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FORMULATION AND EVALUATION OF TIME DEPENDENT DRUG DELIVARY FOR ASTHMA

Mohd. Vaqqas Quraishi, Nishan N. Bobade, Ketakee A. Nichat, Chitralekha G. Therkar, Kajal S. Jumde
Department of Pharmaceutics
Vidyabharati College of Pharmacy,
C. K. Naidu Road , Camp , Amravati, Maharashtra , INDIA 444602

ABSTRACT -

The primary purpose of this study was to design and evaluate a single-unit time-controlled oral pulsatile drug delivery system containing salbutamol sulphate for nocturnal asthma attack prevention. Time-dependent delivery systems are intended to provide a rapid or prolonged release of the medicine after a certain amount of time, referred to as the lag time. These systems can be used for a variety of purposes, including chronotherapeutic formulations and medication administration into the colon. The purpose of this work was to create a time-dependent press-coated tablet. This work seeks to create and assess a chronomodulated drug delivery system of antiasthmatic medication, a selective 2 receptor blocker for the treatment of nocturnal asthma, which is valid and acceptable reasoning. The purpose of this paper is to provide an overview of the rationale for delayed-release dosage forms as well as the primary formulation methodologies. Maintain a lag time of 4-6 hours before drug release and a lag time of 4-5 hours between plasma peak concentration and controlled release of a medication indicated for the pharmacological treatment of asthma. The goal was to have a six-hours lag time. The device is used at bedtime and is expected to deliver the medicine after 6 hours, or around 4 a.m. when asthma episodes are most common.

Method: Drug-containing core tablets with various superdisintegrant compositions such as sodium starch glycolate, croscarmellose sodium, and crospovidone were made using direct compression technique. The fast-dissolving core tablet formulation was chosen, and press-coated tablets were manufactured with hydroxypropyl methylcellulose K4M in varied hydrophobic and hydrophilic polymer compositions. The coated polymers were chosen and measured based on in vitro lag time and drug release profile in simulated stomach and intestinal fluids.

Result : The crospovidone formulation had the fastest dissolving time, 0.31 minutes, and was chosen as the best instant release core tablet. The press-coated tablet formulation with a 360 mg barrier layer over the core tablet exhibited quick and full drug release after a 6-hour lag period. The revised formulation's expedited stability assessments after 6 months found no significant variations in release profile.

Conclusion: The coating amount and kind of coating polymer used had a substantial influence on the lag time before medicine release, according to the in vitro dissolution study. Time-controlled pulsatile release tablets can be created using press-coating methods.

Keywords: Salbutamol sulfate, asthma, Time-controlled pulsatile tablet, Time Dependent Delivery ,Press-coated tablet, 6 h lag time, Burst release .

INTRODUCTION:

The delivery of pharmaceuticals at a time that corresponds to biological requirements for the treatment or prevention of a certain disease is known as chronopharmaceutics . Pulsatile drug delivery systems (PDDS) are a chronopharmaceutical technology in which the medication is released in pre-programmed patterns using a lag time [3]. The most common chronic condition in children is asthma . It's a respiratory inflammatory condition that lasts for years. Nocturnal asthma sufferers experience an increase in airway resistance and a reduction in lung function in the early morning hours. Two-thirds of asthmatics experience symptoms at night. Asthma episodes are 100 times more likely to happen at night than during the day. The forced expiratory volume in one second is lower at 4 a.m. [5,6]. Histamine levels peaked around 4 a.m., at a level that corresponds to the most acute bronchoconstriction [1]. Nocturnal bronchoconstriction is caused by circadian fluctuations in adrenaline, cortisol, histamine, AMP, melatonin, vagal tone, body temperature, lower airway secretions, and other variables . Salbutamol is a rapidly acting, highly selective Beta 2-adrenoceptor agonist with few cardiac side effects. It is used to treat asthma by relaxing the smooth muscle of the bronchial tubes, allowing the bronchi to dilate promptly [9,10]. The GI tract absorbs Oral Salbutamol Sulfate Tablets (2–4 mg) well, with an absolute bioavailability of 44% and a peak plasma concentration of 1–3 hours [11On the other hand, salbutamol sulphate has a short biological half-life (3.8–6 hours) and a high first-pass metabolism. High dosages or prolonged use might result in hypokalemia. These limitations can be reduced by using salbutamol sulphate formulations with time-controlled pulsatile release doses [12].

If asthma symptoms are severe at night or early in the morning, treating asthma with rapid release dose forms may be impractical. Pulsatile-release dose forms can be given after night, with medication release beginning in the early morning hours when asthmatic episodes are most likely [13].

We chose a single pulse system because of the advantages of manufacturing simplicity. When compared to normal pan-coated procedures, compress-coated techniques alleviate the instability of salbutamol sulphate (a hygroscopic medication) [14,15].

METHODS AND MATERIALS:

MATERIALS

Salbutamol sulfate was obtained as a gift sample from Neuland laboratories Pvt. Ltd. Hyderabad, hydroxypropyl methylcellulose K4M (HPMC K4M), low substituted, sodium starch glycolate (SSG), croscarmellose sodium (CCS), crospovidone, polyvinyl pyrrolidone K-30, microcrystalline cellulose , magnesium stearate, aerosil 200, and lactose monohydrate used were of pharmacopoeial grade. A novel technique “time-dependent PDDS” was designed with drug contained in fast disintegrating core and press-coated with suitable barrier layer. Drug-containing core tablets with different composition of super disintegrates such as SSG, CCS, and crospovidone were prepared by direct compression technique. The fast disintegrating core tablet formulation was selected, and press coated tablets were prepared with different compositions of hydrophobic and hydrophilic polymers, HPMC K4M,ethyl cellulose, Eudragit S100. The coating polymers were selected and quantified based on in vitro lag time and drug release profile in simulated gastric and intestinal fluids.

