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ENHANCING BIOAVAILABILITY OF GLIBENCLAMIDE BY THE PREPARATION AND EVALUATION OF FAST DISSOLVING NANO FIBER PATCH

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ABSTRACT

In present investigation we have designed nanofiber patch of Glibenclamide to increase the retention time, bioavailability, onset of action and reducing the pre systemic metabolism. This will ultimately deliver an optimum therapeutic concentration of Glibenclamide in systemic circulation to exert its pharmacological action. Electrospun nanofibers have received special attention as drug delivery systems because of their distinct functional feature and easy fabrication techniques. Glibenclmide is a second-generation sulfonylurea antidiabetic agent. Glibenclamide bind to ATP-sensitive potassium channels on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Depolarization stimulates calcium ion influx through voltage-sensitive calcium channels, raising intracellular concentrations of calcium ions, which induces the secretion, or exocytosis, of insulin.

KEYWORDS: Glibenclamide, Electrospining, nanofiber patch, in vitro release.

INTRODUCTION

Oral medication conveyance is one among the famous courses of medication organization in view of its noninvasive nature, simple use, and better patient consistence. In addition, oral definitions are regularly structured in differed ways that and their creations territory unit cost viable. Contrasted and the contrary courses, the orally regulated uncertain amount kind wants no experience required and is in this way accommodating for endless ailments with incessant inconclusive amount utilization. Consequently, advancement of meds into oral item is liked.

building has been wide examined in oral medication conveyance in light of the comfort and high patient consistence identified with oral organization.[1]

Glibenclamide (GB) or Glyburide is partner oral operator from the second generation of sulfonylureas. This medication is wide utilized for the treatment of sort II diabetes (non-insulin subordinate). moreover, late investigations have incontestible its capacity to stop cerebral ischaemia also, haemorrhagic stroke.[2,3] In 2015, glibenclamide was encased inside the World Health Association model List of Essential Medicines. From a physico-concoction reason for read, glibenclamide demonstrates an oleophilic character and it's credited to the bunch II of the Biopharmaceutical framework (low solvency, high porousness). the most issue of its oral organization is its low bioavailability, outcome of its low solvency in physiological media. In this manner, the disintegration of glibenclamide is considered to be the speed restricting advance, as its ingestion when oral organization achieves forty fifth of the underlying amount of medication.[4]

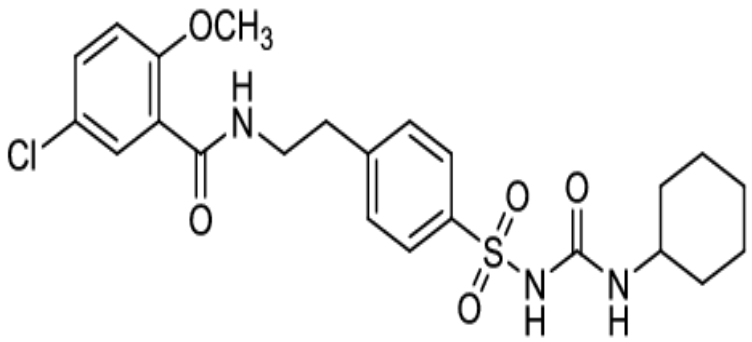

Fig. 1: Stracture of glibenclamide.

Mechanism of action

It is a moment age antidiabetic medicate antidiabetic sedate specialist, appears to bring down the glucose intensely by animating the release of hypoglycemic operator from the exocrine organ, an impression subordinate after working beta cells inside the pipe organ islets. With constant organization in kind II diabetic patients, the glucose bringing down outcome endures regardless of a progressive decrease inside the hypoglycemic operator secretary reaction to the medication. Glibenclamide tie to ATP-delicate K channels on the pipe organ cell surface, diminishing K electrical wonder and incurring change of the film. change invigorates thickening element inflow through voltage-delicate Ca channels, raising intracellular centralizations of Ca particles, that instigates the discharge, or exocytosis, of insulin.

