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Design and development of oral sustained release matrix tablets of didanosine using natural polymer blend

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ABSTRACT

In present study, an attempt was made to design sustained-release tablets containing Didanosine. Formulation of Didanosine matrix tablet was prepared by the polymer combination in order to get required theoretical release profile. Influence of natural polymer on Didanosine was studied. The prepared tablets were selected for DSC and FTIR studies. The tablets were selected for DSC and FTIR studies did not show any chemical interaction between drug and polymer. The values of pre-compression parameters of prepared granules were evaluated the results were within prescribed limits and indicated good free flowing property. The hardness of the tablets ranges from 5.9 to 6.1 kg/cm^2. 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 4.71 to 5.08 mm.. All the evaluation parameters were within acceptable range for all the formulations. The drug content of the tablets was ranges from 96 % to 99%. Thickness, hardness and drug content were within the range of pharmacopoeial limit. The evaluation parameters were within acceptable range for all the formulations. In-vitro release profile was check for 12 hrs to evaluate the SR matrix tablet of Didanosine. The optimized tablets were carried out according to ICH guidelines at 40 ± 2º C/ 75 ± 5% RH for three months. All the prepared tablets were stable at room temperature. Among all the 12 formulations the formulation WGXG-3, WGGK-6 and WGXK-10 shows maximum release within 12 hrs are considered as best formulations. So, it may be concluded that sustained release matrix tablets would improve the patient compliance and bioavailability may be improved by polymer combination.

Keywords: Didanosine, Xanthan gum, Guar gum, Karaya gum, Zero order kinetics, Sustained release matrix Tablets.

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 combinations of Xanthan gum, Guar gum and Karaya gum by wet granulation method. Formulation of Didanosine matrix tablet was prepared by the polymer combination in order to get required theoretical release profile. Influence of combination natural polymer on Didanosine was studied.

EXPERIMENTAL SECTION

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 1**. All the components were screened and then thoroughly mixed in a bottle using tumbling method for a period of 15 mins. The powder mix was granulated with isopropyl alcohol. The wet mass was passed through # 16 and the granules were dried at 50°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: Composition of Didanosine sustained release matrix tablets by wet granulation method (weight in mg)

Ingredients	WGXG 1	WGXG 2	WGXG 3	WGXG 4	WGGK 5	WGGK 6	WGGK 7	WGGK 8	WGXK 9	WGXK 10	WGXK 11	WGXK12
Didanosine	100	100	100	100	100	100	100	100	100	100	100	100
XG	20	40	60	80	-	-	-	-	20	40	60	80
GG	80	60	40	20	20	40	60	80	-	-	-	
KG	-	-	-	-	80	60	40	20	80	60	40	20
MCC	20	20	20	20	20	20	20	20	20	20	20	20
IPA	q.s	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	2
Mg stea	3	3	3	3	3	3	3	3	3	3	3	3
PVP K30	5	5	5	5	5	5	5	5	5	5	5	5
Acacia	20	20	20	20	20	20	20	20	20	20	20	20
Lactose	100	100	100	100	100	100	100	100	100	100	100	100
Total wt	350	350	350	350	350	350	350	350	350	350	350	350

*Note: *XG=Xanthan gum, GG=Guar gum, KG=Karaya gum, IPA=Isopropyl alcohol, MCC=Microcrystalline cellulose, Mg Stea=Magnesium stearate.*

Compatibility studies of Didanosine and polymers:
FTIR Studies: IR spectra for pure drug Didanosine and formulations like WGXG-3, WGGK-6 and WGXK-10 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 optimized formulations 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^{0}C.

Evaluation of granules: The flow properties of the different granules of formulae to be compressed were studied using angle of repose (fixed height cone method) [20], Loose Bulk Density [21], Tapped bulk density, Carr's compressibility index [22], and the Hausner ratio methods [23].

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 [24, 25]: 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.

Tablet hardness [24, 25]: 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 [24, 25]: 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.

$F=W_1/W_2\times100$

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 power was dissolve 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 Whatman filter paper.

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

Determination of swelling and erosion index [26]: 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 1h, the tablet was withdrawn, wiped with tissue paper, and weighed. Then for every 1h, weights of the tablet were noted, and the process was continued till the end of 6 hrs. 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 LABINDIA USP dissolution test apparatus. The details are given as below.

