JOURNAL OF SCIENTIFIC RESEARCH IN ALLIED SCIENCES
ISSN NO. 2455-5800
Contents available at www.jusres.com

Formulation and Evaluation of Metformin loaded Transdermal Patch for the treatment of Diabetes

Rishabh Gupta, Mr. Rajeev, Dr. Sanjar Alam
Department of Pharmaceutics, R. V Northland Institute, Greater Noida, Uttar Pradesh 201306

ARTICLE INFO

Article History
Received: May 2026
Accepted: June 2026

Keywords: Metformin; Transdermal Patch; ICH Q1A (R2) guidelines; Polymer content; Skin.

Corresponding Author
***Rishabh Gupta**

ABSTRACT

ORIGINAL RESEARCH ARTICLE

Metformin, an oral antidiabetic agent, is gaining increasing potential therapeutic indications due to its pleiotropic activity and favorable effects on various pathological conditions, including prediabetes, T1DM, and GDM. Studies have shown that metformin is safe and well-tolerated, and may have cardioprotective and nephroprotective effects. The study aims to develop and evaluate a Metfromin loaded transdermal patch for diabetes treatment. The study investigates the identification and characterization of drugs, including their color, odor, pH, taste, and texture. It identifies Metformin, a drug with a solubility of 1mg/ml in various solvents and a lipophilic nature. The absorption maxima of Metformin were determined using UV scans and calibration curves. The transdermal patch evaluation included thickness, weight variation, hardness, tensile strength, folding endurance, moisture uptake, and drug content. The physiochemical properties of the prepared formulation were also discussed. In vitro drug permeation and diffusion were conducted using Franz diffusion cell, with the maximum permeation found in the F5 patch. The stability studies of the optimized formulation were conducted according to ICH Q1A (R2) guidelines. The results showed optimum drug release up to 24 hours, with smaller pores in the matrix derived from patches tending to fuse readily in the skin. Polymer content resulted as a barrier for drug release, allowing controlled release and decreased drug leakage.

1. INTRODUCTION

Metformin, one of the oldest oral antidiabetic agents and still recommended by almost all current guidelines as the first-line treatment for type 2 diabetes mellitus (T2DM), has become the medication with steadily increasing potential therapeutic indications. A broad spectrum of experimental and clinical studies showed that metformin has a pleiotropic activity and favorable effect in different pathological conditions, including prediabetes, type 1 diabetes mellitus (T1DM) and gestational diabetes mellitus (GDM). Moreover, there are numerous studies, meta-analyses and population studies indicating that metformin is safe and well tolerated and may be associated with cardioprotective and nephroprotective effect (1-5). Recently, it has also been reported in some studies, but not all, that metformin, besides improvement of glucose homeostasis, may possibly reduce the risk of cancer development, inhibit the incidence of neurodegenerative disease and prolong the lifespan. This paper presents some arguments supporting the initiation of metformin in patients with newly diagnosed T2DM, especially those without cardiovascular risk factors or without established cardiovascular disease or advanced kidney insufficiency at the time of new guidelines favoring new drugs with pleotropic effects complimentary to glucose

control. Moreover, it focuses on the potential beneficial effects of metformin in patients with T2DM and coexisting chronic diseases (6, 7). The study aims to develop and evaluate a Metfromin loaded transdermal patch for diabetes treatment. The patch is designed as a self-contained dosage form, delivering the drug at a controlled rate to the systemic circulation. This system avoids first-pass metabolism and enhances bioavailability. It also aims to improve patient compliance by avoiding hazards and discomfort associated with parenteral therapy. The patch provides longer therapy with controlled plasma levels, reducing repeated dosing intervals and potential side effects. It maintains therapeutically effective concentrations over a prolonged period and is non-invasive, free from contamination and irritant compared to parental therapy. The goal is to provide a safer and more effective treatment option for diabetes.

