Criteria 3

Research, Innovations and Extension

Key Indicator 3.3

Research Publication and Awards

3.3.1 Number of research papers published per teacher in the Journals notified on UGC website during the last five years

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2017-2018

Sr. No.	Title of paper	Name of the author/s	Department of the teacher	Name of journal	Impact Factor	Page No. with Link
1	Formulation And Evaluation Of Sustained Release Matrix Tablet Of Glipizide By Using Combination Of Natural And Synthetic Polymer	Bochare Umesh J**, Shelke Satish P,** Ambore Sandeep M, Jain Shirish P, Ghodke Amol D	Pharamceutical Quality Assurance	Journal of Pharma Research: 7 pp. 136-142 (7).	0	**01**
2	Formulation And Evaluation Of Sustained Release Matrix Tablet Of Glipizide By Using Combination Of Natural And Synthetic Polymer	Bochare Umesh J, Shelke Satish P, Ambore Sandeep M, **Jain Shirish P,** Ghodke Amol D	Pharamceutical Quality Assurance	Journal of Pharma Research: 7 pp. 136-142 (7).	0	**08**
3	Formulation And Evaluation Of Sustained Release Matrix Tablet Of Glipizide By Using Combination Of Natural And Synthetic Polymer	Bochare Umesh J, Shelke Satish P, Ambore Sandeep M, Jain Shirish P, **Ghodke Amol D**	Pharamceutical Quality Assurance	Journal of Pharma Research: 7 pp. 136-142 (7).	0	**15**
4	Investigation, Formulation And Evaluation Of Antidibetic Tablet Of Puncagrnatum Peel	**Ghodke Amol D,** Jain Shirish P, Ambore Sandeep M, Shelke Satish P and Bochare Umesh J	Pharamceutical Quality Assurance	International Journal of Pharmacy And Biological Sciences	0	**22**
5	Investigation, Formulation And Evaluation Of Antidibetic Tablet Of Puncagrnatum Peel	Ghodke Amol D**, Jain Shirish P,** Ambore Sandeep M, Shelke Satish P and Bochare Umesh J	Pharamceutical Quality Assurance	International Journal of Pharmacy And Biological Sciences	0	**33**

6	Investigation, Formulation And Evaluation Of Antidibetic Tablet Of Puncagrnatum Peel	Ghodke Amol D, Jain Shirish P, Ambore Sandeep M, **Shelke Satish P** and Bochare Umesh J	Pharamceutical Quality Assurance	International Journal of Pharmacy And Biological Sciences	0	**44**
7	Fabrication and Evaluation Of Herbal Ointment Formulations Of Moringa Oleifera For Topical Delivery	**Saddam C Shaikh**, Dnyaneshwar Sanap, Dipak V Bhusari, Shirish Jain, Pooja P Kochar, Fahim S Memon	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, Doi:https://doi.org/10.22270/ujpr.v3i4.181.	0	**55**
8	Fabrication and Evaluation Of Herbal Ointment Formulations Of Moringa Oleifera For Topical Delivery	Saddam C Shaikh, Dnyaneshwar Sanap, **Dipak V Bhusari,** Shirish Jain, Pooja P Kochar, Fahim S Memon	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, Doi:https://doi.org/10.22270/ujpr.v3i4.181.	0	**60**
9	Fabrication and Evaluation Of Herbal Ointment Formulations Of Moringa Oleifera For Topical Delivery	Saddam C Shaikh, Dnyaneshwar Sanap, Dipak V Bhusari**, Shirish Jain,** Pooja P Kochar, Fahim S Memon	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, Doi:https://doi.org/10.22270/ujpr.v3i4.181.	0	**65**
10	Fabrication and Evaluation Of Herbal Ointment Formulations Of Moringa Oleifera For Topical Delivery	Saddam C Shaikh, Dnyaneshwar Sanap, Dipak V Bhusari, Shirish Jain, Pooja P Kochar, **Fahim S Memon**	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, Doi:https://doi.org/10.22270/ujpr.v3i4.181.	0	**70**
11	Formulation And Evaluation Of Ibuprofen Gastro-Retentive Floating Tablets	**Saddam C Shaikh***, Dnyaneshwar Sanap, Dipak V Bhusari, Shirish Jain, Pooja P Kochar, Vikram N Sanchati	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, DOI: Doi:https://doi.org/10.22270/ujpr.v3i4.178	0	**75**

12	Formulation And Evaluation Of Ibuprofen Gastro-Retentive Floating Tablets	Saddam C Shaikh*, Dnyaneshwar Sanap, **Dipak V Bhusari,** Shirish Jain, Pooja P Kochar, Vikram N Sanchati	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, DOI: Doi:https://doi.org/10.22270/ujpr.v3i4.178	0	**80**
13	Formulation And Evaluation Of Ibuprofen Gastro-Retentive Floating Tablets	Saddam C Shaikh*, Dnyaneshwar Sanap, Dipak V Bhusari, **Shirish Jain**, Pooja P Kochar, Vikram N Sanchati	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, DOI: Doi:https://doi.org/10.22270/ujpr.v3i4.178	0	**85**
14	Formulation And Evaluation Of Ibuprofen Gastro-Retentive Floating Tablets	Saddam C Shaikh*, Dnyaneshwar Sanap, Dipak V Bhusari, Shirish Jain, Pooja P Kochar, **Vikram N Sanchati**	Pharmaceutics	Universal Journal of Pharmaceutical Research, Vol. 3, no. 4, 2018, DOI: Doi:https://doi.org/10.22270/ujpr.v3i4.178	0	**90**

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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF GLIPIZIDE BY USING COMBINATION OF NATURAL AND SYNTHETIC POLYMER

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ABSTRACT

Controlled release delivery system provides a uniform concentration or amount of the drug at the absorption site and thus, after absorption allow maintenance of plasma concentrations within a therapeutic range, which minimizes side effects and also reduces the frequency of administration. The overall objective of this work was to develop a tablet glipizide oral sustained release prepared by the method of direct compression, using hydroxy propyl methyl cellulose (HPMC K-100M) and xanthan gum polymer alone and in combination at various concentrations. Glipizide has a relatively short plasma half-life and low absolute bioavailability. All batches were evaluated for the precompression and post compresson. The hydrophilic matrix of HPMC alone cannot control the release glipizide effective for 12 h while when combined with xanthan gum, may slow down the release of the drug and, therefore, can be successfully employed for the formulation of matrix tablets SR.

KEYWORDS: *Glipizide, Matrix, Polymers, Retardant.*

INTRODUCTION [1]

Oral ingestion is traditionally preferred route of drug administration, providing a convenient method of effectively achieving both local and systemic effects. In conventional oral drug delivery systems, there is very little control over release of drug. The effective concentration at the target site can be achieved by intermittent administration of grossly excessive doses, which in most situations, often results in constantly changing, unpredictable and often sub or supra therapeutic plasma concentrations leaving the marked side effects. An ideal oral drug delivery system should steadily deliver a measurable and reproducible amount of drug to the target site over a prolonged period.

MATERIALS AND METHODOLOGY

Preparation of Standard Curve: [2]

Preparation of Phosphate Buffer pH 6.8:

Placed 11.45 gm of potassium dihydrogen phosphate and 28.80 gm of disodium hydrogen phosphate and made up to 1000 ml with distilled water.

Preparation of Standard Curve of glipizide with Phosphate Buffer pH 6.8:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic phosphate buffer of pH 6.8 as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Preparation of 0.1 N Hydrochloric Acid:

8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Preparation of Standard Curve of glipizide with 0.1 N HCI:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic 0.1 N HCI as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25 µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Drug Excipient Compatibility Studies:

The interaction between the drug and excipients are determined after a specific time period by using suitable analytical techniques like FTIR.

Preformulation Studies: [3-7]

Angle of Repose:

The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation.

$$\theta = \tan^{-1} h/r$$

Where, h = height of the powder heap

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r = radius of the powder heap
θ = is the angle of repose.

Determination of Bulk Density and Tapped Density:

The bulk density and the tapped density were calculated using the following formulae.

Bulk density = Weight of the powder / Initial volume
Tapped density = Weight of the powder / final volume

Carr's Compressibility Index:

Carr's index of each formulation was calculated according to equation given below:

Carr's index = [Tapped density − Bulk density/Tapped density] X 100

Hausner's Ratio:

Hausner's Ratio indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausners Ratio = Tapped density/Tapped density

Formulation Table: The formulation blend was mixed thoroughly by using mortar and pestle and the tablets of glipizide were punched by using Cemach tablet punching machine using 8 mm punch.

Table No. 1: Actual values of Ingredients taken for Matrix Tablet

Sr. No.	Ingredients	Formulation Codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Glipizide	10	10	10	10	10	10	10	10	10
2	HPMC K100-M				15	20	25	15	20	20
3	Xanthan Gum	5	10	15				5	10	12.5
4	Microcrystalline Cellulose	177	172	167	167	162	157	162	152	149.5
5	Magnesium Stearate	4	4	4	4	4	4	4	4	4
6	Talc	4	4	4	4	4	4	4	4	4
	Total weight (mg)	200	200	200	200	200	200	200	200	200

In vitro dissolution studies: [8-9]

The release rate of glipizide from sustain tablets was determined. The dissolution test was performed using United States Pharmacopoeia (USP) type II (paddle) apparatus, 900 ml of phosphate buffer of PH 6.8 at 37 ± 0.5°C and 50 rpm. A sample (10) of the solution was withdrawn from the dissolution apparatus at the appropriate time for 12 hours, and the samples were replaced with fresh dissolution medium. The samples were diluted into a suitable concentration with phosphate buffer. Absorbance of these solutions was measured at 226 nm using a UV/Visible double-beam spectrophotometer.

Data analysis: [10-16]

To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix, Korsmeyar-Peppas and Hixson Crowell model of optimized formulation.

Accelerated stability study: [17]

In order to determine the change in vitro release profile on Storage, stability study of batch F9 was carried out at 40 °C in a Humidity chamber having 75% RH. Sample was withdrawn at various time intervals and the study was conducted for 90 days. The sample was evaluated for change in vitro drug release pattern, hardness, Wetting time, percent drug content and disintegration time.

RESULT AND DISCUSSION

Identification Tests:

Preparation of Standard Curve of glipizide in Phosphate Buffer pH 6.8:

Table No. 2: Calibration Curve of Glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.181
3	10	0.363
4	15	0.544
5	20	0.713
6	25	0.869

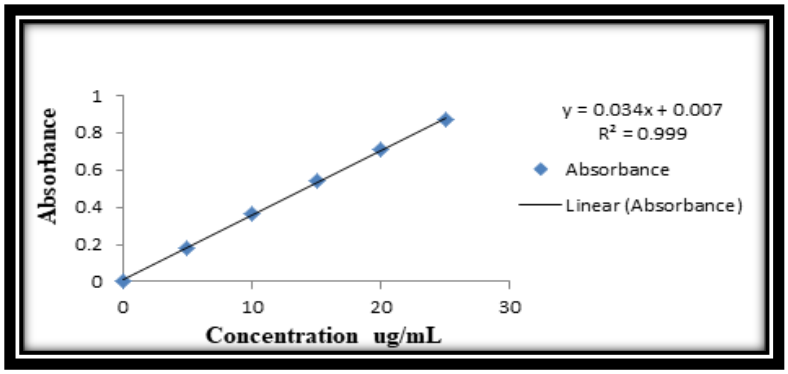

Fig. 1: Calibration curve of glipizide pH 6.8 phosphate buffer at 226 nm

Preparation of Standard Curve of glipizide with 0.1 N HCI:

Table No. 3: Calibration curve of glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.12
3	10	0.258
4	15	0.371
5	20	0.523
6	25	0.624

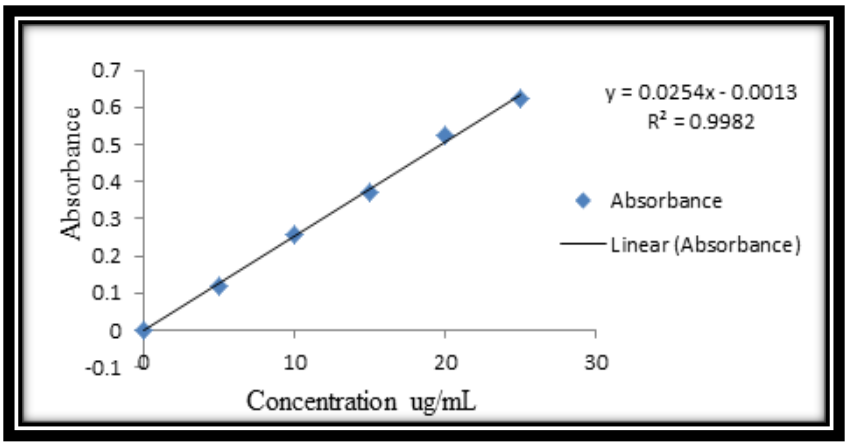

Fig. 2: Calibration curve of glipizide in 0.1 N HCL at 226 nm

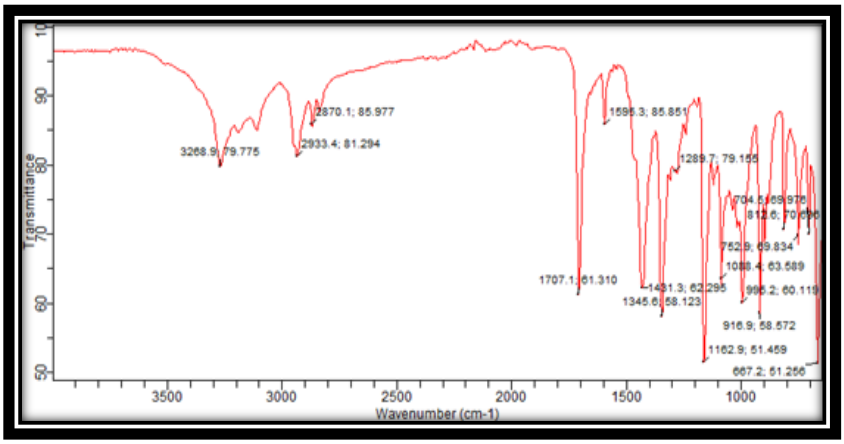

Fig. 3: FTIR Spectrum of glipizide

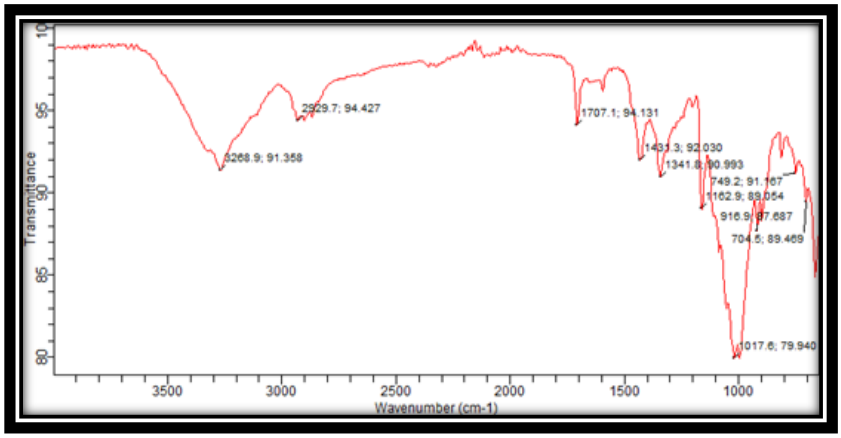

Fig. 4: FTIR spectrum of glipizide with xanthan gum

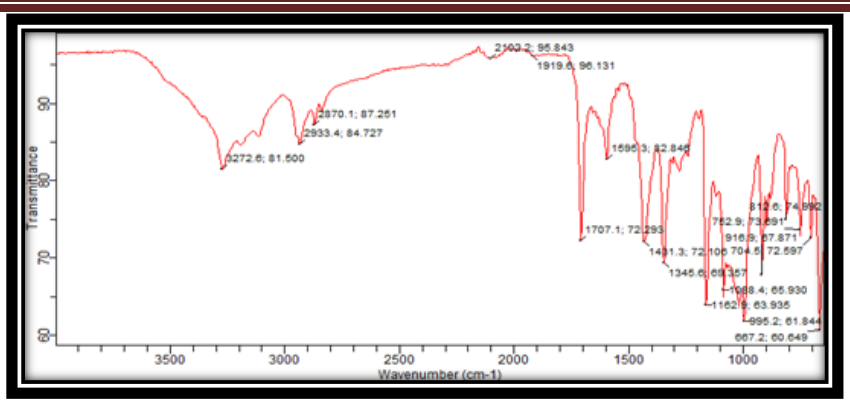

Fig. 5: FTIR spectrum of formulation blend

Preformulation Studies:

Preformulation testing was done for each batch and the result were tabulated in the above table which concluded that all batches are passes with good flow ability and were further proceed for compression of tablets (Table 4).

Evaluation of matrix tablets:

All the prepared matrix tablets were evaluated for following official parameters (Table 5).

After the compression of tablet post compression parameter are evaluated such as hardness, thickness, friability, weight variation and drug content. All parameter possess the standards of Indian pharmacopoeia and found to be within limit. The percent drug content is calculated by performing an assay of glipizide tablet using UV spectrophotometer.

In vitro dissolution studies:

In the dissolution study of various batches formulation the following calculation are done and from that data a graph of various formulation were drawn and compared with marketed formulation (Table 6).

Accelerated Stability Studies:

The optimized batch of F9 glipizide matrix tablet were evaluated for accelerated stability studies at 40^{0}C / 75 % RH condition. The stability details of results are presented as below (Table 7).

Table No. 4: Precompression parameters of glipizide formulation

Formulation code	Bulk density (gm/ ml)	Tapped density (gm/ ml)	Compressibility Index %	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.50	0.617	18.96	18.96	1.23	26.30
F2	0.515	0.580	11.20	11.20	1.14	26.87
F3	0.512	0.595	13.94	13.94	1.16	27.16
F4	0.520	0.591	12.01	12.01	1.13	27.77
F5	0.526	0.606	13.20	13.20	1.15	28.09
F6	0.549	0.617	11.02	11.02	1.12	28.09
F7	0.529	0.602	12.12	12.12	1.13	29.42
F8	0.526	0.609	13.62	13.62	1.15	29.76
F9	0.543	0.632	14.08	14.08	1.16	27.04

Table No. 5: Post Compression parameters of glipizide formulation

Sr. No.	Formulation	Hardness (Kg/cm^2)	Friability (%)	Thickness	Weight variation	% Drug content (mg)
1.	F1	5.3	0.13	3.28	199	102.00
2.	F2	5.1	0.09	5.53	200	98.10
3.	F3	5.5	0.14	3.30	199	98.48
4.	F4	5.2	0.10	3.45	201	97.00
5.	F5	5.0	0.18	3.40	200	98.00
6.	F6	5.5	0.16	3.48	202	101.00
7.	F7	5.4	0.19	3.12	201	96.14
8.	F8	5.6	0.22	3.16	199	95.60
9.	F9	5.4	0.11	3.13	200	99.17

Table No. 6: In-vitro % drug release of formulation F1 to F9

Time	Innovator (Glynase)	% Drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
0.5	19.05	29.91	21.17	11.91	29.91	31.50	27.79	29.91	27.79	21.10
1	26.47	42.00	23.02	13.50	36.79	42.00	29.38	31.50	37.26	26.47
2	36.79	54.00	26.47	19.05	42.00	48.17	37.26	36.79	46.58	29.30
3	46.58	58.00	29.38	21.17	46.58	54.00	51.35	42.00	51.35	37.26
4	51.35	70.41	36.79	26.47	58.00	70.41	58.50	51.35	65.38	46.58
5	60.00	79.41	46.58	27.79	79.41	83.91	87.08	65.38	79.41	54.00

6	68.82	83.91	53.47	29.38	83.91	90.52	87.08	73.58	83.91	65.38
7	75.17	88.14	60.00	31.76	92.91	97.41	87.08	87.08	90.52	73.58
8	83.91	92.91	68.82	36.79	96.88	98.47	90.52	92.91	96.61	81.79
9	90.52	96.35	73.58	40.23	97.67	98.47	97.41	98.20	96.88	88.41
10	94.23	96.88	81.79	46.58	97.67	98.73	97.41	98.73	97.67	92.91
11	97.67	97.67	82.00	48.44	98.47	98.73	101.64	98.73	97.67	96.88
12	100.05	97.67	82.00	51.35	98.47	98.73	101.64	98.73	98.92	99.79

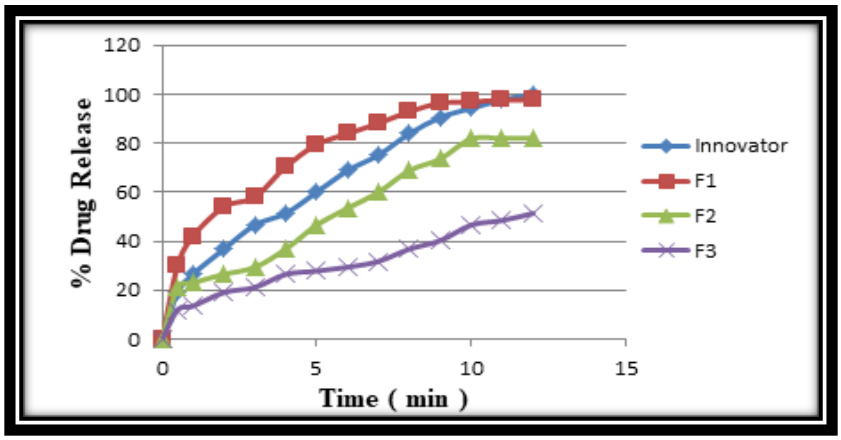

Fig. 6: In-vitro release profile of formulation F1, F2 & F3

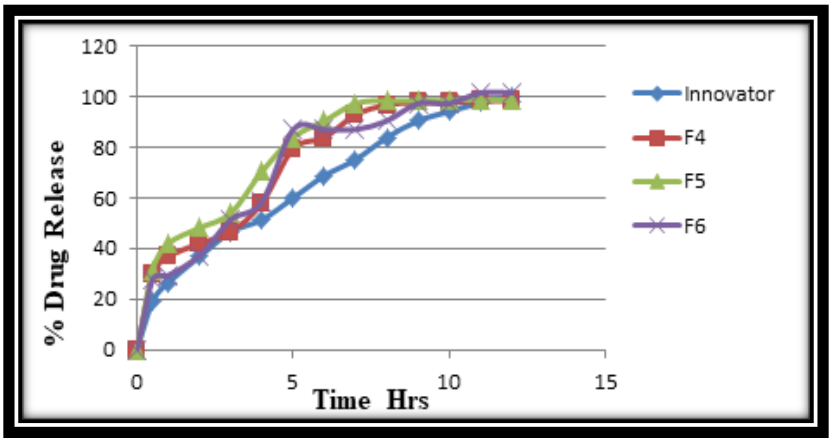

Fig. 7: In-vitro release profile of formulation F4, F5 & F6

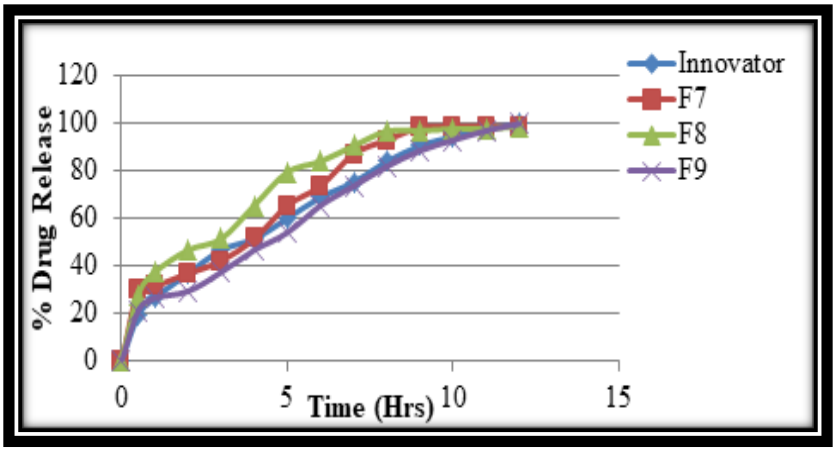

Fig. 8: In-vitro release profile of formulation F7, F8 & F9

Data analysis by various kinetic models:

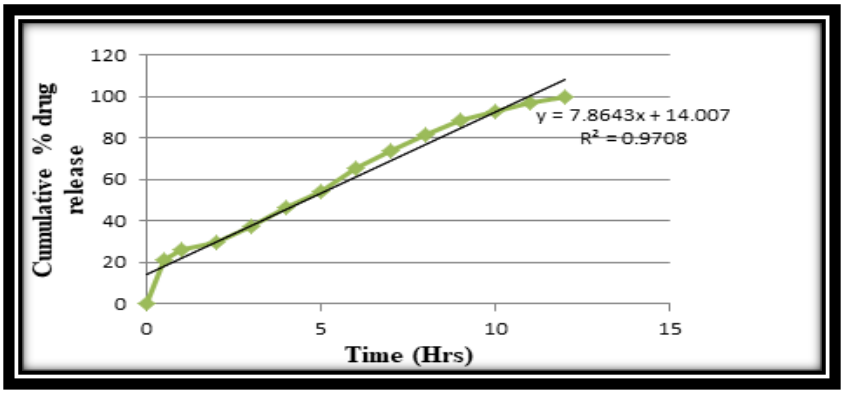

Fig. 9: Zero order kinetic model of optimized formulation

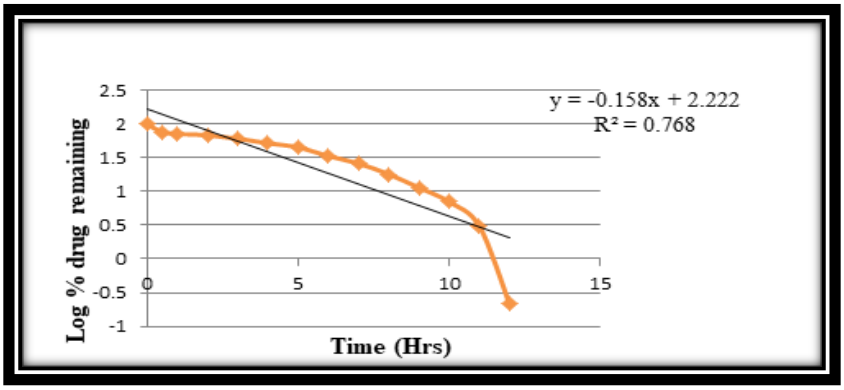

Fig. 10: First order kinetic model of optimized formulation

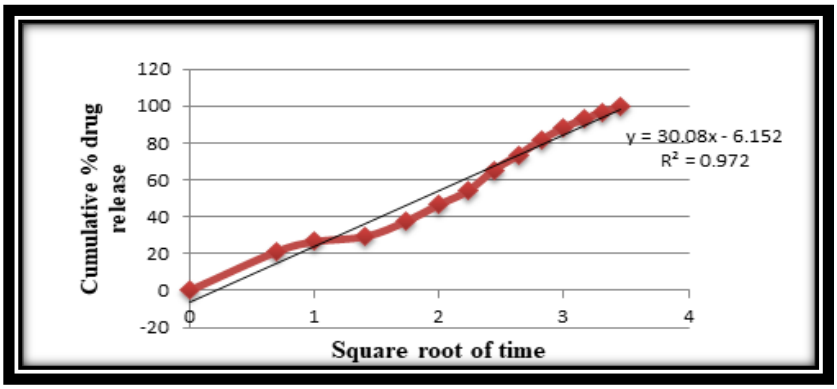

Fig. 11: Higuchi model kinetic release of optimized formulation

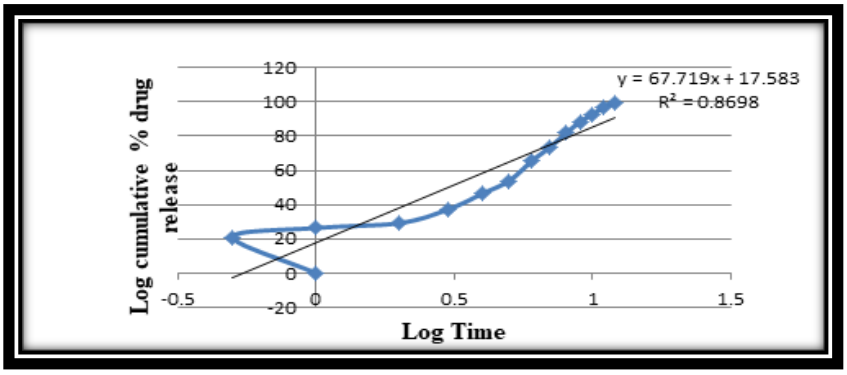

Fig. 12: Korsmeyer-Peppas model for drug release of optimized formulation

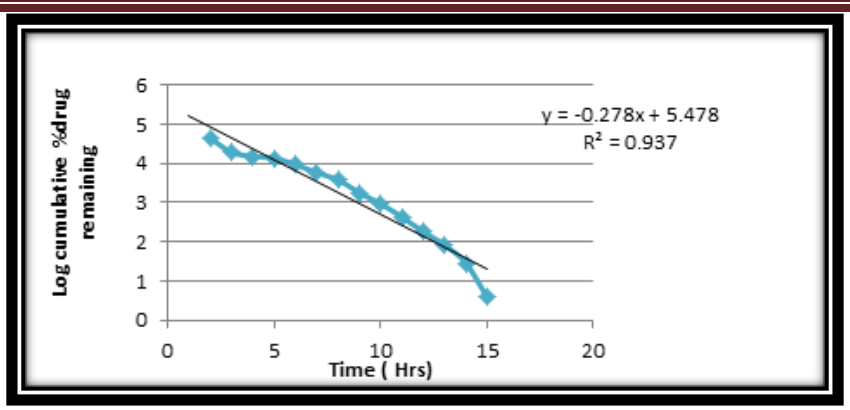

Fig. 13: Hixson-Crowell model kinetic release of optimized formulation

Table No. 7: Results of accelerated stability Study of optimized formulation

Sr. No.	Test	Specifications	Initial	After 1 month	After 2 months	After 3 months
1	**Description**	White/Off-white colored tablets	Complies	Complies	Complies	Complies
2.	**Assay by UV**	NLT 90.0 %and NMT 110.00 %	99.12 %	98.07 %	97.69 %	97.14 %
3	**Dissolution**	NLT 80% release after 12 hours	99.18 %	97.8 %	97.5 %	97.24%

CONCLUSION

The present work was to formulate and evaluate sustain release matrix tablets of glipizide by using natural and synthetic polymer to sustain the drug release from matrix tablet. The sustained release drug delivery was a promising approach to achieve a prolonged therapeutic action of drug. The matrix forming polymers, HPMC K-100M, Xanthan gum alone & in combination were studied.