METHODS

Formulation of core tablets by direct compression The ingredients as depicted in Table 1 except magnesium stearate and aerosil-200 were dry blended for 15 min followed by addition of quitted ingredients and dry blending for another 5 min. The mixed blend of drug and excipients was compressed using a single punch rotary punching machine to produce round tablets weighing 100 mg with a diameter of 9 mm. Evaluation of core tablet

Preparation of press-coated tablets:

The core tablets were press-coated with prepared barrier blends as per the mentioned formulas from T1 to T9. Initially, half of barrier layer material was weighed, and then the core tablet was placed manually at the center. The remaining half of the barrier layer material was added into the die and compressed.

Dissolution rate studies of press-coated tablets:

Dissolution rate studies were performed for all the press coated tablets using, an eight-stage dissolution rate testing apparatus with paddle. The dissolution fluid was 900 ml 0.1 M HCl for 2 h, which was replaced with phosphate buffer pH 6.8. The test was performed at 50 rpm and at a temperature of 37±0.5°C. Samples were withdrawn for every ½ h up to 7 h and the lag times were observed for every batch tablet, and the collected samples were analyzed for the drug released by ultraviolet spectrophotometer at 276 nm to know whether the formulations show sigmoidal release[16]

Table No 1 .Manufacturing formula of the core tablet:

core tablet		Quantity in mg/tablet								
S.N	Ingredients	T1	T2	T3	T4	T5	T6	T7	T8	T9
1	salbutamol Sulphate	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8
2	Microcrystalline cellulose	10	10	10	10	10	10	10	10	10
3	Magnesium stearate	3	3		3	3	3	3	3	3
4	Crospovidone	0	0	0	3	6	9	0	0	0
5	Croscarmellose sodium	0	0	0	0	0	0	3	6	9
6	Lactose monohydrate	73	70	67	73	70	67	73	70	67
7	PVP K30	5	5	5	5	5	5	5	5	5
8	Sodium starch glycolate	3	6	9	0	0	0	0	0	0
9	Aerosile-200	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
	Total Weight(mg)	100	100	100	100	100	100	100	100	100

Table No .2 Manufacturing formula of barrier layer for press-coated tablets:

Coated Tablet		Quantity in mg/tablet				
S.N	Ingredient	F1	F2	F3	F4	F5
1	Core tablet	100	100	100	100	100
2	Eudragit S100	50	100	150	200	250
3	HPMC K4M	250	200	150	100	50
4	Ethyl celluose	50	50	50	50	50
	Total Weight(mg)	450	450	450	450	450

EVALUATION OF TIME DEPENDENT COATED TABLET:

DRUG AND POLYMER COMPATIBILITY STUDIES: The FTIR spectrum of drug was recorded on an infrared spectrophotometer (Shimadzu Affinity-1). IR spectrum the of drug, polymers, and their physical mixture were recorded in the frequency range of 400-4000 cm-1. The recorded peaks were then noted and matched with standard FTIR of the drug.

CALIBRATION CURVE OF SALBUTAMOL SULPHATE : From solution having concentration 100 µg/ml parts of 0.2, 0.4, 0.6, 0.8, 1.0, 1.2,1.4, 1.6, 1.8, and 2 ml were pipette out into 10 ml volumetric flasks. The volume was made up to the mark with 0.1N HCL to get the final concentration of 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 µg/ml respectively. The absorbance of each concentration was measured at 276 nm. A graph of absorbance versus concentration was plotted. It shows the straight line which means calibration curve obeys the Beers Lamberts law[18]

PRECOMPRESSION STUDY :

Angle of Repose - On rotation, the angle of repose is the greatest angle formed by the plane of powder with the horizontal surface. Angle of repose is useful in determining particle flow qualities, which may be connected to particle packing densities and mechanical arrangements. The fixed the funnel and free standing cone method was used to calculate the powder angle of repose. The grains were carefully weighed. The funnel's height was then modified such that the funnel's tip just touched the pinnacle of the granules heap. Granules were permitted to flow freely through the funnel onto the surfaces. The powder cone's diameter and angle of repose were measured.[25]

Bulk density may be calculated by putting preserved bulk powder into a graduated measuring cylinder and measuring the volume and weight of the powder. The following formula can be used to compute bulk density.

$$\text{Bulk Density} = \frac{\text{Weight}}{\text{Bulk Volume (Vo)}}$$

Determination of Tapped density - Tapped density can be determined by pouring preserved powder into a graduated measuring cylinder via a large funnel and tapped for 100 times on a wooden plank and measuring the volume and weight of the powder. Tapped density can be calculated by the following formula

$$\text{Tapped Density} = \frac{\text{Weight}}{\text{Tapped Volume (Vt)}}$$

Compressibility Index (or) Carr' index (I) – An indirect method of measuring powder flow from bulk densities was developed by Carr. The percentages of compressibility of the powder is a direct measure of the potential powder arch and stability. Carr's index of the each formulation prepared was calculated

EVALUATION OF TIME DEPENDENT CORE TABLET:

Dimensions – Control of physical dimension of the tablets such as thickness and is essentials for consumer acceptance and tablets uniformity. The thickness and diameter of the tablets are carried out using digital Vernier Calliper. Three tablets are used from each batch and the results are expressed in Millimetre (mm).

Weight Variation Test – 20 tablets are selected at random, individually weighed in a single pan electronic balance and the average weight is calculated. As per IP not more than two of individual weights should deviate from average weight by more than 5% and none deviate more than twice that Percentage.[25]

Hardness Test –The tablet was held between a fixed and moving jaw. Scale was adjusted to zero and then load is gradually increase till the tablet starts to break. The value of the load at that point gives the hardness of the tablet. Three tablets from each batch are used for hardness test and results are expressed in Kg/cm2 .

