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Formulation and *in- vitro* evaluation of taste masked orodispersible tablet of antipsychotic by using ion exchange resins

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ABSTRACT

Risperidone, a benzisoxazole derivative, is an atypical antipsychotic drug with high affinity for 5-hydrotryptamine (5-HT) and dopamine D2 receptors. But this drug has bitter taste which may leads to patient's non compliance. Ion exchange resins are water–insoluble, cross–linked polymers containing salt forming groups in repeating positions on the polymer chain. It used to mask taste of bitter drug. In this study, Orodispersible tablet of Risperidone was developed. Taste masking of Risperidone were done by two Ion exchange resin Kyron T-104 & Indiaon-204 independently. Formulated Drug Resin Complex was characterized by infrared spectroscopy. λmax and calibration curve of drug were studied. Drug- resin complex were optimized by considering parameters such as optimization of resin concentration, swelling time, stirring time, pH and temperature on maximum drug loading. Taste evaluation done by taste panel method. Optimization of conditions required for maximum drug loading of Risperidone with Resins. Kyron T-134 Superdisintigrant used in formulation so disintegration & drug release in very less time. The In-Vitro drug release of optimized formulation compare with marketed tablet. Thus, results conclusively demonstrated successful masking of taste and rapid disintegration of the formulated tablets in the oral cavity.

Keywords: Risperidone, Kyron T-104, Indiaon-204, Drug-resin complex, Superdisintegrant, taste masking.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. However, geriatric and paediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as fast dissolving tablets or orodispersible tablets. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and paediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market (1).

The oral fast dissolving tablet prepared by many techniques, direct compression is one of main method to prepare oral fast dissolving tablet. Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of Orodispersible tablet because of the availability of improved excipients especially superdisintegrants and sugar based excipients (2). Risperidone, a benzisoxazole derivative, is an atypical antipsychotic drug with high affinity for 5-hydrotryptamine (5-HT) and dopamine D2 receptors (3, 4). It is used primarily in the management of schizophrenia, inappropriate behaviour in severe dementia

and manic episodes associated with bipolar I disorder (3, 4, 5). But this drug has bitter taste which may leads to patient's non compliance. Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care provider, especially for paediatric patients. Conventional taste masking techniques such as use of sweeteners, amino acids, flavouring agent are often unsuccessful in masking the taste of highly bitter drugs.

To mask the bitterness of drug various techniques are available, among those taste masking by use of ion exchange resin is most commonly used commercially (6) Ion exchange resins (IERs) are used to mask bitter taste of drug. Ion exchange resins are water–insoluble, cross–linked polymers containing salt forming groups in repeating positions on the polymer chain. It can be used in the drug formulations to stabilize the sensitive components, sustain release of drug, disintegrate tablets and mask taste. (6) The resin form insoluble adsorbates or resonates through weak ionic bonding with oppositely charged drugs so that dissociation of drug resin complex does not occur under the salivary pH conditions. Bitter cationic drugs can get adsorbed onto the weak cation exchange resin of carboxylic acid functionality to form the complex which is non bitter. Kyron T-104 is Ion exchange resin. Indiaon 204 is a weak acid cation exchange resin based on a cross-linked acrylic-copolymer, divinyl benzene matrix containing carboxylic acid functional groups. It combines with high capacity; it is insoluble in all common solvent, having excellent physical and chemical stability and operating characteristics.

Risperidone is bitter taste drug. Aim of this research work was to develop mouth dissolving orodispersible tablet that disintegrates rapidly in mouth by using two independent tasteless complex of drug and resin i.e. first is Risperidone with Kyron T-104 and another Risperidone with Indiaon 204. Taste masking of of Resperidone done independently by using Kyron T-104 and Indiaon 204 two ion exchange resin. Effect of different parameters such as swelling time, resin activation, drug resin ratio as well as stirring time was optimized by taste and percentage drug loading were evaluated. Formulated DRC (Drug Resin Complex) was characterized by infrared spectroscopy. Taste masking of tablet was done evaluate by taste panel method. The In-Vitro drug release of optimized formulation compare with marketed tablet.

MATERIALS AND METHODS

Materials

Risperidone was obtained from Zim Laboratories, Nagpur, India. Kyron T-104 was obtained from Vama pharma, Nagpur, India. Resin Indiaon 204 was gifted by Ion Exchange (India) Ltd. Microcrystalline cellulose (MCC) from Gujarat Microwax Pvt. Ltd. India. Other chemicals used were of analytical grade.

2. Methods

2.a *Determination maximum absorption (λ max) of drug*

The solution of 10µg/ml concentration containing Risperidone was preparing in 0.1 N HCl and was scanned between the ranges of 200 to 400 nm by Ultra- violet spectrophotometer for getting the maximum absorbance.

2.b *Preparation of standard curve for Risperidone in 0.1 N HCl*

The Standard stock solution of 0.1 N HCl was prepared. From standard stock, sample solution was prepared of following concentration 10ug/ml, 20ug/ml, 30ug/ml, 40ug/ml, 50ug/ml, of risperidone in 0.1 N HCl and analysed at 279nm.

2.1 Taste masking of Risperidone by Kyron T-104

2.1A *Assessment of the bitter taste of the Risperidone (Bitterness threshold)*

The bitter taste threshold value of Risperidone was determined based on the bitter taste recognized by six volunteers (three females and three males). A series of Risperidone aqueous solutions were prepared at different concentrations as standard solutions, i.e. 10, 20, 30, 40 and 50 µg/ml respectively. The test was performed as follows: 1ml of each standard solution was placed on the centre of the tongue, it was retained in the mouth for 30 seconds, and then the mouth was thoroughly rinsed with distilled water (7). The threshold value was correspondingly selected from the different Risperidone concentrations as the lowest concentration that had a bitter taste.

2.1B *Formulation of drug resin complex (DRC)*

Formulation of DRC was done by the batch process; 100 mg of resin Kyron T-104 was placed in a beaker containing 100 ml of deionised water and allowed to swell for a definite period of time (7). Accurately weighed amount of (drug: resin ratio) was added and stirred for desired period of time. The mixture was filtered and residue was washed with deionised water. Filtrate was analyzed by U.V. spectrophotometer at 279 nm for the unbound drug and percentage drug loading was calculated (7).

2.1C *Effect of concentration of resin on drug loading*
An accurately weighed amount of Risperidone was added to the different concentration of Kyron-104 for the determination of optimized ratio with maximum drug loading (8). Amount of maximum bound drug was determined at 279 nm by UV spectroscopy.