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

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 [27]: 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 polymeric films

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

Stability studies: Optimized tablets were selected for stability studies [28, 29]. The stability studies was carried out according to ICH guidelines at 40 ± 2^oC/75 ± 5% RH for three months by storing the samples in (Lab care, Mumbai) stability chamber.

Purpose of Stability Testing
1. To ensure the efficacy, safety and quality of active ingredient(s) and formulation.
2. To establish shelf life or expiry date and to support label claim.
3**.** It provides for a rapid means of quality control.

RESULTS AND DISCUSION

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.

Compatibility studies:

FTIR: The FTIR spectra of pure drug Didanosine and formulations WGXG-3, WGGK-6 and WGXK-10 were carried out. Pure Didanosine displayed characteristic absorption 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 1**. 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 formulations WGXG-3, WGGK-6 and WGXK-10 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 drug. That means it can be justified there is no interaction between drug and excipients.

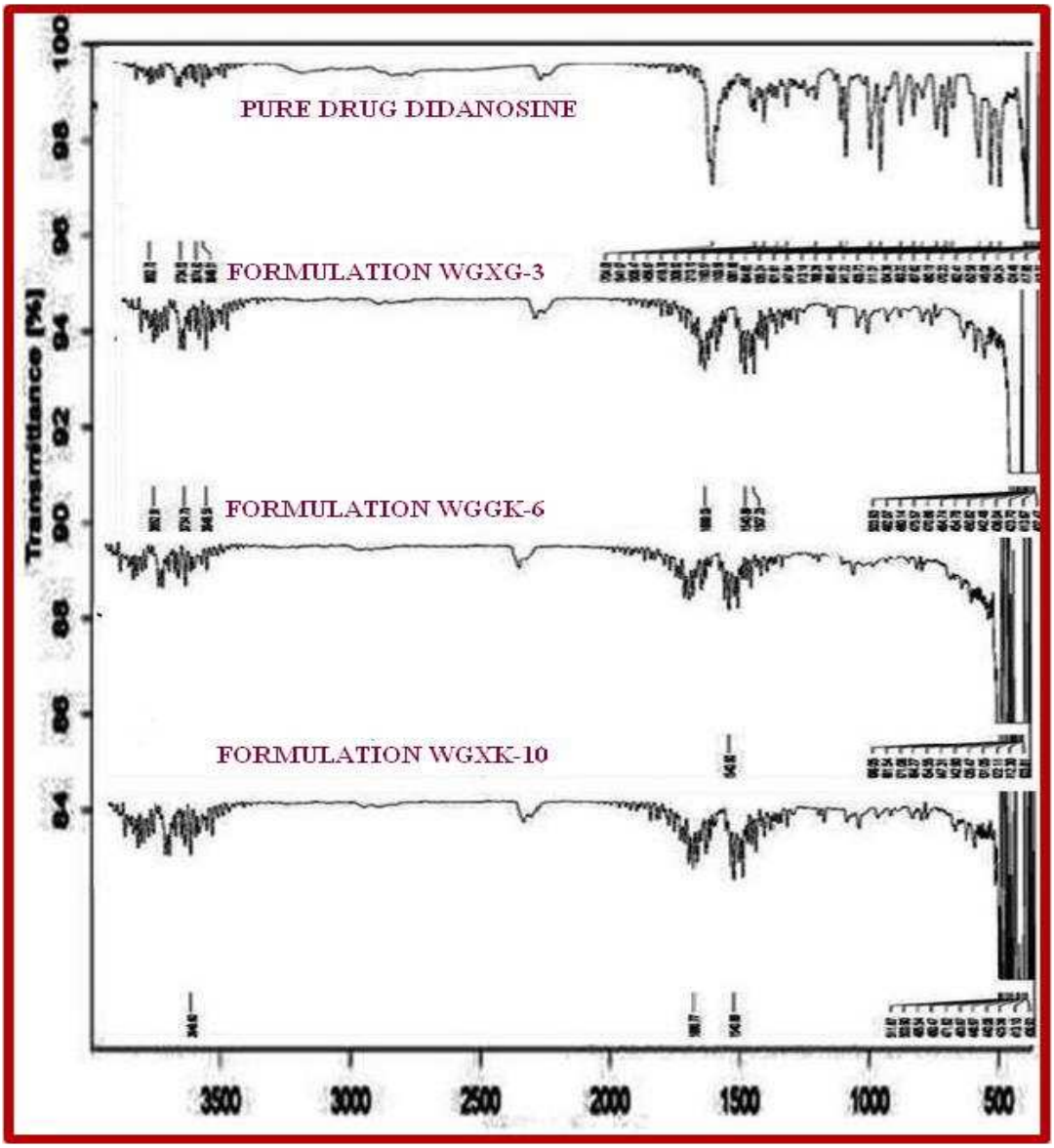

Fig 1: IR Spectra of pure drug Didanosine and Formulations WGXG 3, WGGK 6 and WGXK 10

DSC: The DSC of pure drug Didanosine and formulations WGXG-3, WGGK-6 and WGXK-10 were shown in **Fig 2**. The DSC of pure drug which has shown a sharp melting point at 179^0C. 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. 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.

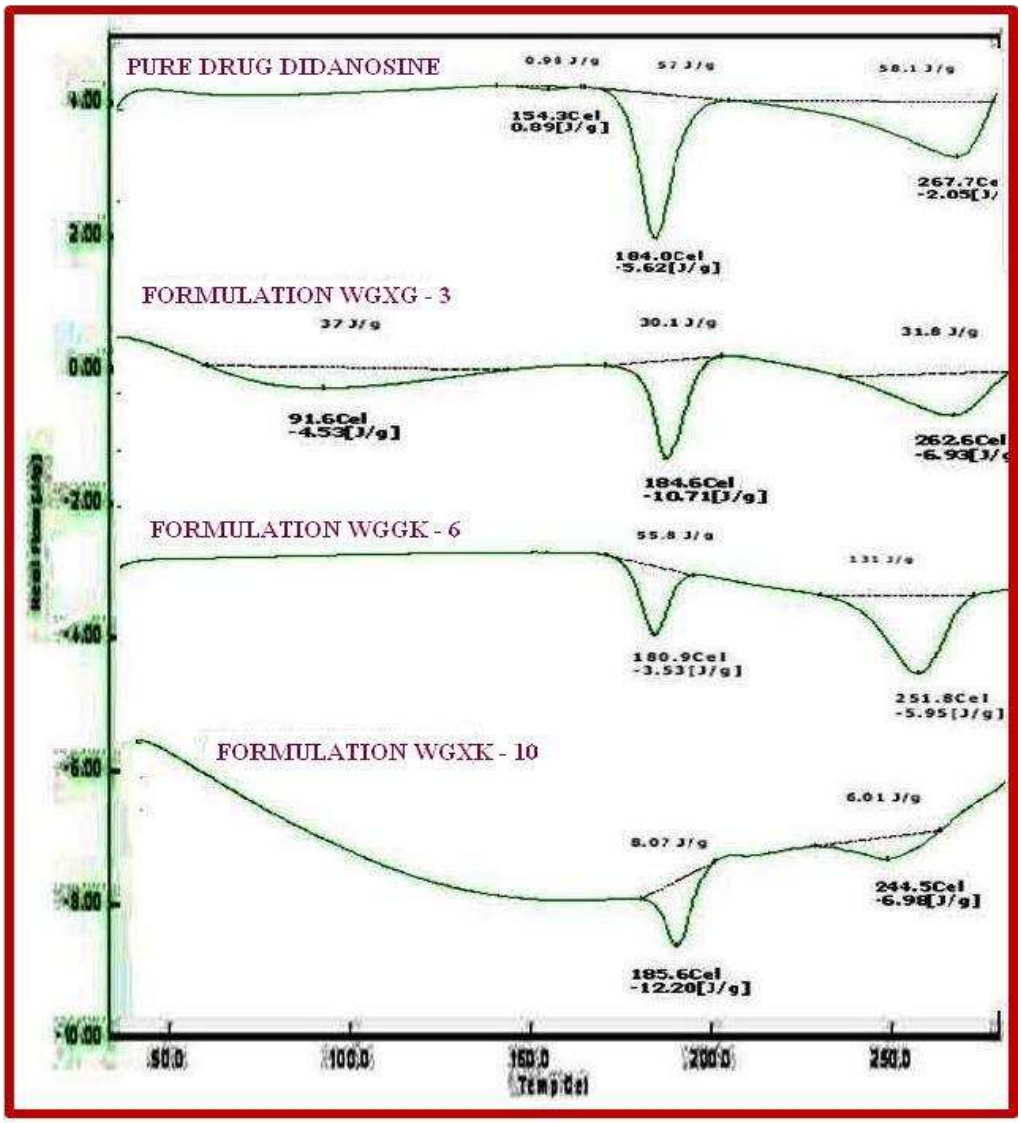

Fig 2: DSC Thermograms of pure drug Didanosine and Formulations WGXG 3, WGGK 6 and WGXK 10

