Formulation and In- Vitro Characterization of Transdermal Patches Containing Glimepiride and Atenolol: A Combination Approach

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Abstract-

In the sector of medical practices, there is a vital impact of Transdermal Drug Delivery System. A Précised quantity of drug is delivered into the blood stream through the skin and it is delivered by the medicated patches. The Transdermal Drug Delivery having various merits over the other conventional system of drug delivery is that, the drug is released in combination form, from the patches into the patients, and usually the drug is released in control manner either from body heat melting thin layers of drug embedded in the adhesive or the drug is released from a reservoir covered by a porous membrane. Then, main objective of the recent study is to prepare a transdermal patches of Glimepiride and Atenolol as a combination approach for the better treatment of patients, by using solvent casting method and the physiochemical parameters were evaluated, the parameters such as weight variation, thickness, moisture uptake, moisture content, drug content, and folding endurance, dissolution and permeation studies. There are total seven transdermal patches were formulated by changing the concentration of ethyl cellulose.

Keywords- Transdermal patches, combinational therapy, Ethyl cellulose, Atenolol, Skin, Glimepiride, Permeation, etc.

Introduction-

Now a days, For systemic therapy or for the local cure and management of tissues beneath the skin can be done with the help of Transdermal Patch, a type of topical delivery of drugs to the healthy undamaged skin. There are various merits of transdermal patches over the other predictable dosage form or controlled release oral system. The transdermal patches facilitates so many things such as avoid dose dumbing, provides constant blood level, increased patient conformity, avoid first pass metabolism [1,2]. When the drug is applied through the skin, it gives a better option for slow and more controlled pathways for release of drug into the systemic circulation, and by pass ―first pass metabolism‖. There are so many benefits of transdermal patches such as, multiple dosing can be avoided, the patient will be able to apply

the transdermal patch, by themselves and they can easily remove it too, the drug level can be maintained for a prolonged time [3,4]. The patient conformity can be enhanced by using Transdermal drug delivery system, it can prevents so many things such as, the hepatic first pass metabolism can be avoided and other side effects can also be reduced in comparison of other Drug delivery system. When the drug were delivered with the help of Transdermal patch system, it is slow, and the drug release and absorption were be controlled. There is no difference due to the over time the plasma drug concentration. In the developing market, there is a lot of demand of Transdermal drug delivery system, that will make a great success in the few upcoming years with the development of new drug delivery system and new inventions [5]. There are so many things in oral route of administration, and to overcome that problems, Transdermal Drug Delivery System play a vital role, such as in terms of long term therapy it enhance the patient conformity, sustained drug delivery, avoiding first pass metabolism to reduce the minimizing inter and intra patient in consistency, to maintain drug level in plasma for prolonged time which consistency, and help to avoid treatment when it is important [6].

Antidiabetic Action-

There is a chronic disease associated with fats, carbohydrates and protein metabolism known as Diabetes mellitus. In Diabetes mellitus there is a defective or decrease secretion of Insulin, which converts into Impaired glucose use, that leads to hyperglycaemia condition . When insulin is absent in body or having insulin resistance in body, and it is most common issue of endocrine system, that is called Diabetes mellitus or in common language known as ‘Sugar’ and an endocrine disorder. The pancreas secretes the hormone Glucagaon and insulin. The alpha and beta cells are located in the islets of Langerhan’s and secrets glucagaon and insulin. By the process of glycogenesis the insulin reduces the level of blood glucose, and then the glucose is transported into adipose tissues, muscles and liver. For the use of glucose the erythrocytes and neural tissues does not required insulin, where as glucagaon accelerates the glycogenolysis process and enhance blood glucose level and glucagaon is produced by alpha cells . Due to this the danger of metabolic and the cardiovascular disorders, obesity and malignancy in new born baby increases. It is observed that, 80 to 90 % of diabetes patients suffer from type-2 diabetes. If we compare diabetic person who perform some physical activity and exercises have less chance of death in comparison of those who does not perform the physical activity. Mostly, it is caused by genetic constitution [7,8].

Anti-Hypertensive Action-

The condition in which an abnormal increase can be seen in the value of systolic or diastolic pressure or mean arterial pressure, is known as hypertension. For assessing hypertension, the diastolic pressure is highlighted in past few years. In the case of coronary diseases and cerebrovascular disease such as strokes, it is observed that systolic pressure enhanced, it is not always hypertension. It concluded that, for measuring hypertension it is essential to note both, systolic and diastolic pressure. The patients suffering from hypertension are mostly asymptomatic and having symptom at the time like headache, dizziness, facial flushing,

ringing sound in the ears. Its symptoms are visual disturbance nausea, vomiting and confusion [9].

Glimepiride-

For the treatment of type-2 diabetes, Glimepiride is used which is a sulphonyl urea. The molecular weight of glimepiride is 490.617 gm/mole and chemical formula is $C_{24}H_{34}N_4O_5S$. In BCS classification system, the glimepiride belongs to class –II. If we observed the glimepiride solubility, it is insoluble in water, slightly soluble in different buffer solution and organic solvent and insoluble in acidic medium . Mostly Glimepiride is orally administered, it is very slightly in methanol, slightly soluble in di-chloro methane and having its solubility as soluble in di-methyl sulfoxide.The solubility of Glimepiride less depends on PH, at 37°C, less than 0.004mg/ml produces very poor solubility in acidic and aqueous medium. At the site of action where, therapeutic action should be produced associated with compatible action of excipients, the poorly water soluble drug face difficulty to send them in absorbable and active form. Due to this, the bioavailability of Glimepiride is unpredictable. The main limitation of Glimepiride is that it is practically insoluble in water and highly hydrophobic in nature [10, 11].

