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Formulation Development and Evaluation of Doxofylline Sustained-Release Tablets by Using Chitosan and Guar Gum

Pawan Avhad [a*†] and Revathi Gupta [b]

[a] Dr. A. P. J. Abdul Kalam University, Arandia, Indore-452016 (M.P.) India.
[b] Faculty of Pharmacy, Dr. A. P. J. Abdul Kalam University, Arandia, Indore-452016 (M.P.) India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

The sustained-release dosage form is a well-characterized and reproducible dosage form that is designed to control drug release profile at a certain rate to reach desired drug concentration in blood plasma or at the target site. There is immense demand in the market for new sustained-release formulations used for new drug molecules which release the drug at a sustained rate. Doxofylline is one of the widely useful drugs in the market and needs to be given in a single dose for a long duration of time. For the same, we have prepared a sustained released Doxofylline tablet.

Aim: This research was done to design, formulate and evaluate Doxofylline sustained-release tablets by using different concentrations of Chitosan and Guar Gum.

Methods: The factorial design was used to prepare Doxofylline sustained-release tablet. Doxofylline sustained-release tablets were prepared to employ different concentrations of Chitosan, Guar Gum, Lactose, and Magnesium Stearate in different combinations by wet granulation technique. Total 9 formulations were designed, formulated, and evaluated for the hardness, thickness, friability, % drug content, and *in-vitro* drug release.

Results: A study of the release of drug by *in-vitro* found that F8 is to be the best efficient formulation which consists of both Chitosan and Guar Gum helped in delayed the release of drug

† Research Scholar;
**Corresponding author: E-mail: pawanavhad@gmail.com;*

up to 24 hours and performs excellent release of drug in starting hours of drug release in the body. The drug released from the F8 formulation indicates the kinetic model of First Order, by anomalous diffusion. The formulation F8 shows optimum thickness, hardness and at 40ºC±2 99.35% drug release after 24 hours shows optimum formulation.

Conclusion: This study concludes that better drug release was observed by using natural polymers. Doxofylline with natural polymer shows good release and better dissolution rate as compared with a single synthetic polymer. Synthetic drug with natural polymer shows more future scope and this work will help the researcher in the future.

Keywords: Chitosan; doxofylline; guar gum; polymer; sustained-release.

1. INTRODUCTION

Most of the traditional oral medications like tablets and others are widely used in the Indian market. Chronic diseases need frequent medication after some time of interval in such cases sustained-release medication helps us for a long duration of action [1]. Many things affect the oral administration of the drug up to its therapeutic activity in that condition new technique or polymer should be used to overcome this. This formulation reduces the frequency of the dose of the drug. Many synthetic polymers play an important role in sustained release formulation, nowadays natural polymers are also useful due to their safety and economical point. Natural polymers are non-carcinogenic, non-toxic, biodegradable, biocompatible, and safe. Oral sustained release formulation by using the wet granulation method and the natural polymer is the most interesting topic for research [2]. The selection of dug for these types of formulation is also challenging. Doxofylline is a new generation methylxanthine drug used in the treatment of asthma belonging to the BCS Class III drug [3]. It is very important to design an optimized formulation with an appropriate dissolution rate in a less period and minimum trials. Different statistical experimental designs were recognized as useful techniques to optimize the process variables. For this purpose, a factorial design was used [4,5].

1.1 Sustained-Release Drug Delivery

Sustained-release drug delivery can show predetermine release by maintaining sustained medication activity at a specified rate while minimizing undesired side effects by keeping a reasonably same, efficacy level of drug in the body [6,7]. Local effect of the drug-related to diseased tissue by keeping the controlled release system in space. Different carriers and particles are used to transfer the drug to the target organ. Many oldest dosage forms suspension, emulsion, tablet capsules, suppositories, etc. have a few drawbacks, like drugs having a short half-life need repeated drug administration, which increases the like hood of skipping a dose of a drug resulting in fewer patient compliance [8]. Drug's steady-state level cannot be maintained in the body because of peak-valley due to absorption and elimination of the drug from the body and this would lead to underdose or overdose, as uniform drug amount increases or decrease above the range of therapeutic. When an overdose occurs, changing drug levels may precipitate undesirable consequences, especially if the substance has a small therapeutic index [9].

1.2 Merits of Sustained-Release Dosage Form

Sustained-release dosage form gives a long-term therapeutic effect by continuously releasing the drug. It reduces frequent dosing of drugs and gives prolong action [10]. It provides patient compliance. It does not require any special storage conditions and handling precautions. Drugs having nauseous taste and smell can be given by the above formulation. It reduces local side effects by reducing the total amount of drugs. The more stable dosage form as compared to others [7,11].

1.3 Types of Sustained Action Systems

1.3.1 Diffusion controlled system

Reservoir Storage System: The inner raw part of the drug is covered by polymer material. Drug release is dependent upon the nature of the membrane. It is possible to release the drug by Zero Order by this system. Those molecules which have high molecular weight have low delivery by using this type of device.

Matrix Devices: This consists of an appropriate combination of a drug molecule with a polymer

matrix. Those compounds having high molecular weight can be easily delivered by this device.

1.3.2 Dissolution controlled release system

Matrix Release System: Drugs are surrounded by a slowly dissolving polymer membrane. The drug also got protection from other things.

Encapsulation Dissolution Control: Similar to microencapsulation by coating seeds, granules, and particles.

1.3.3 Diffusion and dissolution controlled system

Used for those drugs which have high doses and low half-life. The drug is uniformly mixed with matrix and release drug either swelling, hydrolysis, or using enzymatic attack. By imbibing mechanism or by addition of hydrogen or by enzyme action [12,13].

1.4 Drug Removal Mechanism by Matrix Tablet

In a biodegradable matrix system, drug release is determined by polymer erosion from the matrix surface; whereas in hydrophilic matrices gel layer is formed and it depends upon time-release functions. The thickness of the layer of gel will determine the diffusion path length of drug molecules. As soon as swelling continues gel becomes thick and it results in slow drug release from polymer; but, because of regular hydration polymer gets disintegrated from the matrix surface which results in reducing the depilation area and increasing the rate of dissolution in the same system [14,15].

1.5 Kinetics for Drug Release-Suitable Model for Drug release Data

Once a newer formulation enters the market from the manufacturer, it is mandatory to crosscheck that its dissolution is in a good manner. Different research and development laboratory and industry keep their eyes on drugs dissolution studies. Drug dissolution from the dosage form is studied by the different kinetic models. in which the mixed quantity of drug (Q) is a work of test time, t or Q=f(t). Few scientific meanings of the Q(t) function are rarely used, such as zero order, first order, Hixson–Crowell, Higuchi, Korsmeyer–Peppas models.