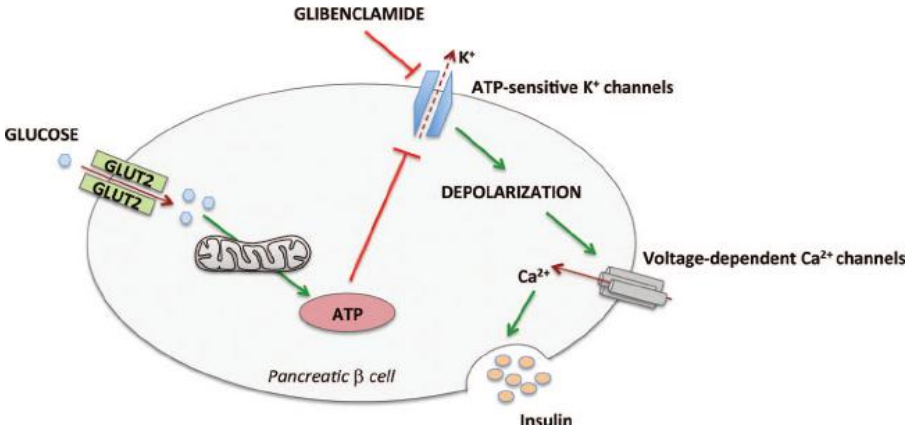

Figure 2.

Electrospinning could be a basic system for generation of nanofibers by sustaining a compound goals in an exceedingly high field of power. a thin fly is made from the appropriate response driblet and drawn by the electric field while the dissolvable dissipates and strong nano-or small scale filaments are regularly prepared. The instrument of nanofiber generation by electrospinning method. Creation of ultrafine filaments by partner power first announced in 1934.[5] In the mean time, in late year's instructive and mechanical investigation are significantly upgraded underway of electrospun nanofibers because of the outstanding qualities of effortlessness, skillfulness, and potential uses in various fields. The high stacking capacity, high epitome strength, conveyance of various prescription, improvement of medication solvency, simple activity, and cost-viability are the clarifications for patterns to use of electrospun nanofibers in medication conveyance.[6,7] changed medication conveyance frameworks with entirely unexpected medication unharness profiles like speedy, pulsatile and biphasic are with progress accomplished bolstered electrospun nanofibers.[8] this content introduces a survey on the improvements of electrospinning and concentrates on utilizations of electrospun nanofibers in medication conveyance.

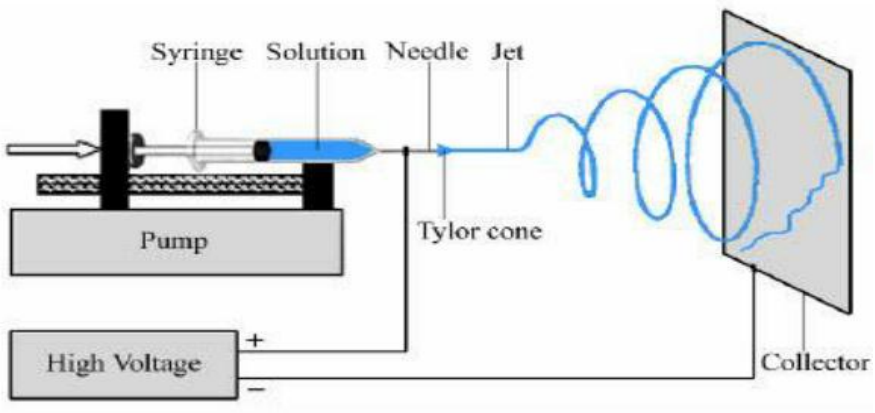

Figure 3.