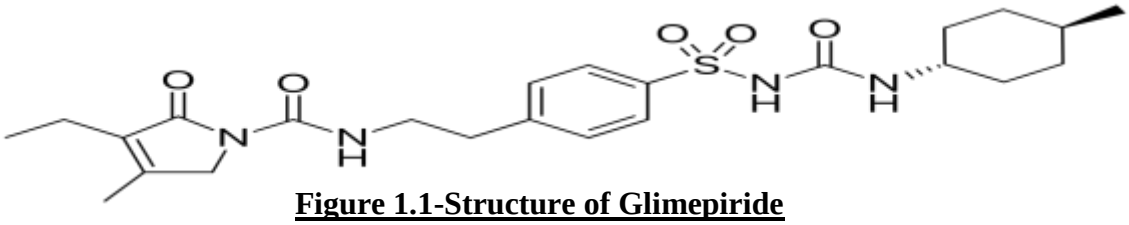

Figure 1.1-Structure of Glimepiride

Atenolol-

If we consider about the anti-hypertensive drug, then it is possible to say that, the Beta blockers are the safest one. Due to this, the Beta blockers are considered as first line of therapy in all drug for the treatment of hypertension by the joint national committee. In the heart fails, the beta blockers are present. By the adrenaline beta receptors gets stimulated and leaves in the elevation of heart rate and blood pressure and due to the vessels of blood get dialated. This is the process by which blood pressure and chest pain is reduced. This machenism leads to less oxygen requirement in the heart. But this is not permanent and help to manage the symptoms. For the treatment of both hypertension and coronary artery diseases a therapeutic agent were introduce by the US FDA, in August 1981 known as “Atenolol” and it was first introduced 1976. Alone in the united state, the Atenolol is prescribed for more than 40 millions prescription And it is mostly common all over the world. Arrhythmias, Angina pectoris, Myocardial infraction and hypertension is mostly treated by Atenolol. Atenolol is mainly develop to cross the blood brain barrier and also used for the therapy of prophylactic treatment of Migraine. In case of bronchial Asthma and diabetes mellitus it does not show the adverse effect [12-14].

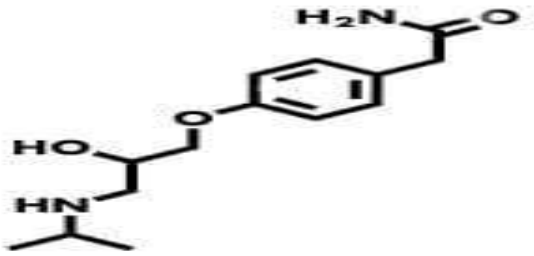

Figure 1.2-Structure of Atenolol

Material and method

Chemical Required-

All the ingredients used in this study were of standard pharmaceutical ranking. Glimepiride and Atenolol were obtained from the Sigma Aldrich, Merck India. Ethyl Cellulose, Dibutylphthalate, Polyethylene Glycol (PEG-400), Chloroform, Methanol, CotranTM9720, Microporous Polyethylene Membrane, Acrylic Adhesives were obtained from SHEAT College of Pharmacy and of analytical reagent ranking.

Apparatus Required-

The apparatus which are needed for making patch Beaker, Glass rod, measuring cylinder, Butter paper, Weighing Balance, Spatula, Petri Dish, Funnel.

Procedure for formulation of Transdermal patches of Glimepiride and Atenolol in combination-

- By using solvent casting method and using different polymer, the transdermal patches were formulated by combining Glimepiride and Atenolol.
- At an optimum temperature the base ingredient were added into the working solution and Glimepiride and Atenolol were also dissolved in it and let it swell properly.
- After that, in the same solution permeation enhancer and plasticizer were added and mixed by using a sonicator.
- A ring containing glass surface were taken and this above solution were casted on it. It was covered with an inverted funnel to control the evaporation of solvent and stand for overnight at 25℃.
- The patches were cut and separated, and the backing membrane were applied and patches were stored in a dessicator.
- After drying process was completed, the single layer transdermal patch were obtained of Glimepiride and Atenolol in combination [15].

Table 1.1- Formulation Composition of Glimepiride + Atenolol Transdermal Patches

Formulation code	Glimepiride (Mg)	Atenolol (Mg)	Ethyl cellulose (%)	PEG-400 (% w/w)	Dibutyl phthalate (%)	Chloroform: Methanol (%)
GA_1	10	25	1	30	1	1:4
GA_2	10	25	1	30	-	1:4
GA_3	10	25	-	30	1	1:4
GA_4	10	25	1	30	0.55	1:4
GA_5	10	25	0.55	30	1	1:4
GA_6	10	25	0.55	30	0.55	1:4
GA_7	10	25	0.75	30	0.75	1:4

Fig 1.3- petri dish is covered with inverted funnel

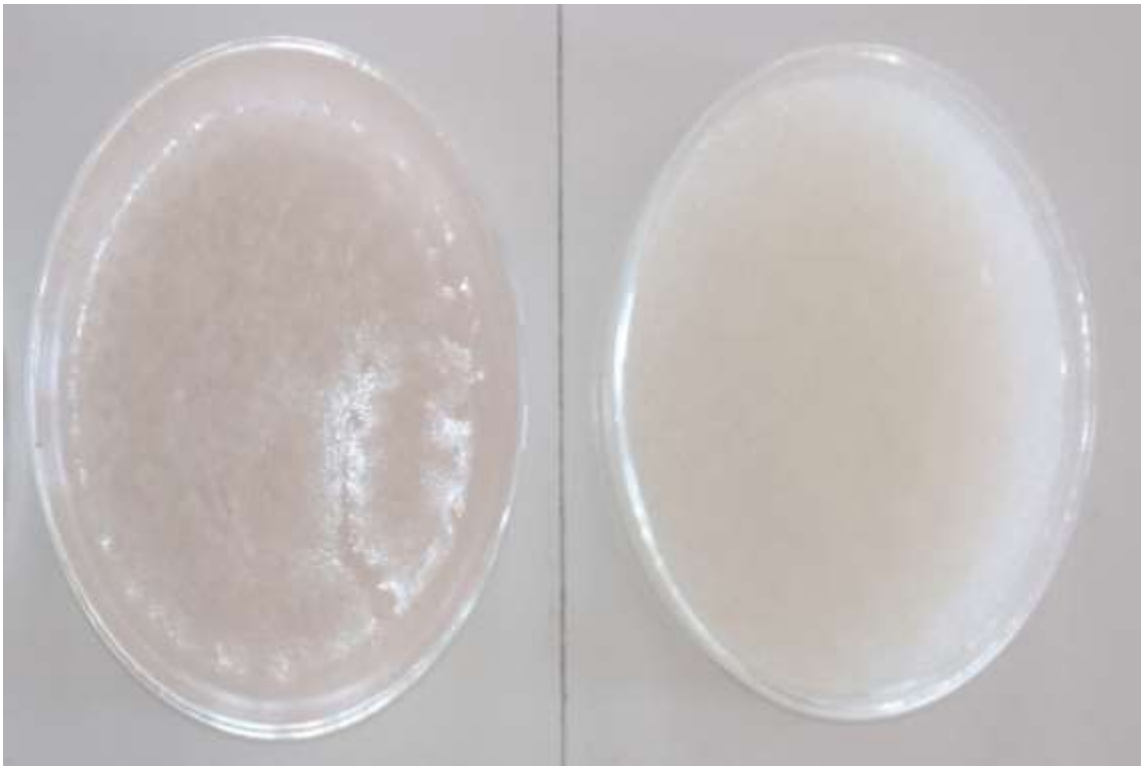

Fig 1.4- Petri dish containing Transdermal Patch Solution

Fig 1.5- Patches after 24 hours

Preformulation Studies [16-18]-

Organoleptic properties of Drug-

For the description of a drug material the preformulation studies were performed such as organoleptic study. In the organoleptic testing, the color, odor, taste and texture of the drug material were tested. For elaborating the properties of a drug material, it is important to perform the organoleptic study for giving a proper description to the dosage form developer.