2. MATERIALS AND METHODS

2.1 Drugs

Metformin, HPMC (w/v), Polyehtylene glycol, and Casting Solvent are available from Maan Pharmaceuticals Pvt Ltd., India, Central Drug House, New Delhi, and Polyehtylene glycol, New Delhi.

2.2 Formulation of Transdermal Patches

A matrix Transdermal patch containing herbal derivative compounds in different ratios using solvent casting technique. The patch was prepared by dissolving polymers and plasticizers in solvents, then transferred to a glass bangle wrapped in aluminum foil. The patches were left undisturbed for 24 hours, then retrieved intact and stored in a desiccator for further evaluation. The patch consists of drug, polymers, and plasticizer to optimize formulation development. The patch was prepared using mercury as a substrate and prepared by dissolving polymers and plasticizers in solvents. The patches were then retrieved intact and stored in a desiccator for further evaluation (Table 1) (8, 9).

Table 1: Formulation composition of Transdermal Patch

Ingredients	Formulation Batches				
	F1	F2	F3	F4	F5
Drug (mg)	500	500	500	500	500
Polymer: HPMC (w/v) (mg)	0.5	1	1.5	2	2.5
30% $^{w}/_{w}$ Plasticizer : (Polyehtylene glycol) (ml)	5	4	3	2	1
Casting Solvent (q.s.) (ml)	10	10	10	10	10

2.3 Evaluation of Metformin loaded Transdermal Patches

Transdermal patches are a method of drug delivery that allows for controlled, slow release of medication through the skin, bypassing the digestive system. The unique formulation of these patches allows for drug penetration through the skin barrier. Design considerations include material selection, size, shape, and thickness. Characterization tests assess drug content uniformity, adhesive properties, permeation rate, and stability to ensure consistent doses over time (10-15).

2.4 Evaluation of Anti Diabetic Potential of Transdermal Patches (F5)

The Wistar rats weighing (Male; 150-200 gm) were selected and housed in propylene cages with free access to water and standard rat pellet diet. Water was given ad libitum during the entire period of the study. They were maintained at a temperature of 25±1℃ and a relative humidity of 45-55% with a 12 hr light or dark cycle. They were acclimatized to the laboratory conditions before carrying out experimental work in a well-ventilated animal house under natural photoperiod conditions for a period of 1 week. The hair on back side of the rat was removed completely on

the previous day of the experiment. Rats were divided into four groups, each group comprised of 5 male rats. Group I was considered as a Normal group, received vehicle only Group II was considered as Disease control group, received 0.1 M citrate buffer (pH 4.5).in distilled water was used as a vehicle. Group III was considered as Standard treatment group (Metformin 500 mg/kg) Group IV was considered as Test treatment group received Optimized transdermal patch (F5) (16, 17).

Group	Group Name	Treatment	No. of Animals
G-I	Normal Control	NPD + Saline	5
G-II	Diabetic control rats	STZ	5
G-III	Standard treated Group	Metformin 500 mg/kg, orally	5
G-IV	Optimized Transdermal Patch (F5)	Metformin 500 mg/kg, Transdermally	5

2.5 Statistical analysis

All the data would be finally analyzed by appropriate statistical tests and test of significance, multiple comparisons, etc. One way ANOVA was used to test the significant difference between the 7 lab groups. The experimental trials were repeated for three times and the average values of the concerned parameters are communicated as means ± S.E.M, n=8 in each group. It is observed F ratio with p-value less than 0.05 of Student's t-test are statistically significant. The examination of the current recorded data has been carried through using MS excel and Graph Pad Prism software.

