FINAL REPORT

of

MAJOR RESEARCH PROJECT of
UNIVERSITY GRANTS COMMISSION, NEW DELHI

[F.N. 42-703/2013(SR), 25-03-2013
W.E.F. April 01, 2013 to March 31, 2017]

for

ENTITLED

"Preparation and Characterization of Novel Nanomaterial Antidiabetic Oral Formulations"

SUBMITTED BY:

Dr. Prabhakar Kumar Verma,
M.Pharm, Ph.D
PRINCIPAL INVESTIGATOR & ASSISTANT PROFESSOR
Department of Pharmaceutical Sciences,
Maharshi Dayanand University, Rohtak-124001 (HR),
India

September, 2017

MAHARSHI DAYANAND UNIVERSITY ROHTAK
(A State University established under Haryana Act No. XXV of 1975)
'A' Grade University accredited by NAAC

No.FO/UGC/17/ 5738
Date 18-10-17

To

Registered

Under Secretary,
University grants Commission
Bhadurshah Zafar Marg,
New Delhi – 110002

Sub:- **Final Report, Statement of Expenditure & Utilization Certificate of the UGC Major Research Project (MRP)-Dr. Prabhakar Kumar Verma, Department of Pharmacy.**

Ref. No. F. No.42-703/2013 (SR) dated 24.05.2014.

Sir/Madam,

Please find enclosed herewith Final Report, Statement of Expenditure & Utilization Certificate, month/year-wise statement of fellowship + HRA due, paid & outstanding and Statement of Expenditure incurred on field work of the Major Research Project assigned to Dr. Prabhakar Kumar Verma in the Department of Pharmacy duly signed by the Finance Officer, Registrar and Joint Director (Audit) of this University for kind consideration. The Principal Investigator has utilized an amount of Rs.12,24,665/- out of total grant of Rs.12,66,144/- released by the Commission.

Further, requested to allow to utilize the unspent balance Rs.41479/- and release more grant Rs.17004/- to meet the outstanding payment of contingency & fellowship.

This is for your kind consideration and necessary action.

Yours faithfully,

Encl: As above.

Asstt. Registrar (Accounts-UGC)
for Director (Research)

Copy to:
Head, Department of Pharmaceutical Sciences, M.D. University, Rohtak.

विश्वविद्यालय अनुदान आयोग
बहादुरशाह जफर मार्ग
नई दिल्ली-110 002
UNIVERSITY GRANTS COMMISSION
BAHADURSHAH ZAFAR MARG
NEW DELHI-110 002

F. No. 42-703/2013 (SR)

The Under Secretary (FD-III)
University Grants Commission
New Delhi-110002

25 MAR 2013

Sub :- UGC support for the Major Research Project in Physical Sciences, Bio-Sciences, Maths , Medical, Agricultural Sciences and Engineering & Chemistry to University/College Teachers – Project entitled,

"Preparation and characterization of novel nanomaterial antidiabetic oral formulations"

Sir,

I am to refer to your letter forwarding the application of Dr. Prabhakar Kumar Verma of your institution for financial assistance under the above scheme and to convey the Commission's approval & sanction an on account grant of Rs. 9,54,300/- (Rupees: nine lakh fifty four thousand three hundred only) to the Registrar, Maharshi Dayanand University, Rohtak-124001, Haryana in r/o Major Research Project of Dr. Prabhakar Kumar Verma, Department of Pharmacy for the period of 3 years w.e.f. 1.4.2013 as detailed below :-

S.No	ITEMS	AMOUNT APPROVED	GRANT RELEASED AS Ist INSTALMENT	Category
A.	Non - Recurring		4,75,000/-	GEN
1.	Books & Journals	25,000/-		
2.	Equipment (Spectrophotometer (double.....))	4,50,000/-		
B.	Recurring		4,79,300/-	
1.	Honorarium to Retd. Teacher @ Rs. 12,000/- p.m.	nil		
2.	Project Fellow @14,000/- p.m. for initial 2 years and Rs. 16,000/- p.m. from the third year onwards.	5,28,000/-		
3.	Chemical/ Glassware / Consumable	1,50,000/-		
4.	Hiring Services	50,000/-		
5.	Contingency	50,000/-		
6.	Travel/Field Work	25,000/-		
7.	Special Need	nil		
8.	Overhead Charges @ Rs. 10% approved recurring Grant (Except Travel & Field Work)	77,800/-		
	Total (A + B)	13,55,800/-	9,54,300/-	

The acceptance Certificate in prescribed format (Annexure-I available on the UGC web-site) may be sent to the undersigned within one month from the issue of the award letter failing which the project may be treated as cancelled

If the terms & conditions are acceptable as per guideline which are available on UGC web-site www.ugc.ac.in the Demand Draft/ Cheque being sent may be retained. Otherwise the same may be returned in original to the UGC by Registered Post in variably with in 15 days from the receipt of the Demand Draft/Cheque in favour of Secretary, UGC, New Delhi

Principal Investigators should ensure that the statement of expenditure & utilization Certificate to the effect that the grant has been utilized for the purpose for which it has been sanctioned shall be furnished to the University Grants Commission in time

The first instalment of the grant shall comprise of 100% of the Non –Recurring including Over Head Charges, and 50% of the total Recurring grant.

12. The sanction is issued in exercise of the delegation of powers vide UGC Order No. 69/2014 [F No 10-1/12 (Admn. IA & B)] dated 26/3/2014

13. The University / Institution shall strictly follow the UGC Regulations on curbing the menace of Ragging in Higher Education Institutions, 2009

14. The University / Institution shall take immediate action for its accreditation by National Assessment & Accreditation Council (NAAC)

15. The accounts of the University / Institution will be open for audit by the Comptroller & Auditor General of India in accordance with the provisions of General Financial Rules, 2005.

16. The annual accounts i.e. balance sheet, income and expenditure statement and statement of receipts and payments are to be prepared strictly in accordance with the Uniform Format of Accounting prescribed by Government

17. An amount of **Rs. 9,02,800/-** out the grant of **Rs. 9,53,300/-**..... Sanctioned vide letter No. **F. No. 42-703/2013 (SR)** dated **22-03-2013 has** been utilized by University/College/Institution for the purpose for which it was sanctioned. **Utilization** Certificate for **Rs** ....NIL... ... has been entered at S. No..... now we may enter Utilization Certificate for **Rs...9,02,800/-** .....S. No..114... and in the U.C. Register at page No. 57.

18. Funds to the extent of Rs are available under the scheme or BE / RBE of the year 2016-17. .

19. These issues with the concurrence of IFD vide Diary No. 6077 (IFD) dated 20.01.2016.

20. This issues with the approval of Joint Secretary (MRP) vide Diary No. 50091 dated 05.02.2016 and revalidated for the financial year 2016-17 with the approval of the Chairman, UGC vide Diary No. 58242 dated 28.04.2016.

Your faithfully,

(G.S. AULAKH)
UNDER SECRETARY

Copy forwarded for information and necessary action for :-

1. The Registrar, Maharashi Dayanand University, Rohtak- 124001 Haryana
2. Office of The Registrar, General of Audit, Central Revenues, AGCR Building, I.P. Estate, New Delhi.
3. Accountant General, State Govt. of Haryana, Chandigarh.
4. Dr. Prabhakar Kumar Verma, Department of Pharmacy, Maharashi Dayanand University, Rohtak- 124001 Haryana
5. Guard file.

(ARUN KUMAR SINHA)
(SECTION OFFICER)

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI 110002
GEN

FD Diary No. 126
Dated : 11.05.2016
24 MAY 201

F. No.42-703/2013 (SR)

May 2016

The Under Secretary (FD-III)
University Grants Commission
Bahadur Shah Zafar Marg
New Delhi – 110002

Sub: Release of Grant-in aid to **Maharashi Dayanand University, Rohtak- 124001 Haryana** for the year 2016-17 under plan in respect of Major Research Project entitled **"Preparation.....formulations"** awarded to **Dr. Prabhakar Kumar Verma, Department of Pharmacy,** tenure of project from **01.04.2013 to 31.03.2017.**

Sir,

I am directed to convey the sanction of the University Grants Commission for payment of grant of **Rs. 3,11,844/- (Rupees Three lakh eleven thousand eight hundred forty four only)** as **2nd installment** for the year 2016-17 towards Major Research Project to **The Registrar, Maharashi Dayanand University, Rohtak- 124001 Haryana** for the plan expenditure.

I am also directed to say that the tenure of the above project has been extended by the UGC upto 31.03.2017 without any additional financial assistance for the extended period.

Name of the Item	Amount Allocated	Head of Account	Grant now Being Sanctioned	Grant already Released	Total Grant
Books & Journal	25,000/-	3.A(56).35	.....	25,000/-	25,000/-
Equipment	4,50,000/-		.....	4,50,000/-	4,50,000/-
Honorarium	.....	3.A(56).31	.....	.....	.....
Project fellow	4,85,877/-		1,73,289/-	2,64,000/-	4,37,289/-
HRA	42,838/-		38,555/-	.....	38,555/-
Chemicals	1,50,000/-		60,000/-	75,000/-	1,35,000/-
Contingency	50,000/-		20,000/-	25,000/-	45,000/-
Hiring Services	50,000/-		20,000/-	25,000/-	45,000/-
Travel/field work	25,000/-		.....	12,500/-	12,500/-
Overhead Charges	77,800/-		.....	77,800/-	77,800/-
Additional Grant	.....		.....	.....	.....
Total	13,62,311/-		3,11,844/-	9,54,300/-	12,66,144/-

1. The sanctioned amount is debit able to **Major Research Project** head Sector **3.A(56).31** and is valid for payment during the financial year **2016-17** only

Annexure – IX

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

PROFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1. Title of the Project: **Preparation and characterization of novel nonmaterial antidiabetic oral formulations**

2. NAME AND ADDRESS OF THE PRINCIPAL INVESTIGATOR: Dr. Prabhakar Kumar Verma
Department of Pharmaceutical Sciences
Maharshi Dayanand University,
Rohtak-124001 (HR)

3. NAME AND ADDRESS OF THE INSTITUTION: Department of Pharmaceutical Sciences
Maharshi Dayanand University,
Rohtak-124001 (HR)

4. UGC APPROVAL LETTER NO. AND DATE: 42-703 (SR) and March 25, 2013

5. DATE OF IMPLEMENTATION: 01-04-2013

6. TENURE OF THE PROJECT: 4 years (One year extension letter attached)

7. TOTAL GRANT ALLOCATED: Rs. 13,62,311 -

8. TOTAL GRANT RECEIVED: Rs. 12,66,144 -

9. FINAL EXPENDITURE: Rs. 12,24665/-

10. TITLE OF THE PROJECT: Preparation and characterization of novel nonmaterial antidiabetic oral formulations

11. OBJECTIVES OF THE PROJECT: See attachment

12. WHETHER OBJECTIVES WERE ACHIEVED: See attachment

13. ACHIEVEMENTS FROM THE PROJECT: See attachment

14. SUMMARY OF THE FINDINGS See attachment
(IN 500 WORDS)

15. CONTRIBUTION TO THE SOCIETY See attachment

16. WHETHER ANY PHD. ENROLLED/PRODUCED OUT OF THE PROJECT 01 Candidate enrolled

17. NO. OF PUBLICATIONS OUT OF THE PROJECT 01 Paper published, 02 papers under consideration, 02 national conference publications (See attachment)

Dr. Prabhakar Kumar Verma

(PRINCIPAL INVESTIGATOR)

PLACE: ROHTAK

Department of Pharmaceutical Sciences
M.D. University, Rohtak-124001 (Haryana)

HOD

18/9/17

Head
Dept. of Pharmaceutical Sciences
M.D. University, ROHTAK

(REGISTRAR PRINCIPAL)
(Seal)

11. OBJECTIVES OF THE PROJECT:

For the development and characterization of novel nanomaterial antidiabetic oral formulations following protocol has been adopted:

1. Selection of antidiabetic drugs like Glipizide, Tolbutamide and Metformin.
2. Preparation of nanoparticles by vapor processing methods (a) Evaporation method i.e by using suitable solvents
3. Characterization of nanoparticles by using Malven particle size analyzer, UV spectrophotometery, DSC, XRD, HPLC and SEM.
4. Selection of excipients: Stearic acid, Pluronic F127, Polycaprolactone, Polyvinyl alcohol
5. Formulation development of nanoparticles
   A. Characterization of nanoformulation by using Malven particle size analyzer, UV spectrophotometery, DSC, XRD, HPLC and SEM.
   B. Determination of antidiabetic activity of formulations with using alloxan or streptozotocin induced animals.
   C. Toxicological study for nanoformulations.
6. Biopharmaceutical and pharmacokinetic evaluation of nanoformulations.
7. Stability study:

   Short term accelerated study will be carried out for 03 months.

12. WHETHER OBJECTIVES WERE ACHIEVED:

The achievement from the project are:-

a) The glipizide nanoformulation were prepared by using various polymeric systems and showed controlled release pattern. The blood glucose level controlled by glipizide nanoformulation was upto 24 hours compared to diabetic control and results were also better at 4h, 6h, 8h, 12h and 24h time intervals compared to standard drug glipizide.

b) The metformin loading nanoformulation was prepared using solvent evaporation method. The results of *in-vitro* drug release studies and in-vivo antidiabetic activity demonstrate the enhanced efficiency and response of nanoencapsulated metformin formulation relative to pure metformin.