Identification of drug-

For performing the identification of drug, the U.V. Spectroscopy and FTIR were performed.
In the U.V-Visible spectroscopy the radiation is passed through the matter.The principle which is involved in UV-visible spectroscopy is the Beer-Lamberts Law. The continue wavelength range is from 200 to 900 nm for the UV- visible spectroscopy. The device which is used in UV- visible is Spectrophotometer device. There are various components components of UV-visible spectroscopy are such as, sources of light (200 nm-900 nm), monochromator, sample solution in cuvette, Detectors, Readout devices, types of Spectrophotometer single and double beam instruments, application of UV-visible spectroscopy qualitative and quantitative analyses.

Solubility of drug-

When to a fixed quantity of the solvent, the solute were added in the little incremental quantity is defined as the semi-quantitative solubility. The solvent system were shaken vigorously after each addition and tested for undissolved solute particulates by visual testing. For serving an estimated rapid solubility, the full quantity of solvent were added up to that level, when few solute particles remains undissolved. When there is requirement of more quantitative result, at a constant temperature, a suspension made up of solute and solvent were shaken. By using an appropriate method, the solvent samples were withdrawn at different-different period, filtered and their concentrations were determined.

Molecular Weight of Drug-

The molecular weight of the drug is defined as the total of the atomic masses of all atoms in a molecule, based on a scale in which atomic masses of Hydrogen, Carbon, Nitrogen, and oxygen are 1, 12, 14 and 16 respectively.

The Molecular weight of Atenolol is – 266.336 Da.

The Molecular weight of Glimepiride is- 490.62 Da.

Partition Coefficient-

Partition coefficient is defined as, when in two immiscible liquids which are in contact of each other, this solute is added in that liquid, the solute will be distributed itself between the two phases of immiscible liquids in a fixed ratio. The partition coefficient is also known as Distribution coefficient. There are various organic solvents were used for the determination of partition coefficient such as ether, amyl acetate, chloroform, carbon tetrachloride, isopropyl myristate, n-octanol.

Melting point of drug-

The Capillary fusion method is generally used for determining the melting point of drug. A capillary tube is used and the drug sample were placed in it and the drug sample were placed in it and the drug sample will be heated until its melting point level comes and recorded.

Infrared spectroscopy-

The infrared spectroscopy is defined as the subset of spectroscopy. It handle the infrared region of the electromagnetic spectrum. The infrared spectroscopy spectrum is a technology that covers a wide range of techniques in which the most common technique in the absorption spectroscopy.The Infrared spectroscopy is generally used to identify a compound or to know a drug sample composition. It is used to determine the fact at discrete energy levels, the molecules have particular frequencies at which they vibrate or rotate and corresponds to these energy levels. By the masses of the atoms, by the associated vibronic coupling and the shape of molecular potential energy surfaces are used to determine these resonant frequencies. The FTIR (Fourier transform infrared investigates the vibrational characteristics of amino acids and its co-factor which are complex to small structural changes. Due to the lack of particular knowledge of this technique, it allows us to investigate the vibrational characteristics directly of all the cofactors, water molecules and all amino acid side chains. While, the reaction-induced FTIR difference spectroscopy it used to choose the vibrations to individual chemical groups which is included in a specific reaction.

Drug excipients Interaction-

To support the manufacture, administration and absorption which are involved in as dosage form the excipients were used. The excipients may participate in the physical or chemical interactions due to which the result of medicament can be disturbed. The active Pharmaceutical ingredients can be degraded due to the chemical interaction, due to the chemical interaction the quantity of the drug available for the therapeutic efficacy can also be reduced, the tolerance or safety can also be altered due to yield product by the reaction. The dissolution rate, dose uniformity or easy administration can also be effected due to the physical interaction. For better understanding, there are various important procedure were used to study the drug-excipient interaction study to determine the residues or impurities of excipients associated with the active pharmaceutical ingredients and their interaction with them and other excipient.

The process of hydrolysis, oxidations or particular interaction of drugs with excipients impurities were the reactions involved in the drug-excipient reactions. The safety and efficacy of the highly potent active pharmaceutical ingredients (API), drug products can also be affected by the presence of excipient impurities.

Standard curve for the quantitative estimation of drug-

The standard curve is also known as calibration curve which is highly used in analytical chemistry. The standard curve is a process which is used to determine a substance concentration in an unknown sample by making its comparison to a set of standard samples of known concentration.

Evaluation of Patches [19,20]-

Thickness of patch-

For measuring the thickness of patch, the thickness gauge is used and the patch were observed at different- different points. At different angles the patch were cut and weighed.

Weight Uniformity-

The drug was spread uniformily all over the patch or not, for this weight uniformity was calculated. The average weight of all patches were determined and weight of single patch was compared with it. From the patches, the random patches were selected for this examination.

Folding Endurance-

Each patch was individually observed and observed for patch cracking and breaking. A patch were taken and at a single point, it was folded for many time as much as possible to evaluate its folding endurance.

Percentage moisture content-

In a dessicator, for 24 hours the patch was stored with calcium chloride after its initial weight and after 24 hours it was again weighed and moisture content percentage were evaluated by using given formula-

$$\text{Moisture content (\%)} = \text{Initial mass} - \text{final mass} / \text{initial mass} \times 100$$

Percentage moisture uptake-

At room temperature that is 25℃, a desiccator were taken and patch was weighed and stored in it. After that potassium chloride saturated solution were added in it and introduced to relative humidity upto 84% and patch weighed were compared. By using given formula, it was calculated.

$$\text{Percentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight X 100}}{\text{Initial weight}}$$

Drug content determination-

A 10 ml of overall solution were prepared of phosphate buffer of pH 7.4 and dichloromethane and patches were introduced in it. The dichloromethane solution from overall mixture was evaporated by using Rotatory Evaporator by maintaining the temperature at 45 ℃ and a blank solution was also prepared. After that the solution was filtered by using membrane filter , then the solution was diluted for bettr absorbance by using double beam UV- Visible spectrophotometer .