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.**

The prepared tablets were subjected to all the quality control tests which showed (Table 3) that they were within the official pharmacopoeial limits. The hardness of the tablets ranges from 5.9 to 6.1 kg/cm^2. 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 4.71 to 5.08 mm.. All 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 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 (^{o}) (±SD), n=3
WGXG1	0.47 ± 0.021	0.55± 0.084	1.11± 0.021	14.5 ± 0.021	30.00 ± 0.086
WGXG2	0.52 ± 0.014	0.59 ± 0.054	1.08 ± 0.023	11.8± 0.035	26.10 ± 0.123
WGXG3	0.51 ± 0.041	0.58 ± 0.026	1.0 ± 0.018	12.0± 0.031	28.01 ± 0.016
WGXG4	0.48 ± 0.014	0.55 ± 0.027	1.10 ±0.010	12.7 ± 0.020	27.41 ± 0.027
WGGK5	0.50 ± 0.021	0.56 ± 0.058	1.10 ± 0.010	10.7 ± 0.024	28.60 ± 0.105
WGGK6	0.55 ± 0.024	0.58 ± 0.012	1.09± 0.045	5.1 ± 0.001	26.80 ± 0.006
WGGK7	0.45 ± 0.051	0.49± 0.032	1.08 ± 0.058	8.2 ± 0.020	28.41 ± 0.012
WGGK8	0.48 ± 0.150	0.51 ± 0.052	1.11 ± 0.015	5.8 ± 0.010	27.55 ± 0.026
WGXK9	0.54 ± 0.036	0.58 ± 0.050	1.05 ± 0.054	6.8 ± 0.010	25 .01± 0.060
WGXK10	0.51 ± 0.034	0.55± 0.013	1.07 ± 0.058	7.2 ± 0.015	24.21 ± 0.020
WGXK11	0.50 ± 0.143	0.54 ± 0.026	1.11 ± 0.015	7.4 ± 0.020	26.25 ± 0.016
WGXK12	0.51 ± 0.020	0.54 ± 0.048	1.06 ± 0.020	5.5 ± 0.031	23.50 ± 0.026

FC=Formulation code

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
WGXG1	4.50 ± 0.204	350.25 ± 0.040	0.30 ± 0.22	6.0 ± 0.08	98.42 ± 0.81
WGXG2	4.81 ± 0.151	350.82 ± 0.161	0.56 ± 0.01	6.1 ± 0.06	98.64 ± 0.54
WGXG3	5.05 ± 0.024	351.24 ± 0.503	0.28 ± 0.03	6.2 ± 0.24	99.98 ± 0.32
WGXG4	4.70 ± 0.150	350.46 ± 0.452	0.57 ± 0.11	5.8 ± 0.14	97.34 ± 0.32
WGGK5	4.81 ± 0.235	352.26 ± 0.211	0.56 ± 0.32	5.9 ± 0.08	99.66 ± 0.42
WGGK6	4.75 ± 0.258	349.51 ± 0.320	0.30 ± 0.12	6.08 ± 0.31	98.12 ± 0.32
WGGK7	4.85 ± 0.031	350.90 ± 0.251	0.52 ± 0.14	6.1 ± 0.24	96.24 ± 0.52
WGGK8	5.01 ± 0.051	351.15 ± 0.530	0.49 ± 0.16	6.0 ± 0.26	97.36 ± 0.46
WGXK9	5.02 ± 0.086	350.01 ± 0.041	0.51 ± 0.08	5.9 ± 0.22	97.24 ± 1.29
WGXK10	5.05 ± 0.045	352.05 ± 0.021	0.53 ± 0.18	6.1 ± 0.14	99.91 ± 1.31
WGXK11	5.08 ± 0.021	351.10 ±0.030	0.48 ± 0.14	5.9 ± 0.12	99.06 ± 1.32
WGXK12	4.95 ± 0.021	352.13±0.021	0.51±0.06	6.0±0.16	98.16 ± 1.36

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 Guar gum and Karaya gum 80:20, as shown in **Table 4**. The least swelling is observed in formulation with Xanthan gum and Guar gum 80:20. 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 Guar gum and Karaya gum, while in case of Xanthan gum and Guar gum initially swelling and then erosion is the mechanism of drug release.

