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Research Article

DESIGN AND DEVELOPMENT OF ORAL SUSTAINED RELEASE MATRIX TABLETS OF DIDANOSINE

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ABSTRACT

Objectives: In present study, an attempt was made to design sustained-release tablets containing Didanosine using natural gums like Xanthan gum, Guar gum and Karaya gum. Methods: The sustained-release tablets containing Didanosine prepared by using natural gums by wet granulation method. Influence of natural polymer on Didanosine was studied. The prepared tablets were selected for DSC and FTIR studies.
Results and Discussions: The tablets were selected for DSC and FTIR studies did not show any chemical interaction between drug and polymer. The prepared formulations were evaluated for Hardness, Thickness, Friability, Weight variation, drug content estimation, Swelling index, *in-vitro* drug release are within the acceptable standard. *In-vitro* release profile was check for 8 hrs to evaluate the SR matrix tablet of Didanosine. The optimized tablets were carried out according to ICH guidelines at 40 ± 2^0 C/ 75 ± 5% RH for three months. All the prepared tablets were stable at room temperature. The values of pre-compression parameters of prepared granules were evaluated the results were within prescribed limits and indicated good free flowing property. The prepared tablets were subjected to all the quality control tests they were within the official pharmacopoeial limits. Friability is less than 1%, indicated that tablets had a good mechanical resistance. Weight variation test revealed that the tablets were within the range of pharmacopoeial limit. Thickness, hardness and drug content were within the range of pharmacopoeial limit. The evaluation parameters were within acceptable range for all the formulations. The *in-vitro* release of Didanosine was conducted for 8 hrs. The optimized formulations WGX3, WGG5 and WGK9 sustained the release up to 8hr. Hence Didanosine along with Xanthan gum, Guar gum and Karaya Gum could be used to prepare sustained released matrix tablets. The *in-vitro* release obeyed zero order kinetics with mechanism of release was erosion followed by non-fickian diffusion.
Conclusion: Among all the formulations WGK9 is the best shows excellent release around 99% after 8 hrs. The prepared matrix tablets of Didanosine were stable. So, it may be concluded that sustained release matrix tablets would improve the patient compliance and bioavailability may be improved.

Keywords: Didanosine, Xanthan gum, Guar gum and Karaya gum.

INTRODUCTION

In recent years the basic aim has been designing of drug products to reduce the frequency of dosing by modifying rate of the drug release from the formulation [1]. Regular research has been carried in this field for the use of naturally occurring biocompatible polymeric material in designing the dosage form for oral controlled release administration [2, 3]. Hydrophilic swellable polymers are widely used to control the release of the drugs from polymer matrix formulations [4, 5]. Gums of natural sources are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media; and these have been used for the preparation of single use dosage forms [6].

Drug release from hydrophilic matrix tablets are sustained by formation of hydrated viscous layer around the tablet which acts as a barrier to drug release by opposing penetration of water in to the tablet and also the movement of dissolved solute out of matrix tablet[7]. Hydrophilic polymers have attracted considerable attention in recent years as sustained controlled release devices for the delivery of water soluble and water insoluble agents. Their characteristics and their ability to hydrate and form a gel layer are well known and essential to sustain and control drug release from matrices [8]. The hydrated gel layer thickness determines the diffusion path of the drug molecules through the polymer mass in to dissolution medium [9]. A number of natural and number of polysaccharides, such as xanthan gum, guar gum and Karaya gum, have been showed to be useful for controlled release due to their hydrophilic properties [10].

AIDS is considered to be an epidemic according to estimates from the UNAIDS/WHO AIDS Epidemic update, December 2005, 38.0 million adults and 2.3 million were living with human immunodeficiency virus (HIV) at the end of 2005. The annual number AIDS patients can be expected to increase for many years to come, unless more effective and patient compliant antiretroviral medications are available at affordable prices[11]. The major drawbacks of antiretroviral drugs for the treatment of AIDS are their adverse side effects during long-term therapy, poor patient compliance and huge cost of the therapy [12, 13]. Didanosine (NRTI) is a potent antiviral agent used in the treatment of AIDS. Conventional formulations of NRTI are administered multiple times a day depending on the dose (100 mg to 400 mg) due to its short half-life ($t_{1/2}$: 1.5±0.4 hrs)[14-16]. Treatment of AIDS using conventional formulations of NRTI is found to have many drawbacks such as adverse side effects due to accumulation of drug in multi-dose therapy [17, 18]. Poor patient compliance [19] and high cost.

