WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 10, 897-914. Research Article ISSN 2277– 7105

FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLET OF ISONIAZID

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Article Received on
09 June 2021,

Revised on 29 June 2021,
Accepted on 19 July 2021

DOI: 10.20959/wjpr202110-21190

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ABSTRACT

Sustained release tablet of isoniazid was formulated and evaluated The study was begun with the drug analysis. The linearity was achieved in the concentration range of 4-20µg/ml in 0.1N HCl at 263 nm with regression coefficient of 0.995. Development was started with guar gum. At the same time to enhance the matrixing ability of the above MCC was also been used. After preformulation work, matrix tablets of drug were prepared by non aqueous wet granulation method. Initially the concentration of polymer was optimized to get better matrixing property and sustain release of the drug, prepared formulation G-1 to G-3 were evaluated and observed that it was not self sufficient to achieve desired matrixing ability for desired time. So further, MCC was also incorporated into the formulations to form GM-1 to GM-3. On the basis of obtained results and release of the drug formula GM-2 was selected with release of total 84.41% drug release. The drug formulation GM-2, the concentration of lactose was optimized as channeling agent. In this regard, Formulations GML-1 and GML-2 were prepared and evaluated in comparison to GM-2. The drug release study of the formulation GML-1 and GML-2 both are showing good release. Formulation GML-2 was taken for further study with release of 94.56%.

KEYWORD: Isoniazid, Antitubercular, Sustained release.

INTRODUCTION

Oral drug delivery is the most preferred and convenient option as the oral route provides maximum active surface area among all drug delivery system for administration of various drugs because of certain advantages such as unit dosage form, low cost, cheapest for packaging. Tablets are one of the most stable and commonly administered oral dosage forms.[1,2,3]

Sustained release dosage form is defined as well characterized and reproducible dosage form, which is designed to control drug release profile at a specified rate to achieve desired drug concentration either in blood plasma or at target site.[4,5] This system will provide actual therapeutic control that would be temporal (time related), spatial (site related) or both.[6,7]

Isoniazid has Antitubercular effect, also known as isonicotinic acid hydrazide (INH). Isoniazid is often used together with rifampicin, pyrazinamide, and either streptomycin or ethambutol.[8] For latent tuberculosis it is often used by itself. It may also be used for atypical types of mycobacteria, such as *M. avium*, *M. kansasii*, and *M. xenopi*.[9,10]

The goal in designing sustained or controlled delivery systems is to reduce frequency of dosing or to increase the effectiveness of the drug by localization at the site of action, reducing the dose required, providing uniform drug delivery. Sustained release system is a type of modified drug delivery system that can be used as an alternative to conventional drug delivery system.[11]

MATERIAL AND MATHOD

Isoniazid was obtained as Gift sample from Sarv Biolab Private Limited, Kala Amb, Sirmour, H P. The Guar Gum, Micro Crystalline Cellulose (MCC), Lactose, Magnesium stearate and Ethyl Cellulose (EC) were bought from Himedia, Mumbai. All used chemicals and solvents were laboratory grade.

Mathods

Preformulation study

Organoleptic evaluation of drug: Organoleptic evaluation was evaluation in which we observed the physical properties of the drug like color, odor, test, physical state etc.

Solubility determination: Solubility of Isoniazid was tested in various solvents. A definite amount (10mg) of drug was dissolved in exact amount (10ml) of solvents at room temperature and observed by the UV- visible spectrometer.

Melting point of isoniazid: Melting point of Isoniazid was determined by Melting point Apparatus. It is performed by filling of drug in capillary tube. The capillary tube and thermometer dipped in apparatus at suitable place and switched on then the point at which drug started melting in the capillary reading of thermometer was recorded.

Partition coefficient of isoniazid: The partition coefficient of drug (Isoniazid) was determined in solvent system n-octanol/distilled water. Accurately weighed quantity of drug

(20mg) was taken in separating funnel containing 20ml n-octanol, 20ml distilled water. Then the funnel was vigorously mixed and kept to equilibrate for 6 hrs. The contents of both phases were separated. After appropriate dilution, the aqueous phase was analysed for Isoniazid against reagent blank solution using UV spectrophotometer. The drug concentration in n-octanol phase determined by subtracting the amount in aqueous phase from the total quantity of drug added to the vial. The partition coefficient value "p" was calculated by the following equation:-

$$P_{O/W} = C_{Oil} / C_{water}$$

Where,

$P_{O/W:}$ Partition coefficient is oil in to water

$C_{oil:}$ concentration of drug in oil

$C_{water:}$ concentration of drug in water

UV Spectrophotometric study of isoniazid

(a) Preparation of stock solution

10mg of exactly weighed Isoniazid was dissolved in adequate quantity of 0.1N HCl in 10ml volumetric flask and shaken (1000 µg/ml). The volume was made upto 10ml.