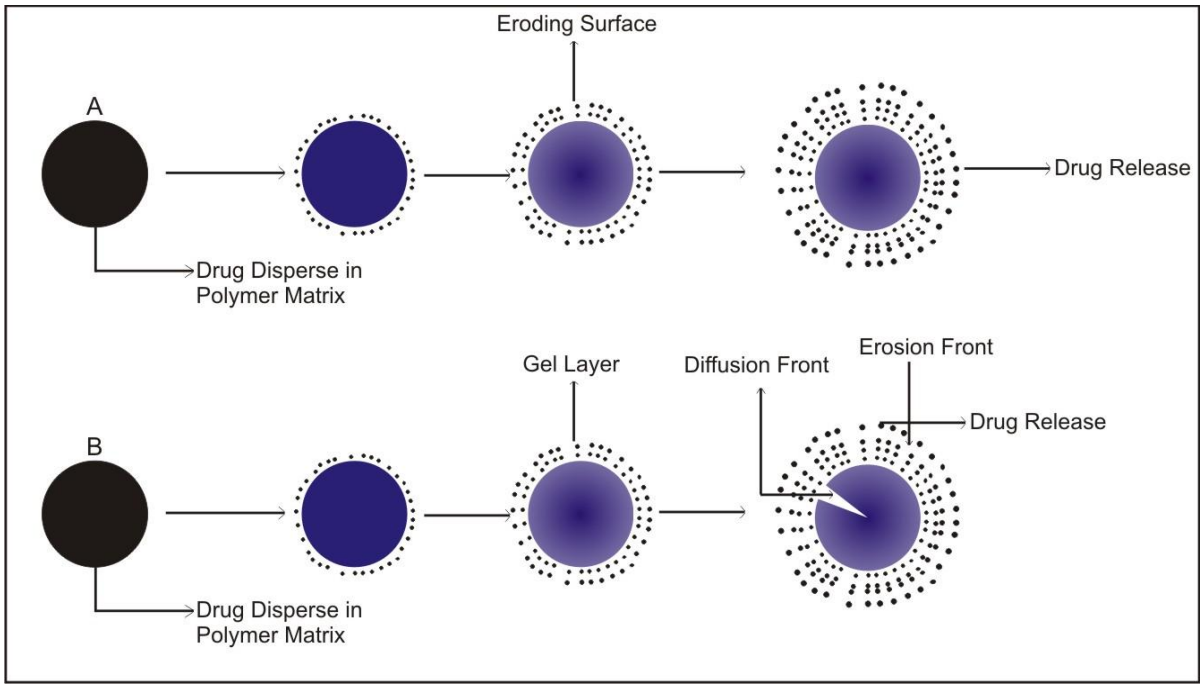


Fig. 1. The hypothetical Diagram shows the release of drugs from a diffusion-controlled drug delivery system. In which there is a homogenous mixture of the polymer matrix (a) and hydrophilic, swellable polymer matrix (b)

1.6 Zero Order Kinetics

Drug released in the same amount from any pharmaceutical formulation by the particular slot of time and this one is the best technique for removal of the drug to reach long pharmacological effect, this is elaborated by the given formula-

$$Qt = Q0 + K0t$$

Where Qt means the quantity of drug release from the formulation in time t.

Q0 is starting quantity of drug in a liquid.
K0 is Constant for Zero Order Release.

The drug release values are plotted on a graph in the form of the cumulative amount of release of drug Vs time. Mostly used for many new modified release dosage forms and matrix tablets or patches dosage forms.

1.7 First Order Kinetics

Such a type is widely used for the absorption and elimination of many drugs.

$$\text{Log } Qt = \text{Log } Q0 + (K1/2.303)$$

In the above equation, Qt denotes the amount of drug release within time t, Q0 is starting quantity of drug release from formulation, K1 is the first-order release constant.

The above-obtained data were plotted on a graph as Log cumulative % of drug remaining Vs time which shows a straight line with the slope as – K/2.303.

This formula is utilized for drug absorption in pharmaceutical dosage form, those containing water-soluble drugs in porous form.

1.8 Higuchi Model

Only one model describes the release of drugs from the matrix system. The model depends on the various hypothesis that the concentration of the drug initially is higher than its solubility. Diffusion of the drug takes place in only one direction. Higuchi explains the release of drugs depends upon scientist Fick's First Law square root dependent.

$$Ft = Q = KH/t$$

Where KH is the Higuchi Dissolution constant.

1.9 Hixson-Crowell Model

Hixson and Crowell (1931) noted that the area of the granular side of particles is proportional to the cubic root of its volume which is derived by the equation described in the following manner.

$$W0\ 1/3 - Wt\ 1/3 = Kst$$

1.10 Mechanism of Drug Release

To determine the drug release mechanism resulting from swelling (due to hydration) and gradual matrix erosion, the first 60% of drug release data can be fitted into the Korsmeyer–Peppas model, which is frequently used to describe drug release behavior from polymeric systems when the mechanism is unknown or when multiple types of release phenomena are present.

$$\text{Log } (Mt / M\infty) = \text{Log } KKP + n \text{ Log } t$$

Where, Mt Quantity of drug release at specific time t, M∞ quantity of drug removes at the infinite time; KKP drug release rate constant related to physical and mechanical properties of the tablet, and n is the release exponent indicative of the mechanism of drug release [16-18].

Table 1. Drug release kinetic

Model Name	Relation	System following the Model
First Order	- Log Qt= Log Q0+ (K1/2.303)	Drugs that are soluble in water
Zero Order	- Qt = Q0 + K0t	Beneath the Skin system and Osmotic systems
Higuchi	- Ft= Q= KH/t	Matrix Formulation
Hixon- Crowell	- W0 1/3-Wt 1/3 = Kst	Erodible isometric matrices

Where, ft = Amount of Drug remove from the system at Time t
KH, Ko, and Ks = constant of the Drug release rate of a particular model
Qo = Remaining quantity of drug to be released at zero order
Qt = Quantity of drug remain to release at time t
Wo= Starting Quantity drug present in the matrix;
Wt = Quantity of released at time t

1.11 Advantages of Doxofylline SR Over Theophylline SR

Doxofylline Sustained bronchodilation for 24 hours including controlling of inflammatory cytokines release. More selective inhibition of phosphodiesterase activities than theophylline reduces the affinity with A1 and A2 Adenosine Receptors. Long action even prevents nocturnal asthma attacks. Devoid of cardiovascular, central nervous, and gastrointestinal side effects. Asthma is a chronic disease, once-daily dosing will increase patient's compliance [19,6].

2. MATERIALS AND METHODS

Doxofylline used as Active Pharmaceutical Agent purchased from Vishal Chemical Supplier Mumbai, similarly Chitosan and Guar Gum, Alcohol was purchased from an above chemical supplier. Lactose, Magnesium Stearate was received as a gift sample from Blue Cross Laboratories, Nashik. The method selected for this research work is the wet granulation tablet manufacturing method by using factorial design. Phosphate Buffer 6.8 PH was prepared by using Indian Pharmacopoeia.

