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Formulation And Evaluation Of Vildagliptin Transdermal Patch

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ABSTRACT: Transdermal drug delivery systems have gained significant attention as an effective alternative to conventional oral administration for various therapeutic agents. In this study, we aimed to develop and evaluate transdermal patches of vildagliptin, a potent dipeptidyl peptidase-4 (DPP-4) inhibitor used in the management of type 2 diabetes mellitus. The transdermal patches were prepared using a combination of polymers, including hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), sodium alginate, permeation enhancer dimethyl sulfoxide and glycerine as plasticizer and formulated into F1 to F6 formulations. Various formulation parameters were optimized to achieve a patch with desirable physicochemical properties, such as flexibility, drug content uniformity, and adhesion to the skin. The formulated patches were evaluated for various parameters, including thickness, weight variation, drug content, moisture content, folding endurance, tensile strength, and in vitro drug release studies. The optimized formulation demonstrated excellent drug content uniformity, desirable thickness and good adhesion to the skin. In vitro drug release studies demonstrated sustained drug release over a period of 24 hours, indicating the potential of the transdermal patches for providing prolonged drug delivery. The developed transdermal patches of vildagliptin showed promising results in terms of physicochemical properties, drug release, and skin irritation. These patches hold potential as an alternative approach for delivering vildagliptin, offering sustained drug release and improved patient compliance in the management of type 2 diabetes mellitus. The drug Vildagliptin

Keywords: Transdermal patches, Type2 diabetes mellitus, Sustained drug release, Vildagliptin, DPP-4 inhibitor, Polymers, Permeation enhancer, Bioavailability, Incretin, Insulin.

I. INTRODUCTION:

The arrival of modern drug delivery system, transdermal drug delivery system recognized itself as an integral part of novel drug delivery systems. Transdermal patches arethe pharmaceutical drug delivery systems of polymeric formulations intended to deliver medications which when applied on skin deliver the drug at a predetermined amount through the dermis into the bloodstream to achieve system effects. Transdermal patches are thin, adhesive patches that typically contain a reservoir or matrix containing the active ingredient(s) that are slowly released over an extended period. These patches are generally prepared by using synthetic or natural polymers by "SOLVENT CASTING METHOD".

As we keep our centre of attention on common disease in our society, many people were suffering from acute or chronic diabetes. To conquer this issue, we chose the anti-diabetic drug "Vildagliptin". Diabetes is a chronic medical condition that effects how your body processes blood sugar (glucose). There are several types of diabetes, but the two most common ones are Type-I and Type-II diabetes. The drug vildagliptin works only on type-II diabetes and should not be used in patients with type-I or diabetic ketoacidosis. Type-II diabetes is a metabolic disorder characterized by insulin resistance and beta-cells dysfunction and inadequate production of insulin. Vildagliptin belongs to the class of drugs known as "Dipeptidyl peptidase-4" (DDP-4) inhibitor, hence used for the management of type-II diabetes mellitus

Vildagliptin works by inhibiting the enzyme DPP-4, which is responsible for the breakdown of incretin hormones. Incretin hormones such as glucagon-like peptidase-1 (GLP-1) and glucose dependent insulinotropic polypeptide (GIP). By inhibiting DPP-4, vildagliptin increases the levels

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of these incretin hormones in the bloodstream. By increasing the levels and prolonging the action of GLP-1 and GIP. Incretin hormones stimulate the release of insulin from pancreatic beta cells. Insulin is responsible for promoting the uptake of glucose from the blood stream into cells, thereby lowering blood sugar or glucose levels. On an over view, the drug vildagliptin promotes insulin release, inhibits glucagon release and slows gastric emptying, all of which contribute to lower blood glucose levels. It is important to note that vildagliptin primarily acts when blood glucose levels are elevated, such as after meals.

Our main aim to choose the drug vildagliptin in transdermal patch is to provide prolonged drug action and to increase its bioavailability. As vildagliptin is present in tablets, it shows decreased action and lower bioavailability. Where as in transdermal patches, it directly entraps into site of action through the skin by reducing dose dumping, side effects and prolonged action with increased bioavailability. We selected Vildagliptin drug over other drugs due to its advantages like efficacy, weight neutrality, low risk of hypoglycaemia, well tolerated and renal safety. Vildagliptin gets metabolized in the liver and approximately 85% of the dose excreted in the urine. The polymers used in the formulations are Hydroxypropyl methyl cellulose (HPMC), Sodium alginate, Sodium carboxymethyl cellulose (CMC). Glycerine acts as a plasticizer. DMSO is used as it acts as permeation enhancer. Ethanol is used to avoid or eliminate air bubbles.