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b) The metformin loading nanoformulation was prepared using solvent evaporation method. The results of *in-vitro* drug release studies and in-vivo antidiabetic activity demonstrate the enhanced efficiency and response of nanoencapsulated metformin formulation relative to pure metformin.

e) The tolbutamide nanoparticles were fabricated by using PCL polymer and phyio-chemical properties were evaluated. The polymeric systems gives prolonged release profiled tolbutamide nanoformulation which was confirmed by *in vitro* and *in vivo* activities.

13. ACHIEVEMENTS FROM THE PROJECT: We have prepared the antidiabetic nanoformulation by using various polymers and copolymers and evaluated for invitro and in vivo activities. We have carried out pharmacokinetic studies and stability studies of different nanoformulations and it was found to be therapeutically active compared to conventional antidiabetic drugs. We have published 01 paper, 02 under consideration and 02 national conference publications.

14. SUMMARY OF THE FINDINGS:

From the present study, it may be concluded that the glipizide loaded SAF127 nanoformulation is a valuable carrier for the design of a controlled drug delivery system of poorly water soluble drugs like glipizide. This nanoformulation can be utilized to improve the therapeutic efficacy of poorly water soluble drugs. The changes in nanoparticles size, zeta potential, PDI and entrapment efficiency was affected with the change in copolymer to drug ratio. PSA results show that there is change in the size of the nanoparticles. There was no interaction between glipizide, SAF127 and PVA has been observed as there was no shift in peaks was observed in physical mixture and optimized glipizide nanoparticles. This indicates that there is no chemical interaction between drug and polymer. The DSC thermogram of SAF127, PVA, pure glipizide physical mixture and optimized drug nanoparticles showed no significant interaction. XRD studies indicates that glipizide encapsulated within the polymer matrix and posses partially amorphous nature. The formulated glipizide nanoparticles showed smooth and spherical shaped appearance under scanning electron microscope. The *in vitro* release of the glipizide from nanoformulation showed initial burst release and then sustained release behaviour upto 24 h. The *in vivo* antidiabetic studies in wister albino rats revealed that the blood glucose level was controlled by glipizide nanoformulation upto 24 hours compared to diabetic control and results were also better at 4h, 6h, 8h, 12h and 24h time intervals compared to standard drug

glipizide. The pharmacokinetic studies showed improvement in C_{max}, t_{max} and biological half-life of nanoformulation compared to standard drug.

The synthesis of metformin nanoparticles were done by selecting suitable polymeric system PCL and Pluronic F127 as surfactant, which can control the drug release of BCS class III water soluble drug candidate. The nanoparticles size, zeta potential and entrapment efficiency was depend upon ratio of drug to polymer and changed with the alteration in ratio. Prepared nanoparticles showed no compatibility issues, which were confirmed by the FT-IR and DSC. XRD analysis revealed that the prepared nanoparticles possess semiamorphous characteristics with slight deviation in its intensity and weakened peaks of the metformin. The *in-vitro* drug release studies showed that the metformin nanoformulation represent controlled drug release as compared to metformin (pure drug) at ratio of 1:2 (drug : PCL). The 100% pure metformin released was observed with in 1 h whereas controlled release was maintained for metformin nanoformulation. The nanoparticles morphology was observed by SEM and was found to be spherical shaped appearance. the *in vivo* studies on wister albino rats showed the better of blood glucose level upto 24 h compared to pure drug which was last upto 4h. Pharmacokinetic studies of optimized metformin nanoformulation showed improvement in C_{max}, t_{max} along with biological half-life of nanoformulation compared to standard drug

The tolbutamide belongs to BCS class 2 and possesses lipophilic characteristics. The nanoparticles were prepared by using SAF127 copolymer and span 80 as emulsifier. Tolbutamide loaded nanoformulation showed polymer to drug ratio controlled parameters. With the increase in amount of drug from 1:1 to 1:4 particle size, PDI, zeta potential and entrapment efficiency was changed. Drug to polymer compatibility was check by using FT-IR and DSC which shows no significant interactions. The *in vitro* and *in vivo* studies showed there was improvement in release profile and blood glucose level compared to pure drug respectively. The pharmacokinetic investigation shows slight improvement in pharmacokinetic parameters compared to standard drug.

Short term stability studies of all these nanoparticles was performed and due to high zeta potential (negative value) and smaller PDI value gives stable nanosuspensions with changes in stability.

15. CONTRIBUTION TO THE SOCIETY:

The prepared antidiabetic nanoformulations were found to have prolonged released profile with respected to polymeric selection. Further, these preclinical studies can be extended upto clinical studies with the target of industrial nanoformulations.

17. NO. OF PUBLICATIONS OUT OF THE PROJECT:

01 Paper published; 02 under consideration, 02 national conference publications

a) Vipan Kumar Kamboj and Prabhakar Kumar Verma. Poloxamers based nanocarriers for drug delivery system. Der Pharmacia Lettre, 2015, 7 (2):264-269

b) S. Kumari, Vipan Kumar Kamboj, Diksha Rajpoot, Anil Kumar Teotia, Prabhakar Kumar Verma, G.N. Singh The Unprecedented Role of Gold Nonmaterial in Diabetes Management.

Communicated: Recent Patents on Drug Delivery & Formulation

c) Vipan Kumar Kamboj, Prabhakar Kumar Verma, Anil Kumar Teotia Preparation, characterization, and in vivo study glipizide loaded Stearic acid coupled Pluronic F127 nanoparticles.

Communicated: Pharmaceutical Development and Technology

National Conference Publication:

d) Vipan Kamboj, Prabhakar Verma. Formulation, evaluation and characterization of metformin HCl nanoformulation, April 15, 2017. National conference on "Recent Advancements in Pharmaceutical Sciences and Clinical Research". Organized by Galgotias University, Greater Noida

e) Vipan Kumar Kamboj, PK Verma. Polymeric nanocarriers for oral nanostructured drug delivery systems. APTI sponsored National conference on "Challenges and Opportunities in Drug Design and Development", April 23, 2016. Organized by JCDV, Sirsa

Annexure-III

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

STATEMENT OF EXPENDITURE IN RESPECT OF MAJOR RESEARCH PROJECT

1. Name of Principal Investigator: Dr. Prabhakar Kumar Verma
2. Deptt. of Principal Investigator: Department of Pharmaceutical Sciences
University/College: Maharshi Dayanand University, Rohtak
3. UGC approval Letter No. and Date: F.No. 42-703 (SR) and March 25, 2013
4. Title of the Research Project: Preparation and characterization of novel nonmaterial antidiabetic oral formulations
5. Effective date of starting the project: 01-04-2013
6. a. Period of Expenditure: From 01-04-2013 to 31-03-2017
b. Details of Expenditure:

S. No.	Name of the Item	Amount Approved	Grant Released	Expenditure	Balance	Outstanding Payments
i.	Book & Journals	25000/-	25000/-	24715/-	285/-	Nil
ii.	Equipment	4,50,000/-	4,50,000/-	4,50,000/-	Nil	Nil
iii	Contingency	50,000/-	45,000/-	43,818/-	1182/-	6,182/-
iv.	Field Work/Travel (Give details in the proforma at Annexure-IV).	25,000/-	12,500/-	12,500/-	Nil	Nil
v.	Hiring Services	50,000/-	45,000/-	5,300/-	39,700/-	Nil
vi.	Chemicals & Glassware	1,50,000/-	1,35,000/-	1,34,688/-	312/-	Nil
vii	Overhead	77,800/-	77,800/-	77,800/-	Nil	Nil
viii.	Any other items (Please specify)	Nil	Nil	Nil	Nil	Nil
A	**Total**	**8,27,800/-**	**7,90,300/-**	**7,48,821/-**	**41,479/-**	**6,182/-**

c. Staff

Date of Appointment: Mr. Dipanshu Sharma – 07-05-2013 (FN)

Mr. Vipan Kumar – 08-10-2013 (AN)

S. No.	Items	From	To	Amount Approved (Rs.)	Grant Released	Expenditure Incurred (Rs.)	Balance (Rs.)	Outstanding Payments (Rs.)
1.	Honorarium to PI (Retired Teachers) @ Rs. 18,000/- p.m.	Nil	Nil	Nil	Nil	Nil	Nil	Nil
2.	**Project fellow:** **i) NET/GATE qualified-** Rs. 16,000/- p.m. for initial 2 years and Rs. 18,000/- p.m. for the third year.	07/05/2013	09/09/2013	4,85,877/-	4,37,289/-	57,490/-	Nil	Nil
	ii) Non-GATE/Non-NET- Rs. 14,000/- p.m. for initial 2 years and Rs. 16,000/- p.m. for the third year.	09/10/2013	31/03/2016			3,79,799/-	Nil	48,070/-
	iii)HRA	08/10/2013	31/03/2016	42,838/-	38,555/-	38,55[illegible]	Nil	4,231/-
	B			5,28,715/-	4,75,844/-	4,75,844/-	Nil	52,301
	Grand Total (A+B)			13,56,515/-	12,66,144/-	12,24665/-	41,479/-	58,483/-

1. It is certified that the appointment(s) have been made in accordance with the terms and conditions laid down by the Commission.

2. If as a result of check or audit objection some irregularly is noticed at later date, action will be taken to refund, adjust or regularize the objected amounts.

3. Payment @ revised rates shall be made with arrears on the availability of additional funds.

4. It is certified that the amount of Rs. **1224665/-** (Rupees **twelve lakh twenty four thousand six hundred sixty five only**) out of grant of Rs. **12,66144/-** (Rupees: **twelve lakh sixty six thousand one hundred forty four only**) received from the University Grants Commission under the scheme of support for Major Research Project entitled "**Preparation and characterization of novel nanomaterial antidiabetic oral formulations**" vide UGC letter No. F. **42-703 (SR)** dated **March 25, 2013** has been utilized for the purpose for which it was sanctioned and in accordance with the terms and conditions laid down by the University Grants Commission.

Note: The request is to allow to utilize the unspent amount Rs. **41479/-** and release the grant Rs. **17004/-** more to meet the outstanding payment of Rs. **6182/-** for contingency and Rs. **52301/-** for the fellowship and HRA (**i.e Rs.48070/- fellowship + 4231/- HRA**).

SIGNATURE OF PRINCIPAL INVESTIGATOR

Dr. Prabhakar Kumar Verma
PI-MRP (UGC)
Department of Pharmaceutical Sciences
M.D. University, Rohtak-124 001

Registrar (Com-finance) Officer
M.D. University
REGISTRAR/PRINCIPAL
ROHTAK (Seal)

HOD

29/9/17
Head
Dept. of Pharmaceutical Sciences
M.D. University, Rohtak

Rs. 12,24,665/- Expenditure verified

Resident Senior Auditor,
Local Audit Haryana,
M.D.U., Rohtak.

Month/Year Wise Statement of Fellowship + HRA Due, Paid and Outstanding Payments

Name of Project Fellow: Dipanshu Sharma

Sr. No.	Month & year	Fellowship Due	Fellowship paid	HRA Due	HRA Paid	Outstanding Fellowship	Outstanding HRA
1	May (7-5-13 to 31-5-13)	11,290/-	11290/-	Nil	Nil	Nil	Nil
2	June, 2013	14,000/-	14,000/-	Nil	Nil	Nil	Nil
3	July, 2013	14,000/-	14,000/-	Nil	Nil	Nil	Nil
4	August, 2013	14,000/-	14,000/-	Nil	Nil	Nil	Nil
5	Sep. (1-9-13 to 09-9-13)	4,200/-	4,200/-	Nil	Nil	Nil	Nil
Name of Project Fellow: Vipan Kumar							
6	Oct. (9-10-13 to 31-10-13)	10,387	10,387/-	1038/-	1038/-	Nil	Nil
7	November, 2013	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
8	December, 2013	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
9	January, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
10	February, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
11	March, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
12	April, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
13	May, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
14	June, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
15	July, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
16	August, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
17	September, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
18	October, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
19	November, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
20	December, 2014	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
21	January, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
22	February, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
23	March, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
24	April, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
25	May, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
26	June, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
27	July, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
28	August, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
29	September, 2015	14,000/-	14,000/-	1400/-	1400/-	Nil	Nil
30	October (1-10-15 to 8-10-15) and (9-10-15 to 31-10-15)	15,482/-	15,482/-	1548/-	1548/-	Nil	Nil
31	November, 2015	16,000/-	16,000/-	1600/-	1600/-	Nil	Nil
32	December, 2015	16,000/-	15930/-	1600/-	1600/-	70/-	Nil
33	January, 2016	16,000/-	00/-	1600/-	569/-	16,000/-	1031/
34	February , 2016	16,000/-	00/-	1600/-	00/-	16,000/-	1600/-
35	March , 2016	16,000/-	00/-	1600/-	00/-	16,000/-	1600/-
Total		**485359/-**	**437289/-**	**42786/-**	**38559/-**	**48070/-**	**4231/-**

Dr. Prabhakar Kumar Verma
PI-MRP (UGC)
Department of Pharmaceutical Sciences
M.D. University, Rohtak-124001 (Haryana)

Principle Investigator

HOD

Head
Dept. of Pharmaceutical Sciences
M.D. University, Rohtak

Registrar/Principal
(Seal)

Resident Senior Auditor,
Local Audit, Haryana,
M.D.U., Rohtak.