The amount of drug release for optimized formulation F9 was found to be 99.79%. The cumulative percentage drug was decreased by increase in polymer concentration. The drug release of optimized formulation F9 correspond to Higuchi model and nearly comparative to zero order as result obtained from r^2 value. It is found be 0.979 for marketed formulation and 0.972 for the optimized formulation. Formulation F9 containing HPMC K-100M. (10%) & Xanthan gum (6.25%) in combination successfully release drug for more than 8 hrs, emerging as best formulation.

The total % drug release from batch F8 and F9 was found to be 98.92 and 99.79 respectively. It shows non-fickian diffusion as per the n value obtained in the Korsmeyer-Peppas release kinetic model was found to be 0.537. FTIR studies proved that there was no chemical interaction in drug and polymer of the developed matrix tablets.

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Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLET OF GLIPIZIDE BY USING COMBINATION OF NATURAL AND SYNTHETIC POLYMER

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Received on: 18-06-2018; Revised and Accepted on: 11-07-2018

ABSTRACT

Controlled release delivery system provides a uniform concentration or amount of the drug at the absorption site and thus, after absorption allow maintenance of plasma concentrations within a therapeutic range, which minimizes side effects and also reduces the frequency of administration. The overall objective of this work was to develop a tablet glipizide oral sustained release prepared by the method of direct compression, using hydroxy propyl methyl cellulose (HPMC K-100M) and xanthan gum polymer alone and in combination at various concentrations. Glipizide has a relatively short plasma half-life and low absolute bioavailability. All batches were evaluated for the precompression and post compresson. The hydrophilic matrix of HPMC alone cannot control the release glipizide effective for 12 h while when combined with xanthan gum, may slow down the release of the drug and, therefore, can be successfully employed for the formulation of matrix tablets SR.

KEYWORDS: *Glipizide, Matrix, Polymers, Retardant.*

INTRODUCTION [1]

Oral ingestion is traditionally preferred route of drug administration, providing a convenient method of effectively achieving both local and systemic effects. In conventional oral drug delivery systems, there is very little control over release of drug. The effective concentration at the target site can be achieved by intermittent administration of grossly excessive doses, which in most situations, often results in constantly changing, unpredictable and often sub or supra therapeutic plasma concentrations leaving the marked side effects. An ideal oral drug delivery system should steadily deliver a measurable and reproducible amount of drug to the target site over a prolonged period.

MATERIALS AND METHODOLOGY

Preparation of Standard Curve: [2]

Preparation of Phosphate Buffer pH 6.8:

Placed 11.45 gm of potassium dihydrogen phosphate and 28.80 gm of disodium hydrogen phosphate and made up to 1000 ml with distilled water.

Preparation of Standard Curve of glipizide with Phosphate Buffer pH 6.8:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic phosphate buffer of pH 6.8 as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Preparation of 0.1 N Hydrochloric Acid:

8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Preparation of Standard Curve of glipizide with 0.1 N HCl:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic 0.1 N HCl as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25 µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Drug Excipient Compatibility Studies:

The interaction between the drug and excipients are determined after a specific time period by using suitable analytical techniques like FTIR.

Preformulation Studies: [3-7]

Angle of Repose:

The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation.

$$\theta = \tan^{-1} h/r$$

Where, h = height of the powder heap

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r = radius of the powder heap
θ = is the angle of repose.

Determination of Bulk Density and Tapped Density:

The bulk density and the tapped density were calculated using the following formulae.

Bulk density = Weight of the powder / Initial volume
Tapped density = Weight of the powder / final volume

Carr's Compressibility Index:

Carr's index of each formulation was calculated according to equation given below:

Carr's index = [Tapped density − Bulk density/Tapped density] X 100

Hausner's Ratio:

Hausner's Ratio indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausners Ratio = Tapped density/Tapped density

Formulation Table: The formulation blend was mixed thoroughly by using mortar and pestle and the tablets of glipizide were punched by using Cemach tablet punching machine using 8 mm punch.

Table No. 1: Actual values of Ingredients taken for Matrix Tablet

Sr. No.	Ingredients	Formulation Codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Glipizide	10	10	10	10	10	10	10	10	10
2	HPMC K100-M				15	20	25	15	20	20
3	Xanthan Gum	5	10	15				5	10	12.5
4	Microcrystalline Cellulose	177	172	167	167	162	157	162	152	149.5
5	Magnesium Stearate	4	4	4	4	4	4	4	4	4
6	Talc	4	4	4	4	4	4	4	4	4
	Total weight (mg)	200	200	200	200	200	200	200	200	200

In vitro dissolution studies: [8-9]

The release rate of glipizide from sustain tablets was determined. The dissolution test was performed using United States Pharmacopoeia (USP) type II (paddle) apparatus, 900 ml of phosphate buffer of PH 6.8 at 37 ± 0.5°C and 50 rpm. A sample (10) of the solution was withdrawn from the dissolution apparatus at the appropriate time for 12 hours, and the samples were replaced with fresh dissolution medium. The samples were diluted into a suitable concentration with phosphate buffer. Absorbance of these solutions was measured at 226 nm using a UV/Visible double-beam spectrophotometer.

Data analysis: [10-16]

To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix, Korsmeyar-Peppas and Hixson Crowell model of optimized formulation.

Accelerated stability study: [17]

In order to determine the change in vitro release profile on Storage, stability study of batch F9 was carried out at 40 °C in a Humidity chamber having 75% RH. Sample was withdrawn at various time intervals and the study was conducted for 90 days. The sample was evaluated for change in vitro drug release pattern, hardness, Wetting time, percent drug content and disintegration time.

RESULT AND DISCUSSION

Identification Tests:

Preparation of Standard Curve of glipizide in Phosphate Buffer pH 6.8:

Table No. 2: Calibration Curve of Glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.181
3	10	0.363
4	15	0.544
5	20	0.713
6	25	0.869

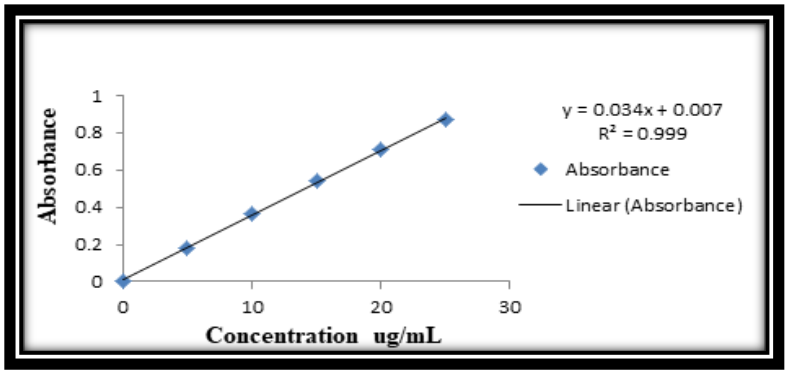

Fig. 1: Calibration curve of glipizide pH 6.8 phosphate buffer at 226 nm

Preparation of Standard Curve of glipizide with 0.1 N HCI:

Table No. 3: Calibration curve of glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.12
3	10	0.258
4	15	0.371
5	20	0.523
6	25	0.624

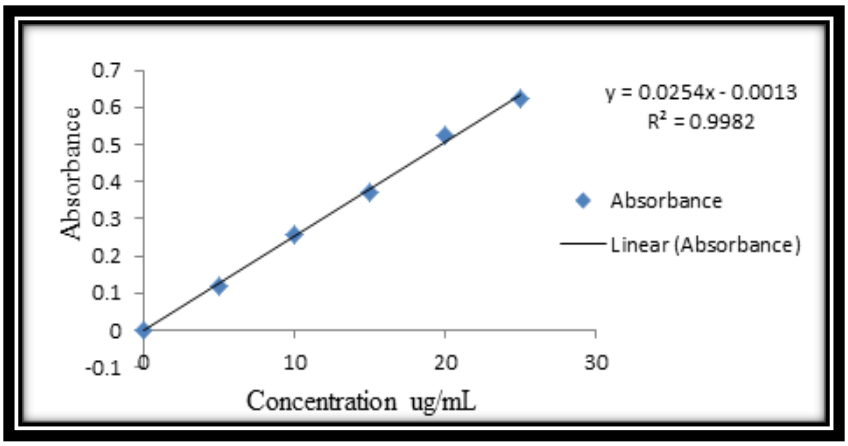

Fig. 2: Calibration curve of glipizide in 0.1 N HCL at 226 nm

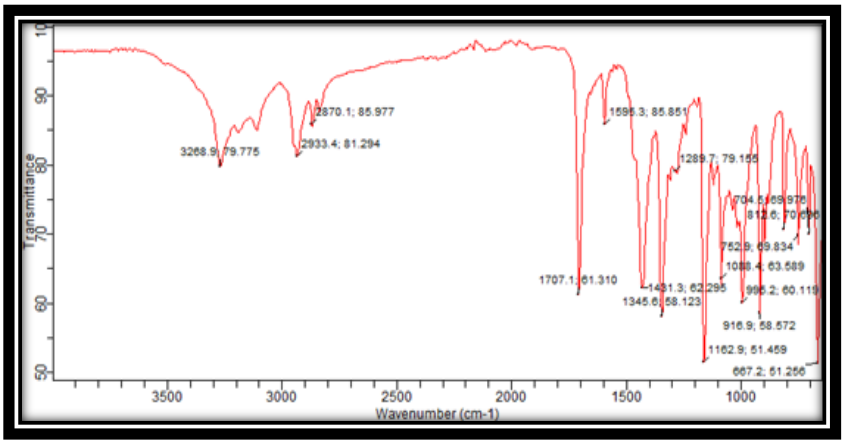

Fig. 3: FTIR Spectrum of glipizide

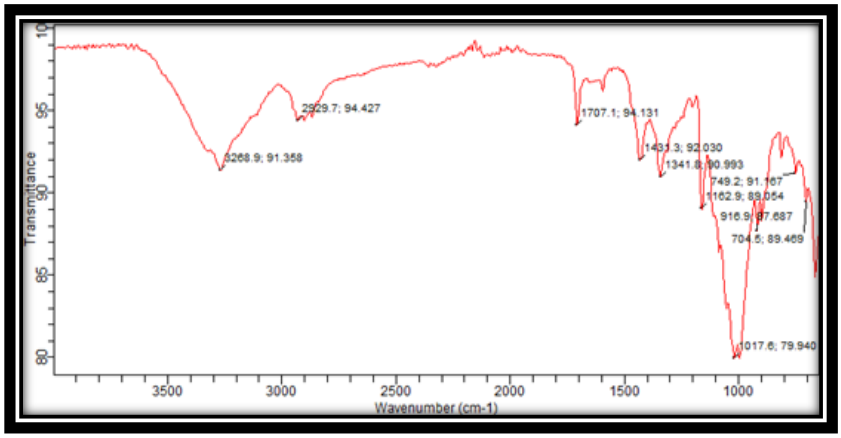

Fig. 4: FTIR spectrum of glipizide with xanthan gum

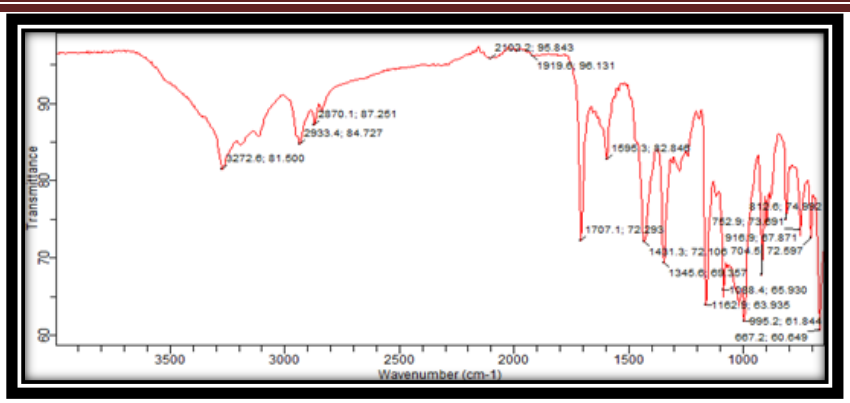

Fig. 5: FTIR spectrum of formulation blend

Preformulation Studies:

Preformulation testing was done for each batch and the result were tabulated in the above table which concluded that all batches are passes with good flow ability and were further proceed for compression of tablets (Table 4).

Evaluation of matrix tablets:

All the prepared matrix tablets were evaluated for following official parameters (Table 5).

After the compression of tablet post compression parameter are evaluated such as hardness, thickness, friability, weight variation and drug content. All parameter possess the standards of Indian pharmacopoeia and found to be within limit. The percent drug content is calculated by performing an assay of glipizide tablet using UV spectrophotometer.

In vitro dissolution studies:

In the dissolution study of various batches formulation the following calculation are done and from that data a graph of various formulation were drawn and compared with marketed formulation (Table 6).

Accelerated Stability Studies:

The optimized batch of F9 glipizide matrix tablet were evaluated for accelerated stability studies at 40^{0}C / 75 % RH condition. The stability details of results are presented as below (Table 7).

Table No. 4: Precompression parameters of glipizide formulation

Formulation code	Bulk density (gm/ ml)	Tapped density (gm/ ml)	Compressibility Index %	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.50	0.617	18.96	18.96	1.23	26.30
F2	0.515	0.580	11.20	11.20	1.14	26.87
F3	0.512	0.595	13.94	13.94	1.16	27.16
F4	0.520	0.591	12.01	12.01	1.13	27.77
F5	0.526	0.606	13.20	13.20	1.15	28.09
F6	0.549	0.617	11.02	11.02	1.12	28.09
F7	0.529	0.602	12.12	12.12	1.13	29.42
F8	0.526	0.609	13.62	13.62	1.15	29.76
F9	0.543	0.632	14.08	14.08	1.16	27.04

Table No. 5: Post Compression parameters of glipizide formulation

Sr. No.	Formulation	Hardness (Kg/cm^2)	Friability (%)	Thickness	Weight variation	% Drug content (mg)
1.	F1	5.3	0.13	3.28	199	102.00
2.	F2	5.1	0.09	5.53	200	98.10
3.	F3	5.5	0.14	3.30	199	98.48
4.	F4	5.2	0.10	3.45	201	97.00
5.	F5	5.0	0.18	3.40	200	98.00
6.	F6	5.5	0.16	3.48	202	101.00
7.	F7	5.4	0.19	3.12	201	96.14
8.	F8	5.6	0.22	3.16	199	95.60
9.	F9	5.4	0.11	3.13	200	99.17

Table No. 6: In-vitro % drug release of formulation F1 to F9

Time	Innovator (Glynase)	% Drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
0.5	19.05	29.91	21.17	11.91	29.91	31.50	27.79	29.91	27.79	21.10
1	26.47	42.00	23.02	13.50	36.79	42.00	29.38	31.50	37.26	26.47
2	36.79	54.00	26.47	19.05	42.00	48.17	37.26	36.79	46.58	29.30
3	46.58	58.00	29.38	21.17	46.58	54.00	51.35	42.00	51.35	37.26
4	51.35	70.41	36.79	26.47	58.00	70.41	58.50	51.35	65.38	46.58
5	60.00	79.41	46.58	27.79	79.41	83.91	87.08	65.38	79.41	54.00

6	68.82	83.91	53.47	29.38	83.91	90.52	87.08	73.58	83.91	65.38
7	75.17	88.14	60.00	31.76	92.91	97.41	87.08	87.08	90.52	73.58
8	83.91	92.91	68.82	36.79	96.88	98.47	90.52	92.91	96.61	81.79
9	90.52	96.35	73.58	40.23	97.67	98.47	97.41	98.20	96.88	88.41
10	94.23	96.88	81.79	46.58	97.67	98.73	97.41	98.73	97.67	92.91
11	97.67	97.67	82.00	48.44	98.47	98.73	101.64	98.73	97.67	96.88
12	100.05	97.67	82.00	51.35	98.47	98.73	101.64	98.73	98.92	99.79

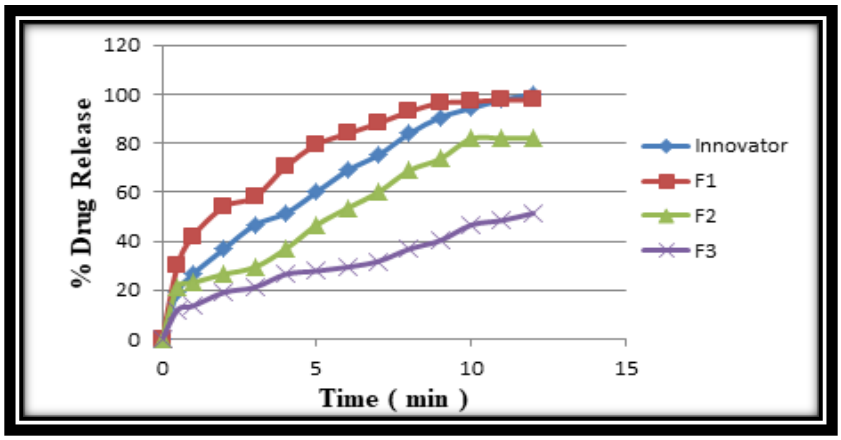

Fig. 6: In-vitro release profile of formulation F1, F2 & F3

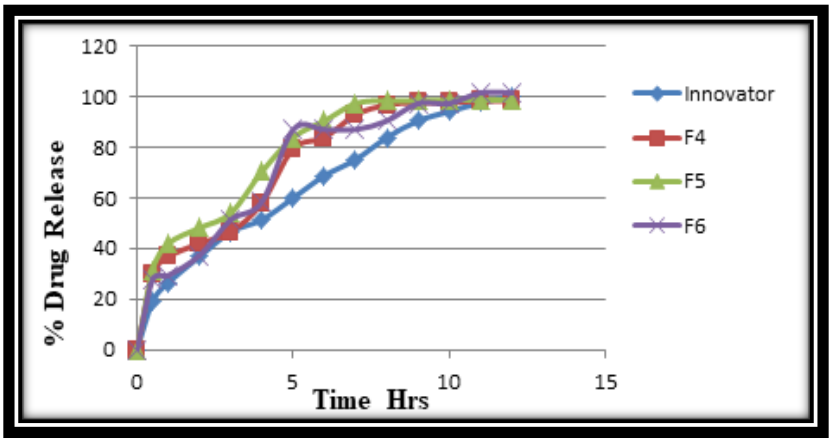

Fig. 7: In-vitro release profile of formulation F4, F5 & F6

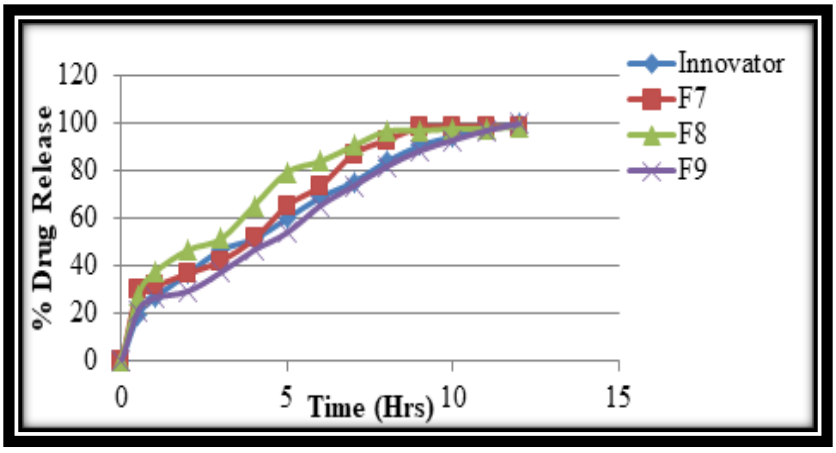

Fig. 8: In-vitro release profile of formulation F7, F8 & F9

Data analysis by various kinetic models:

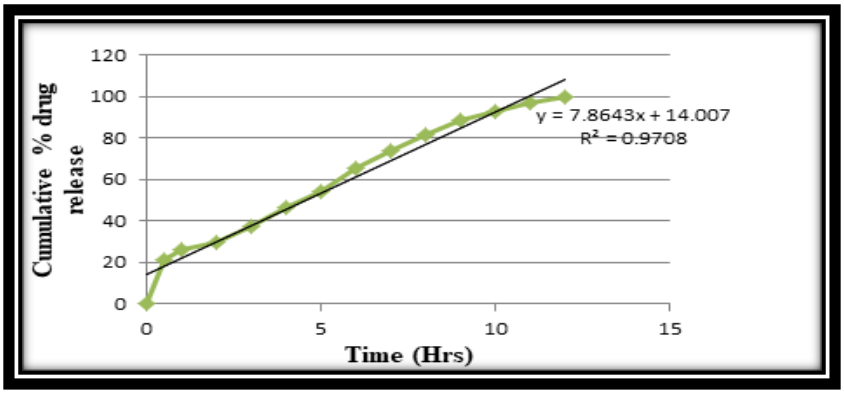

Fig. 9: Zero order kinetic model of optimized formulation

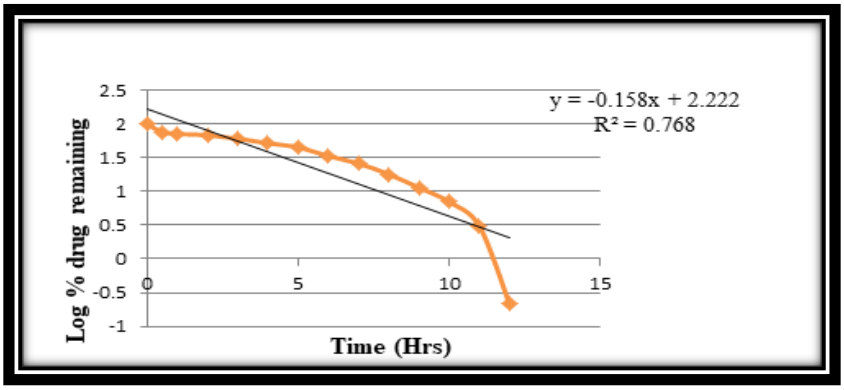

Fig. 10: First order kinetic model of optimized formulation

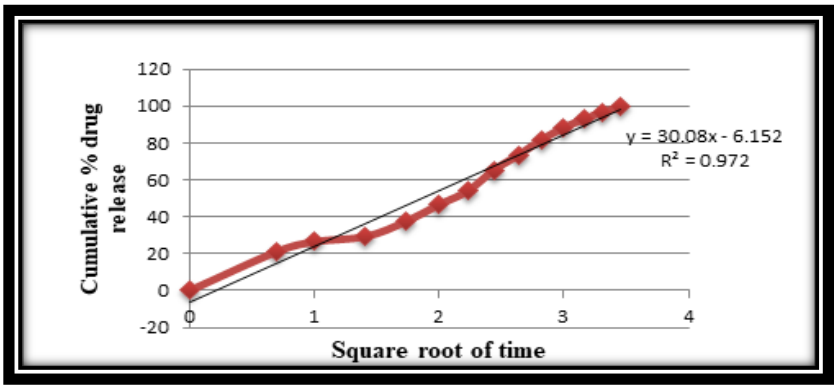

Fig. 11: Higuchi model kinetic release of optimized formulation

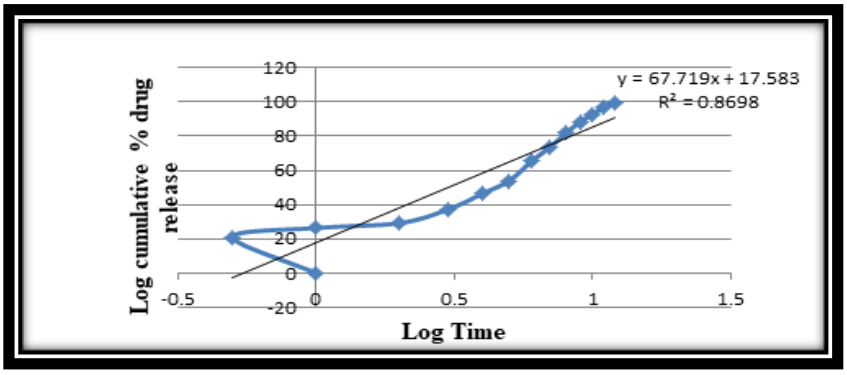

Fig. 12: Korsmeyer-Peppas model for drug release of optimized formulation

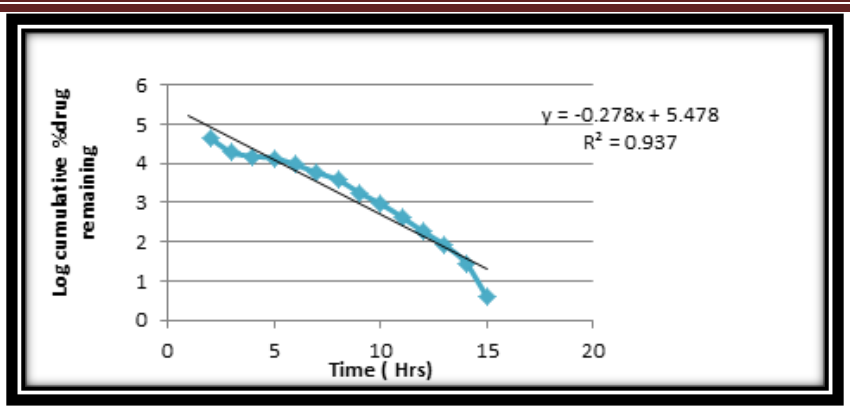

Fig. 13: Hixson-Crowell model kinetic release of optimized formulation

Table No. 7: Results of accelerated stability Study of optimized formulation

Sr. No.	Test	Specifications	Initial	After 1 month	After 2 months	After 3 months
1	**Description**	White/Off-white colored tablets	Complies	Complies	Complies	Complies
2.	**Assay by UV**	NLT 90.0 %and NMT 110.00 %	99.12 %	98.07 %	97.69 %	97.14 %
3	**Dissolution**	NLT 80% release after 12 hours	99.18 %	97.8 %	97.5 %	97.24%

CONCLUSION

The present work was to formulate and evaluate sustain release matrix tablets of glipizide by using natural and synthetic polymer to sustain the drug release from matrix tablet. The sustained release drug delivery was a promising approach to achieve a prolonged therapeutic action of drug. The matrix forming polymers, HPMC K-100M, Xanthan gum alone & in combination were studied.

The amount of drug release for optimized formulation F9 was found to be 99.79%. The cumulative percentage drug was decreased by increase in polymer concentration. The drug release of optimized formulation F9 correspond to Higuchi model and nearly comparative to zero order as result obtained from r^2 value. It is found be 0.979 for marketed formulation and 0.972 for the optimized formulation. Formulation F9 containing HPMC K-100M. (10%) & Xanthan gum (6.25%) in combination successfully release drug for more than 8 hrs, emerging as best formulation.

The total % drug release from batch F8 and F9 was found to be 98.92 and 99.79 respectively. It shows non-fickian diffusion as per the n value obtained in the Korsmeyer-Peppas release kinetic model was found to be 0.537. FTIR studies proved that there was no chemical interaction in drug and polymer of the developed matrix tablets.

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8.5 ml of concentrate hydrochloric acid was taken and diluted with distilled water up to 1000 ml.

Preparation of Standard Curve of glipizide with 0.1 N HCl:

A standard graph of pure drug in suitable medium was prepared by plotting the concentration on X-axis and absorbance on Y-axis. An accurately weighed 100 mg of Glipizide was dissolved in methanolic 0.1 N HCl as per I.P and make up the volume up to 100 ml in a volumetric flask, (Stock Solution: I, This stock solution concentration is 1mg/ml or 1000 µg/ml). From this stock solution 10 ml of solution were pipette out and make up the volume up to 100 ml (Stock Solution: II, 100µg/ml). Then the aliquots were prepared, whose concentration ranging from 5 to 25 µg/ml and the absorbance were measured at 226 nm by using UV Spectrophotometer against the reagent blank. The coefficient of variation and correlation coefficient were determined.

Drug Excipient Compatibility Studies:

The interaction between the drug and excipients are determined after a specific time period by using suitable analytical techniques like FTIR.

Preformulation Studies: [3-7]

Angle of Repose:

The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation.

$$\theta = \tan^{-1} h/r$$

Where, h = height of the powder heap

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r = radius of the powder heap
θ = is the angle of repose.

Determination of Bulk Density and Tapped Density:

The bulk density and the tapped density were calculated using the following formulae.

Bulk density = Weight of the powder / Initial volume
Tapped density = Weight of the powder / final volume

Carr's Compressibility Index:

Carr's index of each formulation was calculated according to equation given below:

Carr's index = [Tapped density − Bulk density/Tapped density] X 100

Hausner's Ratio:

Hausner's Ratio indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

Hausners Ratio = Tapped density/Tapped density

Formulation Table: The formulation blend was mixed thoroughly by using mortar and pestle and the tablets of glipizide were punched by using Cemach tablet punching machine using 8 mm punch.

Table No. 1: Actual values of Ingredients taken for Matrix Tablet

Sr. No.	Ingredients	Formulation Codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Glipizide	10	10	10	10	10	10	10	10	10
2	HPMC K100-M				15	20	25	15	20	20
3	Xanthan Gum	5	10	15				5	10	12.5
4	Microcrystalline Cellulose	177	172	167	167	162	157	162	152	149.5
5	Magnesium Stearate	4	4	4	4	4	4	4	4	4
6	Talc	4	4	4	4	4	4	4	4	4
	Total weight (mg)	200	200	200	200	200	200	200	200	200

In vitro dissolution studies: [8-9]

The release rate of glipizide from sustain tablets was determined. The dissolution test was performed using United States Pharmacopoeia (USP) type II (paddle) apparatus, 900 ml of phosphate buffer of PH 6.8 at 37 ± 0.5°C and 50 rpm. A sample (10) of the solution was withdrawn from the dissolution apparatus at the appropriate time for 12 hours, and the samples were replaced with fresh dissolution medium. The samples were diluted into a suitable concentration with phosphate buffer. Absorbance of these solutions was measured at 226 nm using a UV/Visible double-beam spectrophotometer.

