International Journal of Current Trends in Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijctpr

Research Article Open Access

Formulation and Evaluation of Controlled Release Enteric Coated Respiridone Tablets

Sireesha S*[1], Bala Krishnan M[2], Ramesh Y[3], Kavitha G[1]

[1]*Department of Pharmaceutics, Seshachala College of Pharmacy, Tirupathi - Chennai High way, Puttur, Chittoor, A.P, India*
[2]*Department of Phytochemistry, Seshachala College of Pharmacy, Tirupathi - Chennai High way, Puttur, Chittoor, A.P, India*
[3]*Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur , Muthukur, SPSR Nellore, A.P, India.*

A B S T R A C T

The main objective of pre-formulation testing is to generate information useful in developing the formulation, which is stable, and bioavailability. Further, the use of pre-formulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product. Respiridone is a selective serotonin reuptake inhibitor, chemically unrelated to tricyclic, tetracyclic, or other antidepressants, presumably, the inhibition of serotonin reuptake from brain synapse stimulated serotonin activity in the brain. The drug & excipient Compatibility studies no interaction between polymer and drug. The angles of repose of different formulations were found between 23.91± 0.4 to 28.45± 0.47. The bulk density of blend of Respiridone and excipients were found between 0.57 g/ml to 0.66 g/ml. True density were found between 0.54 g/ml to 0.65/ml. The Carr's index for all the formulations was found to be 17.2 - 19.7. The thickness of the tablets was found out using Vernier Caliper and the thickness found to be in the range of 4.02-4.12 mm for the uncoated tablets (F1-F6), hardness studies and results showed they were in between 6.1-8.0 Kg/cm^2 in all batches. The dissolution rate was found to be increased in the first two hours and the drug release was found to be 53.5%, 44.1%, 38.4% at the end of 2 hrs. Formulation F4 containing HPMCK4M and HPMCK100M showed much prolonged drug release when compared to formulation F5 containing HPMCK4M and ethyl cellulose. Formulation F6 was carried out using three rate controlling polymers HPMCK4M, HPMCK100M and ethyl cellulose. . In the formulations F9, F10 and F11 HPMCKM concentration was decreased and ethyl cellulose was increased. The similarity factor (f^2) of all the formulations ranged from 30 to 68.7. The similarity factor of F10 is high when comparing to other formulations so, it is more similar to that of marketed formulation.

Keywords: Respiridone, Controlled Release, Enteric Coated, *In Vitro* Dissolution.

A R T I C L E I N F O

CONTENTS

Article History: Received 19 January 2016, **Accepted** 24 February 2016, **Available Online** 15 March 2016

***Corresponding Author**
Sireesha S
Department of Pharmaceutics, Seshachala College of Pharmacy, Tirupathi - Chennai High way, Puttur-517 583, Chittoor (dist), Andhra Pradesh, India
Manuscript ID: IJCTPR2884

PAPER-QR CODE

Citation: Sireesha S, *et al.* Formulation and Evaluation of Controlled Release Enteric Coated Respiridone Tablets. *Int. J. Curnt. Tren. Pharm, Res.*, 2016, 4(2): 69-77.

1. Introduction

Oral controlled – release drug delivery is thus a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit [2]. In the exploration of oral controlled release drug administration, one encounters three areas of potential challenges like development of a drug delivery system: To develop a viable oral controlled release drug delivery system capable of delivering a drug at a therapeutically effective rate to a desirable site for duration required for optimal treatment. Modulation of gastrointestinal transit time: To modulate the GI transit time so that the drug delivery system developed can be transported to a target site or to the vicinity of an absorption site and reside there for prolonged period of time to maximize the delivery of a drug dose [1].

Enteric coatings: Enteric coatings are those, which remain intact in the stomach, but will dissolve and release the contents once it reaches the small intestine. Their prime intension is to delay the release of drugs, which are inactivated by the stomach contents or may cause nausea or bleeding by irritation of gastric mucosa.

Important reasons for enteric coating are as follows

1. To protect acid-liable drugs from the gastric fluid
2. To protect gastric distress or nausea due to irritation from drug
3. To deliver drugs intended for local action in the intestines
4. To deliver drug that are optimally absorbed in the small intestine to their primary absorption site in their most concentrated form
5. To provide a delayed release component to repeat actions
6. Protect the drugs from harmful effect of the gastric contents, some of the drugs are prone to be hydrolyzed in acid media (E.g. Omeprazole)

Enteric coating materials

Most enteric coatings won't dissolve in solutions with a pH lower than 5.5. Commonly used enteric coatings may be made from [2]

1. Methacrylic acid copolymers
    a. Cellulose acetate (and its succinate and phthalate version)
2. Polymethacrylic acid/acrylic acid copolymer
3. Hydroxy propyl methyl cellulose phthalate
4. Polyvinyl acetate phthalate
5. Hydroxy methyl ethyl cellulose phthalate

The mechanism of action of risperidone, as with other drugs used to treat schizophrenia, is unknown. However, it has been proposed that the drug's therapeutic activity in schizophrenia is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5HT2) receptor antagonisms. Antagonism at receptors other than D2 and 5HT2 may explain some of the other effects of risperidone [3].