Table 4: Swelling Index of Didanosine matrix tablets

Time (hrs)	WGXG 1	WGXG 2	WGXG 3	WGXG 4	WGGK 5	WGGK 6	WGGK 7	WGGK 8	WGXK 9	WGXK 10	WGXK 11	WGXK 12
0hr	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1hr	50.1	53.2	58.1	64.2	58.7	60.2	71.6	74.3	65.2	70.2	72.1	75
2hr	56.7	62.8	66.2	75.2	65.2	69.5	82.1	89.5	71	79.5	80.2	81.2
3hr	62.6	71.2	75.4	83.6	72	75.1	97.4	98.3	82.6	83.7	90.6	96.3
4hr	70.4	78.5	82.3	92.4	78.2	82.3	108.8	110.5	91.4	93.6	99.4	104.1
5hr	81.8	85.7	89.1	101.3	89.6	92.6	115.3	118.2	101.3	109.4	110.2	114.8
6hr	91.5	98.4	101	110.2	98.3	114.7	122	126.4	119.1	120.6	121.8	123.9
7hr	102.1	108.3	115.1	118	115.8	122.1	132.4	135.1	125.3	129.1	131.7	136.4
8hr	108.3	113.2	118.5	122.3	129.2	132.9	142.4	148.2	132.4	135.6	141.4	143.7

In-vitro dissolution studies of all the formulations of sustained release tablets of Didanosine were carried out in pH 7.4 phosphate buffers for 12 hrs respectively. The study was performed for 12 hrs, and percentage drug release was calculated at 1 hrs time intervals.