In present study, an attempt was made to design sustained-release tablets containing Didanosine using Xanthan gum, Guar gum and Karaya gum. by wet granulation method. Formulation of Didanosine matrix tablet was prepared by the polymer. Influence of natural polymer on Didanosine was studied.

MATERIALS AND METHODS

Didanosine was obtained as a gift sample from Aurobindo Pharma. Hyderabad. Guar Gum obtained from SD Fine Chemicals. Mumbai. Xanthan gum, Karaya gum purchased from ANL laboratories Warangal. All other chemicals used were of analytical grade.

Preparation of sustained release matrix tablets of Didanosine

Wet granulation method: Matrix tablet containing 100mg of Didanosine were prepared by wet granulation technique. The composition of each tablet is shown in table. All the components were screened and then thoroughly mixed in a bottle using tumbling

method for a period of 15 min. The powder mix was granulated with isopropyl alcohol. The wet mass was passed through # 16 and the granules were dried at 50^{0}C for 2 hrs. in a hot air oven. The dried granules were passed through # 20 and lubricated with magnesium stearate by further blending for 3 min and finally talc was added to the blend. Compression was done on 12 station Rimek tablet compression machine (M/s Karnawati Engg. Ltd. Ahmadabad) using 8 mm punches. The weight of the tablets was kept constant for all the formulations **(Table 1)**.

Table 1: Composition of Didanosine sustained release matrix tablets by wet granulation method (weight in mg)

Ingredients	WGX1	WGX2	WGX3	WGX4	WGG5	WGG6	WGG7	WGG8	WGK9	WGK10	WGK11
Didanosine	100	100	100	100	100	100	100	100	100	100	100
XG	80	100	120	140	-	-	-	-	-	-	-
GG	-	-	-	-	80	100	120	140	-	-	-
KG	-	-	-	-	-	-	-	-	100	150	200
MCC	20	20	20	20	20	20	20	20	140	90	40
IPA	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Talc	2	2	2	2	2	2	2	2	2	2	2
Mg stae	3	3	3	3	3	3	3	3	3	3	3
PVP K30	5	5	5	5	5	5	5	5	5	5	5
Acacia	20	20	20	20	20	20	20	20	20	20	20
Lactose	120	100	80	60	120	100	80	60	-	-	-
TOTAL WT	350	350	350	350	350	350	350	350	350	350	350

XG=Xanthan gum, GG=Guar gum, KG=Karaya gum, IPA=Isopropyl alcohol, MCC=Microcrystalline cellulose, Mg Stae=Magnesium stearate

Evaluation of granules

Angle of Repose: The angle of repose of granules was determined by the funnel method. The accurately weighed physical mixture was taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the granules cone measured and angle of repose was calculated using the following equation.

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

Where, h and r are the height and radius of the granules cone, θ is the angle of repose.

Loose Bulk Density (LBD): An accurately weighed granules from each formulation was lightly shaken to break any agglomerates formed and it was introduced in to a measuring cylinder. The volume occupied by the powders was measured which gave bulk volume. The loose bulk density (LBD) of granules was determined using the following formula.

Loose bulk density = Total weight of granules / Total volume of granules

Tapped bulk density (TBD): An accurately weighed granules from each formulation was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The measuring cylinder was tapped until no further change in volume was noted which gave the tapped volume. The TBD of granules was determined by the following formula.

Tapped bulk density= Total weight of granules / Tapped volume

Carr's Compressibility Index: It is a simple index that can be determined on small quantities of granules. In theory, the less compressible a material the more flowable it is. The compressibility index of the granules was determined using following formula [20].

Carr's Compressibility Index (%) = [(TBD-LBD)/ TBD] x100

Where, TBD = Tapped Bulk Density
LBD = Loose Bulk Density

Hausner's Ratio: It is the ratio of tapped density and bulk density. Hausner found that this ratio was related to interparticle friction and, as such, could be used to predict granules flow properties [21]. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index. And greater than 1.5 indicates that poor flow, in between these values passable.

Evaluation of tablets

The prepared tablets were evaluated for weight variation, tablet hardness, friability, and thickness, content uniformity, and in-vitro drug release.

