Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 3, Issue 4, 2011

Research Article

DESIGN AND CHARACTERIZATION OF MODIFIED RELEASE ISONIAZID AND SALBUTAMOL SULPHATE INLAY TABLET

M.SARAT CHANDRA PRASAD, B.NAGENDRA BABU, M.AJAY, S.BRITO RAJ, N.AUDINARAYANA*, K.BHASKAR REDDY

Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, R.V. S. Nagar, Chittoor 517127, Andhra Pradesh, India.
Email: audiguessme1@gmail.com

Received: 20 June 2011, Revised and Accepted: 18 July 2011

ABSTRACT

The objective of the present study was to improve the therapeutic efficacy of a formulation which contains two drugs i.e. Isoniazid and Salbutamol sulphate. The present invention is to provide a dosage form comprising of an active ingredient (Isoniazid) as modified release and another active ingredient (Salbutamol sulphate) as immediate release, wherein the modified release active ingredient is selected for tuberculosis and the immediate release active ingredient is selected with low dose for asthma. Once-daily sustained release matrix tablets of Isoniazid with Inlay Salbutamol sulphate tablet as an immediate release formulation, were prepared by using hydroxyl propyl methyl cellulose (HPMC) and superdisintegrants, with different polymer ratios modified release dosage form has been formulated by wet granulation method. The drug-excipients incompatibility studies were performed by Fourier Transform Infrared spectrophotometer (FTIR).The granules showed satisfactory flow properties and compressibility Index. *In vitro* dissolution test was carried for 12 hours and formulation F4 attained the expected release pattern in both immediate release layer (i.e. 95.20% at the end of 30 mins) and in sustained release layer (i.e. 54.22% at the end of 12 hours). Release kinetics studies revealed that the drug release from formulation F4 (12%) followed zero order kinetics with release exponent value (n) 0.806, which shows that release pattern of tablet follows Non - fickian diffusion mechanism while fitting the drug release data to Korsermeyer- Peppas fitting curve.

Keywords: Isoniazid, Salbutamol sulphate, Hydroxy propyl methyl cellulose, Inlay tablet.

INTRODUCTION

Inlay tablet is a type of layered tablet in which instead of the core tablet being completely surrounded by coating, top surface is completely exposed. While preparation, only the bottom of the die cavity is filled with coating material and core is placed upon it. When compression force is applied, some coating material is displaced to form the sides and compress the whole tablet. It has some advantages over compression coated tablets, Less coating material is required, so cost effective, core is visible, so coreless tablets can be easily detected, reduction in coating forms a thinner tablet and thus freedom from capping of top coating. The present invention also teaches the use of dual retard technique to effectively control the release rate of modified release active ingredient by using small quantity of release controlling agents. This dual retard technique thus sufficiently reduces the size of the dosage form, which is convenient for swallowing[1, 2]

Tuberculosis is chronic granulomatous disease in major health problem in developing countries about 1/3rd of world population infected by mycobacterium tuberculosis it is apprehended with that unless urgent action is taken less than 15 million people worldwide including 4 million in India will die from tuberculosis in 1st decade of 21st century according to WHO as the ICMR 2001 estimate 40% adults in India are effected nearly 2 million people develops active disease every year about 0.5 million people die from it[3].

The WHO recommends Isoniazid dosage ranges from 4 to 6 mg/kg, with the maximum daily dose not to exceed 300 mg[4]. In treatment of tuberculosis it is used as first line drug and it is chemically described as Isonicotinic acid hydrazide 4-Pyridinecarboxylic acid hydrazide[5, 6]. It is a prodrug and must be activated by bacterial catalyse. It is activated by catelase-peroxidase enzyme katG to form isonicotinic acyl anion or radical. These forms will then react with a NADH radical or anion to form isonicotinic acyl- NADH complex. This complex will bind tightly to ketoenoylreductase known as inhA and prevents access of the natural enoyl-AcpM subustrate[7].

Asthma is a common chronic inflammatory disease characterized by variable and recurring symptoms, airflow obstruction, and bronchospasm with wheezing, coughing, chest tightness, and shortness of breath[8]. During asthma attacks, the smooth muscle cells in the bronchi constrict, the airways become inflamed and swollen, and breathing becomes difficult. This is often referred to as a tight chest and is a sign to immediately take medication[9, 10]

Salbutamol is a relatively selective beta-2 adrenoreceptor stimulant. Agonist used for the relief of bronchospasm in conditions such as asthma and COPD (Chronic obstructive pulmonary disease). It is chemically described as 1- (4-hydroxy- 3- hydroxymethylphenyl) - 2- (tert- butyl amino) ethanol sulphate. The elimination half-life of oral salbutamol is between 2.7 and 5 hours. Its short elimination half life calls for frequent daily dosing (2 to 3 times) and therapeutic use in chronic respiratory diseases necessitates its formulation into sustained release dosage form[11].