Transdermal dosage forms, though an alternative to conventional formulations, are becoming popular because of their exclusive advantages. Controlled absorption, more uniform plasma levels, improved bioavailability, reduced side effects, painless and simple application and flexibility of terminating drug administration by simply removing the patch from the skin are some of the potential advantages of transdermal patches.

MATERIALS: Drug – Vildagliptin, Polymer – Hydroxypropyl methyl cellulose (HPMC), Sodium alginate, Sodium carboxymethyl cellulose (CMC), Plasticizer – glycerine, Solvent – Ethanol, water.

II. METHODOLOGY:

INGREDIENTS	F1	F2	F3	F4	F5	F6
Vildagliptin(mg)	20	20	20	20	20	20
Hydroxypropyl methyl cellulose(mg)	500	300	-	-	-	-
Sodium alginate(mg)	-	-	500	600	-	-
Sodium carboxymethyl cellulose(mg)	-	-	-	-	400	500
Glycerine (ml)	1	1	1	1	1	1
Ethanol (ml)	1	1	1	1	1	1
DMSO (ml)	0.1	0.1	0.1	0.1	0.1	0.1
Water (ml)	1.5	1.5	1.5	1.5	15	1.5

Table-1: Formulation Table

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DEVELOPMENT OF TRANSDERMAL PATCHES BY SOLVENT CASTING METHOD:

PROCEDURE:

Transdermal patch was prepared by solvent casting method. Measured amount of drug was dissolved in water in a beaker. In another beaker, polymerwas dissolved in water and stirred on magnetic stirrer at 200-400 rpm, 37 °C for 15 minutes. The dissolved drug was added slowly to the viscous polymeric solution. After 5 minutes, glycerine and dimethyl sulfoxide (DMSO) was added. To avoid air bubbles, ethanol was added. Slowly transfer the solution to the petri dish and spread the solution evenly. Place the funnel in an inverted position on the petri dish. Place the petri dish at room temperature for 24 hours. This results in formation of dried transdermal patch.

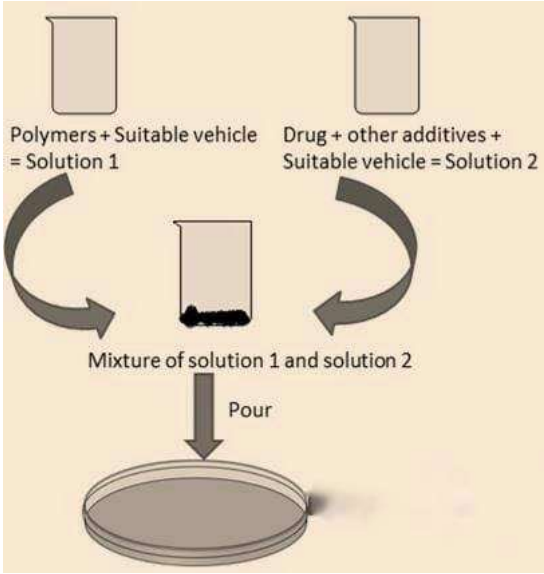

Fig 1: Solvent casting method.

Fig 2a: Magnetic stirrer Fig 2b: Transdermal patch

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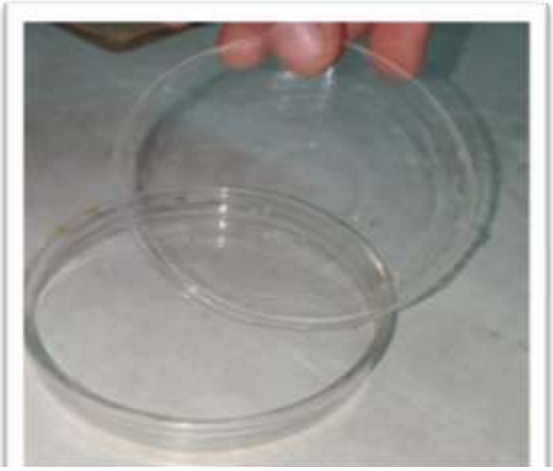

Fig 2c: Transdermal patch

III. EVALUATION PARAMETERS OF TRANSDERMAL PATCH:

3.1 Weight variation:

The prepared patches are to be dried at room temperature for 24hrs before testing. A specified area of 2 cm^2 of patch is to be cut in different parts of the patch and weigh in digital balance.