2.1 Preparation of Stock Solution

Weight 100 mg of Doxofylline and mix with 10 ml methanol in a volumetric flask made volume up to 100 ml with 0.1 N HCL. Dilutions are prepared from the stock solution.

2.2 Mixing, Blending, and compression of Doxofylline Tablet

All material pass through the sieve then mixed properly thoroughly and blended for 15 minutes. Isopropyl alcohol is added to the above-blended material to make the coherent mass of plastic mass. This mass will pass through a sieve to make the granules. Granules after drying send for compression.

2.3 Precompression Blend Evaluation

1. Angle of Repose
2. Determination of Bulk Density and Tapped Density
3. Compressibility Index (Carr's Index)
4. Hauser's Ratio

2.4 Evaluation Parameter of Material Undergone Compression

1. Weight Variation in Tablet
2. Tablet Thickness
3. Hardness of Tablet
4. Friability of Tablet
5. Content of Active Drug in tablet
6. Drug Release Study (*In-vitro*)
7. Kinetics of Dissolution Data
8. Drug Release Mechanism

Table 2. Formula for doxofylline tablet

Drug with Additives	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
					Mg/Tablet				
Doxofylline	800	800	800	800	800	800	800	800	800
Chitosan	20	20	20	30	30	30	40	40	40
Guar Gum	20	30	40	40	30	20	20	30	40
Lactose	45	35	25	15	25	35	25	15	05
Talc Powder	10	10	10	10	10	10	10	10	10
Magnesium Stearate	5	5	5	5	5	5	5	5	5
Isopropyl Alcohol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Final Weight	900	900	900	900	900	900	900	900	900

3. RESULTS

3.1 Organoleptic Properties

The properties of Doxofylline showed similar results reported in IP. It is concluded that Doxofylline is in a pure state.

Table 3. Observation of organoleptic properties of doxofylline

Identification Test	Reported Standards	Result of Sample Obtained
Appearance	Crystalline Powder	Crystalline Powder
Colour	White Colour Powder	White Colour Powder
Odor	Odorless	Odorless

Table 4. Melting point

Sr.No.	Parameter	Drug
1	Melting Point (Sample)	144^0C – 146^0C
2	Melting Point (Reference)	142^0C – 146^0C

3.2 Evaluation of Granules on Basis of Powder Properties

Table 5. Physical properties of drug

Sr.No.	Parameter	Result
1	Bulk Density	0.562 gm/ml
2	Tapped Density	0.624 gm/ml
3	Compressibility Index	11.03%
4	Hauser's Ratio	1.110
5	Angle of Repose	28º

Drug complies with all specifications based on the above result and concluded that drug has very good flow properties.