2. Materials and Methods

Material and Methods:

Respiridone is a gift sample by (Milton Drugs Pvt Limited, Puducherry) Povidone K30 (Signet Chemical, Mumbai), Ethyl Cellulose (Rankem Limited, Mumbai) HPMC (Dow Chemical Company, USA,) Eudragit (Rohm GmbH, Thane), Aerosil (Rankem Limited, Mumbai), Magnesium stearate (Rankem Limited, Mumbai) and all other chemicals & Solvents used were of analytical grade.

Methodology:

Drug Excipient Compatibility Studies

Fourier Transform Infra- Red spectroscopy: The FTIR analysis was conducted for the structure characterization [4]. FTIR spectra of the pure drug, pure polymers and mixture of both were recorded. Formulations were taken in a KBr pellet using bomen MB series FTIR instrument. Approximately 5 mg of samples were mixed with 50 mg of spectroscopic grade KBr; samples were scanned in the IR range from 500 to 3500 cm^{-1}, with a resolution of 4 cm^{-1}.

Formulation of respiridone matrix tablets using different ratios of polymers:

Respiridone Hydrochloride Controlled Release tablet were prepared by direct compression method with different polymer like Ethyl Cellulose, HPMC, in various drug: polymer ratio.

Direct compression technique:

Respiridone Hydrochloride was passed through sieve #40. Ethyl Cellulose, HPMC, spray dried lactose, povidone were passed through sieve # 40. The above sieved materials were mixed thoroughly by tumbling method in a polythene bag. The dry blend was lubricated with aerosil and magnesium stearate. Then the lubricated dry blends were subjected to punching using a tablet punching machine with Punch size: 8.3 mm round concave punches [5].

Determination of bulk density and tapped density:

It refers to a measurement to describe packing of particles and also used to determine the amount of drug that occupies the volume in mg/ml before tapping and after tapping. An accurately weighed quantity of the powder (W), was carefully poured into the graduated cylinder and the volume (V_o) was measured, then the graduated cylinder was closed with lid, set into the density determination apparatus. The density apparatus was set for 500 taps and after that, the volume (V_f) was measured and continued operation till the two consecutive readings were equal [6].

Bulk density= W / V_o

Tapped density = W / V_f

Where,

W = weight of the powder

V_o = intial volume

V_f = final volume

Sieve analysis:

The main aim of sieve analysis is to determine the different size of drug particles present. A series of standard sieve were stacked one above the other so that sieves with larger pore size (less sieve number) occupy top position followed by sieves with smaller pore size (greater sieve number towards the bottom) [7].

Flow Properties:

The flow properties are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by 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 [6].

$\tan\theta = h/r$

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

Where,

h=height of pile.

r= radius of the base of pile.

θ =angle of repose.

Compressibility Index: Compressibility was determined from the powder density using the equation.

$$CI = \frac{(TD - BD)}{TD} x100$$

Where,

TD – Tapped density

BD – Bulk density

Hausner ratio:

It indicates the flow property of the powder and measured by the ratio of tapped density to bulk density.

Evaluation of Tablets.

Post compression parameters

Thickness and diameter:

The thickness and diameter of the tablets were found out using Vernier Caliper and the results were expressed in millimeter. A ± 5% may be allowed depending on the size of the tablet [8].

Hardness test:

Tablets require a certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing and shipping [9]. The hardness of tablet was measured by Monsanto hardness tester. Ten tablets from the batch were used for hardness studies and results are expressed in Kg/cm^2.

Weight variation test:

Ten tablets were selected at random, individually weighed in a single pan electronic balance and the average weight was calculated [10]. The uniformity of weight was determined according to I.P specification. As per I.P. not more than two of Individual weight would deviate from average weight by not more than 5% and none deviate by more than twice that percentage.

Friability test:

It was performed in Roche Friabilator apparatus where the tablets were subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Pre-weighed samples of 20 tablets were placed in the Friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed. Conventional compressed tablets that loose less than 0.5 to 1% of their weight are generally considered acceptable [11].

$$\%\text{Friability} = \frac{\text{Weight loss}}{\text{Weight of tablets before operation}} X100$$

Comparison of dissolution profiles:

The similarity factor (f_2) was employed to evaluate the release profiles of various formulations compared with the ideal release profile [13].

$$f_2 = 50 \log \left\{ \left[1 + \left(\frac{1}{n} \right) \sum_{t=1}^{n} (R_t - T_t)^2 \right]^{-0.5} X\,100 \right\}$$

The similarity factor (f_2) is a logarithmic transformation of the sum-squared error of differences between the experimental drug release T_t and the ideal drug release R_t for over all time points 'n'. The similarity factor fit the result between 0 and 100. It is approached 0 as the dissimilarity of the test and the reference profile increased, whereas, it attained 100 when the test and the reference profile were identical. The two profiles were believed to be similar when the f_2 value of them was larger than 50 for which the mean deviation over all the time points 'n' was less than 10% based on above equation. The reference standard was RES tablets whose dissolution was compared with all formulations in first two hours in acidic medium and then up to 6 h in pH 7.5 buffer.