Annexure - IV

UNIVERSITY GRANTS COMMISSION
BAHADUR SHAH ZAFAR MARG
NEW DELHI – 110 002

STATEMENT OF EXPENDITURE INCURRED ON FIELD WORK

Name of the Principal Investigator: Dr. Prabhakar Kumar Verma

Name of the Place visited	Duration of the Visit		Mode of Journey	Expenditure Incurred (Rs.)
	From	To		
1) PU Chandigarh	20/05/2016	20/5/2016	By Bus	1435/-
2)Blessing Pharma, Nagpur	30/05/2016	29/06/2016	By train	11065/-
			Total	12500/-

Certified that the above expenditure is in accordance with the UGC norms for Major Research Projects.

SIGNATURE OF THE PRINCIPAL INVESTIGATOR

Dr. Prabhakar Kumar Verma
PI-MRP (UGC)
Department of Pharmaceutical Sciences
M.D. University, Rohtak-124001 (Haryana)

REGISTRAR/PRINCIPAL
ROHTAK
(Seal)

STATUTORY AUDITOR
(Govt. Internal Auditor/ Chartered Accountant)
(Seal)

HOD
Head
Dept. of Pharmaceutical Sciences
M.D. University, Rohtak

Resident Auditor,
Local Audit, Haryana,
M.D.U., Rohtak.

Annexure - V

UNIVERSITY GRANTS COMMISSION

BAHADUR SHAH ZAFAR MARG

NEW DELHI – 110 002

Utilization certificate

Certified that the amount of Rs. 1224665/- (Rupees: **twelve lakh twenty four thousand six hundred sixty five only**) out of grant Rs. 12,66144/- (Rupees: **twelve lakh sixty six thousand one hundred forty four only**) received from the University Grants Commission under the scheme of support for Major Research Project entitled "**Preparation and characterization of novel nanomaterial antidiabetic oral formulations**" vide UGC letter No. F. 42-703 (SR) dated March 25, 2013 has been utilized for the purpose for which it was sanctioned and in accordance with the terms and conditions laid down by the University Grants Commission.

If as a result of check or audit objection some irregularly is noticed at later date, action will be taken to refund, adjust or regularize the objected amounts.

Note: The request is to allow to utilize the unspent amount Rs. 41479/- and release the grant Rs. 17004/- more to meet the outstanding payment of Rs. 6182/- for contingency and Rs. 52301/- for the fellowship and HRA (**i.e Rs.48070/- fellowship + 4231/- HRA**).

SIGNATURE OF THE PRINCIPAL INVESTIGATOR
Dr. Prabhakar Kumar Verma
PI-MRP (UGC)
Department of Pharmaceutical Sciences
M.D. University, Rohtak-124001 (Haryana)

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(Seal)
Joint Director,
Local Audit Haryana,
M.D.U. Rohtak.

HOD
Head
Dept. of Pharmaceutical Sciences
M.D. University, Rohtak

Rs 12,24,665/- Expenditure incurred

Annexure – XI

Final Report Assessment / Evaluation Certificate

(Two Members Expert Committee Not Belonging to the Institute of Principal Investigator)

(to be submitted with the final report)

It is certified that the final report of Major Research Project entitled **"Preparation and characterization of novel nanomaterial antidiabetic oral formulations"** by Dr. Prof. **Prabhakar Kumar Verma** Dept. of **Pharmaceutical Sciences, M.D. University, Rohtak** has been assessed by the committee consisting the following members for final submission of the report to the UGC, New Delhi under the scheme of Major Research Project.

Comments/Suggestions of the Expert Committee:-

1. Satisfactory & Good
2. Good

Name & Signatures of Experts with Date:-

	Name of Expert	University/College name	Signature with Date
1.	Dr. Neelam Jain	Dept of Pharmacy BPSMV, Khanpur	18/9/17
2.	Dr. Neeta Chawla	Dept of Pharmacy Jamia Hamdard University, Delhi.	18/09/2017

It is certified that the final report has been uploaded on UGC-MRP portal on .....

It is also certified that final report, Executive summary of the report, Research documents, monograph, academic papers provided under Major Research Project have been posted on the website of the University/College.

18/9/17

Head
Dept. of Pharmaceutical Sciences
M.D. University, ROHTAK

(Registrar/Principal)
Seal

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Poloxamers based nanocarriers for drug delivery system

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ABSTRACT

In last few decades, there has been a considerable research interest in the area of drug delivery using polymer based particulate delivery systems as carriers for small and large molecules. Particulate systems like nanoparticles and micelles have been used as a physical approach to alter and improve the pharmacodynamic and pharmacokinetic profiles of various types of drug molecules. Due to the wide compatibility with drug candidates of diverse nature and ingredients in formulations, poloxamers serve to be excellent polymer for drug delivery vehicles by different routes of administration. This review will highlight the poloxamers-based micelles/nanoparticles that have been developed to date.

Keyword: Poloxamers, Nanoparticles, Drug delivery, Micelles, Nanocarrier.

INTRODUCTION

Polymers are the substances of high molecular weight having repeating monomer units. They are widely used in pharmaceutical systems as suspending, adjuvants, adhesives, emulsifying agents and coating material for controlled and site specific drug delivery systems. Polymer molecules may be branched or linear and separate linear or branched chains may be joined by crosslinks. The chemical reactivity of polymers depends upon the chemistry of monomer units but their properties depend to large extent on the way of arrangement of the monomers. Polymers having identical monomeric units are referred to as homopolymers; those formed from more than one monomer type are called copolymers. Arrangements of various monomers units, say A and B lead to formation of varieties of copolymers. The copolymers may be described as alternating copolymers, graft copolymers or block copolymers. Pluronic is one of the most widely used block copolymer and forms heterogels [1,2].

Nanomaterials have been the subject of increasing research concentration in recent years because of their potential biomedical and life science applications. Polymer nanomaterials have sparked a significant interest as vehicles used for diagnostic and therapeutic agents; research in nanomedicine has not only become a frontier movement but is also a revolutionizing drug delivery field [3].

Poloxamers are interesting copolymers as nanocarrier having amphiphilic characters. Due to large solubility differences between hydrophobic and hydrophilic moieties, in aqueous medium they are able to self-assemble into polymeric micelles characterized by mesoscopic size range. These micelles consist of water-insoluble cores and water-soluble shells. Depending on blocks length, core can assemble into various supramolecular structures characterized by different morphologies [4-6]. This review describes the characteristic features of poloxamers along with its applicability in nano-targeted drug delivery systems.

Characteristic and Properties of Poloxamers

The amphiphilic block copolymer named 'Pluronics or poloxamers' is triblock A-B-A type poly(ethylene oxide)-poly(propylene oxide)-poly-(ethylene oxide) (PEO-PPO-PEO) arrangement, which is non-ionic in nature [7,8]. The block copolymers with different numbers of hydrophilic ethylene oxide and hydrophobic propylene oxide units are characterized by different hydrophilic-lipophilic balance (HLB) values. They consist of a central block of relatively hydrophobic polypropylene oxide (PPO) surrounded on both sides by the blocks of relatively hydrophilic polyethylene oxide (PEO) [9,10]. They form micellar structures above critical micelles concentration in aqueous solvents due to the PEO/PPO ration of 2:1 [11,12].

Generally, pluronic are waxy, white granules of free flowing in nature and are practically tasteless and odorless [13]. Their aqueous solutions in presence of acids, alkalis and metal ions are very stable. The poloxamers are readily soluble in aqueous, nonpolar and polar organic solvents. Poloxamers has been extensively studied as a potential drug delivery vehicle due to their excellent biodegradability and thermosensitivity [14,15]. Due to this fact, Pluronics have been established themselves as a preferred molecule in the formulation and drug delivery techniques. The poloxamers copolymers are available in various grades (Table 1**)** differing in molecular weights and physical forms. Depending upon the physical property, the grades are assigned as F for flakes, L for liquid, P for paste.

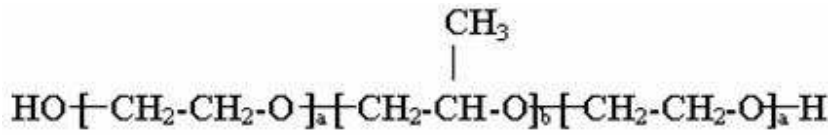

Fig. 1 General structure of Pluronic

Table 1: Pluronic grades and their chemical composition [14,16-17]

Poloxamer	Pluronic®	Physical form	a	b	Content of Oxyethylene (Percent)	Molecular Weight
124	L 44 NF	Liquid	12	20	44.8-48.6	2090-2360
188	F 68 NF	Solid	80	27	79.9-83.7	7680-9510
237	F 87 NF	Solid	64	37	70.5-74.3	6840-8830
338	F 108 NF	Solid	141	44	81.4-84.9	12700-17400
407	F 127 NF	Solid	101	56	71.5-74.9	9840-14600

F127 based Nano-carriers

Due to the long hydrophobic PPO segments and amphiphilic property, F127 can efficiently encapsulate hydrophobic agents with a compact core to efficiently prevent contact of conjugated polymers molecules with oxygen and water to reduce the quenching effect [18].

The gemcitabine loaded nanoparticles have been prepared by an ionic gelation method using chitosan and pluronic F-127 as a carrier and had a spherical shape mean diameter ranging between 80 to 170 nm. The *in vitro* drug release study at 37°C in phosphate-buffered saline (pH 7.4) exhibited controlled release profile for chitosan-pluronic F127 nanoparticles. The cytotoxicity of the gemcitabine loaded nanoparticles was assayed in the HT-29 colon cancer cell line showed increase in the cytotoxicity of gemcitabine embedded in the nanoparticles in comparison to drug alone. The mucoadhesion study reveals that nanoparticles could be considered as an efficient oral formulation for colon cancer treatment [19].

A targeted drug delivery system using folate-conjugated pluronic F127/chitosan core-shell nanoparticles was prepared to deliver doxorubicin to the target cancer cells. First, doxorubicin was encapsulated in pluronic F127 micelle cores in the presence of sodium dodecyl sulfate by self-assembly method. A shell of either chitosan or folate-conjugated chitosan was deposited onto the pluronic F127 micelles with encapsulation efficiency approximately 58.1± 4.7%. The average size of the prepared nanoparticles was 37.4±2.0 nm, while zeta potential was 12.9±2.3mV, indicated the presence of a shell layer and more stable nanoparticles. The *in vitro* doxorubicin release study represents an initial burst release, followed by sustained release, was observed within 24 hours. In addition, the core-shell nanoparticles showed superior cytotoxicity towards MCF-7 cells than free doxorubicin, suggesting a better therapeutic efficacy in treating cancer [20].

The critical micelle concentration (CMC) of pluronic F127 is about 0.26-0.8 wt% [21-22] so that the usefulness of F127 in nanotechnology based drug delivery system is limited since the nano-sized micelles could dissociate upon dilution. The stearic acid (SA) was coupled to F127 between the carboxyl group of SA and the hydroxyl group of pluronic F127, which formed a novel copolymer named as SA-coupled F127, with considerably lower CMC (6.9×10^{-5} wt%). SA-coupled F127 self-assembled to stable nanoparticles with Zeta potential -36 mV. Doxorubicin loaded nanoparticles were prepared with drug loading 5.7 wt% and Zeta potential -36 to -39 mV and the size distribution of nanoparticles was from 20 to 50 nm. Doxorubicin loaded nanoparticles were relatively stable and exhibited doxorubicin dependant cytotoxicity toward MCF-7 cells *in vitro*. These results suggested that SA-coupled F127 potentially could be applied as a nano-technology based drug delivery method [23].

An thermosensitive mixed micelles were prepared from pluronic F127-b-poly(ε-caprolactone) block copolymer by mixing with hydrophilic bovine serum albumin (BSA) and hydrophobic polylactic acid (PLA). Pure micelles with different lengths of caprolactone undergo morphology transition from the rods to the sphere. The addition of PLA and BSA can influence the thermosensitive and drug loaded behaviors of the micelles. Doxorubicin HCl loaded pure and mixed micelles have characteristics ideal for the selective sustained release of doxorubicin HCl in mildly acidic physiological environments rather than at pH 7.4. As observed from cell cytotoxicity, the block polymers showed excellent biocompatibility and the doxorubicin HCl loaded pure and mixed micelles were effective to inhibit the growth of HepG2 tumor cell lines. Therefore, the properties of the micelles can be adjusted by mixing either hydrophilic or hydrophobic molecules and the thermosensitive block polymeric micelles may be an attractive vehicle for doxorubicin HCl delivery [24].

PLGA containing half shells nanostructures were prepared by oil-in-water emulsion solvent evaporation method by adding pluronic F127 to the organic phase. They showed sequential events including phase separation, fast solidification and water escape. These nano-half-shells nanostructures possessed low densities, so the possibility of being used as carriers for pulmonary drug delivery system [25].