In vitro permeation studies-

By using an advanced diffusion cell, the in vitro permeation studies were performed. The formulated transdermal patches were passed across the dialysis membrane. The pH 7.4 of phosphate buffer solution were used to fill the receptor section of the diffusion cell. The transdermal patches were kept on a magnetic stirrer with a bead placed inside it for the uniform distribution of the drug from the patches. The released surface were directed towards the receptor section, so the transdermal patches were placed between the donor section and receptor section. At different time duration, the samples of solution were withdrawn and the spectrophotometrically, drug content were evaluated for which the pH 7.4 phosphate buffer solution were taken as blank solution.

In vitro dissolution studies-

The USP Basket type Dissolution apparatus were used to evaluate the dissolution profile of transdermal patches. The phosphate buffer, pH 7.4 were filled in the basket apparatus and the transdermal patches were introduced in the basket with the exposure of their drug matrix. The temperature were maintained at 32℃ and all the dissolution test were performed at 50 rpm. All dissolution apparatus contains 900 ml of buffer solution. At different time duration, the sample solution were withdrawn and it is detected spectrophotometrically against the blank solution. The graph were plotted for the different formulations against cumulative quantity of drug release versus time.

Result and Discussion-

Result-

Organoleptic properties of Glimepiride –

The organoleptic properties of Glimepiride were evaluated as-

S.No	Color	Odor	Taste	Texture
1	White to Off- White	Odourless	Tasteless	Crystalline powder

Organoleptic properties of Atenolol –

The organoleptic properties of Atenolol were evaluated as-

S.No	Color	Odor	Taste	Texture
1	White	Odourless	Slightly Bitter	Crystalline powder

Identification of Glimepiride-

The U.V Spectroscopy and FTIR were perform for the identification of Glimepiride. The U.V absorbance maxima of Glimepiride was shows at 221 nm.

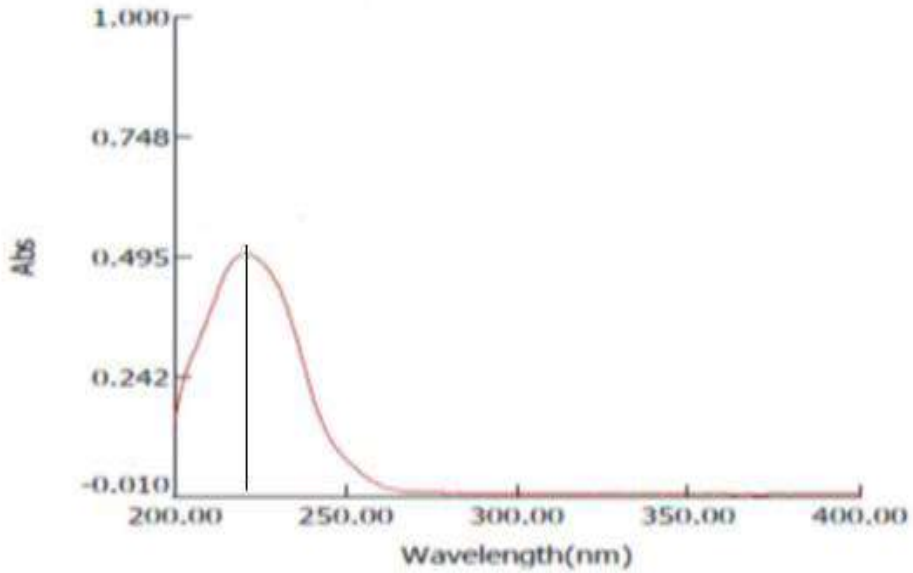

Fig 1.6- UV Spectra of Glimepiride

Identification of Atenolol-

The U.V Spectroscopy and FTIR were perform for the identification of Atenolol.

The U.V absorbance maxima of Glimepiride was shows at 226 nm.

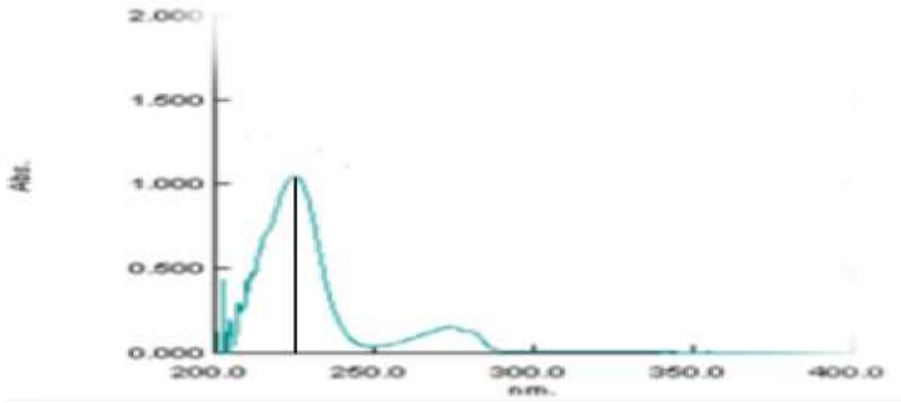

Fig 1.7- UV Spectra of Atenolol

Solubility of Glimepiride and Atenolol-

The solubility of Glimepiride and Atenolol were evaluated and following result were found-

S.NO.	Solvent	Solubility of Glimepiride in mg/ml	Solubility of Atenolol in mg/ml
1	Methanol	6.2	5.5
2	Phosphate buffer of pH 6.8	18.4	1
3	Phosphate buffer of pH 7.2	23.5	3.5

Partition Coefficient of Glimepiride and Atenolol-

Partition coefficient of Glimepiride and Atenolol were observed by taking it's three readings to get an average values-

S. No.	Drug	Partition coefficients of Glimepiride (log p)	Partition coefficients of Atenolol (log p)
1	I reading	3.60 ± 3.63	0.16 ± 0.18
2	II reading	3.65 ± 3.68	0.18 ± 0.20
3	III reading	3.62 ± 3.66	0.15 ± 0.17

mean ± SD (n=3)