Data analysis: [10-16]

To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi matrix, Korsmeyar-Peppas and Hixson Crowell model of optimized formulation.

Accelerated stability study: [17]

In order to determine the change in vitro release profile on Storage, stability study of batch F9 was carried out at 40 °C in a Humidity chamber having 75% RH. Sample was withdrawn at various time intervals and the study was conducted for 90 days. The sample was evaluated for change in vitro drug release pattern, hardness, Wetting time, percent drug content and disintegration time.

RESULT AND DISCUSSION

Identification Tests:

Preparation of Standard Curve of glipizide in Phosphate Buffer pH 6.8:

Table No. 2: Calibration Curve of Glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.181
3	10	0.363
4	15	0.544
5	20	0.713
6	25	0.869

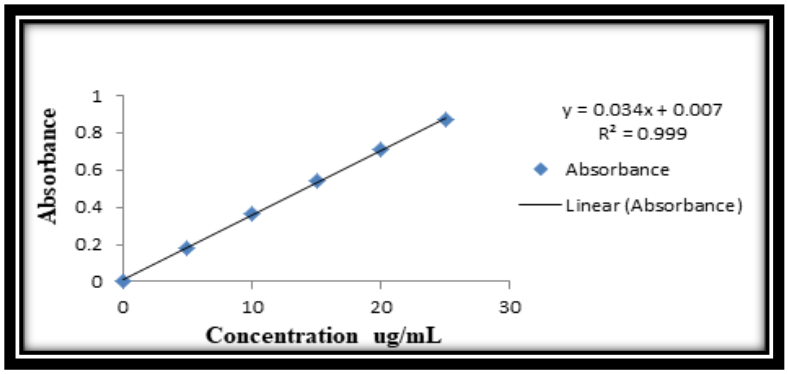

Fig. 1: Calibration curve of glipizide pH 6.8 phosphate buffer at 226 nm

Preparation of Standard Curve of glipizide with 0.1 N HCI:

Table No. 3: Calibration curve of glipizide

Sr. No.	Concentration (ug/ml)	Absorbance
1	0	0
2	5	0.12
3	10	0.258
4	15	0.371
5	20	0.523
6	25	0.624

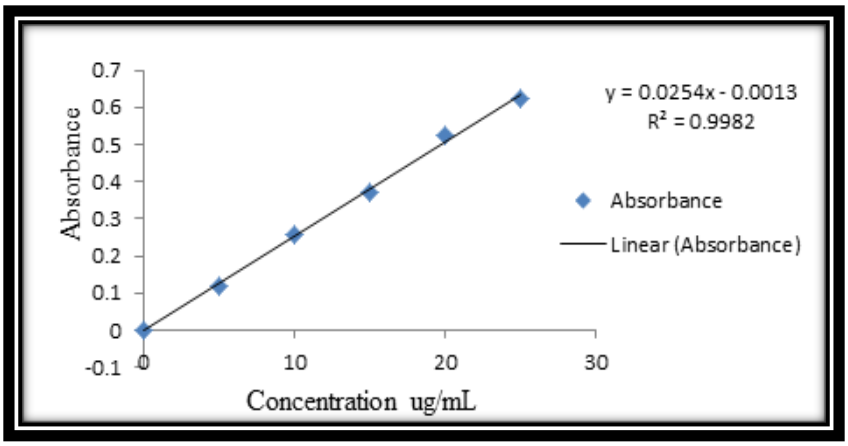

Fig. 2: Calibration curve of glipizide in 0.1 N HCL at 226 nm

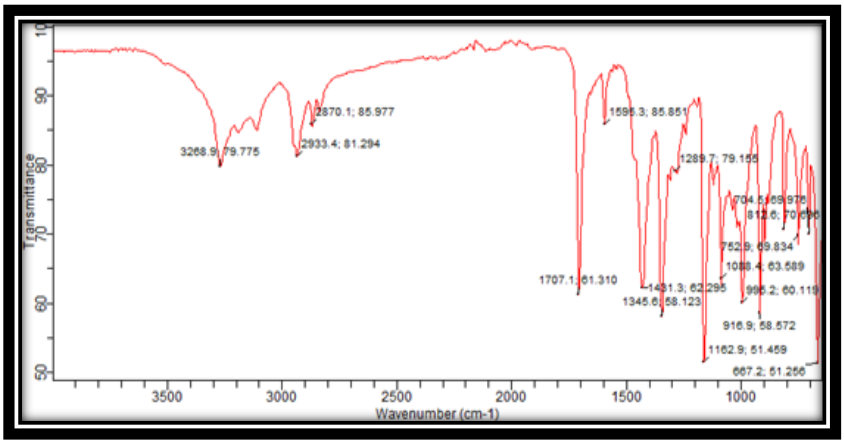

Fig. 3: FTIR Spectrum of glipizide

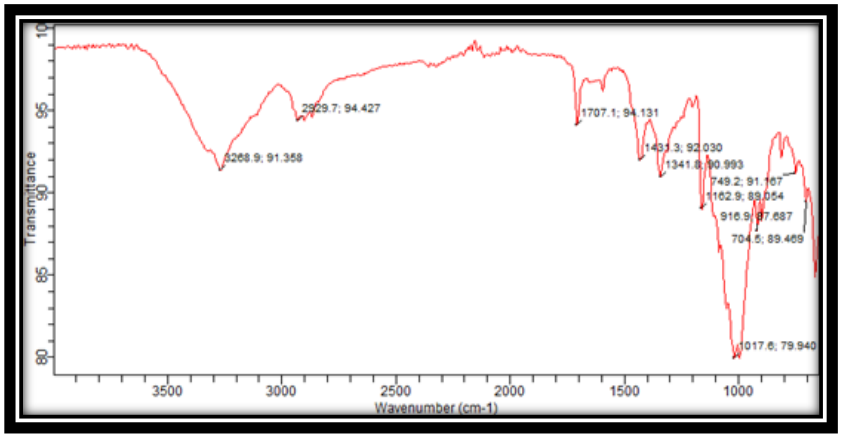

Fig. 4: FTIR spectrum of glipizide with xanthan gum

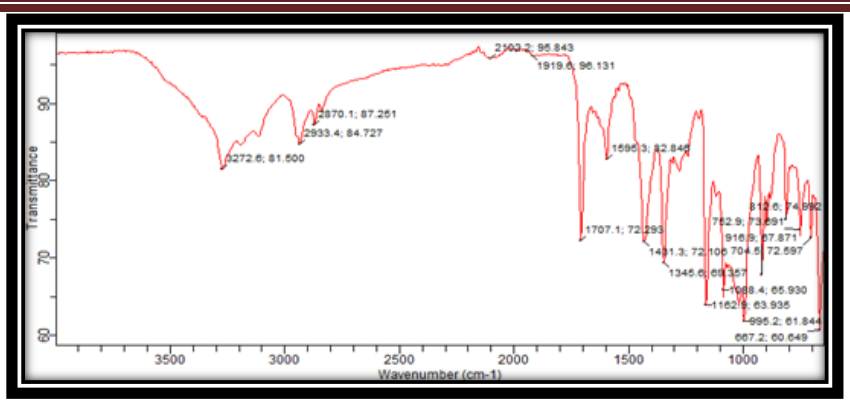

Fig. 5: FTIR spectrum of formulation blend

Preformulation Studies:

Preformulation testing was done for each batch and the result were tabulated in the above table which concluded that all batches are passes with good flow ability and were further proceed for compression of tablets (Table 4).

Evaluation of matrix tablets:

All the prepared matrix tablets were evaluated for following official parameters (Table 5).

After the compression of tablet post compression parameter are evaluated such as hardness, thickness, friability, weight variation and drug content. All parameter possess the standards of Indian pharmacopoeia and found to be within limit. The percent drug content is calculated by performing an assay of glipizide tablet using UV spectrophotometer.

In vitro dissolution studies:

In the dissolution study of various batches formulation the following calculation are done and from that data a graph of various formulation were drawn and compared with marketed formulation (Table 6).

Accelerated Stability Studies:

The optimized batch of F9 glipizide matrix tablet were evaluated for accelerated stability studies at 40^{0}C / 75 % RH condition. The stability details of results are presented as below (Table 7).

Table No. 4: Precompression parameters of glipizide formulation

Formulation code	Bulk density (gm/ ml)	Tapped density (gm/ ml)	Compressibility Index %	Carr's Index (%)	Hausner's Ratio	Angle of repose
F1	0.50	0.617	18.96	18.96	1.23	26.30
F2	0.515	0.580	11.20	11.20	1.14	26.87
F3	0.512	0.595	13.94	13.94	1.16	27.16
F4	0.520	0.591	12.01	12.01	1.13	27.77
F5	0.526	0.606	13.20	13.20	1.15	28.09
F6	0.549	0.617	11.02	11.02	1.12	28.09
F7	0.529	0.602	12.12	12.12	1.13	29.42
F8	0.526	0.609	13.62	13.62	1.15	29.76
F9	0.543	0.632	14.08	14.08	1.16	27.04

Table No. 5: Post Compression parameters of glipizide formulation

Sr. No.	Formulation	Hardness (Kg/cm^2)	Friability (%)	Thickness	Weight variation	% Drug content (mg)
1.	F1	5.3	0.13	3.28	199	102.00
2.	F2	5.1	0.09	5.53	200	98.10
3.	F3	5.5	0.14	3.30	199	98.48
4.	F4	5.2	0.10	3.45	201	97.00
5.	F5	5.0	0.18	3.40	200	98.00
6.	F6	5.5	0.16	3.48	202	101.00
7.	F7	5.4	0.19	3.12	201	96.14
8.	F8	5.6	0.22	3.16	199	95.60
9.	F9	5.4	0.11	3.13	200	99.17

Table No. 6: In-vitro % drug release of formulation F1 to F9

Time	Innovator (Glynase)	% Drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0	0
0.5	19.05	29.91	21.17	11.91	29.91	31.50	27.79	29.91	27.79	21.10
1	26.47	42.00	23.02	13.50	36.79	42.00	29.38	31.50	37.26	26.47
2	36.79	54.00	26.47	19.05	42.00	48.17	37.26	36.79	46.58	29.30
3	46.58	58.00	29.38	21.17	46.58	54.00	51.35	42.00	51.35	37.26
4	51.35	70.41	36.79	26.47	58.00	70.41	58.50	51.35	65.38	46.58
5	60.00	79.41	46.58	27.79	79.41	83.91	87.08	65.38	79.41	54.00

6	68.82	83.91	53.47	29.38	83.91	90.52	87.08	73.58	83.91	65.38
7	75.17	88.14	60.00	31.76	92.91	97.41	87.08	87.08	90.52	73.58
8	83.91	92.91	68.82	36.79	96.88	98.47	90.52	92.91	96.61	81.79
9	90.52	96.35	73.58	40.23	97.67	98.47	97.41	98.20	96.88	88.41
10	94.23	96.88	81.79	46.58	97.67	98.73	97.41	98.73	97.67	92.91
11	97.67	97.67	82.00	48.44	98.47	98.73	101.64	98.73	97.67	96.88
12	100.05	97.67	82.00	51.35	98.47	98.73	101.64	98.73	98.92	99.79

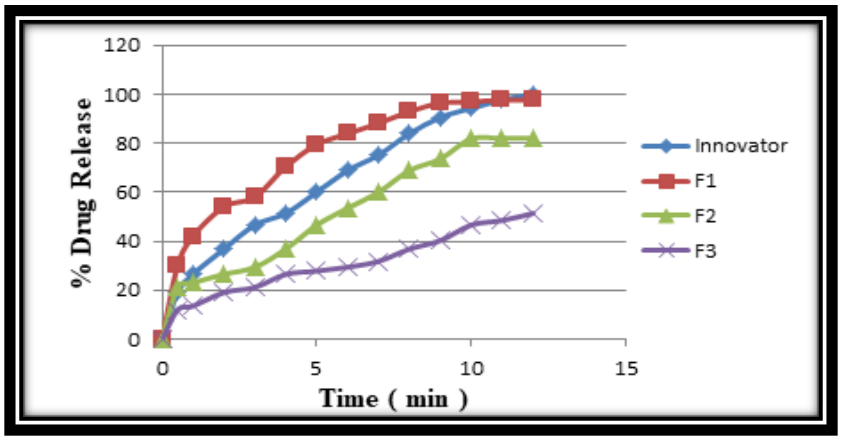

Fig. 6: In-vitro release profile of formulation F1, F2 & F3

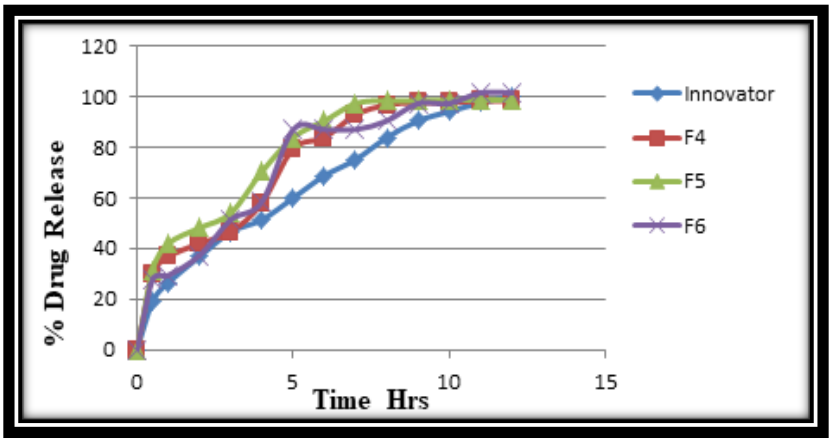

Fig. 7: In-vitro release profile of formulation F4, F5 & F6

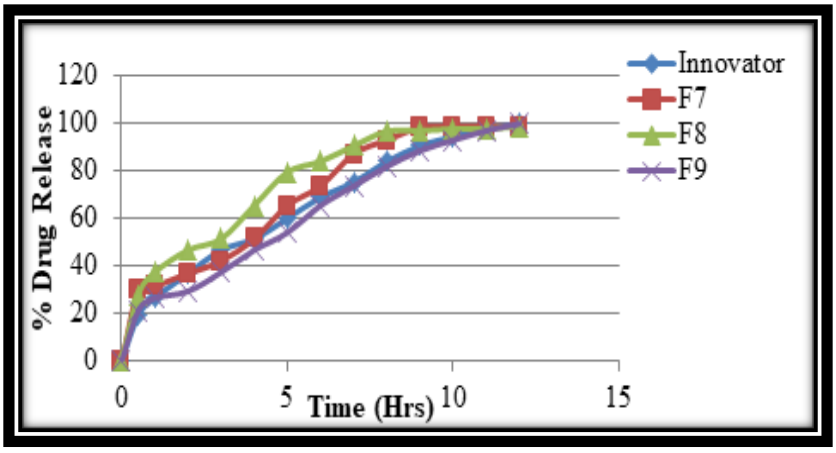

Fig. 8: In-vitro release profile of formulation F7, F8 & F9

Data analysis by various kinetic models:

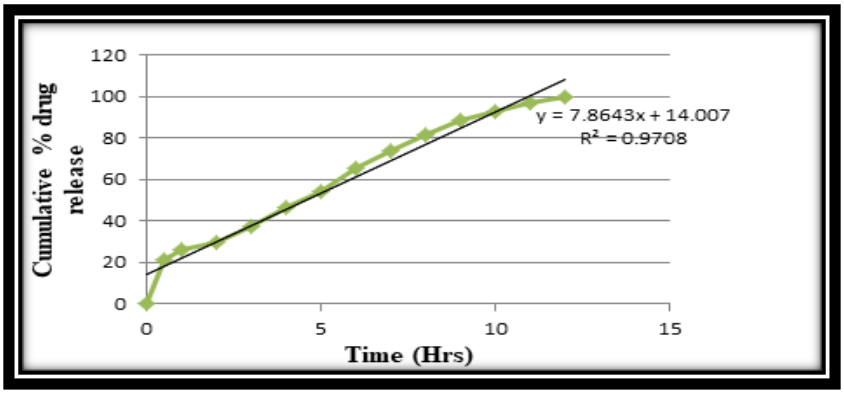

Fig. 9: Zero order kinetic model of optimized formulation

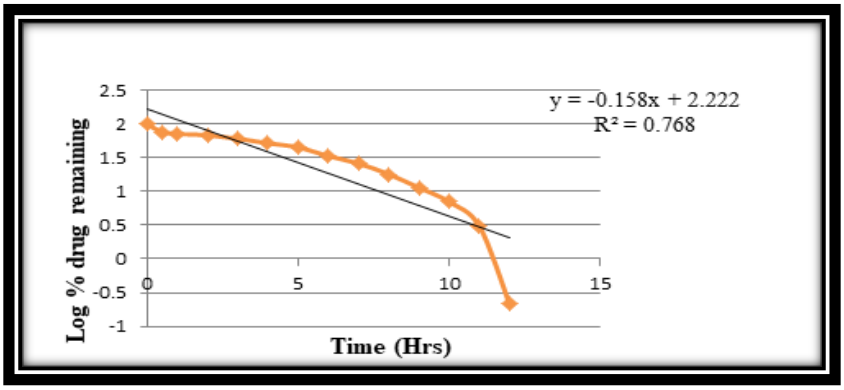

Fig. 10: First order kinetic model of optimized formulation

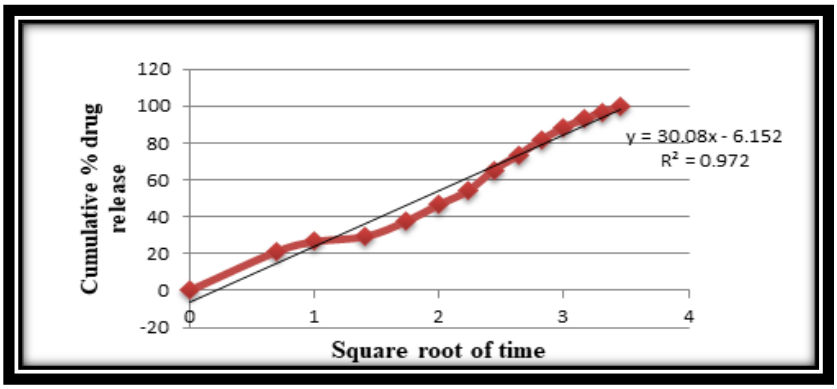

Fig. 11: Higuchi model kinetic release of optimized formulation

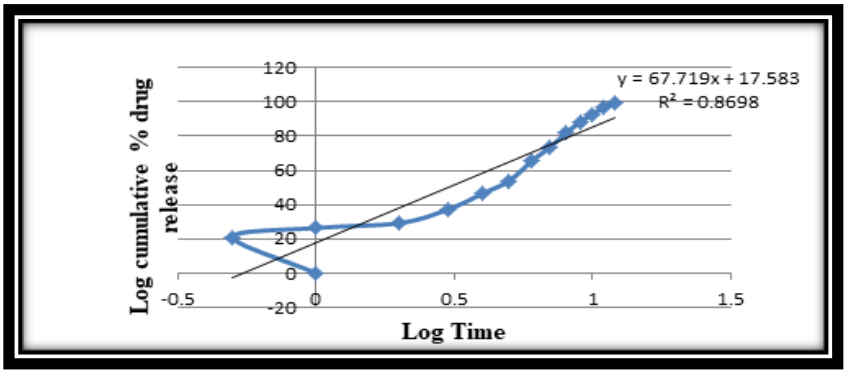

Fig. 12: Korsmeyer-Peppas model for drug release of optimized formulation

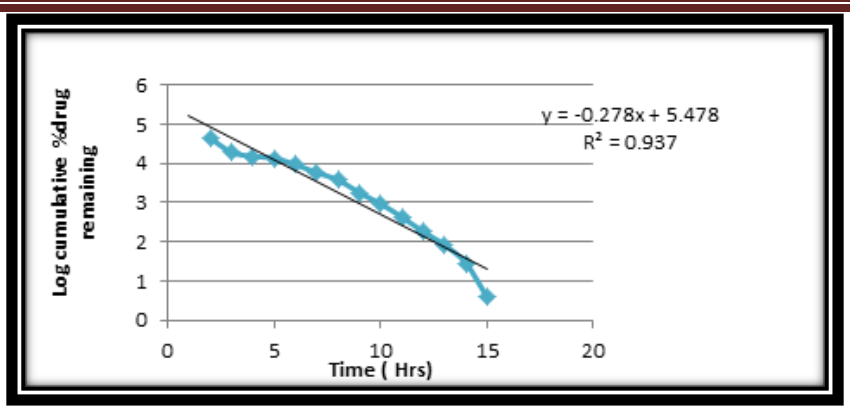

Fig. 13: Hixson-Crowell model kinetic release of optimized formulation

Table No. 7: Results of accelerated stability Study of optimized formulation

Sr. No.	Test	Specifications	Initial	After 1 month	After 2 months	After 3 months
1	**Description**	White/Off-white colored tablets	Complies	Complies	Complies	Complies
2.	**Assay by UV**	NLT 90.0 %and NMT 110.00 %	99.12 %	98.07 %	97.69 %	97.14 %
3	**Dissolution**	NLT 80% release after 12 hours	99.18 %	97.8 %	97.5 %	97.24%

CONCLUSION

The present work was to formulate and evaluate sustain release matrix tablets of glipizide by using natural and synthetic polymer to sustain the drug release from matrix tablet. The sustained release drug delivery was a promising approach to achieve a prolonged therapeutic action of drug. The matrix forming polymers, HPMC K-100M, Xanthan gum alone & in combination were studied.

The amount of drug release for optimized formulation F9 was found to be 99.79%. The cumulative percentage drug was decreased by increase in polymer concentration. The drug release of optimized formulation F9 correspond to Higuchi model and nearly comparative to zero order as result obtained from r^2 value. It is found be 0.979 for marketed formulation and 0.972 for the optimized formulation. Formulation F9 containing HPMC K-100M. (10%) & Xanthan gum (6.25%) in combination successfully release drug for more than 8 hrs, emerging as best formulation.

The total % drug release from batch F8 and F9 was found to be 98.92 and 99.79 respectively. It shows non-fickian diffusion as per the n value obtained in the Korsmeyer-Peppas release kinetic model was found to be 0.537. FTIR studies proved that there was no chemical interaction in drug and polymer of the developed matrix tablets.

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INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF PUNICAGRANATUM PEEL

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INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF *PUNICAGRANATUM* PEEL

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ABSTRACT

The present study was aimed to formulate & evaluate the antidiabetic tablet of Punicagranatum peels waste. Hyperglycemia is the most common metabolic endocrine disorder. It is the chronic condition in which blood glucose level is elevated than normal due to the improper insulin production in body or due to insulin resistance, high blood glucose level and low blood glucose level leads to diabetic condition. Allopathic treatment for diabetes mellitus is too costly so focus on herbal medicines is necessary. Pomegranate peels or rind are considered as an waste material these peels consists of numerous important active chemical constituents such as flavonoids, vitamins and minerals. The main principle active chemical constituents including punicalagin, punicalin, β-sitosterol and valoneic acid dilactone (VAD) from pomegranate peels powder shows potent antidiabetic activity Punicagranatum peels extract have stability problem than other dosage form by converting it into tablet dosage form. We enhance its acceptability, elegance and patient compliance. Manufacturing of tablets was done by using wet granulation method on lab level tablet press (CEMACH) by wet granulation method. Evaluations tests performed on tablets such as Hardness, Weight variation, friability, disintegration test etc

KEY WORDS

punicagranatum, antidiabetic, valoneic acid dilactone (VAD), herbal medicine

1.INTRODUCTION:

Diabetes mellitus is a metabolic disorder identified as increased in blood glucose level than normal. This is happened due to either insufficient insulin production or insulin resistance. High amount of lipids, free fatty acid and glucose in our body affects the B-cells function by various mechanisms such as generation of various reactive oxygen species (ROS). Generally, there are three types of Diabetes occurs one is the Insulin Dependence Diabetes Mellitus (IDDM) second is the (NIDDM) that is Non-Insulin Dependence Diabetes Mellitus and third one is the Gestational Diabetes.

1.1 Biological Sources: [17-20]

a} Botanical Name: *Punicagranatum*
b} Family Name: Puniacaceae
c} Common Name: Pomegranate**,** Anar
d} Part Used: Seeds, flowers, peels, roots etc.

1.2 Common Name: [17-20]

i. **Hindi:** Anar
ii. **English:** Pomegranate
iii. **Latin:** *Punicagranatum*
iv. **Sanskrit:** Dadimah
v. **Marathi:** Dalimba

2. MATERIALS:

Fresh Fruits of *punicagranatum* was collected from local market of Buldana, Maharashtra and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra. This authentification is done by Prof. Dr. S.V. Ambekar Sir. The fruits were washed with purified water, rinsed well and dried at room temperature for about 10min in open air. The peel from the fruit was removed carefully by knife and allowed to sun-drying. The dried material was

properly ground into powder. This powder material was separated according to particle size with the help of sieves no; #44, #60, #80, #85 to obtained different batches for further Preformulation Study.

Excipients: - Lactose, Starch & Amaranth obtained from Research Lab Akola.

Method: -

3. Preformulation study: -

3.1 Bulk Density: [22-39]

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity of tablet blend was transferred into 100ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was calculated by using formula

$$\textbf{Bulk Density} = \frac{\textbf{m}}{\textbf{Vi}}$$

Where, **m** = mass of the blend, Vi = Bulk volume

3.2 Tapped density: [22-39] Weighed accurate quantity of powder sample was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 & 300 taps in tap density apparatus.

Tapped density was calculated.

$$\text{Tapped Density} = \frac{m}{Vt}$$

Where, m = mass of the blend, Vt = tapped volume

3.3 Carr's Index (Compressibility): [22-39] The compressibility index and Hausner's ratio was measures the property of powder to be compressed. The packing ability of powder material was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated by following formula:

$$\text{Carr s index} = [TD-BD]/TD \times 100$$

3.4 Hausner s' Ratio: [22-39] **It** is measurement of frictional resistance of tablet blend. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density.

$$\text{Hausner s' Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

3.5 Angle of Repose (θ): [22-39] It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is determined by the equation;

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

Where, **θ** = Angle of repose; h = height of powder heap; r = Radius of the powder cone.

Procedure: Weighed quantity of the powder sample was passed through a funnel kept at a height 2cm from the base. The **powder** was passed till it forms a heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated by using above formula.

3.6 Flow Rate [22-39]: -

1. Weighed accurate quantity of powder sample
2. Place a cotton plug at the neck of a clean and dry funnel of stem diameter 1-2.5cm.
3. Place powder sample in the funnel.
4. Remove plug from the neck & Record the total time required for all the powder to flow. Calculate flow rate by using formula.

$$\text{Flow Rate} = \frac{\text{Weight powder}}{\text{Time required to flow}}$$

3.7 Water Soluble Extractive: [19-21]**:**

Useful for the evaluation of a crude drug. Give idea about the nature of the chemical constituents present in a crude drug.

1. Weigh about 5gm of the coarsely powdered drug and transfer it to a dry 250ml conical flask.
2. Fill a 100 ml graduated flask with water and transfer into conical flask.
3. Cork the flask and set aside for 24 hours, shaking frequently. (Maceration).
4. Filter into a 50 ml cylinder. When sufficient filtrate has collected, transfer 25ml of the filtrate to a weigh thin porcelain dish.
5. Evaporate to dryness on a water- bath and complete the drying in an oven at 105^0C for 6 hours.
6. Cool and weigh immediately.
7. Calculate the percentage w/w of extractive with reference to the air-dried drug.

Calculation:

a) Weight of empty porcelain dish =.....(X).....gm

b) Weight of porcelain dish with residue =..... (Y).....gm

c) Weight of residue = ...(X –Y).....gm

$$\text{W.S.E.}(\%) = \frac{\text{Weight of residue X 100 X 100}}{\text{Weight of drug taken X Volume of filtrate (25 ml)}}$$

3.8 Alcohol Soluble Extractive: [19-21] Same as water soluble extractives only water is replacing with alcohol.

3.9 Moisture contents: [19-21] Weigh 1.5g of sample in a porcelain dish containing 6-8 cm diameter and 2-4 cm depth in it. Dry the sample in an oven at 105^0 C. cool & weigh. Calculate the moisture contents by using formula.

Moisture Contents(%)=Final weight-Initial weight×100

3.10 Total Ash Value: [19-21] Used to determine quality and purity of crude drug and to establish the identity of it.

Procedure:

1. Weigh 2gm of powder drug into the crucible
2. Ignite sample on burner (flame) until all the carbon is burned off.
3. Cool it and weigh the ash.
4. Calculate the percentage of total ash with references to the air-dried sample of crude drug.

Calculation:

a) Weight of the empty dish = x
b) Weight of the drug taken = y
c) Weight of the dish with ash = z
d) Weight of the ash = (z - x)

$$\text{Total ash} = \frac{100(Z-X)}{y}$$

3.11 Antimicrobial test: Antimicrobial test Perform against *Escherichia coli* & *Staphylococcus aureus* culture medium.

1. Weigh accurately all the ingredients & prepared nutrient broth and agar medium.
2. Used nutrient brouth for sub-culturing of phathogen (freshly prepared bacterial culture).
3. Take petri plate and test tube wash it properly with tap water & autoclave it (at 121^0C 15 lb pressure for 15-30 minute).
4. Prepared aceptic area in aceptic room.
5. Dilute the testing sample in test tube in a range of 10^{-1}, 10^{-2}, & 10^{-3} respectively.
6. Transfer the agar medium in Petri plate in aceptic condition allowed it cool & solidify.
7. Then transfer the microbial culture which is required (*E. coli & S.aureus*) with the help of sterile disposable syringe.
8. Shake it properly 2-3 times for proper mixing.
9. Then transfer the sample which is diluted with the help of disc or bohr plate technique.
10. Then incubate the plate for 24-48 hours in Incubator.
11. Calculate the zone of inhibition by comparing with standard.