Weight variation: The weight of the tablet being made was routinely determined to ensure that a tablet contains the proper amount of drug. The USP weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablets met the USP specification that not more than 2 tablets are outside the percentage limits and no tablet differs by more than 2 times the percentage limit. USP official limits.

Tablet hardness: The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of each batch of tablet was checked by using Pfizer hardness tester. The hardness was measured in terms of kg/cm^2. Six tablets were chosen randomly and tested for hardness. The average hardness of six determinations was recorded.

Friability: Friability determines the resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage. Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients. If there is any chipping, capping, cracking or breaking of tablet; then the batch should be rejected.

Method: 20 tablets were weighed and the initial weight of these tablets was recorded and placed in Roche friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the friabilator, dusted off the fines and again weighed and the weight was recorded.

$F=W_1/W_2\times100$

Where: F = Friability

W_1= weight of the tablet before test.

W_2= weight of the tablet after test

Dimensions: The dimensions of the tablets are thickness and diameter. The tablets should have uniform thickness and diameter. The manufacturer normally states these. Thickness and diameter of a tablet were measured using vernier callipers. These values were checked and used to adjust the initial stages of compression.

Drug content studies: The study to find out the actual drug content in different formulation against the standard drug was performed by taking the ratio of absorbance for the sample and the pure drug. Five tablets were taken and amount of drug present in each tablet was determined and the tablets were crushed in a Pestle mortar into powder which was transferred as amount equivalent to 40mg to 100ml standard flask. The powder was dissolving in 7.4 pH buffer and made up to volume with 7.4 pH buffer solution and the sample was mixed thoroughly and filtered through Whatmann filter paper.

The filtered solution was diluted suitably and analyzed for drug content by UV-VIS Spectrophotometer at wavelength 200nm and 400nm. Percentage of drug content was determined by comparing of standard with the prepared formulations.

Determination of swelling and erosion index: The swelling index of all the tablet formulations was studied. The extent of swelling was measured in terms of percent weight gain by the tablet. One tablet from each formulation was kept in a petri dish containing 15 ml of phosphate buffer pH 7.4. At the end of 1hr, the tablet was withdrawn, wiped with tissue paper, and weighed. Then for every 1hrs, weights of the tablet were noted, and the process was continued till the end of 6 h. The percent weight gain of the tablets was calculated

To determine matrix erosion, swollen tablets were placed in a vacuum oven at 40^0C and after 48 hrs, tablets were removed and weighed. Swelling (%) and erosion (%)was calculated according to the following formula, where S is the weight of the matrix tablets after swelling; R is the weight of the eroded tablet and T is the initial weight of the matrix tablets.

Swelling index= (S-T)/T×100
% Erosion = (T-R)/T×100

***In-vitro* Dissolution studies:** *In-vitro* dissolution study of Didanosine was carried using Electrolab TDT-08L USP dissolution test apparatus. The details are given as below.

LABINDIA USP dissolution test apparatus

Medium : pH 7.4 buffer solution
RPM : 50
Time : 12 hrs
Temp : 37^0 C ± 5^0 C
Volume : 900ml
Wave length : 249 nm

Procedure: Tablet was introduced into dissolution test apparatus and the apparatus was set at 50 rpm. 5 ml of sample was withdrawn at every 1hr interval and replaced by the respective buffer solutions. Samples withdrawn were analyzed by UV spectrophotometer at 249 nm in 7.4 pH for estimation of amount of drug released using buffer solution as blank.

Release kinetics: Data obtained from *in-vitro* release studied was evaluated to check the goodness of fit to various kinetics equations for quantifying the phenomena controlling the release from microspheres. The kinetic models used were zero order, first order, and Higuchi and Korsmeyer-peppas model. The goodness of fit was evaluated using the correlation coefficient values (R^2).

Interpretation of diffusion release mechanisms from tablets

N	Mechanism
0.5	Fickian diffusion
0.5<n<1	Non- fickian diffusion
1	Class II transport
>1.0	Class II transport

Characterization of Didanosine tablets

FTIR Studies: IR spectra for drug Didanosine, formulation with xanthan gum, formulation with guar gum and formulation with karaya gum were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR 1615, Perkin Elmer, USA) with KBr pellets.