Melting point of Glimepiride and Atenolol –

The capillary fusion method were used to evaluate the melting point of Glimepiride and Atenolol and the observation were as follows-

S. No.	Method Used	Experimental values of Glimepiride	Experimental values of Atenolol
1	Capillary Fusion Method (I reading)	207℃- 210 ℃	153℃- 156 ℃
2	Capillary Fusion Method (II reading)	210 ℃- 212 ℃	157℃- 159 ℃
3	Capillary Fusion Method (III reading)	208 ℃– 211 ℃	151℃- 153℃

FTIR of Glimepiride and Atenolol –

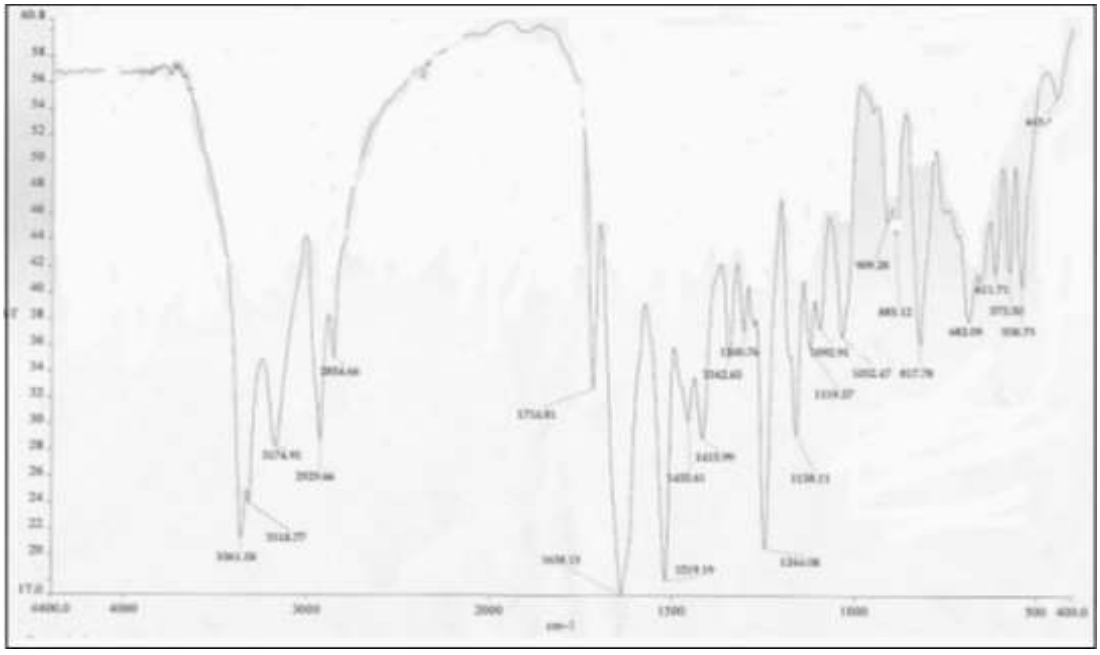

Fig 1.8- FTIR Spectra of Glimepiride and Atenolol

FTIR Spectra of drug-excipient interaction-

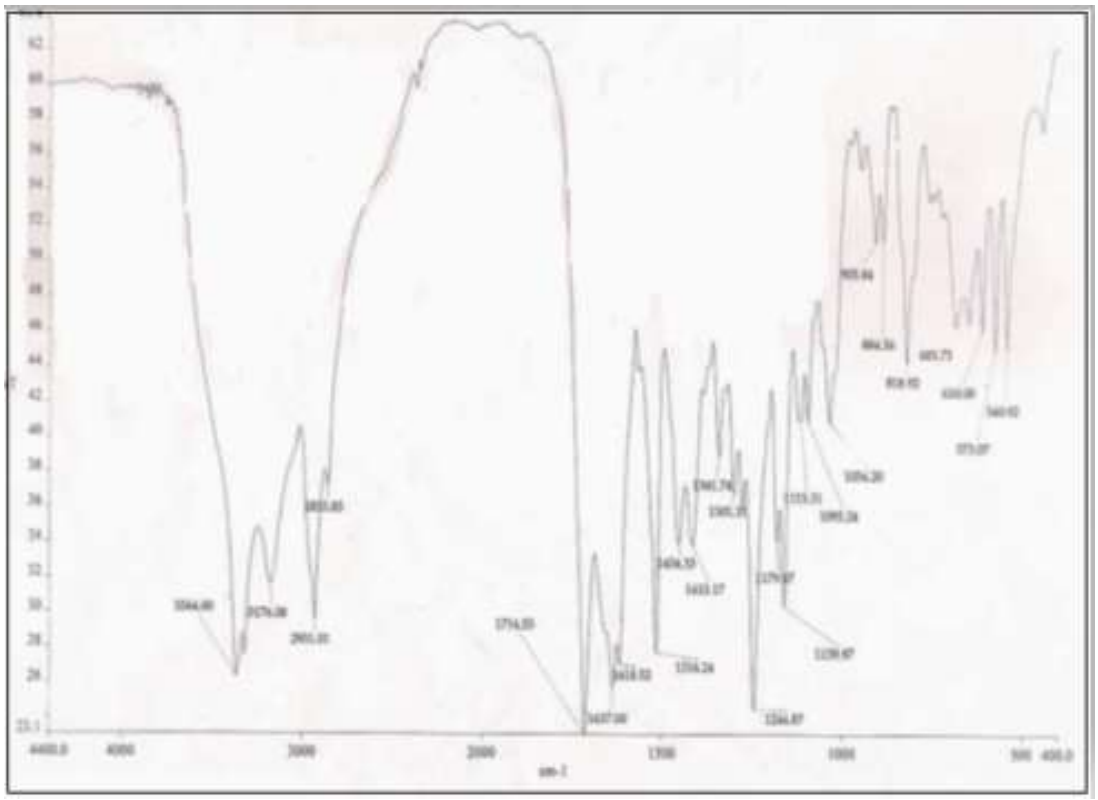

Fig 1.9- FTIR Spectra of Glimepiride and Atenolol with it's Excipients