3.12 Drug Excipient Compatibility study: [33-38]
Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combining it with the excipients. The samples were taken for FT-IR study

3.13 Formulation Designing:

Table 1 Formulation Designing

Sr.no	Ingredients in (mg)	F1	F2	F3	F4	F5	F6
01	Pomegranate powder	20	40	60	80	100	120
02	Lactose	100	100	80	80	50	60
03	Starch	130	110	110	90	100	70
04	Amaranth	q.s	q.s	q.s	q.s	q.s	q.s
Total		250mg	250mg	250mg	250mg	250mg	250mg

3.14 Wet Granulation Method: [33-36]

1. Starch was weighed and made into an emulsion and cooked well on a water bath until translucent semisolid mass was formed.
2. The Amaranth solution was prepared by using required quantity of water separately.
3. The weighed quantities of excipients were mixed thoroughly with powder drug, the cooked starch and Amaranth solution were added slowly till the powder became a damp mass.
4. This damp mass was passed through sieve number 22# and dried in an oven at a temperature of 105°C, until granules were dried properly.
5. Then the dried granules subjected to compression.

6. Finally, the tablets were compressed with 8 mm punches by using multiple punch Tablet press machine (CEMACH).

4. Evaluation of prepared tablets:

4. 1 General appearance: [22-39] Physical examination is done by visual inspection, Color, Odor Size, Shape Unique Identification Marking etc.

4.2 Thickness: [22-39] Ten Tablets were selected randomly from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement. The average of 3 readings was taken as thickness of the tablet.

4.3 Weight variation: [22-39] Twenty tablets were taken randomly, weigh individually and average weight was determined. The individual tablet weight was compared with average tablet weight.

4.4 Hardness: [22-39] Tablets require certain amount of strength or hardness, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (strength) is the pfizer hardness tester.

Method: Ten tablets were randomly selected and hardness was measured in Pfizer hardness tester. The average of 3 readings was taken as hardness of the tablet.

4.5 Friability: [22-39] **Friability** is related to the ability of tablet to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus friabilator. Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered as acceptable.

Method: Ten tablets were randomly select and weighed (initial wt.) and then transfer into friabilator. It was subjected to 100 revolutions in 4 minutes. The tablets were dedusted and reweighed (final wt). These two weights (i.e. initial and final) were applied to calculate the friability.

$$\%\text{Friability} = \frac{(\text{Initial Weight} - \text{final weight})}{(\text{Initial weight})} \times 100$$

4.6 Disintegration test: [22-39] In vitro disintegration time was measured using USP disintegration test apparatus. For DT test randomly one tablet were selected from each batch and test was performed in 900 ml distilled water at 37 ± 0.5 °C temperature and at the rate of 30 ± 2 cycles/min.

4.7 Stability Study: [33&37] The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. The International Conference on Harmonization (ICH) Guidelines titled "Stability Testing of New Drug substance and Products" (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

Stability conditions: (ICH guidelines)

25°C / 60%RH Long term Testing for 12 months

30°C / 65% RH Intermediate condition if significant change occurs due to accelerated testing

40 ºC / 75% RH Accelerated testing for 06 month

Method:

The selected formulation was exposed to different storage condition. As per ICH guidelines for 3 months and evaluated.

5. RESULTS & CONCLUSION:

Table no 2: Preformulation Study of Powder Sample

Sr.no:	Parameters	Sieve no: #44	Sieve no: #60	Sieve no: #80	Sieve no: #85
01	Colour	Light Brown	**Light Brown**	Light Brown	Light Brown
01	Bulk Density (gm/ml)	0.645	**0.56**	0.476	0.454
02	Tapped Density (gm/ml)	0.772	**0.64**	0.638	0.556
03	Carr's Index (%)	16.45	**12.29**	17.39	18.34
04	Hausner's ratio	1.19	**1.14**	1.24	1.22
05	Porosity (%)	25	**16.66**	23.80	19.047
06	Angle of Repose (θ)	33^0 42"	**29^0 98"**	26^0 56"	31^0 29"

07	Moisture contents (%)	10	**09**	10	20
08	Flow Rate (gm/sec)	0.78	**0.66**	0.44	0.33
09	Ash value (NMT4%)	0.32	**0.32**	0.32	0.32
10	Water Soluble Extractive (%)	45.6	**45.6**	45.6	45.6
11	Alcohol Soluble Extractive (%)	49.6	**49.6**	49.6	49.6
12	Antimicrobial Test *(E. coli & S.aureus)*	+ve	**+ve**	+ve	+ve

From above preformulation data powder from Sieve no: #60 shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, Moisture contents. The batch shows good data as compared with other batches. Therefore, it was concluded that the Powder from Sieve no: #60 consider as an optimized batch.

Table No 3: Antimicrobial test

		Zone of Inhibition in mm diameter			
Sr. no	**Name of Pathogens**	**Dilutions**	**Sample A**	**Sample B**	**Std. Ciprofloxacin**
01	*Escherichia coli*	10^{-1}	17	16	15
		10^{-2}	14	12	12
		10^{-3}	12	11	10
02	*Staphylococcus aureus*	10^{-1}	15	14	14
		10^{-2}	13	12	12
		10^{-3}	10	11	10

Sample A = Pomegranate peel powder, Sample B = Pomegranate Tablet

From the above evaluation details it can be concluded that *punicagranatun* peel powder shows +ve antimicrobial activity against *E.coli* & *S.aureus*, shows more potency than that of Standard Ciprofloxacin.

❖ **Drug Excipient Compatibility study**

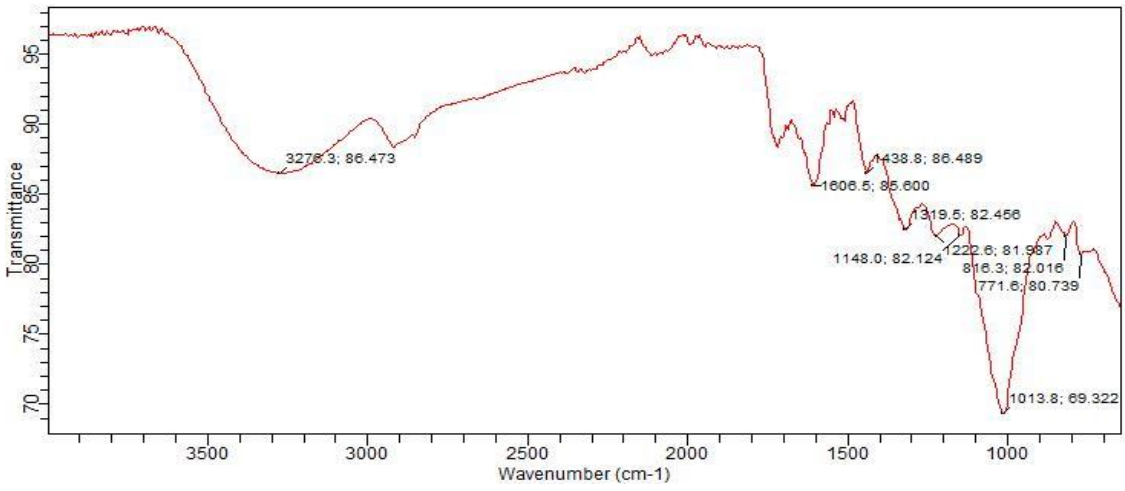

Figure 1: FTIR Spectra of pomegranate peel powder

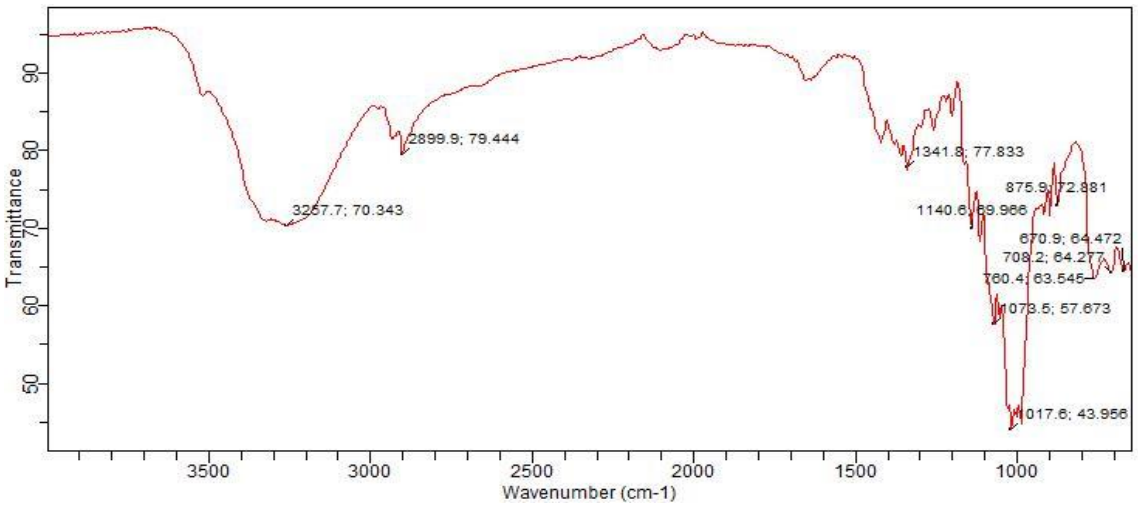

Figure 2: FTIR Spectra of pomegranate peel tablet

Table No 4: Preformulation Study of Granules

Sr.No:	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
01	Bulk Density (gm/ml)	0.645	0.640	0.540	0.769	0.689	0.740
02	Tapped Density (gm/ml)	0.952	0.740	0.689	0.833	0.740	0.866
03	Carr's Index (%)	33.24	13.51	21.62	7.68	6.89	14.54
04	Hausner's ratio	1.475	1.156	1.275	1.083	1.074	1.170
05	Porosity (%)	10	32.25	9.37	13.33	25	6.896
06	Angle of Repose (θ)	$35^0 52''$	$36^0 02''$	$34^0 59''$	$33^0 69''$	$34^0 13''$	$33^0 69''$
07	Moisture contents (%)	07	09	08	06	09	08
08	Flow Rate (gm/sec)	0.77	0.44	0.66	0.33	0.85	0.75

From above preformulation study of granules, F_4 and F_5 batch shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, and Moisture contents.

Table No 5: Evaluation of Formulation

Sr.No:	Parameters	Formulation Batch					
	General appearance	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**
01	a) Colour	Pink	Pink	**Pink**	Pink	Pink	**Pink**
	b) Odour	None	None	**None**	None	None	**None**
	c) Taste	None	None	**None**	None	None	**None**
	d) Size (Diameter)	1.7mm	1.8mm	**1.7mm**	1.8mm	1.7mm	**1.7mm**
	e) Shape	Round	Round	**Round**	Round	Round	**Round**
02	Hardness (kg/cm^2)	3.5	5	**3.5**	3	3.5	**4**
03	Thickness (mm)	3	3.2	**3**	3	3	**3.5**
04	Friability (%)	0.79	0.85	**0.50**	0.70	0.85	**0.16**
05	Weight variation test	Pass	Pass	**Pass**	Pass	Pass	**Pass**
06	Dis. time (sec.)	20	25	**20**	15	30	**25**
07	Antimicrobial Test	+ve	+ve	**+ve**	+ve	+ve	**+ve**
08	Moisture content (%)	7	8	**6**	9	8	**9**

From the above evaluation parameter like thickness, average weight, hardness, friability, disintegration time etc. It can be concluded that the F_1 and F_4 batch show all parameter within acceptable limit, as compared to other batches therefore it is considered as a good formulation.

Table No 6: Comparative Study

Sr.no	Parameters	Batch		
	General appearance	**F1**	**F4**	**MF**
01	a) Color	Pink	Pink	White
	b) Odor	None	None	None
	c) Taste	None	None	Bitter
	d) Size (Diameter)	1.7mm	1.8mm	1.5mm
	e) Shape	Round	Round	Round
02	Hardness (kg/cm^2)	3.5	3	3.5
03	Thickness (mm)	3	3	3
04	Friability (%)	0.79	0.70	0.49
05	Weight variation test	Pass	Pass	Pass
06	Dis. time(sec.)	20	15	280
07	Antimicrobial Test	+ve	+ve	+ve
08	Moisture content (%)	7	9	8

Stability Study of optimized batch: -

The effects of temperature and humidity, on the physical characteristics of the tablets, were evaluated for assessing the stability (40 ^{0}C ± 2 ^{0}C/ 75 % ± 5% RH) of the prepared formulation.

Table No 7: Stability Study of Optimized Formulation

Duration (Months)	General Appearance	Hardness (kg/cm^2)	Weight Variation	Friability (%)	Disintegration Time (sec)
1 Month	No change	3.5	249	0.70	20
2 Months	No change	3	248	0.60	15
3 Months	No change	3	250	0.79	25

Stability study of the tablets at 40^{0}C ± 2^{0}C/ 75% ± 5% RH for 3 months showed no significant changes in the mechanical strength or in disintegration time of the tablets.

Figure 3 Pomegranate Fruit

Figure 4 Pomegranate Peel

Figure 5 Pomegranate peel powder

Figure 6 Pomegranate Tablet

7. DISCUSSION AND CONCLUSION:

Herbs plays major role in the treatment than the allopathic medicines because of less side effects, low cost and easy availability. The research work done on that basis and the selected plant for the formulation was proved for the use of antidiabetic purpose. The *Punicagranatum* peel powder were used to formulate tablets and evaluated for physical parameters and standardize as per pharmacopoeial standards. Preformulation study and Physical Parameter revealed that all the values were within acceptable limit shown in table no 5. The herbal formulation showed significant antidiabetic activity and the tablet standardize as per Pharmacopoeial standards. From the above evaluation parameters, it can be concluded that overall batches the F1 & F4 batch show all parameter in acceptable limit. Therefore, it is considered as a good Formulation.

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INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF PUNICAGRANATUM PEEL

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INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF *PUNICAGRANATUM* PEEL

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ABSTRACT

The present study was aimed to formulate & evaluate the antidiabetic tablet of Punicagranatum peels waste. Hyperglycemia is the most common metabolic endocrine disorder. It is the chronic condition in which blood glucose level is elevated than normal due to the improper insulin production in body or due to insulin resistance, high blood glucose level and low blood glucose level leads to diabetic condition. Allopathic treatment for diabetes mellitus is too costly so focus on herbal medicines is necessary. Pomegranate peels or rind are considered as an waste material these peels consists of numerous important active chemical constituents such as flavonoids, vitamins and minerals. The main principle active chemical constituents including punicalagin, punicalin, β-sitosterol and valoneic acid dilactone (VAD) from pomegranate peels powder shows potent antidiabetic activity Punicagranatum peels extract have stability problem than other dosage form by converting it into tablet dosage form. We enhance its acceptability, elegance and patient compliance. Manufacturing of tablets was done by using wet granulation method on lab level tablet press (CEMACH) by wet granulation method. Evaluations tests performed on tablets such as Hardness, Weight variation, friability, disintegration test etc

KEY WORDS

punicagranatum, antidiabetic, valoneic acid dilactone (VAD), herbal medicine

1.INTRODUCTION:

Diabetes mellitus is a metabolic disorder identified as increased in blood glucose level than normal. This is happened due to either insufficient insulin production or insulin resistance. High amount of lipids, free fatty acid and glucose in our body affects the B-cells function by various mechanisms such as generation of various reactive oxygen species (ROS). Generally, there are three types of Diabetes occurs one is the Insulin Dependence Diabetes Mellitus (IDDM) second is the (NIDDM) that is Non-Insulin Dependence Diabetes Mellitus and third one is the Gestational Diabetes.

1.1 Biological Sources: [17-20]

a} Botanical Name: *Punicagranatum*
b} Family Name: Puniacaceae
c} Common Name: Pomegranate**,** Anar
d} Part Used: Seeds, flowers, peels, roots etc.

1.2 Common Name: [17-20]

i. **Hindi:** Anar
ii. **English:** Pomegranate
iii. **Latin:** *Punicagranatum*
iv. **Sanskrit:** Dadimah
v. **Marathi:** Dalimba

2. MATERIALS:

Fresh Fruits of *punicagranatum* was collected from local market of Buldana, Maharashtra and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra. This authentification is done by Prof. Dr. S.V. Ambekar Sir. The fruits were washed with purified water, rinsed well and dried at room temperature for about 10min in open air. The peel from the fruit was removed carefully by knife and allowed to sun-drying. The dried material was

properly ground into powder. This powder material was separated according to particle size with the help of sieves no; #44, #60, #80, #85 to obtained different batches for further Preformulation Study.

Excipients: - Lactose, Starch & Amaranth obtained from Research Lab Akola.

Method: -

3. Preformulation study: -

3.1 Bulk Density: [22-39]

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity of tablet blend was transferred into 100ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was calculated by using formula

$$\textbf{Bulk Density} = \frac{\textbf{m}}{\textbf{Vi}}$$

Where, **m** = mass of the blend, Vi = Bulk volume

3.2 Tapped density: [22-39] Weighed accurate quantity of powder sample was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 & 300 taps in tap density apparatus.

Tapped density was calculated.

$$\text{Tapped Density} = \frac{m}{Vt}$$

Where, m = mass of the blend, Vt = tapped volume

3.3 Carr's Index (Compressibility): [22-39] The compressibility index and Hausner's ratio was measures the property of powder to be compressed. The packing ability of powder material was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated by following formula:

$$\text{Carr s index} = [TD-BD]/TD \times 100$$

3.4 Hausner s' Ratio: [22-39] **It** is measurement of frictional resistance of tablet blend. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density.

$$\text{Hausner s' Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

3.5 Angle of Repose (θ): [22-39] It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is determined by the equation;

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

Where, **θ** = Angle of repose; h = height of powder heap; r = Radius of the powder cone.

Procedure: Weighed quantity of the powder sample was passed through a funnel kept at a height 2cm from the base. The **powder** was passed till it forms a heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated by using above formula.

3.6 Flow Rate [22-39]: -

1. Weighed accurate quantity of powder sample
2. Place a cotton plug at the neck of a clean and dry funnel of stem diameter 1-2.5cm.
3. Place powder sample in the funnel.
4. Remove plug from the neck & Record the total time required for all the powder to flow. Calculate flow rate by using formula.

$$\text{Flow Rate} = \frac{\text{Weight powder}}{\text{Time required to flow}}$$

3.7 Water Soluble Extractive: [19-21]**:**

Useful for the evaluation of a crude drug. Give idea about the nature of the chemical constituents present in a crude drug.

1. Weigh about 5gm of the coarsely powdered drug and transfer it to a dry 250ml conical flask.
2. Fill a 100 ml graduated flask with water and transfer into conical flask.
3. Cork the flask and set aside for 24 hours, shaking frequently. (Maceration).
4. Filter into a 50 ml cylinder. When sufficient filtrate has collected, transfer 25ml of the filtrate to a weigh thin porcelain dish.
5. Evaporate to dryness on a water- bath and complete the drying in an oven at 105^0C for 6 hours.
6. Cool and weigh immediately.
7. Calculate the percentage w/w of extractive with reference to the air-dried drug.

Calculation:

a) Weight of empty porcelain dish =.....(X).....gm

b) Weight of porcelain dish with residue =..... (Y).....gm

c) Weight of residue = ...(X –Y).....gm

$$\text{W.S.E.}(\%) = \frac{\text{Weight of residue X 100 X 100}}{\text{Weight of drug taken X Volume of filtrate (25 ml)}}$$

3.8 Alcohol Soluble Extractive: [19-21] Same as water soluble extractives only water is replacing with alcohol.

3.9 Moisture contents: [19-21] Weigh 1.5g of sample in a porcelain dish containing 6-8 cm diameter and 2-4 cm depth in it. Dry the sample in an oven at 105^0 C. cool & weigh. Calculate the moisture contents by using formula.

Moisture Contents(%)=Final weight-Initial weight×100

3.10 Total Ash Value: [19-21] Used to determine quality and purity of crude drug and to establish the identity of it.

Procedure:

1. Weigh 2gm of powder drug into the crucible
2. Ignite sample on burner (flame) until all the carbon is burned off.
3. Cool it and weigh the ash.
4. Calculate the percentage of total ash with references to the air-dried sample of crude drug.

Calculation:

a) Weight of the empty dish = x
b) Weight of the drug taken = y
c) Weight of the dish with ash = z
d) Weight of the ash = (z - x)

$$\text{Total ash} = \frac{100(Z-X)}{y}$$

3.11 Antimicrobial test: Antimicrobial test Perform against *Escherichia coli* & *Staphylococcus aureus* culture medium.

1. Weigh accurately all the ingredients & prepared nutrient broth and agar medium.
2. Used nutrient brouth for sub-culturing of phathogen (freshly prepared bacterial culture).
3. Take petri plate and test tube wash it properly with tap water & autoclave it (at 121^0C 15 lb pressure for 15-30 minute).
4. Prepared aceptic area in aceptic room.
5. Dilute the testing sample in test tube in a range of 10^{-1}, 10^{-2}, & 10^{-3} respectively.
6. Transfer the agar medium in Petri plate in aceptic condition allowed it cool & solidify.
7. Then transfer the microbial culture which is required (*E. coli & S.aureus*) with the help of sterile disposable syringe.
8. Shake it properly 2-3 times for proper mixing.
9. Then transfer the sample which is diluted with the help of disc or bohr plate technique.
10. Then incubate the plate for 24-48 hours in Incubator.
11. Calculate the zone of inhibition by comparing with standard.

3.12 Drug Excipient Compatibility study: [33-38]
Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combining it with the excipients. The samples were taken for FT-IR study

3.13 Formulation Designing:

Table 1 Formulation Designing

Sr.no	Ingredients in (mg)	F1	F2	F3	F4	F5	F6
01	Pomegranate powder	20	40	60	80	100	120
02	Lactose	100	100	80	80	50	60
03	Starch	130	110	110	90	100	70
04	Amaranth	q.s	q.s	q.s	q.s	q.s	q.s
Total		250mg	250mg	250mg	250mg	250mg	250mg

3.14 Wet Granulation Method: [33-36]

1. Starch was weighed and made into an emulsion and cooked well on a water bath until translucent semisolid mass was formed.
2. The Amaranth solution was prepared by using required quantity of water separately.
3. The weighed quantities of excipients were mixed thoroughly with powder drug, the cooked starch and Amaranth solution were added slowly till the powder became a damp mass.
4. This damp mass was passed through sieve number 22# and dried in an oven at a temperature of 105°C, until granules were dried properly.
5. Then the dried granules subjected to compression.

6. Finally, the tablets were compressed with 8 mm punches by using multiple punch Tablet press machine (CEMACH).

4. Evaluation of prepared tablets:

4. 1 General appearance: [22-39] Physical examination is done by visual inspection, Color, Odor Size, Shape Unique Identification Marking etc.

4.2 Thickness: [22-39] Ten Tablets were selected randomly from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement. The average of 3 readings was taken as thickness of the tablet.

4.3 Weight variation: [22-39] Twenty tablets were taken randomly, weigh individually and average weight was determined. The individual tablet weight was compared with average tablet weight.

4.4 Hardness: [22-39] Tablets require certain amount of strength or hardness, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (strength) is the pfizer hardness tester.

Method: Ten tablets were randomly selected and hardness was measured in Pfizer hardness tester. The average of 3 readings was taken as hardness of the tablet.

4.5 Friability: [22-39] **Friability** is related to the ability of tablet to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus friabilator. Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered as acceptable.

Method: Ten tablets were randomly select and weighed (initial wt.) and then transfer into friabilator. It was subjected to 100 revolutions in 4 minutes. The tablets were dedusted and reweighed (final wt). These two weights (i.e. initial and final) were applied to calculate the friability.

$$\%\text{Friability} = \frac{(\text{Initial Weight} - \text{final weight})}{(\text{Initial weight})} \times 100$$

4.6 Disintegration test: [22-39] In vitro disintegration time was measured using USP disintegration test apparatus. For DT test randomly one tablet were selected from each batch and test was performed in 900 ml distilled water at 37 ± 0.5 °C temperature and at the rate of 30 ± 2 cycles/min.

4.7 Stability Study: [33&37] The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. The International Conference on Harmonization (ICH) Guidelines titled "Stability Testing of New Drug substance and Products" (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

Stability conditions: (ICH guidelines)

25°C / 60%RH Long term Testing for 12 months

30°C / 65% RH Intermediate condition if significant change occurs due to accelerated testing

40 ºC / 75% RH Accelerated testing for 06 month

Method:

The selected formulation was exposed to different storage condition. As per ICH guidelines for 3 months and evaluated.

5. RESULTS & CONCLUSION:

Table no 2: Preformulation Study of Powder Sample

Sr.no:	Parameters	Sieve no: #44	Sieve no: #60	Sieve no: #80	Sieve no: #85
01	Colour	Light Brown	**Light Brown**	Light Brown	Light Brown
01	Bulk Density (gm/ml)	0.645	**0.56**	0.476	0.454
02	Tapped Density (gm/ml)	0.772	**0.64**	0.638	0.556
03	Carr's Index (%)	16.45	**12.29**	17.39	18.34
04	Hausner's ratio	1.19	**1.14**	1.24	1.22
05	Porosity (%)	25	**16.66**	23.80	19.047
06	Angle of Repose (θ)	33^0 42"	**29^0 98"**	26^0 56"	31^0 29"

07	Moisture contents (%)	10	**09**	10	20
08	Flow Rate (gm/sec)	0.78	**0.66**	0.44	0.33
09	Ash value (NMT4%)	0.32	**0.32**	0.32	0.32
10	Water Soluble Extractive (%)	45.6	**45.6**	45.6	45.6
11	Alcohol Soluble Extractive (%)	49.6	**49.6**	49.6	49.6
12	Antimicrobial Test *(E. coli & S.aureus)*	+ve	**+ve**	+ve	+ve

From above preformulation data powder from Sieve no: #60 shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, Moisture contents. The batch shows good data as compared with other batches. Therefore, it was concluded that the Powder from Sieve no: #60 consider as an optimized batch.

Table No 3: Antimicrobial test

		Zone of Inhibition in mm diameter			
Sr. no	**Name of Pathogens**	**Dilutions**	**Sample A**	**Sample B**	**Std. Ciprofloxacin**
01	*Escherichia coli*	10^{-1}	17	16	15
		10^{-2}	14	12	12
		10^{-3}	12	11	10
02	*Staphylococcus aureus*	10^{-1}	15	14	14
		10^{-2}	13	12	12
		10^{-3}	10	11	10

Sample A = Pomegranate peel powder, Sample B = Pomegranate Tablet

From the above evaluation details it can be concluded that *punicagranatun* peel powder shows +ve antimicrobial activity against *E.coli* & *S.aureus*, shows more potency than that of Standard Ciprofloxacin.

❖ **Drug Excipient Compatibility study**

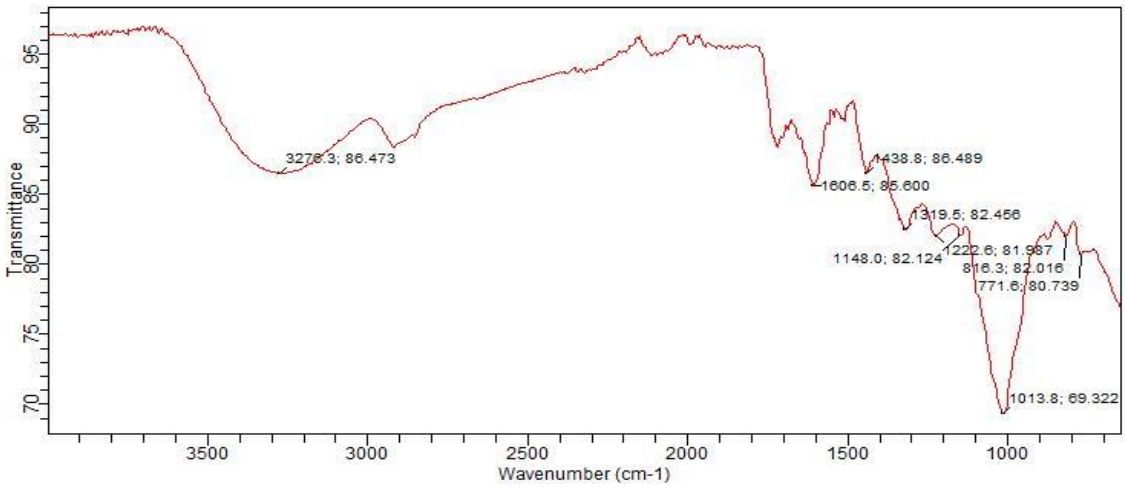

Figure 1: FTIR Spectra of pomegranate peel powder

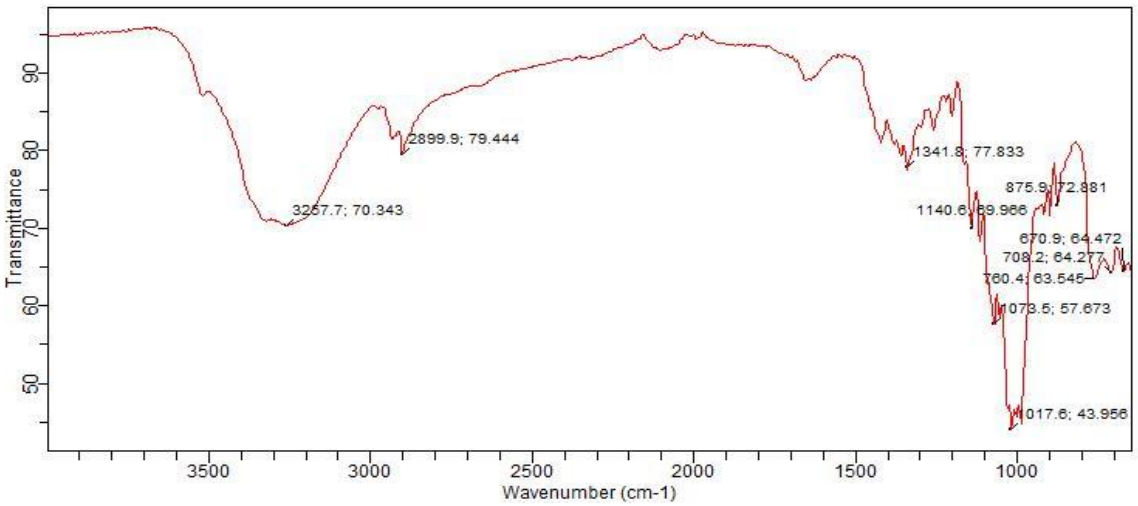

Figure 2: FTIR Spectra of pomegranate peel tablet

Table No 4: Preformulation Study of Granules

Sr.No:	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
01	Bulk Density (gm/ml)	0.645	0.640	0.540	0.769	0.689	0.740
02	Tapped Density (gm/ml)	0.952	0.740	0.689	0.833	0.740	0.866
03	Carr's Index (%)	33.24	13.51	21.62	7.68	6.89	14.54
04	Hausner's ratio	1.475	1.156	1.275	1.083	1.074	1.170
05	Porosity (%)	10	32.25	9.37	13.33	25	6.896
06	Angle of Repose (θ)	$35^0 52''$	$36^0 02''$	$34^0 59''$	$33^0 69''$	$34^0 13''$	$33^0 69''$
07	Moisture contents (%)	07	09	08	06	09	08
08	Flow Rate (gm/sec)	0.77	0.44	0.66	0.33	0.85	0.75

From above preformulation study of granules, F_4 and F_5 batch shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, and Moisture contents.