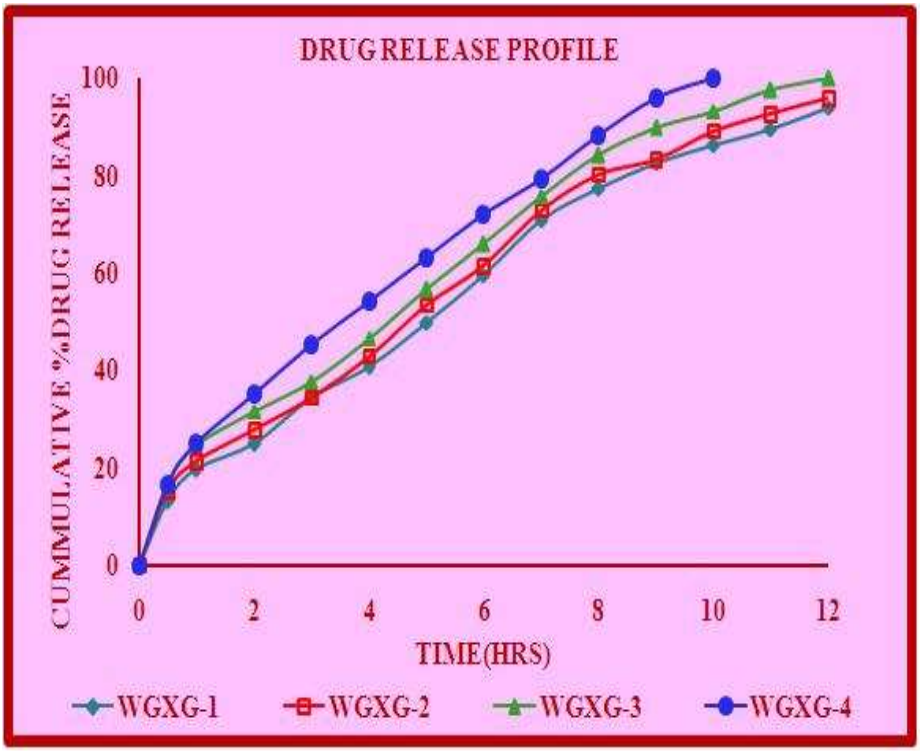

Fig 3: *In- vitro* release profile of formulation WGXG-1 to WGXG-4

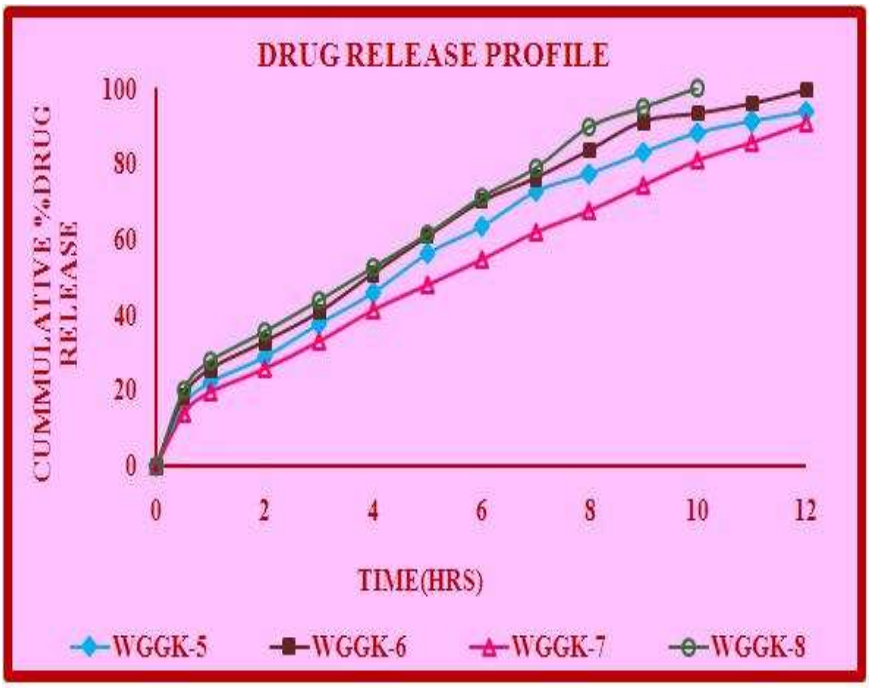

Fig 4: *In- vitro* release profile of formulation WGGK-5 to WGGK-8

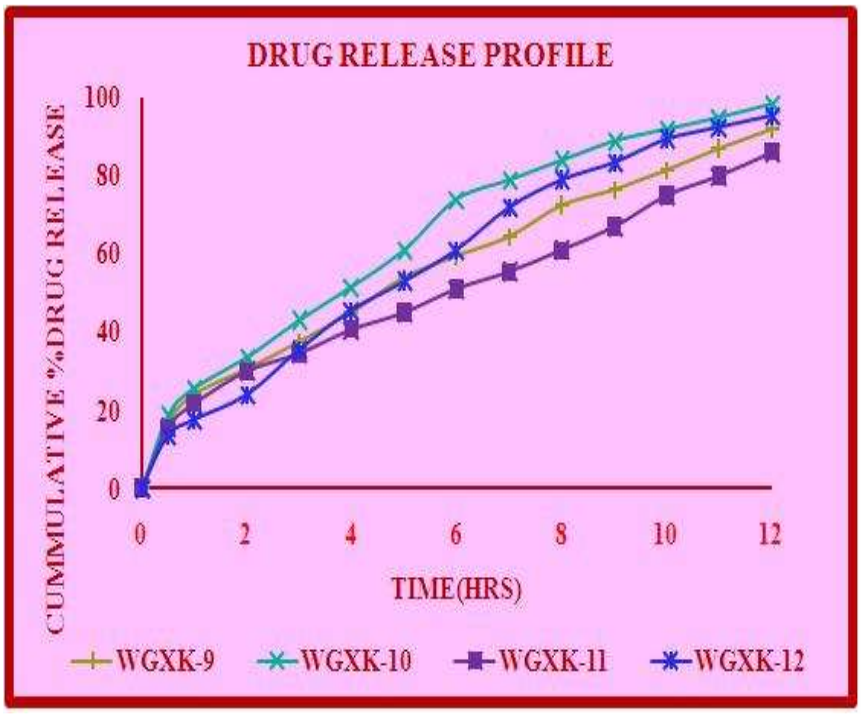

Fig 6: *In- vitro* release profile of formulation WGXK-9 to WGXK-12

The dissolution profile of Didanosine tablets (350mg) containing combination of Xanthan Gum and Guar gum in varying concentrations (WGXG-1, WGXG-2, WGXG-3, and WGXG-4). Among all the four formulations WGXG-3 showed drug release up to 99.72% in 12 hrs, but formulation WGXG-4 100% drug released within 10 hrs as shows in **Fig 3**. The Didanosine tablets (350mg) containing combination of Guar gum and Karaya gum in varying concentrations (WGGK-5, WGGK-6, WGGK-7, WGGK-8). Among all the four formulations WGGK-6 showed drug release up to 99.81% in 12 hrs, where as WGGK-8 formulation shows 100 % release within 10 hrs as showed in **Fig 4.**The Didanosine tablets (350mg) containing combination of Xanthan gum and Karaya gum in varying concentrations (WGXK-9, WGXK-10, WGXK-11, WGXK-12). Among all the 4 formulations the WGXK-10 showed drug release up to 98.55 % in 12 hrs as shown in **Fig 5**. Among all the 12 formulations the formulation WGXG-3, WGGK-6 and WGXK-10 shows maximum release within 12 hrs are considered as best formulations.

Table 5: Kinetic parameters of Didanosine matrix tablets

Formulation code	First order (r^2)	Zero orde (r^2)	Higuchi model (r^2)	Kors.-Peppas (r^2)	Kors.-Peppas (n)
WGXG1	0.898	0.982	0.915	0.945	0.75
WGXG2	0.906	0.995	0.954	0.993	0.794
WGXG3	0.780	0.993	0.936	0.985	0.801
WGXG4	0.931	0.983	0.945	0.957	0.669
WGGK5	0.915	0.986	0.939	0.954	0.116
WGGK6	0.790	0.983	0.911	0.937	0.159
WGGK7	0.951	0.989	0.945	0.968	0.210
WGGK8	0.962	0.988	0.949	0.965	0.281
WGXK9	0.924	0.984	0.984	0.962	0.667
WGXK10	0.789	0.981	0.981	0.937	0.778