Honokiol, a multi-functional drug possessed low water solubility and has great potential in cancer therapy [26-32]. Honokiol micelles based on poly(ethylene glycol)-poly(ε-caprolactone)-poly(ethylene glycol) and pluronic F127 copolymer were prepared which underwent thermosensitive sol-gel-sol transition. Due to high hydrophobic character, honokiol could not be well-disperse in the composite hydrogel to form homogeneous solution. Above mentioned problem were solved by preparing honokiol micelles. The obtained honokiol micelles with average particle size of 33.34 nm and polydisperse index of 0.036 could be well dispersed in water with good stability. Cytotoxicity assay was conducted by using human HEK293 cells and suggested biocompatibility with low cell cytotoxicity [33].

In another study, honokiol nanoparticles were prepared with pluronic F127 by emulsion- solvent evaporation method. The obtained honokiol showed amorphous character and well dispersed in water [34]. The pluronic block copolymers were shown to be potent biological response modifiers capable of sensitizing and overcoming multidrug resistance (MDR) in cancer therapy and enhancing drug transport across cellular barriers, such as polarized intestinal epithelial cells, brain and Caco-2 endothelium [3,35-36]. From the above fact, the prepared honokiol nanoparticles might be anti-MDR formulation for cancer therapy.

Poly(lactic acid)-b-pluronic-b-poly(lactic acid) (PLA-F127-PLA) vesicular nanoparticles as oral delivery carrier for insulin were reported [37]. These polymeric vesicles aggregate with complicated onion-like structure containing three layers, which possessed microstructure similar to many biological systems. The biphasic release behavior was observed for the *in vitro* release of insulin from PLAF127-29 vesicles. In diabetic mice tests the blood glucose concentration of oral insulin-loaded PLA-F127-29 vesicles decreased from 18.5 to 5.3 mmol/L within 4.5 hours and the minimum blood glucose concentration about 4.5 mmol/L were achieved after 5 hours. This blood glucose concentration was maintained for at least an additional 18.5 hours. Due to prolonged hypoglycemic effect, PLA-F127-PLA vesicles could be promising polymeric carriers for oral insulin delivery application [38].

F68 based Nano-carriers

Paclitaxel loaded poly(ε-caprolactone)(PCL)/pluronic F68 (F68) nanoparticle formulation was prepared by solvent evaporation method as an intratumoral delivery system to assess its potential for future neoadjuvant chemotherapy application in the treatment of breast cancer [39]. Pluronic F68 incorporated into the PCL matrix acted as both pore-forming agent and to enhance drug release from the particles [40]. The murine breast cancer model has shown that

when using equivalent paclitaxel doses, paclitaxel loaded PCL/F68 nanoparticles administered by a single intratumoral injection were more efficient in impeding tumor development than conventional paclitaxel injections administered by multiple intraperitoneal injections [39].

The doxorubicin loaded pluronic F68 nanoparticles in size range of 632.8 nm were prepared in a molten mixture of doxorubicin dissolved in soybean oil/Tween 80 mixtures and pluronic F-68 through temperature induced phase. For detailed understanding of the tumor microenvironment, elevated interstitial tumor pressure and dense tumor extracellular matrix have been known as formidable barriers to the extravasation of nanoparticles. The increased targeting at tumor and effective extravasation into interior cells in the tumor tissue were demonstrated using pluronic nanoparticles using high-intensity focused ultrasound (HIFU) exposure. This approach transiently enhance the effective pore size of tumor tissue with the increased permeability of pluronic nanoparticles through non-thermal mechanisms and was confirmed by observing the *in vivo* biodistribution of pluronic nanoparticles with HIFU exposure. The results demonstrated that HIFU exposure through non thermal mechanisms can aid the extravasation of nanopartcles into interior cells in tumors and increase the therapeutic effect in targeted cancer therapy [41].

Curcumin loaded mixed micelles (Cur-PF), composed of Pluronic P123 (P123) and Pluronic F68 was prepared using the thin-film hydration method. The nano-sized micelles improved the solubility and biological activity of the drug. The *in vitro* cytotoxicity assay showed that the IC_{50} values on MCF-7 cells for Cur-PF and free curcumin in DMSO solution were 5.04 g/mL and 8.35 g/mL, while 2.52 g/mL and 8.27 g/mL on MCF-7/ADR cells [42].

Nisin loaded tripolymeric nanoformulation was synthesized using three biocompatible polymers viz. chitosan, sodium alginate and pluronic F68 by ionotropic pre-gelation method followed by polycationic cross linking. The controlled and sustained *in vitro* release profile of nisin was achieved. The used polymers and nisin exhibited synergistic antimicrobial activity that was retained over a prolonged period [43].

Silver nanoparticles (AgNps) co-stabilization with the bioactive copolymer pluronic F68, was shown improved antimicrobial activity against gram-negative microorganisms (*E. coli* and *P. aeruginosa*) in comparison to unstabilized AgNps [44].

The protein-pluronic covalent conjugates described were antibodies and insulin attached to pluronic analogs, which were used as targeting moieties for the delivery of polymeric micelles to the brain [45]. Pluronic P85 is an amphiphilic block copolymer with a molecular mass of ca. 4600 dalton having approximately equal by mass content of PPO and PEO chains. The unconjugated pluronic P85 was formulated with haloperidol (neuroleptic drug) in the form of polymeric micelles and then blended either with pluronic P85 modified insulin or antibodies. The protein molecules get incorporated into the PEO shell of the polymeric micelles while the solubilized drug remained in the core of micelle formed by PPO chains. The antibodies used in this study included either brain specific antibodies against alpha-2-glycoprotein or brain non-specific antibodies against alcohol dehydrogenase. The micelles were intraperitoneally administered into mice and biological activity was determined. All haloperidol micelle formulations showed better central response than the haloperidol alone. Among micelle groups, the most pronounced augment of haloperidol action was observed with the micelles linked to the brain specific antibody, followed by insulin linked micelles and then non-specific antibody or untargeted micelles. Similar micelles incorporated with fluorescence dye confirmed that the dye was in fact delivered to the brain parenchyma [46-47].

CONCLUSION

The difunctional block copolymer, poloxamers exhibits various desired characteristics of pharmaceutical formulations like its amphiphilic micellar behavior, desirable delivery rate, thermo-sensitivity and biocompatibility. The amphiphilic characteristics of micelles makes delivery systems capable of solubilizing poorly soluble or water insoluble drugs and of protecting labile molecules such as peptides and proteins. There has been remarkable progress in development of poloxamers based nano-carriers drug delivery systems. The new wave of pharmaceutical products will definitely make use of this polymer and a range of formulation problems incurred will get solved.

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A-507

Preparation and *In- Vitro & In- Vivo* Evaluation of Fexofenadine Hydrochloride Orodispersible Films

R.Divya, R.V.Koteswararao, G.Navya and Y.Vamshi Vishnu

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Abstract:

The aim of present study of this research was to select a suitable drug with negligible side effects and to formulate and evaluate it as Orodispersible films and to improve cumulative drug release. Fexofenadine Hydrochloride is a non sedative, no impairing antihistamine used to treat seasonal allergic rhinitis (sneezing, runny nose, itchy nose, palate and throat or watery eyes), and urticaria (hives). Unlike most other antihistamines Fexofenadine Hydrochloride does not cross the blood brain barrier and therefore will not cause any drowsiness which can gradually effect child's learning ability, drowsiness can also interfere with driving vehicles or operating machinery. Orodispersible films were formulated using different polymers like HPMC E3 and HPMC E6 in different concentrations by Solvent Casting method; these films were evaluated and all the physical characteristics were within the acceptable limits.

Keywords: Fexofenadine Hydrochloride, Oro Dispersible Films, HPMC Polymers

A-508

Glipizide Loaded Stearic Acid-Coupled F127 Nanoparticles as an Effective Antidiabetic Agent for Controlled Drug Release

Vipan Kumar Kamboj, Rashmi Shah and Prabhakar Kumar Verma

Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India-124001
vk.kamboj123@gmail.com

Abstract:

The glipizide nanoparticles have been prepared by solvent evaporation technique using stearic acid-coupled F127 copolymer and polyvinyl alcohol. The prepared glipizide nanoparticles were subjected to various studies for characterization including particle size analysis, FTIR, XRD, DSC and SEM. *In vivo* studies with best-optimized batch were performed in Wistar albino rats. These studies favorably revealed that the mean particle diameter of optimized glipizide nanoparticles was 249.30 ± 3.20 nm, poly dispersity index 0.187± 0.0157, zeta potential -19.86 ± 0.586 mV and had spherical morphology with amorphous nature. The results of FTIR and DSC analysis showed that there was no significant interaction between drug and excipients. The optimized glipizide nanoparticles demonstrated favorable *in vitro* controlled drug release characteristics. The *in vivo* toxicity study in Wister albino rats showed no mortality. The formulated nanoparticles of glipizide could be able to manage sugar level in streptozotocin-induced diabetes in Wister albino rats compared to conventional glipizide and support the *in vitro* controlled drug release pattern. The copolymer selected for this study was found to be a good carrier for nanotechnology-based controlled release drug delivery system.

Keywords: Glipizide, Nanoparticles, Solvent Evaporation, Streptozotocin

A-509

Development and Evaluation of Salbutamol-Loaded Sodium Alginate-Pectin Floating Beads

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Abstract:

In the present study, an attempt has been made to development and evaluation of salbutamol-loaded sodium alginate-pectin based floating beads for the gastro-retentive system. The floating property contributed mainly by the reduction in the density of beads due to entrapped air during beads preparation. The effect of polymer concentration studies showed an increase in bead size and decrease in beads density with increase of pectin amounts in the formulation. The effect of sodium alginate and pectin weight masses on drug loading efficiency (% DLE) and % drug release ($\%R_{6h}$) was analyzed by 32 factorial designs and optimization indicated mainly the effect of pectin concentration on these properties. The optimized formulation showed % DLE of 95.17±0.87%, $\%R_{6h}$ >85%, size 3.65 mm, and density equals to 0.40 g/cm3. In vitro flotation studies of beads showed good floating time > 6 h for all batches with a lag time of ~10 minutes. The in vivo studies of formulation

Abstract number- GU083

Formulation, Evaluation and Characterization of Metformin HCl Nanoformulation

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Abstract:
Nanoparticle based materials have tremendous application in every field of human activity, with a lot of economic benefit increasing nanoparticle research and use. There are numbers of nanomaterial based products are already available commercially and many others are in queue. Therefore, there is a pressing need for careful consideration of benefits and side effects of the use of nanoparticles in medicine. With the objective to achieve prolonged drug release for the treatment of diabetes mellitus, metformin HCl loaded stearic acid coupled F127 nanoparticles have been formulated. These nanoparticles have been developed by solvent evaporation technique and were subjected to various studies for characterization including particle size analysis, XRD and SEM. These studies favorably revealed that the mean particle diameter of optimized formulation was 211.50 nm, poly dispersity index 0.112, zeta potential -21.92 mV and had spherical morphology with amorphous nature. Moreover, these nanoparticles were also subjected to FTIR and DSC for compatibility analysis between drug and polymer. The results were positive and showed that, there were no interaction between drug and polymer. The optimized formulation demonstrated the favorable *in vitro* prolonged release characteristics.The *in vivo* toxicity study in albino rats showed no mortality. Hence, the designed nanoformulation could possibly be advantageous in terms of prolonged release, to achieve reduced dose frequency and improve patient compliance of metformin HCl.

Keywords: Diabetes mellitus, Metformin HCl, Nanoparticles, Polymer.

P-123

Polymeric Nanocarriers for Oral Nanostructured Drug Delivery Systems

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Despite the widespread research and success stories with other routes of drugs administration, oral route is most preferred way of delivering drugs with better patient acceptance. In last two decades, nanoparticles have been extensively studied for oral drug delivery for specific organ or to act locally in gastrointestinal tract. Nanostructure such as liposomes, solid lipid nanoparticles, nanocrystals, nanospheres and micelles possess unique physiological properties due to ultra-small size, large surface area to mass ratio. The hydrophilic and hydrophobic drugs candidates have been loaded into biodegradable and biocompatible nanocarriers to achieve the stability of active pharmaceutical ingredient (APIs) in gastrointestinal juice to improve the oral bioavailability and targeted drug release patron. These APIs are entrapped in the polymeric network as solid solutions or particulates enmesh or may be attached to particle surface by chemical or by physical adsorption. The targeted oral bioavailability, scale-up manufacturing process and batch to batch consistency are the main challenges faced by the pharmaceutical scientists. Literature is abounding with use of natural, semi-synthetic and synthetic polymers with concerning their safety, toxicology and biodegradation aspect. This paper emphasize on advantage and disadvantage of polymeric systems for oral nanoparticles, organ targeted delivery and problems faced during fabrication process.

P-124

Synthesis and Spectral Study of Benzothiazole – GABA Analogs

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Benzothiazole and GABA analogs repeatedly presented as neurologically acting molecules in literature. In present study we synthesize some novel benzothiazole – GABA analogs and structures of target compounds were confirmed by spectral data. The synthesized compounds may leads to a new pharmacophore for developing the central nervous system acting molecules.