(b) UV-Scanning of t Isoniazid in 0.1N HCl to Determination of λ_{max}

1ml solution was taken from the stock solution in 10ml volumetric flask and make upto 10ml with 0.1N HCl resultant solution was 100µg/ml.

10µg/ml, Aliquot was scanned between 200-400 nm on a UV-Visible spectrophotometer against 0.1N HCl as blank.

(c) **Preparation of standard curve 0.1N HCl buffer**

Aliquots of the above solution were taken and dilute to get drug concentration in the range of 0-20µg/ml. The resulting dilutions (0-20 µg/ml) were scanned and Absorbance was measured by using UV/Visible spectrophotometer at λ_{max} 263 nm against 0.1N HCl as blank. Linear regressed calibration curve was created.

Compatibility studies of isoniazid with excipients: Compatibility study of Isoniazid with excipient was performed under different storage condition for one month. Drug and excipients were physically mixed and the physical mixture was divided in four parts, filled in glass vial and kept under different temperature and relative humidity condition. The control sample and a vial containing only drug was sealed and kept as such in low temperature

condition (2-8^{0}C). After one month the samples were withdrawn and physically observed for change in the physical characteristic of the drug-excipient mixture.

IR Spectroscopic study for drug excipients interaction: The IR spectra of drug and polymer (MCC) in ratio (1:1) were recorded to determine the suitability of selected polymer for Isoniazid using Infrared spectrophotometer. The IR analysis was performed with spectra measures over the frequency range 750-4000 cm^{-1}. The study was performed on FT-IR spectrometer, observed the spectra for, major deviation in comparison to the spectra of standard drug.

Method of formulation of granules

Granules were prepared by wet granulation method. Guar gum and Isoniazid were mixed homogeneously by pestle mortar. Lactose was used as filler and channeling agent. MCC solution in Ethanol was used as granulating agent. Granules were prepared by 30 mesh screen. Prepared granules were dry on hot air oven and stored in dry and cool place or in desiccator.

Characterization of prepared granules

Bulk density (D_b): It is the ratio of the total mass of the granules to the bulk of volume of the granules. It was measured by poured the weighed granules (passed through standard sieve) into a measuring cylinder and the initial volume was noted. This initial volume is called the bulk volume. From this, the bulk density was calculated according to the formula mention below. It is expressed in g/cc and is given by-

$$D_b = m/V_0$$

Where,

m – Mass of the granules

V_0 – Bulk volume of t`he granules

Tapped density (D_t): It is the ratio of total mass of granules to the tapped volume of the granules. The volume was measured by tapping the granules for 50 times. Then the tapping was done. Then the tapping was done for 75 times and the taped volume was noted (the different between these two volume should be less than 2%). If it is more than 2% tapping is continue for 125 times and tapped volume was note.

$$D_t = m/V_I$$

Where,

m – Mass of the granules

V_I – tapped volume of the granules

Angle of repose (θ): This is the maximum angle possible between the surface of a pile of the granules or granules and the horizontal plane.

The angle of repose of granules was determined by the funnel method. The funnel was fixed at a particular height (2.5 cm) on a burette stand. The granules sample was passed through the funnel until it forms a heap. Further, adding of the granules was stopped as soon the heap touches the tip of the funnel. The circle was drawn across it without disturbing pile. The radius and the height of the heap were noted down. The same procedure was repeated for three times and the average value was taken. The angle of repose was calculated by using equation.

$$\mathbf{Tan\ \theta = h/r}$$

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

Where, θ = Angle of repose; h = Height of the heap; r = Radius of the heap

Measurement of granules compressibility

(a) Compressibility index

The flow ability of the granules can be evaluated by comprising the Bulk Density (BD) and Tapped Density (TD) of granules and the rate at which it packed down. Compressibility Index of the granules was determined by the Carr's compressibility index:

$$\mathbf{CI\ (\%) = TD\text{-}BD/TD\ X\ 100}$$

(b) Hausner's ratio

It is the measurement of frictional resistance of the drug. The ideal range should be 1.2-1.5, it was determined by the ratio of tapped density and bulk density.

$$\mathbf{HR = Tapped\ Density/\ Bulk\ Density}$$

Formulation of matrix tablets

In Granules, talc (5% w/w) and magnesium stearate (5% w/w) were added as a glidant and lubricant respectively. Tablets were compressed using 9 mm die/punch set in a single punch tablet compression machine.

Evaluation of prepared matrix tablets

The evaluation of Matrix tablet dosage form with respect to various characteristics is vital to precisely control the dosage form behavior and to ensure batch-to-batch uniformity. The tablets were evaluated for thickness, weight variation, hardness, friability, matrixing property and *in vitro* drug release.

Thickness: The thickness of the tablets was determined using a thickness gauge. Five tablets from each batch were used, and average values were calculated.