3.3 Infrared Spectra of Doxofylline

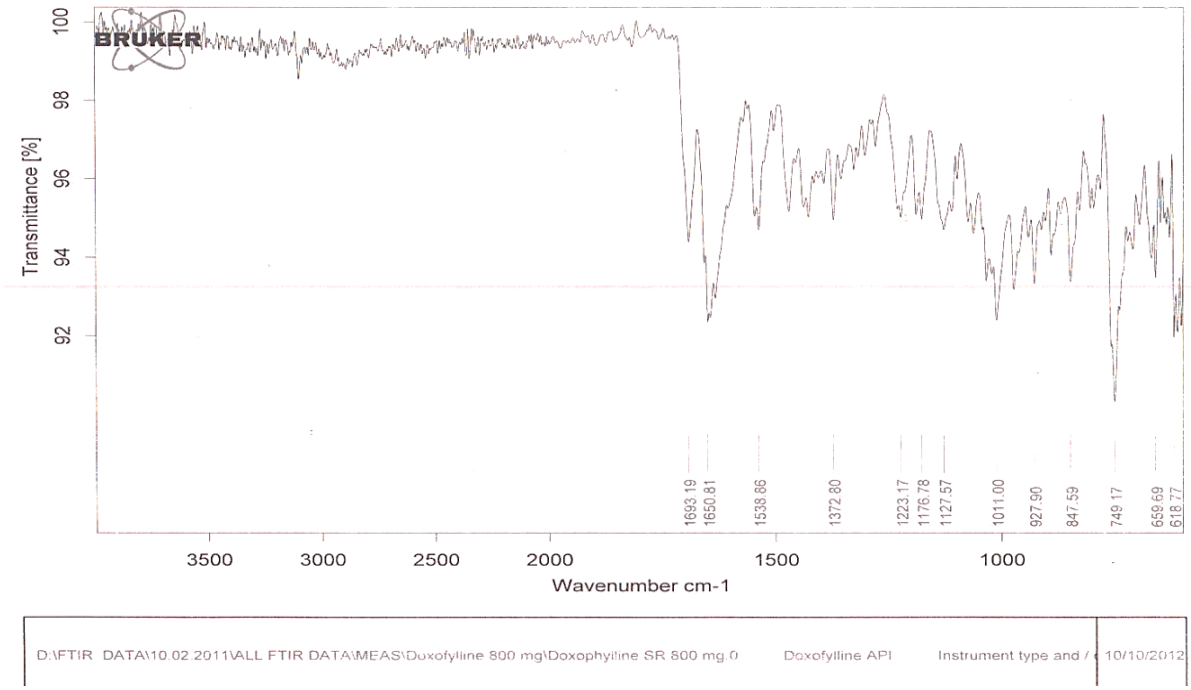


Fig. 2. IR Graph of drug doxofylline

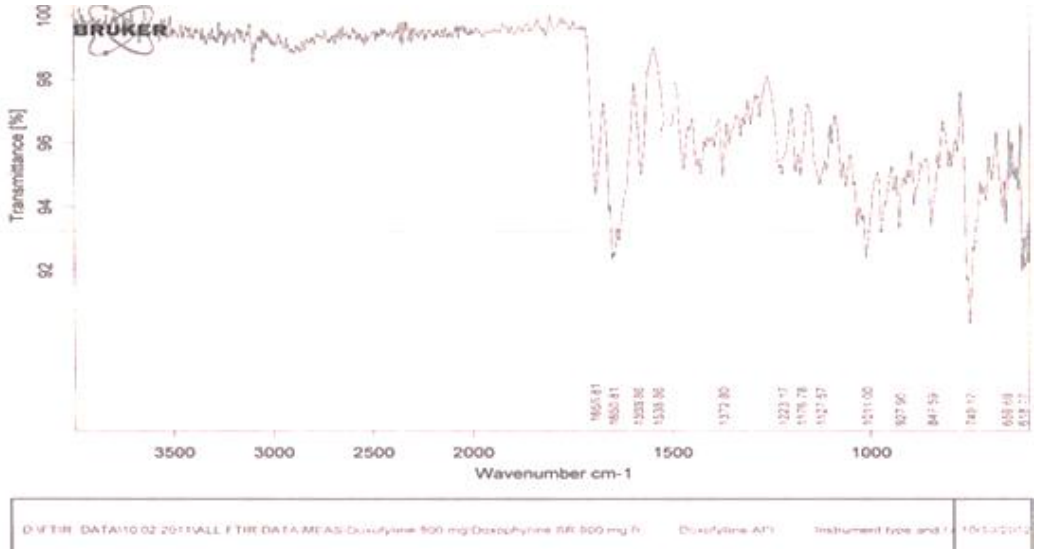


Fig. 3. IR Graph of drug doxofylline + polymer

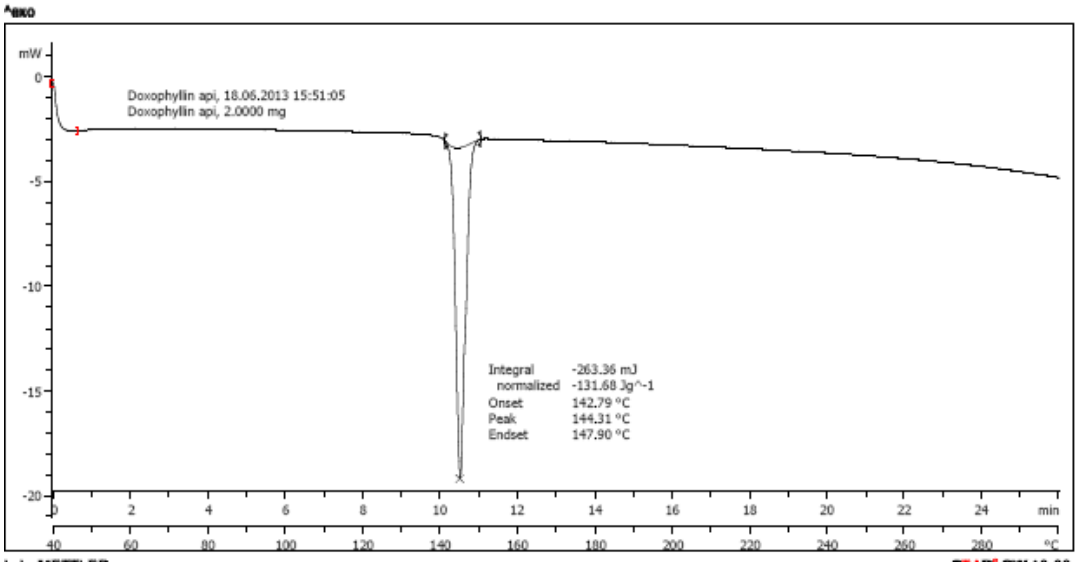
Table 6. IR bands of doxofylline

Groups	Std. Freq. (cm^{-1})	Observed Freq. (cm^{-1})
C-H Stretch	3130-3070	3110.10
C-H Stretch	1090-1010	1011.00
C-H Stretch	1700-1690	1693.19
C-H Stretch	1680-1620	1650.81
C-O-C	1140-1070	1127.57

Table 7. Interpretation of IR bands of doxofylline + polymer

Groups	Std. Freq. (cm^{-1})	Observed Freq. (cm^{-1})
C=N Stretch	1500-1600	1595.20
C=C Stretch	1680-1620	1656.10
C-H Stretch	1400-1500	1430.00

3.4 Differential Scanning Calorimetry (DSC)



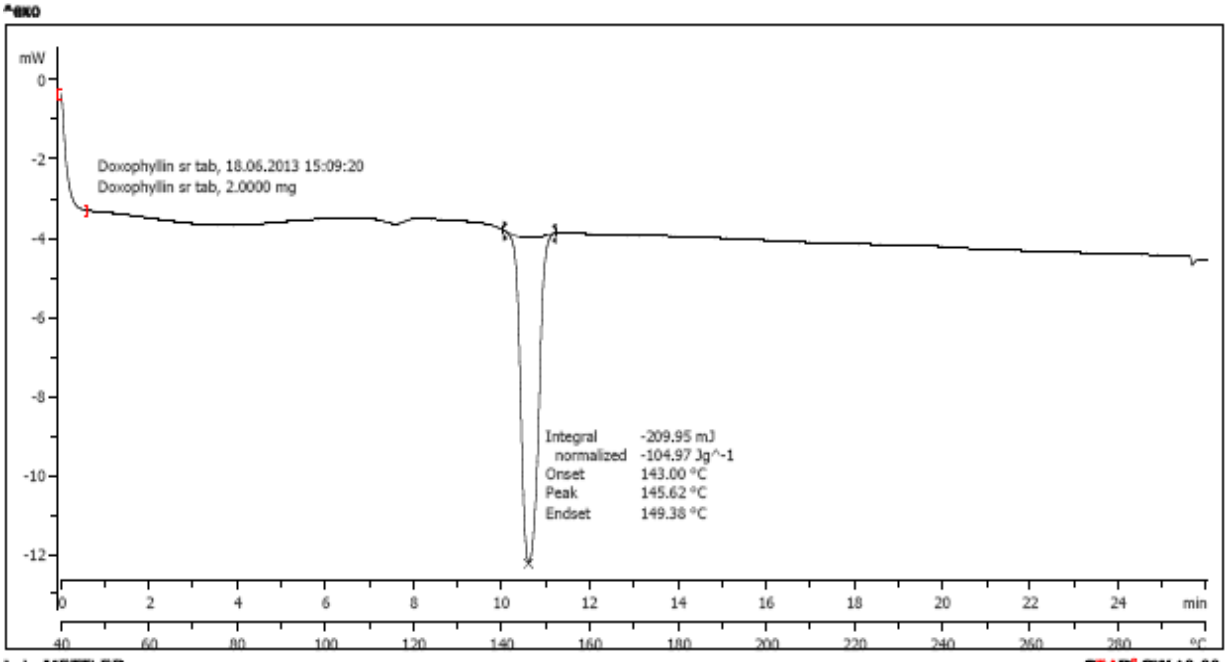


Fig. 4. DSC of physical mixture

DSC Study shows that combination of physical misture of drug and API does not changes energetics of phase transition. Melting point of each ingredient remain same as of their own individual melting point.

3.5 Solubility

Table 8. Solubility data of doxofylline

Sr. No.	Water	Drug Dissolved(mg/ml)
1	Water	0.014
2	0.1 N HCL	0.025
3	Phosphate Buffer of PH 6.8	0.018

According to the above results, 0.1N HCL shows more solubility than other media for that 0.1N HCL used further study.