Present study is to develop a sustain release Isoniazid tablet with HPMC as release retarding polymer with different concentrations. On other hand Salbutamol sulphate which is used as asthmatic drug was designed as immediate release core tablet by using various super disintegrants.

MATERIALS

Salbutamol sulphate and Isoniazid was obtained as gift sample from Milton Labs, Pondicherry, Xanthum Gum, Sodium starch glycolate, Cross povidone, Cross carmellose sodium, HPMC K 100, was obtained as gift sample Novel Drugs Limited, Trichy. Disodium hydrogen phosphate, Con Hcl, Sodium chloride purchased from S. D. Fine chemicals, Mumbai.

METHODS

Preparation of Inlay Tablet Dual -Retard delivery system

Inlay Tablet dual-retard drug delivery system was prepared by compressing a smaller tablet, forming a core tablet and then surrounded with a powder mixture compressed to produce a bigger tablet (Fig 3).[2]

Different tablet formulations were prepared by Wet granulation technique. The formulations were composed of polymer as HPMC K100 in various proportions for the sustained release matrix. The Salbutamol sulphate immediate release core for the Inlay tablets were formulated using super disintegrants like Cross povidone, sodium starch glycolate and cross carmellose sodium by wet granulation method. All the powders were passed through 44 mesh sieve for uniformity and breaking of lumps in powders. Required quantity of drugs, polymers and diluents were mixed thoroughly and a sufficient quantity of granulating agent was added slowly to get wet mass. The mass was sieved through 10 and semi dried at 60°.The dried granules were passed sieve no 22 mixed with 2% talc and 1% magnesium stearate. The granules 1 of Salbutamol sulphate

were compressed to small tablet by 8X32 punches and then placed centrally in the granules 2 of Isoniazid for final compression by 16X 32 punches to form I inlay tablets. Formulation of immediate and sustained release is shown in Table 1 and 2.

Table1: Formulation of IR Salbutamol Sulphate Granules 1 Fi1-Fi6[12, 19]

Ingredient (mg/ tablet)	Formulation (mg)					
	FI1	**FI2**	**FI3**	**FI4**	**FI5**	**FI6**
Salbutamol sulphate	4	4	4	4	4	4
Lactose	75	55	75	50	75	50
Sodium starch glycolate	20	40	-	-	-	-
Cross povidone	-	-	20	40	-	-
Cross carmellose sodium	-	-		-	20	40
Magnesium stearate	1%	1%	1%	1%	1%	1%
Talc	2%	2%	2%	2%	2%	2%
Starch mucilage	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	100	100	100	100	100	100

*IR indicates immediate release

Table 2: Formulation of SR Isoniazid Granules 2 Fs1-Fs6[13]

Ingredient (mg/ tablet)	Formulation					
	FS1	**FS2**	**FS3**	**FS4**	**FS5**	**FS6**
Isoniazid	300	300	300	300	300	300
HPMC K 100	15	30	45	60	90	120
Microcrystalline cellulose	185	170	155	140	110	80
Talc	2%	2%	2%	2%	2%	2%
Magnesium stearate	1%	1%	1%	1%	1%	1%
Starch mucilage	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	500	500	500	500	500	500

*SR indicates sustained release, HPMC indicates hydroxypropyl methylcellulose.

Preformulation studies

Compatibility studies

FTIR studies

Compatibility studies were performed by using FTIR technique for the drug, excipients and polymers to determine any incompatibility between the ingredients and shown in FIG 1a-1d.