DSC Studies: DSC scan of about 5mg, accurately weighed drug Didanosine and formulation with xanthan gum, formulation with guar gum and formulation with karaya gum were performed by using an automatic thermal analyzer system. (DSC60 Shimadzu Corporation, Japan) Sealed and perforated aluminum pans were used in the experiments for all the samples. Temperature calibrations were performed using Indium as standard. An empty pan sealed in the same way as for the sample was used as a reference. The entire samples were run at a scanning rate of 100C/min from 50-300^0C.

Stability studies: Optimized Didanosine matrix tablets were selected for stability studies [7]. The stability studies was carried out according to ICH guidelines at 40 ± 2^0C/75 ± 5% RH for three months by storing the samples in (Labcare, Mumbai) stability chamber.

Purpose of Stability Testing

To ensure the efficacy, safety and quality of active ingredient(s) and formulation.

To establish shelf life or expiry date and to support label claim.

It provides for a rapid means of quality control.

RESULTS AND DISCUSSION:

Granulation is the key process in the production of many dosage forms. To ensure good content uniformity and avoid flow related inter tablet weight variation problems. Wet granulation is preferred in routine commercial production. Wet granulation was thus used in the present study.

The values of pre-compression parameters of prepared granules were evaluated the results were within prescribed limits and indicated good free flowing property. The results of pre-compression parameters were given in **Table 2.**

Table 2: Pre-compressional parameters of Didanosine matrix tablets

FC	Loose bulk density (g/ml) (±SD), n=3	Tapped bulk density (g/cm^2) (±SD), n=3	Hausner's ratio (±SD), n=3	Compresssibity Index (%) (±SD), n=3	Angle of repose (^{0}) (±SD), n=3
WGX1	0.56 ± 0.026	0.59 ± 0.015	1.05 ± 0.054	5.1 ± 0.001	30.80 ± 0.006
WGX2	0.45 ± 0.054	0.48 ± 0.036	1.07 ± 0.058	6.2 ± 0.020	30.41 ± 0.012
WGX3	0.45 ± 0.153	0.50 ± 0.054	1.11 ± 0.015	10.0 ± 0.010	28.55 ± 0.026
WGX4	0.50 ± 0.041	0.53 ± 0.084	1.06 ± 0.020	5.70 ± .020	30.50 ± 0.076
WGG5	0.50 ± 0.016	0.56 ± 0.054	1.12 ± 0.032	10.7 ± 0.041	27.11 ± 0.113
WGG6	0.48 ± 0.028	0.50 ± 0.026	1.04 ± 0.018	4.0 ± 0.051	30.30 ± 0.006
WGG7	0.45 ± 0.023	0.50 ± 0.027	1.11 ±0.008	10.0 ± 0.020	26.41 ± 0.017
WGG8	0.50 ± 0.058	0.56 ± 0.058	1.12 ± 0.002	10.7 ± 0.021	29.60 ± 0.115
WGK9	0.50 ± 0.016	0.58 ± 0.012	1.10 ± 0.052	13.7 ± 0.014	29.70 ± 0.006
WGK10	0.49 ± 0.041	0.56 ± 0.036	1.09 ± 0.021	12.5 ± 0.040	28.51 ± 0.012
WGK11	0.45 ± 0.150	0.52 ± 0.054	1.10 ± 0.014	13.4 ± 0.101	29.45 ± 0.026

FC=Formulation code

The prepared tablets were subjected to all the quality control tests which showed (Table 3) that they were within the official pharmacopoeial limits. Friability is less than 1%, indicated that tablets had a good mechanical resistance. Weight variation test revealed that the tablets were within the range of pharmacopoeial limit. Thickness of the tablets was ranges from 4.24 to 5.08 mm. The evaluation parameters were within acceptable range for all the formulations. The drug content of the tablets was ranges from 96 % to 99%. The results of hardness, friability, weight variation, thickness and drug content were given in **Table 3.**