2.1D *Effect of pH on maximum drug loading*
Accurately weighed Risperidone was added to 100 mg of Kyron T-104 solution and slurred in 100 ml each of pH 1.2, 2, 3, 4, 5, 6, 7, and 8 solutions (prepared from standard solutions of hydrochloric acid and potassium hydroxide, maintained at 25°C (9). The maximum drug-loading at particular pH was estimated.

2.1E *Effect of temperature on maximum drug loading*
Accurately weighed Risperidone was added to 100 mg of Kyron T-104 solution and slurred in 100 ml of deionised water, maintained at different temperature such as, 40°C, Room temperature using temperature-controlled magnetic stirring for 6 hour (10). Amount of maximum bound drug at the particular temperature was estimated.

2.1F *Effect of time on maximum drug loading*
Accurately weighed, 100 mg of Risperidone was added to 500 mg of Kyron T-104 solution and slurred in deionised water. Three batches with stirring time of 1, 2, 3, 4, 5, 6 hr were processed (11). Amount of maximum bound drug at the end was estimated.

2.1G *Characterization of Risperidone - Kyron T-104 complexes*
The drug, resin and resinate were subjected to Fourier Transform Infra Red (FTIR) studies to check drug resin interaction using FT/IR (Jasco – 470 plus).

2.1H *Taste evaluation of Drug-resin complex (DRC)*
Taste evaluation of DRC was performed by volunteers in the age group of 19 to 22 years. The study protocol was explained and written consent was obtained from volunteers. DRC equivalent to 10 mg Risperidone was held in the mouth for 30 seconds by each volunteer. Bitterness levels were recorded instantly and then after 30 sec, 60 sec. The bitterness level was recorded against pure drug using a numerical scale. A numerical scale was used with the following values: 0 = tasteless, 1= acceptable bitterness, 2= slight bitterness, 3= moderately bitterness and 4= strong bitterness (12).

2.1I *Determination of drug content*
Resinate prepared by above process was evaluated for the drug content. Resinate equivalent to 10 mg of drug was stirred with 100 ml of 0.1N HCl for 60 minutes, till the entire drug leached out, then the solution was filtered. Dilutions were made with 0.1N HCl and the drug content was noted spectrophotometrically at 279 nm using 0.1 N HCl as blank (13).

2.1J *In Vitro drug release study from resinate*
Resin ate equivalent to 4.16 mg of drug was subjected to dissolution studies using USP type II dissolution apparatus at 50 rpm with temperature of 37±0.5ºC and 900 ml of SSF (Simulated salivary fluid), similarly SGF (Simulated gastric fluid) was also used as the dissolution medium. Aliquot equal to 5 ml was withdrawn at specific time interval and it was filtered through what man filter, the solution was checked by UV spectroscopy at 279 nm and quantity of drug release was determined periodically (14). The testing was carried out in triplicate.

2.8K *Evaluation of the Tablet Blend*
Physical properties such as bulk density, tapped density, compressibility index, and the angle of repose of blend were determined (15).

Table No.1: Composition of Tablet of taste masking by Kyron T-104 (B1-B3)

Sr.no	Tablet ingredient (mg)	B1	B2	B3
1	DRC	4.7	4.7	4.7
2	Kyron T-314	5	7.5	10
3	Mannitol	60.84	58.34	55.84
4	Mcc	20	20	20
5	Aspartame	5	5	5
6	Talc	3	3	3
7	Mag.stearate	1	1	1
8	Aerosil	1	1	1
	Total	100	100	100

2.8L *Formulation and optimization*
The tablet consist of resin ate equivalent to 30 mg drug. Avicel (PH 102) and Pearlitol SD200 were selected as diluents (Table No. 1). All the 3 batches were prepared by direct compression method using single punch machine. The hardness of the tablet of each batch were tried to keep constant (3 kg/cm2). The weight of the tablet of each batch was adjusted to 100 mg. The tablet was evaluated for its tensile strength, weight variation, % friability, disintegration time. Dissolution study of tablets was carried out in simulated gastric fluids (16).

2.8M *Comparison of optimized formulation with conventional marketed tablet*
The In-Vitro drug release study of optimized formulation and marketed tablet was done and compare the drug release.

2.2 Taste masking of Risperidone by Indiaon-204
In Experimental study for taste masking by Indiaon-204 are same as in taste masking of Risperidone by Kyron T-104 with little difference in some procedure. Parameter like effect of pH, temperature and taste evaluation was studied in same manner as in taste masking in Kyron T-104.

2.2A *Preparation of resinate*
Resinate were prepared by batch process in which given quantity (mg) of resin was placed in a beaker containing deionised water and allowed to swell for 30 minutes. Accurately weighed Risperidone (drug: resin ratio) was added and stirred for 30 minutes. The resinate obtained were washed with copious amount of deionised water. The complexes were dried overnight in a hot air oven at 40 ºC (Gohel *et al*, 2005).

2.2B *Optimization of concentration of resin on drug loading*
An accurately weighed amount of Risperidone was added to the different concentration of indion 204 for the determination of optimized ratio with maximum drug loading (Birader, S.S., Bhagwati, S., Kuppasad I.J., 2006). Amount of maximum bound drug was determined at 279 nm by UV spectroscopy.

2.2C *Effect of pH on maximum drug loading*
Accurately weighed Risperidone was added to 200 mg of Indiaon 204 solution and slurred in 25 ml each of pH 1.2, 2, 3, 4, 5, 6, 7, and 8 solutions (prepared from standard solutions of hydrochloric acid and potassium hydroxide), maintained at 25°C. (Chatap, V.K., Sharma, D.K., Gupta V.B., 2008) The maximum drug-loading at particular pH was estimated.

2.2D *Effect of temperature on maximum drug loading*
Accurately weighed Risperidone was added to 200 mg of Indiaon 204 solution and slurred in 25 ml of deionised water, maintained at different temperature such as, 40°C, Room temperature using temperature-controlled magnetic stirring for 6 hour (Sohi *et al*,2004). Amount of maximum bound drug at the particular temperature was estimated.

2.2E *Characterization of Risperidone -Indiaon 204 complexes*
The drug, resin and resinate were subjected to Fourier Transform Infra Red (FTIR) studies to check drug resin interaction using FT/IR (Jasco – 470 plus).

2.2F *Taste evaluation:*
Taste evaluation of DRC was performed by volunteers in the age group of 19 to 22 years. The study protocol was explained and written consent was obtained from volunteers. DRC equivalent to 10 mg risperidone was held in the mouth for 30 seconds by each volunteer. Bitterness levels were recorded instantly and then after 30 sec, 60 sec. The bitterness level was recorded against pure drug using a numerical scale. A numerical scale was used with the following values: 0 = tasteless, 1= acceptable bitterness, 2= slight bitterness, 3= moderately bitterness and 4= strong bitterness (Chandrashekar *et al*, 2006).