3.2Thickness:

The thickness of the patch was assessed by using digital verniercaliper at different points of the patch. From each formulation three randomly selected patches were used. The average value for thickness of a single patch was determined.

3.3 Folding Endurance:

The patch of specific area (2cm ×2cm) was cut and repeatedly folded in the same place until it broken and hence the folding endurance was obtained.

3.4 Drug Content:

A specified area of patch (2cm×2cm) was dissolved in 100ml of phosphate buffer solution of pH 7.4 and stir continuously with the help of shaker. After filtration the drug was estimated by UV spectrophotometer at 233nm and determined the drug content.

3.5 Surface pH:

The surface pH of the specified patch was determined by placing the pH meter in close contact with the wetted surface of patch. The pH of selected patch was measured using a pH meter.

3.6 Percent Moisture content:

The patches were weighed individually and kept in a desiccator containing activated silica at room temperatures for 24hr. Individual patch were weighed repeatedly until they show constant weight. Percentage moisture content was calculated by using subsequent formula:

3.7 Percent Moisture uptake:

Percent moisture content= Initial weight- final weight/ final weight×100

Percentage moisture uptake= Final wt – initial wt/ initial wt×100

The patches were also subjected to moisture uptake studies by exposing the patches to 84% RH and ambient temperature in a desiccator containing saturated solution of potassium chloride until a constant weight was achieved. Then the patches were weighed and percentage moisture

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uptake was calculated by using the following formula:

IV. RESULTS AND DISCUSSION:

4.1 Organoleptic properties of drug:
The colour, odour and taste of the drug were characterized and recorded using descriptive terminology; the results are shown in Table2.

S.NO	PARAMETER	OBSERVATIONS
1	Colour	White
2	Odour	Odourless
3	Appearance	White crystalline powder

Table-2: Results of organoleptic properties of Vildaglipt

4.2 Solubility of drug:

S.NO	SOLVENT	SOLUBILITY
1	Methanol	Freely soluble
2	Ethanol	Slightly soluble
3	Distilled water	Very slightly soluble
4	chloroform	Soluble
5	Buffer 7.2	Slightly soluble

Table-3: Solubility of vildagliptin.

4.3 Drug polymer compatibility studies:

Drug- Excipient interactions play an important role in the release of drug from formulations.Vildagliptin with IR grade KBr was scanned over a range 400-4500 cm-1 using FTIR instrument .The drug exhibits peaks due to carboxylic group, alcohol group, secondary amine and C=O Stretching in COOH and CONH. The main peaks of Vildagliptin were present in mixture of drug and polymerand no change in main peaks of drug IR spectra in a mixture of drug and polymers was found. Drug-Excipient compatibility studies by FTIR revealed no interaction between drug and the polymers used in the formulation thus showing compatibility.