Friability Test – Pre weighed samples of 20 tablets are placed in the friabilator, which is then operated for 100 revolutions (5 min). The tablets are then dusted and reweighted. Compressed tablets that loss less than 0.5 to 1.0% of their weight are generally considered acceptable.

In vitro Study - The lag time capacity of the tablets was determined using USP Dissolution apparatus II containing 900 ml of simulated gastric fluid. The time interval between introduction of the tablet in to the dissolution medium and its buoyancy to the dissolution medium was taken as buoyancy Lag Time and then the after 2hr transfer in buffer 7.4 and 6.8 and calculated lag time capacity of coated tablet[26,28]

Determination of Drug Content - Ten tablets are weighed and taken in a mortar and crushed to make powder form. A quantity of powder weighing equivalent to 10 mg of drug is taken in a 100 ml volumetric flask and 0.1 N HCl was added. The solution is filtered using membrane filter (0.45µm) and 10 ml of filtrate is taken into 100 ml volumetric flask and made up to final volume with buffer pH 6.8. Then its absorbance is measured at 200-400nm using UV Visible spectrometer. Then the amount of total drug present in the one tablet is calculated

IN - VITRO DRUG RELEASE STUDIES: Dissolution characteristics of the formulated press coated tablets of salbutamol sulphate was carried out using USP Type II (paddle) dissolution test apparatus for 9 hrs. Method - 900 ml of 0.1 N HCl .PH 7.4 and 6.8 was filled in dissolution vessel and temperature of the medium is set at 37°C ± 0.5°C. One tablet of different batch is placed in each dissolution vessel and the rotational speed of paddle was set at 50 rpm. 5ml of sample is withdrawn at pre-determined time interval of every one hour for up to 9 hours and same volume of fresh medium is replaced immediately. The withdrawn sample is diluted to 10 ml in volumetric flask and filtered through 0.45µ membrane filter. The resultant samples are analyzed for drug content at 200-400 nm using UV-Visible spectrophotometer.

DETERMINATION OF SWELLING INDEX: For each formulation batch, one tablet was weighed and placed in a beaker containing 100 ml of media. After each interval, the tablet should be removed from the media and weighed again up to 24 hours and note down the readings

STABILITY STUDIES: In the present study, stability studies were carried out at 40°C ± 2°C, 70 ± 5% RH), (24°C ± 2°C ,70% ± 5% RH) and (40°C ± 2°C, 70% ± 5% RH) for a specific time period up to 4week for the optimized formulation. The optimized formulation was analyzed for the drug contents study, pH, lag time (hr), cumulative drug release (%). Experiments were performed in triplicate and average values are noted. The stability studies data was then recorded.

RESULTS AND DISCUSSION:

EVALUATION OF TIME DEPENDENT PRESS COATED TABLET:

Drug and polymer compatibility studies –

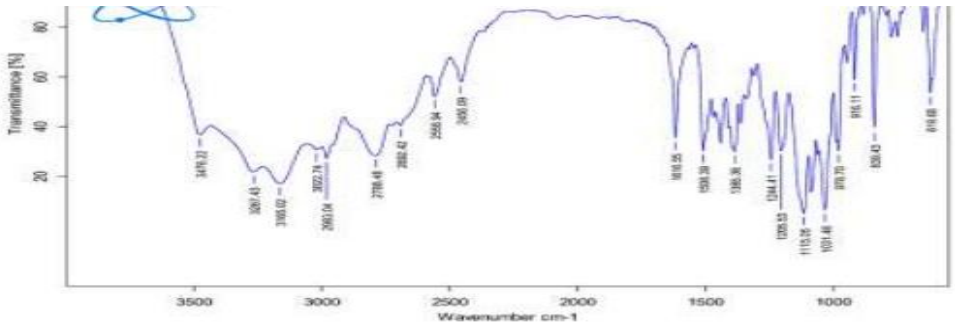


Fig. 1: FT-IR spectrum of Salbutamol sulphate drug

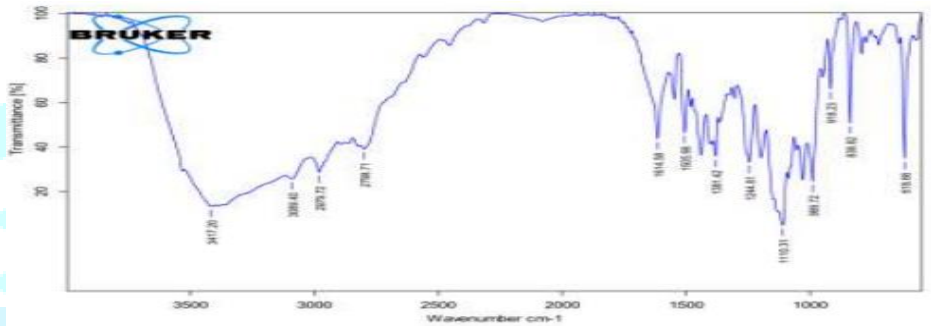


Fig. 2: FTIR graph of Salbutamol sulphate +Croscarmellose sodium

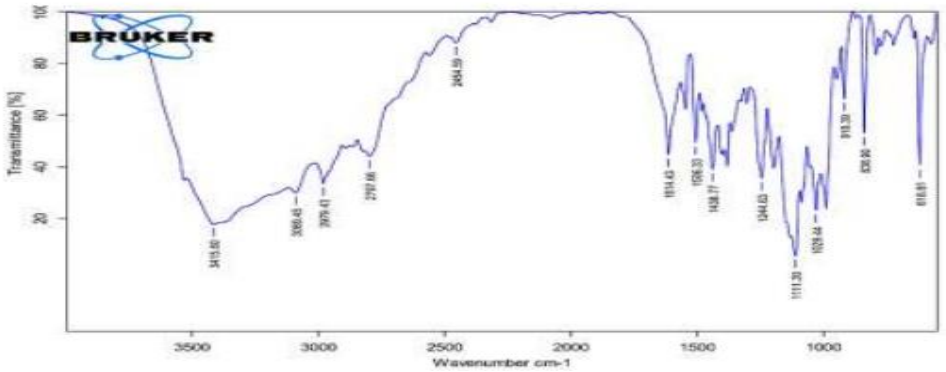


Fig. 3: FTIR graph of Salbutamol sulphate +Sodium starch glycolate.