3. RESULTS AND DISCUSSION

3.1 Evaluation of Metformin loaded Transdermal Patches

The Thickness has been found to be in the range of 0.429 to 0.512 mm. The Weight Variation has been found to be in the range of 141 to 148 gm. The Hardness has been found to be in the range of 244 to 248 Pascals. The Tensile Strength has been found to be in the range of 0.5080 to 0.5727 Kg/m3. The Folding Endurance has been found to be in the range of 267 to 270 units. The Moisture Uptake has been found to be in the range of 5.013 to 5.050 %. The Drug content has been found to be in the range of 89±0.3 to 90±0.5 %. The values for all the formulations are tabulated in the graph. (Figure 1-6; Table 2)

Table 2: Physiochemical properties of prepared formulation

Patches	Thickness (mm)	Weight uniformity (mg)	Hardness (Pascal)	Tensile Strength (Kg/m^3)	Folding endurance	Moisture uptake	Drug content (%)
F1	0.4297±02028	141.7±1.202	244.0±2.082	0.5080±0.5773	267.3±0.6667	5.013±0.8819	79.80±0.4583
F2	0.4657±0.2848	147.7±0.8819	246.0±2.517	0.5197±0.1202	266.7±0.8819	5.020±0.1528	80.63±0.9770
F3	0.4970±0.2646	144.7±0.578	247.0±0.5774	0.5780±0.5773	266.3±1.856	5.040±0.2646	80.27±0.4978
F4	0.5040±0.1528	141.0±0.878	246.0±1.155	0.5690±0.8819	270.0±1.010	5.060±0.3055	80.53±1.048
F5	0.5127±0.1202	148.0±0.619	248.0±0.5774	0.5727±0.8889	270.0±0.5774	5.050±0.3786	80.23±0.7839

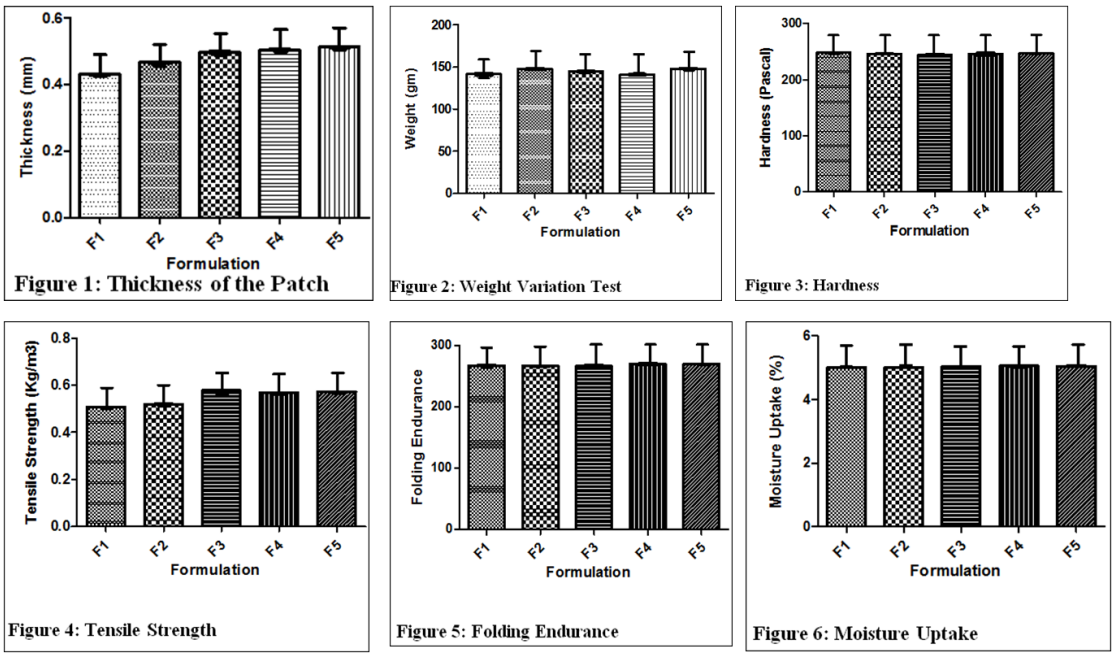

Figure 1-6: Different Parameters showing the Characteristics of Transdermal Patches