3.6 Calibration Curve of API in 0.1N HCL

Table 9. Drug absorbance in 0.1 N HCL

Quantity of Drug (µg/ml)	Absorbance (nm)
9	0.3044
13	0.4767
18	0.6916
22	0.8457
26	0.9791

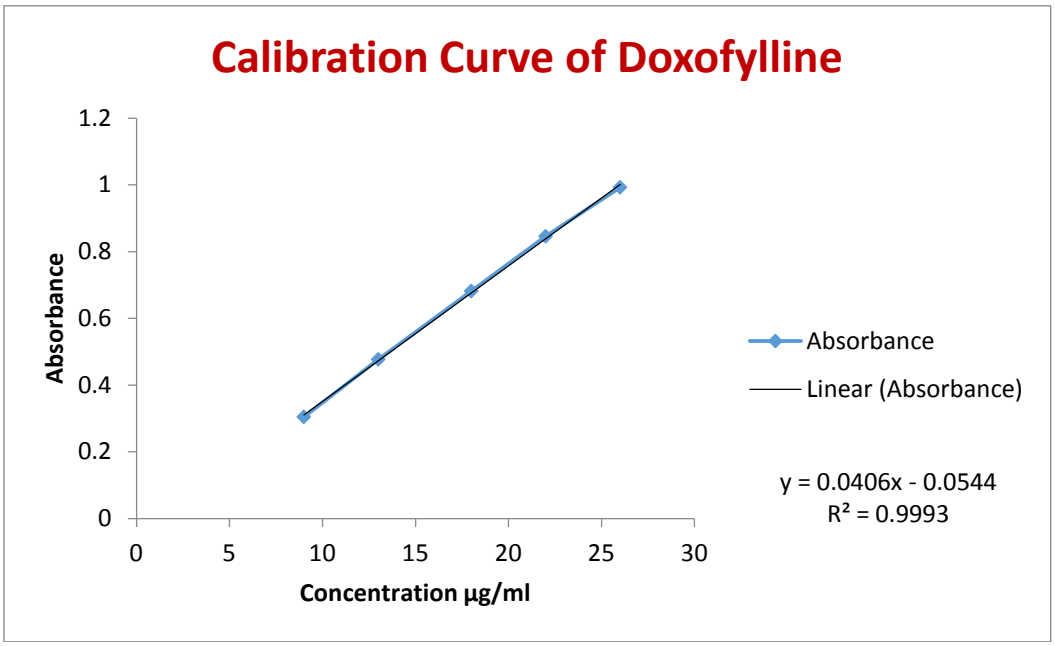


Fig. 5. Calibration Curve of Doxofylline by UV

From the Calibration curve Line Equation is given as

Y =0.04x - 0.044

The value of R2 is 0.999 by obtaining the result it has been concluded that API Obeyed Beer-Lambert's Law.

3.6.1 UV spectrum of doxofylline

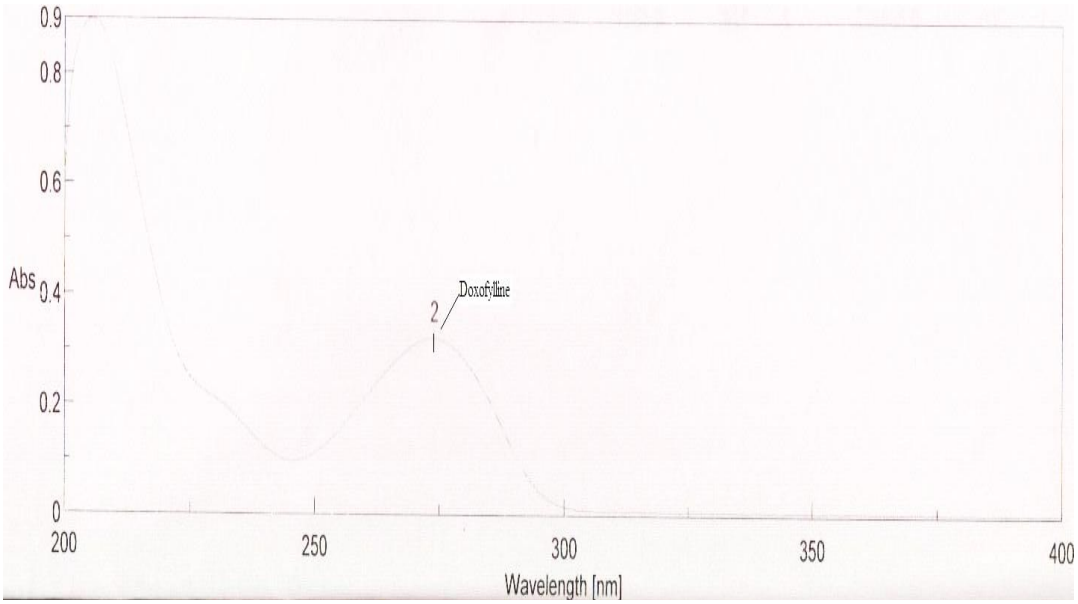


Fig. 6. UV Spectra of Doxofylline

Doxofylline spectrum (λmax) was found at 274 nm

3.7 Drug-Excipient Compatibility Study Data

Table 10. Drug absorbance in 0.1 N HCL

Sr. No.	Physical Admixture	Drug excipient ratio	Initial description	Observation 40ºC/75%RH		
				1St Week	2nd Week	4th Week
1	Doxofylline API	Plain API	White Powder	No Change	No Change	No Change
2	Doxofylline + Chitosan	1:1	White Powder	No Change	No Change	No Change
3	Doxofylline + Guar Gum	1:1	White Powder	No Change	No Change	No Change
4	Doxofylline + Lactose	1:1	White Powder	No Change	No Change	No Change
5	Doxofylline + Purified Talc	1:1	White Powder	No Change	No Change	No Change
6	Doxofylline + Mg Stearate	1:1	White Powder	No Change	No Change	No Change
7	Doxofylline + Alcohol	1:1	White Powder	No Change	No Change	No Change

3.8 In-process Results

3.8.1 In process Evaluation of in compression blend

Table 11. Evaluation of blend before compression

Batch No.	Bulk density (mg/ml)	Tapped density (mg/ml)	Compressibility Index (%)	Hauser's ratio	LOD %
F1	0.495	0.590	19.19	1.191	1.23
F2	0.469	0.533	13.64	1.136	1.04
F3	0.458	0.521	13.75	1.137	0.97
F4	0.468	0.545	16.45	1.164	1.16
F5	0.464	0.527	13.57	1.135	0.81
F6	0.576	0.679	17.40	1.178	0.77
F7	0.558	0.681	22.04	1.223	0.65
F8	0.632	0.790	25.00	1.250	0.58
F9	0.561	0.676	20.49	1.204	0.58

