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THE STUDY OF SALBUTAMOL MATRIX TABLETS USING DIFFERENT POLYMERS AS RELEASE RETARDING AGENT

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ABSTRACT

Salbutamol sulphate is an antiasthamatic and bronchodilator agent, with half life of 1.6 hours and requires multiple daily doses to maintain adequate plasma concentrations. The present study was undertaken with an aim to formulation development and evaluation of Salbutamol sulphate sustained release tablets using different polymers as release retarding agent. Preformulation study was done initially and results directed for the further course of formulation. Based on Preformulation studies different batches of Salbutamol sulphate were prepared using Xanthan gum, carbopol and ethyl cellulose chosen for their different hydrophilic properties to calculate the suatained release properties. Analysis of Salbutamol is done by UV visible spectrophometer using wavelength 276nm. Results of in-vitro swelling study indicate that the formulation F6 was having considerable swelling index. From the discussion it is concluded that the tablets of batch F4 had considerable swelling behaviors and *in vitro* drug release. Batch F6 can be taken as an ideal or optimized formulation of sustained release tablets for 12 hour release as it fulfills all the requirements for sustained release tablet.

KEYWORDS: Sustained Release, Xanthan Gum, Carbopol 934, Ethyl Cellulose, Salbutamol, Retarding Agents

1. INTRODUCTION

Oral route of drug administration is oldest and safest mode of drug administration. It posses several advantage. It dose not pose the sterility problem and minimal risk of damage at the site of administration. Hydrophilic polymers are widely used in oral controlled drug delivery due to their flexibility to produce desirable drug release profile, cost effectiveness, and broad regulatory acceptance.

In the case of oral sustained released dosage form, an effect is for several hours depending upon residence time of formulation in the GIT.

By considering the facts about drug, the present study was aim to formulate and evaluate the sustained release oral matrix tablet by using Salbutamol sulphate as a model drug and see the effects of different polymers to prolong the release of drug for extended period of time in order to

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- Improve patient compliance
- Reduce dosing frequency.
- Increase bioavailability of the drug.

Salbutamol sulphate is an antiasthamatic and bronchodilator agent, with half life of 1.6 hours and requires multiple daily doses to maintain adequate plasma concentrations. So it is selected to prepare a sustained release tablet.

The objective of this present study is to develop a sustained release tablet of salbutamol sulphate which releases the drug in a sustained manner over a period of 12 hours, by using different polymers and study on polymer concentration effect on release pattern.

- To formulate the sustained release dosage form of Salbutamol.
- To study the effect of polymer concentration on tablet characteristic.
- To study the effect of combination and composition of various polymer materials on tablet characteristic.
- To study the effect of temperature and relative humidity on tablet characteristic.

2. MATERIALS & METHODS

2.1 U.V. Spectrophotometric Method of Analysis:

Stock solution: An accurately weighed 100 mg of Salbutamol Sulphate was dissolved in 100 ml of phosphate buffer of pH 1.2, Ph 5.8, pH 7.4 to get solutions of 1000 µg/ml. From this 10ml of solution was withdrawn and diluted upto 100 ml with phosphate buffer to get Salbutamol sulphate stock solution of 100 µg/ml.

Standard solutions: From above stock solutions different aliquot prepared in the range of 10-100 µg/ml.

Solution of Salbutamol sulphate was prepared and scanned and the result showed maxima at 276 nm.

2.2 Method of granulation:

The different formulation was prepared by using different ratios shown in Table-1.

Table-1: Formulation of salbutamol matrix tablet.

Batch ingredients	F.1	F 2	F3	F 4	F 5	F 6	F 7	F 8	F 9	F10	F11	F 12
Drug	4	4	4	4	4	4	4	4	4	4	4	4
Ethyl cellulose	20	-	-	40	-	-	60	-	-	20	40	60
Carbopol 934P	-	20	-	-	40	-	-	60	-	20	40	60
Xanthan gum	-	-	20	-	-	40	-	-	60	20	40	60
Compressible Lactose	170	170	170	150	150	150	130	130	130	130	70	10
Magnesium Sterate	4	4	4	4	4	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2	2	2	2	2	2

Each quantity mentioned will be taken in mgs

2.3 Determination of bulk density and tapped density:

The bulk density, and tapped density were calculated using the following formulas.

Bulk density $= W/V_o$
Tapped density $= W/V_f$

Where,

V_o = initial volume
V_f = final volume.

2.4 Compressibility index:

The compressibility index and Hausner ratio may be calculated using measured values for bulk density (ρ_{bulk}) and tapped density (ρ_{tapped}) as follows:

$$\text{Compressibility index} = \frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} X\,100$$

$$\text{Hausner ratio} = \frac{\rho_{tapped}}{\rho_{bulk}}$$

2.5 Loss on Drying:

Determination of loss on drying of granules is important drying time during granulation was optimized depending LOD value. LOD of each batches were tested at 105°C for 2.5 minutes by using "Sartorius" electronic LOD apparatus.