Standard curve of Glimepiride –

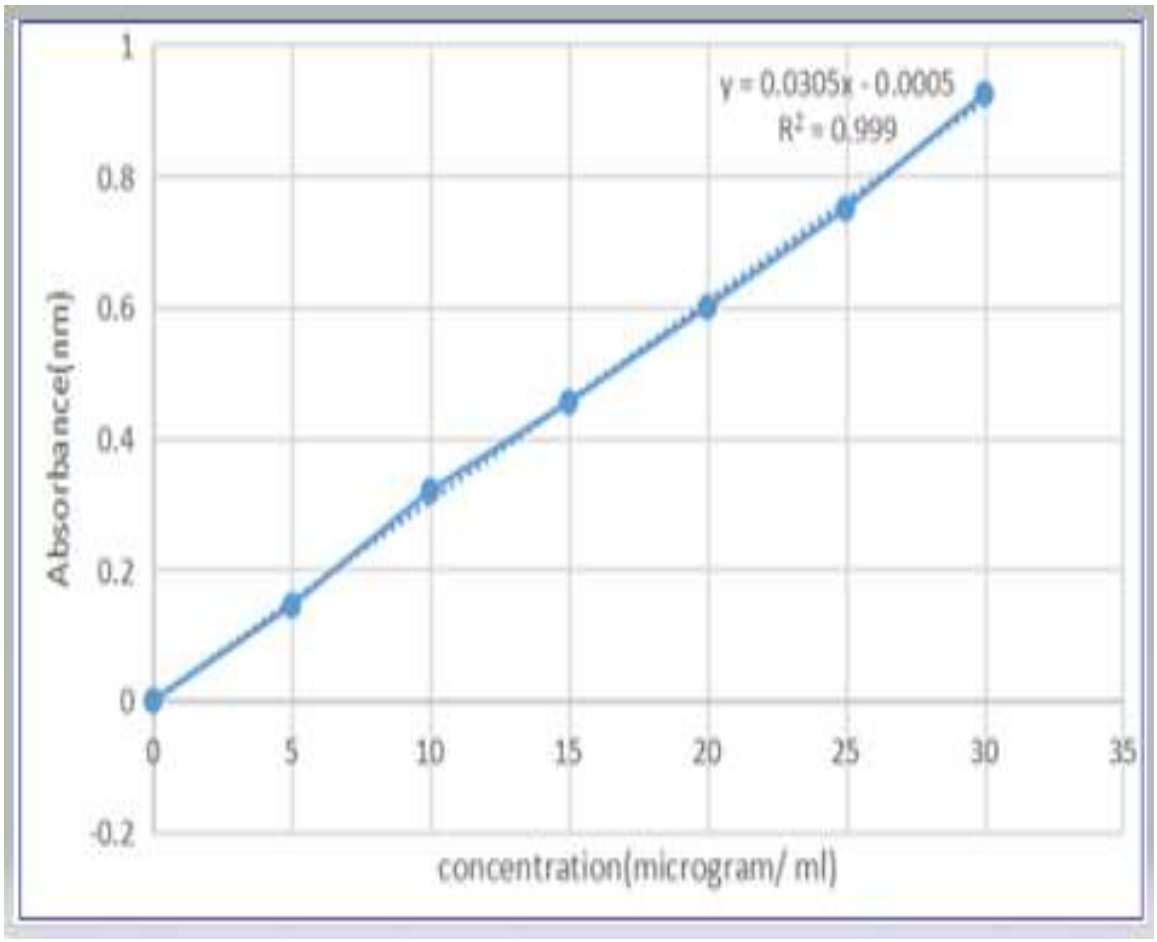

Fig 1.10- Standard curve of Glimepiride

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.145
3	10	0.320
4	15	0.455
5	20	0.600
6	25	0.750
7	30	0.925

Standard curve of Atenolol –

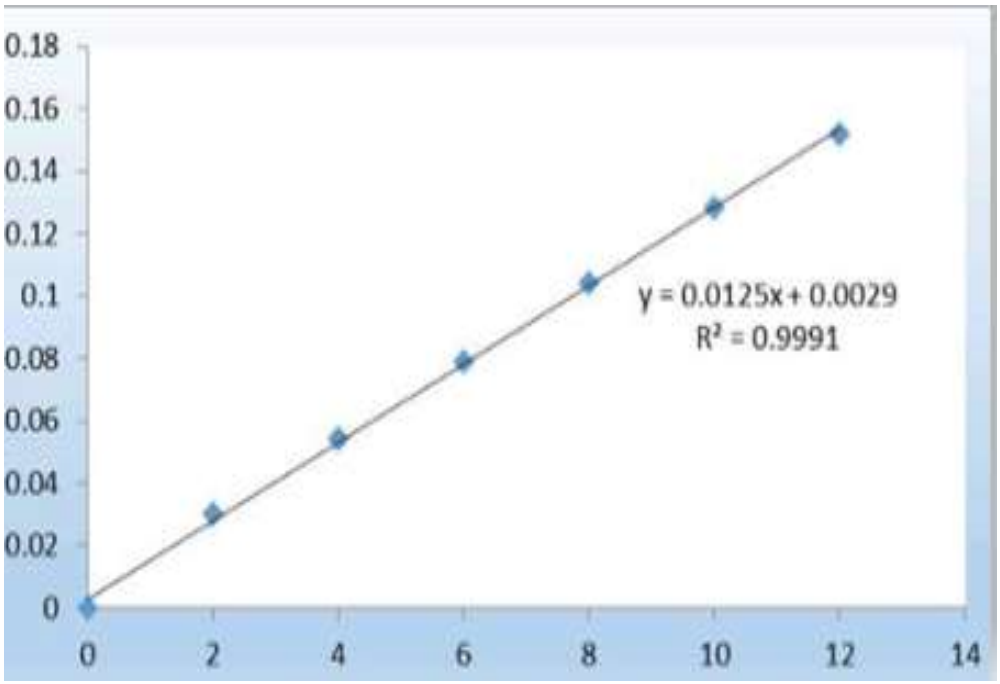

Fig 1.11- Standard curve of Atenolol

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.030
3	4	0.054
4	6	0.079
5	8	0.104
6	10	0.128
7	12	0.152

Characterization of working solution of Transdermal patches of Glimepiride + Atenolol-

S. No.	Working Solution	pH Values
1	**GA_1**	5.8
2	**GA_2**	6.2
3	**GA_3**	6.8
4	**GA_4**	5.6
5	**GA_5**	6.9
6	**GA_6**	6.4
7	**GA_7**	6.3

