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Research Article

Design and Development of Sustained Release Matrix Tablets of Furosemide

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ABSTRACT

Sustained release matrix system are favored because of their simplicity, patient compliance etc, than traditional drug delivery which have many drawbacks like repeated administration, fluctuation in blood concentration level etc. For the purpose of enhancement the bioavailability of furosemide, a dosage form with sustained release of furosemide was designed in this study.

Sustained release tablets of furosemide were fabricated using xanthan gum (13.33 % to 66.67 %). The prepared tablets were evaluated for pre compression and post compression studies like angle of repose, bulk density, tapped density, hardness, weight variation, fraibilty, drug content, *in-vitro* releaseof drug etc. among the five formulations A better controlled drug release (85 %) was obtained with the matrix tablet SX_5containing xanthan gum 66.67%. Short-term stability studies of all formulations indicates that there were no significant changes in drug content and dissolution parameter values after 3 month storage at 40° ± 2°C/75 ± 5% RH.

Key Words: Furesemide, Xanthan Gum, Sustained Release Matrix Tablets etc.

INTRODUCTION

Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in developing a sustained-release drug delivery system. Recent trend in development of sustained-release drug delivery systems was the use of gums of plant origin to fulfill the aim of retarding the drug release[1,2,3,4]. Natural gums are biodegradable, non-toxic and have capability to swell on contact with aqueous media. The natural polymers used do hold advantages over the synthetic polymers generally because they are non toxic, less expensive and freely available. Most common examples of natural gums are Guargum, Xanthan gum, Pectin and GumTragacanth.

Xanthan gum is a high molecular weight extracellular polysaccharide, produced on commercial scale by the viscous fermentation of gram negative bacterium *Xanthomonascampesteris*. The molecule consists of a backbone identical to that of cellulose, with side chains attached to alternate glucose residues. It is a hydrophilic polymer, which until recently had been limited for use in thickening, suspending and emulsifying water based systems. [5]

Furosemide (4-chloro-2- furfurylamino-5-sulphamoyl benzoic acid) is a drug with a diuretic action which acts at the renal level on the ascending limb of the loop of Henle. [6]Furosemide is absorbed mostly in the stomach and upper small intestine, possibly due to its weak acidic properties, Furosemide undergoes first pass metabolism resulting in a narrow absorption window, leads to its low

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bioavailability (43-69 %). The biological half life of furosemide is 100 minutes.

MATERIALS AND METHODS

Furosemide was obtained as a gift sample from Wokhardth Aurangabad. Xanthan gumwas obtained from Bangalore fine chem, Bangalore. Other materials like MCC, PVP K-30, Magnesium stearate, talc were obtained from SD fine chem, Mumbai.

PREPATION OF SUSTAINED RELEASE MATRIX TABLETS

Sustained release matrix tablets of furosemide were prepared by using different drug: polymer ratios viz. 1:1, 1:2, 1:3, 1:4 and 1:5 for SX_1, SX_2, SX_3, SX_4 and SX_5respectively for all formulations as per the composition given in Table-1. The lubricated formulations were compressed by a direct-compression technique.

Table 1: Composition of matrix tablets of furosemide.

Ingredients mg/tablet	Formulation code					
	SF_0	SX_1	SX_2	SX_3	SX_4	SX_5
Furosemide	20	20	20	20	20	20
Xanthan gum	---	20	40	60	80	100
Microcrystalline cellulose	113	93	73	53	33	13
Talc	2.0	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0
PVP K 30	3.0	3.0	3.0	3.0	3.0	3.0
Lactose	10	10	10	10	10	10
Total weight	150	150	150	150	150	150

SF = Sustained formulation not containing any polymer.
SXF = Sustained formulation containing Xanthan Gum.

EVALUATION OF MATRIX TABLETS OF FUROSEMIDE

All the prepared matrix tablets were evaluated for uniformity of weight and drug content as per IP method. The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Hardness was measured by using Pfizer hardness tester. Thickness was measured by Vernier caliper.

In vitro drug release studies

The *in vitro* dissolution studies of sustained release matrix tablets of furosemide were carried out using USP XXIII tablet dissolution test apparatus (Electrolab TDT-08L), employing a paddle stirrer at 50 rpm in 900 ml of pH 6.8 phosphate buffer at 37.0° ± 0.5°C. Then 5 ml of samples were collected and replaced with the same amount of dissolution medium at 1hr time intervals for 12 hr. The samples withdrawn were analyzed spectrophotometrically at 276.0 nm using UV-visible double-beam spectrophotometer (Shimadzu UV-1800 spectrophotometer).