Evaluation of Granular Flow Property

Angle of repose

A funnel is fixed at a particular height 'h' cm on a burette stand. A white paper is placed below the funnel on the tablet. The given powdered drug whose angle is to be determined is passed slowly through the funnel, until it forms a pile, care is taken to see that the drug particles slip and roll over each other through the sides of the funnel. Further addition of drug is stopped as soon as the drug pile touches the tip of the funnel. Circumference of the pile of drug is drawn with a pencil and measure the height of the pile without disturbing the pile. The radius of the pile is noted down as 'r' cm. and is calculated by following formula.

$$\tan\theta = h/r$$

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

Where, h = height of the pile: r = radius of the pile

Bulk density

Apparent bulk density was determined by placing pre-sieved drug excipients blend in to a graduated cylinder and measuring the volume and weight. 25 g of Salbutamol sulphate and Isoniazid granules were weighed respectively and transfer the powder into a graduated measuring cylinder, via a large funnel the volume of the powder was measured. The Thermonik bulk density apparatus was used to measure bulk density. The volume of the powder is measured after 100 tapping. Bulk density of the powder can be determined by the formula given below[14].

LBD = Wt of Powder / Vol. of Powder

Tapped density

Tapped density was determined by USP method II tablet blend was filled in 100 ml graduated cylinder of tap density tester which was operated for fixed number of taps until the powder bed volume has reached a minimum, thus was calculated by following formula[14].

$$Dt = M/Vb$$

Where, M = Weight of powder taken; Vb = tapped volume.

Compressibility Index and Hausner's Ratio

This was measured for the property of a powder to be compressed, as such they are measured for relative importance of inter particulate interactions. Compressibility index and was calculated by following equation[15].

$$\text{Compressibility index} = [(Dt - Db)] / Dt \times 100$$

Where, Dt = tapped density; Db = bulk density;

Hausner ratio was calculated by following equation:

$$\text{Hausner's ratio} = Dt/ Do$$

Where, Dt = tapped density; Do = bulk density

Evaluation of tablet

Physical evaluation of tablets

Weight variation

Tablet designed to contain a specific amount of drug .The weight of the tablet being made is routinely measured to ensure the tablet contains the proper amount of drug. 20 tablets were selected randomly from each batch and average weight was calculated. Then the deviation (as per IP limit ±5% for 500 mg tablet) of individual weights from the average weight and then standard deviation was calculated[15].

Hardness

The Monsanto hardness tester consists of a barrel containing a compressible spring held between two plungers. Then lower

plunger is placed in contact with the tablet and a zero reading is taken. The upper plunger is then forced against or spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force and the force of fracture is recorded[16].

Friability

The laboratory friability tester is known as the Roche friabilator. 10 tablets are weighed and placed in the plastic chamber which revolves at 25 rpm dropping the tablets a distance of six-inches with each revolution which is operated for 100 revolutions. The tablets are then dusted and reweighed to find out the % of loss in weight (as per IP limit it should be <1%). The friability of the tablet is determined by the formula given below. Then average hardness and standard deviation was calculated[17].

$$\text{Friability} = \frac{\text{Final Weight-initial weight}}{\text{Initial weight}} \times 100$$

Determination of Thickness

Thicknesses of five randomly selected tablets from each batch were measured with a Vernier caliper. Then the average Thickness and standard deviation were calculated. Tablet thickness should be controlled within 5% variation of a standard value[18].

***In Vitro* Release Studies**

The dissolution test for the tablets is carried out using USP apparatus II, 900ml of 0.1 N HCL, and the paddle is rotated at 50 RPM for the first 2 hour. And then 0.1N Hcl is replaced by phosphate buffer 6.8pH and the paddle is rotated continuously for upto 12hours. Samples for immediate release layer is collected at the interval of 0,5,10,15,20,30,45,60 min and for sustained release layer 0,2,4,6,8,10,12 hours. The collected samples are analyzed at 276 nm for Salbutamol sulphate and 263 nm Isoniazid by UV spectrophotometrically.

Release kinetics

Data obtained from *in- vitro* release study were fitted to various kinetic equations.

The kinetic models used were[20],

- Zero order equation : ($Q=k_0t$)
- First order equation : ($\ln (100 - Q) = \ln Q - k_1t$)
- Higuchi equation : ($Q= kt^{1/2}$)

Further, to find out the mechanism of drug release, first 60% drug release was fitted in Korsmeyer and Peppas equation ($Q = kpt^n$). Where, Q is the percent of the drug release at time 't' and k_0 and kt are the coefficients of the equations and 'n' is the release exponent. The 'n' value was used to characterize different release mechanism. For swelling controlled release system, the diffusion exponent value n, is 1.this type of transport is known as case II transport and results in zero order release kinetics. However in some cases, drug release occurs due to a combination of macromolecular relaxation and Fickian diffusion. In this case, the diffusional exponent is between 0.5-1. This type of transport is known as Anomalous or Non-Fickian diffusion transport.