Nanofibers may help in the improved care of: Intense injuries, just as those brought about by consumes, careful or awful injuries • Chronic injuries, similar to ulcers, not proceeding through the regular phases of recuperating

- Permeability of gases and fluids
- High retention capacity of fluids (exudate)
- High filtration intensity for bacterium prompting limited diseases
- Possibility to include drug – haemostatic or antimicrobial dressing
- Swelling and gel framing ability to remain wet environment
- Anti glue result to the dermis - effortless expulsion of the dressing while not obliterating new molded tissue

Materials

The following materials was from Glibenclamide *(*Aurobindo Pharmaceuticals, Hyderabad), Potassium di-hydrogen-*o* phosphate (Signet Chemical Corp. Pvt. Ltd., Mumbai), Sodium hydroxide palates, Ethanol (Changshu Yanguan Chemical, China), Methanol (Fisher Chemical Ltd., Ahmedabad), Acetone (Fisher Chemical Ltd., Mumbai), Di-chloro methane (Fisher Chemical Ltd., Mumbai), Chloroform (Fisher Chemical Ltd., Mumbai), Di-methyl sulphur oxide (Fisher Chemical Ltd., Mumbai), Di- methyl foramide (Fisher Chemical Ltd., Mumbai), n-octanol (Fisher Chemical Ltd., Mumbai), HPC(Fisher Chemical Ltd., Mumbai).

RESULT AND DISCUSSION

Preformulation studies

Preformulation studies area unit associate integral a part of the whole drug development method. it's the study of the physical and chemical properties of the drug previous change of integrity method. These studies target those chemistry properties of the drug that would {affect|have associate effect on} its execution and advancement of an adequate indefinite quantity type. a radical understanding of those properties could at last offer a explanation for formulation style. within the most straightforward case, these preformulation examinations could simply make sure that there aren't any important obstructions to the compound's advancement. These studies are indispensable protocol for development of safe, effective and stable dosage form. The obtained drug sample was identified by various analytical techniques such as UV spectroscopy, IR spectroscopy, melting point, solubility etc.

Organoleptic properties of medication (Glibenclamide): presented in Table.

Table 1: Organoleptic properties of medication (glibenclamide).

Description	Crystalline
Taste	without taste
Odor	Odorless
Colour	White

Melting point

Table 2: Data of glibenclamide melting point.

Drug	Specification	Observation
Glibenclamide	169°C-178°C	172°C-175°C

Discussion: The dissolving purpose of medication was observed to be range 172-175°C, hence drug sample was free from any type of impurities.

Determination Absorption Maxima by UV Spectroscopy of Glibenclamide

UV-VIS spectroscopy is basically utilized for quantitative examination and fills in as a helpful assistant instrument for basic explanation of various drugs to obtain specific information on the chromophoric part of the molecules in solution when exposed to light in the UV area of the range retaining light of specific wavelength relying upon the sort of electronic change related with the ingestion. The UV range is commonly recorded as a plot of absorbance versus wavelength.

A double beam UV-visible spectrophotometer was used for quantitative analysis of the drug. A 5 µg/ml solution of Glibenclamide in ethanol was varying in the limit of 300 nm. The result of UV spectrum of Glibenclamide is depicted in Figure.

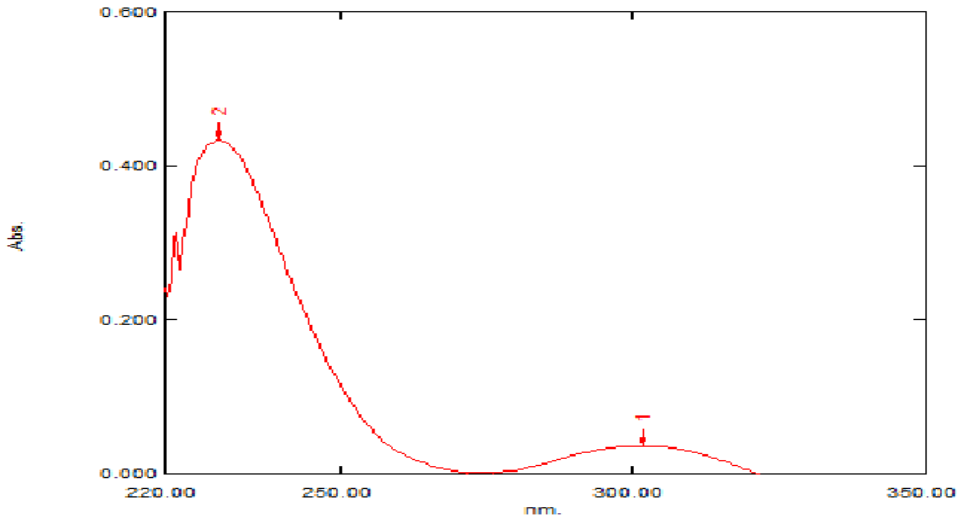

Figure 4: UV spectrum of glibenclamide in ethanol.