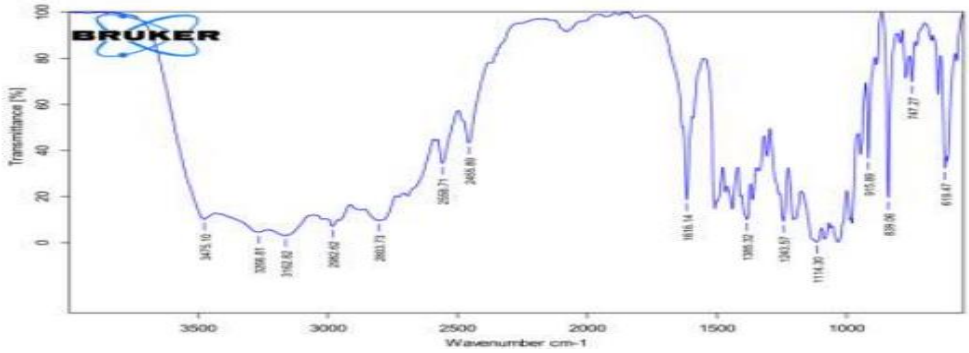


Fig. 4: FTIR spectrum of Salbutamol sulphate +HPMCK4M.

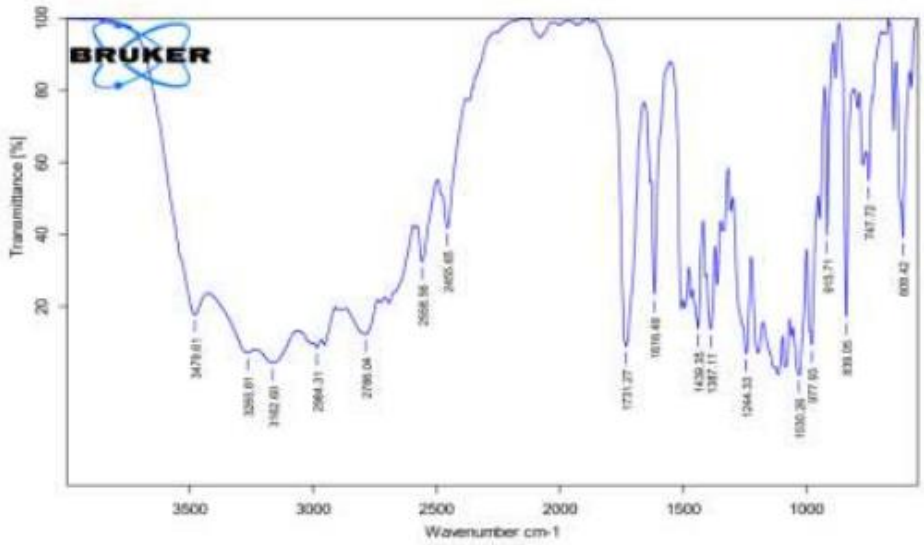


Fig. 5: FTIR spectrum of Salbutamol sulphate +Eudragit S100.

The results of FTIR study shows that, the drug was not found to show any interactions with the polymers i.e. Eudragit S100 , Croscarmellose sodium and HPMC K4M. Hence we can use the chosen polymers for further study.

Calibration Curve of salbutamol sulphate with distill water:

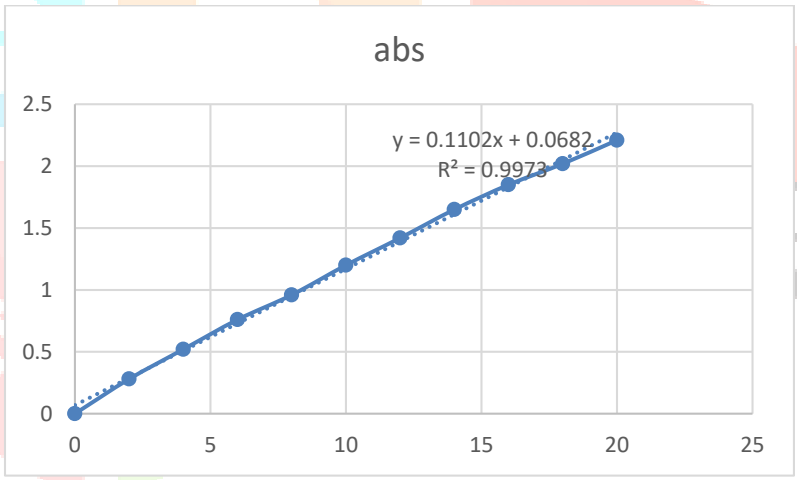


Fig.6 Calibration Curve of salbutamol sulphate with distill water

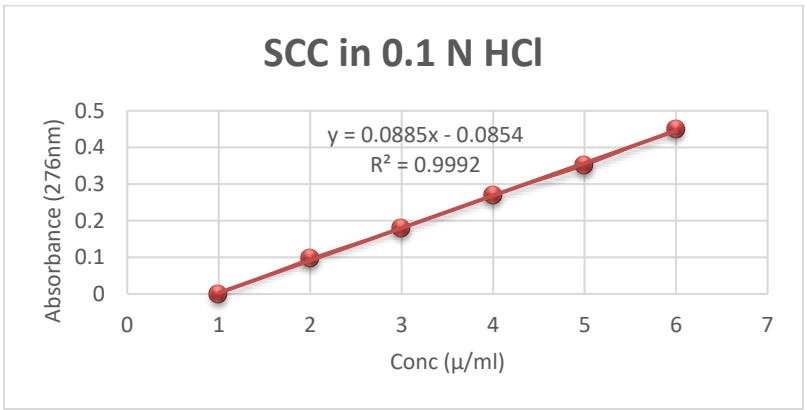


Fig.7 Calibration Curve of salbutamol sulphate with 0.N HCL

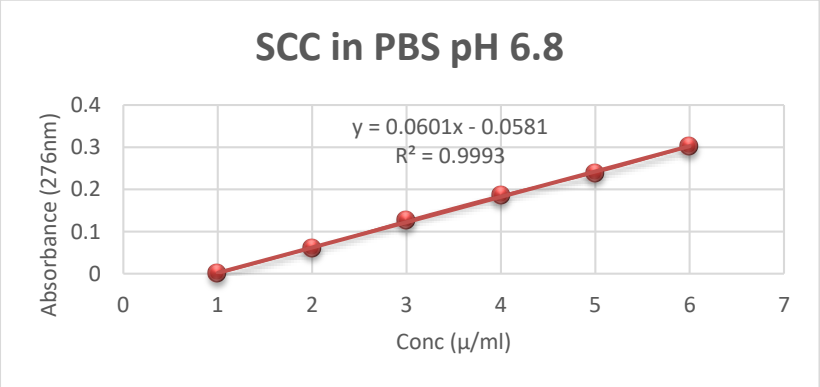


Fig.8 Calibration Curve of salbutamol sulphate with Ph6.8

The calibration curve of salbutamol sulphate shows the R2 value which is equals to 0.999 nearly a straight line which shows that the study follows beers law

Table No .3 Evaluation of directly compressible of core tablet powder

formulation batch	bulk density (g/cm3 ± SD)	tapped density (g/cm3 ± SD)	carr's index (% ± SD)	Hausner's ratio(± SD)	angle of repose(± SD)
T1	0.56±0.02	0.63±0.02	12.91±1.08	1.13±0.01	24.9±0.38
T2	0.57±0.01	0.66±0.01	12.31±1.04	1.12±0.02	24.23±0.34
T3	0.56±0.01	0.67±0.03	12.80±1.10	1.12±0.01	23.17±0.44
T4	0.58±0.02	0.65±0.02	13.25±0.89	1.14±0.01	23.29±0.38
T5	0.59±0.00	0.63±0.12	12.4±0.96	1.13±0.00	24.76±0.32
T6	0.60±0.02	0.66±0.15	13.2±0.59	1.14±0.01	22.87±0.40
T7	0.54±0.01	0.63±0.05	12.36±0.79	1.15±0.02	24.54±0.39
T8	0.52±0.01	0.66±0.08	12.3±0.82	1.14±0.01	24.47±0.39
T9	0.53±0.01	0.63±0.09	12.34+_0.45	1.13±0.00	24.44±0.33

Table No .4 Evaluation of formulations of core tablet

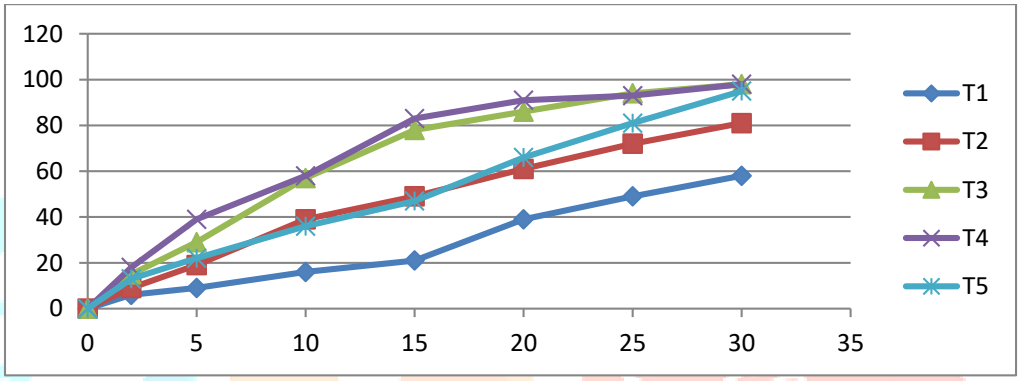
Formulation batch	Weight variation(mg)	Hardness (kg/cm3)	Thickness (mm)	Friability	Drug content	Disintegration Time
T1	101.1±1.42	3.76±0.19	1.96±0.04	0.29	98.6±0.21	12.61±0.30
T2	99.7±1.39	3.69±0.16	1.97±0.08	0.31	98.7±0.23	6.71±0.79
T3	100.8±1.43	3.66±0.18	1.99±0.03	0.35	99.6±0.24	3.95±0.39
T4	101.6±1.34	3.68±0.11	1.98±0.08	0.32	97.67±0.18	2.19±0.24
T5	101.9±1.47	3.74±0.17	2.01±0.07	0.31	99.56±0.17	2.76±0.20
T6	99.8±1.54	3.79±0.9	1.99±0.09	0.37	99.23±0.27	1.45±0.09
T7	99.9±1.45	3.73±0.21	2.02±0.03	0.38	97.91±0.32	1.20±0.10
T8	100.2±1.59	3.65±0.20	1.98±0.10	0.36	99.16±0.29	0.58±0.06
T9	101.1±1.41	3.63±0.23	1.98±0.11	0.28	99.69±0.33	0.35±0.03