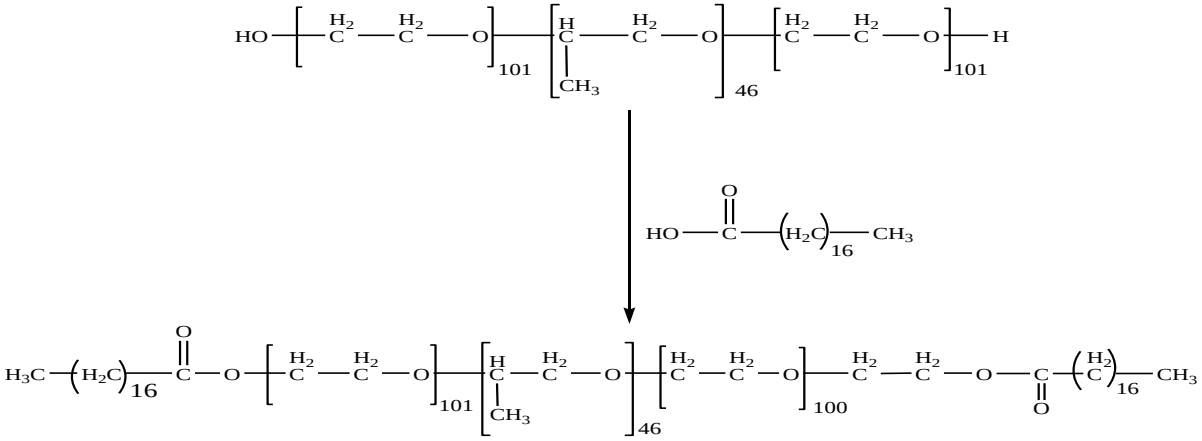
MATERIALS AND METHOD

Materials

Pharmaceutical grade of Glipizide was procured as a gift sample from Swapnroop Drugs and Pharmaceuticals, Aurangabad, India. Stearic acid, Pluronic F127, Polyvinyl alcohol and Streptozotocin were of analytical grade and have been purchased from Sigma Aldrich. Other chemical and solvents were from analytical grade and have been purchased from Molychem, Mumbai. The calibration curve was prepared by using double beam UV-Vis spectrophotometer (Lab India 3000). SA-F127 was synthesized Scheme 1(Ref) and structure was confirmed by spectrum of FTIR (Bruker 1-206-0280, KBr pellets) and ^{1}H NMR (Bruker Model Advance II 400 (400 MHz, ^{1}H NMR) spectroscopy.

Synthesis of Stearic acid-coupled F127 (Polymer)

Stearic acid was coupled to Pluronic F127 (**Scheme 1**) at the melting phase through esters between the carboxyl group of SA and the hydroxyl of F127. 10 g F127 and 10 g Stearic acid (SA) were added into a 50 ml round bottom flask and the mixture was heated with continuous stirring to produce a well-mixed molten phase and reacted at 160°C for 5 h. SA-coupled F127 was obtained by dropping the resulting solution into the ethyl acetate/petroleum ether 1:1 (v/v) mixture solution to remove the un-reacted SA by filtering, which was insoluble in the mixture solution. Finally, SA-coupled F127 was obtained by evaporating the solvent on room temperature and was dried at room temperature under vacuum. The polymer structure was confirmed by spectrum of FTIR (Bruker 1-206-0280, KBr pellets) and ^{1}H NMR (Bruker Model Advance II 400 (400 MHz, 1H NMR) spectroscopy.



Scheme 1. Synthesis of Stearic acid-coupled F127 (Polymer)

Calibration curve of drug

Standard curve of Glipizide has been prepared by using double beam UV-Vis spectrophotometer (Lab India 3000) in chloroform which showed λ_{max} at 274 nm. The concentration (2.5-15 µg/ml) range was used and compiled in Figure 1.

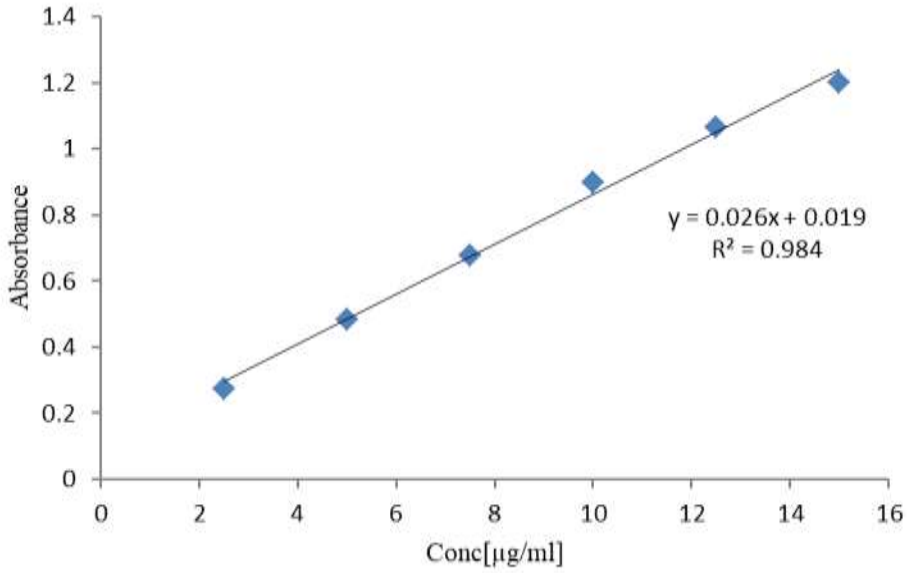


Figure 1. Standard Curve of Glipizide in phosphate buffer

Preparation of Glipizide nanoparticles

Glipizide loaded nanoparticles were prepared by modifying the previously reported procedure(Gao et al., 2011). A mixture of methylene chloride and chloroform (50:50) were prepared and Glipizide were dissolved in it. The copolymer (SAF127) dissolved in chloroform. Copolymer solution was added into drug solution drop by drop with continues stirring. Polyvinyl alcohol (PVA) 0.5ml (2%) has been dissolved in water and 3ml ethanol was added as co-solvent. The PVA mixture were added drop wise into drug and copolymer mixture with continuously homogenization for 30 min with gap of 30 sec at each 2 min intervals. The solvent was evaporated by stirring and stored in vacuum desiccators over night at room temperature in order to remove remaining solvent. The resultant thin film was hydrated with 10 ml of distilled water in warm water bath at 40°C for 30 min and the mixture was stirred at 700 rpm for 30 min to obtain a clear nano-suspension solution. The unincorporated drug aggregates were removed during the filter sterilization process and then nanoparticles were collected by centrifugation followed by lyophilization.

Particle Size Analysis and Zeta Potential

The average particle size, zeta potential and particle size distribution (PDI) of glipizide loaded SAF127 nanoparticles was measured at 25°C using Zetasizer Nano ZS (Malvern Instruments, Malvern, UK).

Entrapment efficiency, drug loading, percentage yield

Accurately weighed nanoparticles were dissolved in methylene chloride : chloroform (50:50). The amount of drug in the solution was measured using UV-Vis spectrophotometer (Lab India-3000) at 274 nm. Drug loading (%), drug entrapment (%) and percentage yield were represented by following equation:

$$\text{Drug Loading (\%)} = \frac{\text{Mass of drug in nanoparticles}}{\text{Mass of nanoparticles recovered}} \times 100 \qquad \text{Eq. 1}$$

$$\text{Drug Entrapment (\%)} = \frac{\text{Mass of drug in nanoparticles}}{\text{Mass of drug used in formulation}} \times 100 \qquad \text{Eq. 2}$$

$$\text{Percentage yield (\%)} = \frac{\text{Total nanoparticles weight}}{\text{Total solid weight}} \times 100 \qquad \text{Eq. 3}$$

Fourier Transform Infrared Spectroscopy

The interaction between drug and polymer were studied by using FTIR. FTIR spectra of the pure glipizide, polymer SAF127, PVA and physical mixture (1:1) were taken in KBr Pellet using Bruker (1-206-0280).

Differential Scanning Calorimetry (DSC) analysis

DSC measurements were carried out on DSC Q10 V9.9, US. The instrument was calibrated using Indium as standard. Samples were placed in sealed aluminium pans and heated from 35ºC to 280ºC at a rate of 10ºC/min under nitrogen atmosphere (60 ml/min), with empty pan as reference.

X-ray Diffraction (XRD) analysis

XRD analysis was carried out using RigakuMiniflex-600 diffractometer. A Cu Kα source operation (40 kV, 15 mA) was employed. The diffraction pattern was recorded over a 2θ angular range of 10-70.

Surface Morphology

The surface morphology of the best optimized batch was examined using field emission scanning electron microscopy (FESEM; JEOL-JSM-7600F).

In vitro dissolution studies

In vitro dissolution studies were performed using dialysis sac method(Rani et al., 2017). Accurately weighed glipizide nanoformulations suspension was placed in dialysis membrane bags (12-14 kDa cut-off, HiMedia, India) tied with dialysis clips. The dialysis bags containing glipizide nanosuspension were immersed in conical flask with 150 ml of phosphate buffer solution (0.1 M) with pH 7.4. The conical flask were stirred at 100 rpm and 37±05°C. At fix time intervals, the samples were withdrawn from the conical flask and replaced with equal amount of fresh phosphate buffer and assay were performed using UV-Vis spectrophotometer (Lab India 3000) 274 nm.

In Vivo Study

Animals

Experiments were performed in adult either sex Wistar albino rats weighing from 200 to 250 g. Rats were procured from Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar, India and were housed in stainless steel cages in groups of Six and housed in animal house of Mahrshi Dayanand University, Rohtak under standard environmental conditions (23 ± 1°C, 55 ± 5% humidity and a 12 h/12 h light/dark cycle) and maintained with free access to water and a standard laboratory diet ad libitum. The protocol of the animal study was approved by Institutional Ethical Committee (151/57 dated 30/03/2015).

Toxicity Study in Wister Albino Rats

The animals were randomly selected and assigned to following two test groups (6 mice in each group) namely Group I (Control groups, treated with normal saline), Group II (Test group; treated with drug nanoparticles F1 equivalent to 800µg/kg B.W). The respective doses of glipizide loaded nanoparticles were freshly prepared and administered by oral gavaged in a single dose. Acute toxicity was measured by mortality and survival time for 30 days.

Streptozotocin (STZ)-Induced Diabetic Rat Model

Diabetes was induced in female wister albino rats by intraperitoneal injection of streptozotocin at a dose of 50 mg/kg body weight. STZ was dissolved in 0.1 M cold sodium citrate buffer, pH 4.5 (Torrico et al., 2007). The animals were allowed to drink 5% glucose solution to overcome the drug induced hypoglycemia. The serum glucose levels were monitored with Glucose Estimation

Kit (Agappe Diagnostics Ltd., India). The animals with glucose levels above 300 mg/dL were selected further for study (Jana, Bera, & Ghosh, 2015).

Pharmacokinetic evaluation

The overnight fasted rats were (n=6) treated with glipizide nanoparticles F1 and blood samples were withdrawn at different time intervals through retro orbital sinuses using heparinised capillaries. Plasma was separated by centrifugation (Plasto craft) and stored at -20 ºC until further analysis. Glipizide in rat blood plasma was estimated by earlier reported RP-HPLC (Mutalik et al., 2006).

Chromatographic conditions

The pharmacokinetic was performed on Dionex UHPLC ultimate 3000 RS containing pump, autosampler, column compartment and Diode array detector. The data acquisition was achieved through Chromoleon software. The mobile phase consisted of 20mM monobasic potassium dihydrogen orthophosphate in water, which was adjusted to pH 3.5 with phosphoric acid and acetonitrile in the proportion of 65:35 v/v. The mobile phase was filtered through 0.22 µm membrane filter and sonicated. The flow rate was maintained at 1 ml/min and the total run time of the method was set at 15 min. the effluent was monitored at 274 nm.

Standard solutions

A standard stock solution of glipizide (100µg/ml) was prepared by dissolving accurately weighed sample in acetonitrile. The calibration curve were prepared by spiking the known amounts of glipizide (25-2500ng/ml) with plasma

Extraction Procedure

A volume of 0.1 ml of blank rat plasma and 0.1 ml of 0.1N hydrochloric acid was mixed thoroughly. The plasma was spiked with standard glipizide solutions to yield concentrations of 25-2500 ng/ml. Then the mixture was gently shaken for duration of 3 min and it was added with 5 ml benzene in a 20 ml glass tube. The mixture was smoothly shaken using cyclomixer for 5 min and centrifuged for 10 min at 6000 rpm. After centrifugation, the organic phase was evaporation to dryness under nitrogen. The residue was dissolved in 0.1 ml of equilibrated mobile phase by vortexing. An aliquot of 20 µl was injected into the chromatographic system by autosapler. The calibration curve was obtained by plotting peak area ratios of glipizide to concentration (x-axis).