Evaluation of Transdermal patches of Glimepiride + Atenolol-

Table 1.2- Thickness of Patches

S. No.	Formulation code (GA)	Thickness (mm)
1	GA_1	0.32 ± 0.01
2	GA_2	0.36±0.03
3	GA_3	0.34±0.05
4	GA_4	0.30 ±0.04
5	GA_5	0.37±0.01
6	GA_6	0.39±0.04
7	GA_7	0.35±0.04

mean ± SD (n=3)

Table 1.3- Weight uniformity of Patches

S. No.	Formulation code (GA)	Weight Uniformity (mg)
1	GA_1	181.7±0.50
2	GA_2	160.2±0.31
3	GA_3	171.3±0.21
4	GA_4	185.1±0.33
5	GA_5	193.4±0.56
6	GA_6	212.5±0.41
7	GA_7	180.4±0.23

mean ± SD (n=3)

Table 1.4- Folding endurance of Patches

S. No.	Formulation code (F)	Folding Endurance (cm)
1	GA_1	253 ± 1.0
2	GA_2	229±2.0
3	GA_3	251±2.0
4	GA_4	274±2.0
5	GA_5	284±2.0
6	GA_6	223±1.0
7	GA_7	268±1.0

mean ± SD (n=3)

Table 1.5- Percentage moisture content of Patches

S. No.	Formulation code (F)	Percentage Moisture Content(%)
1	GA_1	9.12 ± 0.023
2	GA_2	3.15±0.016
3	GA_3	8.23±0.01
4	GA_4	5.92±0.021
5	GA_5	11.21±0.031
6	GA_6	10.21±0.011
7	GA_7	3.26±0.014

mean ± SD (n=3)

Table 1.6- Percentage moisture uptake of Patches

S. No.	Formulation code (GA)	Percentage Moisture Uptake(%)
1	GA_1	5.1 ± 0.016
2	GA_2	11.21±0.03
3	GA_3	4.23±0.017
4	GA_4	11.42±0.01
5	GA_5	7.32±0.011
6	GA_6	9.36±0.031
7	GA_7	8.38±0.025

mean ± SD (n=3)

Table 1.7- Drug content of Patches

S. No.	Formulation code (GA)	Drug Content(%) of Glimepiride	Drug Content(%) of Atenolol
1	GA_1	99.30	99.11
2	GA_2	99.55	99.41
3	GA_3	98.53	98.26
4	GA_4	98.26	99.25
5	GA_5	98.16	98.54
6	GA_6	98.26	99.38
7	GA_7	99.64	98.55

Time	Cumulative % drug release						
Hours	GA_1	GA_2	GA_3	GA_4	GA_5	GA_6	GA_7
0	0	0	0	0	0	0	0
0.5	2.7	5.65	5.2	4.31	3.5	3.8	5.9
1	4.94	8.1	6.48	9.15	6.22	6.3	7.4

2	12.35	10.15	15.3	10.32	12.6	12.62	12.5
3	16.15	16.48	23.39	18.67	18.82	18.85	16.7
4	20.72	24.75	26.39	23.15	25.59	25.62	21.1
5	31.15	28.6	28.25	32.21	29.85	29.9	24.41
6	34.15	31.75	38.74	50.24	34.43	34.46	28.72
7	38.73	34.4	45	71.54	40.48	41	35.66
8	43.2	42.63	48.79	94.26	45.8	45.82	39.15

Table 1.8- Drug content of Patches

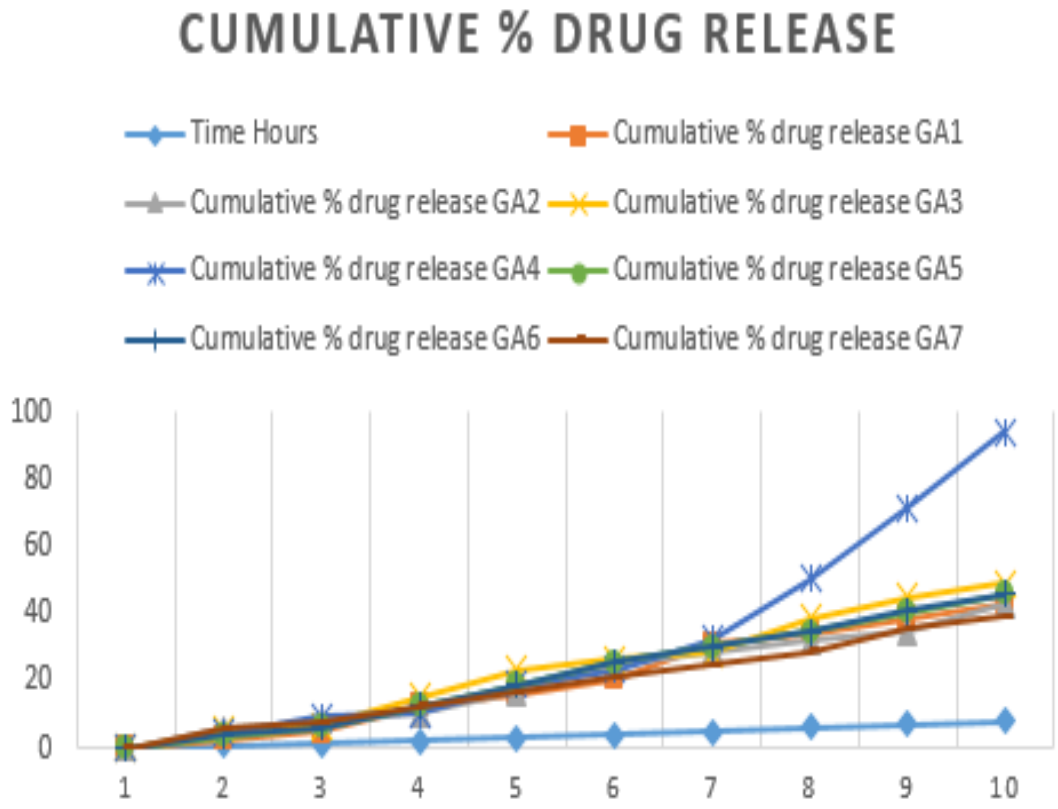

Fig 1.12- Zero order kinetic release graph for all seven formulations

Table 1.9- In vitro dissolution studies of Glimepiride + Atenolol Transdermal Patches