Discussion: The maximum wavelength of Glibenclamide was observed at 300 nm.

Table 3: Absorption maxima (λ_{max}) of Glibenclamide in ethanol.

Absorption maxima (λ_{max})	
Observed	**Reference**
300	220-310

Table 4: Preparation of standard calibration curve of glibenclamide in ethanol.

Concentration(µg/ml)	Max. Absorbance	Statistical data
10	0.086±0.0032	R^2 value= 0.999 Regression equation y = 0.138x - 0.005
20	0.178±0.0006	
30	0.263±0.0006	
40	0.353±0.0006	
50	0.448±0.0006	
60	0.544±0.0006	
70	0.638±0.0015	
80	0.733±0.0010	
90	0.850±0.0010	

The standard stock solution of Glibenclamide (1 mg/ml) was prepared in ethanol. This solution was diluted with ethanol to obtain suitable dilutions (10-100 µg/ml) and analyzed spectrophotometrically at 300 nm. The results obtained are shown below in Table 13 and graphically shown in Figure. The standard curve of Glibenclamide as shown in graph indicated the regression equation Y = 0.0095x -0.0201 and R^2 value is 0.999, which shows good linearity as shown in Tables, respectively.

Table: Standard curve data of Glibenclamide in ethanol.

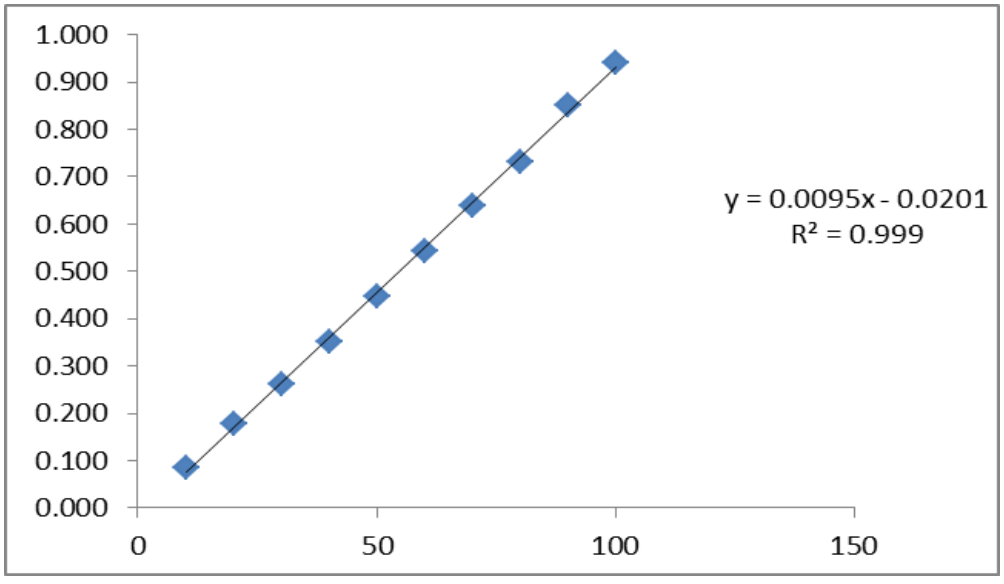

Figure 5: Standard curve of Glibenclamide in ethanol.

Solubility studies

The spontaneous interaction of two or more substances to form a homogenous molecular dispersion is called solubility. For solubility determination, excess amount of drug (100 mg) was added in each solvent (5.0 ml) in separate test tubes. These test tubes were kept in water bath shaker at 50 rpm for 24 hours at room temperature. After 24 hour, each sample was centrifuge and then sample was suitably diluted and analysed for the drug content using UV-VIS spectrophotometer. The observed solubility profile of the drug is shown in Table and Figure.