Weight variation test: To study weight variation, 20 tablets were weighted individually and the arithmetic mean weight calculated. Not more than two tablets differ from the average weight by more than 5%.

Hardness and Friability: For each formulation, the hardness and friability tests of six tablets were performed using the Pfizer hardness tester and Roche friabilator, respectively.

Swelling behavior of the tablet: The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of all formulation was studied in a petridish containing pH 0.1N HCl. At the end of 0.5h and 1 h, the tablet was withdrawn, soaked with tissue paper, and weighed. Then for every 1 h, weights of the tablet were noted, and the method was continued till the end of 8 h. Percentage weight gain by the tablet was calculated by formula;

$$\mathbf{S.I = \{(Mt\text{-}Mo) / Mo\} X 100}$$

Where, S.I = swelling index; Mt = weight of tablet at time t (h) and

Mo = weight of tablet at zero time

***In-vitro* drug release study:** *in-vitro* release studies were carried out in the dissolution test apparatus USP Type II. The tests were done out in 900 ml of 0.1N HCl for 12 hrs at 75 rpm at 37±0.5^{o}C. 5 ml of the aliquot were withdrawn at different predetermined time intervals (1, 2, 4, 6, 8, and 12) and filtered. Sample was analyzed at 263 nm using UV/Visible spectrophotometer, 0.1N HCl was used as blank. 5 ml of 0.1N HCl was replaced in the vessel after each withdrawal to maintain the sink condition. The percentage drug release was calculated using the calibration curve and was plotted against function of time to study the pattern of drug release from tablets.

Optimization of formulation

The duty of formulating a dosage form to accomplish a desirable controlled release with the selection of potential excipients that allow the formulation of matrices having controlled

delivery characteristics and it should dissolve slowly enough to work as a reservoir for the delivery. Initial dummy batches were prepared using guar gum.

Optimization of 'drug: Polymer' ratio

In preliminary trial batches, dummy batches were prepared by using guar gum. Ratio of drug and guar gum were optimized to get better matrixing property and prolonged release for the desired time. Three formulations comprising changed ratio of guar gum is mentioned in the table.

Statistical treatment of data

Numerous theories/kinetics models describe drug dissolution from immediate and modified release dosage form. The release of drug from a polymeric matrix is complicated. It often involves drug diffusion, interface movement and various interactions.

In order to determine the mechanism of drug release from sustained release floating matrix tablets, the data were treated using following mathematical models:-

1. Zero order (cumulative percentage of drug released versus time)
2. First order (log percent of drug unreleased versus time)
3. Higuchi model (cumulative percentage of drug released versus square root of time)
4. Korsmeyer'- Peppas model (log of cumulative percentage of drug released versus log time)

The released data were plotted according to following equations,

1. Zero order : $M= M_0 – K_0t$
2. First order : $\text{Log } C= \text{Log } C_0 – K_t/2.303$
3. Higuchi square root law : $Q= kt^{1/2}$
4. Korsmeyer's model : $M_t/M_\infty= kt^n$

Where, M, C and Q is the amount of drug released at time t, M_0 and C_0 is total amount of drug and K_0, K_t and k are corresponding rate constant.

From the above equations the correlation coefficient and exponential (n) values for the final formulation have been calculated to identify the drug release mechanism the graphs for various mathematical treatment models.

RESULT AND DISCUSSION

Preformulation study

Organoleptic properties of drug isoniazid

Isoniazid was a solid, white, odorless, powder which is sweet in starting but bitter at last.

Solubility of isoniazid in different solvents

Solubility of Isoniazid was tested in various solvents at room temperature and observed, it was freely soluble in water and 6.8 pH buffer and soluble in ethanol, 0.1 N HCl, 0.1 N NaOH and methanol.

Melting point: Reported melting point of Isoniazid was 171.4^{0}C and Observed at 170.5 ^{0}C.

Partition coefficient: Partition coefficient of the drug was observed at 0.35±0.04.

Preparation of standard curve in 0.1N HCl

Table no. 9: Absorbance of different aliquots of Isoniazid at 263 nm.