Table 3: Post compressional parameters Didanosine matrix tablets

FC	Thickness (mm) (±SD), n=3	Weight variation(%) (±SD), n=20	Friability% (±SD),n=3	Hardness (±SD), n=3	Drug content (±SD), n=3
WGX1	4.24 ± 0.402	351.23 ± 0.250	0.28 ± 0.245	6.2 ± 0.201	96 ± 0.48
WGX2	4.50 ± 0.204	350.82 ± 0.361	0.56 ± 0.302	6.0 ± 0.045	98 ± 0.45
WGX3	5.02 ± 0.307	352.24 ± 0.503	0.28 ± 0.450	6.3 ± 0.420	99 ± 0.54
WGX4	4.60 ± 0.415	351.46 ± 0.452	0.57 ± 0.105	5.9 ± 0.325	97 ± 0.85
WGG5	4.80 ± 0.350	350.26 ± 0.211	0.56 ± 0.450	5.8 ± 0.220	99 ± 0.24
WGG6	4.72 ± 0.409	351.51 ± 0.320	0.30 ± 0.320	6.1 ± 0.450	98 ± 0.36
WGG7	4.95 ± 0.305	350.90 ± 0.251	0.58 ± 0.452	6.2 ± 0.500	96 ± 0.25
WGG8	5.05 ± 0.405	353.15 ± 0.530	0.48 ± 0.040	6.0 ± 0.105	97 ± 0.50
WGK9	5.01 ± 0.025	351.01 ± 0.023	0.25 ± 0.026	6.0 ± 0.029	96 ± 1.25
WGK10	5.04 ± 0.032	350.02 ± 0.032	0.32 ± 0.029	6.1 ± 0.015	97 ± 1.30
WGK11	5.01 ± 0.041	352.05 ± 0.035	0.36 ± 0.035	6.0 ± 0.040	99 ± 1.50

FC=Formulation code

The swelling study of prepared Didanosine tablets was performed in phosphate buffer pH 7.4 and the results are presented as percentage weight change with respect to time. The swelling behavior is an important property for uniform and sustained release of drugs. The swelling behavior depends upon the nature of polymer, concentration of polymer and pH of the medium. The highest swelling observed in the formulation with karaya gum, as shown in **Table 4**. The least swelling is observed in formulation with xanthan gum. Because weight gain by tablet was increased proportionally with rate of hydration. Later on, it decreases gradually due to dissolution of outer most gel layer of the tablet in dissolution medium from the swelling data it is concluded that swelling is the dominant mechanism of drug release in karaya gum, while in case of xanthan gum initially swelling and then erosion is the mechanism of drug release.

Table 4: Swelling Index of Xanthan Gum, Guar Gum and Karaya Gum of Didanosine matrix tablets

ime (hrs)	WGX1	WGX2	WGX3	WGX4	WGG5	WGG6	WGG7	WGG8	WGK9	WGK10	WGK11
0hr	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1hr	65.25	68.4	70	74.2	69.2	75.8	78.7	80	65.2	71.1	72
2hr	88.66	90.2	92.02	97.4	78.5	80.5	83.1	87.2	75.8	86.3	92.5
3hr	95.4	98.2	99.7	104.5	88.8	90.2	95.8	98.14	95.1	98.8	102.3
4hr	98.5	104.2	106.5	110.14	101.5	105.14	108.2	112.1	106.8	112.3	120.4
5hr	101.1	109.1	111.5	115	106.2	110.2	112.8	120.2	115.1	120.5	129.8
6hr	106.7	114.5	116.2	119.1	110.2	115.1	119.4	124.1	125.4	125.3	135.2
7hr	115.1	118.3	121.1	123.1	116.1	119.8	123.4	128.6	135.2	138.1	142
8hr	119.24	122.1	125.6	129.2	120.5	125.1	128.3	131	150.2	152.3	155

In-vitro dissolution studies of all the formulations of sustained release tablets of Didanosine were carried out in pH 7.4 phosphate buffers for 8 hrs respectively. The study was performed for 8 hrs, and percentage drug release was calculated at 1 hrs time intervals.

The dissolution profile of Didanosine tablets (350mg) containing Xanthan gum (WGX1, WGX2, WGX3, WGX4) showed a maximum drug release 80<% within 8 hrs as and among all the formulations WGX3 showed best release of 96% at 8hrs as shown in **Fig 1**. The Didanosine tablets (350mg) containing Guar gum (WGG5, WGG6, WGG7, WGG8) showed a maximum drug release 75<% within 8 hrs and among all the formulations WGG5 showed best release of 95% at 8 hrs, as shown in **Fig 2**. The Didanosine tablets (350mg) containing Karaya Gum (WGK9, WGK10, WGK11) showed a maximum drug release 80<% within 8 hrs and among all the formulations WGK9 showed best release of 99% at 8hrs as shown in **Fig 3**.