Table No 5: Evaluation of Formulation

Sr.No:	Parameters	Formulation Batch					
	General appearance	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**
01	a) Colour	Pink	Pink	**Pink**	Pink	Pink	**Pink**
	b) Odour	None	None	**None**	None	None	**None**
	c) Taste	None	None	**None**	None	None	**None**
	d) Size (Diameter)	1.7mm	1.8mm	**1.7mm**	1.8mm	1.7mm	**1.7mm**
	e) Shape	Round	Round	**Round**	Round	Round	**Round**
02	Hardness (kg/cm^2)	3.5	5	**3.5**	3	3.5	**4**
03	Thickness (mm)	3	3.2	**3**	3	3	**3.5**
04	Friability (%)	0.79	0.85	**0.50**	0.70	0.85	**0.16**
05	Weight variation test	Pass	Pass	**Pass**	Pass	Pass	**Pass**
06	Dis. time (sec.)	20	25	**20**	15	30	**25**
07	Antimicrobial Test	+ve	+ve	**+ve**	+ve	+ve	**+ve**
08	Moisture content (%)	7	8	**6**	9	8	**9**

From the above evaluation parameter like thickness, average weight, hardness, friability, disintegration time etc. It can be concluded that the F_1 and F_4 batch show all parameter within acceptable limit, as compared to other batches therefore it is considered as a good formulation.

Table No 6: Comparative Study

Sr.no	Parameters	Batch		
	General appearance	**F1**	**F4**	**MF**
01	a) Color	Pink	Pink	White
	b) Odor	None	None	None
	c) Taste	None	None	Bitter
	d) Size (Diameter)	1.7mm	1.8mm	1.5mm
	e) Shape	Round	Round	Round
02	Hardness (kg/cm^2)	3.5	3	3.5
03	Thickness (mm)	3	3	3
04	Friability (%)	0.79	0.70	0.49
05	Weight variation test	Pass	Pass	Pass
06	Dis. time(sec.)	20	15	280
07	Antimicrobial Test	+ve	+ve	+ve
08	Moisture content (%)	7	9	8

Stability Study of optimized batch: -

The effects of temperature and humidity, on the physical characteristics of the tablets, were evaluated for assessing the stability (40 ^{0}C ± 2 ^{0}C/ 75 % ± 5% RH) of the prepared formulation.

Table No 7: Stability Study of Optimized Formulation

Duration (Months)	General Appearance	Hardness (kg/cm^2)	Weight Variation	Friability (%)	Disintegration Time (sec)
1 Month	No change	3.5	249	0.70	20
2 Months	No change	3	248	0.60	15
3 Months	No change	3	250	0.79	25

Stability study of the tablets at 40^{0}C ± 2^{0}C/ 75% ± 5% RH for 3 months showed no significant changes in the mechanical strength or in disintegration time of the tablets.

Figure 3 Pomegranate Fruit

Figure 4 Pomegranate Peel

Figure 5 Pomegranate peel powder

Figure 6 Pomegranate Tablet

7. DISCUSSION AND CONCLUSION:

Herbs plays major role in the treatment than the allopathic medicines because of less side effects, low cost and easy availability. The research work done on that basis and the selected plant for the formulation was proved for the use of antidiabetic purpose. The *Punicagranatum* peel powder were used to formulate tablets and evaluated for physical parameters and standardize as per pharmacopoeial standards. Preformulation study and Physical Parameter revealed that all the values were within acceptable limit shown in table no 5. The herbal formulation showed significant antidiabetic activity and the tablet standardize as per Pharmacopoeial standards. From the above evaluation parameters, it can be concluded that overall batches the F1 & F4 batch show all parameter in acceptable limit. Therefore, it is considered as a good Formulation.

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INVESTIGATION, FORMULATION AND EVALUATION OF ANTIDIABETIC TABLET OF *PUNICAGRANATUM* PEEL

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ABSTRACT

The present study was aimed to formulate & evaluate the antidiabetic tablet of Punicagranatum peels waste. Hyperglycemia is the most common metabolic endocrine disorder. It is the chronic condition in which blood glucose level is elevated than normal due to the improper insulin production in body or due to insulin resistance, high blood glucose level and low blood glucose level leads to diabetic condition. Allopathic treatment for diabetes mellitus is too costly so focus on herbal medicines is necessary. Pomegranate peels or rind are considered as an waste material these peels consists of numerous important active chemical constituents such as flavonoids, vitamins and minerals. The main principle active chemical constituents including punicalagin, punicalin, β-sitosterol and valoneic acid dilactone (VAD) from pomegranate peels powder shows potent antidiabetic activity Punicagranatum peels extract have stability problem than other dosage form by converting it into tablet dosage form. We enhance its acceptability, elegance and patient compliance. Manufacturing of tablets was done by using wet granulation method on lab level tablet press (CEMACH) by wet granulation method. Evaluations tests performed on tablets such as Hardness, Weight variation, friability, disintegration test etc

KEY WORDS

punicagranatum, antidiabetic, valoneic acid dilactone (VAD), herbal medicine

1.INTRODUCTION:

Diabetes mellitus is a metabolic disorder identified as increased in blood glucose level than normal. This is happened due to either insufficient insulin production or insulin resistance. High amount of lipids, free fatty acid and glucose in our body affects the B-cells function by various mechanisms such as generation of various reactive oxygen species (ROS). Generally, there are three types of Diabetes occurs one is the Insulin Dependence Diabetes Mellitus (IDDM) second is the (NIDDM) that is Non-Insulin Dependence Diabetes Mellitus and third one is the Gestational Diabetes.

1.1 Biological Sources: [17-20]

a} Botanical Name: *Punicagranatum*
b} Family Name: Puniacaceae
c} Common Name: Pomegranate**,** Anar
d} Part Used: Seeds, flowers, peels, roots etc.

1.2 Common Name: [17-20]

i. **Hindi:** Anar
ii. **English:** Pomegranate
iii. **Latin:** *Punicagranatum*
iv. **Sanskrit:** Dadimah
v. **Marathi:** Dalimba

2. MATERIALS:

Fresh Fruits of *punicagranatum* was collected from local market of Buldana, Maharashtra and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra. This authentification is done by Prof. Dr. S.V. Ambekar Sir. The fruits were washed with purified water, rinsed well and dried at room temperature for about 10min in open air. The peel from the fruit was removed carefully by knife and allowed to sun-drying. The dried material was

properly ground into powder. This powder material was separated according to particle size with the help of sieves no; #44, #60, #80, #85 to obtained different batches for further Preformulation Study.

Excipients: - Lactose, Starch & Amaranth obtained from Research Lab Akola.

Method: -

3. Preformulation study: -

3.1 Bulk Density: [22-39]

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity of tablet blend was transferred into 100ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was calculated by using formula

$$\textbf{Bulk Density} = \frac{\textbf{m}}{\textbf{Vi}}$$

Where, **m** = mass of the blend, Vi = Bulk volume

3.2 Tapped density: [22-39] Weighed accurate quantity of powder sample was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 & 300 taps in tap density apparatus.

Tapped density was calculated.

$$\text{Tapped Density} = \frac{m}{Vt}$$

Where, m = mass of the blend, Vt = tapped volume

3.3 Carr's Index (Compressibility): [22-39] The compressibility index and Hausner's ratio was measures the property of powder to be compressed. The packing ability of powder material was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated by following formula:

$$\text{Carr s index} = [TD-BD]/TD \times 100$$

3.4 Hausner s' Ratio: [22-39] **It** is measurement of frictional resistance of tablet blend. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density.

$$\text{Hausner s' Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

3.5 Angle of Repose (θ): [22-39] It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is determined by the equation;

$$\text{Angle of repose } (\theta) = \tan^{-1}(h/r)$$

Where, **θ** = Angle of repose; h = height of powder heap; r = Radius of the powder cone.

Procedure: Weighed quantity of the powder sample was passed through a funnel kept at a height 2cm from the base. The **powder** was passed till it forms a heap and touches the tip of the funnel. The radius was measured and angle of repose was calculated by using above formula.

3.6 Flow Rate [22-39]: -

1. Weighed accurate quantity of powder sample
2. Place a cotton plug at the neck of a clean and dry funnel of stem diameter 1-2.5cm.
3. Place powder sample in the funnel.
4. Remove plug from the neck & Record the total time required for all the powder to flow. Calculate flow rate by using formula.

$$\text{Flow Rate} = \frac{\text{Weight powder}}{\text{Time required to flow}}$$

3.7 Water Soluble Extractive: [19-21]**:**

Useful for the evaluation of a crude drug. Give idea about the nature of the chemical constituents present in a crude drug.

1. Weigh about 5gm of the coarsely powdered drug and transfer it to a dry 250ml conical flask.
2. Fill a 100 ml graduated flask with water and transfer into conical flask.
3. Cork the flask and set aside for 24 hours, shaking frequently. (Maceration).
4. Filter into a 50 ml cylinder. When sufficient filtrate has collected, transfer 25ml of the filtrate to a weigh thin porcelain dish.
5. Evaporate to dryness on a water- bath and complete the drying in an oven at 105^0C for 6 hours.
6. Cool and weigh immediately.
7. Calculate the percentage w/w of extractive with reference to the air-dried drug.

Calculation:

a) Weight of empty porcelain dish =.....(X).....gm

b) Weight of porcelain dish with residue =..... (Y).....gm

c) Weight of residue = ...(X –Y).....gm

$$\text{W.S.E.}(\%) = \frac{\text{Weight of residue X 100 X 100}}{\text{Weight of drug taken X Volume of filtrate (25 ml)}}$$

3.8 Alcohol Soluble Extractive: [19-21] Same as water soluble extractives only water is replacing with alcohol.

3.9 Moisture contents: [19-21] Weigh 1.5g of sample in a porcelain dish containing 6-8 cm diameter and 2-4 cm depth in it. Dry the sample in an oven at 105^0 C. cool & weigh. Calculate the moisture contents by using formula.

Moisture Contents(%)=Final weight-Initial weight×100

3.10 Total Ash Value: [19-21] Used to determine quality and purity of crude drug and to establish the identity of it.

Procedure:

1. Weigh 2gm of powder drug into the crucible
2. Ignite sample on burner (flame) until all the carbon is burned off.
3. Cool it and weigh the ash.
4. Calculate the percentage of total ash with references to the air-dried sample of crude drug.

Calculation:

a) Weight of the empty dish = x
b) Weight of the drug taken = y
c) Weight of the dish with ash = z
d) Weight of the ash = (z - x)

$$\text{Total ash} = \frac{100(Z-X)}{y}$$

3.11 Antimicrobial test: Antimicrobial test Perform against *Escherichia coli* & *Staphylococcus aureus* culture medium.

1. Weigh accurately all the ingredients & prepared nutrient broth and agar medium.
2. Used nutrient brouth for sub-culturing of phathogen (freshly prepared bacterial culture).
3. Take petri plate and test tube wash it properly with tap water & autoclave it (at 121^0C 15 lb pressure for 15-30 minute).
4. Prepared aceptic area in aceptic room.
5. Dilute the testing sample in test tube in a range of 10^{-1}, 10^{-2}, & 10^{-3} respectively.
6. Transfer the agar medium in Petri plate in aceptic condition allowed it cool & solidify.
7. Then transfer the microbial culture which is required (*E. coli & S.aureus*) with the help of sterile disposable syringe.
8. Shake it properly 2-3 times for proper mixing.
9. Then transfer the sample which is diluted with the help of disc or bohr plate technique.
10. Then incubate the plate for 24-48 hours in Incubator.
11. Calculate the zone of inhibition by comparing with standard.

3.12 Drug Excipient Compatibility study: [33-38]
Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combining it with the excipients. The samples were taken for FT-IR study

3.13 Formulation Designing:

Table 1 Formulation Designing

Sr.no	Ingredients in (mg)	F1	F2	F3	F4	F5	F6
01	Pomegranate powder	20	40	60	80	100	120
02	Lactose	100	100	80	80	50	60
03	Starch	130	110	110	90	100	70
04	Amaranth	q.s	q.s	q.s	q.s	q.s	q.s
Total		250mg	250mg	250mg	250mg	250mg	250mg

3.14 Wet Granulation Method: [33-36]

1. Starch was weighed and made into an emulsion and cooked well on a water bath until translucent semisolid mass was formed.
2. The Amaranth solution was prepared by using required quantity of water separately.
3. The weighed quantities of excipients were mixed thoroughly with powder drug, the cooked starch and Amaranth solution were added slowly till the powder became a damp mass.
4. This damp mass was passed through sieve number 22# and dried in an oven at a temperature of 105°C, until granules were dried properly.
5. Then the dried granules subjected to compression.

6. Finally, the tablets were compressed with 8 mm punches by using multiple punch Tablet press machine (CEMACH).

4. Evaluation of prepared tablets:

4. 1 General appearance: [22-39] Physical examination is done by visual inspection, Color, Odor Size, Shape Unique Identification Marking etc.

4.2 Thickness: [22-39] Ten Tablets were selected randomly from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement. The average of 3 readings was taken as thickness of the tablet.

4.3 Weight variation: [22-39] Twenty tablets were taken randomly, weigh individually and average weight was determined. The individual tablet weight was compared with average tablet weight.

4.4 Hardness: [22-39] Tablets require certain amount of strength or hardness, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (strength) is the pfizer hardness tester.

Method: Ten tablets were randomly selected and hardness was measured in Pfizer hardness tester. The average of 3 readings was taken as hardness of the tablet.

4.5 Friability: [22-39] **Friability** is related to the ability of tablet to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus friabilator. Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered as acceptable.

Method: Ten tablets were randomly select and weighed (initial wt.) and then transfer into friabilator. It was subjected to 100 revolutions in 4 minutes. The tablets were dedusted and reweighed (final wt). These two weights (i.e. initial and final) were applied to calculate the friability.

$$\%\text{Friability} = \frac{(\text{Initial Weight} - \text{final weight})}{(\text{Initial weight})} \times 100$$

4.6 Disintegration test: [22-39] In vitro disintegration time was measured using USP disintegration test apparatus. For DT test randomly one tablet were selected from each batch and test was performed in 900 ml distilled water at 37 ± 0.5 °C temperature and at the rate of 30 ± 2 cycles/min.

4.7 Stability Study: [33&37] The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives. The International Conference on Harmonization (ICH) Guidelines titled "Stability Testing of New Drug substance and Products" (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

Stability conditions: (ICH guidelines)

25°C / 60%RH Long term Testing for 12 months

30°C / 65% RH Intermediate condition if significant change occurs due to accelerated testing

40 ºC / 75% RH Accelerated testing for 06 month

Method:

The selected formulation was exposed to different storage condition. As per ICH guidelines for 3 months and evaluated.

5. RESULTS & CONCLUSION:

Table no 2: Preformulation Study of Powder Sample

Sr.no:	Parameters	Sieve no: #44	Sieve no: #60	Sieve no: #80	Sieve no: #85
01	Colour	Light Brown	**Light Brown**	Light Brown	Light Brown
01	Bulk Density (gm/ml)	0.645	**0.56**	0.476	0.454
02	Tapped Density (gm/ml)	0.772	**0.64**	0.638	0.556
03	Carr's Index (%)	16.45	**12.29**	17.39	18.34
04	Hausner's ratio	1.19	**1.14**	1.24	1.22
05	Porosity (%)	25	**16.66**	23.80	19.047
06	Angle of Repose (θ)	33^0 42"	**29^0 98"**	26^0 56"	31^0 29"

07	Moisture contents (%)	10	**09**	10	20
08	Flow Rate (gm/sec)	0.78	**0.66**	0.44	0.33
09	Ash value (NMT4%)	0.32	**0.32**	0.32	0.32
10	Water Soluble Extractive (%)	45.6	**45.6**	45.6	45.6
11	Alcohol Soluble Extractive (%)	49.6	**49.6**	49.6	49.6
12	Antimicrobial Test *(E. coli & S.aureus)*	+ve	**+ve**	+ve	+ve

From above preformulation data powder from Sieve no: #60 shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, Moisture contents. The batch shows good data as compared with other batches. Therefore, it was concluded that the Powder from Sieve no: #60 consider as an optimized batch.

Table No 3: Antimicrobial test

		Zone of Inhibition in mm diameter			
Sr. no	**Name of Pathogens**	**Dilutions**	**Sample A**	**Sample B**	**Std. Ciprofloxacin**
01	*Escherichia coli*	10^{-1}	17	16	15
		10^{-2}	14	12	12
		10^{-3}	12	11	10
02	*Staphylococcus aureus*	10^{-1}	15	14	14
		10^{-2}	13	12	12
		10^{-3}	10	11	10

Sample A = Pomegranate peel powder, Sample B = Pomegranate Tablet

From the above evaluation details it can be concluded that *punicagranatun* peel powder shows +ve antimicrobial activity against *E.coli* & *S.aureus*, shows more potency than that of Standard Ciprofloxacin.

❖ **Drug Excipient Compatibility study**

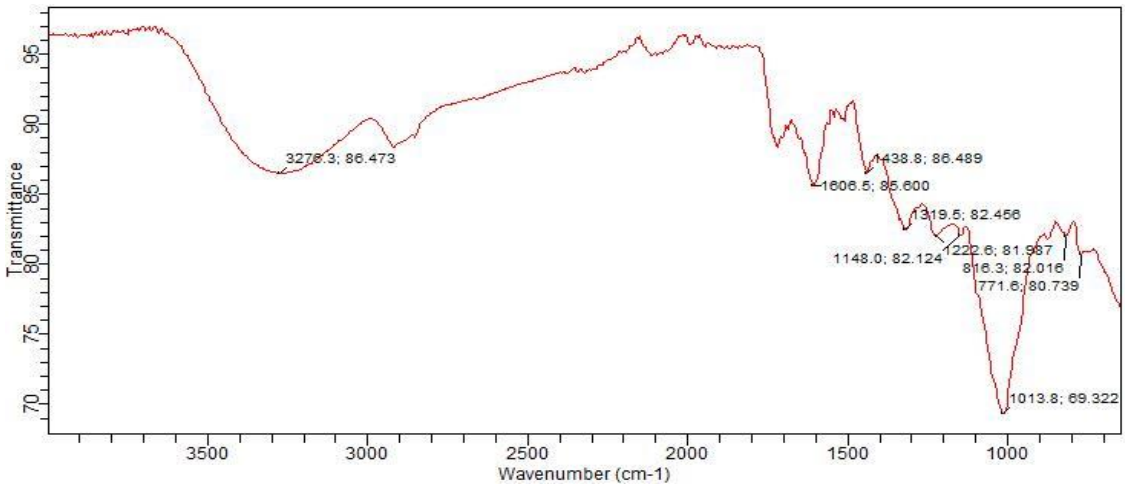

Figure 1: FTIR Spectra of pomegranate peel powder

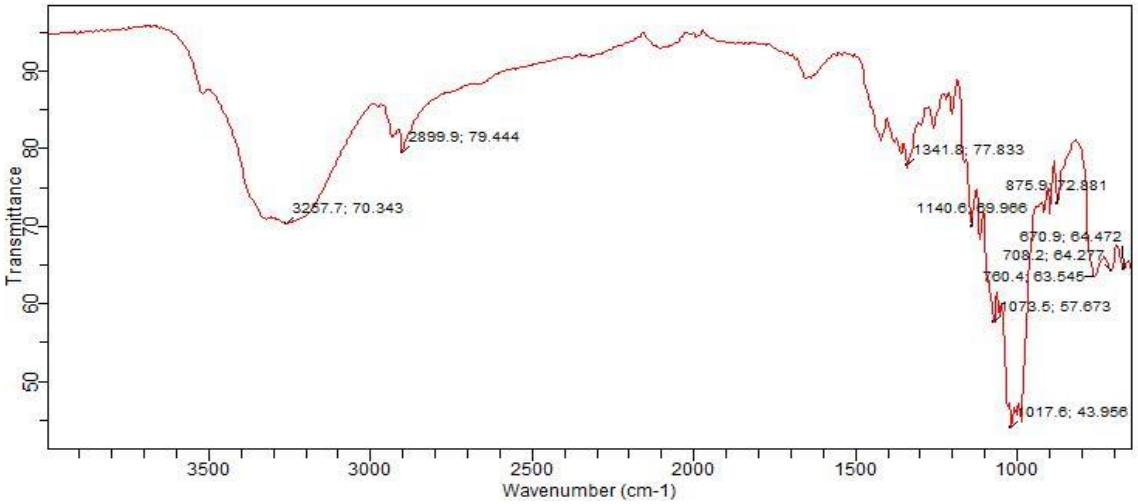

Figure 2: FTIR Spectra of pomegranate peel tablet

Table No 4: Preformulation Study of Granules

Sr.No:	Parameters	F_1	F_2	F_3	F_4	F_5	F_6
01	Bulk Density (gm/ml)	0.645	0.640	0.540	0.769	0.689	0.740
02	Tapped Density (gm/ml)	0.952	0.740	0.689	0.833	0.740	0.866
03	Carr's Index (%)	33.24	13.51	21.62	7.68	6.89	14.54
04	Hausner's ratio	1.475	1.156	1.275	1.083	1.074	1.170
05	Porosity (%)	10	32.25	9.37	13.33	25	6.896
06	Angle of Repose (θ)	$35^0 52''$	$36^0 02''$	$34^0 59''$	$33^0 69''$	$34^0 13''$	$33^0 69''$
07	Moisture contents (%)	07	09	08	06	09	08
08	Flow Rate (gm/sec)	0.77	0.44	0.66	0.33	0.85	0.75

From above preformulation study of granules, F_4 and F_5 batch shows acceptable angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, Flow rate, and Moisture contents.

Table No 5: Evaluation of Formulation

Sr.No:	Parameters	Formulation Batch					
	General appearance	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**
01	a) Colour	Pink	Pink	**Pink**	Pink	Pink	**Pink**
	b) Odour	None	None	**None**	None	None	**None**
	c) Taste	None	None	**None**	None	None	**None**
	d) Size (Diameter)	1.7mm	1.8mm	**1.7mm**	1.8mm	1.7mm	**1.7mm**
	e) Shape	Round	Round	**Round**	Round	Round	**Round**
02	Hardness (kg/cm^2)	3.5	5	**3.5**	3	3.5	**4**
03	Thickness (mm)	3	3.2	**3**	3	3	**3.5**
04	Friability (%)	0.79	0.85	**0.50**	0.70	0.85	**0.16**
05	Weight variation test	Pass	Pass	**Pass**	Pass	Pass	**Pass**
06	Dis. time (sec.)	20	25	**20**	15	30	**25**
07	Antimicrobial Test	+ve	+ve	**+ve**	+ve	+ve	**+ve**
08	Moisture content (%)	7	8	**6**	9	8	**9**

From the above evaluation parameter like thickness, average weight, hardness, friability, disintegration time etc. It can be concluded that the F_1 and F_4 batch show all parameter within acceptable limit, as compared to other batches therefore it is considered as a good formulation.

Table No 6: Comparative Study

Sr.no	Parameters	Batch		
	General appearance	**F1**	**F4**	**MF**
01	a) Color	Pink	Pink	White
	b) Odor	None	None	None
	c) Taste	None	None	Bitter
	d) Size (Diameter)	1.7mm	1.8mm	1.5mm
	e) Shape	Round	Round	Round
02	Hardness (kg/cm^2)	3.5	3	3.5
03	Thickness (mm)	3	3	3
04	Friability (%)	0.79	0.70	0.49
05	Weight variation test	Pass	Pass	Pass
06	Dis. time(sec.)	20	15	280
07	Antimicrobial Test	+ve	+ve	+ve
08	Moisture content (%)	7	9	8

Stability Study of optimized batch: -

The effects of temperature and humidity, on the physical characteristics of the tablets, were evaluated for assessing the stability (40 ^{0}C ± 2 ^{0}C/ 75 % ± 5% RH) of the prepared formulation.

Table No 7: Stability Study of Optimized Formulation

Duration (Months)	General Appearance	Hardness (kg/cm^2)	Weight Variation	Friability (%)	Disintegration Time (sec)
1 Month	No change	3.5	249	0.70	20
2 Months	No change	3	248	0.60	15
3 Months	No change	3	250	0.79	25

Stability study of the tablets at 40^{0}C ± 2^{0}C/ 75% ± 5% RH for 3 months showed no significant changes in the mechanical strength or in disintegration time of the tablets.

Figure 3 Pomegranate Fruit

Figure 4 Pomegranate Peel

Figure 5 Pomegranate peel powder

Figure 6 Pomegranate Tablet

7. DISCUSSION AND CONCLUSION:

Herbs plays major role in the treatment than the allopathic medicines because of less side effects, low cost and easy availability. The research work done on that basis and the selected plant for the formulation was proved for the use of antidiabetic purpose. The *Punicagranatum* peel powder were used to formulate tablets and evaluated for physical parameters and standardize as per pharmacopoeial standards. Preformulation study and Physical Parameter revealed that all the values were within acceptable limit shown in table no 5. The herbal formulation showed significant antidiabetic activity and the tablet standardize as per Pharmacopoeial standards. From the above evaluation parameters, it can be concluded that overall batches the F1 & F4 batch show all parameter in acceptable limit. Therefore, it is considered as a good Formulation.

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RESEARCH ARTICLE

FABRICATION AND EVALUATION OF HERBAL OINTMENT FORMULATIONS OF *MORINGA OLEIFERA* FOR TOPICAL DELIVERY

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ABSTRACT
Objective: Traditional medicine is an important source of potentially useful new compounds for the development of chemotherapeutic agents. *Moringa oleifera* Lam. is a multipurpose and exceptionally nutritious vegetable tree with a variety of potential uses. It is distributed in many countries of the tropics and subtropics. Ointments are semisolid systems which behave as viscoelastic materials when shear stress is applied. They contain medicaments and are intended to be applied externally to the body or to the mucous membrane.
Methods: In present study the *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations were evaluated for different parameters such as general appearance, spreadability, pH, extrudability, centrifugation, irritancy, loss on drying, stability study *etc*.
Results: All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4. Formulations were found to be stable at different temperature.
Conclusion: On the basis of results it can be concluded that ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments.
Keywords: Herbal ointment leaves extract, *Moringa oleifera* Lam, semisolid systems.

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INTRODUCTION
Ointments are topical formulations that offer better patient compliance and hence become more acceptable to patients[1]. It is a semisolid dosage form that contains <20% water and volatiles and >50% hydrocarbons, waxes or polyethylene glycols as the vehicle for external application to the skin[2]. Ointments are used topically for several purposes, *e.g.*, as protectant, antiseptics, emollients, antipruritic, kerotolytic, and astringents[3]. Plants had been used for medicinal purposes long before recorded history. According to survey report by WHO, about 25 per cent of prescribed human medicines are derived from plants and 80 per cent people still depend on traditional system of medicines[4]. The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety, and efficacy[5].

Figure 1: Leaves of *Moringa oleifera*

Herbal medicine, also called botanical medicine or phytomedicine, refers to the use of any plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Long practiced outside of conventional medicine, herbalism is becoming more main stream an

up-to-date analysis and research shows their value in the treatment and prevention of disease[6].

Figure 2: *Moringa oleifera* leaf powder

Moringa oleifera is one of the vegetables of the Brassica order and belongs to the family Moringaceae. *Moringa* trees have been used to combat malnutrition, especially among infants and nursing mothers[7]. *Moringa oleifera* is a small native tree of the sub-Himalayan regions of North West India, which is now indigenous to many regions in West India, Africa, Arabia, South East Asia, Islands and South America[8].

Traditionally, besides being a daily used vegetable among people of these regions, the Moringa is also widely known as 'the miracle tree' and used for its abilities for various ailments and even some chronic diseases including anemia, skin infections, blackheads, anxiety, bronchitis, catarrh, chest congestion, asthma, blood impurities, cholera, glandular, swelling, headaches, conjunctivitis, cough, diarrhea, eye and ear infections, fever, abnormal blood pressure, hysteria, pain in joints, pimples, psoriasis, respiratory disorders, scurvy, semen deficiency, sore throat, sprain, tuberculosis, for intestinal worms, lactation, diabetes and pregnancy[9]. The healing properties of Moringa oil have been documented by ancient cultures. Moringa oil has tremendous cosmetic value and is used in body and hair care as a moisturizer and skin conditioner. Moringa oil has been used in skin preparations and ointments since Egyptian times. Moringa is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce. They contain high amount of vitamin C, vitamin A, calcium, potassium, and proteins, the basic building blocks of all our body cells. Another important point is that *Moringa oleifera* leaves contain all of the essential amino acids in a good proportion, which are the building blocks of proteins[10]. Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. Leaves were also used for food fortification. Spoonful of the powder can then be added to baby food, soups, and vegetables, adding nutrition but not changing the taste.

The delivery of drug through the skin has long been a promising concept because of the ease of access, large surface area, vast exposure to the circulatory and lymphatic networks and non-invasive nature of the treatment. In present study four different ointment formulations of *Moringa oleifera* were prepared and evaluated for different parameters[11].

MATERIALS AND METHODS

Fresh leaves of *Moringa oleifera* was collected from local Area Buldana, Maharashtra, India and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra, India.

Extraction of Plant Material

Collected leaves are washed in running tap water till the removal of dirt. After this leaves are soaked in 1% saline solution (NaCl) for 5 minutes to remove microbes. Leaves are further washed with 70 % ethanol followed by twice washing with distilled water. This step plays a substantial role in removal of dust, pathogens as well as microbes present on the leave surface. The excess water can be removed by spreading the leaves in sunlight for a brief period till the removal of water present on the leaf surface[12-15].

The leaves (1 kg) were crushed with little amount of water to obtain the leaf juice. The leaf juice was filtered through a muslin cloth and later through Whatman filter paper to obtain a greenish brown juice. The juice was shade dried and a little amount of absolute alcohol was added to the juice to prevent the growth of microorganisms. The dried leaf juice was collected as a brown colored powder (about 30 g). It was refluxed at 50°C for 5-6 hours with absolute alcohol. The alcohol fraction was separated from the residue and dried to obtain the alcoholic fraction of *Moringa oleifera* leaf juice.