RESULTS AND DISCUSSION

Inlay tablet is a novel technology which overcomes the difficulties that faced in other compression coated tablets, Once daily dosage form of Inlay tablet of Salbutamol sulphate with sustained release Isoniazid were formulated using HPMC K 100 , Six different formulation (F1- F6) were prepared and their physical and release characteristic are studied.

Compatibility studies

Compatibility study was accessed by Fourier Transformer Infrared Spectroscopy.The FTIR spectra results are shown in FIG: 1a-1d. The spectra indicated that there is no drug – drug interaction and drug – polymer interaction.

Preformulation studies

The preformulation studies of both Isoniazid SR and Salbutamol sulphate IR granules were evaluated for various physical properties and the values are shown in the Table 3 & 4. Angle of repose shows that the flow property for both the granules was good and it is within the acceptable limits, less than 35 Bulk density of both the granules indicates good packaging character. The Carr's index for all the formulation was found to be below 15%, which indicate acceptable flow properties. The Hausner's ratio for all the granules was less than 2%, which also indicates the good flow property and packaging characters.

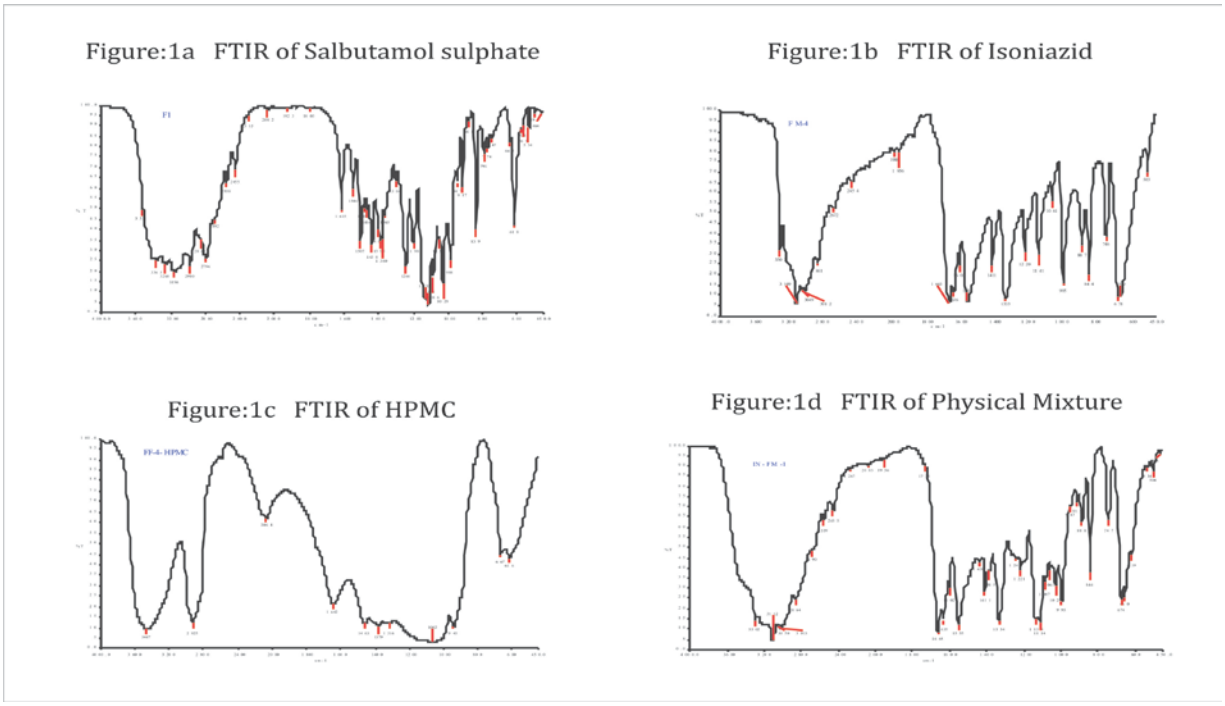

Fig: 1a-1d

Table 3: Physical evaluation of Isoniazid Granules

Parameters	FS1	FS2	FS3	FS4	FS5	FS6
Angle of repose	30.42 ± 0.02	31.20 ± 0.01	26.41±1.73	30.41±0.73	30.41±0.01	29.78±1.41
Bulk Density	0.35 ± 0.01	0.43 ± 0.01	0.36±0.01	0.40±0.01	0.42±0.02	0.44±0.01
Tapped density	0.41 ± 0.01	0.50 ± 0.01	0.53±0.01	0.53±0.05	0.58±0.01	0.59±0.01
Carr's index	7.33 ± 0.11	14.26 ± 0.02	13.03±0.55	7.81±1.50	15.08±0.90	7.66±1.45
Hausner's ratio	1.06 ± 0.01	1.14 ± 0.02	1.15±0.01	1.05±0.01	1.12±0.01	1.09±0.02