IN-VITRO DISSOLUTION PROFILE OF CORE TABLET :

In Vitro drug release of Core tablet

Table No .5 %Cumulative Drug Release in Different Trial

time	T1	T2	T3	T4	T5
0	0	0	0	0	0
2	6.68±0.26	9.36±0.16	15.59±0.26	18.59±0.34	13.26±0.46
5	9.16±0.19	19.49±0.03	29.49±0.25	39.76±0.29	22.35±0.65
10	16.43±0.14	39.59±0.21	57.59±0.16	58.69±0.06	36.86±0.39
15	21.68±0.28	49.59±0.14	78.48±0.09	83.34±0.35	47.49±0.48
20	39.63±0.11	61.19±0.23	86.67±0.21	91.48±0.25	66.68±0.16
25	49.43±0.02	72.49±0.16	94.68±0.18	93.86±0.04	81.16±0.32
30	58.59±0.09	81.68±0.06	98.49±0.04	98.26±0.03	95.49±0.03

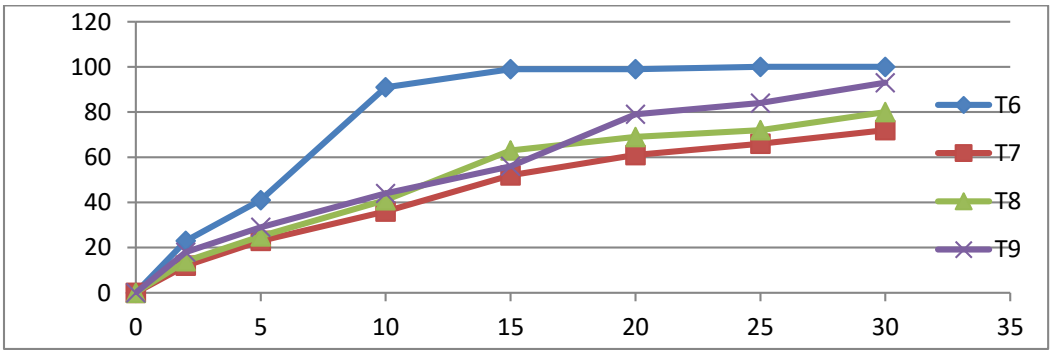


%Cumulative Drug Release of core tablet

Table No .6 %Cumulative Drug Release in Different Trial

T6	T7	T8	T9
0	0	0	0
23.26±0.16	12.86±0.06	14.59±0.29	18.68±0.12
41.95±0.19	23.48±0.07	25.59±0.07	29.46±0.26
91.19±0.24	36.36±0.14	41.68±0.21	44.19±0.04
99.56±0.11	52.48±0.29	63.19±0.06	56.68±0.14
99.48±0.16	61.91±0.06	69.69±0.19	79.32±0.04
100.02±0.01	66.82±0.21	72.48±0.13	84.61±0.06
100.03±0.04	72.48±0.09	80.47±0.09	93.49±0.03

All values are expressed as mean ± standard deviation, n=3



%Cumulative Drug Release of core tablet

Table No.7: Evaluation of press-coated tablet

Formulation batch	Weight variation	Hardness (kg/cm3)	Thickness(mm)
F1	448.3±3.87	6.79±0.69	3.86±0.03
F2	447.7±2.64	7.46±0.75	3.91±0.02
F3	450.8±4.46	9.65±0.43	3.93±0.05
F4	451.4±3.76	8.18±0.41	3.87±0.04
F5	450.3±3.91	7.78±0.56	3.82±0.03

The Average Weight of all time dependent core tablets within formulation was found to be uniform. This indicates uniform filling of the die cavity during tablet compression.

The Hardness of all time dependent core tablets was found to be in the range of 3.63±0.23to 3.79±0.9 kg/cm2. This insures good mechanical strength.

The Thickness of all time dependent core tablets was found in the range of 1.96±0.04 to 2.02±0.03mm. There were no marked variations in the thickness of all formulation indicating uniform behavior of powder throughout the compression process.

The Friability of all time dependent core tablets was found to be in range 0.28 to 0.38,which indicates the good flow ability.

The Drug Content of all formulations was found to be in between 97.67±0.18 to 99.69±0.33%. The values ensures good uniformity of drug content in the tablet.

From the results it was observed that,Lag Time of all formulations was in range 4.33 to 5.56 h.

Table No .8 %swelling index

TIME	F1±SD	F2±SD	F3±SD	F4±SD	F5±SD
0	0±0	0±0	0±0	0±0	0±0
1	5.6±0.659	3.7±0.946	4.8±0.458	4.2±0.486	3.8±0.459
2	12.4±0.349	9.5±0.491	11.4±0.365	9.1±0.963	8.5±0.756
3	28.8±0.465	22.3±0.459	23.7±0.893	17.6±0.489	14.9±0.953
4	39.5±0.683	34.2±0.763	32.6±0.148	25.7±0.256	23.6±0.415
5	54.2±0.861	42±0.369	45.3±0.349	33.9±0.346	29.7±0.563
6	66.3±0.684	56.7±0.159	58.6±0.843	41.4±0.692	38.4±0.489
7	74.2±0.629	66.4±0.986	69.7±0.459	51.6±0.315	47.9±0.256
8	79.5±0.734	70.9±0.146	76.5±0.136	56.8±0.852	54.6±0.864
9	92.7±0.364	74.6±0.356	82.9±0.896	64.9±0.469	61.8±0.789