3.3 In vitro Drug Release Study

Optimized batch showed steady state diffusion through 24 hours. This slow diffusion rate will maintain the concentration of Extract drug up to 24 hours. The cumulative percent drug was released from formulation batch of F1, F2, F3, F4 and F5 were 59.200 ± 0.6004. 61.350 ± 0.5501, 79.050 ± 0.5492, 89.100 ± 1.000 and 96.250 ± 0.6515 respectively. The maximum percent cumulative drug release was shown by F5 formulation. It is clear that the patches showed optimum drug release up to 24 hrs. The permeation data fitted in zero order drug release indicating controlled release of the Extract from the formulations. It is observed that smaller pores size in the matrix derived from patches tend to fuse readily in the skin, polymer content resulted as a barrier for drug release and helped as a controlled release and also decrease drug leakage (Figure 7; Table 3)

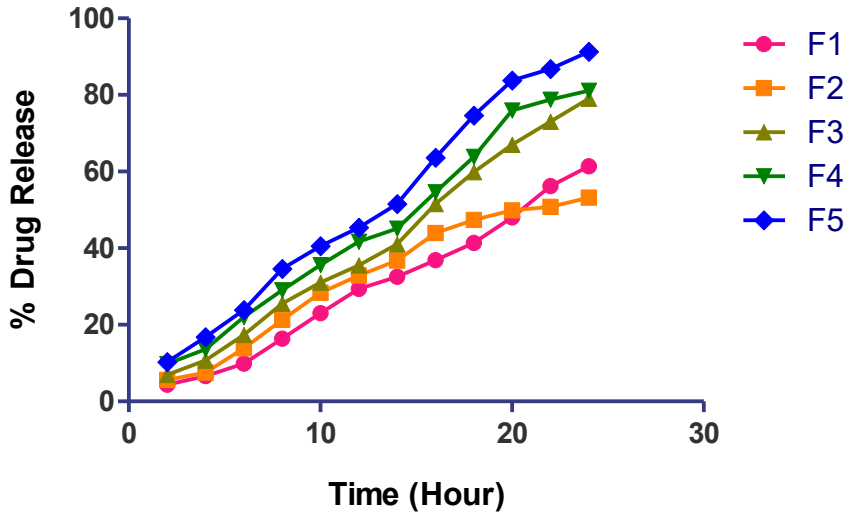

Figure 7: In vitro drug release studies

Table 3: In-vitro drug release studies of Transdermal patch

S.No	Time (hrs)	Rate of Drug Diffusion (%)				
		F1	F2	F3	F4	F5
1	2	4.35 ±0.1500	5.600 ±0.200	6.950 ±0.1499	9.750 ±0.3504	10.250 ±0.1996
2	4	6.650 ±0.1500	7.500 ±0.3002	10.700 ±0.500	13.600 ±0.2003	16.800 ±0.3002
3	6	9.850 ±0.1500	13.900 ±0.2003	17.350 ±0.0509	22.000 ±0.500	23.900 ±0.3996
4	8	16.350 ±0.1499	21.250 ±0.6496	25.500 ±0.3996	29.000 ±0.3996	34.650 ±0.4489
5	10	23.000 ±0.500	28.350 ±0.0519	31.050 ±0.1506	35.650 ±0.250	40.500 ±0.4015
6	12	29.350 ±0.7499	32.850 ±0.250	35.500 ±0.2992	41.700 ±0.6004	45.350 ±0.4499
7	14	32.550 ±0.9498	36.800 ±0.2992	41.050 ±0.7499	45.150 ±0.4499	51.550 ±0.4508
8	16	36.850 ±0.0114	43.950 ±0.250	51.550 ±0.5492	54.600 ±0.3996	63.650 ±0.4499
9	18	41.350 ±0.4499989	47.400 ±0.1999	59.850 ±0.250	63.850 ±0.3495	74.64999 ±0.4508
10	20	48.050 ±0.8504	49.850 ±0.250	67.000 ±0.1969	75.950 ±0.1477	83.800 ±0.3977
11	22	50.750 ±0.1515	56.200 ±0.2992	73.000 ±0.1969	78.800 ±0.2992	86.800 ±0.2992
12	24	59.200 ±0.6004	61.350 ±0.5501	79.050 ±0.5492	89.100 ±1.000	96.250 ±0.6515