Table 5: Solubility profile of Glibenclamide in different solvent.

Solvents	Solubility Observed (mg/ml)
Water	0.051333± 0.000608
PH-6.8	0.067123± 0.000608
PH-7.4	0.739754± 0.533011
Ethanol	3.102802± 0.006077
Methanol	5.337895± 0.010526
Acetone	26.18596±0.60774
DCM	31.02807 ± 0.160792
Chloroform	34.43158±0.105263

(Mean ± SD, N=3)

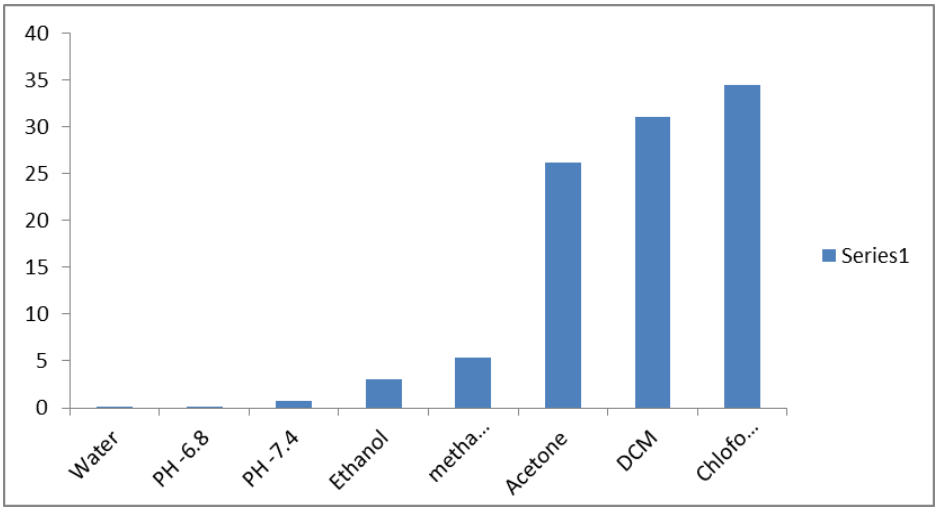

Figure 6: Solubility profile of Glibenclamide in different solvent.

Discussion: The drug Glibenclamide was more soluble in water < PH-6.8 < PH-7.4 < Ethanol < Methanol < Acetone < DCM < Chloroform.

Partition coefficient determination

The partition coefficient determination study was performed by using shake flask method. The Partition-coefficient of Glibnclamide is shown in Table.

Table 6: Partition coefficient of glibenclamide.

Drug	Partition coefficient (log P)	
	Observed	Reported
Glibencamide	1.463636 ± 0.019242072	4.7

(Mean ± SD, n=3)

Discussion: The partition coefficient of Glibenclamide in n- Octanol: Water was found to be 1.463636 ± 0.019242072. This indicates that the drug is lipophilic in nature.

FTIR analysis of pure drug

The FTIR spectrum and its interpretation for Glibenclamide is shown in Figure and Table, respectively.

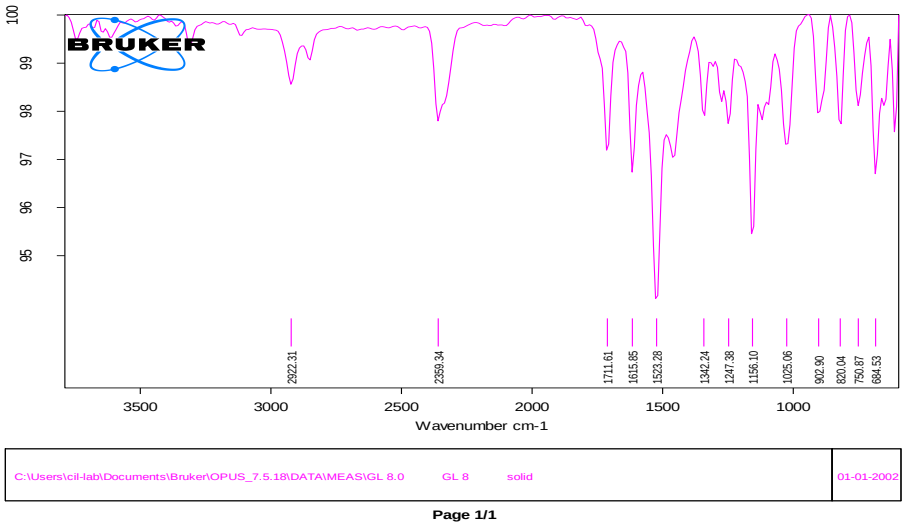

Figure 7: FTIR spectrum of Glibenclamide.