3. Results and discussions

Drug Excipient Compatibility Studies: FTIR analysis was conducted for the structure characterization and drug excipient Compatibility to which Respiridone showed the following character. All the FTIR characterization of drug excipient was analyzed and results showed that there was no shift of peak that corresponds to pure drug shown in figure 6 & 7.

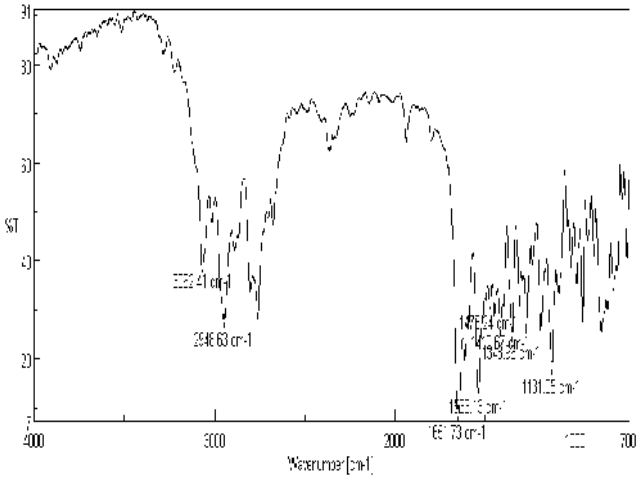

Figure 1: FTIR of Respiridone

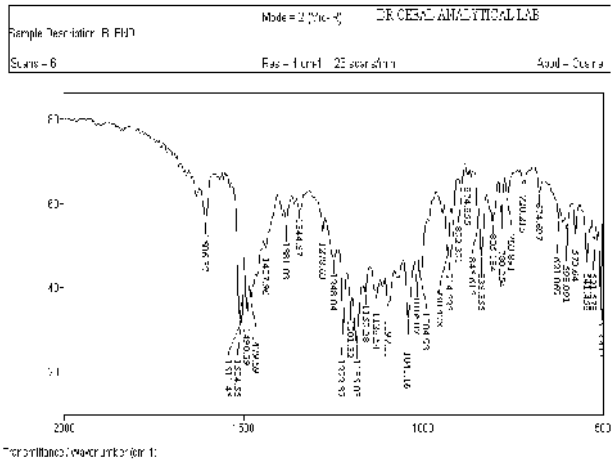

Figure 2: FTIR of API +Excipients

The FTIR of Respiridone (drug) showed intense band at 3402.68 cm-1, 1606.26 cm-1, 2364.94 cm-1 corresponding to the functional groups , NH, C=C and C-H bending. The FTIR of drug and excipients shown intense bands at 3403.24 cm-1,1606.37 cm-1 , 2923.51 cm-1 indicates no change in the functional groups NH, C=C and C-H. From the above interpretation, it is understood that there is no major shifting in the frequencies of above said functional groups. Hence, these drug and polymers are compatible with each other.

Characterization of respiridone blends:

The blends of matrix tablet were prepared and Pre compression parameters like the angle of repose, bulk density, tapped density and Carr's index was characterized.

Angle of repose:

The angle of repose for the blend of Respiridone and excipients was done. The angles of repose of different formulations were found between 23.91± 0.4 to 28.45± 0.47. The angle of repose of different formulations was ≤ 28.45 which indicates that material had excellent flow property. So it was confirmed that the flow property of blends were free flowing. All the values were mentioned in the table 8.

Bulk density and True density:

The bulk density of blend of Respiridone and excipients were found between 0.57 g/ml to 0.66g/ml. True density were found between 0.54g/ml to 0.65/ml.

Carr's index:

The measurement of free flowing powder can also be done by Carr's index. The Carr's index for all the formulations was found to be 17.2-19.7 which reveals that the blends have fair flow character. The results are shown in table 8.

Characterization of respiridone matrix tablets (post compression parameters)

The tablets of different formulations of Respiridone were subjected to various evaluation tests, such as hardness, thickness weight variation, friability and drug content. All the result is shown in Table 9.

Thickness:

The thickness of the tablets was found out using Vernier Caliper and the thickness found to be in the range of 4.02-4.12 mm for the uncoated tablets (F1-F6). For the enteric-coated tablets, the thickness ranged from 4.21-4.30. Thus all formulations showed uniform thickness.

Hardness test:

The hardness of tablet was measured by Monsanto hardness tester. Ten tablets from the batch were used for hardness studies and results showed they were in between 6.1-8.0 Kg/cm^2. This is appropriate for matrix tablet.

Weight variation test:

In a weight variation, the pharmacopoeial limit for the percentage deviation for tablets of more than 250 mg is ±5%. The average percentage deviation of all tablet formulations was found to be within the above limit, and hence all formulations passed the test for uniformity of weight as per official requirements.

Friability test:

The Friability of all the formulation was below 1% as per IP specification.