Table 4: Physical evaluation of Salbutamol sulphate Granules

Parameters	FS1	FS2	FS3	FS4	FS5	FS6
Angle of repose	35.18±1.35	34.60±0.02	35.53±0.01	33.85±0.85	37.17±2.48	35.76±1.76
Bulk Density	0.53±0.05	0.54±0.03	0.51±0.01	0.55±0.05	0.53±0.01	0.54±0.05
Tapped density	0.60±0.05	0.48±0.05	0.44±0.02	0.55±0.05	0.46±0.05	0.58±0.02
Carr's index	14.46±2.03	14.25±0.95	13.15±0.75	14.22±1.88	13.61±0.77	12.10±1.90
Hausner's ratio	1.15±0.03	1.14±0.01	1.12±0.06	1.14±0.03	1.15±0.01	1.15±0.05

Assay of Tablet

The linear methodology shows good reproducibility, the calibration curve was found to be linear. The amount present in the tablet was calculated by using UV spectrophotometry and the results are shown in Table 5 .From the results it was observed that the formulations containing Salbutamol sulphate shows the amount of drug ranges from 98.05 ± 4.34 to 102.09 ± 2.75 % W/V and the formulations containing Isoniazid shows the amount of drug ranges from 100.05±2.32 to 101.89±2.43% W/V.

Physical evaluation of Inlay Tablets

Tablets are selected randomly from all the six batches and physical evaluation of tablets were studied and tabulated in Table 5**.** The table shows the average weight of tablet 0.599±0.01 to 0.602±0.02 mg. The hardness was found to be 6.7±0.2 to 7.8±0. kg/cm^2 and the friability were found to be 0.28±0.02 to 0.59±0.02 %. The thickness of the tablet was found to be 4.59±0.02 to 4.82±0.02 mm. From the above discussion it was found that all the parameters were within the acceptable limits.

Table 5: Physical evaluation of Inlay tablets

Formulation	Parameters				Assay %W/W – UV	
	Weight variation (mg)	Hardness kg/cm2	Friability %	Thickness mm	Salbutamol sulphate	Isoniazid
F1	0.602±0.02	6.7±0.2	0.37±0.14	4.77±0.02	102.09±2.75	100.25±2.72
F2	0.599±0.01	7.8±0.3	0.58±0.04	4.59±0.02	100.69±3.42	101.89±2.43
F3	0.600±0.02	7.3±0.2	0.45±0.14	4.82±0.02	102.05±2.25	100.54±2.23
F4	0.599±0.01	7.5±0.2	0.28±0.02	4.80±0.02	101.34±3.45	100.74±2.54
F5	0.601±0.02	7.4±0.2	0.59±0.02	4.81±0.02	98.05± 4.32	101.98±2.36
F6	0.600±0.02	7.5±0.2	0.38±0.02	4.79±0.02	99.65±2.76	100.05±2.32

***In Vitro* release studies**

Six different formulations (F1-F6) were prepared and the release characteristics were studied for 12 hrs. Among the six formulations (F1-F6), F4 attained expected release pattern in both immediate release layer (i.e., 95.20% at the end of 30 mins) and in sustained release layer (i.e., 54.22% at the end of 12 hours). The results are shown in Table: 6 & 7 and Fig: 2a & 2b.

Table 6: Comparative *In vitro* drug release profile for IR layer FI1- FI6 in 0.1N HCL

Time (min)	% Drug Release					
	F1	F2	F3	F4	F5	F6
0	0.45	1.62	1.37	8.52	4.21	6.78
5	19.15	18.27	25.22	27.03	19.13	24.14
10	18.23	28.22	27.51	48.31	28.31	32.24
15	30.23	55.35	59.23	77.90	50.43	46.17
30	60.22	70.23	88.16	95.20	77.12	65.20
60	95.76	98.33	94.15	101.23	92.44	98.26

Mean of 3 determinations

Table 7: Comparative *In vitro* drug release profile for SR FS1- FS6 in 6.8 pH buffer