Preparation of Ointment

Four topical ointment formulations were prepared by means of different ingredients as shown in Table 1. The constituents of the base were placed together in a melting pan and allowed to melt together at 70°C. After melting, the ingredients were stirred gently maintaining temperature of 70°C for about 5 minutes and then cooled with continuous stirring. Formulation of ointment was done by incorporating 10 % w/w of the semisolid extract of *Moringa oleifera* into the various bases by triturating in a ceramic mortar with a pestle to obtain 100g of herbal ointments containing 10 % w/w of *Moringa oleifera*. The prepared herbal ointments were put in ointment jars, labelled and were stored at room temperature pending the evaluation[16-18].

Table 1: Composition of *Moringa oleifera* ointment formulations

Ingredients (% w/w)	Formulation code			
	F1	F2	F3	F4
Extract	10	10	10	10
Cetostearyl alcohol	5	5	-	-
Chlororesol	-	-	5	5
Wool fat	-	5	5	-
Liquid Paraffin	20	20	-	-
Hard Paraffin	5	-	-	5

Evaluation of formulations

Prepared *Moringa oleifera* ointment formulations were evaluated for the following parameters.

1. Organoleptic Parameters

Moringa oleifera ointment formulations were evaluated based on their appearance, texture and consistency.

Texture was determined on the basis of grittiness/ smoothness. Texture was found to be smooth; it can be spreadable and washable easily.

2. pH

Total 2.5gm *Moringa oleifera* ointment formulations of each batch was taken in 100 ml dry beaker, 50 ml water was added to it. Beaker was heated on water bath maintained at about 60ºC to 70ºC for 10 minutes, cooled to room temperature, and then centrifuged at 3000 rpm for 10 minutes. The pH of water extract was measured by using pH meter. The pH measurements were done by using a digital type pH meter by dipping the glass electrode into the ointment formulation[19].

3. Spreadability

The spreadability is expressed in terms of time in seconds taken by two slides to slip off from ointment, placed in between two slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability of ointment[20].

Spreadability of *Moringa oleifera* ointment formulations was determined by using the formula-

$$S = \frac{MxL}{T}$$

Where S =spreadability, M =Weight tied to upper slide, L =Length of glass slides and T =Time taken to separate the slides.

4. Viscosity

The measurement of viscosity of prepared ointments was carried out with Brookfield Viscometer (model LV -DV-II, Helipath spindle type S-96). The values of each *Moringa oleifera* ointment formulation were done in triplicate[21].

5. Extrudability

Extrudability test is the measure of the force required to extrude the material from a collapsible tube when certain amount of force has been applied on it in the form of weight. In the present study the quantity in percentage of ointment extruded from the tube on application of certain load was determined. The extruadibility of prepared *Moringa oleifera* ointment formulations was calculated by using following formula[22].

$$\text{Ext.} = \frac{\text{Amount of ointment extruaded from the tube x 100}}{\text{Total amount of ointment filled in the tube}}$$

6. Loss on drying

The loss in weight, in the sample so tested, principally is due to loss of water and small amount of other volatile material from it. Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations of different batches in a petri dish on a water bath and dried until constant weight was obtained[23].

7. Centrifugation

It is believed to be a unique tool for the evaluation of accelerated deterioration of ointments. It was determined by using Remi centrifuge in 10ml graduated cylinder at 10,000 rpm for 10 min[24].

8. Washability

Moringa oleifera ointment formulations were applied on the skin and then ease extend of washing with water was checked. Washability was checked by keeping applied skin area under the tap water for about 10 min[25].

9. Stability study

Moringa oleifera ointment formulations were evaluated for their stability at an ambient condition of pressure and temperature for two weeks. Formulations were observed for phase separation and particle agglomeration[26].

10. Acute skin irritation study

This test was performed on albino rats weighing between 150-200g. The animals were given standard animal feed and had free access to water *ad libitum*. The total mass was separated into four groups, each batch containing five animals. Dorsal hair at the back of the rats were removed one day prior to the commencement of the study and kept individually in cages to avoid contact with the other rats. Two groups of each were used for control and standard irritant. Other two groups were used as test. The 50mg of *Moringa oleifera* ointment formulations were applied over one square centimeter area of whole and abraded skin to different animals. Aqueous solution of 0.8 % formalin was used as standard irritant. The animals were observed for seven days for any signs of oedema and erythema[27].

RESULTS AND DISCUSSION

Four different ointment formulations were prepared using *Moringa oleifera* extract in different ratio (Table1). All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance (Table 2). The mechanical evaluation parameters are important tests to evaluate pharmaceutical ointment formulations. Formulations complied with the physical evaluation parameters like pH, physical stability, centrifugation, viscosity, spreadability, extrudability was found to be acceptable.

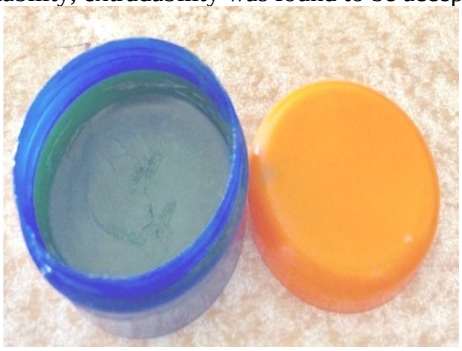

Figure 3: *Moringa oleifera* ointment formulation of batch F1

The pH of the formulations was in the range of 5.5 to 6.5, which lies in the normal pH range of the skin and would not produce any skin irritation. There was no significant change in pH values as a function of time for all formulations**.** Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations was found to be in the range of 20-38%. The results of viscosity gives an idea about measurement of strength and the result of spreadability denote the extent of area to which the prepared formulations readily spreads on application to skin or affected part and homogeneity confirms no lumps. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4.

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As per results of spreadability studies, the spreading area was found to decrease with increase in viscosity, as spreadability and viscosity are inversely proportional. All the formulations did not produce any skin irritation, i.e. erythema and oedema for about a week when applied over the skin. All formulations were found to be safe for clinical practice. No phase separation was observed during centrifugation among all ointment formulations. Formulations were found to be stable at different temperature i.e. 20°C, 25°C, 37°C.

Table 2: Evaluation of Formulation

Parameters	F1	F2	F3	F4
Colour	Green	Green	Green	Green
Odour	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth, soft semisolid	Soft semisolid	Smooth, Soft semisolid	Soft semisolid
Viscosity (cps)	34.5±0.8	35.3±0.4	33.5±0.21	32.21±0.51
pH	5.5	6.5	5.0	5.6
Spreadability (sec)	9	10	8	7
Extrudability (gm)	0.5	0.4	0.9	0.8
Centrifugation	No phase separation	No phase separation	No phase separation	No phase separation
Loss on drying	20%	35%	38%	25%
Washability	Good	Good	Good	Good
Non irritancy	Non irritant	Non irritant	Non irritant	Non irritant
Stability study	Stable	Stable	Stable	Stable

CONCLUSION

Since ancient time, herbs plays major role in the treatment because of less side effects, low cost and easy availability. The *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations evaluated for physical parameters and standardize as per pharmacopoeial standards. The results of the physical evaluation of ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments. Further investigations are necessary to determine the therapeutic efficiency of the prepared *Morenga oleifera* ointment formulations.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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Traditionally, besides being a daily used vegetable among people of these regions, the Moringa is also widely known as 'the miracle tree' and used for its abilities for various ailments and even some chronic diseases including anemia, skin infections, blackheads, anxiety, bronchitis, catarrh, chest congestion, asthma, blood impurities, cholera, glandular, swelling, headaches, conjunctivitis, cough, diarrhea, eye and ear infections, fever, abnormal blood pressure, hysteria, pain in joints, pimples, psoriasis, respiratory disorders, scurvy, semen deficiency, sore throat, sprain, tuberculosis, for intestinal worms, lactation, diabetes and pregnancy[9]. The healing properties of Moringa oil have been documented by ancient cultures. Moringa oil has tremendous cosmetic value and is used in body and hair care as a moisturizer and skin conditioner. Moringa oil has been used in skin preparations and ointments since Egyptian times. Moringa is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce. They contain high amount of vitamin C, vitamin A, calcium, potassium, and proteins, the basic building blocks of all our body cells. Another important point is that *Moringa oleifera* leaves contain all of the essential amino acids in a good proportion, which are the building blocks of proteins[10]. Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. Leaves were also used for food fortification. Spoonful of the powder can then be added to baby food, soups, and vegetables, adding nutrition but not changing the taste.

The delivery of drug through the skin has long been a promising concept because of the ease of access, large surface area, vast exposure to the circulatory and lymphatic networks and non-invasive nature of the treatment. In present study four different ointment formulations of *Moringa oleifera* were prepared and evaluated for different parameters[11].

MATERIALS AND METHODS

Fresh leaves of *Moringa oleifera* was collected from local Area Buldana, Maharashtra, India and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra, India.

Extraction of Plant Material

Collected leaves are washed in running tap water till the removal of dirt. After this leaves are soaked in 1% saline solution (NaCl) for 5 minutes to remove microbes. Leaves are further washed with 70 % ethanol followed by twice washing with distilled water. This step plays a substantial role in removal of dust, pathogens as well as microbes present on the leave surface. The excess water can be removed by spreading the leaves in sunlight for a brief period till the removal of water present on the leaf surface[12-15].

The leaves (1 kg) were crushed with little amount of water to obtain the leaf juice. The leaf juice was filtered through a muslin cloth and later through Whatman filter paper to obtain a greenish brown juice. The juice was shade dried and a little amount of absolute alcohol was added to the juice to prevent the growth of microorganisms. The dried leaf juice was collected as a brown colored powder (about 30 g). It was refluxed at 50°C for 5-6 hours with absolute alcohol. The alcohol fraction was separated from the residue and dried to obtain the alcoholic fraction of *Moringa oleifera* leaf juice.

Preparation of Ointment

Four topical ointment formulations were prepared by means of different ingredients as shown in Table 1. The constituents of the base were placed together in a melting pan and allowed to melt together at 70°C. After melting, the ingredients were stirred gently maintaining temperature of 70°C for about 5 minutes and then cooled with continuous stirring. Formulation of ointment was done by incorporating 10 % w/w of the semisolid extract of *Moringa oleifera* into the various bases by triturating in a ceramic mortar with a pestle to obtain 100g of herbal ointments containing 10 % w/w of *Moringa oleifera*. The prepared herbal ointments were put in ointment jars, labelled and were stored at room temperature pending the evaluation[16-18].

Table 1: Composition of *Moringa oleifera* ointment formulations

Ingredients (% w/w)	Formulation code			
	F1	F2	F3	F4
Extract	10	10	10	10
Cetostearyl alcohol	5	5	-	-
Chlororesol	-	-	5	5
Wool fat	-	5	5	-
Liquid Paraffin	20	20	-	-
Hard Paraffin	5	-	-	5

Evaluation of formulations

Prepared *Moringa oleifera* ointment formulations were evaluated for the following parameters.

1. Organoleptic Parameters

Moringa oleifera ointment formulations were evaluated based on their appearance, texture and consistency.

Texture was determined on the basis of grittiness/ smoothness. Texture was found to be smooth; it can be spreadable and washable easily.

2. pH

Total 2.5gm *Moringa oleifera* ointment formulations of each batch was taken in 100 ml dry beaker, 50 ml water was added to it. Beaker was heated on water bath maintained at about 60ºC to 70ºC for 10 minutes, cooled to room temperature, and then centrifuged at 3000 rpm for 10 minutes. The pH of water extract was measured by using pH meter. The pH measurements were done by using a digital type pH meter by dipping the glass electrode into the ointment formulation[19].

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The spreadability is expressed in terms of time in seconds taken by two slides to slip off from ointment, placed in between two slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability of ointment[20].

Spreadability of *Moringa oleifera* ointment formulations was determined by using the formula-

$$S = \frac{MxL}{T}$$

Where S =spreadability, M =Weight tied to upper slide, L =Length of glass slides and T =Time taken to separate the slides.

4. Viscosity

The measurement of viscosity of prepared ointments was carried out with Brookfield Viscometer (model LV -DV-II, Helipath spindle type S-96). The values of each *Moringa oleifera* ointment formulation were done in triplicate[21].

5. Extrudability

Extrudability test is the measure of the force required to extrude the material from a collapsible tube when certain amount of force has been applied on it in the form of weight. In the present study the quantity in percentage of ointment extruded from the tube on application of certain load was determined. The extruadibility of prepared *Moringa oleifera* ointment formulations was calculated by using following formula[22].

$$\text{Ext.} = \frac{\text{Amount of ointment extruaded from the tube x 100}}{\text{Total amount of ointment filled in the tube}}$$

6. Loss on drying

The loss in weight, in the sample so tested, principally is due to loss of water and small amount of other volatile material from it. Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations of different batches in a petri dish on a water bath and dried until constant weight was obtained[23].

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It is believed to be a unique tool for the evaluation of accelerated deterioration of ointments. It was determined by using Remi centrifuge in 10ml graduated cylinder at 10,000 rpm for 10 min[24].

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9. Stability study

Moringa oleifera ointment formulations were evaluated for their stability at an ambient condition of pressure and temperature for two weeks. Formulations were observed for phase separation and particle agglomeration[26].

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RESULTS AND DISCUSSION

Four different ointment formulations were prepared using *Moringa oleifera* extract in different ratio (Table1). All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance (Table 2). The mechanical evaluation parameters are important tests to evaluate pharmaceutical ointment formulations. Formulations complied with the physical evaluation parameters like pH, physical stability, centrifugation, viscosity, spreadability, extrudability was found to be acceptable.

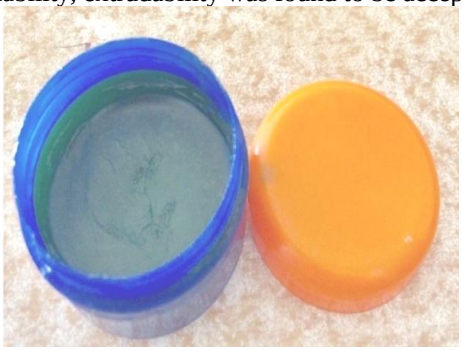

Figure 3: *Moringa oleifera* ointment formulation of batch F1

The pH of the formulations was in the range of 5.5 to 6.5, which lies in the normal pH range of the skin and would not produce any skin irritation. There was no significant change in pH values as a function of time for all formulations**.** Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations was found to be in the range of 20-38%. The results of viscosity gives an idea about measurement of strength and the result of spreadability denote the extent of area to which the prepared formulations readily spreads on application to skin or affected part and homogeneity confirms no lumps. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4.

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As per results of spreadability studies, the spreading area was found to decrease with increase in viscosity, as spreadability and viscosity are inversely proportional. All the formulations did not produce any skin irritation, i.e. erythema and oedema for about a week when applied over the skin. All formulations were found to be safe for clinical practice. No phase separation was observed during centrifugation among all ointment formulations. Formulations were found to be stable at different temperature i.e. 20°C, 25°C, 37°C.

Table 2: Evaluation of Formulation

Parameters	F1	F2	F3	F4
Colour	Green	Green	Green	Green
Odour	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth, soft semisolid	Soft semisolid	Smooth, Soft semisolid	Soft semisolid
Viscosity (cps)	34.5±0.8	35.3±0.4	33.5±0.21	32.21±0.51
pH	5.5	6.5	5.0	5.6
Spreadability (sec)	9	10	8	7
Extrudability (gm)	0.5	0.4	0.9	0.8
Centrifugation	No phase separation	No phase separation	No phase separation	No phase separation
Loss on drying	20%	35%	38%	25%
Washability	Good	Good	Good	Good
Non irritancy	Non irritant	Non irritant	Non irritant	Non irritant
Stability study	Stable	Stable	Stable	Stable

CONCLUSION

Since ancient time, herbs plays major role in the treatment because of less side effects, low cost and easy availability. The *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations evaluated for physical parameters and standardize as per pharmacopoeial standards. The results of the physical evaluation of ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments. Further investigations are necessary to determine the therapeutic efficiency of the prepared *Morenga oleifera* ointment formulations.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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RESEARCH ARTICLE

FABRICATION AND EVALUATION OF HERBAL OINTMENT FORMULATIONS OF *MORINGA OLEIFERA* FOR TOPICAL DELIVERY

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ABSTRACT
Objective: Traditional medicine is an important source of potentially useful new compounds for the development of chemotherapeutic agents. *Moringa oleifera* Lam. is a multipurpose and exceptionally nutritious vegetable tree with a variety of potential uses. It is distributed in many countries of the tropics and subtropics. Ointments are semisolid systems which behave as viscoelastic materials when shear stress is applied. They contain medicaments and are intended to be applied externally to the body or to the mucous membrane.
Methods: In present study the *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations were evaluated for different parameters such as general appearance, spreadability, pH, extrudability, centrifugation, irritancy, loss on drying, stability study *etc*.
Results: All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4. Formulations were found to be stable at different temperature.
Conclusion: On the basis of results it can be concluded that ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments.
Keywords: Herbal ointment leaves extract, *Moringa oleifera* Lam, semisolid systems.

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INTRODUCTION
Ointments are topical formulations that offer better patient compliance and hence become more acceptable to patients[1]. It is a semisolid dosage form that contains <20% water and volatiles and >50% hydrocarbons, waxes or polyethylene glycols as the vehicle for external application to the skin[2]. Ointments are used topically for several purposes, *e.g.*, as protectant, antiseptics, emollients, antipruritic, kerotolytic, and astringents[3]. Plants had been used for medicinal purposes long before recorded history. According to survey report by WHO, about 25 per cent of prescribed human medicines are derived from plants and 80 per cent people still depend on traditional system of medicines[4]. The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety, and efficacy[5].

Figure 1: Leaves of *Moringa oleifera*

Herbal medicine, also called botanical medicine or phytomedicine, refers to the use of any plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Long practiced outside of conventional medicine, herbalism is becoming more main stream an

up-to-date analysis and research shows their value in the treatment and prevention of disease[6].

Figure 2: *Moringa oleifera* leaf powder

Moringa oleifera is one of the vegetables of the Brassica order and belongs to the family Moringaceae. *Moringa* trees have been used to combat malnutrition, especially among infants and nursing mothers[7]. *Moringa oleifera* is a small native tree of the sub-Himalayan regions of North West India, which is now indigenous to many regions in West India, Africa, Arabia, South East Asia, Islands and South America[8]. Traditionally, besides being a daily used vegetable among people of these regions, the Moringa is also widely known as 'the miracle tree' and used for its abilities for various ailments and even some chronic diseases including anemia, skin infections, blackheads, anxiety, bronchitis, catarrh, chest congestion, asthma, blood impurities, cholera, glandular, swelling, headaches, conjunctivitis, cough, diarrhea, eye and ear infections, fever, abnormal blood pressure, hysteria, pain in joints, pimples, psoriasis, respiratory disorders, scurvy, semen deficiency, sore throat, sprain, tuberculosis, for intestinal worms, lactation, diabetes and pregnancy[9]. The healing properties of Moringa oil have been documented by ancient cultures. Moringa oil has tremendous cosmetic value and is used in body and hair care as a moisturizer and skin conditioner. Moringa oil has been used in skin preparations and ointments since Egyptian times. Moringa is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce. They contain high amount of vitamin C, vitamin A, calcium, potassium, and proteins, the basic building blocks of all our body cells. Another important point is that *Moringa oleifera* leaves contain all of the essential amino acids in a good proportion, which are the building blocks of proteins[10]. Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. Leaves were also used for food fortification. Spoonful of the powder can then be added to baby food, soups, and vegetables, adding nutrition but not changing the taste.

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RESULTS AND DISCUSSION

Four different ointment formulations were prepared using *Moringa oleifera* extract in different ratio (Table1). All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance (Table 2). The mechanical evaluation parameters are important tests to evaluate pharmaceutical ointment formulations. Formulations complied with the physical evaluation parameters like pH, physical stability, centrifugation, viscosity, spreadability, extrudability was found to be acceptable.

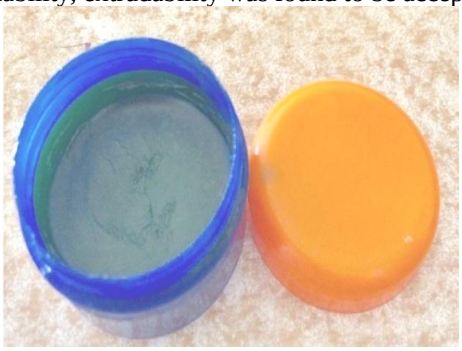

Figure 3: *Moringa oleifera* ointment formulation of batch F1

The pH of the formulations was in the range of 5.5 to 6.5, which lies in the normal pH range of the skin and would not produce any skin irritation. There was no significant change in pH values as a function of time for all formulations**.** Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations was found to be in the range of 20-38%. The results of viscosity gives an idea about measurement of strength and the result of spreadability denote the extent of area to which the prepared formulations readily spreads on application to skin or affected part and homogeneity confirms no lumps. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4.

As per results of spreadability studies, the spreading area was found to decrease with increase in viscosity, as spreadability and viscosity are inversely proportional. All the formulations did not produce any skin irritation, i.e. erythema and oedema for about a week when applied over the skin. All formulations were found to be safe for clinical practice. No phase separation was observed during centrifugation among all ointment formulations. Formulations were found to be stable at different temperature i.e. 20°C, 25°C, 37°C.

Table 2: Evaluation of Formulation

Parameters	F1	F2	F3	F4
Colour	Green	Green	Green	Green
Odour	Characteristic	Characteristic	Characteristic	Characteristic
Consistency	Smooth, soft semisolid	Soft semisolid	Smooth, Soft semisolid	Soft semisolid
Viscosity (cps)	34.5±0.8	35.3±0.4	33.5±0.21	32.21±0.51
pH	5.5	6.5	5.0	5.6
Spreadability (sec)	9	10	8	7
Extrudability (gm)	0.5	0.4	0.9	0.8
Centrifugation	No phase separation	No phase separation	No phase separation	No phase separation
Loss on drying	20%	35%	38%	25%
Washability	Good	Good	Good	Good
Non irritancy	Non irritant	Non irritant	Non irritant	Non irritant
Stability study	Stable	Stable	Stable	Stable

CONCLUSION

Since ancient time, herbs plays major role in the treatment because of less side effects, low cost and easy availability. The *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations evaluated for physical parameters and standardize as per pharmacopoeial standards. The results of the physical evaluation of ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments. Further investigations are necessary to determine the therapeutic efficiency of the prepared *Morenga oleifera* ointment formulations.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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RESEARCH ARTICLE

FABRICATION AND EVALUATION OF HERBAL OINTMENT FORMULATIONS OF *MORINGA OLEIFERA* FOR TOPICAL DELIVERY

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ABSTRACT
Objective: Traditional medicine is an important source of potentially useful new compounds for the development of chemotherapeutic agents. *Moringa oleifera* Lam. is a multipurpose and exceptionally nutritious vegetable tree with a variety of potential uses. It is distributed in many countries of the tropics and subtropics. Ointments are semisolid systems which behave as viscoelastic materials when shear stress is applied. They contain medicaments and are intended to be applied externally to the body or to the mucous membrane.
Methods: In present study the *Morenga oleifera* leaves extract was used to formulate four different ointment formulations with different bases like cetostearyl alcohol, hard paraffin, and liquid paraffin. Formulations were evaluated for different parameters such as general appearance, spreadability, pH, extrudability, centrifugation, irritancy, loss on drying, stability study *etc*.
Results: All formulations were found to be free of grittiness, homogeneous, without phase separation with green colour with a smooth homogeneous texture and glossy appearance. Viscosity of the ointment formulations was in the range of 32.21±0.51 to 35.3±0.4. Formulations were found to be stable at different temperature.
Conclusion: On the basis of results it can be concluded that ointment preparations with extract of *Morenga oleifera* leaves indicated the suitability of method for the production of ointments.
Keywords: Herbal ointment leaves extract, *Moringa oleifera* Lam, semisolid systems.

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INTRODUCTION
Ointments are topical formulations that offer better patient compliance and hence become more acceptable to patients[1]. It is a semisolid dosage form that contains <20% water and volatiles and >50% hydrocarbons, waxes or polyethylene glycols as the vehicle for external application to the skin[2]. Ointments are used topically for several purposes, *e.g.*, as protectant, antiseptics, emollients, antipruritic, kerotolytic, and astringents[3]. Plants had been used for medicinal purposes long before recorded history. According to survey report by WHO, about 25 per cent of prescribed human medicines are derived from plants and 80 per cent people still depend on traditional system of medicines[4]. The World Health Organization (WHO) has appreciated the importance of medicinal plants for public health care in developing nations and has evolved guidelines to support the member states in their efforts to formulate national policies on traditional medicine and to study their potential usefulness including evaluation, safety, and efficacy[5].

Figure 1: Leaves of *Moringa oleifera*

Herbal medicine, also called botanical medicine or phytomedicine, refers to the use of any plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Long practiced outside of conventional medicine, herbalism is becoming more main stream an

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up-to-date analysis and research shows their value in the treatment and prevention of disease[6].

Figure 2: *Moringa oleifera* leaf powder

Moringa oleifera is one of the vegetables of the Brassica order and belongs to the family Moringaceae. *Moringa* trees have been used to combat malnutrition, especially among infants and nursing mothers[7]. *Moringa oleifera* is a small native tree of the sub-Himalayan regions of North West India, which is now indigenous to many regions in West India, Africa, Arabia, South East Asia, Islands and South America[8]. Traditionally, besides being a daily used vegetable among people of these regions, the Moringa is also widely known as 'the miracle tree' and used for its abilities for various ailments and even some chronic diseases including anemia, skin infections, blackheads, anxiety, bronchitis, catarrh, chest congestion, asthma, blood impurities, cholera, glandular, swelling, headaches, conjunctivitis, cough, diarrhea, eye and ear infections, fever, abnormal blood pressure, hysteria, pain in joints, pimples, psoriasis, respiratory disorders, scurvy, semen deficiency, sore throat, sprain, tuberculosis, for intestinal worms, lactation, diabetes and pregnancy[9]. The healing properties of Moringa oil have been documented by ancient cultures. Moringa oil has tremendous cosmetic value and is used in body and hair care as a moisturizer and skin conditioner. Moringa oil has been used in skin preparations and ointments since Egyptian times. Moringa is especially promising as a food source in the tropics because the tree is in full leaf at the end of the dry season when other foods are typically scarce. They contain high amount of vitamin C, vitamin A, calcium, potassium, and proteins, the basic building blocks of all our body cells. Another important point is that *Moringa oleifera* leaves contain all of the essential amino acids in a good proportion, which are the building blocks of proteins[10]. Leaves can be eaten fresh, cooked, or stored as dried powder for many months without refrigeration, and reportedly without loss of nutritional value. Leaves were also used for food fortification. Spoonful of the powder can then be added to baby food, soups, and vegetables, adding nutrition but not changing the taste.

The delivery of drug through the skin has long been a promising concept because of the ease of access, large surface area, vast exposure to the circulatory and lymphatic networks and non-invasive nature of the treatment. In present study four different ointment formulations of *Moringa oleifera* were prepared and evaluated for different parameters[11].

MATERIALS AND METHODS

Fresh leaves of *Moringa oleifera* was collected from local Area Buldana, Maharashtra, India and transported to laboratory, authenticated from Center for Biodiversity Jijamata Mahavidyalaya, Buldana, Maharashtra, India.

Extraction of Plant Material

Collected leaves are washed in running tap water till the removal of dirt. After this leaves are soaked in 1% saline solution (NaCl) for 5 minutes to remove microbes. Leaves are further washed with 70 % ethanol followed by twice washing with distilled water. This step plays a substantial role in removal of dust, pathogens as well as microbes present on the leave surface. The excess water can be removed by spreading the leaves in sunlight for a brief period till the removal of water present on the leaf surface[12-15].

The leaves (1 kg) were crushed with little amount of water to obtain the leaf juice. The leaf juice was filtered through a muslin cloth and later through Whatman filter paper to obtain a greenish brown juice. The juice was shade dried and a little amount of absolute alcohol was added to the juice to prevent the growth of microorganisms. The dried leaf juice was collected as a brown colored powder (about 30 g). It was refluxed at 50°C for 5-6 hours with absolute alcohol. The alcohol fraction was separated from the residue and dried to obtain the alcoholic fraction of *Moringa oleifera* leaf juice.

Preparation of Ointment

Four topical ointment formulations were prepared by means of different ingredients as shown in Table 1. The constituents of the base were placed together in a melting pan and allowed to melt together at 70°C. After melting, the ingredients were stirred gently maintaining temperature of 70°C for about 5 minutes and then cooled with continuous stirring. Formulation of ointment was done by incorporating 10 % w/w of the semisolid extract of *Moringa oleifera* into the various bases by triturating in a ceramic mortar with a pestle to obtain 100g of herbal ointments containing 10 % w/w of *Moringa oleifera*. The prepared herbal ointments were put in ointment jars, labelled and were stored at room temperature pending the evaluation[16-18].

Table 1: Composition of *Moringa oleifera* ointment formulations

Ingredients (% w/w)	Formulation code			
	F1	F2	F3	F4
Extract	10	10	10	10
Cetostearyl alcohol	5	5	-	-
Chlororesol	-	-	5	5
Wool fat	-	5	5	-
Liquid Paraffin	20	20	-	-
Hard Paraffin	5	-	-	5

Evaluation of formulations

Prepared *Moringa oleifera* ointment formulations were evaluated for the following parameters.

1. Organoleptic Parameters

Moringa oleifera ointment formulations were evaluated based on their appearance, texture and consistency.

Texture was determined on the basis of grittiness/ smoothness. Texture was found to be smooth; it can be spreadable and washable easily.

2. pH

Total 2.5gm *Moringa oleifera* ointment formulations of each batch was taken in 100 ml dry beaker, 50 ml water was added to it. Beaker was heated on water bath maintained at about 60ºC to 70ºC for 10 minutes, cooled to room temperature, and then centrifuged at 3000 rpm for 10 minutes. The pH of water extract was measured by using pH meter. The pH measurements were done by using a digital type pH meter by dipping the glass electrode into the ointment formulation[19].

3. Spreadability

The spreadability is expressed in terms of time in seconds taken by two slides to slip off from ointment, placed in between two slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability of ointment[20].