2.2G *Determination of drug content:*
Resinate prepared by above process was evaluated for the drug content. Resinate equivalent to 10 mg of drug was stirred with 100 ml of 0.1N HCl for 60 minutes, till the entire drug leached out, then the solution was filtered. Dilutions were made with 0.1N HCl and the drug content was noted spectrophotometrically at 279 nm using 0.1 N HCl as blank (Mahajan *et al*, 2004).

2.2H *In-Vitro drug release study from resinate:*
Resinate equivalent to 4.6 mg of drug was subjected to dissolution studies using USP type II dissolution apparatus at 50 rpm with temperature of 37±0.5ºC and 900 ml of SSF (Simulated salivary fluid), similarly SGF (Simulated gastric fluid) was also used as the dissolution medium. Aliquot equal to 5 ml was withdrawn at specific time interval

and it was filtered through whatman filter, the solution was checked by UV spectroscopy at 279 nm and quantity of drug release was determined periodically (Devi *et al*, 2006). The testing was carried out in triplicate.

2.2I *Characterization of Risperidone Indiaon-204 complexes*

The drug, resin and resinate were subjected to Fourier Transform Infra Red (FTIR) studies to check drug resin interaction using FT/IR (Jasco – 470 plus).

2.2J *Evaluation of the tablet blend*

Physical properties such as bulk density, tapped density, compressibility index, and the angle of repose of blend were determined (Shirwaikar *et al*, 2004).

2.2K *Formulation and optimization*

The tablet consist of resinate equivalent to 30 mg drug (Table No.2). All the 3 batches were prepared by direct compression method using single punch machine. The hardness of the tablet of each batch were tried to keep constant (3 kg/cm2). The weight of the tablet of each batch was adjusted to 100 mg (Tablet No.2). The tablet was evaluated for its tensile strength, weight variation, % friability, disintegration time. Dissolution study of tablets was carried out in simulated gastric fluids (Seong *et al*, 2005).

Table No. 2: Composition of taste masked Tablet by Indioan-204 (B4-B6)

Sr.no	Tablet ingredient (mg)	B4	B5	B6
1	DRC	4.7	4.7	4.7
2	Kyron T-314	5	7.5	10
3	Mannitol	60.84	58.34	55.84
4	Mcc	20	20	20
5	Aspartame	5	5	5
6	Talc	3	3	3
7	Mag.stearate	1	1	1
8	Aerosil	1	1	1
	Total	100	100	100

2.2L *Comparison of optimized formulation with conventional marketed tablet*

The In-Vitro drug release study of optimized formulation and marketed tablet was done and compare the drug release.

RESULTS AND DISCUSSION

3.*a Determination of maximum absorption (λmax) of drug*

The maximum wavelength of Risperidone *(λ max)* was observed at 279 nm which match with reported wavelength. It was illustrated in figure no. 1.

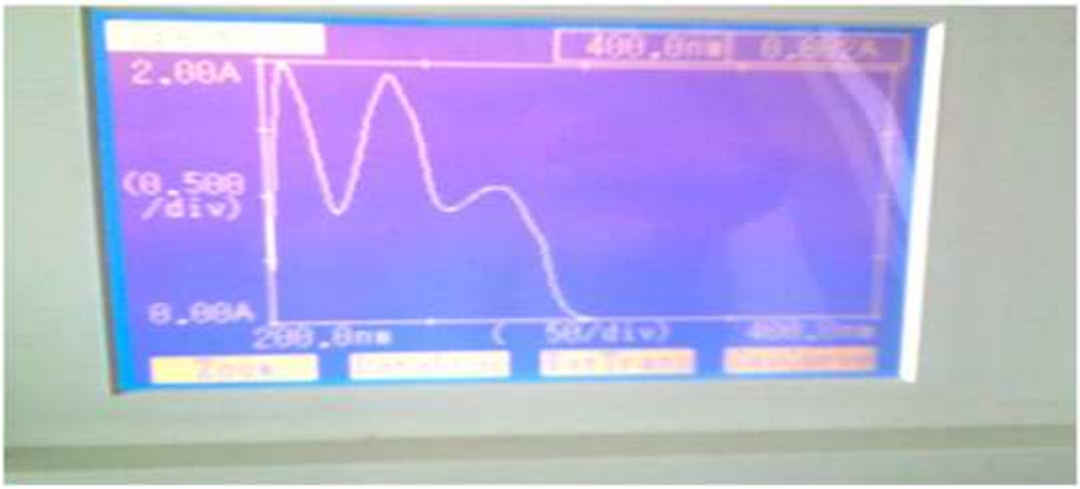

Figure No. 1 Ultra Violet spectroscopy spectra of Risperidone show *λmax.*

3b. *Standard curve for Risperidone in 0.1 N HCl*

The standard calibration curve of Resperidone in 0.1NHCl was established, when the absorption plotted against concentration (Fig no.2) the linear curves developed (Table No.3). From above it conclude that drug follows Beer's Lambert law and hence authentic one.