Time (hr)	% drug released						
	F1	F2	F3	F4	F5	F6	USP Limits
2	11.94	11.26	9.22	10.28	9.13	8.36	Not more than 10% - 25%
4	33.80	33.37	28.52	27.28	25.27	21.11	Between 25% - 40%
6	40.97	40.12	34.39	33.25	30.16	28.12	-
8	49.66	46.32	42.12	42.20	39.88	37.29	Between 40% - 60%
10	64.93	55.68	45.13	48.32	49.54	41.80	-
12	74.64	69.12	61.18	54.22	55.21	46.69	-

Mean of 3 determinations

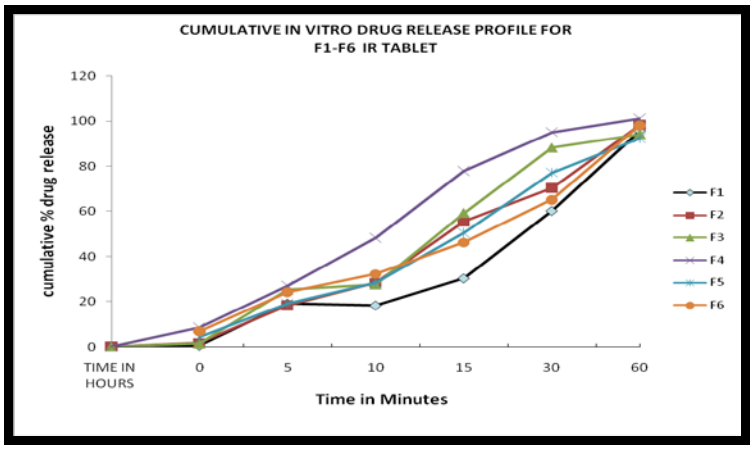

Fig. 2a: Comparative *In vitro* drug release profile for IR layer in 0.1N HCL

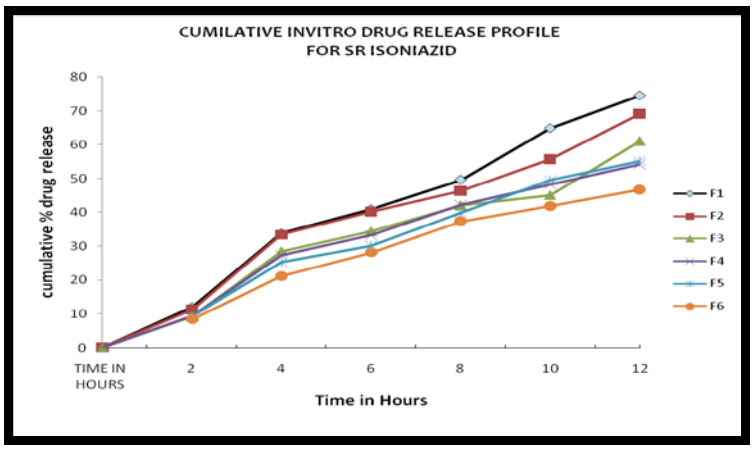

Fig. 2b: Comparative *In vitro* drug release profile for SR in 6.8 phosphate buffer