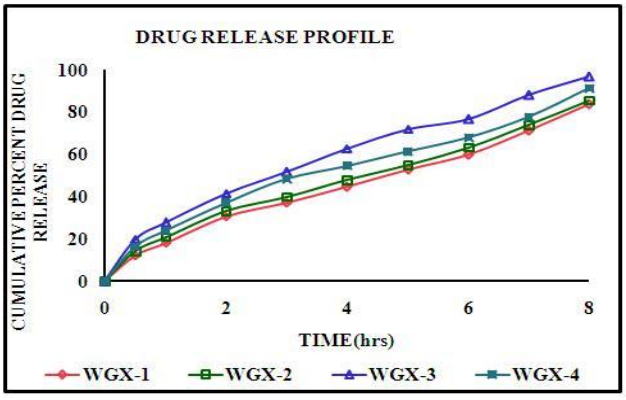

Fig 1: *In- vitro* release profile of formulation WGX-1 to WGX-4.

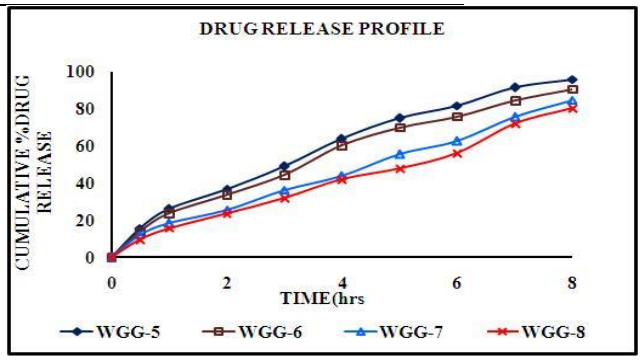

Fig 2: *In- vitro* release profile of formulation WGG-5 to WGG-8.

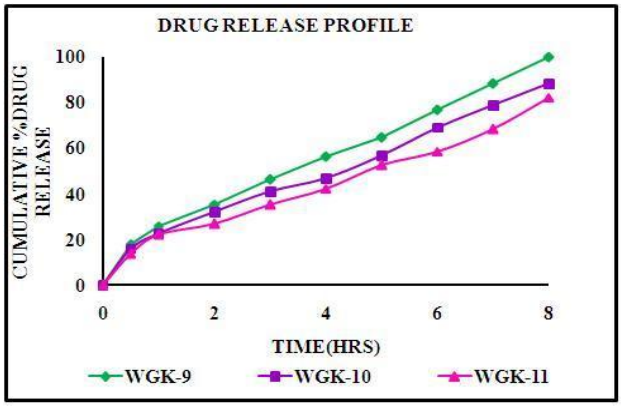

Fig 3: *In- vitro* release profile of formulation WGK-9 to WGK-11.

The values of release parameters, n and k, are incersely related. A higher value of k may suggest burst drug release from the matrix. According to the criteria for release kinetics from swellable systems, a value of release exponent, n= 0.45, 0.45<n<0.89 and 0.89<n<1.0 indicates Fickian (case I) diffusion, non-Fickian (anamalous) diffusion and zero order (case II) transport, respectively. A result reveals that all formulations follow zero order kinetics as correlation coefficient (r^2) values are higher than that of first order release kinetics. The correlation coefficient (r^2) values >0.94, suggest that drug release mechanism from Didanosine tablets followed non-Fickian (anomalous) transport mechanism. Kinetic results were given **Table 5**.

Table5: Kinetic parameters of Didanosine matrix tablets.

Formulation code	First order (r^2)	Zero order (r^2)	Higuchi model (r^2)	Kors.-Peppas (r^2)	Kors.-Peppas (n)
WGX1	0.929	0.975	0.963	0.946	0.645
WGX2	0.884	0.974	0.959	0.958	0.592
WGX3	0.865	0.978	0.977	0.990	0.677
WGX4	0.915	0.975	0.964	0.965	0.595
WGG5	0.814	0.981	0.976	0.990	0.682
WGG6	0.958	0.975	0.979	0.991	0.682
WGG7	0.926	0.993	0.941	0.981	0.777
WGG8	0.845	0.944	0.856	0.902	0.738
WGK9	0.759	0.986	0.941	0.960	0.699
WGK10	0.840	0.985	0.934	0.955	0.712
WGK11	0.942	0.972	0.978	0.981	0.594