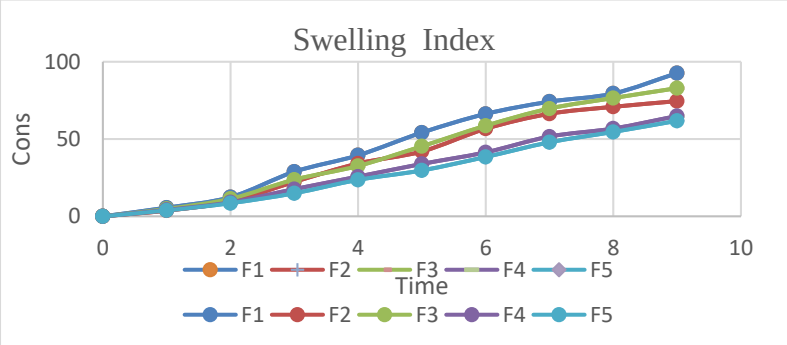


Fig.10%swelling index

Table No 9 : IN VITRO DISSOLUTION PROFILE OF PRESS COATED TABLET

Dissolutions Media	TIME	Cumulative % Drug Release in Different Trial				
		F1	F2	F3	F4	F5
Simulated gastric fluid (0.1 HCL)	0.5	0	0	0	0	0
	1	0	0	0	0	0
	1.5	0	0	0	0	0
	2	0	0	0	0	0
Simulated pH 7.4	2.5	0	0	6.2±0.56	0	0
	3	0	0	15.3±0.29	0	0
	3.5	0	3.16±0.36	30.8±0.43	5.3±0.61	3.18±0.35
	4	1.12±0.16	10.15±0.63	46.2±0.32	8.2±0.27	9.17±0.36
	4.5	2.28±0.42	17.3±0.25	58.9±0.16	13.6±0.16	21.9±0.43
	5	3.74±0.36	38.61±0.53	78.3±0.76	19.7±0.31	34.33±0.65
Simulated pH 6.8	5.5	38.8±0.19	56.32±0.41	87.3±0.62	29.8±0.39	47.3±0.16
	6	53.58±0.49	70.2±0.39	91.6±0.54	53.12±0.65	72.56±0.54
	6.25	72.65±0.68	84.2±0.23		68.2±0.46	89.62±0.41
	6.5	86.7±0.76	96.52±0.16		78.33±0.65	96.8±0.62
	6.75	93.09±0.56	99.82±0.35		81.96±0.19	
	7	99.15±0.62				