2.6 Angle of repose:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

$\text{Tan}\,\theta = h/r$
$\theta = \tan^{-1} h/r$

Where h = height of pile
r = radius of the base of the pile
θ = angle of repose

2.7 Modeling of Dissolution Profiles:

In the present study, data of the *in vitro* release were fitted to different equations and kinetic models to explain the release kinetics of salbutamol sulphate from the matrix tablets. The kinetic models used were a Zero order equation, First order, Higuchi release and Korsmeyer-Peppas models.

3. RESULT AND DISCUSSION

3.1 Standard curve of Salbutamol sulphate

Table-2: Drug Calibration Data

S. no.	Concentration (mcg/ml)	Abs (pH 1.2)	Abs (pH 5.4)	Abs (pH 7.4)
1	10	0.087	0.053	0.041
2	20	0.178	0.108	0.089
3	30	0.260	0.168	0.132
4	40	0.340	0.220	0.169
5	50	0.425	0.276	0.215
6	60	0.510	0.329	0.259
7	70	0.594	0.380	0.317
8	80	0.673	0.430	0.352
9	90	0.749	0.480	0.401
10	100	0.836	0.536	0.456

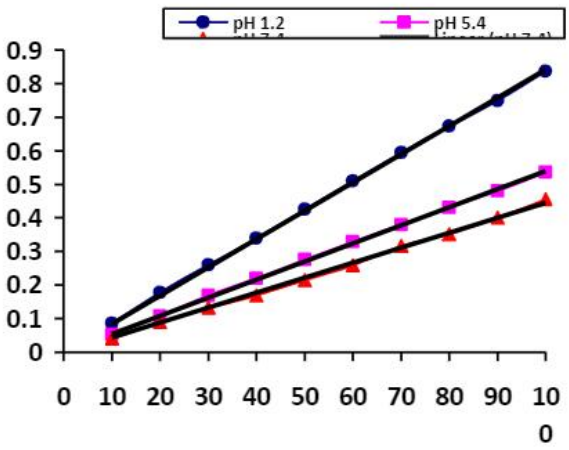

Fig-1Standard Calibration Curve

Table-3: Preformulation studies

Batch	Bulk Density	Tapped Density	Carrs Index	Hausners Ratio	Θ (degree)
F 1	0.488	0.526	7.22	1.08	22.14±0.03
F 2	0.512	0.574	10.80	1.12	19.16±0.06
F 3	0.486	0.526	7.22	1.08	24.18±0.05
F 4	0.502	0.581	13.60	1.16	18.16±0.04
F 5	0.523	0.602	13.12	1.15	19.14±0.02
F 6	0.543	0.592	8.47	1.09	21.14±0.02
F 7	0.499	0.564	11.52	1.13	20.42±0.01
F 8	0.544	0.601	9.48	1.10	18.21±0.02
F 9	0.561	0.611	8.19	1.08	24.14±0.04
F 10	0.491	0.566	13.25	1.15	19.42±0.41
F 11	0.544	0.601	9.48	1.10	20.64±0.02
F 12	0.442	0.506	12.65	1.14	21.42±0.04

Table-4: Results of Thickness and Disintegration time

Parameter Batch	Thickness (mm)*	Disintegration Time(sec)*	Weight Variation(mg)	Hardness (Kg/cm2)*	Friability (%)	Drug Content (%)
F 1	3.3	190±	200.1	5.53	0.52	99.50
F 2	3.1	210	198.9	5.60	0.58	92.89
F 3	3.3.	145	202.1	5.86	0.62	100.02

F 4	3.3	205	201.4	6.00	0.55	99.59
F 5	3.2	250	199.3	6.18	0.64	99.38
F 6	3.3	197	198.4	6.23	0.59	97.05
F 7	3.1	240	200.7	6.40	0.67	99.60
F 8	3.2	300	201.5	6.46	0.70	91.69
F 9	3.2	243	199.3	6.63	0.66	95.62
F 10	3.3	207	200.1	6.73	0.54	99.50
F 11	3.1	275	203.1	6.80	0.53	100.02
F 12	3.3.	310	199.3	6.93	0.64	99.60

Table-5: Drug Release Profile

Serial no.	Time (min)	F 1	F 2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	M
1	10	3.21	4.28	3.75	2.94	4.28	4.01	3.21	4.82	3.21	2.94	2.67	2.67	2.41
2	20	6.71	9.13	6.71	5.10	8.59	8.32	5.10	6.99	5.37	6.44	4.83	3.49	4.03
3	30	9.96	15.34	9.96	7.54	14.53	12.38	6.20	9.17	8.35	7.81	7.00	4.58	6.19
4	60	17.25	21.31	14.57	15.35	21.04	15.94	9.45	11.36	10.54	9.73	7.84	5.95	11.05
5	90	19.72	25.67	21.04	19.16	25.93	21.07	12.08	16.47	15.65	12.97	10.00	7.84	15.91
6	120	22.27	33.90	23.61	20.36	32.82	26.05	16.71	19.82	18.72	15.48	11.96	9.510	22.18
7	150	29.46	46.8	37.47	25.92	42.82	35.71	18.60	28.30	26.39	24.01	19.70	14.79	29.04
8	180	32.00	58.97	50.46	29.28	57.05	46.18	23.22	33.35	31.85	29.89	23.07	18.15	34.08
9	210	34.97	69.94	59.78	32.25	63.21	52.13	24.95	41.76	39.43	37.06	25.64	20.70	42.48
10	240	41.29	77.64	64.98	39.82	72.75	61.02	27.94	51.05	47.04	43.85	32.38	22.84	47.60
11	300	52.03	93.50	79.81	44.93	86.04	70.74	33.57	62.30	57.78	59.70	45.68	30.00	53.73
12	360	58.23		87.05	49.05	88.67	77.95	35.13	70.03	63.47	63.88	49.33	32.09	57.86
13	420	62.41		93.82	50.12	93.88	85.72	40.80	75.76	68.16	69.10	55.56	34.70	66.10
14	480	64.58			53.76	97.06	89.94	43.94	83.57	71.86	73.84	58.76	37.83	77.45
15	540	67.26			56.39		92.66	46.58	88.352	75.06	77.08	62.99	40.98	85.79
16	600	70.98			62.11		94.86	49.75	92.13	76.75	81.86	65.20	43.13	93.68