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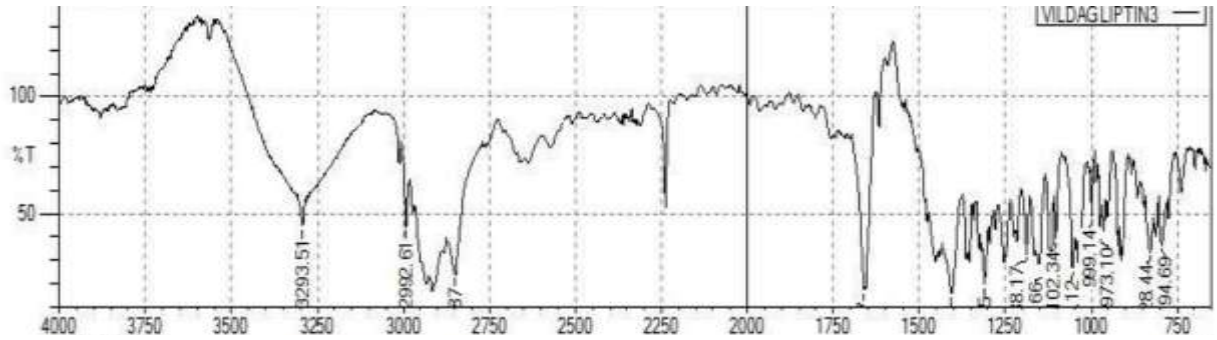
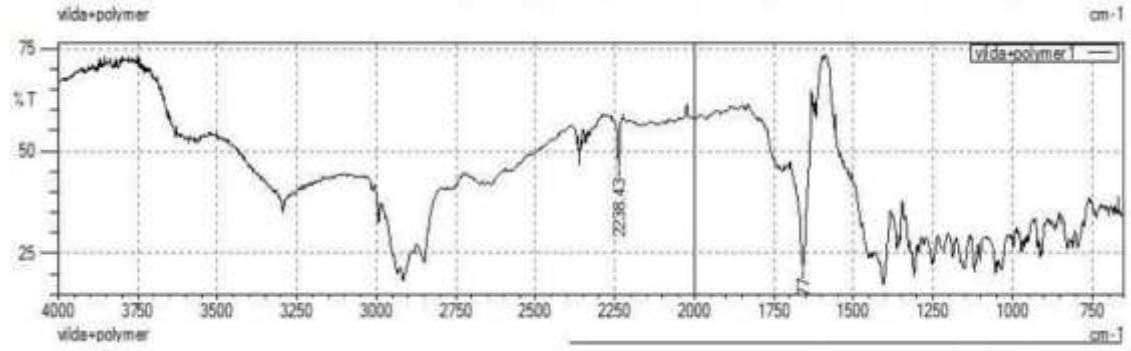


Graph-1: FTIR spectra of pure drug vildagliptin



Graph-2: FTIR spectra of vildagliptin and polymer

4.4 In vitro drug release study:

In vitro drug release studies of Vildagliptin patch formulation through Frans diffusion cell showed slow and sustained release of drug up to 8hrs.

Time	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	18.68	12.40	14.68	15.65	13.96	15.75
2	31.92	17.60	19.92	26.89	23.79	24.96
3	47.67	23.40	26.39	44.60	40.28	35.94
4	58.92	34.90	38.90	55.75	54.27	52.96
5	67.25	49.37	57.85	63.27	62.19	61.27
6	78.84	59.21	63.96	72.47	70.16	72.96
7	89.65	75.78	81.25	83.70	84.59	82.67
8	96.86	90.27	93.94	93.78	91.25	93.68

Table-4: In vitro drug release.

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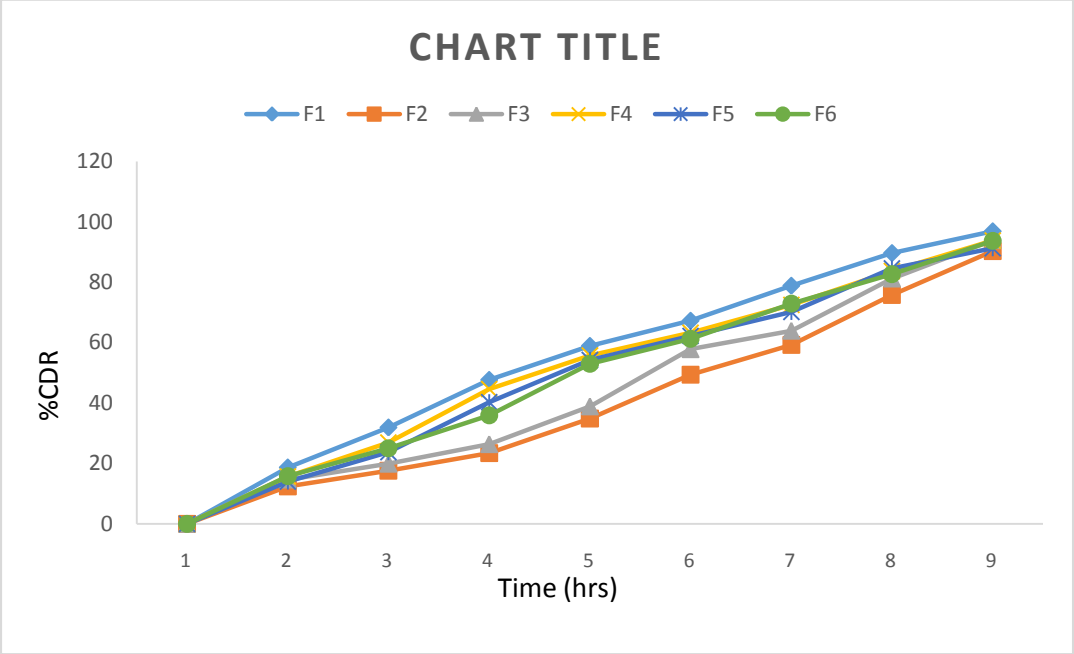