S. no.	Concentration (µg/ml)	Absorbance
1	0	0
2	4	0.162
3	8	0.337
4	12	0.512
5	16	0.657
0	20	0.901

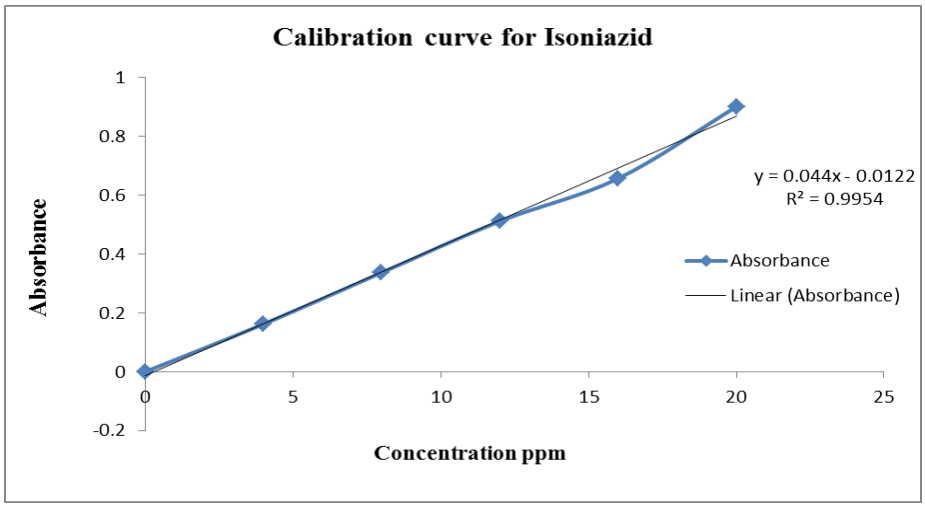

Figure no. 2: Graph showing calibration curve of Isoniazid (0.1N HCl).

Compatibility studies of isoniazid with excipients

Compatibility study of Isoniazid drug-excipient mixture was performed. The observations were given in the table below.

Table no. 10: Physical drug-polymer compatibility studies.

S. no.	Drug-Excipient	Initial	30 Days study Condition			Comments
			CS	RT	Oven	
1.	Drug +Polymer (1:1)	Cream Color	NC	NC	NC	Compatible
2.	Drug +Polymer (1:1)	Cream Color	NC	NC	NC	Compatible
3.	Drug +Polymer (1:1)	Cream Color	NC	NC	NC	Compatible
4.	Drug +Polymer (1:1)	Cream Color	NC	NC	NC	Compatible
5.	Drug +Polymer (1:1)	Cream Color	NC	NC	NC	Compatible

In one-month study no change was observed in the physical characteristics of the drug in presence of the excipients. This shows that there is no incompatibility between Isoniazid and excipients.

FT-IR Spectroscopic study for Drug-Excipients Interaction

The study was performed on FT-IR, the spectra shows no major deviation, in comparison to the spectra of standard drug.

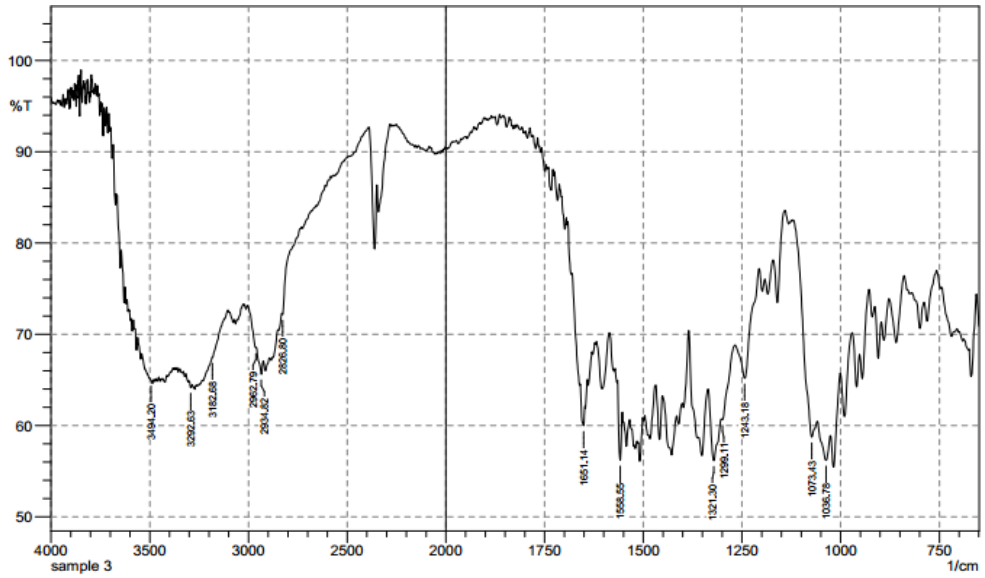

Figure no. 4: FT-IR graph of drug (Isoniazid) and polymer (Guar gum).

Pharmaceutical characterization of granules

Table no. 11: Micromeritic properties of granules.

Formulation	Parameter				
	BD (g/ml)	TD (g/ml)	CI (%)	HR	Angle of Repose
G-1	0.64±0.02	0.75±0.02	14.67±0.13	1.17±0.01	30.06±0.23
G-2	0.64±0.02	0.67±0.01	04.48±0.04	1.04±0.01	29.56±0.21
G-3	0.58±0.01	0.69±0.01	15.94±0.11	1.19±0.02	29.20±0.13
GM-1	0.56±0.01	0.67±0.01	16.42±0.16	1.19±0.01	29.24±0.19
GM-2	0.62±0.01	0.74±0.01	16.21±0.07	1.19±0.02	29.10±0.21
GM-3	0.68±0.01	0.78±0.01	12.82±0.13	1.15±0.01	30.01±0.23

Optimization of drug: Polymer ratio

In preliminary trial batches, dummy batches were prepared by using guar gum. Ratio of drug and guar gum were optimized to get better matrixing property and prolonged release for the desired time. Three formulations comprising changed ratio of guar gum is mentioned in the table below:

Table no. 12: Formulation of isoniazid matrix tablet with different concentration of guar gum.