RESULTS

Hardness test

The hardness of tablets was found to be in range of 4.86±0.11 to 5.08 ±0.82 kg/cm^2.

Friability test

The % weight loss in friability test of all the

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formulations was found to be less than 1%, indicating that the can withstand the mechanical shock or during handling.

Weight Variation Test: The average weight of tablets was found to be 149-152 mg for all formulations. Overall the all prepared formulations were good quality with regard to weight uniformity. The standard deviation values were within the acceptable limits.

Table 2:Results of physical characteristics of Matrix tablets with Xanthan gum

Formulation Code	Hardness (kg/cm^2) Mean ± SD (n=3)	Thickness (mm) Mean ± SD (n=3)	Average weight (mg) Mean ± SD (n=10)	Friability (%)	Drug content (%) Mean ± SD (n=3)
SX_1	4.86 ± 0.11	3.22 ± 0.11	150.4 ± 0.9	0.19	97.49 ± 1.08
SX_2	4.87 ± 0.06	3.31 ± 0.06	151.7 ± 0.8	0.12	99.78 ± 0.96
SX_3	4.91 ± 0.18	3.21 ± 0.18	149.3 ± 1.1	0.70	98.22 ± 0.69
SX_4	5.08 ± 0.12	3.16 ± 0.12	149.2 ± 0.9	0.75	97.75 ± 0.38
SX_5	4.93 ± 0.11	3.25 ± 0.11	152.4 ± 0.8	0.86	101.21 ± 1.07

Drug Content Uniformity

Uniformity in drug content was found according to I.P specifications and percentage of drug content was more than 95%. All the formulations comply with official standards.

In vitro drug release study

In vitro drug release was studied using USP XXIII tablet dissolution test apparatus (Electrolab TDT-08L), with 900 ml of dissolution medium maintained at 37±1°C for 12 h, at 50 rpm. pH 6.8 phosphate buffer used as a dissolution medium 5ml of sample was withdrawn after every hour, and was replaced by an equal volume of fresh dissolution medium of same pH. Collected samples were analyzed spectrophotometrically at 272 nm, and cumulative percent drug release was calculated.

The data obtained in the in-vitro dissolution study is grouped according to four modes of data treatment as follows:

1. Cumulative percentage drug released Vs time in hrs.

2. Cumulative percentage drug released Vs square root of time in hrs. (Higuchi's classical diffusion)

3. Cumulative percentage drug released Vs time in hrs.

4. Cumulative percentage drug released Vs square root of time in hrs. (Higuchi's classical diffusion)

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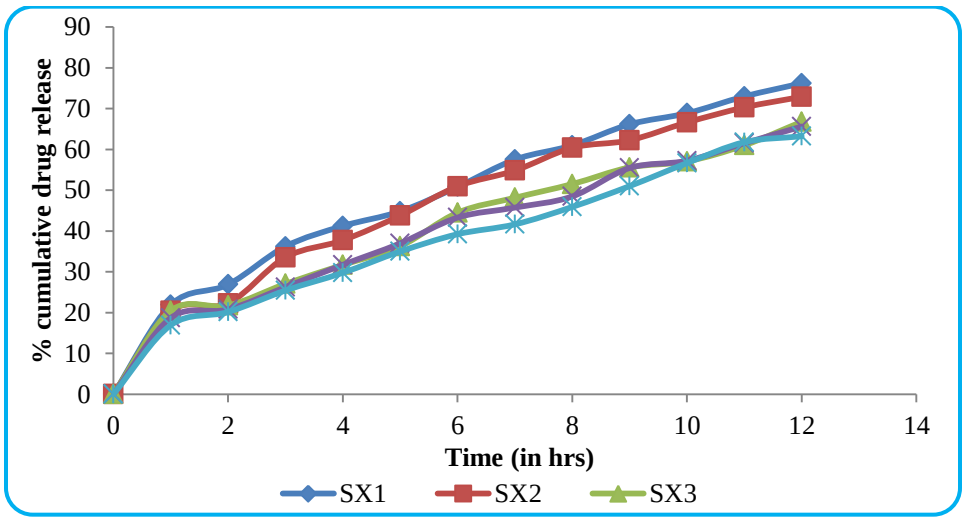