All the above values are means ± SD (n=3)
Formulation F1 to F9 shows good flow properties

3.8.2 In-process evaluation of tablet

IPQC Test

Table 12. In process evaluation of tablet

Batch No.	Average Weight (mg) (n= 10)	Thickness (mm) (n= 5)	Hardness (N) (n= 5)	Friability (%)
F1	899±2.05	5.28±0.008	186±1.34	0.240
F2	901±2.83	5.29±0.114	195±1.22	0.177
F3	898±2.31	5.28±0.013	177±1.87	0.119
F4	899±2.95	5.30±0.011	197±1.30	0.175
F5	897±2.22	5.28±0.013	189±1.51	0.118
F6	899±2.60	6.00±0.013	293±1.64	0.329
F7	899±2.53	6.05±0.012	298±1.30	0.468
F8	900±1.59	6.01±0.016	289±1.30	0.400
F9	900±2.37	6.04±0.023	296±1.87	0.334

All the above values are means ± SD (n=3)
All the F1 to F9 batches have passed all parameters like thickness, Variation in weight, Hardness of Tablet, Friability shows it within the limit

3.9 Dissolution Results of Formulations

Table 13. Comparative dissolution profile for F1-F9 formulation

Formula Code	% Drug Release (In Hours) Percent drug release at the time (hrs)									
	1	**2**	**4**	**6**	**8**	**10**	**12**	**16**	**18**	**24**
F1	8.47±0.25	15.14±0.21	22.92±1.32	33.12±2.26	47.82±2.78	53.42±2.96	61.15±4.61	73.21±1.02	84.70±2.78	91.60±2.3
F2	8.80±1.56	15.24±1.50	20.85±2.04	34.24±1.63	40.70±4.3	53.88±1.74	66.79±2.93	75.08±2.20	84.26±4.30	90.50±2.20
F3	9.34±3.02	21.34±3.02	30.54±1.06	48.07±3.05	57.30±3.05	64.88±2.40	70.35±2.03	78.97±2.0	86.36±3.05	95.38±2.01
F4	9.56±2.94	19.01±2.42	23.74±1.00	29.57±2.03	39.11±1.00	48.19±1.92	53.84±1.09	61.10±1.2	78.04±1.00	94.16±2.20
F5	9.08±4.01	18.84±4.01	28.78±3.29	34.40±3.45	40.54±1.13	51.36±1.8	70.70±2.93	74.09±2.322	84.26±2.30	97.48±2.30
F6	8.16±1.98	15.62±1.98	19.60±2.92	24.26±0.94	33.10±1.3	45.03±3.00	65.23±3.01	72.83±1.20	83.91±1.30	98.08±1.31
F7	9.02±1.34	14.21±1.21	20.89±2.34	28.91±3.20	34.168±1.2	48.88±2.35	57.93±1.13	71.93±2.10	78.60±1.20	98.93±1.10
F8	09.00±2.12	13.55±2.03	20.90±2.20	24.75±2.21	36.66±3.23	45.42±1.13	54.17±2.10	69.93±2.500	76.93±3.24	9.35±2.15
F9	9.24±2.32	16.38±2.20	21.60±2.12	26.3±1.26	35.83±1.40	46.18±2.23	56.33±3.21	72.48±1.6	81.64±1.41	98.87±3.20

All the above values are means ± SD (n=3)

3.9.1 Drug release for F1- F9 formulation

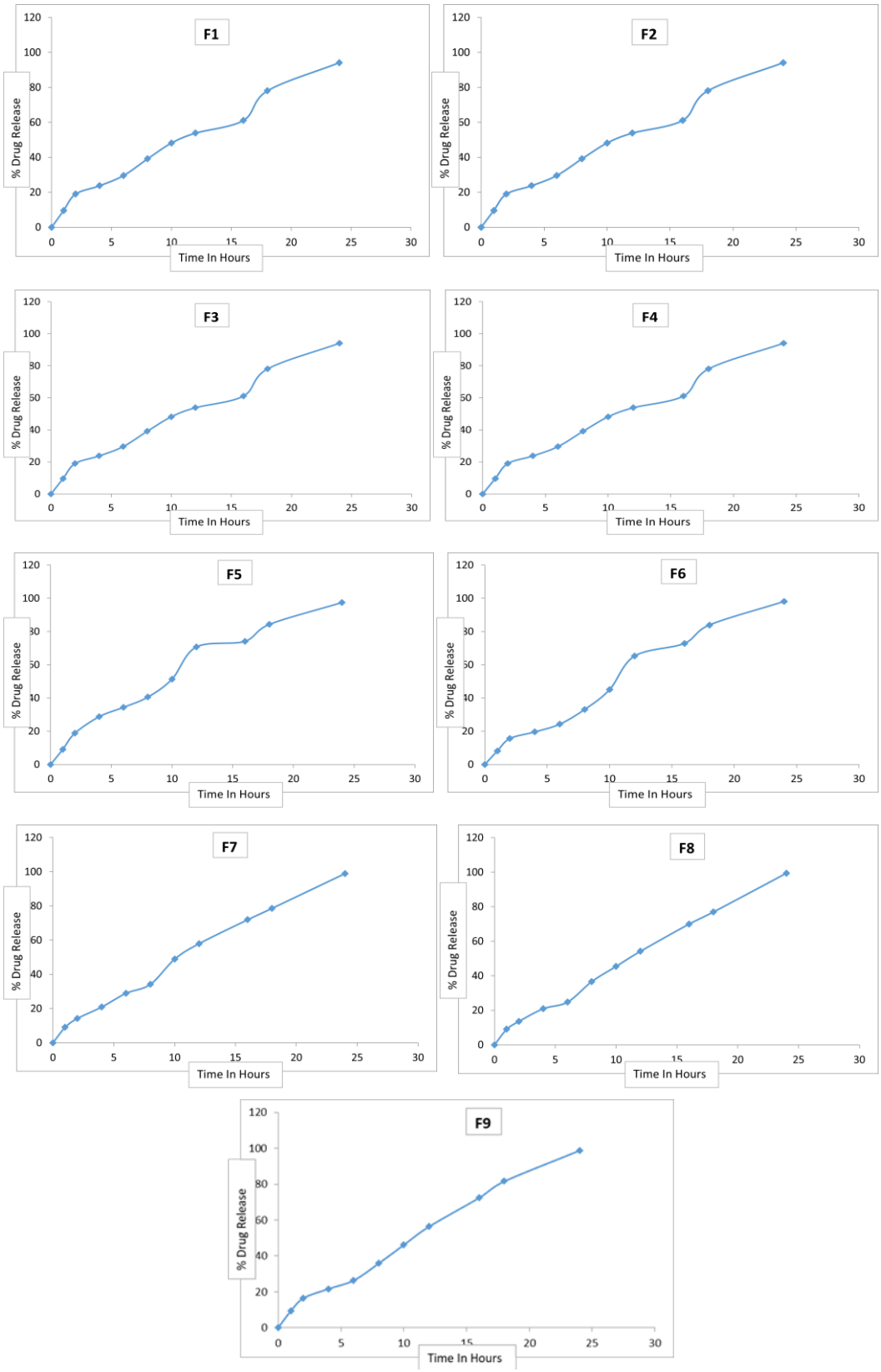


Fig. 7. % Drug release for F1- F9 formulation

3.9.2 Drug Release Kinetics

Data received by studying drug release, above parameters were followed zero-order, first-order, Higuchi, Kosermayer's for the establishment of the release of drug mechanism and Drug release Kinetic of prepared tablet formulation. A regression coefficient (r^2) indicated the proper model for the formulation and is the important criteria for the selection of the model.