S. no.	Ingredients (mg/tab)	G-1	G-2	G-3
1.	Drug (Isoniazid)	200	200	200
2.	Guar gum	200	300	400
3.	Lactose	100	100	100
4.	EC in alcohol 1% w/v	50	50	50
5.	Talc	50	50	50
6.	Mg stearate	100	100	100
7.	Total weight of tablet	700	800	900

Evaluation of batches G-1 to G-2

The Monsanto hardness tester was used to define the hardness of the tablets. The diameter and thickness of the tablets were determined using measuring scale and Vernier's calipers. As the hardness of the tablet was not optimum and breaking frequently so these were taken for the further study and it was decided to incorporate MCC too to provide sufficient strength and martrixing ability to the tablet.

Table no. 13: Formulation of isoniazid matrix tablet containing Guar gum with different concentration of MCC.

S. no.	Ingredients (mg/tab)	GM-1	GM-2	GM-3
1.	Drug (Isoniazid)	200	200	200
2.	Guar gum	300	300	300

3.	MCC	50	100	150
4.	Lactose	100	100	100
5.	EC in alcohol 1% w/v	50	50	50
6.	Talc	50	50	50
7.	Mg stearate	100	100	100
8.	Total weight of tablet	850	900	950

Evaluation of batches GM-1, GM-2 and GM-3

Determination of hardness, thickness and diameter of the tablets were determined and results were showed in the table below:

Table no. 14: Hardness, Thickness and Diameter isoniazid tablets.

S. no.	Parameter	Formulation code		
		GM-1	GM-2	GM-3
1.	Hardness (kg/cm^2)	4.1 ± 0.5	5.5 ± 0.43	5.8 ± 0.31
2.	Thickness (mm)	2.3	2.5	2.7
3.	Diameter (mm)	9.1	9.1	9.1

Weight variation, content variation friability and Swelling behavior in terms of swelling Index were also calculated. The results obtained for the different batches are stated in the table below:

Table no. 15: General characteristics of tablets.

Code	Weight variation test (%)	Content Variation	Hardness (Kg/cm^2)	% Friability	Swelling Index
GM-1	2.52 ± 0.11	94.6%	5.5 ± 0.50	0.21	55
GM-2	1.25 ± 0.17	93.8%	5.8 ± 0.43	0.25	60
GM-3	1.32 ± 0.08	95.4%	5.7 ± 0.31	0.18	66

Swelling behavior in terms of swelling Index was calculated and the swelling Index for the various formulations is reported in the table below:

Table no. 16: Swelling Index and Observation for swelling.

Sr. no.	Formulation	Swelling Index	General observation related to swelling
1	G-1	45	Swell and burst (not able to measure)
2	G-2	48	Slow swell But get deform after 2-3 hr release propertis
3	G-3	52	Swelling occurs but get deformed
4	GM-1	53	Slow swelling but get deformed
5	GM-2	63	Slow swelling
6	GM-3	69	Slow swelling

In-vitro drug release study of GM-2 and GM-3

Formulation GM1 was not having the sufficient matrixing property for the desired time so it is discarded for further study. For the further study formulation GM-2 and GM-3 were subjected to the dissolution study.

Table no. 17: *In vitro* drug release of batch GM-2 and GM-3.

Time(hr)	Cumulative percentage of drug release	
	GM-2 ± SD	GM-3 ± SD
0	0	0
1	19.42±1.21	16.21±0.42
2	29.93±1.52	27.29±0.34
4	43.24±0.89	37.48±1.22
6	54.82±1.43	49.44±1.33
8	71.38±2.04	63.25±2.04
12	77.84±0.82	74.87±1.83
24	84.41±1.82	79.45±1.23