Drug content analysis:

Respiridone matrix tablet was tested for their drug content and all the formulation showed drug content more than 95%. All the tablet formulations showed acceptable pharmacotechnical properties and complied with the in-house specifications for weight variation, drug content, hardness and friability.

***In-vitro* dissolution studies-F1, F2, F3 batch:**

The formulations F1, F2, F3 contains HPMCK4M in different concentrations. The trials with the use of single rate controlling polymer increased the dissolution rate in the first two hrs and hence combination of the polymers was used.

Table 1*: In-vitro* dissolution profile - F1, F2, F3 batch's

Batch No.	F1	F2	F3
% Drug release in acid stage	0.0	0.0	0.0
% Drug release in buffer stage			
1 Hr	38±0.90	30.3±0.64	25±0.93
2 Hr	53.5±1.23	44.1±1.21	38.4±1.63
4 Hr	77.8±0.92	67.5±2.12	60.9±1.23
6 Hr	79.2±2.2	82.1±1.68	79.2±0.52

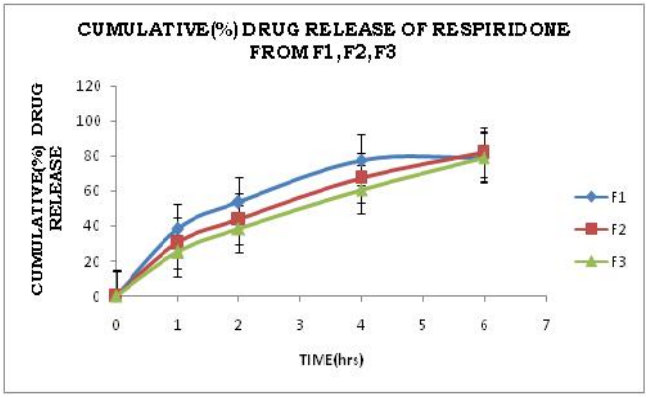

Figure 3: *In-vitro* dissolution profile - F1, F2, F3 batch's

***In-vitro* dissolution studies-F4, F5, F6 batches:** The formulation F4 containing a combination of HPMCK4M

and HPMCK100M the drug release was prolonged when compared to the formulation F5 containing a combination of HPMCK4M and ethyl cellulose and formulation F6 containing three rate controlling polymers.

Table 2: *In-vitro* dissolution profile – F4, F5, F6 batch's

Batch No.	F4	F5	F6
%Drug release in acid stage	0.0	0.0	0.0
% Drug release in buffer stage			
1 Hr	11.4 ± 1.62	37.7±0.82	31.9±1.21
2 Hr	29.2±0.52	45.2±0.42	52.8±0.63
4 Hr	48.5±1.21	76.3±1.62	68.2±2.12
6 Hr	68.0±0.85	91.0±2.12	83.2± 0.21

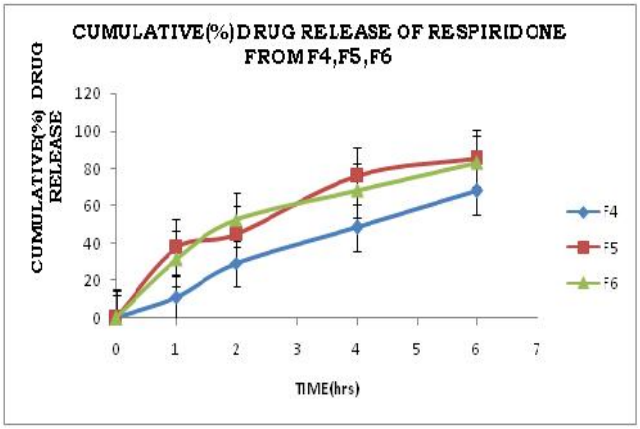

Figure 4: *In-vitro* dissolution profile – F4, F5, F6 batch's

***In-vitro* dissolution studies-F7, F8 batch:**

Enteric coating was developed for the formulation F5 and as the percentage of coating was increased the drug release was found to be decreased. In the formulation F8 Ethyl cellulose concentration was decreased and HPMC K4M was increased.

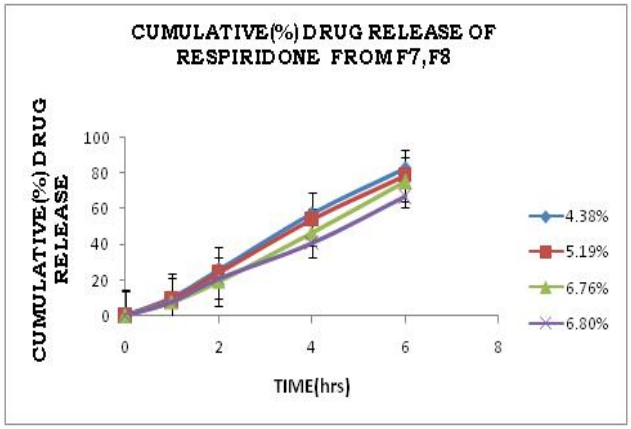

Figure 5: *In-vitro* dissolution profile-F7, F8 batch's

***In-vitro* dissolution studies F9:** In this formulation concentration of ethyl cellulose was increased and HPMC K4M was decreased and enteric coating was developed. The drug release was not matched with the innovator.