Figure 1: Cumulative percent drug released Vs time plots (zero order) of formulations SX_1, SX_2, SX_3, $SX_4$and SX_5

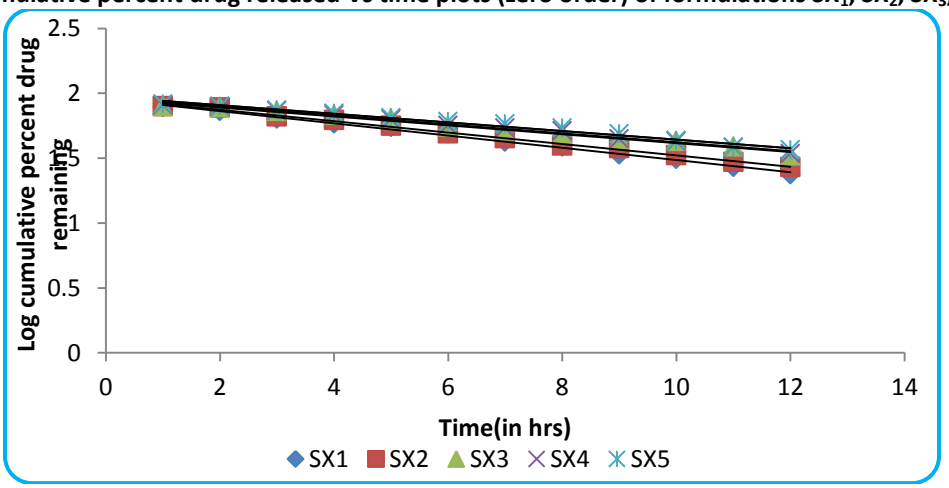

Figure 2: Log cumulative percent drug released Vs time plots (first order) of formulations SX_1, SX_2, SX_3, SX_4 and SX_5

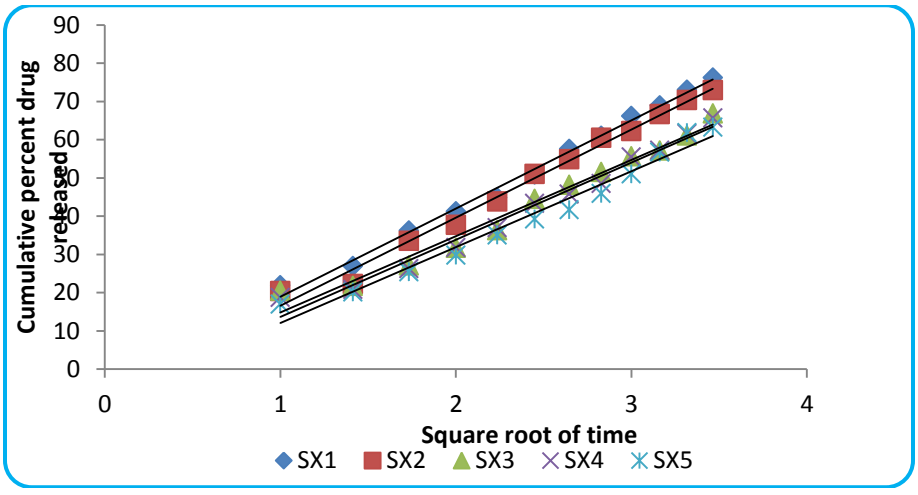

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Figure 3: Cumulative percent drug released Vs square root of time (Higuchi plots) of formulations SX_1, SX_2, SX_3, SX_4 and SX_5