3.4 Stability Study

Stability of the drug has been defined as ability of the formulation in specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability was to provide evidence on the quality of the drug substance or drug product which varies with time under the influence of the variety of factors such temperature and humidity. Stability studies were conducted according to the ICH Q1A (R2) guidelines; the formulation in container wrapped in aluminum foil and were kept in stability chamber at temperature 40° ± 2°C and 75% ± 5 RH and at room temperature for 1 month. Samples were withdrawn at the end of the month and were analyzed for drug content (Table 4).

Table 4: Influence of storage condition and storage duration on drug content and particle size for 1 month at accelerated temperature (40° ± 2°C and 75% ± 5 RH) and room temperature.

Time Duration (Days)	Drug Content (%)	
	At Room Temp.	At Accelerated Temp.
30	88.2	87.9

3.5 Evaluation of Anti Diabetic Activity

3.5.1 Blood Glucose Level

One-way ANOVA showed that Metformin orally and transdermally have significant influence on Plasma glucose levels. Post hoc test indicated the Plasma glucose levels was significantly decreased by treatment with high dose level of Metformin orally and transdermally (500 mg/kg, $P<0.01$). The information displayed in representative Table 5 shows the fasting Plasma glucose levels of 7 exploratory group rats amid the test time frame.

Table 5 : Effect on Plasma Glucose Levels

Plasma Glucose levels (mg/dl)					
Group	**Initial day**	**15th day**	**30th day**	**45th day**	**60th day**
I	82.23±1.21[a]	83.93±0.52[a]	85.82±0.61[a]	84.14±0.78[a]	85.80±1.28[a]
II	325.47±4.16[b]	331.7±28.43[b]	343.41±1.05[c]	356.04±2.73[c]	368.84±3.72[b]
III	339.64±4.60[b]	280.11±9.15[c]	181.57±4.90[b]	120.52±3.16[b]	90.30±1.34[a]
IV	341.24±0.60[b]	290.04±2.14[c]	179.01±0.11	129.22±0.70[b]	100.20±2.04[a]

4. CONCLUSIONS

The study investigates the identification and characterization of drugs, including their color, odor, pH, taste, and texture. Organoleptic characterization is crucial in pharmaceutical sciences, as it helps determine the physical and chemical characteristics of medications. The study identifies Metformin, a drug with a solubility of 1mg/ml in various solvents. The absorption maxima of Metformin was determined using a UV scan and a calibration curve. The transdermal patch evaluation included thickness, weight variation, hardness, tensile strength, folding endurance, moisture uptake, and drug content. The formulation was prepared using a Franz diffusion cell and the maximum permeation was found in the F5 patch. The formulation showed optimum drug release up to 24 hours, with smaller pores in the matrix derived from patches tending to fuse readily in the skin. Polymer content resulted as a barrier for drug release, helping to control release and decrease drug leakage. The stability studies were conducted according to the ICH Q1A (R2) guidelines, with the formulation in a container wrapped in aluminum foil and kept in a stability chamber at 40° ± 2°C and 75% ± 5 RH and room temperature for 1 month. The influence of storage condition and storage duration on drug content and particle size for 1 month at accelerated temperature and room temperature was also examined. The selection of the Metformin-loaded transdermal patch **F5** for *in vivo* animal study is justified by its superior performance in *in vitro* evaluation assays and stability studies compared to formulations F1-F4. The *in vitro* drug release studies demonstrated that **F5** achieved a more favorable controlled and sustained release profile, as compared to F1-F4, which in some studies showed higher initial burst releases or lower overall cumulative release at specified time points. All five Metformin-loaded transdermal patch formulations (F1-F5) showed increasing drug diffusion over 24 hours in *in vitro* testing. Formulation F5 demonstrated the highest diffusion rate, releasing 96.25% of the drug at 24 hours, while F1 and F2 had the lowest cumulative release. The provided table contains the full diffusion rates for each formulation over time. This sustained release characteristic is crucial for maintaining consistent therapeutic drug levels in the bloodstream over prolonged periods, bypassing the rapid first-pass metabolism associated with oral administration. Furthermore, stability studies confirmed that **F5** maintained its integrity, drug content, and release kinetics within acceptable limits over the storage period, ensuring a reliable and consistent dosage form for the *in vivo* trials. The combination of optimal *in*