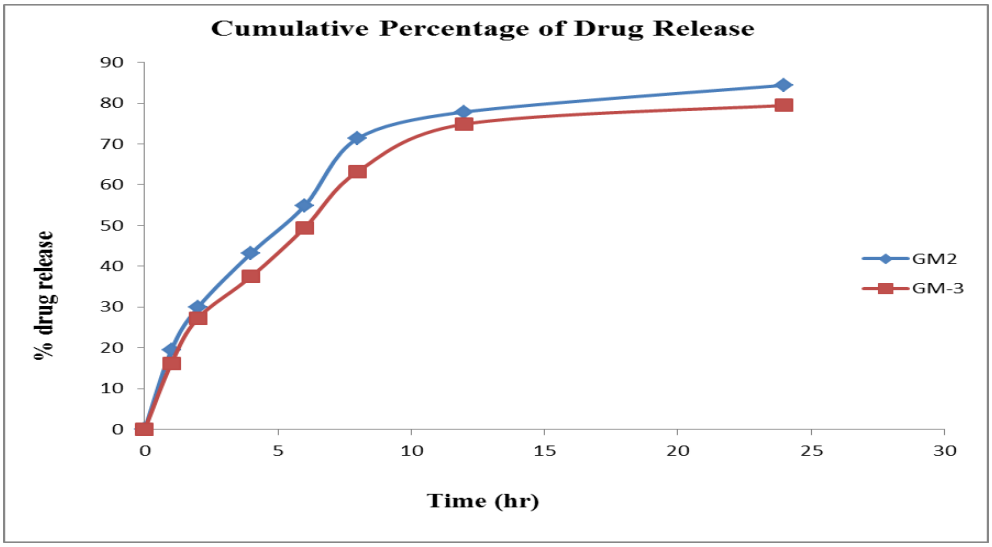

Figure no. 6: Dissolution profiles of formulation GM-2 and GM-3.

Optimization of concentration of lactose as channeling agent

On the basis of matrixing property and release behavior, formulation GM-2 was selected for the further study. It is clearly mentioned in the literature that lactose work as channeling agent to enhance the release of the drug. So in the further steps concentration of lactose was optimized for getting the optimum release of the Isoniazid. Three basic formulations with variable lactose concentration mentioned in the table below:

Table no. 18: Formulas for isoniazid matrix tablet containing different concentrations of lactose.

S. no.	Ingredients (mg/tab)	GM-2	GML-1	GML-2
1.	Drug (Isoniazid)	200	200	200
2.	Guar gum	300	300	300
3.	MCC	100	100	100
3.	Lactose	100	125	150
4.	EC in alcohol 1% w/v	50	50	50
5.	Talc	50	50	50
6.	Mg stearate	100	100	100
7.	Total weight of tablet	900	925	950

Evaluation of Batches GM-2, GML-1 and GML-2

Determination of hardness, Thickness and Diameter of tablets

The Monsanto hardness tester was used to define the hardness of the tablets. The diameter and thickness of the tablets were determined using measuring scale and Vernier's calipers and results are shown in the table below:

Table no. 19: Hardness, Thickness and Diameter isoniazid tablets.

S. no.	Parameter	Formulation code		
		GM-2	GML-1	GML-2
1.	Hardness (kg/cm^2)	5.8 ± 0.43	5.6 ± 0.50	5.9 ± 0.41
2.	Thickness (mm)	2.4	2.5	2.6
3.	Diameter (mm)	9.1	9.1	9.1

Determination of weight variation, content Variation and Friability

Weight variation test, content variation test and friability test for the different batches were achieved as per the I.P 2010. Swelling behavior in terms of swelling Index was also calculated as per the procedure mentioned above. The results achieved for the different batches are mentioned in the table below:

Table no. 20: General characteristics of tablets.

Code	Weight variation test (%)	% Drug Content	Hardness (Kg/cm^2)	% Friability	Swelling Index
GM-2	5.15 ± 0.27	82.4%	5.8 ± 0.43	0.11	61
GML-1	5.82 ± 0.61	96.2%	5.6 ± 0.50	0.13	63
GML-2	6.52 ± 0.54	94.3 %	5.9 ± 0.41	0.09	71

***In-vitro* drug release study**

Formulation GM-2 was showing the release of approx. 82.4% in 24 hr so it is not further taken for the release study. Further study was continued with the formulation GML-1 and

GML-2 and these were subjected to the dissolution study with the media and conditions as mentioned above.

Table no. 21: *In-Vitro* release profile of GML-1 Formulation.

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	20.88	1.319	79.12	1.898
2	1.141	0.301	29.54	1.470	70.46	1.848
4	2	0.602	38.06	1.580	61.94	1.792
6	2.449	0.777	47.62	1.677	52.38	1.719
8	2.828	0.903	58.38	1.766	41.62	1.619
12	3.464	1.079	70.84	1.850	29.16	1.465
24	4.898	1.380	90.54	1.957	09.46	0.976

Table no. 22: *In-Vitro* release profile of GML-2 formulation.