Statistical Analysis

The *in vivo* data were statistically analyzed by anova followed by Dunnets Multticomparison test. Results are quoted as significant where $p < 0.05$ and $p < 0.01$. The pharmacokinetic parameters were calculated using Non-compartmental Pharmacokinetic analysis software (PK Solutions 2.0)

Result and Discussion

Synthesis of SAF127 Copolymer

The esterification reaction occurs between the carboxyl group of SA and the hydroxyl group of F127 (Scheme 1). The FTIR spectra of synthesized polymer having ester band (stretching vibration of C=O) around 1700.77 cm^{-1} were observed which confirmed the reaction between SA and F127 (Figure 2). The structure and composition of SAF127 were determined by ^{1}HNMR spectroscopy in $CDCl_3$ (Figure 3) and δ (ppm) of different groups are shown in table 1.

Table 1. Major features of ^{1}H NMR spectra of Stearic acid-coupled F127

δ (ppm)	**Assign**
C**H$_2$**-O in PEO	3.68-3.66
C**H$_2$**CH$_2$-O in PEO	2.37-2.34
C**HH**CH(CH$_3$)-O in PEO	1.66-1.62
C**HH**CH(C**H$_3$**)-O in PEO	1.31-1.27
CH$_2$ in SA	1.17-1.14

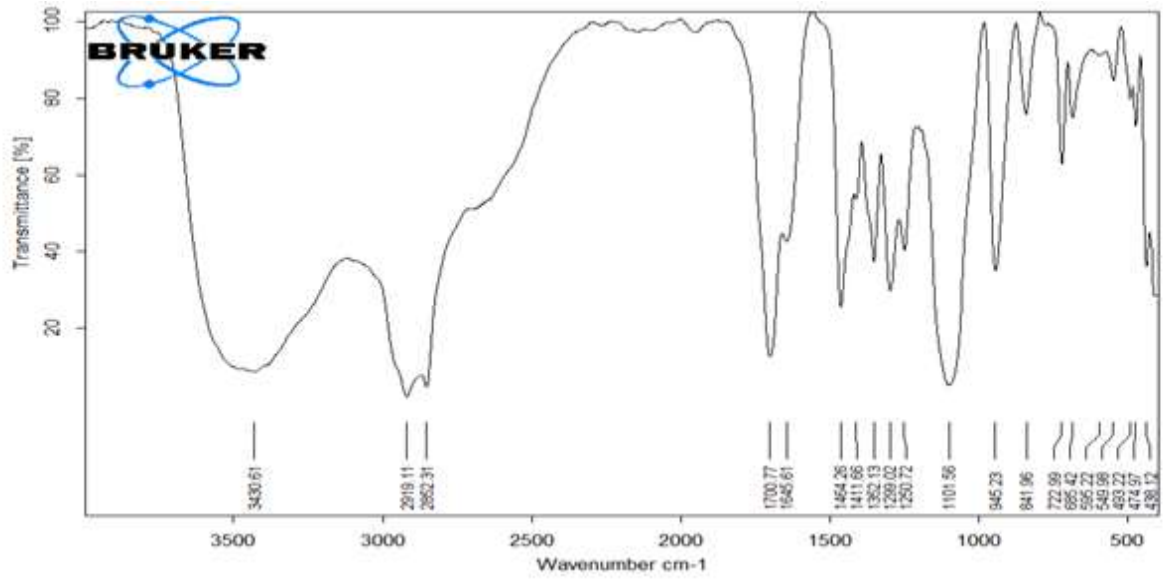


Figure 2 FT-IR spectra of Stearic acid-coupled F127 (Polymer)

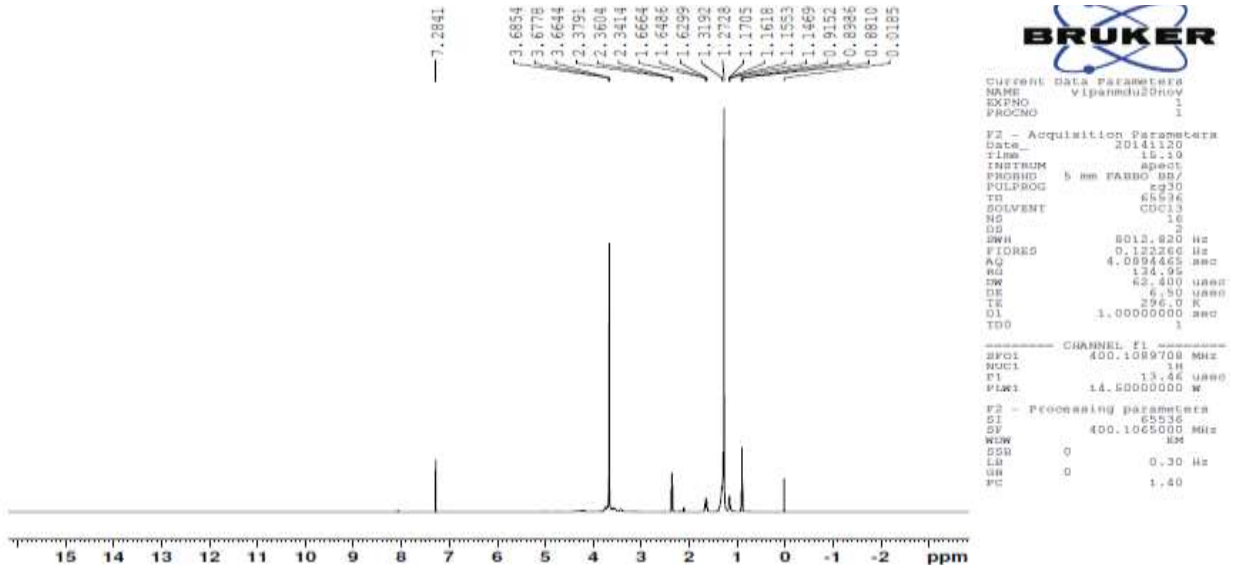


Figure 3 ^{1}H NMR spectra of Stearic acid-coupled F127

Identification of drug

Various parameters like physical appearance melting point analysis, uv-visible spectroscopic analysis and solubility studies were performed and results were compared with standards (Table 2).

Synthesis of Glipizide nanoparticles

The glipizide is encapsulated with copolymer SAF127 and PVA using solvent evaporation technique. Different glipizide: polymer SAF127 ratios were tried. The effect of drug: polymer ratio on particle size, polydispersity index, zeta potential, entrapment efficiency, percentage yield is shown in Table 3 and 4. Glipizide drug: polymer ratios tried were 1:1, 1:2, 1:3 and 1:4. The F1 nanoformulation having drug to copolymer ratio 1:1 showed significantly improvement in particle size (249.30±3.20), zeta potential (-19.86±0.586), entrapment efficiency (81.1±3.12%) and percentage yield (76.4±2.23%).

As the polymer amount is increase from F1 to F4, values of studied parameter were decreased. During preparation of all batches, concentration of PVA was kept fixed 0.5ml (2%). In nanoparticles preparation process, PVA along with SAF127 add controlled release properties(Mansour, Sohn, Al-Ghananeem, & DeLuca, 2010)(Gao et al., 2011).

Table 2: Identification parameters of pure glipizide

Sr. No.	Parameter	Result	Standard
1.	Physical Appearance	White crystalline, odourless powder.	Complies as per Vol-II, IP 2007
2.	Melting Point Analysis	201±2^{o}C.	Complies as per USP 30 NF 25
3.	UV-Visible Analysis	λ_{max} - 274 nm in chloroform	Complies as per EP 5.0
4	Solubility	Insoluble in water, ethanol Slightely soluble in methylene chloride, acetone Soluble in DMF	Complies as per Vol-I, IP 2007

Table 3 Ratio of Drug:Polymer, Particle size, Polydispersity index (PDI) and Zeta potential

Batch	Drug : Polymer Ratio	Particle size (nm)	PDI	Zeta potential (mV)
F1	1:1	249.30 ± 3.20	0.187 ± 0.0157	-19.82 ± 0.586
F2	1:2	631.46 ± 4.05	0.555 ± 0.0362	-16.31 ± 0.153
F3	1:3	722.30 ± 6.77	0.329 ± 0.0238	-11.33 ± 0.513
F4	1:4	890.20 ± 7.80	0.472 ± 0.0264	-6.03 ± 0.737
F5	2:1	530.24 ± 3.51	0.162 ± 0.0211	-15.51 ± 0.561

n = 3, mean values ± SD

Table 4. Percentage Yield and entrapment efficiency batches

Batch	Entrapment Efficiency (%)	Yield (%)
F1	81.1±3.12	76.4±2.23
F2	60.1±4.41	59.31±4.22
F3	60±3.34	49.84±3.41
F4	35.4±1.98	23.2±3.45
F5	70.6±2.51	66.3 ± 4.14

n = 3, mean values ± SD

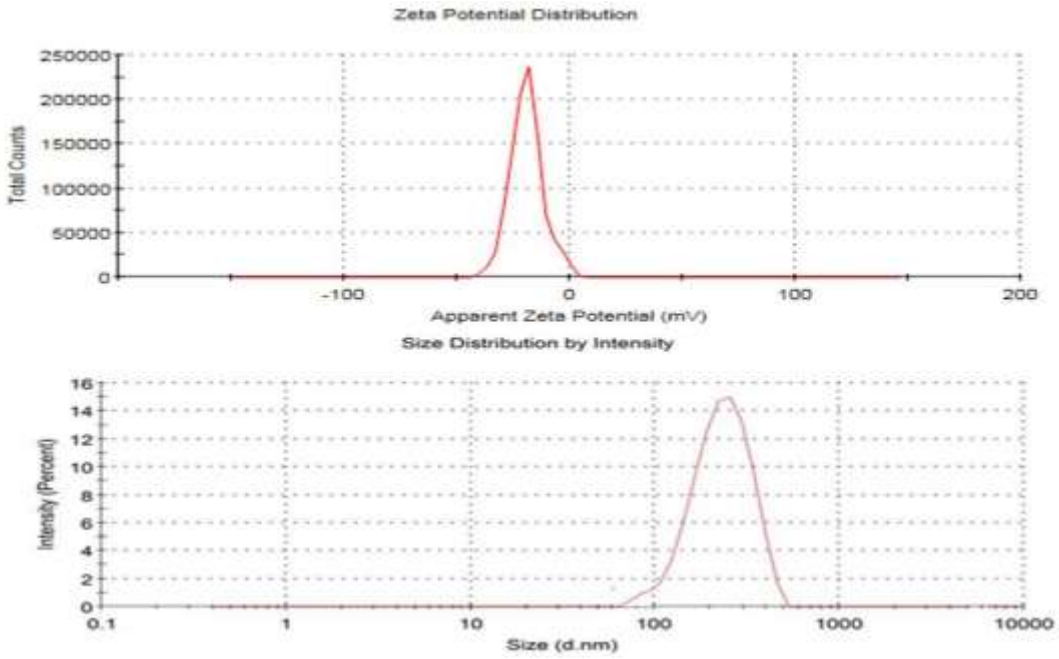


Figure 4 PSA and Zeta potential of glipizide nanoformulation F1

Drug Excipients Compatibility Study

FTIR

In order to develop a sustained release delivery system, interaction between drug and excipients is an important study by which the desire release pattern of drug and other requisite physico-chemical properties may be achieved (Mukherjee et al., 2005). FTIR spectroscopy is an available method, which gives us a distinct idea regarding interaction(s) between different functional groups present in drug and excipients(Mukherjee, Santra, Pattnaik, & Ghosh, 2008).

The possible interactions between SAF127, glipizide, PVA, physical mixture and optimized glipizide nanoparticles (F1) were investigated by comparing the peaks. The IR spectra of pure glipizide shows C=O stretch at 1688 cm^{-1} which is also observed in physical mixture and batch F1 nanoformulation. There was no interaction between glipizide, SAF127 and PVA has been observed as there was no shift in peaks was observed in physical mixture and optimized glipizide nanoparticles (F1) (Figure 5). This indicates the drug and polymers were compatible and suitable for this study.

Differential scanning calorimetry (DSC) analysis

DSC analysis was found to be useful in the investigation of thermal properties of the nanoparticles, providing quantitative and qualitative information about the physico-chemical

state of drug inside the nanoparticles as well as drug-polymer interactions(Ramazani, Keramati, Malvandi, Danafar, & Kheiri Manjili, 2017)

A characteristics sharp endothermic peak at 212.18°C was observed for pure drug glipizide which is absent in SAF127 whereas PVA shows endothermic peak at 215.31°C. The DSC thermogram of SAF127, PVA, pure glipizide physical mixture and optimized batch F1 are shown in Figure 6. A close look at overlay suggests that there was no significant interaction between drug and polymers.

Both FTIR and DSC studies support the compatibility between polymers and drug, hence we have selected these polymers for the preparation and optimization of glipizide nanoparticles.