Table 7: Interpretation of FTIR spectrum of Glibenclamide.

Reported peak	Observed peak	Functional group (cm^{-1})
3000-3700		N-H stretching
2950-2850	2922.31	Alkyl C-H stretching
1715	1711.61	OCH3 stretching
1600-1900	1615.85	C=O stretching
1060	1025.06	S=O stretching

Drug excipient compatibility study by FTIR spectroscopy.

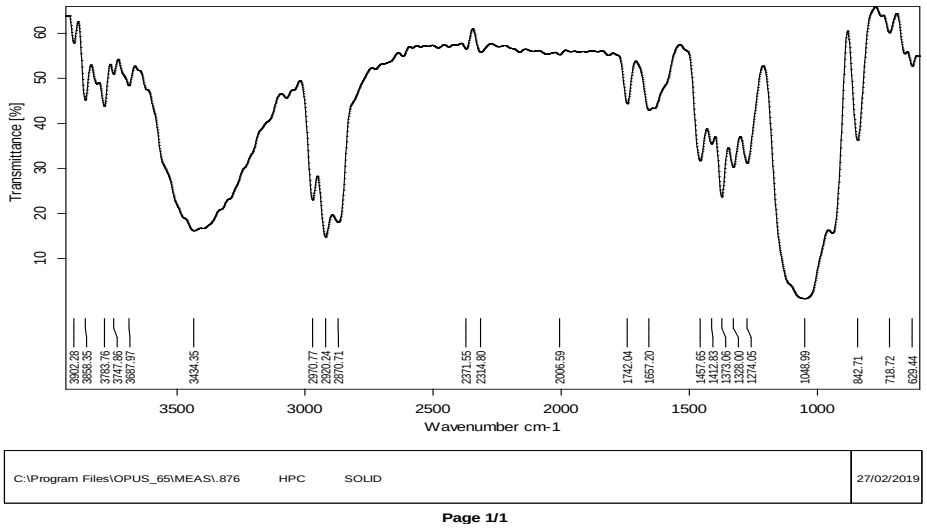

Figure 8: FTIR spectrum of pure HPC.

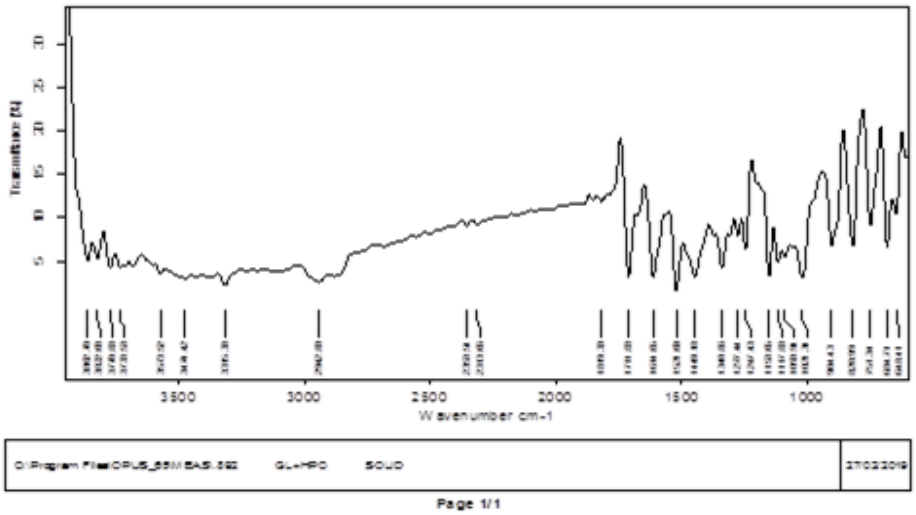

Figure 9: FTIR spectrum of Physical mixture (HPC+ Drug).