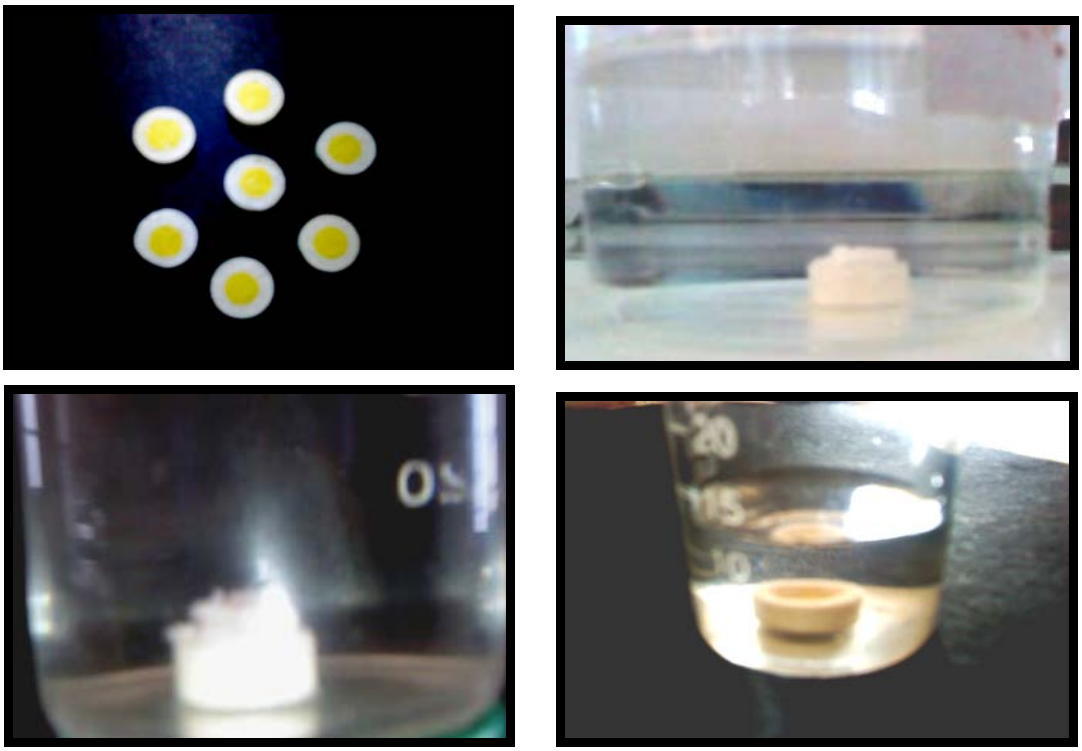

Fig. 3: Simultaneous release pattern of IR and swelling of SR layer of Inlay tablet

***In Vitro* release kinetics**

From the Release kinetics was revealed that the drug release for formulation F4 follows zero order kinetics with release exponent value (n) 0.806, which shows that the mechanism of pattern of tablet follows Non - fickian diffusion sustained mechanism in peppas fitting curve. The *K* values are release rate constants according to the models considered; R^2 values are determination Coefficients; and exponent *n* value of the korsmeyer-peppas model are shown in Table 8 and Fig: 4a &4b.

Table 8: Drug Release kinetics data

Formulation	Zero order R^2	First order R^2	Korsermayer-Peppa's *n*
F1	0.9506	0.9806	0.769
F2	0.9638	0.9929	0.697
F3	0.9725	0.9989	0.749
F4	0.9747	0.9915	0.806
F5	0.9859	0.9839	0.775
F6	0.9536	0.9144	0.618

K values are release rate constants according to the models considered; R^2 values are determination Coefficients; and *n* is the exponent of the korsmeyer-peppas model.

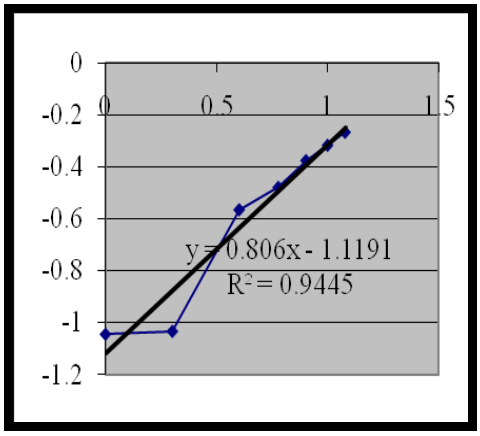

Fig. 4a: F4-Peppa's curve

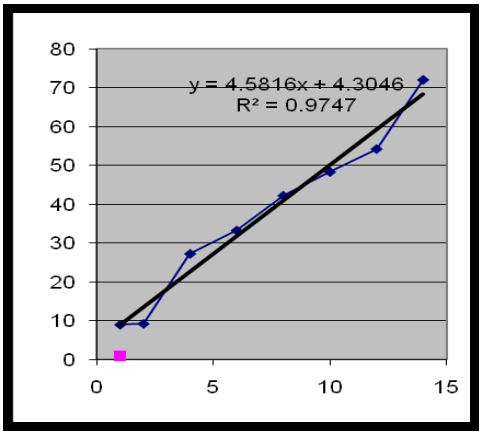

Fig. 4b: F4-Zero order curve

CONCLUSION

The formulation F4 has achieved the objective of sustained drug delivery with prolonged release, cost effective, decrease dose and frequency of administration, and hence improved patient compliance. Thus it may conclude that the once daily Inlay tablet of Salbutamol sulphate with sustained release of Isoniazid can be administered to Tuberculosis cum Asthma.