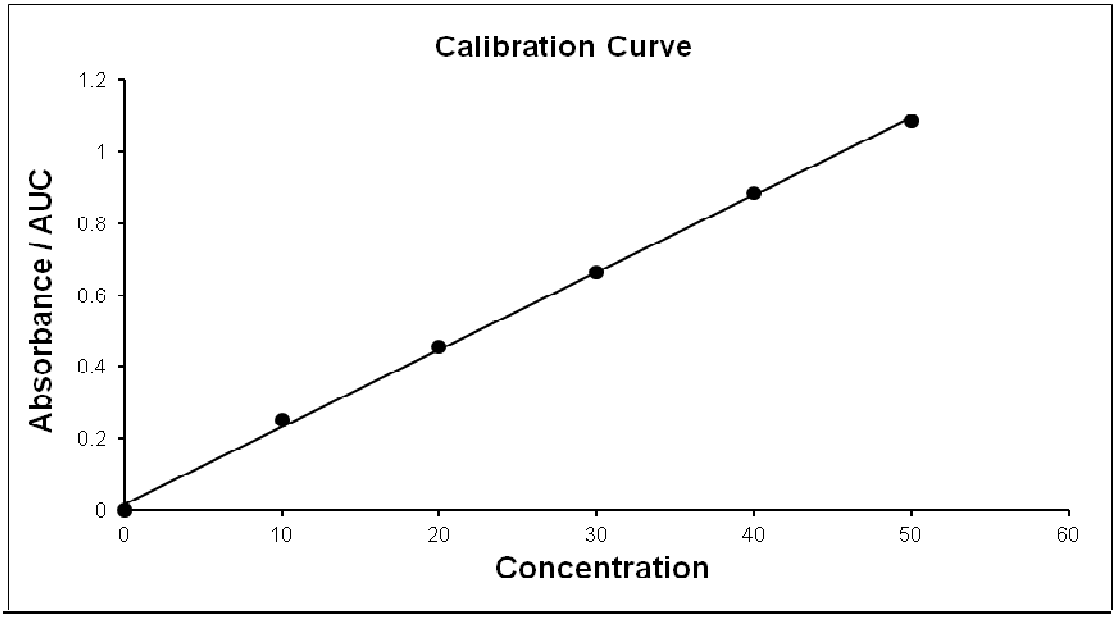

Figure No.2 Standard Calibration curve of Risperidone

Table 3 Standard Calibration Curve

Sr.No.	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.251
3	20	0.455
4	30	0.662
5	40	0.885
6	50	1.086

3.1 Result and discussion for Taste masking of Risperidone by Kyron T-104

3.1A *The bitterness threshold of Risperidone*

The bitterness threshold of Risperidone recognized by the volunteers was between 35-45 µg/ml. From the majority of volunteers it was found that the threshold value of Risperidone was found to be 40µg/ml.

3.1B *Result of effect of concentration of resin (on drug loading), pH, temperature and time on maximum drug loading and optimization*.

While studying the effect of concentration of resin on drug loading, maximum drug loading was found in ratio 1:1 (drug: Kyron T-104) (Table No.4). Complexation between the drug and resin is essentially a process of diffusion of ions between the resin and surrounding drug solution. As the reaction is an equilibrium phenomenon, maximum efficiency is best achieved in batch process. Equilibrium time was shorter due to thinner barrier for diffusion of ions, as it is a continuous motion. Also higher swelling efficiency in the batch process result in more surface area for ion exchange. Hence the batch process is suitable for smaller particles. The swelling and hydrating properties of Kyron T-104 affect the rate of ion exchange, which in turn affects the percentage drug loading.

In unswollen resin matrix, the exchangeable groups are latent and coiled toward the backbone, hence less drug-loading efficiency. The optimized percentage drug loading (w/w) was found to be 98.10±0.16 for Kyron T-104 with swelling time 30 minute. The equilibrium ion exchange in solution occurs stoichiometrically and hence is affected by stirring time (Table No**.** 5)

The optimized percentage drug loading (wt/wt) was found to be 98.12±.14 for Kyron T-104 with stirring time 60 minutes (Table No.5). Drug complexation involved exchange of ionisable drug and metal ion in resin. Such a mode

of complexation between drug and resin affected by pH of media. Complexation was enhanced and was found maximum at pH 6 (Table No.6).

Table No. 4. Effect of drug resin ratio on DRC (Drug-Resin complex) formation using Kyron T-104

Resins	Ratio	% drug bound to resins
Kyron T-104	1:1	11.7
	1:1	25.2
	1:1	11.55
	1:1	14.25
	1:2	12.6
	1:2	15.75
	1:2	15
	1:2	11
	1:3	16.5
	1:3	0.3

Table No. 5 Effect of time on DRC (Drug-Resin complex) formation using Kyron T-104

Resins	Time (Hr)	% drug bound to resins
Kyron T-104 pH-6 Ratio-1:1	1	82.11
	2	87.34
	3	91.21
	4	94.42
	5	96.23
	6	96.53

Table No. 6. Effect of pH on DRC (Drug-Resin complex) formation using Kyron T-104

Resins	pH	Ratio	%drug bound to resins
Kyron T-104	5	1:1	11.7
	6	1:1	21
	7	1:1	11.55
	8	1:1	14.25
	5	1:2	12.6
	6	1:2	15.75
	7	1:2	15
	8	1:2	11
	8	1:3	16.5
	7	1:3	0.3

Table No.7 Effect of room temperature on DRC (Drug-Resin complex) formation Kyron T-104

Resins	Time (hr)	% drug bound to resins
KYRON T-104(room temp) pH -6 Ratio-1:1	0.5	20.60
	1	26.33
	1.50	33.21
	2	38.32
	2.50	44.12
	3	53.32
	3.50	58.45
	4	66.24
	4.50	77.21
	5	79.27
	5.50	85.44
	6	92.22

Efficient drug loading on Kyron T-104 in the experimental range 25-80^{0}C (Table No.7 and 8)**.** Increased temperature during complexation increases the ionization of drug and resin. The effect is more pronounced for poorly water soluble and unionized drugs. Higher temperature tends to increase the diffusion rate of ions by decreasing the thickness of exhaustive exchange zone. As Risperidone is water soluble ionizable drug, temperature does not show any significant effect on drug absorption and also cation exchange resins are significantly affected by temperature changes.

Table No. 8 Effect of temperature at 40^{0}C on DRC (Drug-Resin complex) formation using Kyron T-104

Resins	Time(hr)	% drug bound to resins
Kyron T-104 At 40^{0c} pH-6 Ratio- 1:1	0.5	18.21
	1	27.20
	1.50	36.45
	2	42.12
	2.50	50.22
	3	58.33
	3.50	66.77
	4	74.32
	4.50	82.24
	5	89.56
	5.50	94.35
	6	98.21

3.1C *Taste evaluation by panel method*

Taste evaluation revealed that Kyron T-104 masks the bitter taste of the drug completely (Table No. 9).