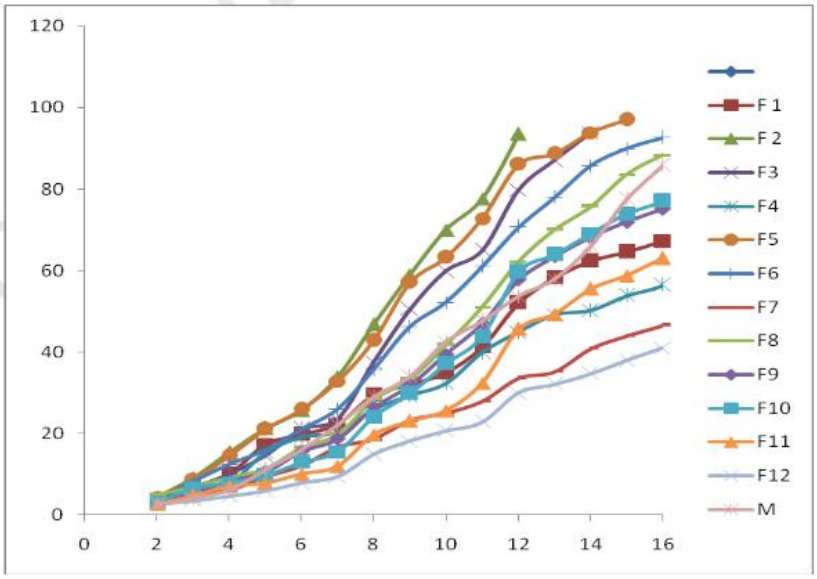

Fig-2: Comparative study of drug release of different formulations

Table-6: Comparison of all kinetic modals

Batch code	Zero order	First order	Higuchi	Korsmeyer-Peppas	Similarity Factor
F1	0.9580	0.7371	0.9855	0.9895	48.75
F2	0.9911	0.8616	0.9507	0.9838	34.38
F3	0.9765	0.8344	0.9547	0.9846	38.01
F4	0.9447	0.7092	0.9905	0.9885	38.78
F5	0.9471	0.7559	0.973	0.9876	62.57
F6	0.9471	0.7573	0.9696	0.9863	94.88
F7	0.9736	0.8136	0.9796	0.9833	29.54
F8	0.9653	0.8256	0.9655	0.9713	61.31
F9	0.9533	0.7821	0.9697	0.9858	57.076
F10	0.9641	0.8141	0.9568	0.9713	59.213
F11	0.9734	0.8385	0.9514	0.967	35.493
F12	0.9744	0.8308	0.9718	0.9718	38.434

SUMMARY AND CONCLUSION

The present study was undertaken with an aim to formulation development and evaluation of Salbutamol sulphate sustained release tablets using different polymers as release retarding agent. Preformulation study was done initially and results directed for the further course of formulation. Based on Preformulation studies different batches of Salbutamol sulphate were prepared using selected excipients.

Various formulations of sustained release tablets of Salbutamol sulphate were developed using various polymers viz, ethyl cellulose, carpool and Xanthan Gum in different proportions and combinations by wet granulation technique.

Results of *in vitro* release profile indicated that formulation (F6) was the most promising formulation as the extent of drug release from this formulation was high as compare to other formulations.

Results of in-vitro swelling study indicate that the formulation F6 was having considerable swelling index.

Stability study was conducted on tablets of Batch F6 stored at room temperature, 40^0C and 2-8^0C for one month. Tablets were evaluated for hardness, friability, in-vitro release profile and drug content, after one month no significant changes were observed in any of the studied parameters during the study period, thus it could be concluded that formulation was stable.

From the discussion it is concluded that the tablets of batch F4 had considerable swelling behaviors and *in vitro* drug release. It was observed that tablets of batch F4 followed the Non-Fickenian release profiles.

From the above results and discussion it is concluded that formulation of sustained release tablet of Salbutamol sulphate containing Xanthan gum(10%),

Batch F6 can be taken as an ideal or optimized formulation of sustained release tablets for 12 hour release as it fulfills all the requirements for sustained release tablet.

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