ACKNOWLEDGEMENT

The authors wish to thank Sri Dr. Ravuri Venkataswamy, Chairman and Mr.R.V.srinivasulu, vice chairman, Sri Venkateswara college of pharmacy, R.V.S Nagar, Chittoor for providing facilities to carry out this research work . Also thank Milton Labs, Pondicherry. And Novel Drugs Limited, Trichy. Indian Institute of Technology, Chennai for providing necessary facilities to conduct the work.

REFERENCES

1. Liberman and Lachman, Tablet dosage forms, 2 Ed; (1), 72-104,274,275; (2) 34-98; (3)101-154.
2. Manoranjan Sahu, S.C.Dinda Formulation and development of modified release Inlayered tablet, Journal of Pharmacy Research 2010, 3(4),794-798
3. K D Tripathi, Essential of Medical Pharmacology, 6th (Ed), 2008, 698-700.
4. The Merck Index, An encyclopedia of chemicals, drugs, and biologicals 13th edition. 2005.
5. WHO, The International Pharmacopoeia. General Methods of Analysis, Quality Specifications for Pharmaceutical Substances, Excipients and Dosage Forms. 2004, 3 edition.
6. WHO. Treatment of tuberculosis: Guidelines for national programmes, 3rd Edition. 2003.http://whqlibdoc. who.int/hq/2003/WHO_CDS_TB_2003.313_eng. pdf.
7. Indian pharmacopoeia, The Controller of Publications, New Delhi, Vol.1 **1996**; 408.
8. Zhao J, Takamura M, Yamaoka A, Odajima Y, Iikura Y. Altered eosinophil levels as a result of viral infection in asthma exacerbation in childhood. J Pediatr Allergy Immunol. 2002, 13(1):47-50.
9. Bradley JU, Lawrence ML. Drugs used in treatment of asthma. In: Hardman JG, Lee E., editors. Goodman and Gillman's: The pharmacological basis of therapeutics, 10 th ed. New York; the Mc Graw-Hill Companies: 2001. 735.
10. Peter JB, Robert AM, George RB, Principles of pharmacology: Basic concepts and clinical applications. New York; Thomson Publishing Company: 1995.589.
11. Md. Qamrul Ahsan, Md. Mofizur Rahman, Mithilesh Kumar Jha , Ishtiaq Ahmed , Md. Mizanur Rahman Moghal and Md. Habibur Rahman "Development and In-Vitro Evaluation of Sustained Release Matrix Tablets of Salbutamol Sulphate Using Methocel K100M Cr polymer", IJPSR, (2011); Vol. 2 Issue 3, 567-576.
12. Arvind K. Singh, Ramesh K. Singh "Development And Evaluation of Fast Disintegrating Tablets Of Salbutamol Sulphate by Superdisintegrating Agents", IJPSR (2010), Vol. 1, Issue 7, 47-53.
13. Suresh. S, Mohammad Zakir Hussain, Saravanan. C, Venkatesh. S, Narayana SwamyV.B "Formulation and evaluation of sustained release matrix tablets of Isoniazid", Der Pharmacia Lettre, 2011, 3(1): 237-246.
14. Aulton ME: Pharmaceutics -The Science of Dosage Form Design. 2nd Edition, Churchill Livingstone. 2002; 200-206.

15. Krishanaiah YS, Lath K, Nageshwara L, Karthikeyan RS, Bhaskar Pand Satyanarayana V. "Development of colon target oral guar gum matrix tablet of Albendazolefor the treatment of Helminthiasis". Indian J. Pharm. Sci. 2003; 65 (4): 378-385.
16. The United State of Pharmacopoeia 24/ Nf19 Asian Edition, The official compendia of standard United States pharmacopoeial convection Inc. Rockville. 1995; 1015, 1016, 1791.
17. Chaudhari PD. "Formulation and Evaluation of fast dissolving tablet of famotidine" Indian Drug. 2005; 42(10): 641-649.
18. The British Pharmacopoeia, department of health/by stationary office on behalf of the medicine and health care product regulatory agency, crown copy right, 2005;5th Ed. 1303-1304, 2588-2589, A133.
19. Sharad N. Shinde 'Development and Evaluation of Floating Tablets of Salbutamol Sulphate' International Journal of Pharma Research and Development, 2010; Volume-2, 1-7.
20. Sandhiya.K. M, Shanmugam.S and Vetrichelvan.T Design and Development of Ambroxol Hydrochloride Sustained Release Matrix Tablets International Journal of Pharmacy and Pharmaceutical Sciences 2011.Vol 3 Suppl 3.