Drug loading capacity (%).

Table 8: Percentage Drug loading capacity of nanofiber patch.

Formulation code	Drug loading capacity (%)
F19	87.63 ±0.60
F20	94.78 ±0.86
F22	85.99 ±0.33
F24	89.95 ±1.017

In vitro release kinetics

In-vitro drug release kinetic study data of formulation F20 was given below.

- **Zero order kinetics models**

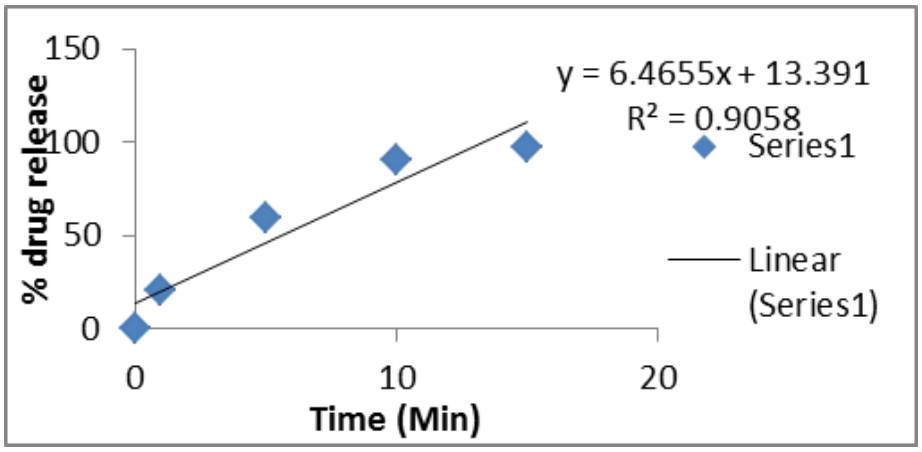

Figure 12: Zero order graph of formulation F20.

- **First order kinetics model**

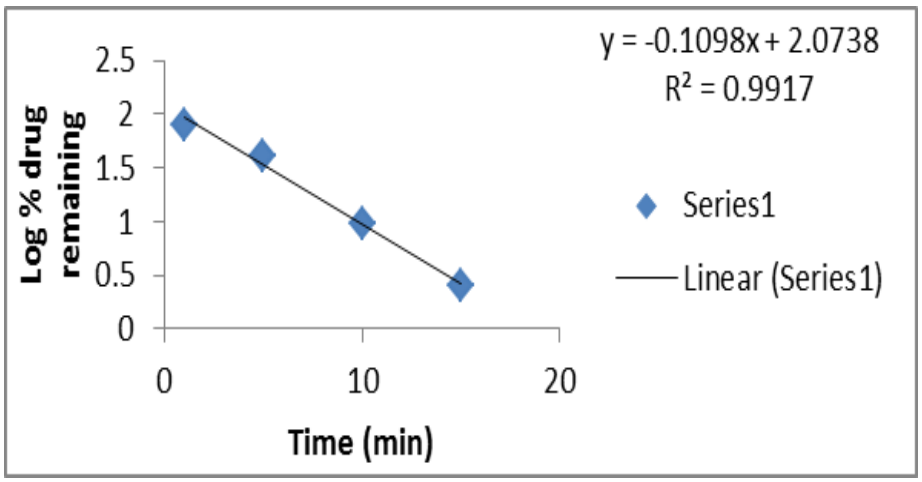

Figure 13: First order graph of formulation F20.