Table 3: *In- vitro* dissolution profile F9 batch.

Batch No.	F9	
	A	B
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	6.9±1.23	9.7±2.12
2 Hr	19.2±1.24	24.1±1.78
4 Hr	46.6±0.89	48.1±0.99
6 Hr	75.6±0.99	72.8±0.67

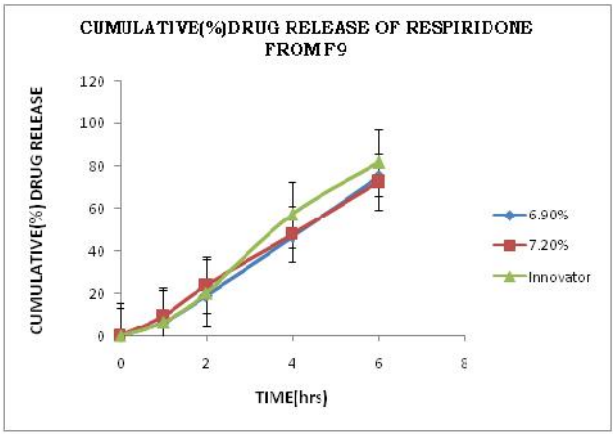

Figure 6: *In-vitro* dissolution profile – F9 batch

***In-vitro* dissolution studies–F10:**

In this formulation concentration of ethyl cellulose was further increased and HPMC K4M was decreased and enteric coating of different % was developed.

Table 4: *In-vitro* dissolution profile F10 batch

Batch No.	F10	
	A	B
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	13.2±0.55	10.2±0.93
2 Hr	31.5±3.01	26.3±1.69
4 Hr	57.8±3.78	54.8±1.05
6 Hr	88.1±2.08	84.9±0.65

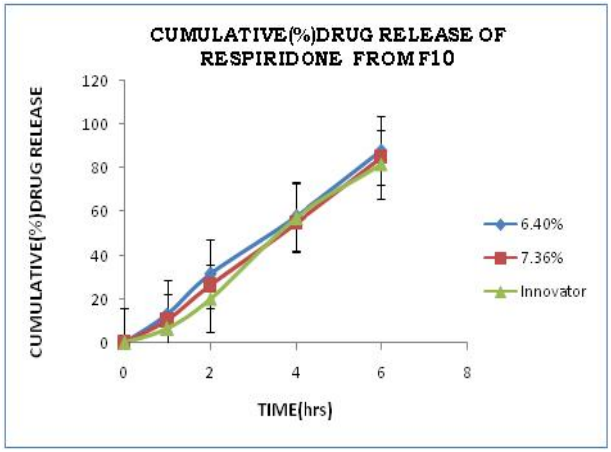

Figure 7: *In-vitro* dissolution profile – F10 batch

***In-vitro* dissolution studies F11:**

In this formulation concentration of ethyl cellulose was further increased and HPMC K4M was decreased and enteric coating of different % was developed.

Table 5: *In-vitro* dissolution profile – F11 batch

Batch No.	F11	
	A	B
% Drug release in acid stage	0.0	0.0
% Drug release in buffer stage		
1 Hr	8.6±1.22	10.2±1.25
2 Hr	29.4±1.26	24.6±0.96
4 Hr	43.7±0.59	53.7±1.25
6 Hr	69.6±2.23	82.7±3.23

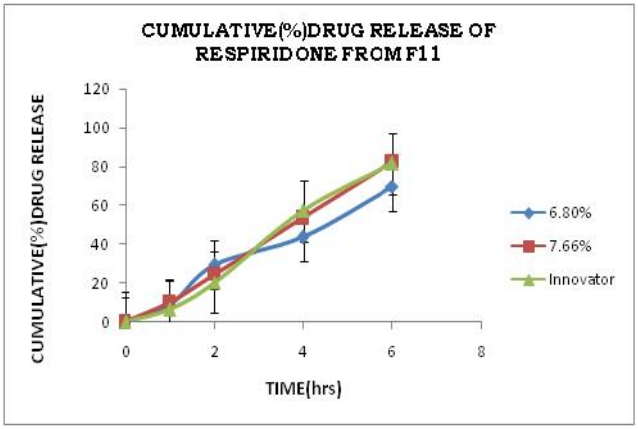

Figure 8: *In-vitro* dissolution profile F11 batch

Comparison of formulations with marketed formulation respiridone using similarity factor (f_2): The similarity factor (f_2) was calculated for all the formulations as per the procedure and the values are shown in the table.

Table 6: Similarity factor (f_2)

Formulations		Similarity factor (f_2)
F1		30
F2		37.4
F3		44
F4		50
F5		32
F6		33.5
F7	A	64.7
	B	64.2
	C	49.6
F8	A	47.6
F9	A	60.4
	B	58.1
F10	A	56.7
	B	68.7
F11	A	49.6
	B	67.2

The similarity factor of all the formulation ranged from 30-70. The f_2 value of formulation F10 (7.36%) was higher when compared to other formulations therefore F10 formulation was found to be similar to that of the marketed formulation.

