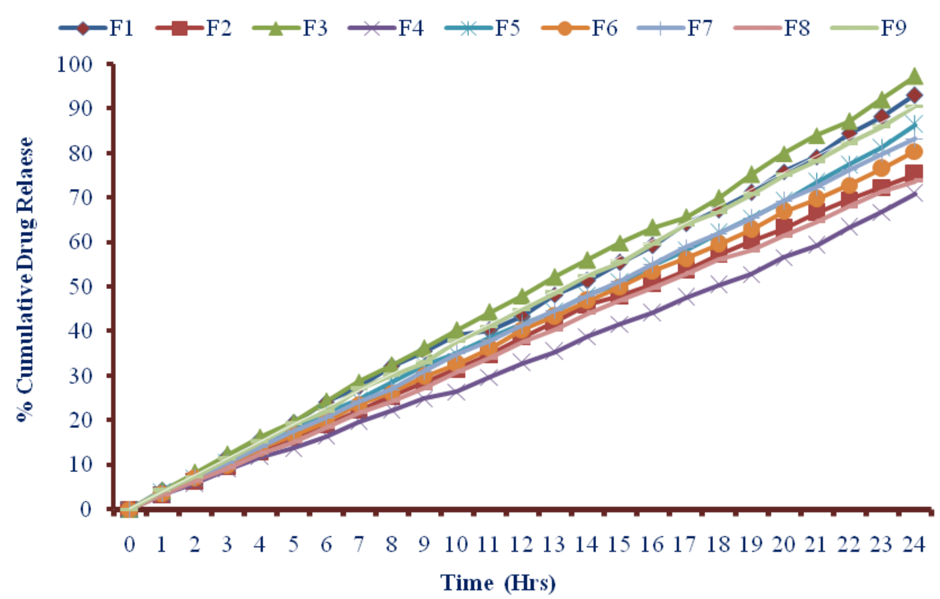

Fig: 09: Zero Order Plots for Glimepiride Transdermal Patches

- **First order plots for Prepared Glimepiride Transdermal Patches(F_1-F_9)**

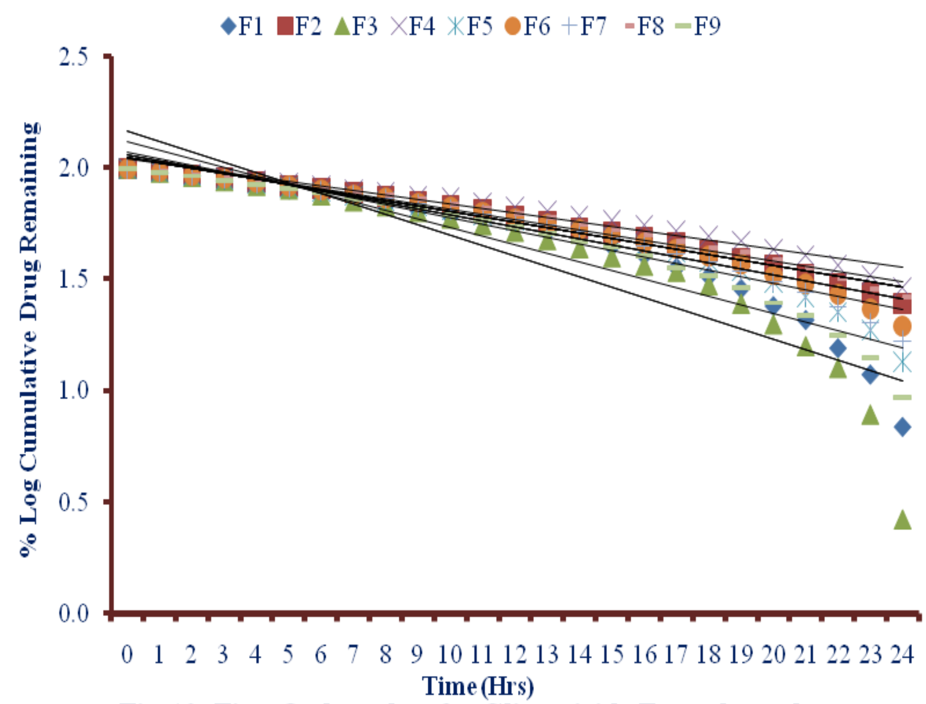

Fig:10: First Order plots for Glimepiride Transdermal Patches

- **Higuchi's plots for Prepared Glimepiride Transdermal Patches(F_1-F_9)**

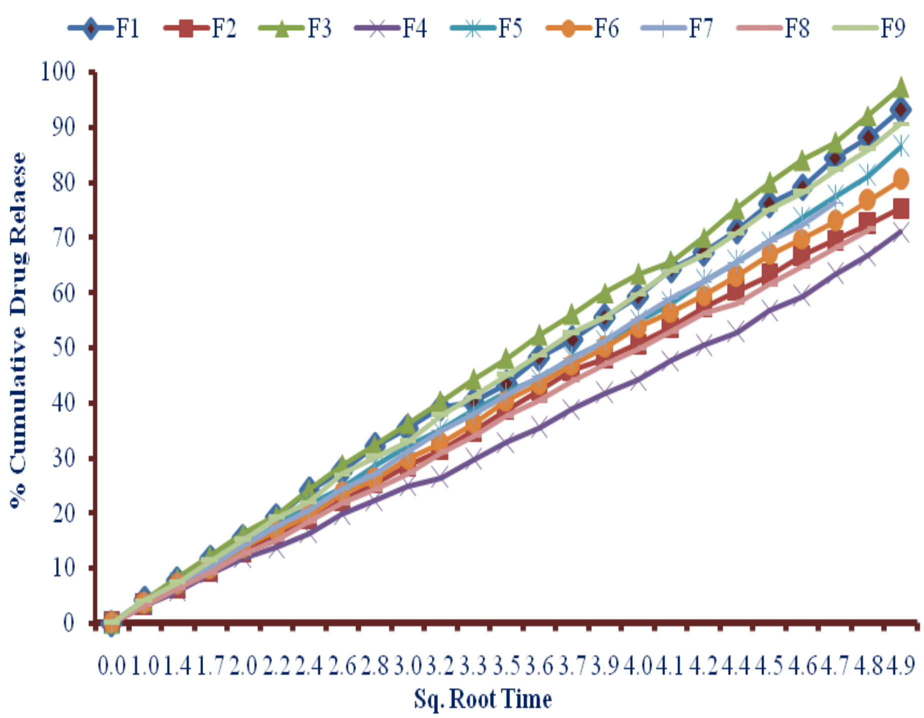

Fig:11: Higuchi's plots for Glimepiride Transdermal Patches

- **Korsmeyer- Peppa's Plots for Prepared Glimepiride Transdermal Patches(F_1-F_9)**

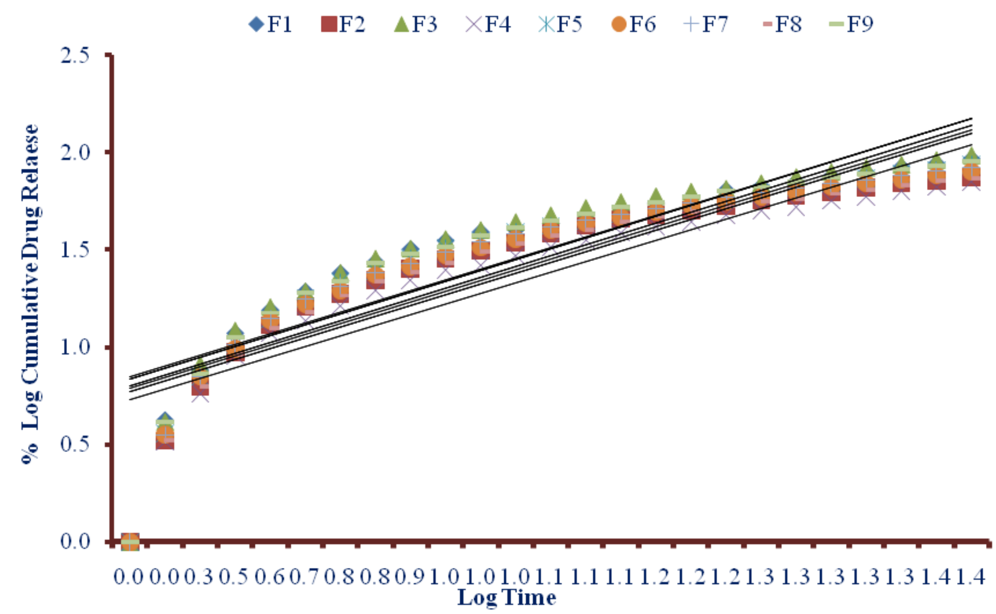

Fig:12:Peppa's plots for Glimepiride Transdermal Patches

CONCLUSION

Transdermal patches of Glimepiride using polymers like HPMC and ERS100 in various proportions and combinations showed satisfactory physicochemical characteristics. The proportional amounts of various hydrophilic polymers in various formulations have influence on drug release from these formulated Glimepiride transdermal patches. From the present study it can be concluded that, Transdermal drug delivery system for Glimepiride with HPMC K100M and Eudragit RS100 meet the ideal requirement for Transdermal devices which can be good way to bypass the extensive hepatic first pass metabolism and increase bioavailability. Transdermal patches of Glimepiride may provide sustained transdermal delivery for prolonged periods in the therapy of Diabetics, which can be HPMC and ERS100 of moderate level useful for preparation of sustained release matrix transdermal patch formulation. Further, from the above findings it can be concluded that formulation F_3 is the best formulation which is substantiated by its higher *in vitro* drug release.

COMPETING INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper

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