- **Higuchi kinetics model**

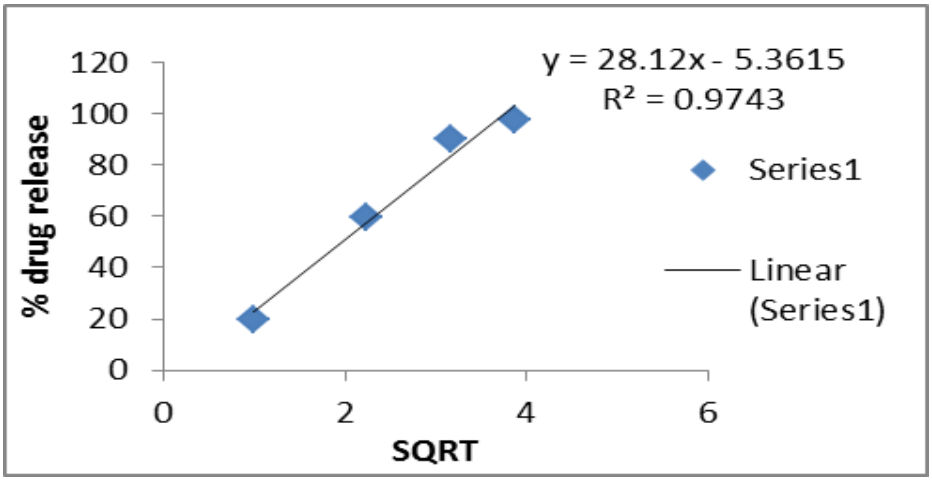

Figure 14: Higuchi order graph of formulation F20.

➢ **Korsmeyer peppas kinetics model**

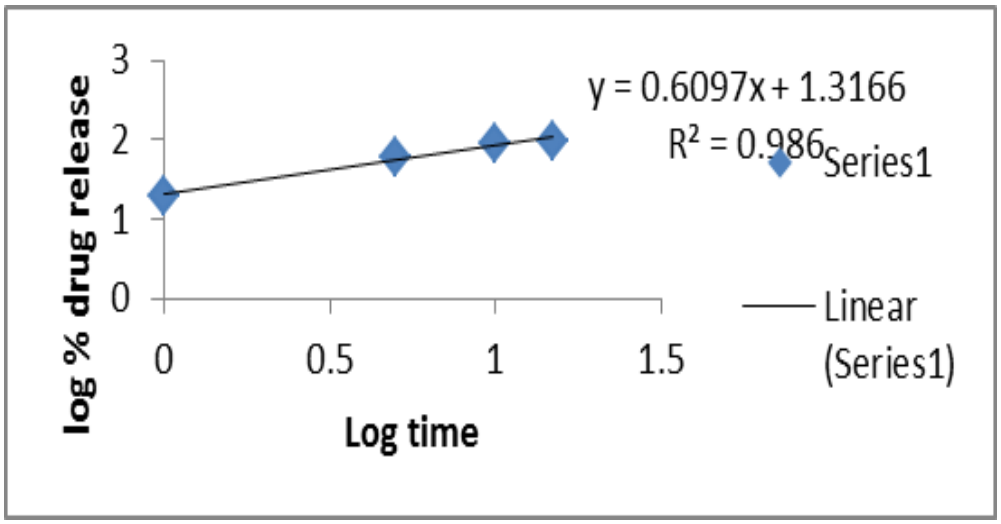

Figure 15: Korsmeyer peppas order graph of formulation F20.

Table 9: Kinetic equation parameter of formulation F20.

Formulation Name	Zero order		First order		Higuchi		Peppas	
	R^2	K_0	R^2	K_0	R^2	K_0	R^2	K_0
F20	0.905	6.4655	0.9917	-0.1098	0.9743	28.12	0.986	0.609

The data obtained for in vitro release shown in Table were fitted into equation for the zero order, first order, higuchi, and Korsmeyer peppas models. The interpretation of data was based on the value of the resulting regression coefficients.

CONCLUSION

Fast dissolving patch of Glibenclamide enhances the, bioavailability, absorption and reduces the side effect. It is convenient for paedriatic and geriatric patient. Polymers are widely used in the pharmaceutical field. They are easily available in market and non toxic in nature. Polymer's is effectively used for the preparation of fast dissolving patch. It was found to be nano fiber patch enhance the in vitro release. Polymer (HPC) Patch containing Glibenclamide loaded nano fiber patch appeared clear with best characteristics.

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