Spreadability of *Moringa oleifera* ointment formulations was determined by using the formula-

$$S = \frac{MxL}{T}$$

Where S =spreadability, M =Weight tied to upper slide, L =Length of glass slides and T =Time taken to separate the slides.

4. Viscosity

The measurement of viscosity of prepared ointments was carried out with Brookfield Viscometer (model LV -DV-II, Helipath spindle type S-96). The values of each *Moringa oleifera* ointment formulation were done in triplicate[21].

5. Extrudability

Extrudability test is the measure of the force required to extrude the material from a collapsible tube when certain amount of force has been applied on it in the form of weight. In the present study the quantity in percentage of ointment extruded from the tube on application of certain load was determined. The extruadibility of prepared *Moringa oleifera* ointment formulations was calculated by using following formula[22].

$$\text{Ext.} = \frac{\text{Amount of ointment extruaded from the tube x 100}}{\text{Total amount of ointment filled in the tube}}$$

6. Loss on drying

The loss in weight, in the sample so tested, principally is due to loss of water and small amount of other volatile material from it. Loss on drying was determined by placing the 1gm of *Moringa oleifera* ointment formulations of different batches in a petri dish on a water bath and dried until constant weight was obtained[23].

7. Centrifugation

It is believed to be a unique tool for the evaluation of accelerated deterioration of ointments. It was determined by using Remi centrifuge in 10ml graduated cylinder at 10,000 rpm for 10 min[24].

8. Washability

Moringa oleifera ointment formulations were applied on the skin and then ease extend of washing with water was checked. Washability was checked by keeping applied skin area under the tap water for about 10 min[25].

9. Stability study

Moringa oleifera ointment formulations were evaluated for their stability at an ambient condition of pressure and temperature for two weeks. Formulations were observed for phase separation and particle agglomeration[26].

10. Acute skin irritation study

This test was performed on albino rats weighing between 150-200g. The animals were given standard animal feed and had free access to water *ad libitum*. The total mass was separated into four groups, each batch containing five animals. Dorsal hair at the back of the rats were removed one day prior to the commencement of the study and kept individually in cages to avoid contact with the other rats. Two groups of each were used for control and standard irritant. Other two groups were used as test. The 50mg of *Moringa oleifera* ointment formulations were applied over one square centimeter area of whole and abraded skin to different animals. Aqueous solution of 0.8 % formalin was used as standard irritant. The animals were observed for seven days for any signs of oedema and erythema[27].

RESULTS AND DISCUSSION

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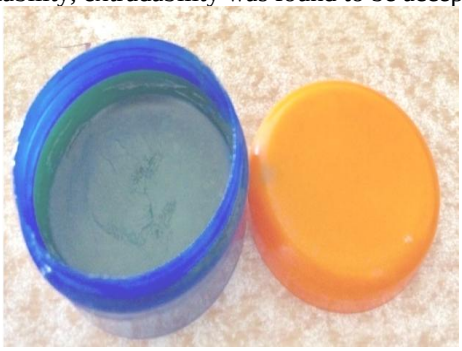

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AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF IBUPROFEN GASTRO-RETENTIVE FLOATING TABLETS

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ABSTRACT
Objective: The objective of the present study was to formulate the gastro-retentive floating tablets containing Ibuprofen, which would remain in stomach and/or upper part of GIT for prolonged period of time. Floating systems have low bulk density so that they can float on the gastric juice in the stomach. Ibuprofen is an anti inflammatory drug.
Methods: On trial and error basis formulation design was done. Four different batches of floating tablets of Ibuprofen were prepared using HPMC, Xanthan gum, and gas generating agent sodium bicarbonate and citric acid. The tablets were characterized for the pre and post compression parameters such as friability, hardness, thickness, drug content, weight variation, *in-vitro* buoyancy studies and 13 hrs *in-vitro* drug release studies and the results were within the limits.
Results: There was no interaction found in between drug and other ingredients. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs.
Conclusion: From the results obtained, it was concluded that the optimized formulation F4 desired drug release properties and floating behavior.
Keywords: Citric acid, gastro-retentive floating tablets, HPMC K4M, Ibuprofen, sodium bicarbonate, xanthan gum.

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INTRODUCTION
Administration of drugs by oral route offers ease administration and gastrointestinal physiology offers more flexibility in dosage form design than other routes[1]. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half lives are eliminated quickly from the systemic circulation. So, there is need of frequent dosing of these drugs is required to achieve desired therapeutic activity. To avoid this, the development of oral sustained/controlled release formulations is an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. Floating drug delivery systems (FDDS) were first described by Davis in 1968[2]. Floating systems or Hydro-dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time while the system is floating on the gastric content; the drug is released slowly at the desired rate from the floating system. After release of drug, the residual system is emptied from the stomach[3]. This results in an increased Gastric retention time and a better control of the fluctuations in plasma drug concentration[4]. Gastro retentive systems confine the dosage forms for several hours inside the stomach and considerably prolong the gastric residence time of drugs[5]. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It is also beneficial for local drug delivery to the stomach and proximal small intestines[6]. Ibuprofen (iso-butyl-propanoic-phenolic acid) is a non-steroidal anti-inflammatory drug (NSAID). It is a propionic acid derivatives[7]. It is used for treatment of rheumatoid arthritis, degenerative joint disease, osteoarthritis, acute musculoskeletal disorders, and low back pain, fever. The bioavailability of the drug is 87-100% and the protein binding capacity is 98%[8]. It is metabolized by liver and it has a plasmatic half-life of 1.8–2.0 h as a result, it has to be administered three to six times a day. It is excreted through urine[9]. Hydrophilic polymer matrix is widely used for formulating sustained release dosage form. HPMC is widely used hydrophilic polymer to prolong

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drug release due to its rapid hydration, good compression and gelling characteristics along with its ease of use, availability, and very low toxicity. It regulates the release of drug by controlling the swelling and cross-linking[10,11].

The main intention of this work was to formulate a single unit floating tablets of ibuprofen with use of HPMC for the release of the drug after a definite lag time and provides required concentration of drug at regular intervals of time which results reduction in frequency of dose of administration and will improve patient compliance[12].

MATERIALS AND METHODS

Ibuprofen was obtained as a gift sample from Leben Parma, Akola, Maharashtra, India. HPMC K4M, Xanthan gum, Citric acid, lactose and Sodium bicarbonate, Talc and MCC were obtained from Research Lab, Akola, Maharashtra, India. All the chemicals and reagents required for the present experimental work are of analytical grade.

Standard Calibration Curve

10 mg of Ibuprofen was weighed and dissolved in 10 ml of phosphate buffer 6.8, to give a solution of 1000 µg/ml concentration. From this solution 1 ml was taken and diluted to 10ml using Phosphate buffer 6.8 to produce a stock solution of 100µg/ml. From this stock solution different concentrations were prepared. The absorbance of these solutions was measured at 221 nm by UV spectrophotometer (Jasco V530 plus)[13].

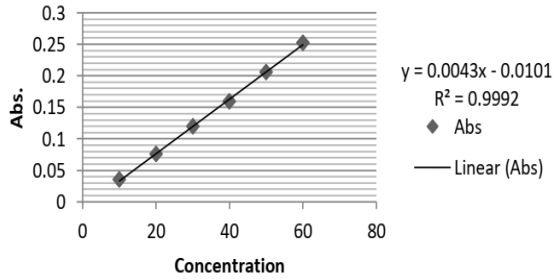

Figure 1: Standard calibration curve of Ibuprofen

Fourier Transform Infra-Red (FTIR) Spectroscopy

Interaction of drug with excipients was confirmed by carrying out IR interactions studies. Drug and excipients used in study were placed in air tight screw cap amber colored vials, then vials were kept at room temperature as well as in hot air oven at 40^0C for one week to get them moisture free and FT-IR analysis was carried out with saturated potassium bromide using pellet making method. Standard and KBr were taken in the ratio of 1:300 to make a solid disc or pellet with the help of Hydraulic Pellet Machine[14, 15].

Powder characterization

1. Bulk Density: It refers to packing of particles. The bulk density of the formulated granules was evaluated using a bulk density apparatus[16]. It is expressed in gm/ml and is given by below equation-

$$\text{Bulk density} = \frac{\text{Mass of the powder}}{\text{Volume of the bulk powder}}$$

2. Tapped density

Weighed quantity of tablet blend was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 and300 taps in tap density apparatus[17].

$$\text{Tapped density} = \frac{\text{Mass of the powder}}{\text{Tapped volume of the powder}}$$

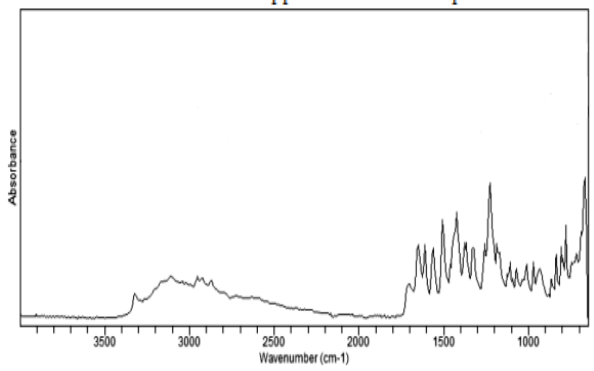

Figure 2: FTIR spectrum of Ibuprofen

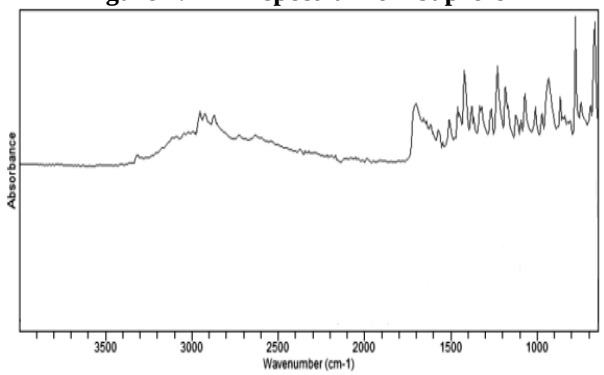

Figure 3: FTIR spectrum of mixture of Ibuprofen, HPMC K4M

3. Carr's Index (Compressibility)

The compressibility index and Hausner ratio was measures the property of powder to be compressed. The packing ability of tablet blend was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping[18].

It was indicated as Carr's compressibility index was calculated by following formula-

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{X100}$$

4. Hausner Ratio

It is measurement of frictional resistance of tablet blend[19]. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

5. Angle of Repose

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane2^0. It was determined by the following equation:

$$\tan\theta = \frac{h}{r}$$

Where, θ = Angle of repose, h = of powder heap.
r = Radius of the powder cone.

Preparation of Ibuprofen floating tablets

The composition of different formulations of Ibuprofen floating tablets is shown in Table 2. All the ingredients were accurately weighed and passed through mesh 60#. In order to mix the ingredients thoroughly drug and

polymer were blended and geometrically in a mortar and pestle for 15 minutes then magnesium stearate, sodium bicarbonate, talc, lactose and magnesium stearate were mixed one by one. After thoroughly mixing the ingredients, the powder was blend was passed through 44# sieve and compressed on rotary tablet punching machine[21,22].

Post compression parameters of Ibuprofen floating tablets

1. Weight uniformity test

Twenty Ibuprofen tablets were weighed individually, average weight was calculated and individual tablet weights were compared to the, average weight. The tablets met the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit[23].

2. Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked from each formulation and the mean and standard deviation values were calculated[24].

3. Friability

A friability test was conducted on Ibuprofen floating tablets using a Roche friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again[25,26]. The percentage friability was then calculated by,

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \text{X100}$$

4. Lag Time

The *In-vitro* buoyancy was determined by the lag time. The Ibuprofen tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for a tablet to rise to the surface for floating was determined as the lag time[27].

5. Floating Time

The Ibuprofen tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. The time for which the tablet remained floating on the surface of medium was determined as floating time[28].

6. Drug Content

Ten Ibuprofen tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 5 ml of Methanol and made up to 100 ml of 0.1 N HCl. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10 ml using 0.1 N HCl. Absorbance was measured at 221 nm using 0.1 N HCl as a blank. The amount of drug present in one tablet was calculated[29].

***7. In vitro* release studies**

In vitro drug release study for the prepared Ibuprofen floating tablets were conducted for period of 13 hours using a six station USP XXVI type II (paddle) apparatus at 37±0.5^{0}C and 50 rpm speed. The dissolution studies were carried out in triplicate for 10 hours in phosphate buffer of pH 6.8 under sink condition. At first half an hour and then every 1 hour interval samples of 5ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 221 nm for Ibuprofen by a UV- spectrophotometer[29].

RESULTS AND DISCUSSION

Floating tablets of Ibuprofen were developed in order increase the gastric residence time of drug, so that they can be retained in stomach for longer time to reduce the frequency of administration. Four different batches of tablets were made using HPMC K4M, along with effervescing agent sodium bicarbonate and citric acid to optimize the drug content, *in-vitro* buoyancy and *in-vitro* drug dissolution studies.

Table 1: Results of physical evaluation of pre-compression blend

Batch code	Angle of repose (θ)	Bulk Density	Tapped Density	Carr's Index	Hausner's ratio
F1	21	0.224	0.264	15.15	1.17
F2	22	0.222	0.260	14.61	1.17
F3	26	0.251	0.289	13.14	1.15
F4	25	0.229	0.260	11.92	1.13

The selection of viscosity grade of a polymer is an important consideration in the formulation of tablet. All the formulations were prepared by direct compression method. Preformulation is the first step in development of new formulation. Characteristic absorption bands in FTIR spectrum of the drug sample showed and proved identity of drug. There was no interaction found in between drug and other ingredients. Absorption maxima of the Ibuprofen were determined by UV spectrophotometric method using UV/Visible spectrophotometer. The λ_{max} of Ibuprofen in phosphate buffer 6.8 is 221 nm. The standard curves of Ibuprofen were prepared in Phosphate buffer 6.8 in the concentration range of 10 to 50µg/ml. A straight line with r^2=0.9992 was found indicating that the drug follows Beer's law within the specified concentration range. The value of Hausner's ratio varies from 1.13-1.17. Bulk density varies from 0.222-0.251 and tapped density varies from 0.260-0.289. Whereas angle of repose varied from 22-31° which ensured good flow properties of powder. Carr's Index varies from 11.92 - 15.15. The general appearance of tablets, its visual identity and overall 'elegance' is essential for acceptability, the shape of all the formulation remained off white, smooth, flat faced circular and no visible cracks. In a weight variation test, the Pharmacopoeial limit for percentage deviation for the tablets of more than 250 mg is ±5%[18]. The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. The hardness of the tablet was measured by Monsanto tester and was ranged between 3.7±0.93 to 6.3±0.98 Kg/cm^2. Increasing tablet hardness provided a much great control over dissolution rate. The resistance of tablets to shipping or

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breakage, under conditions of storage, transportation and handling before usage depends on its hardness[22]. Friability is the measure of tablet strength. The friability was measured by Roche friabilator and was found 0.2 to 0.7 %, and this parameter given the satisfactory mechanical resistance of the tablet. In the present study the percentage friability for all the formulations was below 1% indicating that the friability is within the prescribed limits[26].

Table 2: Composition of different Ibuprofen floating tablets

Batch code	Ibuprofen (mg)	HPMC K4M (mg)	Xanthan gum (mg)	$NaHCo_3$ (mg)	M.C.C (mg)	Citric acid (mg)	Lactose (mg)	Mg stearate (mg)	Talc (mg)
F1	100	25	12	20	38	15	13	5	5
F2	100	12	25	18	38	12	11	5	5
F3	100	37	37	25	38	18	18	5	5
F4	100	50	50	30	38	25	20	5	5

Table 3: Evaluation parameters of Ibuprofen floating tablets

Batch code	Average weight (gm.), n=20	Hardness (kg/cm^3), n=6	Friability (%), n=20	Buoyancy lag time (sec)	Total floatation time (hrs)	% Drug Content, n=10
F1	0.485±0.03	3.7 ±0.93	0.7	120±1.01	>10	98.86±0.15
F2	0.492±0.14	6.3 ±0.98	0.3	100±1.78	>8	98.32±0.09
F3	0.500±0.25	4.2 ±1.26	0.5	200±1.46	>10	97.58±0.47
F4	0.468±0.09	5.9 ±1.35	0.2	240±1.59	>11	99.57±0.63

The drug content estimations showed values in the range of 97.58±0.47 to 99.57±0.06 %. These results showed the good drug content uniformity of the tablet. The release profiles of formulations F1, F2, F3 and F4, are shown in Figure 4. The release of drug mainly depends upon the polymer concentration. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs. The release profiles showed tri-phasic with initial burst effect (less than 30 min) followed by a polymer-controlled slower release in the second phase.

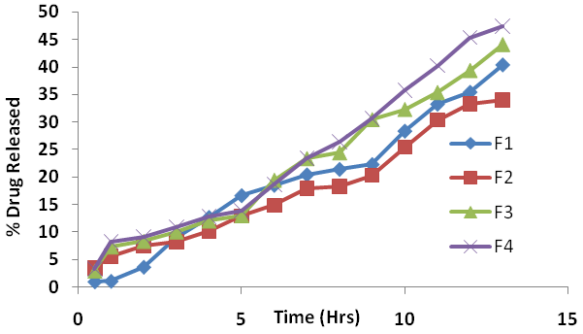

Figure 4: *In-vitro* % drug release profiles of Ibuprofen floating tablets

The difference in burst effect was the result of difference in the viscosity of the polymers. It is reported that citric acid level greatly influenced the drug release, irrespective of hydroxypropyl methyl cellulose grade. Lactose was used as diluents as well as channeling agent in the floating delivery of the drug.

In vitro release profile showed that on increasing the concentration of lactose release rate increased. Floating lag time for formulations of batches was found to in the range of 100±1.78 to 240±1.59 sec. The concentration of gas generating agent affected the floating lag time, as the amount of gas-generating agent was increased, the floating lag time decreased. The incorporation of gas generating agent exhibited reduction in the floating lag time. After the analysis of the above formulation and optimization study we can conclude that optimized formulation of batch F4 is the best and promising formulation for the delivery of the Ibuprofen in order to provide the controlled release and increased gastro retentive drug delivery system to reduce frequency of its administration.

CONCULSION

The ultimate aim of the present study was to prepare gastroretentive floating tablet of Ibuprofen using polymers like HPMC K4M by direct compression method. FTIR study concludes no drug polymer interaction. Different pre compression properties like Carr's Index, Hausner's ratio indicate good flow properties of powder. The formulations were evaluated for various parameters like hardness, friability, weight variation, floating lag time, floating time, *in-vitro* drug release etc. Based on different evaluation parameters formulation of batch F4 was concluded as an optimum formulation. The present research work was successful in improving the efficacy of Ibuprofen oral therapy as the drug release was extended reducing dosing frequency thereby improving patient compliance.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

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INTRODUCTION
Administration of drugs by oral route offers ease administration and gastrointestinal physiology offers more flexibility in dosage form design than other routes[1]. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half lives are eliminated quickly from the systemic circulation. So, there is need of frequent dosing of these drugs is required to achieve desired therapeutic activity. To avoid this, the development of oral sustained/controlled release formulations is an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. Floating drug delivery systems (FDDS) were first described by Davis in 1968[2]. Floating systems or Hydro-dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time while the system is floating on the gastric content; the drug is released slowly at the desired rate from the floating system. After release of drug, the residual system is emptied from the stomach[3]. This results in an increased Gastric retention time and a better control of the fluctuations in plasma drug concentration[4]. Gastro retentive systems confine the dosage forms for several hours inside the stomach and considerably prolong the gastric residence time of drugs[5]. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It is also beneficial for local drug delivery to the stomach and proximal small intestines[6]. Ibuprofen (iso-butyl-propanoic-phenolic acid) is a non-steroidal anti-inflammatory drug (NSAID). It is a propionic acid derivatives[7]. It is used for treatment of rheumatoid arthritis, degenerative joint disease, osteoarthritis, acute musculoskeletal disorders, and low back pain, fever. The bioavailability of the drug is 87-100% and the protein binding capacity is 98%[8]. It is metabolized by liver and it has a plasmatic half-life of 1.8–2.0 h as a result, it has to be administered three to six times a day. It is excreted through urine[9]. Hydrophilic polymer matrix is widely used for formulating sustained release dosage form. HPMC is widely used hydrophilic polymer to prolong

drug release due to its rapid hydration, good compression and gelling characteristics along with its ease of use, availability, and very low toxicity. It regulates the release of drug by controlling the swelling and cross-linking[10,11].

The main intention of this work was to formulate a single unit floating tablets of ibuprofen with use of HPMC for the release of the drug after a definite lag time and provides required concentration of drug at regular intervals of time which results reduction in frequency of dose of administration and will improve patient compliance[12].

MATERIALS AND METHODS

Ibuprofen was obtained as a gift sample from Leben Parma, Akola, Maharashtra, India. HPMC K4M, Xanthan gum, Citric acid, lactose and Sodium bicarbonate, Talc and MCC were obtained from Research Lab, Akola, Maharashtra, India. All the chemicals and reagents required for the present experimental work are of analytical grade.

Standard Calibration Curve

10 mg of Ibuprofen was weighed and dissolved in 10 ml of phosphate buffer 6.8, to give a solution of 1000 µg/ml concentration. From this solution 1 ml was taken and diluted to 10ml using Phosphate buffer 6.8 to produce a stock solution of 100µg/ml. From this stock solution different concentrations were prepared. The absorbance of these solutions was measured at 221 nm by UV spectrophotometer (Jasco V530 plus)[13].

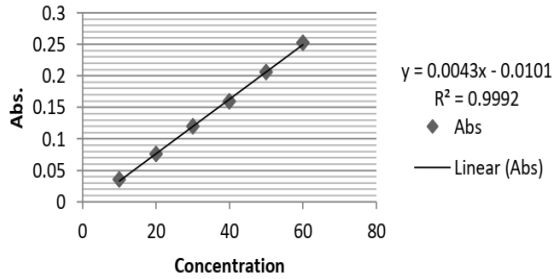

Figure 1: Standard calibration curve of Ibuprofen

Fourier Transform Infra-Red (FTIR) Spectroscopy

Interaction of drug with excipients was confirmed by carrying out IR interactions studies. Drug and excipients used in study were placed in air tight screw cap amber colored vials, then vials were kept at room temperature as well as in hot air oven at 40^0C for one week to get them moisture free and FT-IR analysis was carried out with saturated potassium bromide using pellet making method. Standard and KBr were taken in the ratio of 1:300 to make a solid disc or pellet with the help of Hydraulic Pellet Machine[14, 15].

Powder characterization

1. Bulk Density: It refers to packing of particles. The bulk density of the formulated granules was evaluated using a bulk density apparatus[16]. It is expressed in gm/ml and is given by below equation-

$$\text{Bulk density} = \frac{\text{Mass of the powder}}{\text{Volume of the bulk powder}}$$

2. Tapped density

Weighed quantity of tablet blend was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 and300 taps in tap density apparatus[17].

$$\text{Tapped density} = \frac{\text{Mass of the powder}}{\text{Tapped volume of the powder}}$$

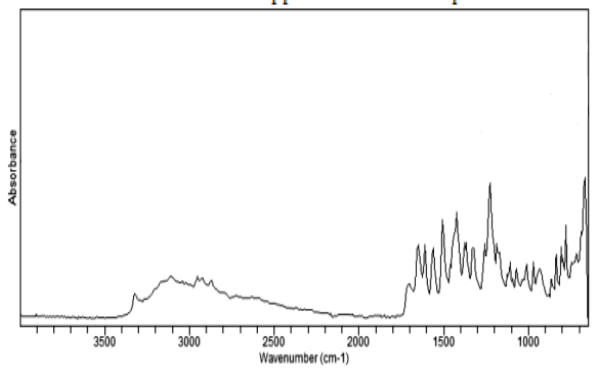

Figure 2: FTIR spectrum of Ibuprofen

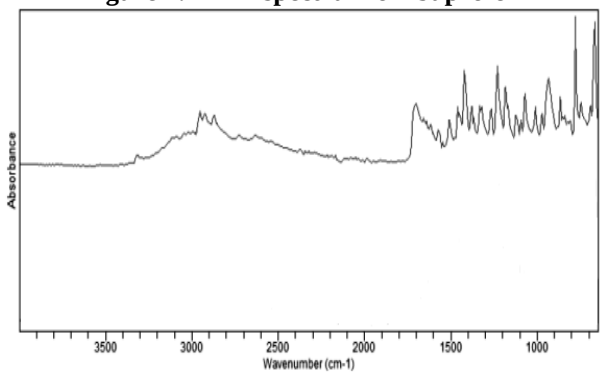

Figure 3: FTIR spectrum of mixture of Ibuprofen, HPMC K4M

3. Carr's Index (Compressibility)

The compressibility index and Hausner ratio was measures the property of powder to be compressed. The packing ability of tablet blend was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping[18].

It was indicated as Carr's compressibility index was calculated by following formula-

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{X100}$$

4. Hausner Ratio

It is measurement of frictional resistance of tablet blend[19]. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

5. Angle of Repose

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane2^0. It was determined by the following equation:

$$\tan\theta = \frac{h}{r}$$

Where, θ = Angle of repose, h = of powder heap.
r = Radius of the powder cone.

Preparation of Ibuprofen floating tablets

The composition of different formulations of Ibuprofen floating tablets is shown in Table 2. All the ingredients were accurately weighed and passed through mesh 60#. In order to mix the ingredients thoroughly drug and

polymer were blended and geometrically in a mortar and pestle for 15 minutes then magnesium stearate, sodium bicarbonate, talc, lactose and magnesium stearate were mixed one by one. After thoroughly mixing the ingredients, the powder was blend was passed through 44# sieve and compressed on rotary tablet punching machine[21,22].

Post compression parameters of Ibuprofen floating tablets

1. Weight uniformity test

Twenty Ibuprofen tablets were weighed individually, average weight was calculated and individual tablet weights were compared to the, average weight. The tablets met the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit[23].

2. Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked from each formulation and the mean and standard deviation values were calculated[24].

3. Friability

A friability test was conducted on Ibuprofen floating tablets using a Roche friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again[25,26]. The percentage friability was then calculated by,

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \text{X100}$$

4. Lag Time

The *In-vitro* buoyancy was determined by the lag time. The Ibuprofen tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for a tablet to rise to the surface for floating was determined as the lag time[27].

5. Floating Time

The Ibuprofen tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. The time for which the tablet remained floating on the surface of medium was determined as floating time[28].

6. Drug Content

Ten Ibuprofen tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 5 ml of Methanol and made up to 100 ml of 0.1 N HCl. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10 ml using 0.1 N HCl. Absorbance was measured at 221 nm using 0.1 N HCl as a blank. The amount of drug present in one tablet was calculated[29].

***7. In vitro* release studies**

In vitro drug release study for the prepared Ibuprofen floating tablets were conducted for period of 13 hours using a six station USP XXVI type II (paddle) apparatus at 37±0.5^{0}C and 50 rpm speed. The dissolution studies were carried out in triplicate for 10 hours in phosphate buffer of pH 6.8 under sink condition. At first half an hour and then every 1 hour interval samples of 5ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 221 nm for Ibuprofen by a UV- spectrophotometer[29].

RESULTS AND DISCUSSION

Floating tablets of Ibuprofen were developed in order increase the gastric residence time of drug, so that they can be retained in stomach for longer time to reduce the frequency of administration. Four different batches of tablets were made using HPMC K4M, along with effervescing agent sodium bicarbonate and citric acid to optimize the drug content, *in-vitro* buoyancy and *in-vitro* drug dissolution studies.

Table 1: Results of physical evaluation of pre-compression blend

Batch code	Angle of repose (θ)	Bulk Density	Tapped Density	Carr's Index	Hausner's ratio
F1	21	0.224	0.264	15.15	1.17
F2	22	0.222	0.260	14.61	1.17
F3	26	0.251	0.289	13.14	1.15
F4	25	0.229	0.260	11.92	1.13

The selection of viscosity grade of a polymer is an important consideration in the formulation of tablet. All the formulations were prepared by direct compression method. Preformulation is the first step in development of new formulation. Characteristic absorption bands in FTIR spectrum of the drug sample showed and proved identity of drug. There was no interaction found in between drug and other ingredients. Absorption maxima of the Ibuprofen were determined by UV spectrophotometric method using UV/Visible spectrophotometer. The λ_{max} of Ibuprofen in phosphate buffer 6.8 is 221 nm. The standard curves of Ibuprofen were prepared in Phosphate buffer 6.8 in the concentration range of 10 to 50µg/ml. A straight line with r^2=0.9992 was found indicating that the drug follows Beer's law within the specified concentration range. The value of Hausner's ratio varies from 1.13-1.17. Bulk density varies from 0.222-0.251 and tapped density varies from 0.260-0.289. Whereas angle of repose varied from 22-31° which ensured good flow properties of powder. Carr's Index varies from 11.92 - 15.15. The general appearance of tablets, its visual identity and overall 'elegance' is essential for acceptability, the shape of all the formulation remained off white, smooth, flat faced circular and no visible cracks. In a weight variation test, the Pharmacopoeial limit for percentage deviation for the tablets of more than 250 mg is ±5%[18]. The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. The hardness of the tablet was measured by Monsanto tester and was ranged between 3.7±0.93 to 6.3±0.98 Kg/cm^2. Increasing tablet hardness provided a much great control over dissolution rate. The resistance of tablets to shipping or

breakage, under conditions of storage, transportation and handling before usage depends on its hardness[22]. Friability is the measure of tablet strength. The friability was measured by Roche friabilator and was found 0.2 to 0.7 %, and this parameter given the satisfactory mechanical resistance of the tablet. In the present study the percentage friability for all the formulations was below 1% indicating that the friability is within the prescribed limits[26].