Table No. 9. Evaluation of taste of Drug-resin complex (DRC)

Volunteers	Bitterness level after					
	10 sec.	1 min.	2 min.	5 min.	10 min.	15min.
1	X	0	0	0	0	0
2	X	X	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	X	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0

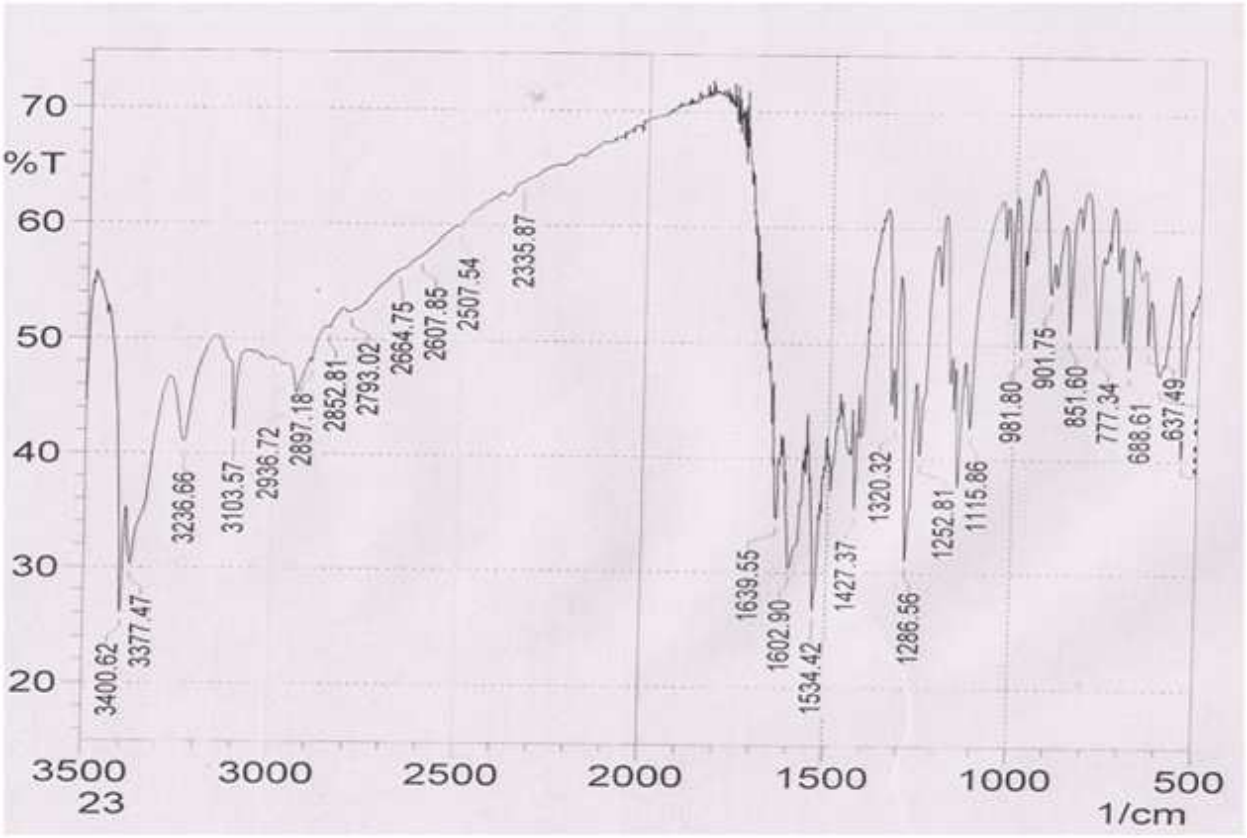

Figure No.3 FTIR Spectra of Risperidone

3.1D *Characterization of Risperidone- Kyron T-104 complexes*

The interaction between the drug and the resin often leads to identifiable change in the IR profile of drug dispersion. So Risperidone: Kyron T-104 was subjected to IR analysis in order to evaluate possible interaction between drug and Kyron T-104. The FTIR spectra of Risperidone and Risperidone-Kyron T-104 complex were shown in Figure no. 3 and 4 respectively.

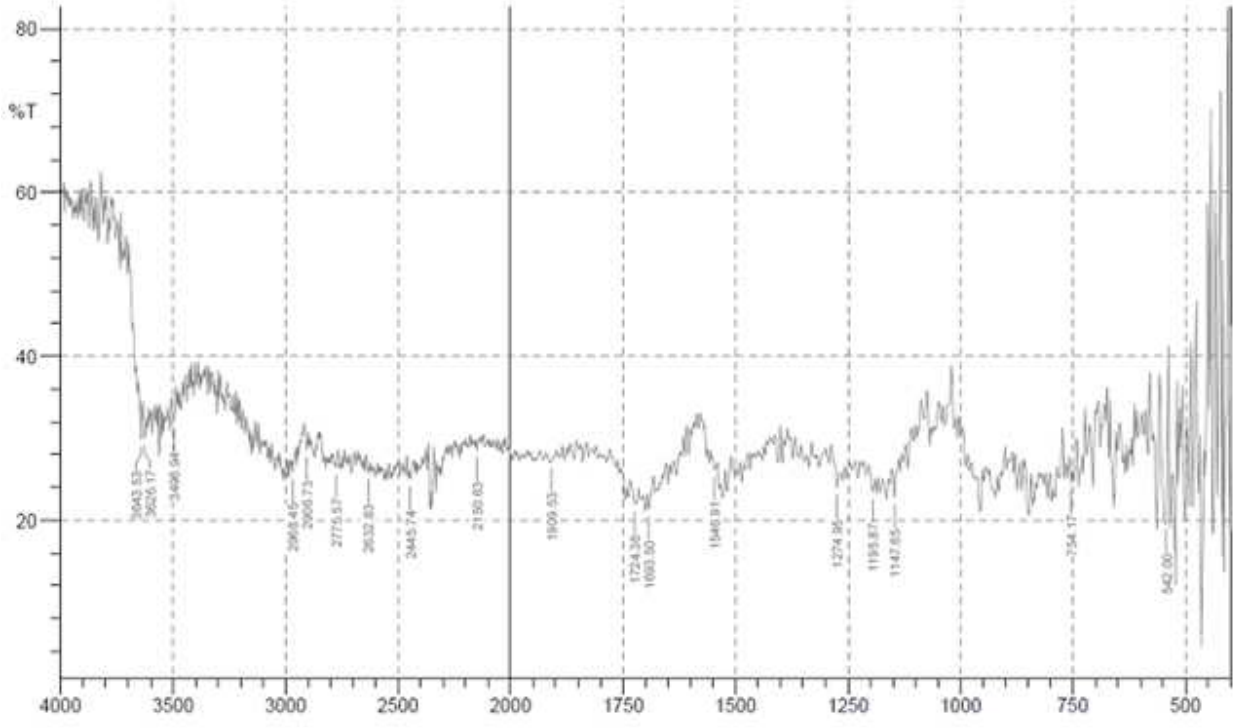

Figure No.4 FTIR spectra of Risperidone- Kyron T-104 resin

3.1E *Drug content*

The drug content of resin was found to be 98.34 ± 0.054 %.