Discussions of *in vitro drug* release:

In vitro drug release: The results of *In-vitro* release studies of formulae F1, F2, F3 prepared by single rate controlling polymer HPMC. The dissolution rate was found to be increased in the first two hours and the drug release was found to be 53.5%, 44.1%, 38.4% at the end of 2 hrs.

The release rate of HPMC was higher, probably due to faster dissolution of the highly water soluble drug from the core and its diffusion out of the matrix forming the pores for the entry of solvent molecule. Formulations F4, F5, were carried out using two rate-controlling polymers and the results showed that the formulation F4 containing HPMCK4M and HPMCK100M showed much prolonged drug release when compared to formulation F5 containing HPMCK4M and ethyl cellulose.

This is probably due to use of higher viscosity grade of HPMC in matrix. Increasing the molecular weight or viscosity of the polymer in the matrix formulation increases the gel layer viscosity and thus slows drug dissolution. Also, the greater viscosity of the gel, the more resistant the gel is to dilution and erosion, thus controlling the drug dissolution. Formulation F6 was carried out using three-rate controlling polymers HPMCK4M, HPMCK100M and ethyl cellulose.

There was no much difference in the release profile compared to the formulation containing two polymers. In the formulation F7 core tablets of formulation F5 were coated with coating solution of Acryl EZE up to average weight buildup of 4.37% w/w, 5% w/w, 6.76% w/w. In vitro release profile was compared with innovator it was observed that F7 was not complied. Further trials were conducted by varying the concentration of HPMC and ethyl cellulose. In the formulation F8 ethyl cellulose concentration was decreased and tablets were coated up to average weight buildup of 6.8%.

The drug release at the end of 6 hrs was found to be 66.7%.As HPMCK4M concentration was increased causes an increase in the viscosity of gel as well as formulation of gel layer with a longer diffusion path. This could cause a decrease in the effective diffusion coefficient of the drug and therefore reduction in drug release. In the formulations F9, F10 and F11 HPMCKM concentration was decreased and ethyl cellulose was increased. The drug release was found to be increased when compared to F8. The formulation F10 continued with an average weight buildup of 7.36%. Similarity factor (f_2) value was calculated for all formulations. The similarity factor (f_2) of all the formulations ranged from 30 to 68.7. The similarity factor of F10 is high when comparing to other formulations so, it is more similar to that of marketed formulation.

Table 7: Formulation of Respiridone Hydrochloride matrix tablets using different ratios of polymers (F1-F6)

S. No.	Ingredients (in mg)	Formulation					
		F1	F2	F3	F4	F5	F6
1	Respiridone	42.66	42.66	42.66	42.66	42.66	42.66
2	HPMC K4M	30.00	40.00	50.00	40.00	40.00	30.00
3	HPMC K100M	-	-	-	10.00	-	10.00
4	Ethyl Cellulose	-	-	-	-	10.00	10.00
5	Povidone	10.00	10.00	10.00	10.00	10.00	10.00
6	Spray Dried Lactose	141.34	131.34	121.34	121.78	121.78	121.78
7	Aerosil	2.00	2.00	2.00	2.00	2.00	2.00
8	Magnesium steareate	4.00	4.00	4.00	4.00	4.00	4.00
9	Total Weight	230	230	230	230	230	230

From the above 6 formulations F5 was selected and enteric coating was developed.

Table 8: Enteric coating of formulation F7

S. No	Ingredients (in mg)	Formulation (F7)		
		E1	E2	E3
	Enteric Coating	**4.378%**	**5.19%**	**6.76%**
1	Respiridone Hydrochloride	42.66	42.66	42.66
2	HPMC K4M	40.00	40.00	40.00
3	HPMC K100M	-	-	-
4	Ethyl Cellulose	10.00	10.00	10.00
5	Povidone	10.00	10.00	10.00
6	Spray Dried Lactose	121.78	121.78	121.78
7	Aerosil	2.00	2.00	2.00
8	Magnesium stearate	4.00	4.00	4.00

Table 9: Formulation of Respiridone hydrochloride matrix with varied concentrations of HPMC K4M and Ethyl cellulose Enteric Coating for formulations F8, F9, F10, F11

S. No	Ingredients (in mg)	Formulation						
		F8	F9		F10		F11	
		6.8%	6.9%	7.2%	6.4%	7.36%	6.8%	7.66%
1	Respiridone Hydrochloride	42.66	42.66	42.66	42.66	42.66	42.66	42.66
2	HPMC K4M	45.00	35.00	35.00	30.00	30.00	30.00	30.00
3	HPMC K100M	-	-	-	30.00	30.00	-	-
4	Ethyl Cellulose	5.00	15.00	15.00	-	-	30.00	30.00
5	Povidone	10.00	10.00	10.00	20.00	20.00	20.00	20.00
6	Spray Dried Lactose	141.34	131.34	131.34	121.34	121.34	121.34	121.34
7	Aerosil	2.00	2.00	2.00	2.00	2.00	2.00	2.00
8	Magnesium steareate	4.00	4.00	4.00	4.00	4.00	4.00	4.00
9	Total Weight	**250**	**250**	**250**	**250**	**250**	**250**	**250**