Table 2: Composition of different Ibuprofen floating tablets

Batch code	Ibuprofen (mg)	HPMC K4M (mg)	Xanthan gum (mg)	$NaHCo_3$ (mg)	M.C.C (mg)	Citric acid (mg)	Lactose (mg)	Mg stearate (mg)	Talc (mg)
F1	100	25	12	20	38	15	13	5	5
F2	100	12	25	18	38	12	11	5	5
F3	100	37	37	25	38	18	18	5	5
F4	100	50	50	30	38	25	20	5	5

Table 3: Evaluation parameters of Ibuprofen floating tablets

Batch code	Average weight (gm.), n=20	Hardness (kg/cm^3), n=6	Friability (%), n=20	Buoyancy lag time (sec)	Total floatation time (hrs)	% Drug Content, n=10
F1	0.485±0.03	3.7 ±0.93	0.7	120±1.01	>10	98.86±0.15
F2	0.492±0.14	6.3 ±0.98	0.3	100±1.78	>8	98.32±0.09
F3	0.500±0.25	4.2 ±1.26	0.5	200±1.46	>10	97.58±0.47
F4	0.468±0.09	5.9 ±1.35	0.2	240±1.59	>11	99.57±0.63

The drug content estimations showed values in the range of 97.58±0.47 to 99.57±0.06 %. These results showed the good drug content uniformity of the tablet. The release profiles of formulations F1, F2, F3 and F4, are shown in Figure 4. The release of drug mainly depends upon the polymer concentration. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs. The release profiles showed tri-phasic with initial burst effect (less than 30 min) followed by a polymer-controlled slower release in the second phase.

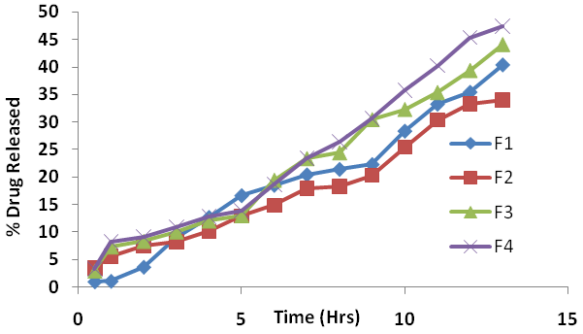

Figure 4: *In-vitro* % drug release profiles of Ibuprofen floating tablets

The difference in burst effect was the result of difference in the viscosity of the polymers. It is reported that citric acid level greatly influenced the drug release, irrespective of hydroxypropyl methyl cellulose grade. Lactose was used as diluents as well as channeling agent in the floating delivery of the drug.

In vitro release profile showed that on increasing the concentration of lactose release rate increased. Floating lag time for formulations of batches was found to in the range of 100±1.78 to 240±1.59 sec. The concentration of gas generating agent affected the floating lag time, as the amount of gas-generating agent was increased, the floating lag time decreased. The incorporation of gas generating agent exhibited reduction in the floating lag time. After the analysis of the above formulation and optimization study we can conclude that optimized formulation of batch F4 is the best and promising formulation for the delivery of the Ibuprofen in order to provide the controlled release and increased gastro retentive drug delivery system to reduce frequency of its administration.

CONCULSION

The ultimate aim of the present study was to prepare gastroretentive floating tablet of Ibuprofen using polymers like HPMC K4M by direct compression method. FTIR study concludes no drug polymer interaction. Different pre compression properties like Carr's Index, Hausner's ratio indicate good flow properties of powder. The formulations were evaluated for various parameters like hardness, friability, weight variation, floating lag time, floating time, *in-vitro* drug release etc. Based on different evaluation parameters formulation of batch F4 was concluded as an optimum formulation. The present research work was successful in improving the efficacy of Ibuprofen oral therapy as the drug release was extended reducing dosing frequency thereby improving patient compliance.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF IBUPROFEN GASTRO-RETENTIVE FLOATING TABLETS

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ABSTRACT
Objective: The objective of the present study was to formulate the gastro-retentive floating tablets containing Ibuprofen, which would remain in stomach and/or upper part of GIT for prolonged period of time. Floating systems have low bulk density so that they can float on the gastric juice in the stomach. Ibuprofen is an anti inflammatory drug.
Methods: On trial and error basis formulation design was done. Four different batches of floating tablets of Ibuprofen were prepared using HPMC, Xanthan gum, and gas generating agent sodium bicarbonate and citric acid. The tablets were characterized for the pre and post compression parameters such as friability, hardness, thickness, drug content, weight variation, *in-vitro* buoyancy studies and 13 hrs *in-vitro* drug release studies and the results were within the limits.
Results: There was no interaction found in between drug and other ingredients. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs.
Conclusion: From the results obtained, it was concluded that the optimized formulation F4 desired drug release properties and floating behavior.
Keywords: Citric acid, gastro-retentive floating tablets, HPMC K4M, Ibuprofen, sodium bicarbonate, xanthan gum.

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Standard Calibration Curve

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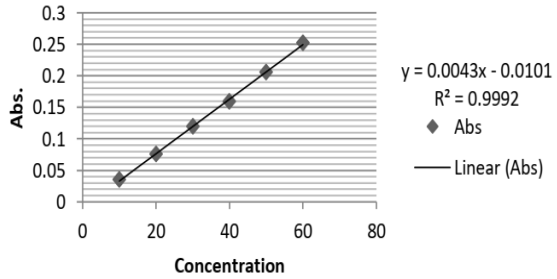


Figure 1: Standard calibration curve of Ibuprofen

Fourier Transform Infra-Red (FTIR) Spectroscopy

Interaction of drug with excipients was confirmed by carrying out IR interactions studies. Drug and excipients used in study were placed in air tight screw cap amber colored vials, then vials were kept at room temperature as well as in hot air oven at 40^0C for one week to get them moisture free and FT-IR analysis was carried out with saturated potassium bromide using pellet making method. Standard and KBr were taken in the ratio of 1:300 to make a solid disc or pellet with the help of Hydraulic Pellet Machine[14, 15].

Powder characterization

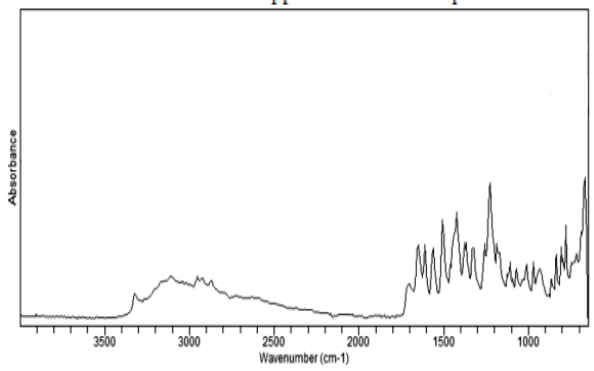
1. Bulk Density: It refers to packing of particles. The bulk density of the formulated granules was evaluated using a bulk density apparatus[16]. It is expressed in gm/ml and is given by below equation-

$$\text{Bulk density} = \frac{\text{Mass of the powder}}{\text{Volume of the bulk powder}}$$

2. Tapped density

Weighed quantity of tablet blend was into a graduated cylinder. Volume occupied by the drug was noted down. Then cylinder was subjected to 100, 200 and300 taps in tap density apparatus[17].

$$\text{Tapped density} = \frac{\text{Mass of the powder}}{\text{Tapped volume of the powder}}$$



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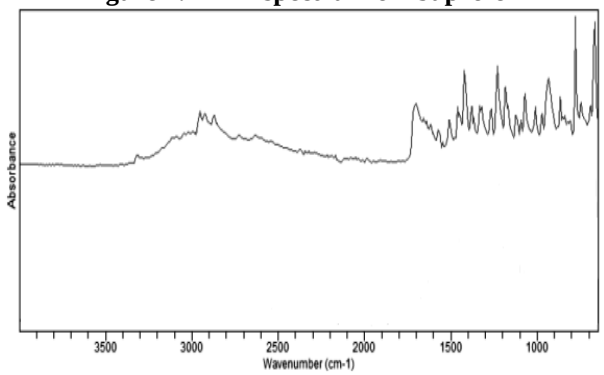

Figure 3: FTIR spectrum of mixture of Ibuprofen, HPMC K4M

3. Carr's Index (Compressibility)

The compressibility index and Hausner ratio was measures the property of powder to be compressed. The packing ability of tablet blend was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping[18].

It was indicated as Carr's compressibility index was calculated by following formula-

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \text{X100}$$

4. Hausner Ratio

It is measurement of frictional resistance of tablet blend[19]. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

5. Angle of Repose

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane2^0. It was determined by the following equation:

$$\tan\theta = \frac{h}{r}$$

Where, θ = Angle of repose, h = of powder heap.
r = Radius of the powder cone.

Preparation of Ibuprofen floating tablets

The composition of different formulations of Ibuprofen floating tablets is shown in Table 2. All the ingredients were accurately weighed and passed through mesh 60#. In order to mix the ingredients thoroughly drug and

polymer were blended and geometrically in a mortar and pestle for 15 minutes then magnesium stearate, sodium bicarbonate, talc, lactose and magnesium stearate were mixed one by one. After thoroughly mixing the ingredients, the powder was blend was passed through 44# sieve and compressed on rotary tablet punching machine[21,22].

Post compression parameters of Ibuprofen floating tablets

1. Weight uniformity test

Twenty Ibuprofen tablets were weighed individually, average weight was calculated and individual tablet weights were compared to the, average weight. The tablets met the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit[23].

2. Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked from each formulation and the mean and standard deviation values were calculated[24].

3. Friability

A friability test was conducted on Ibuprofen floating tablets using a Roche friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again[25,26]. The percentage friability was then calculated by,

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \text{X100}$$

4. Lag Time

The *In-vitro* buoyancy was determined by the lag time. The Ibuprofen tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for a tablet to rise to the surface for floating was determined as the lag time[27].

5. Floating Time

The Ibuprofen tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. The time for which the tablet remained floating on the surface of medium was determined as floating time[28].

6. Drug Content

Ten Ibuprofen tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 5 ml of Methanol and made up to 100 ml of 0.1 N HCl. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10 ml using 0.1 N HCl. Absorbance was measured at 221 nm using 0.1 N HCl as a blank. The amount of drug present in one tablet was calculated[29].

***7. In vitro* release studies**

In vitro drug release study for the prepared Ibuprofen floating tablets were conducted for period of 13 hours using a six station USP XXVI type II (paddle) apparatus at 37±0.5^{0}C and 50 rpm speed. The dissolution studies were carried out in triplicate for 10 hours in phosphate buffer of pH 6.8 under sink condition. At first half an hour and then every 1 hour interval samples of 5ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 221 nm for Ibuprofen by a UV- spectrophotometer[29].

RESULTS AND DISCUSSION

Floating tablets of Ibuprofen were developed in order increase the gastric residence time of drug, so that they can be retained in stomach for longer time to reduce the frequency of administration. Four different batches of tablets were made using HPMC K4M, along with effervescing agent sodium bicarbonate and citric acid to optimize the drug content, *in-vitro* buoyancy and *in-vitro* drug dissolution studies.

Table 1: Results of physical evaluation of pre-compression blend

Batch code	Angle of repose (θ)	Bulk Density	Tapped Density	Carr's Index	Hausner's ratio
F1	21	0.224	0.264	15.15	1.17
F2	22	0.222	0.260	14.61	1.17
F3	26	0.251	0.289	13.14	1.15
F4	25	0.229	0.260	11.92	1.13

The selection of viscosity grade of a polymer is an important consideration in the formulation of tablet. All the formulations were prepared by direct compression method. Preformulation is the first step in development of new formulation. Characteristic absorption bands in FTIR spectrum of the drug sample showed and proved identity of drug. There was no interaction found in between drug and other ingredients. Absorption maxima of the Ibuprofen were determined by UV spectrophotometric method using UV/Visible spectrophotometer. The λ_{max} of Ibuprofen in phosphate buffer 6.8 is 221 nm. The standard curves of Ibuprofen were prepared in Phosphate buffer 6.8 in the concentration range of 10 to 50µg/ml. A straight line with r^2=0.9992 was found indicating that the drug follows Beer's law within the specified concentration range. The value of Hausner's ratio varies from 1.13-1.17. Bulk density varies from 0.222-0.251 and tapped density varies from 0.260-0.289. Whereas angle of repose varied from 22-31° which ensured good flow properties of powder. Carr's Index varies from 11.92 - 15.15. The general appearance of tablets, its visual identity and overall 'elegance' is essential for acceptability, the shape of all the formulation remained off white, smooth, flat faced circular and no visible cracks. In a weight variation test, the Pharmacopoeial limit for percentage deviation for the tablets of more than 250 mg is ±5%[18]. The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. The hardness of the tablet was measured by Monsanto tester and was ranged between 3.7±0.93 to 6.3±0.98 Kg/cm^2. Increasing tablet hardness provided a much great control over dissolution rate. The resistance of tablets to shipping or

breakage, under conditions of storage, transportation and handling before usage depends on its hardness[22]. Friability is the measure of tablet strength. The friability was measured by Roche friabilator and was found 0.2 to 0.7 %, and this parameter given the satisfactory mechanical resistance of the tablet. In the present study the percentage friability for all the formulations was below 1% indicating that the friability is within the prescribed limits[26].

Table 2: Composition of different Ibuprofen floating tablets

Batch code	Ibuprofen (mg)	HPMC K4M (mg)	Xanthan gum (mg)	$NaHCo_3$ (mg)	M.C.C (mg)	Citric acid (mg)	Lactose (mg)	Mg stearate (mg)	Talc (mg)
F1	100	25	12	20	38	15	13	5	5
F2	100	12	25	18	38	12	11	5	5
F3	100	37	37	25	38	18	18	5	5
F4	100	50	50	30	38	25	20	5	5

Table 3: Evaluation parameters of Ibuprofen floating tablets

Batch code	Average weight (gm.), n=20	Hardness (kg/cm^3), n=6	Friability (%), n=20	Buoyancy lag time (sec)	Total floatation time (hrs)	% Drug Content, n=10
F1	0.485±0.03	3.7 ±0.93	0.7	120±1.01	>10	98.86±0.15
F2	0.492±0.14	6.3 ±0.98	0.3	100±1.78	>8	98.32±0.09
F3	0.500±0.25	4.2 ±1.26	0.5	200±1.46	>10	97.58±0.47
F4	0.468±0.09	5.9 ±1.35	0.2	240±1.59	>11	99.57±0.63

The drug content estimations showed values in the range of 97.58±0.47 to 99.57±0.06 %. These results showed the good drug content uniformity of the tablet. The release profiles of formulations F1, F2, F3 and F4, are shown in Figure 4. The release of drug mainly depends upon the polymer concentration. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs. The release profiles showed tri-phasic with initial burst effect (less than 30 min) followed by a polymer-controlled slower release in the second phase.

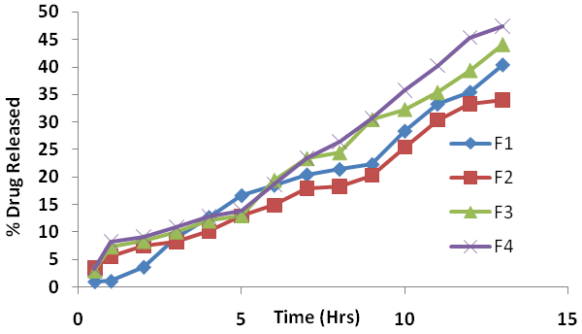

Figure 4: *In-vitro* % drug release profiles of Ibuprofen floating tablets

The difference in burst effect was the result of difference in the viscosity of the polymers. It is reported that citric acid level greatly influenced the drug release, irrespective of hydroxypropyl methyl cellulose grade. Lactose was used as diluents as well as channeling agent in the floating delivery of the drug.

In vitro release profile showed that on increasing the concentration of lactose release rate increased. Floating lag time for formulations of batches was found to in the range of 100±1.78 to 240±1.59 sec. The concentration of gas generating agent affected the floating lag time, as the amount of gas-generating agent was increased, the floating lag time decreased. The incorporation of gas generating agent exhibited reduction in the floating lag time. After the analysis of the above formulation and optimization study we can conclude that optimized formulation of batch F4 is the best and promising formulation for the delivery of the Ibuprofen in order to provide the controlled release and increased gastro retentive drug delivery system to reduce frequency of its administration.

CONCULSION

The ultimate aim of the present study was to prepare gastroretentive floating tablet of Ibuprofen using polymers like HPMC K4M by direct compression method. FTIR study concludes no drug polymer interaction. Different pre compression properties like Carr's Index, Hausner's ratio indicate good flow properties of powder. The formulations were evaluated for various parameters like hardness, friability, weight variation, floating lag time, floating time, *in-vitro* drug release etc. Based on different evaluation parameters formulation of batch F4 was concluded as an optimum formulation. The present research work was successful in improving the efficacy of Ibuprofen oral therapy as the drug release was extended reducing dosing frequency thereby improving patient compliance.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

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RESEARCH ARTICLE

FORMULATION AND EVALUATION OF IBUPROFEN GASTRO-RETENTIVE FLOATING TABLETS

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Rajarshi Shahu College of Pharmacy, Buldana, Maharashtra, India

ABSTRACT
Objective: The objective of the present study was to formulate the gastro-retentive floating tablets containing Ibuprofen, which would remain in stomach and/or upper part of GIT for prolonged period of time. Floating systems have low bulk density so that they can float on the gastric juice in the stomach. Ibuprofen is an anti inflammatory drug.
Methods: On trial and error basis formulation design was done. Four different batches of floating tablets of Ibuprofen were prepared using HPMC, Xanthan gum, and gas generating agent sodium bicarbonate and citric acid. The tablets were characterized for the pre and post compression parameters such as friability, hardness, thickness, drug content, weight variation, *in-vitro* buoyancy studies and 13 hrs *in-vitro* drug release studies and the results were within the limits.
Results: There was no interaction found in between drug and other ingredients. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs.
Conclusion: From the results obtained, it was concluded that the optimized formulation F4 desired drug release properties and floating behavior.
Keywords: Citric acid, gastro-retentive floating tablets, HPMC K4M, Ibuprofen, sodium bicarbonate, xanthan gum.

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INTRODUCTION
Administration of drugs by oral route offers ease administration and gastrointestinal physiology offers more flexibility in dosage form design than other routes[1]. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half lives are eliminated quickly from the systemic circulation. So, there is need of frequent dosing of these drugs is required to achieve desired therapeutic activity. To avoid this, the development of oral sustained/controlled release formulations is an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the systemic circulation for a long time. Floating drug delivery systems (FDDS) were first described by Davis in 1968[2]. Floating systems or Hydro-dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time while the system is floating on the gastric content; the drug is released slowly at the desired rate from the floating system. After release of drug, the residual system is emptied from the stomach[3]. This results in an increased Gastric retention time and a better control of the fluctuations in plasma drug concentration[4]. Gastro retentive systems confine the dosage forms for several hours inside the stomach and considerably prolong the gastric residence time of drugs[5]. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. It is also beneficial for local drug delivery to the stomach and proximal small intestines[6]. Ibuprofen (iso-butyl-propanoic-phenolic acid) is a non-steroidal anti-inflammatory drug (NSAID). It is a propionic acid derivatives[7]. It is used for treatment of rheumatoid arthritis, degenerative joint disease, osteoarthritis, acute musculoskeletal disorders, and low back pain, fever. The bioavailability of the drug is 87-100% and the protein binding capacity is 98%[8]. It is metabolized by liver and it has a plasmatic half-life of 1.8–2.0 h as a result, it has to be administered three to six times a day. It is excreted through urine[9]. Hydrophilic polymer matrix is widely used for formulating sustained release dosage form. HPMC is widely used hydrophilic polymer to prolong

drug release due to its rapid hydration, good compression and gelling characteristics along with its ease of use, availability, and very low toxicity. It regulates the release of drug by controlling the swelling and cross-linking[10,11].

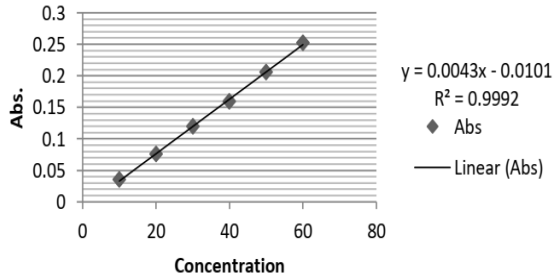
The main intention of this work was to formulate a single unit floating tablets of ibuprofen with use of HPMC for the release of the drug after a definite lag time and provides required concentration of drug at regular intervals of time which results reduction in frequency of dose of administration and will improve patient compliance[12].

MATERIALS AND METHODS

Ibuprofen was obtained as a gift sample from Leben Parma, Akola, Maharashtra, India. HPMC K4M, Xanthan gum, Citric acid, lactose and Sodium bicarbonate, Talc and MCC were obtained from Research Lab, Akola, Maharashtra, India. All the chemicals and reagents required for the present experimental work are of analytical grade.

Standard Calibration Curve

10 mg of Ibuprofen was weighed and dissolved in 10 ml of phosphate buffer 6.8, to give a solution of 1000 µg/ml concentration. From this solution 1 ml was taken and diluted to 10ml using Phosphate buffer 6.8 to produce a stock solution of 100µg/ml. From this stock solution different concentrations were prepared. The absorbance of these solutions was measured at 221 nm by UV spectrophotometer (Jasco V530 plus)[13].



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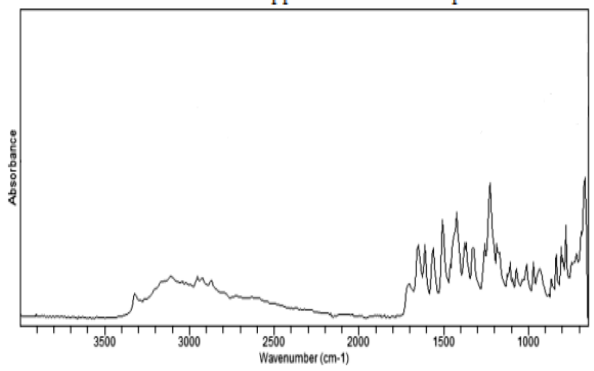
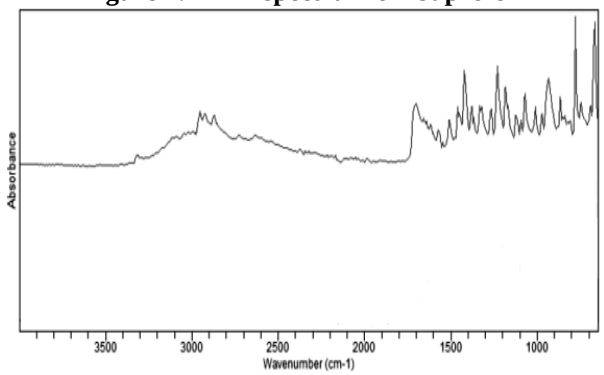


Figure 2: FTIR spectrum of Ibuprofen



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It is measurement of frictional resistance of tablet blend[19]. The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

5. Angle of Repose

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane2^0. It was determined by the following equation:

$$\tan\theta = \frac{h}{r}$$

Where, θ = Angle of repose, h = of powder heap.
r = Radius of the powder cone.

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Twenty Ibuprofen tablets were weighed individually, average weight was calculated and individual tablet weights were compared to the, average weight. The tablets met the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit[23].

2. Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked from each formulation and the mean and standard deviation values were calculated[24].

3. Friability

A friability test was conducted on Ibuprofen floating tablets using a Roche friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again[25,26]. The percentage friability was then calculated by,

$$\% \text{ Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \text{X100}$$

4. Lag Time

The *In-vitro* buoyancy was determined by the lag time. The Ibuprofen tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for a tablet to rise to the surface for floating was determined as the lag time[27].

5. Floating Time

The Ibuprofen tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. The time for which the tablet remained floating on the surface of medium was determined as floating time[28].

6. Drug Content

Ten Ibuprofen tablets were weighed and average weight was calculated. All the 10 tablets were crushed in a mortar. The powder equivalent to 10 mg was accurately weighed, dissolved in 5 ml of Methanol and made up to 100 ml of 0.1 N HCl. The volumetric flask was then shaken for approximately 20 minutes. The solution was filtered and 1 ml of filtrate was diluted to 10 ml using 0.1 N HCl. Absorbance was measured at 221 nm using 0.1 N HCl as a blank. The amount of drug present in one tablet was calculated[29].

***7. In vitro* release studies**

In vitro drug release study for the prepared Ibuprofen floating tablets were conducted for period of 13 hours using a six station USP XXVI type II (paddle) apparatus at 37±0.5^{0}C and 50 rpm speed. The dissolution studies were carried out in triplicate for 10 hours in phosphate buffer of pH 6.8 under sink condition. At first half an hour and then every 1 hour interval samples of 5ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 221 nm for Ibuprofen by a UV- spectrophotometer[29].

RESULTS AND DISCUSSION

Floating tablets of Ibuprofen were developed in order increase the gastric residence time of drug, so that they can be retained in stomach for longer time to reduce the frequency of administration. Four different batches of tablets were made using HPMC K4M, along with effervescing agent sodium bicarbonate and citric acid to optimize the drug content, *in-vitro* buoyancy and *in-vitro* drug dissolution studies.

Table 1: Results of physical evaluation of pre-compression blend

Batch code	Angle of repose (θ)	Bulk Density	Tapped Density	Carr's Index	Hausner's ratio
F1	21	0.224	0.264	15.15	1.17
F2	22	0.222	0.260	14.61	1.17
F3	26	0.251	0.289	13.14	1.15
F4	25	0.229	0.260	11.92	1.13

The selection of viscosity grade of a polymer is an important consideration in the formulation of tablet. All the formulations were prepared by direct compression method. Preformulation is the first step in development of new formulation. Characteristic absorption bands in FTIR spectrum of the drug sample showed and proved identity of drug. There was no interaction found in between drug and other ingredients. Absorption maxima of the Ibuprofen were determined by UV spectrophotometric method using UV/Visible spectrophotometer. The λ_{max} of Ibuprofen in phosphate buffer 6.8 is 221 nm. The standard curves of Ibuprofen were prepared in Phosphate buffer 6.8 in the concentration range of 10 to 50µg/ml. A straight line with r^2=0.9992 was found indicating that the drug follows Beer's law within the specified concentration range. The value of Hausner's ratio varies from 1.13-1.17. Bulk density varies from 0.222-0.251 and tapped density varies from 0.260-0.289. Whereas angle of repose varied from 22-31° which ensured good flow properties of powder. Carr's Index varies from 11.92 - 15.15. The general appearance of tablets, its visual identity and overall 'elegance' is essential for acceptability, the shape of all the formulation remained off white, smooth, flat faced circular and no visible cracks. In a weight variation test, the Pharmacopoeial limit for percentage deviation for the tablets of more than 250 mg is ±5%[18]. The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. The hardness of the tablet was measured by Monsanto tester and was ranged between 3.7±0.93 to 6.3±0.98 Kg/cm^2. Increasing tablet hardness provided a much great control over dissolution rate. The resistance of tablets to shipping or

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breakage, under conditions of storage, transportation and handling before usage depends on its hardness[22]. Friability is the measure of tablet strength. The friability was measured by Roche friabilator and was found 0.2 to 0.7 %, and this parameter given the satisfactory mechanical resistance of the tablet. In the present study the percentage friability for all the formulations was below 1% indicating that the friability is within the prescribed limits[26].

Table 2: Composition of different Ibuprofen floating tablets

Batch code	Ibuprofen (mg)	HPMC K4M (mg)	Xanthan gum (mg)	$NaHCo_3$ (mg)	M.C.C (mg)	Citric acid (mg)	Lactose (mg)	Mg stearate (mg)	Talc (mg)
F1	100	25	12	20	38	15	13	5	5
F2	100	12	25	18	38	12	11	5	5
F3	100	37	37	25	38	18	18	5	5
F4	100	50	50	30	38	25	20	5	5

Table 3: Evaluation parameters of Ibuprofen floating tablets

Batch code	Average weight (gm.), n=20	Hardness (kg/cm^3), n=6	Friability (%), n=20	Buoyancy lag time (sec)	Total floatation time (hrs)	% Drug Content, n=10
F1	0.485±0.03	3.7 ±0.93	0.7	120±1.01	>10	98.86±0.15
F2	0.492±0.14	6.3 ±0.98	0.3	100±1.78	>8	98.32±0.09
F3	0.500±0.25	4.2 ±1.26	0.5	200±1.46	>10	97.58±0.47
F4	0.468±0.09	5.9 ±1.35	0.2	240±1.59	>11	99.57±0.63

The drug content estimations showed values in the range of 97.58±0.47 to 99.57±0.06 %. These results showed the good drug content uniformity of the tablet. The release profiles of formulations F1, F2, F3 and F4, are shown in Figure 4. The release of drug mainly depends upon the polymer concentration. Maximum release was shown by formulation of batch F4 (47.38%), and minimum by the formulations of batch F2 (34.46%) in the duration of 13 hrs. The release profiles showed tri-phasic with initial burst effect (less than 30 min) followed by a polymer-controlled slower release in the second phase.

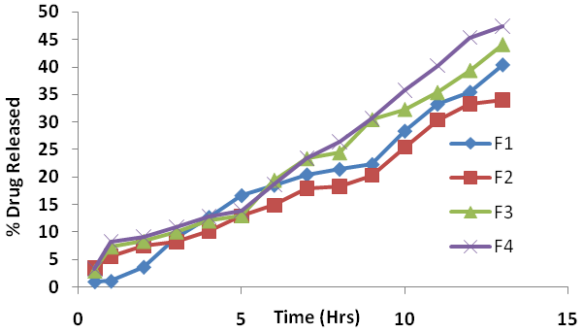

Figure 4: *In-vitro* % drug release profiles of Ibuprofen floating tablets

The difference in burst effect was the result of difference in the viscosity of the polymers. It is reported that citric acid level greatly influenced the drug release, irrespective of hydroxypropyl methyl cellulose grade. Lactose was used as diluents as well as channeling agent in the floating delivery of the drug.

In vitro release profile showed that on increasing the concentration of lactose release rate increased. Floating lag time for formulations of batches was found to in the range of 100±1.78 to 240±1.59 sec. The concentration of gas generating agent affected the floating lag time, as the amount of gas-generating agent was increased, the floating lag time decreased. The incorporation of gas generating agent exhibited reduction in the floating lag time. After the analysis of the above formulation and optimization study we can conclude that optimized formulation of batch F4 is the best and promising formulation for the delivery of the Ibuprofen in order to provide the controlled release and increased gastro retentive drug delivery system to reduce frequency of its administration.

CONCULSION

The ultimate aim of the present study was to prepare gastroretentive floating tablet of Ibuprofen using polymers like HPMC K4M by direct compression method. FTIR study concludes no drug polymer interaction. Different pre compression properties like Carr's Index, Hausner's ratio indicate good flow properties of powder. The formulations were evaluated for various parameters like hardness, friability, weight variation, floating lag time, floating time, *in-vitro* drug release etc. Based on different evaluation parameters formulation of batch F4 was concluded as an optimum formulation. The present research work was successful in improving the efficacy of Ibuprofen oral therapy as the drug release was extended reducing dosing frequency thereby improving patient compliance.

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

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