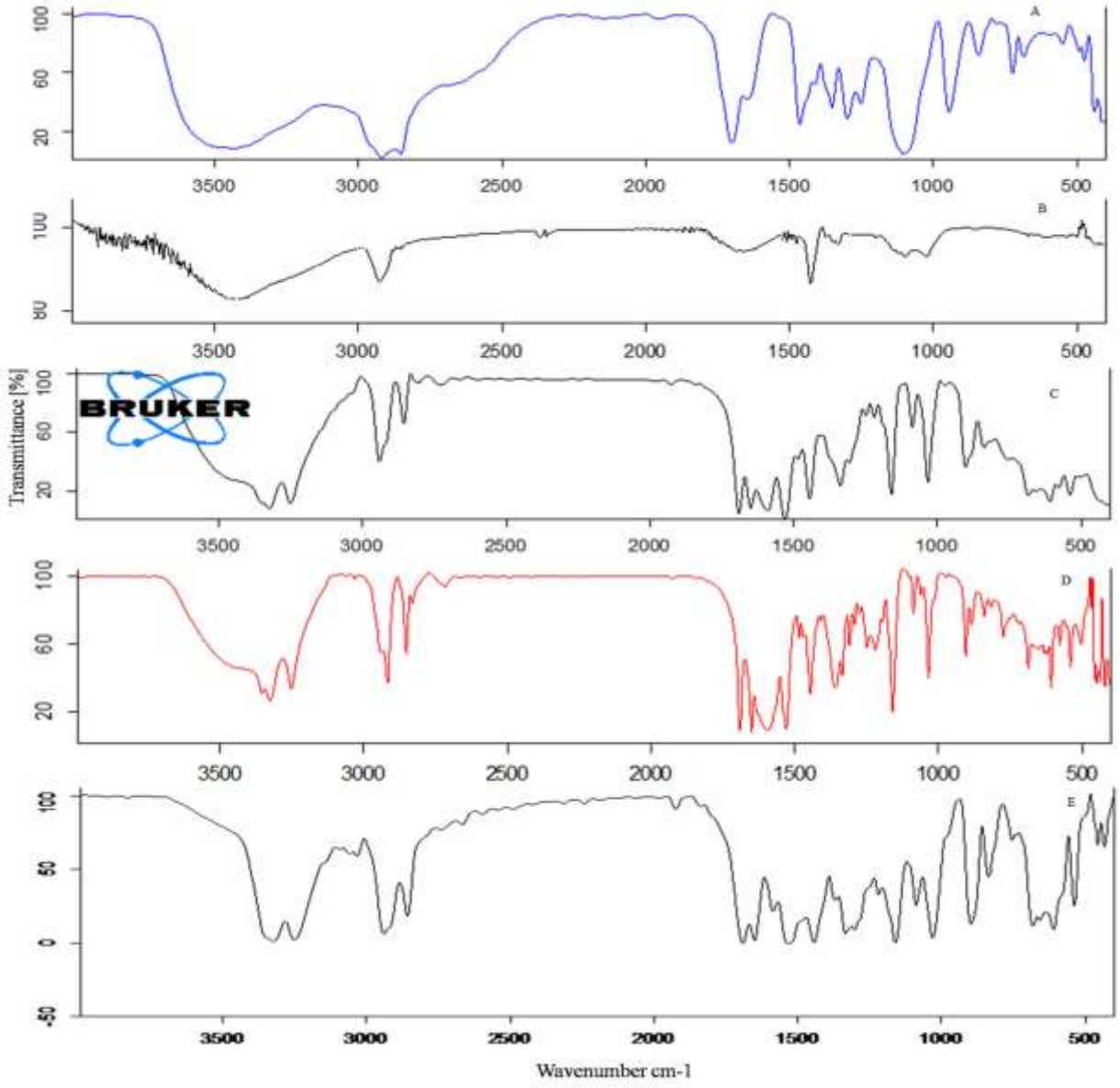


Figure 5 FTIR spectra of A) SAF127, B) PVA, C) Glipizide (pure drug), D) Physical mixture and E) Optimized glipizide nanoformulation (F1)

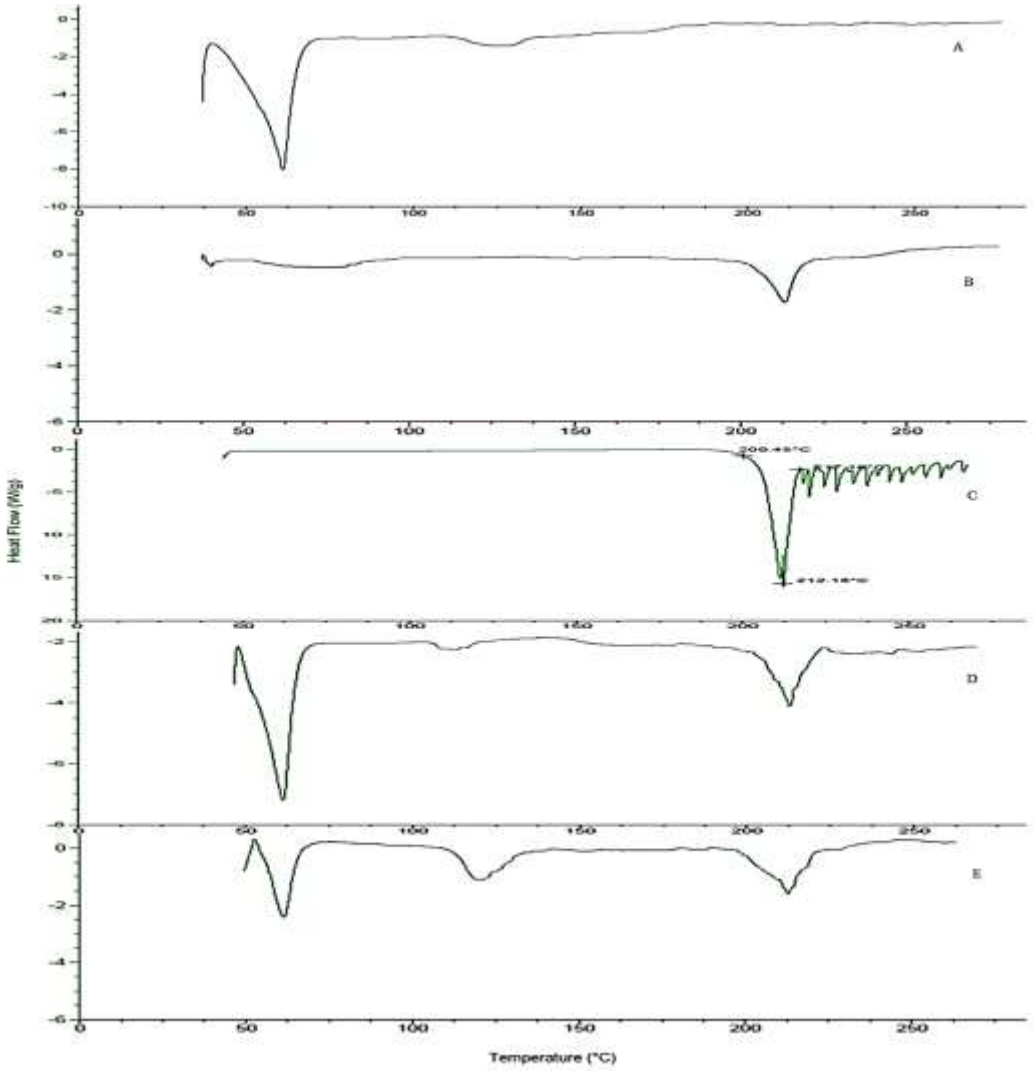


Figure 6. DSC thermograms of A) SAF127, B) PVA, C) Glipizide (pure drug), D) Physical mixture and E) Optimized glipizide nanoformulation (F1)

X-Ray Diffraction studies of Nanoparticles

XRD is useful in the investigation of crystalline properties of the nanoformulations (Purnomo & Sumadiyasa, 2016). The glipizide shows several sharp peaks in its XRD pattern indicating the crystalline nature (Figure 7C) and this obtained pattern was found to be in line with the earlier report of (Dash, Mohammed, Humaira, & Reddy, 2015). The sharp diffraction peaks due to the pure glipizide and polymers such as SAF127, PVA can be seen in the physical mixture (Figure 7D). However, PVA (Figure 7B) showed a diffused spectrum having fewer peaks. After being formulated into nanoparticals, the XRD pattern showed comparatively less sharp peaks (Figure

7E), indicating that glipizide encapsulated within the polymer matrix and posses partially amorphous nature. The presence of the glipizide within the polymeric matrix could be responsible for the controlled drug release nanoformulation(Chen et al., 2012).

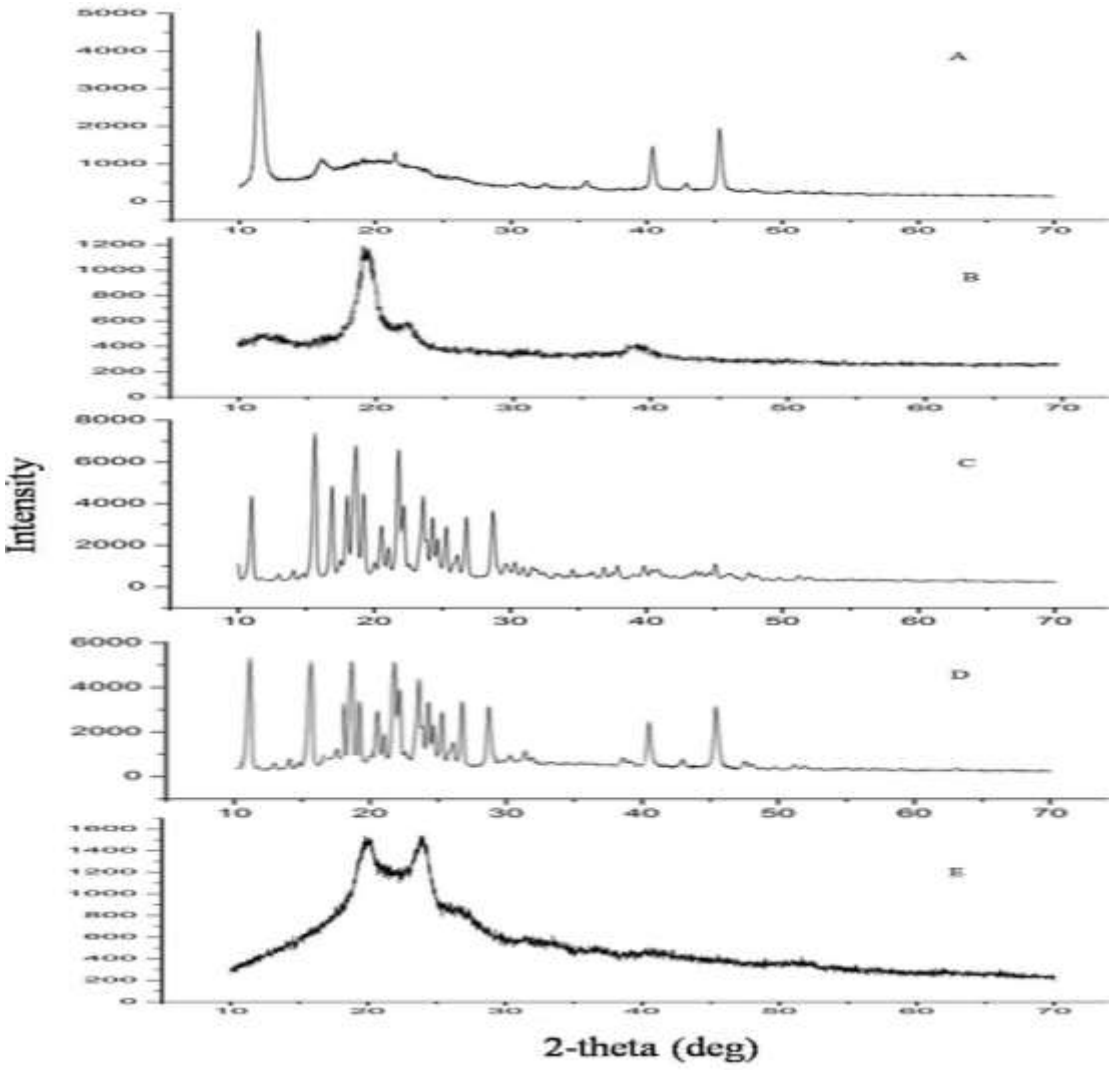


Figure 7 X-ray diffraction patterns of A) SAF127, B) PVA, C) Glipizide (pure drug), D) Physical mixture and E) Optimized glipizide nanoformulation (F1)

Surface morphological studies

Optimized glipizide nanoparticles (F1) showed smooth and spherical shaped appearance (Figure 8). This smooth surface property of nanoparticles reveals complete removal of solvent from the glipizide nanoparticles and is the indication of good quality. It is reported that, incomplete removal of organic solvents affects the saturation of polymer and produces irregular shaped

particles (Dhana Lekshmi, Kishore, & Neelakanta Reddy, 2011). Glipizide showed smooth surfaced crystals in physical mixture which are not seen in final nanoparticles F1 indicates that glipizide is encapsulated in polymeric matrix.