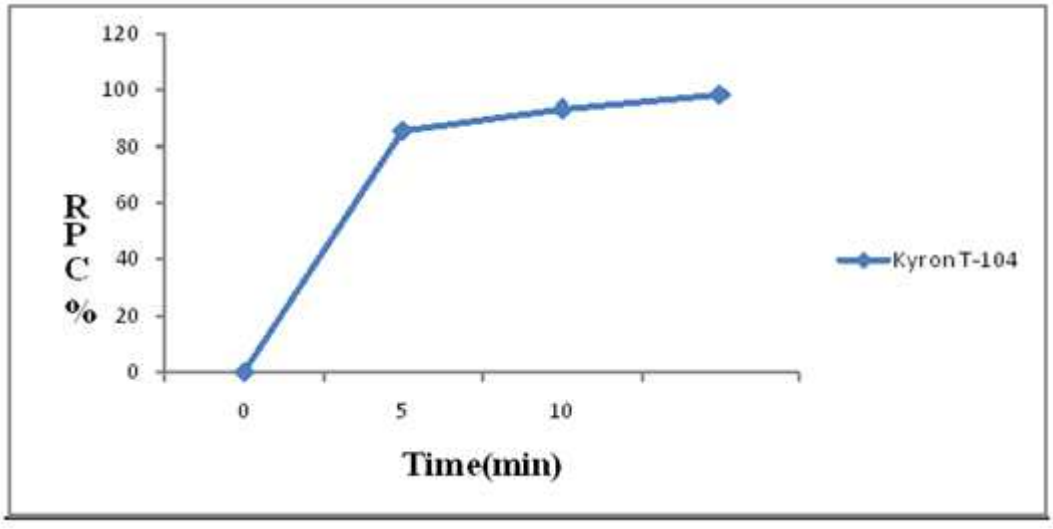

Figure No. 5 In-Vitro drug release study from Risperidone- Kyron T-104 resinate

3.1F *In-Vitro drug release study from resinate:*

Samples were withdrawn, analyzed at 279 nm and percentage cumulative drug release was determined. The presence of exchangeable ions of ionisable electrolytes in the salivary fluid may be responsible for this release. So the drug resin complex is stable in salivary pH for a period of administration. The amount released is insufficient to impart bitter taste while the formulation passes through the mouth to further parts of the gastrointestinal (GI) tract. *In vitro* drug release study was also performed in simulated gastric fluids (SGF) pH 1.2 (Fig. No.5). The drug release

from Kyron T-104 was found to be more than 85 % within 10 minutes in simulated gastric fluids (SGF) which shown in figure no.5.

3.1G *Evaluation of tablets blend and tablet*

The various evaluation test of tablet were done and their results were in the standard limits prescribed in officially in Indian Pharmacopoeia (Table No. 10).

Table No.10: Powder and tablet evalution of optimized batch

Parameter	Optimized batch
Bulk density	0.535 gm/ml
Tapped density	0.614 gm/ml
Compressibility index	13.84
Hauners ratio	1.178
Angle of repose	28.52°
Friability	0.60 %
Disintegration	20 Secound
Weight variation	100.1 Kg/cm^2
Thickess	3.4 mm
Diameter	5.3 mm

3.1H *Dissolution study of Tablet*

Dissolution study of tablets revealed that more than 85 % of the drug was released within ten minutes (Table No 11). Drug release pattern was shown in figure no. 6.

Table No. 11: Dissolution study of optimized tablet formulation

S .No	Time (min)	% Cumulative release
1.	5	83.51 ± 0.19
2.	10	98.12 ± 0.14

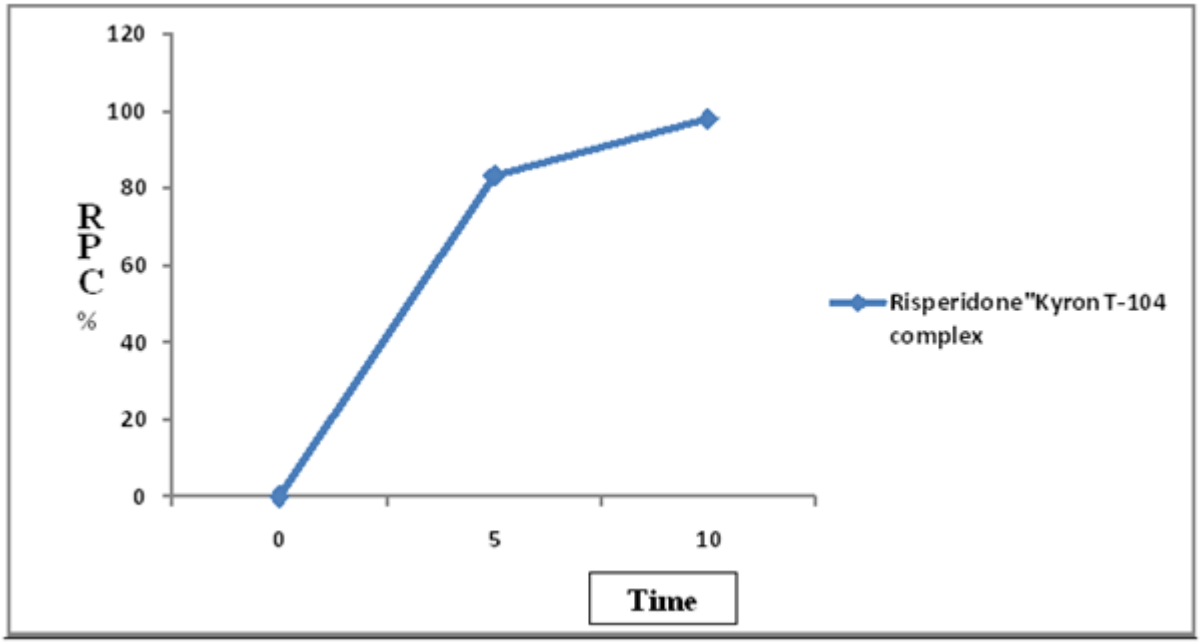

Figure No. 6 In-Vitro drug release of taste masked Orodispersible tablet by Kyron T-104 resin

3.1I *Comparison of optimized formulation with conventional marketed tablet*

The In-Vitro drug release study of optimized formulation and marketed tablet was done and compare the drug release. Result was illustrated in table no.12 and comparative drug release pattern of conventional Risperidone tablet and optimized tablet represent in figure no. 7. Optimized tablet had more drug released compare to conventional marketed tablet.

