ORIGINAL RESEARCH PAPER

Pharma

DESIGN & OPTIMIZATION OF FDDS OF ACYCLOVIR USING XANTHAN GUM

KEY WORDS: Acyclovir, Non fickain diffudion, Floating drug delivery.

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ABSTRACT

The drug Acyclovir widely prescribed as antiviral drug used for the treatment of HIV/AIDS. The purpose of the present work was to design and optimize FDDS of acyclovir using Xanthan gum. The tablets were prepared by wet granulation method. All the formulations were evaluated for pre & post compressional parameters. Floating lag time was in the range of 120sec and constantly floated for upto 24 hrs. The obtained results revealed that, release of drug was by mixed order kinetics. All the formulations indicating a dissolution behaviour controlled by Non Fickain Diffusion. From these studies it can be concluded that, the formulation retained for longer periods of time in the stomach and provides controlled release of the drug & improve the therapeutic effect of the drug by increasing its bioavailability.

INTRODUCTION:

During the last decade, many studies have been performed concerning the sustained release dosage form of drugs, which have aimed at the prolongation of gastric emptying time (GET). The GET has been reported to be from 2 to 6 hours in humans in the fed state[1]. In present situation, the AIDS is causing more threatens, AIDS is not a disease, it is the damage done to immune system by the infection of HIV[2]. Novel oral controlled dosage form that is retained in the stomach for prolonged and predictable period is of major interest among academic and industrial research groups[3]. Conventional drug delivery system achieves as well as maintains the drug concentration within the therapeutically effective range needed for treatment only when taken several times a day. This results in significant fluctuations in drug levels[4]. Oral ingestion is the most convenient and commonly used method of drug delivery[5] which has narrow absorption window in GI restricted by poor bioavailability because of incomplete release of drug[6].

Factors Affecting Gastric Retension:

Gastric retention time (GRT) is affected by several factors which include[7,8]:

a) size and shape of the dosage form
b) density
c) concaminant intake of food and drugs
d) biological factors like age, gender, posture, body weight and disease states.

Acyclovir is a guanine analogue used in the treatment of viral diseases. The reported oral bioavailability is 10-20% with a plasma elimination half life of 1-2 h[9].

Preparation of Floating tablets of Acyclovir[10,11]:

According to the present invention, the FDDS includes a swelling agent PVP, gas generating component generated by sodium bicarbonate, swelling controlled by xanthan gum, which acts both as swellability and a release controlling agent. The gas generating component sodium bicarbonate contacts with gastric fluid to generate carbon dioxide that gets entrapped within the hydrated gel matrix of the swelling composition. Sodium bicarbonate ($NaHCO_3$) was incorporated in the formulation in such a way that when in contact with the acidic gastric contents, CO_2 is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage form. Magnesium stearate and talc as lubricant and glidant.

Table 1: Acyclovir formulations (mg)

	AF1	AF2	AF3	AF4	AF5	AF6	AF7
Acyclovir	400	400	400	400	400	400	400
Xanthan gum	25	50	75	100	125	150	175
Sod aliginate	175	150	125	100	75	50	25
Sod CMC	50	50	50	50	50	50	50
PVP K30	25	25	25	25	25	25	25
Sod bicarbonate	200	200	200	200	200	200	200
Mg Stearate	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10

RESULTS AND DISCUSSION:

In-Vitro Release Study:

Dissolution studies were performed for Floating tablets using USP XXIII dissolution test apparatus-II at 50rpm, 900ml of 0.1N HCl as dissolution media.

The Formulations AF1 to AF7 containing drug & Xanthan gum of 25mg, 50mg, 75mg, 100mg, 125mg, 150mg & 175mg exhibited 100% of drug release in 4, 7, 8, 9, 10 and 11 hours respectively.

In the above results, it was observed that as the concentration of the polymers increased, there is a decrease in the drug release rates. An increase in polymer concentration causes increase in viscosity of the gel as well as the gel layer with longer diffusional path. This could cause a decrease in effective diffusion coefficient of the drug and a reduction in drug release rate.

Formulation AF7 containing Xanthan gum of 175mg showed a drug release of 100% in 11 hours, so selected as promising formulation.

Table 2: Invitro release data of AF1 to AF7

Timings	AF1	AF2	AF3	AF4	AF5	AF6	AF7
1 hr	67.23± 0.11	42.90± 0.67	39.99± 0.89	32.44± 0.78	30.01± 0.73	28.47± 0.19	26.15± 0.91
2 hr	79.87± 0.32	53.56± 0.90	48.56± 0.14	44.92± 0.61	37.68± 1.54	36.90± 0.27	34.89± 0.13
3 hr	86.43± 0.88	67.10± 0.78	58.99± 0.89	56.89± 1.87	49.97± 0.90	47.67± 0.79	43.11± 0.67
4 hr	100.00 ±0.00	74.55± 0.11	67.11± 1.89	64.11± 0.23	56.55± 0.61	54.88± 1.89	51.21± 0.36
5 hr	100.00 ±0.00	89.30± 0.89	78.53± 0.98	75.51± 0.90	64.66± 0.22	57.90± 0.62	56.78± 1.02
6 hr	100.00 ±0.00	99.98± 0.13	87.22± 0.55	84.94± 0.88	71.88± 0.43	65.77± 0.44	62.44± 0.34
7 hr	100.00 ±0.00	100.00 ±0.00	98.99± 0.91	95.17± 0.19	80.12± 0.65	76.61± 1.01	70.39± 0.73
8 hr	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.89	99.97± 0.76	87.28± 0.36	78.55± 0.99
9 hr	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	99.38± 0.76	85.80± 0.22

10 hr	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	98.00± 0.45
11 hr	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.97
12 hr	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.00	100.00 ±0.97

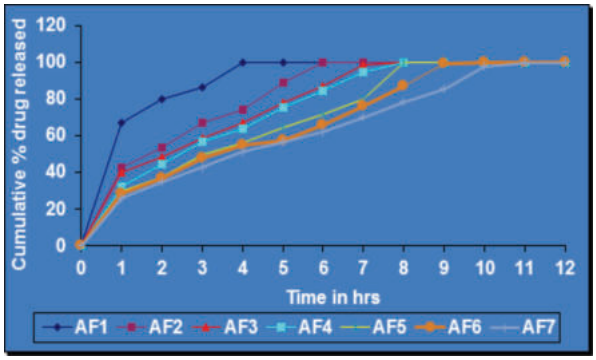

Fig 1: Invitro drug release of AF1 to AF7

CONCLUSION

From the present study, the following conclusions can be drawn:

- From study it is evident that, floating tablets of Acyclovir can be developed to increase gastric residence time and thereby increasing its bioavailability. Further detailed investigations are required to establish chemical efficacy of these formulations.
- All the prepared tablet formulations were found to be good without capping and chipping.
- Formulated FDDS tablets gave satisfactory results for various pre & post-compressional parameters.
- As the amount of polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent (NaHCO3) increases the drugs releases increases and at the same time floating lag time decreases.
- Sodium alginate and Xanthan gum has given extra adhesion property and helped to maintain the integrity of the tablet.
- Swelling index has a significant effect on the drug release.

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