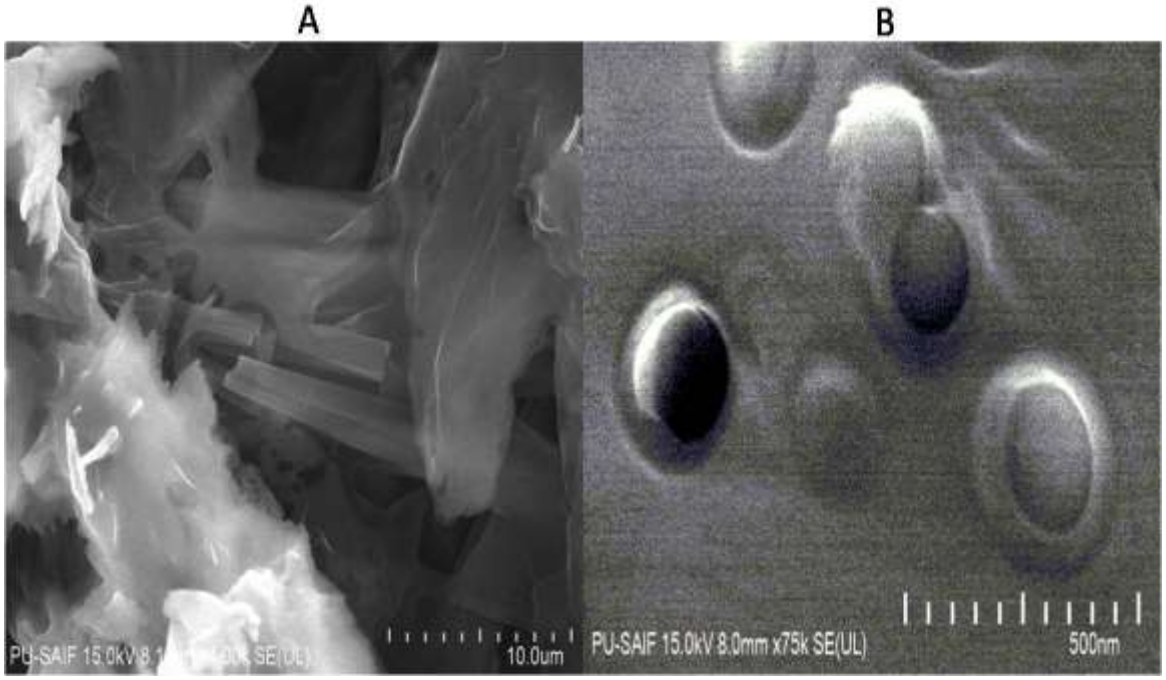


Figure 8 SEM images of A) Physical mixture (drug + polymers), B) Optimized glipizide nanoformulation (F1)

***In Vitro* studies**

The *in vitro* release of the glipizide from nanoformulation F1 showed initial burst release and then sustained release. The release of drug at 8 h was 51.1±4.6% and 89.1±4.12% unto 24h (Figure 9). The initial burst release of glipizide may be due to the loosely associated glipizide on the interface of nanoparticles of SAF127 nanoparticles. The drug incorporated into the inner core compartment stayed firmly inside the nanoparticles showing a sustained release pattern(Gao et al., 2011).

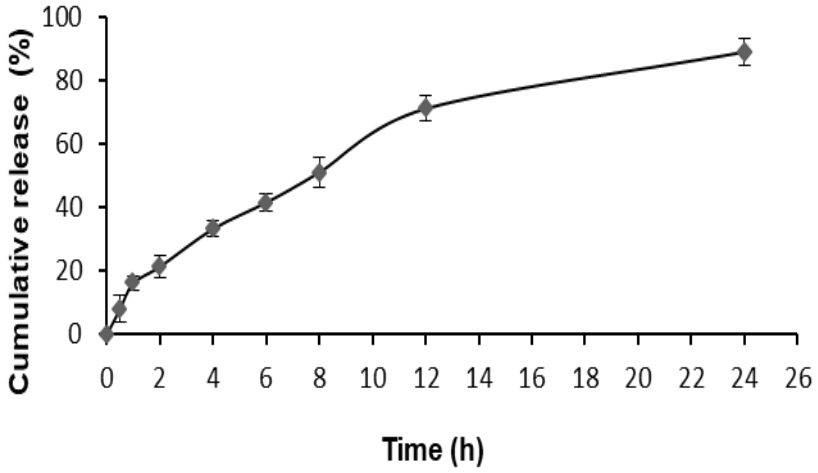


Figure 9 Percentage Cumulative release of glipizide nanoformulation F1

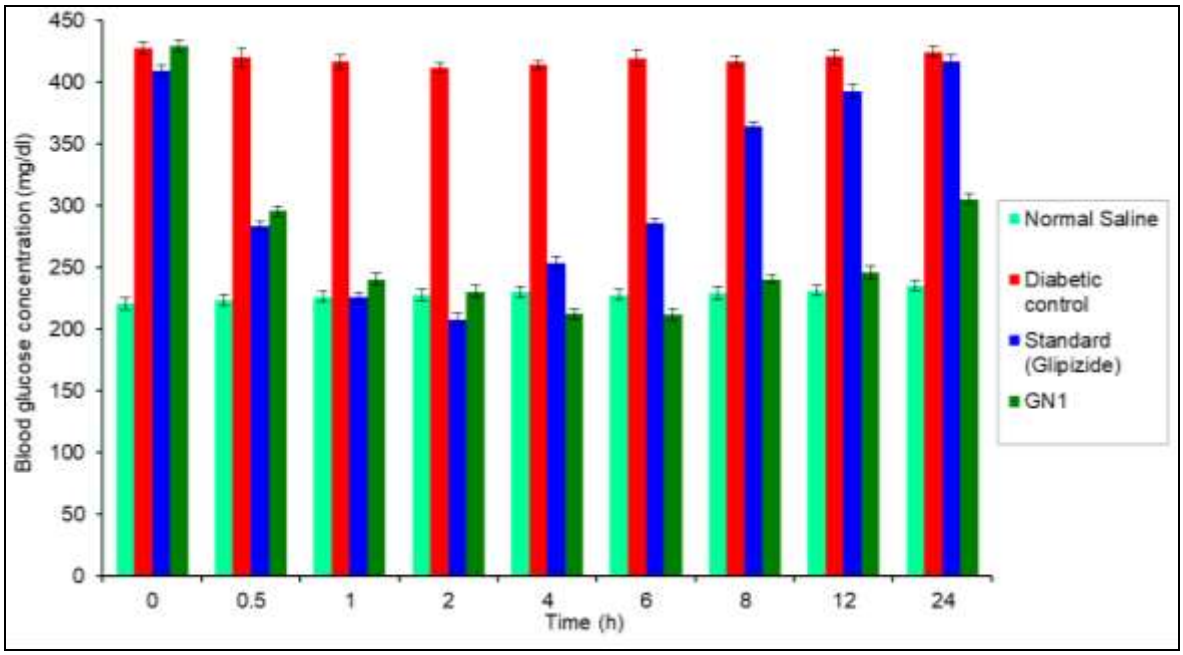


Figure 10. Effect of GN1 (1.5 mg/kg b.w.) in streptozotocin-induced diabetic rat model (mean ± SD; n = 6); N = 6. Anova followed by Dunnett's Multiple comparison test where ; ** = $p < 0.05$; * = $p < 0.01$; compared to control

***In vivo* studies**

The efficacy of the glipizide nanoparticles was evaluated in female Wistar albino rats at doses of 800 µg/Kg body weight. The nanoformulation F1 were selected for *in vivo* studies and results are shown in table 5. It was observed that the nanoformulations F1 reduced the blood glucose level in a sustained manner up to 24h. A significant ($p \leq 0.05$) reduction in blood glucose level was

observed as compared to diabetic control group. A significant ($p < 0.01$) blood glucose reduction was observed at 2 and 4 h time period compared to normal saline group. The blood glucose level controlled by glipizide nanoformulation (F1) upto 24 hours compared to diabetic control and results were also better at 4h, 6h, 8h, 12h and 24h time intervals compared to standard drug glipizide. *In vivo* blood glucose control pattern is similar to *in vitro* release profile of nanoformulation. The nanoencapsulated glipizide formulation was found to be much better than the conventional glipizide which maintains blood glucose level for 4 to 6 hours from a single oral dose.

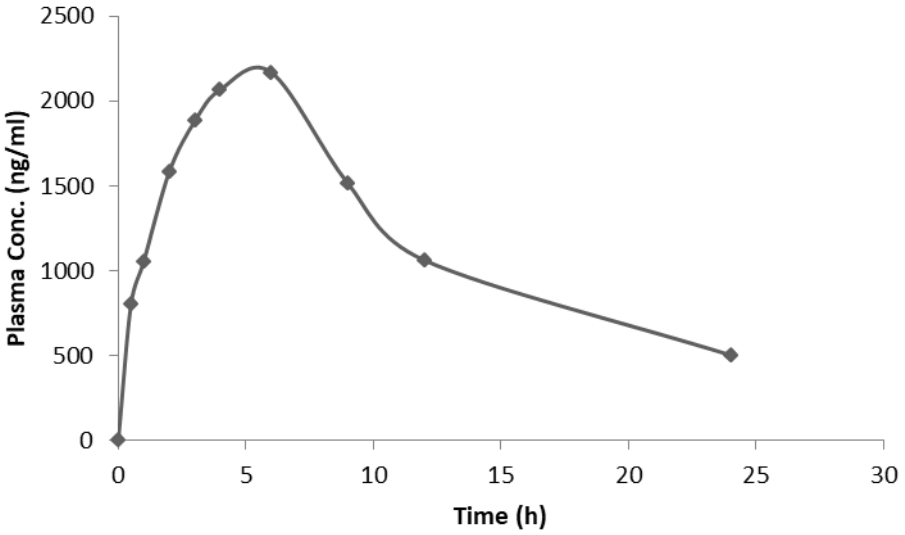


Figure 11 Blood plasma concentrations of glipizide vs. time graph after oral administration of glipizide nanoformulation(F1)

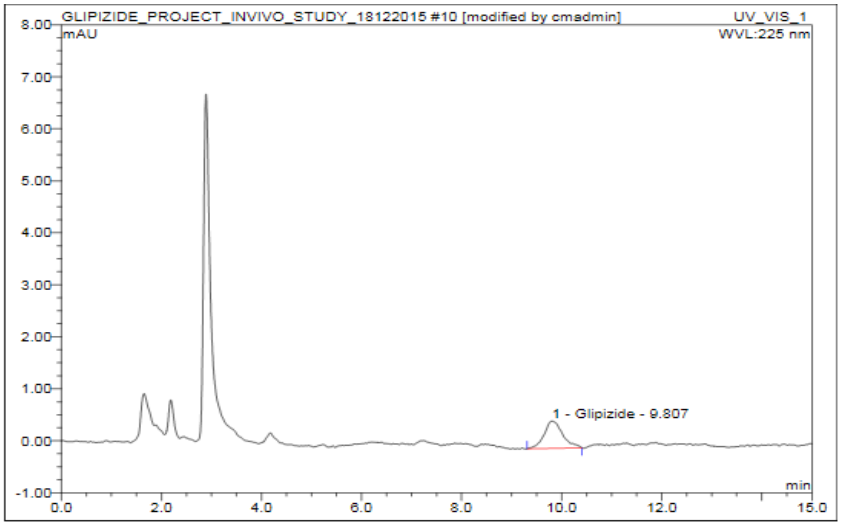


Figure 102 Chromatogram of *in vivo* pharmacokinetic studies of glipizide nanoformulation (F1)

Pharmacokinetic parameter

The plasma concentrations of glipizide vs. time are shown in Figure 10. The C_{max} (ng.h/ml) and t_{max} (h) after oral administration of glipizide nanoparticles were 2205±0.13 ng/ml and 6.23±0.41 h, respectively. The biological half-life ($t_{1/2}$) of glipizide was prolonged to about 9 h. The AUC $_{(0\rightarrow\infty)}$ was found to be 29.1 (ng.h/ml).

Stability studies

Three month stability studies were performed for nanoparticles size variation and aggregation factor. Overall, no significant variation in these parameters was observed. The high zeta potential (negative value) of nanoparticles batch F1 and low PDI value suggested that no aggregation of nanoparticles was occurred due to steric and electrostatic forces.

Conclusion

From the present study, it may be concluded that the glipizide loaded SAF127 nanoformulation is a valuable carrier for the design of a controlled drug delivery system of poorly water soluble drugs like glipizide. This nanoformulation can be utilized to improve the therapeutic efficacy of poorly water soluble drugs. The changes in nanoparticles size, zeta potential, PDI and entrapment efficiency was affected with the change in copolymer to drug ratio. PSA results show that there is change in the size of the nanoparticles. There was no interaction between glipizide, SAF127 and PVA has been observed as there was no shift in peaks was observed in physical mixture and optimized glipizide nanoparticles. This indicates that there is no chemical interaction between drug and polymer. The DSC thermogram of SAF127, PVA, pure glipizide physical mixture and optimized drug nanoparticles showed no significant interaction. XRD studies indicates that glipizide encapsulated within the polymer matrix and posses partially amorphous nature. The formulated glipizide nanoparticles showed smooth and spherical shaped appearance under scanning electron microscope. The *in vitro* release of the glipizide from nanoformulation showed initial burst release and then sustained release behaviour upto 24 h. The *in vivo* antidiabetic studies in wister albino rats revealed that the blood glucose level was controlled by glipizide nanoformulation upto 24 hours compared to diabetic control and results were also better at 4h, 6h, 8h, 12h and 24h time intervals compared to standard drug glipizide. The pharmacokinetic studies showed improvement in C_{max}, t_{max} and biological half-life of nanoformulation compared to standard drug.

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