vitro release kinetics and proven stability makes **F5** the most promising candidate for effective transdermal drug delivery and successful animal study evaluation.

5. CONFLICT OF INTEREST

None

6. REFERENCES

1. Bailey CJ. Metformin: Therapeutic profile in the treatment of type 2 diabetes. Diabetes, Obesity and Metabolism. 2024 Aug;26:3-19.
2. LaMoia TE, Shulman GI. Cellular and molecular mechanisms of metformin action. Endocrine reviews. 2021 Feb 1;42(1):77-96.
3. Lv Z, Guo Y. Metformin and its benefits for various diseases. Frontiers in endocrinology. 2020 Apr 16;11:191.
4. Foretz M, Guigas B, Viollet B. Metformin: update on mechanisms of action and repurposing potential. Nature Reviews Endocrinology. 2023 Aug;19(8):460-76.
5. He L. Metformin and systemic metabolism. Trends in pharmacological sciences. 2020 Nov 1;41(11):868-81.
6. Kristófi R, Eriksson JW. Metformin as an anti-inflammatory agent: a short review. Journal of Endocrinology. 2021 Sep 1;251(2):R11-22.
7. Cwynar-Zając Ł. Metformin–a new approach. Pediatric Endocrinology Diabetes and Metabolism. 2021 Jun 20;27(2):134-40.
8. Khandelwal KR. Practical pharmacognosy. 15th edition. Nirali prakashan, pune 2006;15:149-56.
9. Sharma A, Sisodia SS. Preliminary Phytochemical Evaluation of Aerial Parts of Sphaeranthus indicus Linn.(Asteraceae). IJP, 2022; Vol. 9(2): 36-40.
10. Valeveti SK, Pashikanti S. Design, development, and evaluation of transdermal patches containing memantine hydrochloride. Int J App Pharm. 2023;48481:181-97.
11. Purnamasari N, Alatas F, Gozali D. Formulation and evaluation of diclofenac potassium transdermal Patch. J Ilmiah Farmasi. 2019;7(1):43-8.
12. Hardainiyan S, Kumar K, Nandy BC, Saxena R. Design, formulation and in vitro drug release from transdermal patches containing imipramine hydrochloride as model drug. Int J Pharm Pharm Sci. 2017;9(6):220-5.
13. Reveny J, Sumaiyah S. Formulation and evaluation of in vitro transdermal patch diclofenac sodium using chitosan polymer and polyvinyl alcohol cross-linked tripolyphosphate sodium. Asian J Pharm Clin Res. 2018;11(8):171.
14. Allena RT, Yadav HKS, Sandina S, Prasad SC. Preparation and evaluation of transdermal patches of metformin hydrochloride using natural polymer for sustained release. Int J Pharm Pharm Sci. 2012;4:297-302.
15. Patel DJ, Vyas AM, Rathi SG, Shah SK. Formulation and evaluation of transdermal patch of apixaban. IJPSRR. 2021;69(2):57-63.
16. Akhtar N, Akram M, Daniyal M, Ahmad S. Evaluation of antidiabetic activity of Ipomoea batatas L. extract in alloxan-induced diabetic rats. International journal of immunopathology and pharmacology. 2018 Nov;32:2058738418814678.
17. Chauhan L, Vashisht S. Formulation and evaluation of novel herbal antidiabetic transdermal patch. Inno Pharm Pharmacother. 2018;6(4).