FTIR: The FTIR spectra of pure Didanosine alone and its physical mixture with other excipients were carried out. Pure Didanosine displayed characteristic peaks at γ (cm^{-1}): 1820-1660 (-C=O strong absorption) 3400 (-CONH medium absorption) 1300-1000(-O- absorption) 3400(-OH – absorption). The FT-IR spectra of pure drug and drug + excipients are shown in **Fig 4.** The FTIR spectrum of Didanosine pure drug exhibited characteristic absorption at 3400 cm^{-1} representing the presence of –CONH. Whereas a characteristic absorption band at 1820-1660 cm^{-1} is due to the presence of -C=O, and absorption band at 1300-1000. Similarly the IR spectrum of Didanosine and other polymers namely Xanthan gum, Guar gum and Karaya gum showed characteristic absorption bands for the functional groups -CONH, -N, COC and -OH at or near that of Didanosine absorption bands values indicating that there was no chemical and physical change in the functional groups present in Didanosine.

DSC: The DSC of pure drug and formulations were shown in **Fig 5.** The DSC of pure drug was subjected to DSC which has shown a sharp melting point at 179^{0}C. The DSC of formulation containing Didanosine and Xanthan gum shows a little range of melting process. Melting point at 184.0^{0}C. The DSC of formulation containing Didanosine and guar gum produced a warm melting point at 184.6^{0}C. The DSC of the formulation containing Didanosine and Karaya gum produced a warm melting point at 185.6^{0}C in all the cases which leads to a physical mixture. Looking at the DSC date observed in all the case one can conclude that during the formulation with various excipients no chemical reaction takes place between drug and excipients during process. The melting point of product will be same range with negligible variation. That means it can be justified there is no interaction between drug and excipients.

The stability studies of the optimized tablets WGX3, WGG5 and WGK9 were carried out according to ICH guidelines at 40±2^{0}C/ 75±5 % RH for three months. After three month the tablets were again analyzed for the hardness, friability and drug content uniformity. No change was observed in the hardness, friability and disintegration time of tablets prepared by co-processed technique. No significant change was observed in all the formulations. The results were shown in **Table 5.**

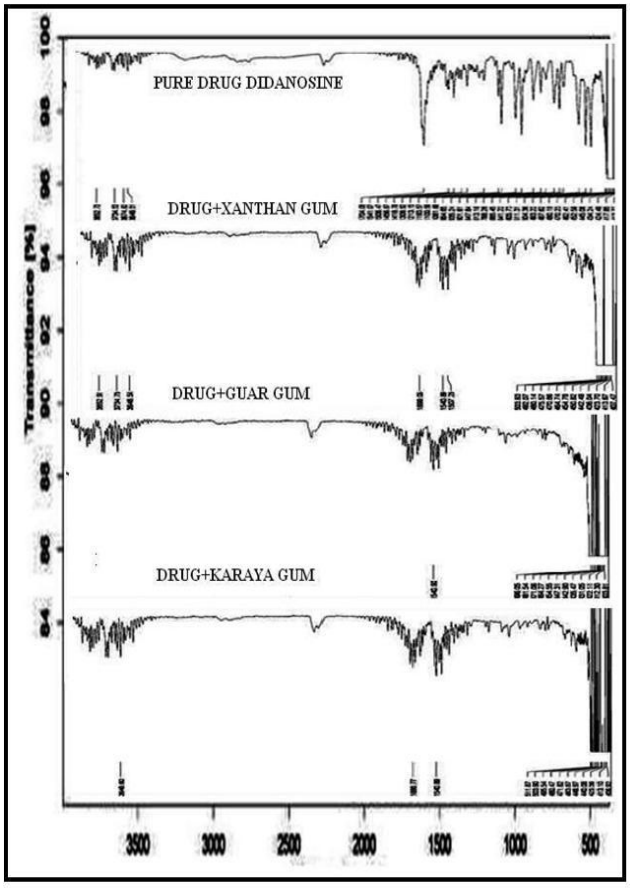

Fig 4: IR Spectra of Didanosine, Formulation with xanthan gum, Formulation with guar gum and Formulation with karaya gum