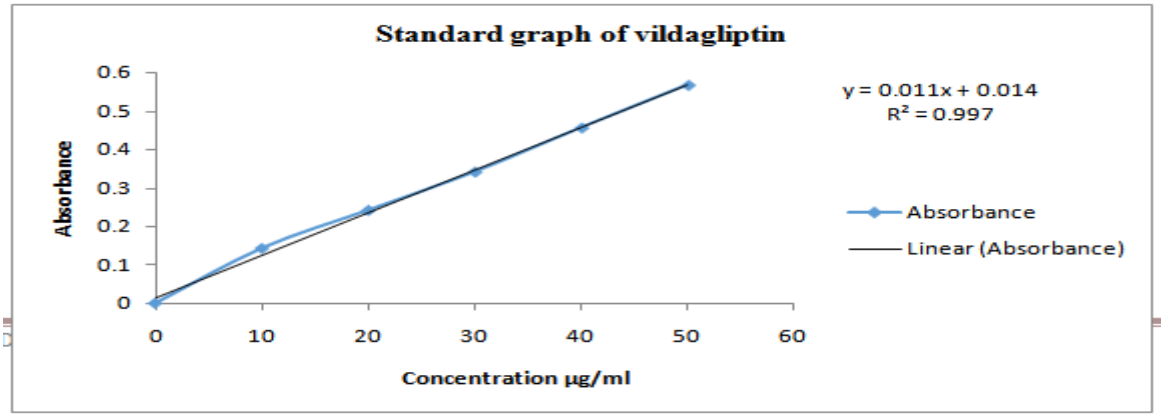
Graph-3: In vitro drug release.

4.5 Calibration curve:

The analytical wavelength and calibration data of vildagliptin in 7.4 phosphate buffer was determined. The λ max was found to be 233nm. The calibration curve for vildagliptin is given in graph 4.

Drug concentration (µg/ml)	**Absorbance**
0	0
10	0.143
20	0.242
30	0.342
40	0.457
50	0.568

Table-5: Standard graph of vildagliptin



Graph-4: linear regression analysis for standard curve.

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4.6 Entrapment efficiency:
Entrapment efficiency is the parameter in which the amount of drug entrapped is vildagliptin can be determined.

Table-6: Entrapment Efficiency

Formulation	Drug entrapment efficiency
F1	92.67
F2	80.59
F3	85.96
F4	89.67
F5	90.18
F6	91.52

4.7 Stability Studies:
There are no significant changes in physical and chemical properties of the formulation 1 after 30 days. Parameters qualified at various time intervals are shown below-

Time in days	**Drug content (%)**	**Folding endurance**	**PHYSICAL APPEARENCE**	**% CUMULATIVE DRUG RELEASE**
0	92.67	45	No change in colour	96.86
30	92.05	47	No change in colour	96.67

V. CONCLUSION:

The aim of this research was to formulate Vildagliptin incorporated transdermal patches for anti-diabetic action to reduce side effects and prolonged drug action with increased bioavailability. By using solvent casting method F1 to F6 formulations were prepared. Formulations were developed by using different polymers at different ratios. Among all the six formulations F1 formulation was found to be satisfactory formulation with 96.86% drug release. The FTIR studies shows that there is no interaction between the excipients and drug. Formulations were developed by using different polymers at different proportions. Among all the polymers HPMC has given the best satisfactory results. The present study concludes that transdermal patch containing vildagliptin, enhances the drug permeation, increased bioavailability and prolongeddrug action with decreased side effects.

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