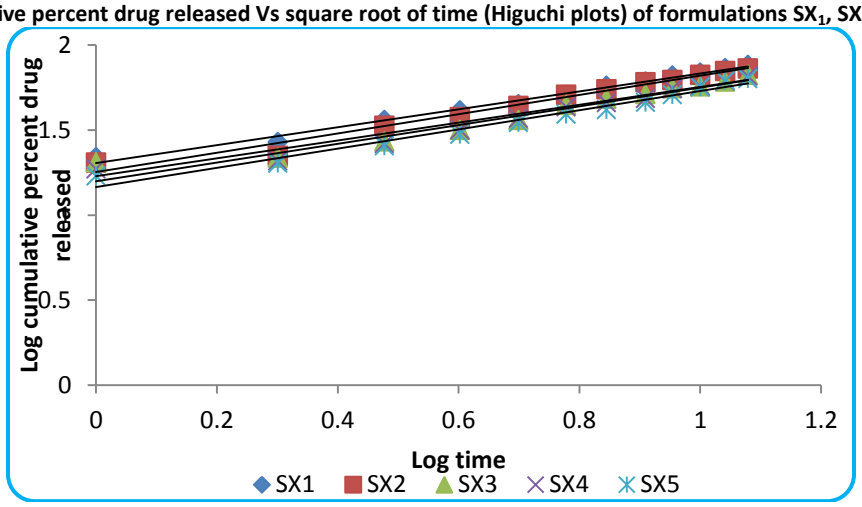

Figure 4: Log cumulative percent drug released Vs log time (Peppas plots) of formulations SX1, SX2, SX3, SX4 and SX5

Kinetic data of the formulations

Formulation code		Zero order	First order	Higichi equation	Peppas equation
SX_1	a	14.33	1.957	4.057	1.305
	b	5.620	0.047	23.02	0.528
	r^2	0.945	0.994	0.993	0.988
SX_2	a	12.65	1.961	6.487	1.253
	b	5.533	0.044	23.04	0.562
	r^2	0.947	0.996	0.989	0.975
SX_3	a	11.06	1.959	5.087	1.1227
	b	4.487	0.034	19.93	0.525
	r^2	0.954	0.987	0.974	0.953
SX_4	a	10.45	1.965	6.458	1.199
	b	4.855	0.034	20.15	0.550
	r^2	0.962	0.990	0.981	0.967
SX_5	a	8.923	1.974	7.803	1.164
	b	4.755	0.033	19.84	0.565
	r^2	0.971	0.982	0.973	0.972

Table 3: Dissolution parameters for the formulations

Sl.No	Formulation code	t_{25} (hrs)	t_{50} (hrs)	t_{75} (hrs)	Cumulative % drug release in 12 hrs
1	**SX_1**	1.36	5.48	10.12	76.23
2	**SX_2**	2.24	5.48	11	72.92
3	**SX_3**	2.36	7.36	---	66.79
4	**SX_4**	2.48	8.12	---	65.63
5	**SX_5**	2.48	8.48	---	63.24

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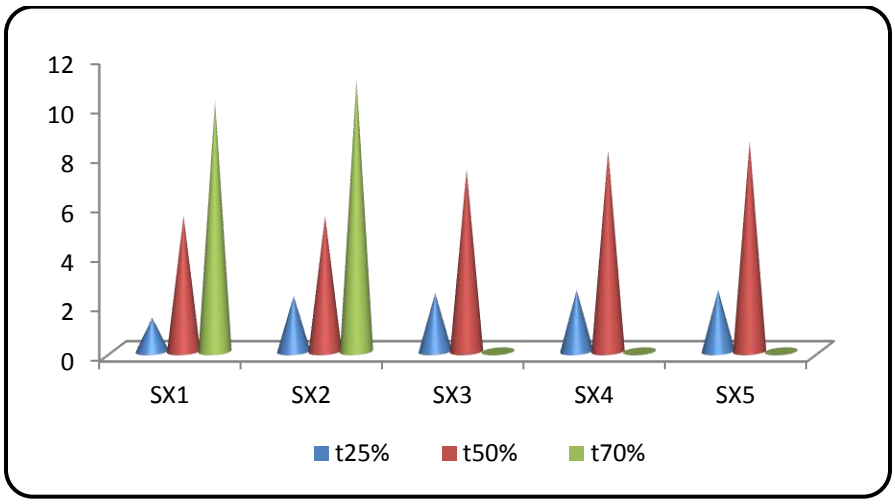

Figure 5: Comparison of dissolution parameters ($t_{25\%}$, $t_{50\%}$ and $t_{70\%}$) of sustained tablets of furosemide.

CONCLUSION

Result of the present study ascertains that natural gum employed was found to be successful informulating the sustained-release matrix tablets of Furosemide. The prepared matrix tablets were evaluated for various parameters like hardness, thickness, weight variation, friability, percent drug content and *in vitro* drug release studies as per USP guidelines. Out of 10 formulations, the formulation SX_1 is selected as best formulation which shows 76.23 % drug release in 12 hrs.

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