To find the drug release mechanism above data is analyzed by Zero Order Kinetic, First Order Kinetic, Higuchi's, and Korsmeyer equations.

Table 14. Dissolution model for F1- F9 formulation for R^2 value

Sr. No.	Zero Order Model	First –Order Model	Higuchi Model	Kosmeyer Model Papa's Model	Hixon and Crowel Model
1	0.9727	0.9616	0.9688	0.7836	0.9931
2	0.9528	0.9779	0.9578	0.7836	0.9854
3	0.9196	0.9756	0.9844	0.7836	0.9934
4	0.9821	0.8756	0.9525	0.7836	0.9481
5	0.9661	0.8900	0.9660	0.7836	0.9699
6	0.9769	0.8234	0.9185	0.7836	0.9407
7	0.9920	0.7717	0.9424	0.7836	0.9207
8	0.9960	0.7203	0.9341	0.7836	0.8915
9	0.9922	0.7736	0.9332	0.7836	0.9190

The most suitable and fitted model was found to be Zero Order Kinetic Model

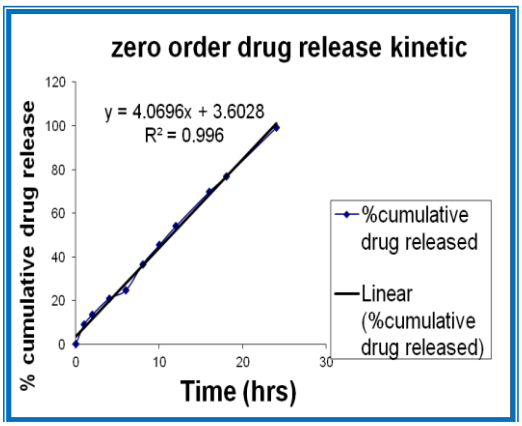


Fig. 8. Comparative zero-order drug release

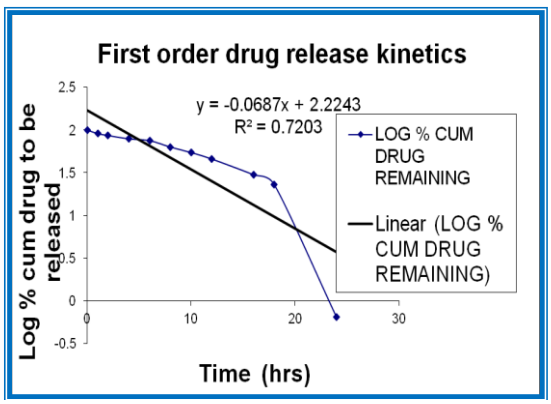


Fig. 9. Comparative first-order drug release kinetics

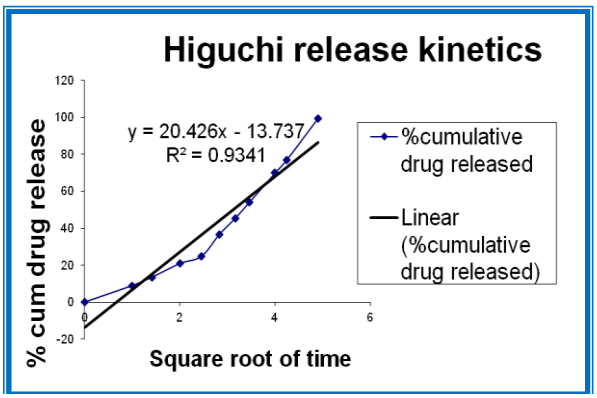


Fig. 10. Comparative Higuchi release kinetics

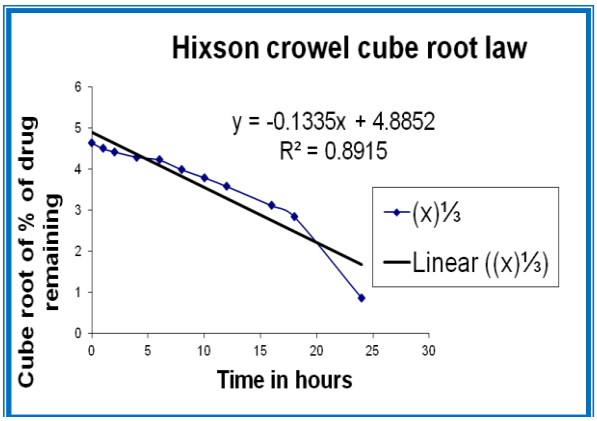


Fig. 11. Comparative Hixon Crowell cube root law

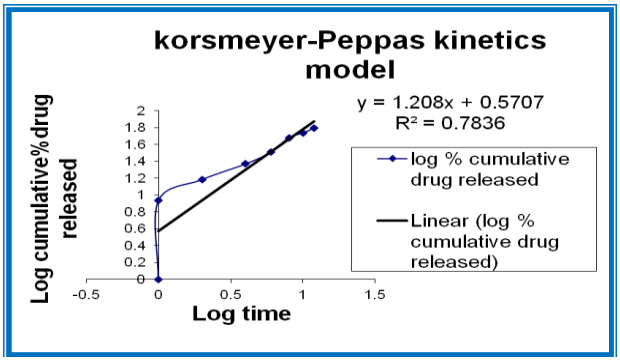


Fig. 12. Comparative Korsmeyer-Peppas kinetics model

4. DISCUSSION

Doxofylline sustained release tablets were prepared by the wet granulation method with a factorial design. Chitosan and Guar Gum were used as natural polymers to control the release of drugs from the matrix. Total nine formulations were prepared with three levels and two factors containing 800 mg of Doxofylline. Granules were studied for powder properties such as angle of repose, bulk density, tapped density. The bulk density of optimized F8 formulation was 0.632 mg/ml, tapped density was found to be 0.790 mg/ml, compressibility index was found 25.00%, Hausner's ratio was found to be 1.250. Prepared tablets were evaluated for the content of the drug in tablet, hardness, friability, thickness, uniformity of weight. The average weight of tablet 900 mg, Harness of optimized F8 formulation was 289±1.30 N, Thickness 6.01 mm, and friability 0.400%. Drug release after 24 hours was found to be 99.35%. *In-vitro* drug release study was

done using Phosphate buffer PH 6.8 at Temp 37.8^{o}C. The cumulative % drug release of the factorial design was in the range of 91 to 99 %. Hence it has been discussed earlier all result parameters were optimized and a suitable formulation was found to be F8.