Table 10: Development of different % of enteric coating

Parameters	F8	F9	F10	F11
Uncoated tablets				
100 tablets wt. (gm)	22.92	23.1	23.05	23.01,
50 tablets (gm)	11.487	11.559	11.869	--
Wt. of tablets taken (gm)	57.365	57.841	11.869	64.597
Average wt. (mg)	229.46	231.36	237.38	230.7

Tablets wt. after warming (gm)	56.867	57.373	11.7414	64.174
Average wt. (mg)	227.46	229.49	234.83	229.19
Tablets wt. after coating (gm)	60.76	61.369	12.4997	68.60
Average wt. (mg)	243.04	245.47	249.99	245
% Coated	6.845	6.96	6.46	6.89

Table 11: Development of different% of enteric coating

Parameters	**F10**	**F11**
Uncoated tablets	----	---
Wt. of tablets (gm)	91.857	68.998
No. of tablets	400	300
Average wt. (gm)	229.65	229.99
After warming Wt. of tablets (gm)	91.5956	68.764
Average wt. (gm)	228.99	229.21
After coating		
Wt. of tablets (gm)	98.339	74.031
Average wt. (gm)	245.847	246.77
% Coated	7.36	7.66

Table 12: Characterization of Respiridone blends

Batch		**Angle of repose (θ)**	**Bulk density (g/ml)**	**Tapped density (g/ml)**	**Carr's index**
Uncoated tablets					
F1		26.07 ± 0.8	0.62± 0.01	0.72 ± 0.01	14.28 ± 0.3
F 2		25.25 ± 0.6	0.65± 0.0	0.71 ± 0.01	13.88 ± 0.6
F 3		28.45± 0.47	0.64± 0.01	0.74 ± 0.02	15.14 ± 0.6
F 4		25.12 ± 0.6	0.66± 0.02	0.74 ± 0.01	15.31 ± 0.08
F 5		26.10 ± 0.5	0.67± 0.03	0.74 ± 0.03	14.46 ± 0.4
F 6		26.91 ± 0.4	0.64± 0.02	0.73 ± 0.03	14.34 ± 0.02
Enteric coated tablets					
F7	4.378%(A)	27.46 ± 0.5	0.65± 0.01	0.75 ± 0.04	14.60 ± 0.24
	5%(B)	26.20 ± 0.2	0.64± 0.01	0.73 ± 0.03	14.57 ± 0.54
	6.76%(C)	25.45 ± 0.4	0.63± 0.01	0.71 ± 0.05	14.48 ± 0.21
F8	6.8%(A)	27.01 ± 0.7	0.67± 0.03	0.72 ± 0.01	15.56 ± 0.36
F9	6.9%(A)	25.92 ± 0.8	0.62± 0.03	0.74 ± 0.03	15.57 ± 0.24
	7.2%(B)	26.23 ± 0.5	0.594± 0.01	0.76 ±0.01	14.08 ± 0.20
F10	6.4%(A)	27.21 ± 0.4	0.56± 0.01	0.74 ± 0.01	15.39 ± 0.21
	7.36%(B)	24.91 ± 0.45	0.487± 0.01	0.74 ± 0.03	15.39 ± 0.21
F11	6.8%(A)	27.81±0.6	0.62± 0.01	0.72 ± 0.01	13.31 ± 0.08
	7.66%(B)	26.07±0.7	0.61± 0.02	0.76 ±0.01	14.34 ± 0.02

Table 13: Characterization of Respiridone matrix tablets

Batch		**Thickness (mm)**	**Hardness (Kg/cm^2)**	**Friability (%)**	**Weight Variation (mg)**	**Content Uniformity (%)**
Uncoated tablets						
F1		4.02 ± .012	6.2 ± 0.5	0.45± 0.005	225 ± 2	100.2 ±2.4
F 2		4.01 ± 0.09	6.6 ± 0.3	0.32±0.0041	227 ± 2	98.2 ± 1.6
F 3		4.05 ± 0.16	6.4 ± 0.5	0.19± 0.003	226 ± 4	98.7 ±2.2
F 4		4.09 ± 0.07	6.6 ± 0.2	0.21± 0.002	220 ± 2	101.2 ±2.4
F 5		4.11 ± 0.05	7.1 ± 0.3	0.54± 0.004	228 ± 4	102.3 ±1.3
F 6		4.02 ± 0.19	6.8 ± 0.2	0.49± 0.011	232 ± 2	101.5 ±1.6
Enteric coated tablets						
F7	A	4.28± 0.12	7.4±0.05	0.502±0.01	228± 2	98.2 ±1.2