Table No. 12. Comparison of optimized with conventional marketed tablet

Sr. No	Time(min)	Cumulative % release from conventional marketed tablet	Cumulative % release from optimized batch
1.	5	80.12 ± 0.23	84.57 ± 0.15
2.	10	95.33 ± 0.18	100.16 ± 0.26

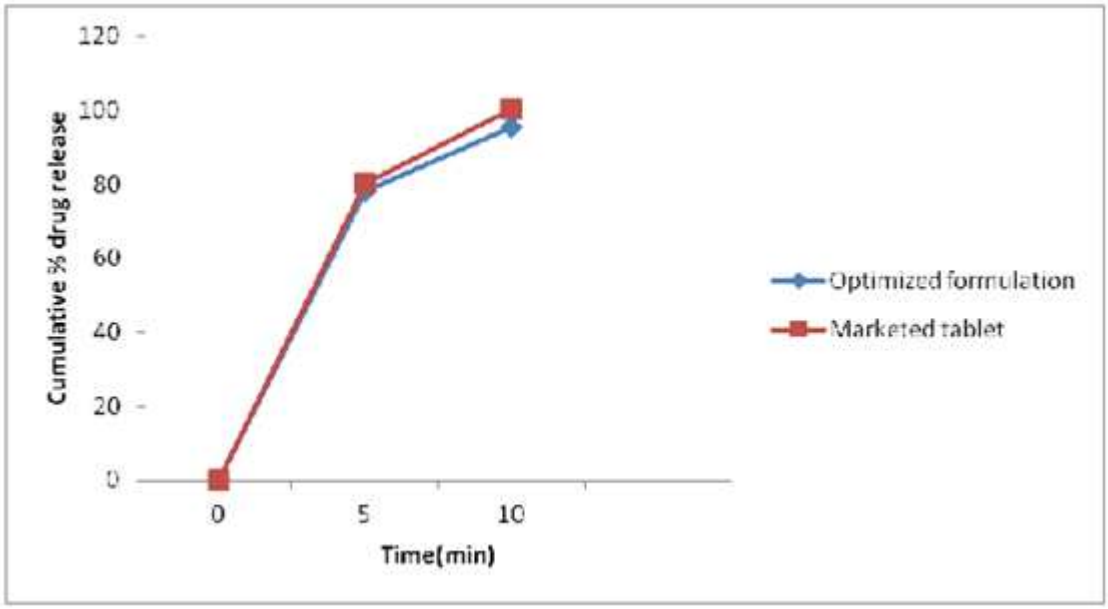

Figure No.7 Comparison of optimized formulation of taste masked Orodispersible tablet by Kyron T-104 with conventional marketed tablet of Risperidone

3.2 Result and discussion for Taste masking of Risperidone by Indiaon-204

3.2A *The bitterness threshold of Risperidone:*

The bitterness threshold of Risperidone recognized by the volunteers was between 35-45 µg/ml. From the majority of volunteers it was found that the threshold value of Risperidone was found to be 40 µg/ml.

3.2B *Result of effect of concentration of resin (on drug loading), pH, temperature and time on maximum drug loading and optimization*.

While studying the effect of concentration of resin on drug loading, maximum drug loading was found in ratio 1:2 (drug: indiaon 204) (Table No.13). Complexation between the drug and resin is essentially a process of diffusion of ions between the resin and surrounding drug solution. As the reaction is an equilibrium phenomenon, maximum efficiency is best achieved in batch process. Equilibrium time was shorter due to thinner barrier for diffusion of ions, as it is a continuous motion. Also higher swelling efficiency in the batch process result in more surface area for ion exchange. Hence the batch process is suitable for smaller particles. The swelling and hydrating properties of Indiaon 204 affect the rate of ion exchange, which in turn affects the percentage drug loading. In unswollen resin matrix, the exchangeable groups are latent and coiled toward the backbone, hence less drug-loading efficiency. The optimized percentage drug loading (wt/wt) was found to be 100.40±0.16 for Indiaon 204 with swelling time 30 minute.

The equilibrium ion exchange in solution occurs stoichiometrically and hence is affected by stirring time**.** The optimized percentage drug loading (wt/wt) was found to be 100.22±.14 for Indiaon 204 with stirring time 60 minutes.

Drug complexation involved exchange of ionisable drug and metal ion in resin. Such a mode of complexation between drug and resin affected by pH of media. Complexation was enhanced and was found maximum at pH 8 (Table no.14).

Efficient drug loading on indiaon 204 in the experimental range 25-80◦C (Table No. 15 and 16) Increased temperature during complexation increases the ionization of drug and resin. The effect is more pronounced for poorly water soluble and unionized drugs. Higher temperature tends to increase the diffusion rate of ions by decreasing the thickness of exhaustive exchange zone. As Risperidone is water soluble ionizable drug, temperature does not show any significant effect on drug absorption and also cation exchange resins are significantly affected by temperature changes.

Table No. 13 Effect of drug resin ratio on DRC formation using Indion-204

Resins	Ratio	% drug bound to resins
Indion-204	1:2	17.7
	1:2	19.8
	1:2	21
	1:2	11.1
	1:2	25.2
	1:2	13.5
	1:2.5	9.6

Table No. 14 Effect of pH on DRC formation usuing Indion 204

Resins	pH	Ratio	%drug bound to resins
Indion 204	4	1:2	17.7
	5	1:2	19.8
	6	1:2	21
	7	1:2	11.1
	8	1:2	25.2
	8	1:2.5	13.5
	9	1:2	9.6

Table No. 15 Effect of room temperature on DRC formation using indion 204

Resins	Time (hr)	% drug bound to resins
Indion 204 (Room temp) pH-8 Ratio-1:2	0.5	17.12
	1	24.12
	1.50	30.11
	2	35.23
	2.50	41.56
	3	48.21
	3.50	54.26
	4	60.23
	4.50	67.22
	5	72.26
	5.50	80.23
	6	87.33

Table No. 16 Effect of temperature at 40^0C on DRC formation using Indion 204

Resins	Time(hr)	% drug bound to resins
Indion 204 At 40^{0c} pH-9 Ratio-1:1	0.5	14.11
	1	23.11
	1.50	32.44
	2	40.43
	2.50	47.23
	3	56.80
	3.50	62.22
	4	69.21
	4.50	77.13
	5	85.66
	5.50	90.21
	6	95.45

Table No. 17 Evalution of taste resinate of Risperidone and Indion 204

Volunteers	Bitterness level after					
	10 sec.	1 min.	2 min.	5 min.	10 min.	15min.
1	X	0	0	0	0	0
2	X	X	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	X	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0

3.2C*Taste evaluation by panel method:*
Taste evaluation revealed that Indiaon-204 masks the bitter taste of the drug completely (Table No. 17).