5. CONCLUSION

In this way, Doxofylline sustained-release tablets were prepared and developed, by using different combinations of natural polymers like Chitosan and Guar Gum (release retarding polymers). The tablet containing Doxofylline were prepared by wet granulation technique. From the physical evaluation, FTIR, in which stretching vibrations are observed, C=C at 1650 cm-1, C-O-C at 1127 cm-1, C-N at 1011 cm-1, UV shows spectrum (λmax) at 274 nm, and DSC studies show Sharp Peak at 144^{0}C, hence the identified drug is Doxofylline. By studying stability, and DSC study we observed that API and additives are compatible with each other. There should not be any interaction between API and additives. We observed the melting point of the above formulation in the range of 144^{0}C to 148^{0}C. Tablets were prepared by using chitosan and guar gum as natural polymer using the wet granulation method of tablet manufacturing. Prepared tablets were evaluated using parameters such as physicochemical parameters like Hardness of the tablet, friability, average weight of the tablet, the thickness of tablet, and drug content, all these indicate that prepared tablets were physically and mechanically stable. From the dissolution studies formulation, No F8 showed 99% drug release that complies with IP. The stability testing of formulation No F8 at 40ºC±2 99.3 % ±5 RH revealed no specific changes related to assay and release of drug pattern which indicates the stability of the prepared formulation. Used polymers Guar Gum and Chitosan shows good release as that of synthetic polymer. At last, it has been concluded that the method used for manufacturing of above formulation meets all the stated specifications as well as quality parameters. This technique will produce reproducibility and robustness in the prepared formulation.

6. FUTURE SCOPE

The above research work has several scopes in the future for developing new drug formulations and study of different natural polymers as we have used in the above project. Also, different methods were used for formulation instead of wet granulation. There are different ways to treat chronic pulmonary obstructive disease and asthma. Therefore, various formulations can be made in the future for the betterment and curing of this disease. Certain future scopes like bioequivalence study of various formulations, manufacture and develop new techniques for release pattern of the drug by using a combination of polymers and advanced new drug delivery can be used for the above project.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

STUDY SIGNIFICANCE

The study highlights the release of the drug more slowly into the bloodstream due to the use of polymers, which provides the ability to maintain a constant level of medicament in the body.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Alasvand N, Urbanska AM, Rahmati M, Saeidifar M, Gungor-Ozkerim PS, Sefat F, et al. Therapeutic Nanoparticles for

Targeted Delivery of Anticancer Drugs [Internet]. Multifunctional Systems for Combined Delivery, Biosensing and Diagnostics. Elsevier Inc. 2017;245–259.
Available:http://dx.doi.org/10.1016/B978-0-323-52725-5/00013-7

2. Rajeswari S. Natural Polymers: a Recent Review. World J Pharm Pharm Sci. 2017;6(June):472–94.
3. Rangasamy M, Palnati VKR, Bandaru LNR. Formulation development and evaluation of voriconazole sustained release tablets. Int Curr Pharm J. 2013; 2(10):165–9.
4. HIGUCHI T. Theoretical Analysis of Rate of Release of Solid Drugs Dispersed in Solid Matrices. Mech Sustain Action Medicat. 1963;52(12):1145-1149.
5. Sampath Kumar KP, Bhowmik D, Chandira M, KTripathi K. Innovations in Sustained Release Drug Delivery System and Its Market Opportunities. J Chem Pharm Res. 2010;2(1):349–60.
6. Raghavendra Kumar Gunda JNSK. Formulation development and evaluation of Zidovudine sustained release tablets using factorial design. Der Pharm Sin Pelagia Res Libr. 2015;6(6):59-67.
7. Senthilkumar KL, Ehizilmuthu RP. Formulation, development and evaluation of metformin hydrochloride sustained release tablets. Int J Pharma Bio Sci. 2011;2(2):77–82.
8. Mandhar P, Joshi G. Development of Sustained Release Drug Delivery System: A Review. Asian Pacific J Heal Sci. 2015;2(1):179–85.
9. Raghavendra Kumar Gunda JNSK. Formulation Development and Evaluation of Doxofylline Sustained Release Tablets. FABAD J Pharm Sci, 42,. 2017;42(3):199-208.
10. Gunda RK, Manchineni PR. Formulation Development and Evaluation of Rosuvastatin Sustained Release Tablets. J Pharm Ther. 2019;4(1):238–47.
11. Gilbert Banker CR. Modern Pharmaceutics. Marcel Dekker, Inc. 2002. 1–1688 p.
12. Swapna K, Kothamasu S, Swain S, Babu MS, Kusumpudi Swapna C. Formulation and evaluation of Gliclazide sustained release tablets. Pharma Innov J [Internet]. 2018;7(7):649–54.
Available:www.thepharmajournal.com
13. Isha C, Nimrata S, Rana AC, Surbhi G. Oral Sustained Release Drug Delivery System: An Overview. Int Res J Pharm. 2012;3(5):57–62.
14. Gunda RK, Department. Formulation Development and Evaluation of Rosiglitazone Maleate Sustained Release Tablets using Factorial Design. Int J PharmTech Res. 2015;8(4):713-724.
15. Prakash Pawan, Porwal Mayur SA. Role of natural polymers in sustained release drug delivery system: Applications and recent approaches. Int Res J Pharm. 2011;2(9):6–11.
16. Maderuelo C, Zarzuelo A, Lanao JM. Critical factors in the release of drugs from sustained release hydrophilic matrices. J Control Release [Internet]. 2011;154(1):2–19.
Available:
http://dx.doi.org/10.1016/j.jconrel.2011.04.002
17. Swati Jain, Neelesh Kumar Mehra AKS and GKS, Department. Development and Evaluation of Sustained Release Matrix Tablet of Lamivudine. Int J Pharm Sci Res. 2011;2(July):454–61.
18. Gunda RK, Kumar JNS, Brahma CK, Satyanarayana V, Prashant KN. Design, formulation and evaluation of atenolol gastro retentive floating tablets. Asian J Pharm. 2015;9(4):S34–42.
19. Gunda RK, Suresh Kumar JN, Satyanarayana V, Ameer Pasha SK, Batta S. Formulation design, optimization and evaluation of domperidone maleate gastro retentive floating tablets. Der Pharm Lett. 2016;8(4):198–207.

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