Time	**Glimepiride + Atenolol dissolution release (%)**						
Hours	**GA_1**	**GA_2**	**GA_3**	**GA_4**	**GA_5**	**GA_6**	**GA_7**
0	0	0	0	0	0	0	0
5	48.2	52.31	54.21	58.32	40.14	50.55	36.5
10	62.34	68.02	60.15	65.31	66.48	68.12	65.32
15	81.21	78.11	71.24	79.21	82.34	76.14	79.14

20	85.11	82.33	80.1	80.1	86.14	83.28	88.34
25	90.03	89.04	90.23	96.24	89.28	89.67	91.50

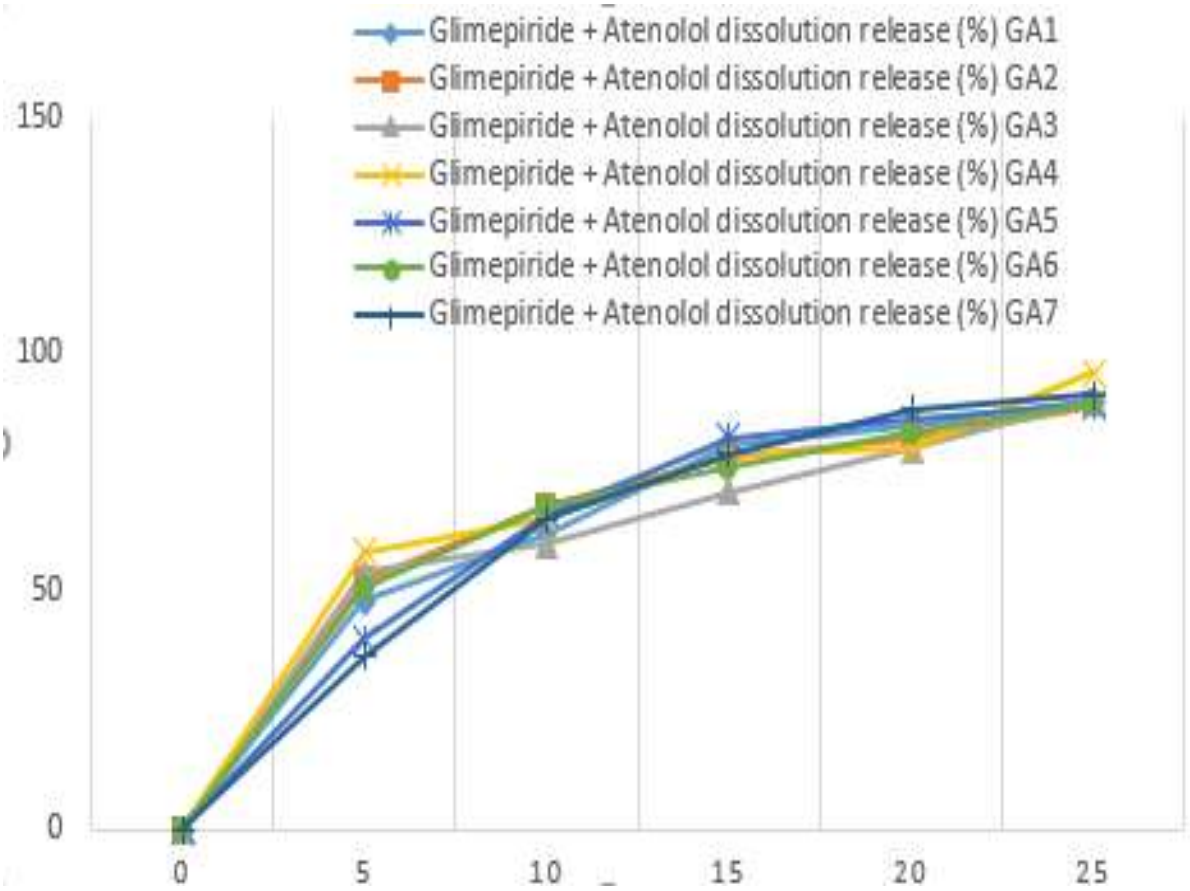

Fig 1.13- In vitro dissolution profile of Glimepiride + Atenolol Transdermal Patches

Discussion-

For the formulation of transdermal patches of Glimepiride + Atenolol the pre-formulation studies of Glimepiride, Atenolol and it's excipients were performed.

The organoleptic properties of Glimepiride and Atenolo were evaluated. Glimepiride is white to off white in colour, odourless, it is tasteless and it is consist of crystalline powder texture. All these parameters showed in table 1.2. Atenolol is white in colour, odourless, slightly bitter in taste and it consist of crystalline powder texture. All these parameters showed in table 1.3.

The maximum absorbance of Glimepiride and Atenolol in UV Spectra were observed at 221 nm and 226 nm.

The Solubility of Glimepiride and Atenolol in Methanol were found to be freely soluble , in phosphate buffer PH 7.2 it is found to be soluble and freely soluble. The partition coefficient of Glimepiride and Atenolol were observed at 3.65±3.68 and Atenolol was observed

0.16±0.18. The melting point of Glimepiride and Atenolol were obtained from Capillary fusion method as 207℃ and 151℃.

FTIR spectra were performed for Glimepiride and Atenolol and drug with its excipients interactions and the peak were shown in above figure with its interpretation. The standard curve for Glimepiride and Atenolol were plotted.

After that total 7 formulation of the transdermal patches were formed by using solvent casting method and the post evaluation of these patches were performed.

The PH of the working solution was observed as 6.9 and it is good.

Conclusion-

The main aim of research work is to formulate the transdermal patches of Glimepiride and Atenolol in combination and to observe the drug permeation and the release of the drug, and it's dissolution. As we know, the Glimepiride and Atenolol is used in the treatment of Diabetes and hypertension, as anti- diabetic and beta blocker drug. Due to it's lipophilic property and it's molecular weight, it is able to provide good permeation activity. The post evaluation of Glimepiride and Atenolol transdermal patches were performed such as thickness of Glimepiride + Atenolol patches, weight uniformiry, folding endurance, drug content, percentage moisture content, percentage moisture uptake , in vitro permeation studies and in vitro dissolution studies. These patches will provide better patient compliance.
The transdermal patches were formulated successfully by taking different concentrations of ethyl cellulose by solvent casting method. We had concluded from the present work that these patches show good permeation and dissolution properties, and passed all mentioned evaluation test successfully, so these patches can be used as a combination therapy for the patient suffering from diabetic conditions, hypertension and other heart related disorder.

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Conflict of Interest-

There is no conflict of interest among the authors of this research paper.

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