WGXK11	0.921	0.982	0.982	0.948	0.667
WGXK12	0.927	0.985	0.985	0.945	0.727

The values of release parameters, n and k, are incersely related. A higher value of k may suggest brust 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**.

The stability studies of the optimized tablets WGXG-3, WGGK-6 and WGXK-10 were carried out according to ICH guidelines at 40±2ºC/ 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 the of all formulation. The results were shown in **Table 6.**

Table 6: Data after stability study

Formulation Code	Stability period	Drug content (±SD), n=3	Hardness (kg/cm^2) (±SD), n=3	Friability (%), (±SD), n=3
WGXG3	30 days	99.98 ± 0.21	6.24 ± 0.10	0.27 ± 0.10
	60 days	98.65 ± 0.19	6.06 ± 0.18	0.34 ± 0.03
	90 days	98.96 ± 0.17	6.09 ± 0.41	0.31 ± 0.07
WGGK6	30 days	98.12 ± 0.32	6.08 ± 0.31	0.30 ± 0.12
	60 days	97.86 ± 0.14	6.06 ± 0.22	0.29 ± 0.08
	90 days	97.72 ± 0.18	6.04 ± 0.14	0.28 ± 0.16
WGXK10	30 days	99.91 ± 0.01	6.19 ± 0.08	0.53 ± 0.10
	60 days	99.01 ± 0.01	5.76 ± 0.27	0.31 ± 0.18
	90 days	98.64 ± 0.04	6.44 ± 0.12	0.39 ± 0.11

CONCLUSION

The sustained release matrix tablets of Didanosine could be prepared using Xanthan gum, Guar gum and Karaya gum in different combination of polymers 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 6hr in phosphate buffer pH 7.4 maintaining the integrity of formulation. The *in-vitro* release of Didanosine was conducted for 12 hrs. The optimized formulations WGXG-3, WGGK-6 and WGXK-10 sustained the release up to 12 hrs. Hence Didanosine along with Xanthan gum and Guar gum could be used to prepared sustained released matrix tablets. The *in-vitro* release obeyed zero order kinetics with mechanism of release was erosion followed by non-fickian diffusion. 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 by polymer combination.

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