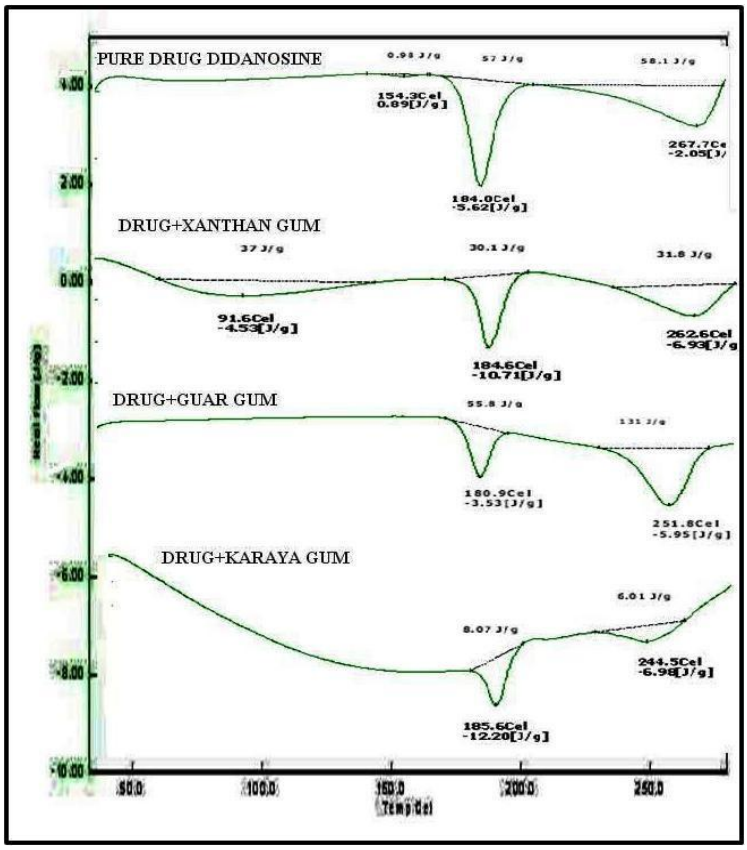

Fig 5: DSC Thermograms of Didanosine, Formulation with xanthan gum, Formulation with guar gum and Formulation with karaya gum

Table 6: Data after stability study

Formulation Code	Stability period	Drug content (±SD), n=3	Hardness(kg/cm²) (±SD), n=3	Friability (%), (±SD), n=3
WGX3	30 days	98.12 ± 0.14	6.16 ± 0.28	0.31 ± 0.10
	60 days	99.54 ± 0.41	5.76 ± 0.18	0.39 ± 0.11
	90 days	98.98 ± 0.11	6.14 ± 0.14	0.26 ± 0.02
WGG5	30 days	99.94 ± 0.12	6.03 ± 0.43	0.34 ± 0.02
	60 days	99.11 ± 0.10	6.07 ± 0.51	0.30 ± 0.07
	90 days	98.54 ± 0.24	6.03 ± 0.13	0.29 ± 0.01
WGK9	30 days	99.44 ± 0.14	5.97 ± 0.45	0.28 ± 0.11
	60 days	97.99 ± 0.19	6.03 ± 0.08	0.43 ± 0.17
	90 days	99.25 ± 0.20	6.13 ± 0.41	0.31 ± 0.04

CONCLUSION

The sustained release matrix tablets of Didanosine could be prepared using Xanthan gum, Guar gum and Karaya gum by wet granulation method. The prepared sustained release matrix tablets subjected to FTIR and DSC Study suggested that there was no drug-polymer and polymer-polymer interaction. The matrix tablets showed good Swelling up to 6 hrs in phosphate buffer pH 7.4 maintaining the integrity of formulation. The release of Didanosine was conducted for 8 hrs. The optimized formulations WGX3, WGG5 and WGK9 sustained the release up to 8 hrs. Hence Didanosine along with Xanthan gum, Guar gum and Karaya Gum could be used to prepared sustained released matrix tablets. The release obeyed zero order kinetics with mechanism of release was erosion followed by non-fickian diffusion. Among all the formulations WGK9 is the best shows excellent release around 99% after 8 hrs. The prepared matrix tablets of Didanosine were stable. So, it may be concluded that sustained release matrix tablets would improve the patient compliance and bioavailability may be improved.

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