All values are expressed as mean ± standard deviation, n=3

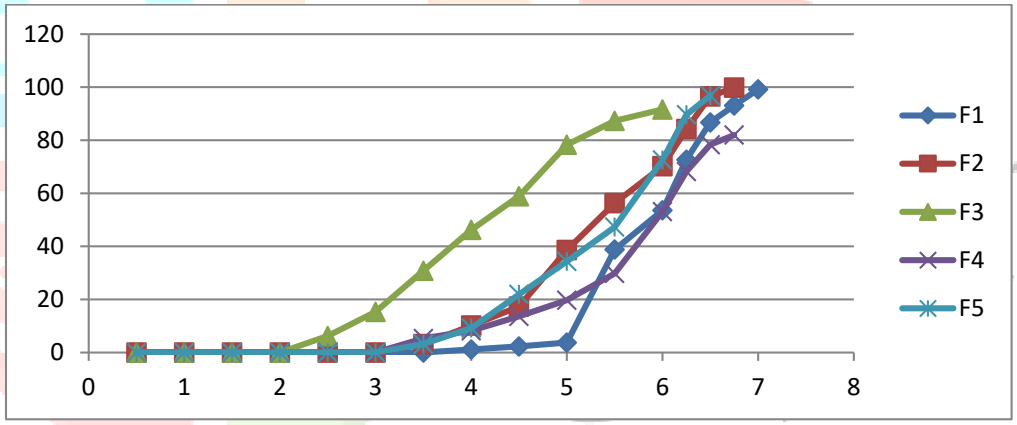


Fig.11. Cumulative % Drug Release in Different Trial

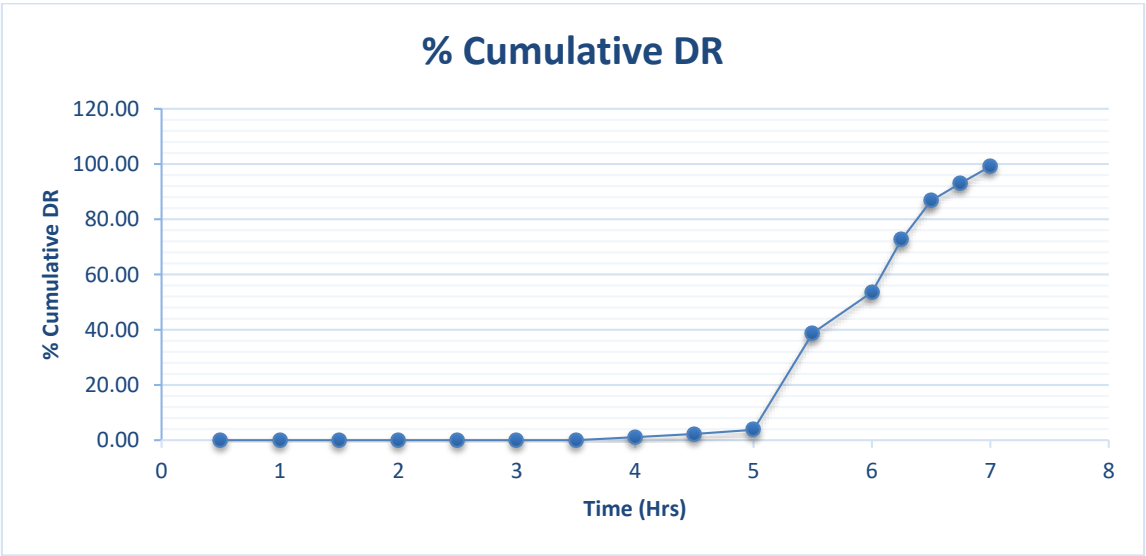


Fig.12 Cumulative % Drug Release in optimize F1batch

Table No.9 Lag time and t90% of all batch press-coated tablets

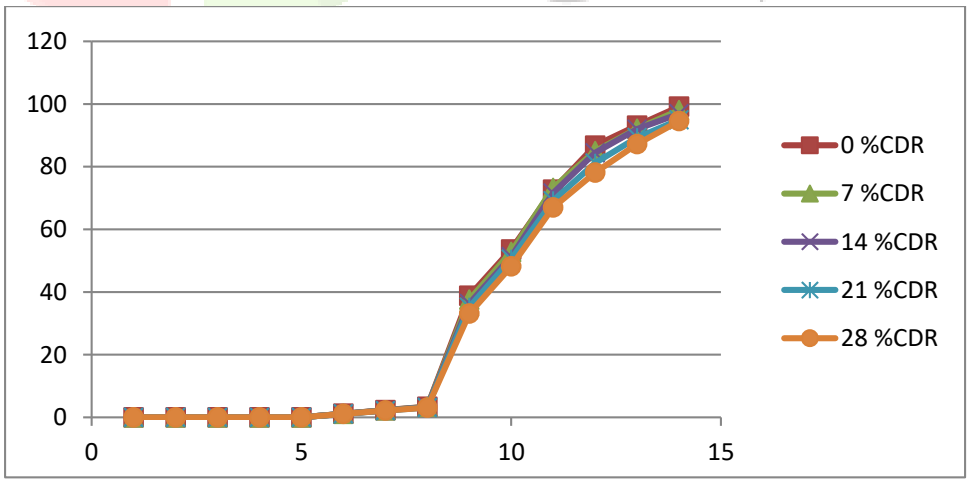
Formulation	F1	F2	F3	F4	F5
Lag time (h)	5.5	4.5	3	3	4.3
t90% (h)	6.90	6.36	6	6.55	6.45

The results obtained in the in-vitro drug release study are tabulated. The cumulative percentage of salbutamol sulphate released as a function of time for all the formulations are the optimize batch F1 shown in graph . Coating of tablets with Eudragit S-100 :HPMC K4M :Ethyl cellulose in combination showed the lag time of nearly before burst effect. From the result, concluded that the combination of Eudragit S-100:HPMC K4M :Ethyl cellulose can be successfully utilized to create desired release profile similar to the targeted release profile in future study. From the results, we have seen that press coating gave us more appropriate results as the release of drug at pH 7.4 was less and the drug release at pH 6.8 was more, i.e the drug release was more in the colonic region.

Stability study of tablet

Table No 10 : Drug release profile of formulation F1 for stability study

	days	0 %CDR	7 %CDR	14 %CDR	21 %CDR	28 %CDR
Sr. No	time	0	0	0	0	0
1	0	0	0	0	0	0
2	1	0	0	0	0	0
3	2	0	0	0	0	0
4	3	0	0	0	0	0
5	4	1.16±0.02	1.14±0.01	1.13±0.01	1.1±0.02	1.1±0.01
6	4.5	2.32±0.02	2.26±0.01	2.21±0.01	2.15±0.02	2.18±0.02
7	5	3.39 ±0.04	3.35±0.02	3.29±0.03	3.12±0.01	3.11±0.01
8	5.5	38.8±0.01	37.56±0.03	36.33±0.07	35.2±0.03	33.13±0.02
9	6	53.58±0.06	16.8±0.08	51.3±0.04	50.51±0.09	48.19±0.05
10	6.25	72.65±0.21	52.8±0.12	71.6±0.11	69.15±0.8	67.01±0.1
11	6.5	86.7±0.05	73.24±0.14	84.41±0.17	81.15±0.16	78.12±0.19
12	6.75	93.09±0.13	92.12±0.19	91.96±0.19	89.3±0.29	87.2±0.31
13	7	99.15±0.17	97.03±0.23	95.89±0.16	94.96±0.38	94.54±0.21



Stability study	% Drug Content	Lag Time (hr)	Appearance
0days	99.15±0.17	5.5	No Change
1week	97.03±0.23	5.5	No Change
2week	95.89±0.16	5.5	No Change
3week	94.96±0.38	5.5	No Change
4week	94.54±0.21	5.5	No Change

It was concluded that F1 were having sufficient lag time of 5.5hr . The greater the lag time, more will be the time taken by the dosage form to release the drug.
The selected formulation (F1) was found to be stable upon storage for 4 week. No change was observed in the appearance, hardness and average weight of the tablet. Also no significant change was observed in the in-vitro release of the drug

CONCLUSION

From the above results we can conclude that Salbutamol sulphate press coated(pulsatile) tablet formulations prepared with Eudragit , HPMC K4M, Ethyl cellulose showed acceptable properties like friability, weight variation, hardness etc and in-vitro drug release which remained unchanged upon storage for 4 week. Eudragit S100 and was the most successfully coating polymer. Salbutamol sulphate tablets with the formulation code T6 proved to be the formula of choice, While coating ratio 0.5:2.5:0.5.F1 Batch was selected for coating, using the press coating, small amount of drug was degraded in the small intestine. But the main site release of drug in the pH 6.8 (colonic pH) was more drug release as compared to the F2,F3 F4, and F5 Batch coating. So, the optimized formula of coating consisted of F1 Batch coating of tablets. since it showed the highest drug release and lag time. So, Salbutamol sulphate tablets can be used in bust release drug delivery in treatment of asthma so as to improve the absorption of drug in colon and also to reduce the dosing frequency of the drug.

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