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	23.11	1.363	76.89	1.886
2	1.141	0.301	32.88	1.516	67.12	1.827
4	2	0.602	42.52	1.628	57.48	1.759
6	2.449	0.777	51.62	1.713	48.38	1.685
8	2.828	0.903	63.88	1.805	36.12	1.558
12	3.464	1.079	76.44	1.883	23.56	1.372
24	4.898	1.380	94.56	1.976	05.44	0.736

Statistical treatment of data

Zero order kinetics of GML-1 and GML-2

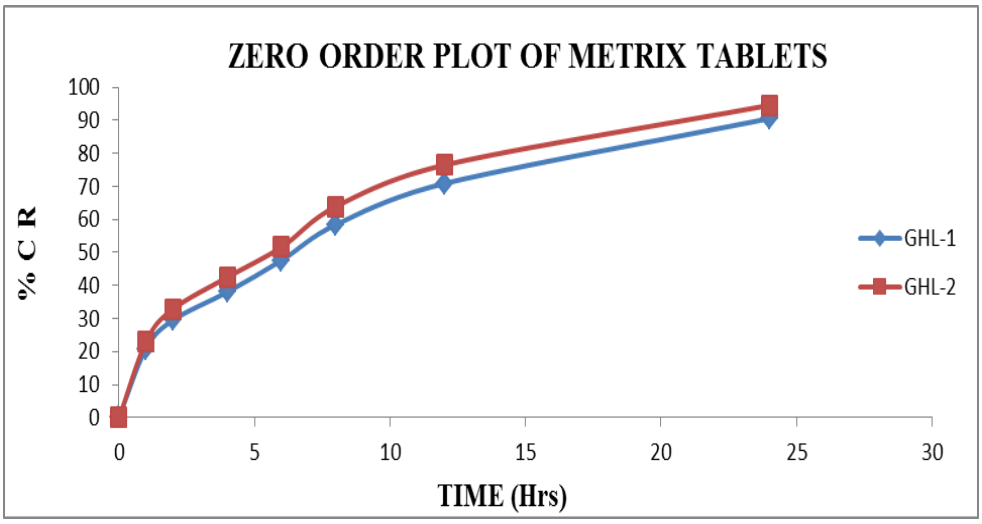

Figure no. 7: Zero order plot for matrix tablets.

First order kinetics for GML-1 and GML-2

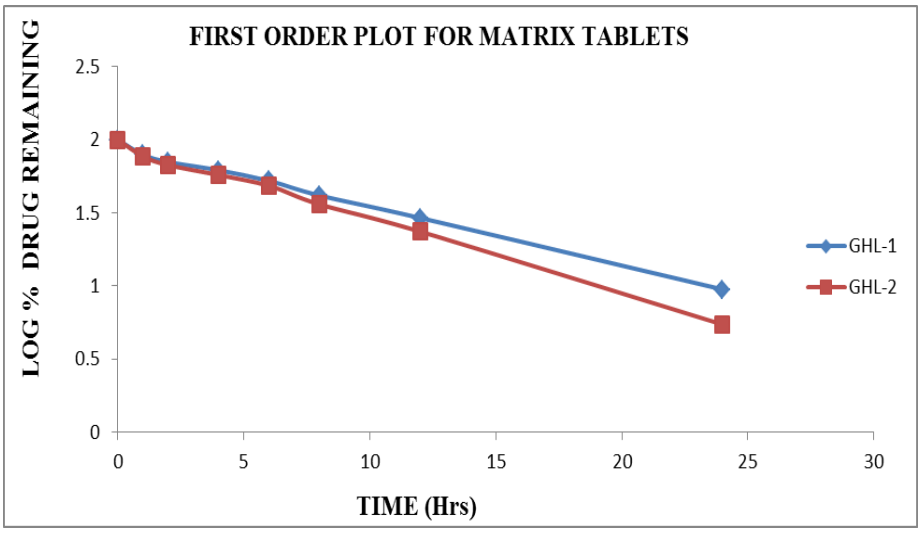

Figure no. 8: First order plot for matrix tablets.

Higuchi Model for GML-1and GML-2

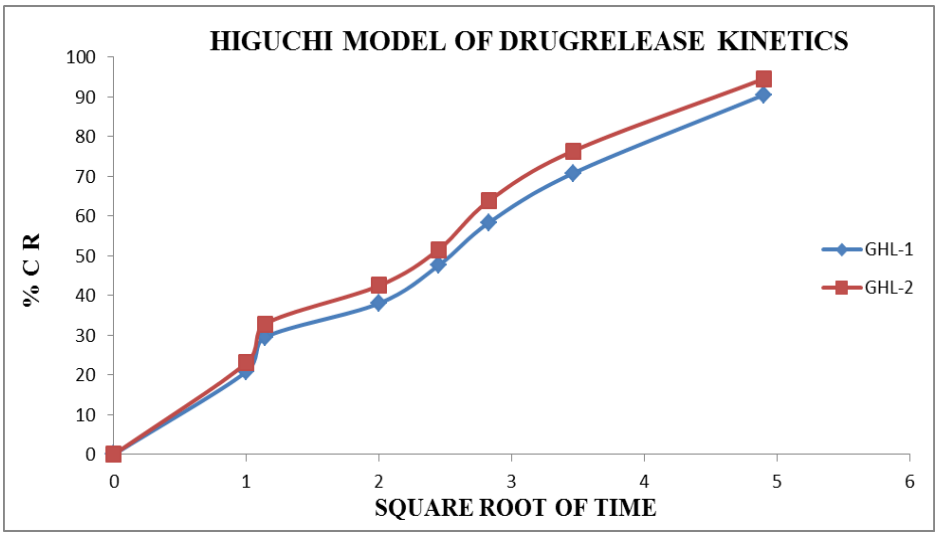

Figure no. 9: Higuchi model for matrix tablets.