	B	4.21± 0.08	7.2±0.04	0.408±0.027	232± 2	99.2 ±1.8
	C	429.± 0.09	6.8±0.11	0.418±0.012	226± 2	98.23±1.4
F8	A	4.24± 0.01	6.4 ± 0.5	0.501±0.010	231± 2	98.4 ± 1.6
F9	A	4.26± 0.13	7.1±0.04	0.41± 0.011	229± 2	102.3 ±1.3
	B	4.28± 0.09	6.6 ± 0.2	0.538±0.013	230± 2	101.5 ±1.6
F10	A	4.28± 0.12	7.4 ± 0.5	0.11± 0.003	227± 2	98.8± 1.6
	B	4.27± 0.08	7.0 ± 0.2	0.034±0.012	229± 2	101.1±1.4
F11	A	4.29± 0.13	6.8 ± 0.5	0.05± 0.005	228± 2	101.5 ±2.4
	B	4.30± 0.09	6.6 ± 0.2	0.32± 0.004	226± 2	100.2 ±2.4

Table 14: *In-vitro* dissolution profile – F7, F8 batch's

Batch No.	**F7**			**F8**
	A	**B**	**C**	**A**
% Drug release in acid stage	0.0	0.0	0.0	0.0
% Drug release in buffer stage				
1 Hr	10.3±0.42	9.0±0.96	7.6±0.56	7.9±0.65
2 Hr	25.6±1.21	24.2±1.61	19.4±0.78	21.1±0.32
4 Hr	57.3±0.56	54.1±1.22	46.6±1.23	40.8±0.98
6 Hr	83.1±1.21	78.7±0.41	75.0±1.56	66.7±1.23

4. Conclusion

Resperidone controlled release tablets were formulated and optimized at the polymer concentration ratio of 30:20 (HPMC: EC) at the coating percentage of an average weight buildup of 7.36%w/w. *In vitro* release studies complied with the innovator and the formulation was found to be equal. The drug and Polymer there is no compatibility, the similarity factor of F10 is shows high as compared to the other formulations are compared with that of marketed formulation.

5. Acknowledgement

I thank full to the Principal Seshachala College of Pharmacy, Puttur & Industrial Guide Aurobindo Pharma Limited, (Unit XII), Hyderabad for providing necessary facilities to carry out this work.

6. References

[1] Robert Langer, Donald Wise, editors. Medical Application of Controlled release: classes of system. CRC Press: Inc; **1984**. pp.159.

[2] Lippincott Williams, Wilkins, Thomas Wai- Yip Lee, Joseph R Robinson, editors. Remington's The Science and Practice of Pharmacy. 20th ed. Maryland; **2000**. pp.903-914.

[3] Robinson JR, Lee VH. Controlled drug delivery: fundamentals & application. 2nd ed. New York (NY): Marcel Dekker; **1987** .p. 36.

[4] Welling PG, Dobrinska MR, Robinson JR, Lee VH. Controlled Drug Delivery: Fundamentals and Applications, 2nd Ed. New York: Marcel Dekker; **1987** .p. 255-259.

[5] Basak SC, Jayakumar Reddy, Lucas Mani. Formulation and release behaviour of sustained release ambroxol hydrochloride HPMC matrix tablet. Indian J Pharm Sci., **2006,** 68(5):594-598.

[6] Gohel MC, Parikh RK, Padshala MN. Formulation of directly compressible Isoniazid modified release matrix tablet. Indian J Pharma Sci., **2007**, 69(5): 640-645.

[7] Punna Rao Ravi, Sindhura Ganga, Ranendra Narayan Saha1.Design and Study of Lamivudine Oral Controlled Release Tablets, AAPS Pharm Sci Tech **2007**;8(4):E1- E9.

[8] Gohel MC, Parikh RK, Padshala MN, Sarvaiya KG, Jena., Formulation and optimization of directly compressible isoniazid modified release matrix tablet. Indian J Pharma Sci **2008**;69:640-645.

[9] Selim Reza MD, Mohiuddin Abdul Quadir, Syed Shabbir Haider Comparative evaluation of plastic, hydrophobic and hydrophilic polymers as matrices for controlled-release drug delivery. J Pharma Sci **2003**;6(2):274-291.

[10] Ranjani V Nelloreb, Gurvinder Singh Rekhia, Ajaz S Hussainc, Lloyd G Tillmand, Larry L Augsburger. Development of metoprolol tartrate extended-release matrix tablet formulations for regulatory policy consideration. Journal of Control Rel., **1998**, 50(3): 247–256.

[11] Meena Rani, Brahmeshwar Mishra. Comparative In Vitro and In Vivo Evaluation of Matrix, Osmotic Matrix, and Osmotic Pump Tablets for Controlled Delivery of Diclofenac Sodium, AAPS Pharm Sci Tech., **2004**, 5(4): 1-6.

[12] Reddy KR, Mutalik S, Reddy S. Once-daily Sustained-release matrix tablets of nicorandil: Formulation and in vitro evaluation. AAPS Pharm Sci Tech., **2003**, 4(4): 61.

[13] Silvina A Bravo, Maria C Lamas, Claudio J Salomon. In-vitro studies of diclofenac sodium controlled-release from biopolymeric hydrophilic matrices. J Pharm Pharmaceut Sci., **2002**, 5(3): 213-219.