DISCUSSION

Isoniazid has Antitubercular effect, also known as isonicotinic acid hydrazide (INH). Isoniazid is often used together with rifampicin, pyrazinamide, and either streptomycin or ethambutol. The study was begun with the drug analysis as the isoniazid is white, odorless, and sweet to bitter solid and preparation of calibration on a UV-Visible spectrophotometer. The linearity was achieved in the concentration range of 4-20µg/ml in 0.1N HCl at 263 nm with regression coefficient of 0.995 following to the equation Y=0.044x + 0.012. The FT-IR spectra study also checks the drug and excipient compatibility.

Hydrophilic matrices are always had been point of interest during the development of an oral sustained-release formulation. Such polymeric system particularly from the natural origin can be used for sustained release of both water-soluble and water-insoluble drugs.

Development was started with guar gum. At the same time to enhance the matrixing ability of the above MCC was also been used. To rule out any type of physical incompatibility between drug and excipient, 1:1 blends of drug and excipient were kept under different temperature conditions for one month. Isoniazid was found to be compatible with the guar gum and other excipients selected in the present studies like MCC and EC etc.

The interference of selected polymer was also studied to rule out the negative effects because of polymer. Spectrophotometric estimation of Isoniazid in presence of guar gum was studied and it was found that that there is no major change in absorbance or wavelength. The IR spectra of drug and polymer combination show no major deviation, in comparison to the spectra of standard drug.

After preformulation work, matrix tablets of drug were prepared by non aqueous wet granulation method. Initially the concentration of polymer was optimized to get better matrixing property and sustain release of the drug, prepared formulation G-1 to G-3 were evaluated and observed that it was not self sufficient to achieve desired matrixing ability for desired time. So further, MCC was also incorporated into the formulations to form GM-1 to GM-3. On the basis of obtained results and release of the drug formula GM-2 was selected with release of total 84.41% drug release. But the release of the drug in this formulation was not optimum so for increasing the release of the drug formulation GM-2, the concentration of lactose as channeling agent was further optimized to improve the release of the drug from polymer matrix. In this regard, Formulations GML-1 and GML-2 were prepared and evaluated for the various properties in comparison to GM-2 and the results are mentioned in the table. The drug release study of the formulation GML-1 and GML-2 both are showing good release but the formulation GML-1 get deform during the study so formulation GML-2 was taken for further study with release of 94.56%. During the study it was also been saw that if the concentration of lactose is increased more than optimum it resulted in the burst release of the formulation which in not desired so the formulation with higher lactose was not considered for the drug release study.

To find out the mechanism of drug released from the final formulations GML-1 and GML-2 of Isoniazid matrix tablets, the data was fitted to zero order, first order and Higuchi model.

When the data obtained for release of drug for final formulation GHL-1 and GHL-2 were plotted according to the first order equation, the formulation shows a fair linearity, with correlation coefficient values of 0.967 and 0.965 respectively which indicates greater the concentration faster the release rate of drug from tablet.

Release of the drug from a matrix tablet containing hydrophilic polymers generally includes factor of diffusion. Diffusion is related to transport of drug from the dosage matrix in to the *in-vitro* study fluid depending on the concentration. As gradient varies, the drug was released and the distance for diffusion increases. This could explain why the drug diffuses at a comparatively slower rate as the distance for diffusion increases, which was referred as square root kinetics or Higuchi's kinetics. In this experiment, the *in vitro* release profiles of drug the formulation could be best expressed by Higuchi's equation showing high linearity for both the formulation GML-1 and GML-2, representing the release process under the drug diffusion through polymer matrix.

CONCLUSION

The use of hydrophilic polymer matrix is one of the most widespread approaches in formulating a sustained-release dosage form. This is due to the fact that these formulations are relatively flexible and a well-designed system usually gives reproducible release profile. In the present work initially the polymers: drug ratio was optimized to get the better matrixing property and sustained release of the drug. The optimum ratio of drug-polymer was found in formulation GML-2.

In the present study it was found that Micro Crystalline cellulose (MCC) in combination with guar gum can be successfully used for the formulation of matrix tablet of Isoniazid without any interference with Isoniazid, it can also be concluded that this polymer alone or in combination with other polymers may be used for the formulation of any drug delivery system where matrix formation is required.

CONFLICTS OF INTEREST

There are no conflicts of interests.

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