3.2D *Characterization of Risperidone Indaion-204 complex*
The interaction between the drug and the resin often leads to identifiable change in the IR profile of drug dispersion. So Risperidone: indiaon 204 were subjected to IR analysis in order to evaluate possible interaction between drug and Indiaon 204. The FTIR spectra of Risperidone and Risperidone-Indiaon 204 complex were shown in figure no.3 and 8 respectively.

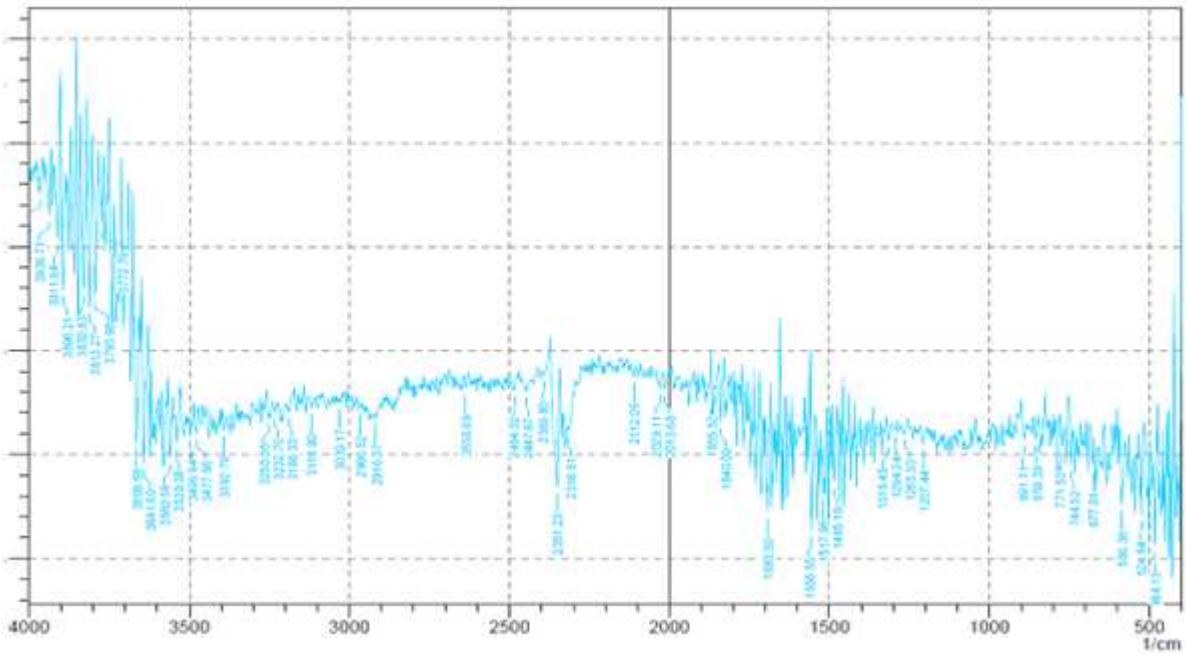

Figure No.8 FTIR spectra of Risperidone- Indiaon 204 resin

3.2E *Drug content*
The drug content of resin was found to be 94.34 ± 0.054 %.

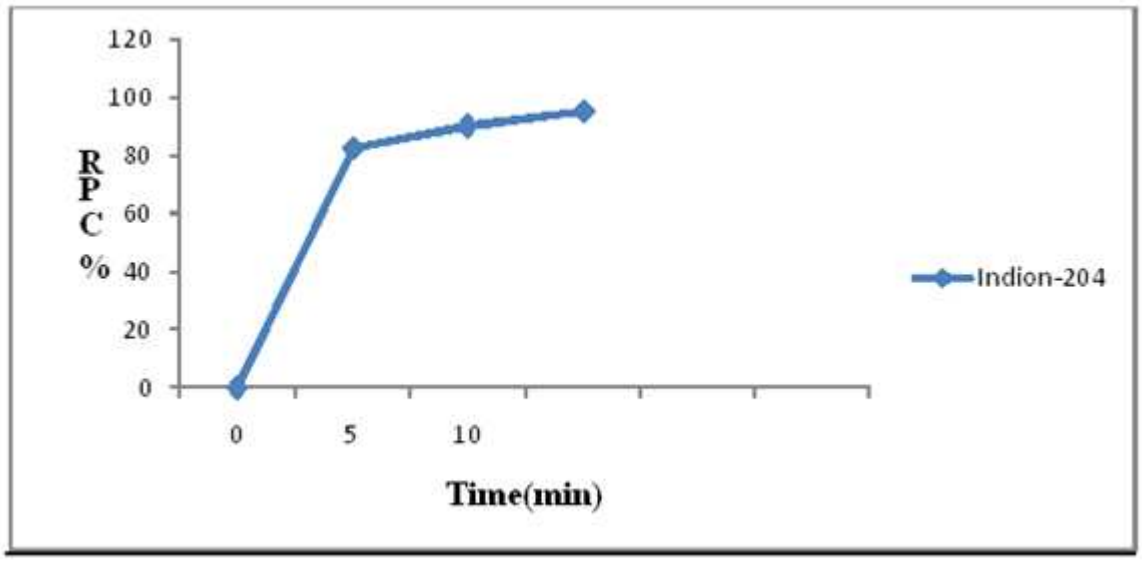

Figure No.9 In-Vitro drug release study from Risperidone- Indiaon 204 resin resinate

3.2F *In-Vitro drug release study from resinate*
Samples were withdrawn, analyzed at 279 nm and percentage cumulative drug release was determined. The presence of exchangeable ions of ionisable electrolytes in the salivary fluid may be responsible for this release. So

the drug resin complex is stable in salivary pH for a period of administration. The amount released is insufficient to impart bitter taste while the formulation passes through the mouth to further parts of the gastrointestinal (GI) tract. *In vitro* drug release study was also performed in simulated gastric fluids (SGF) pH 1.2 (Fig. No.9). The drug release from Indiaon 204 was found to be more than 85 % within 10 minutes in simulated gastric fluids (SGF).

3.2G *Evaluation of tablet blend and tablets*

The various evaluation test of tablet were done and their results were in the standard limits prescribed in officially in Indian Pharmacopoeia (Tablet No.18).

Table No. 18 Evalution of taste resinate of Risperidone and Indion 204

Volunteers	Bitterness level after					
	10 sec.	1 min.	2 min.	5 min.	10 min.	15min.
1	X	0	0	0	0	0
2	X	X	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	X	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0

3.2H *Dissolution study of Tablet*

Dissolution study of tablets revealed that more than 85 % of the drug was released within ten minutes (Table No.19). Drug release patter was shown in figure no. 10.

Table No. 19: Dissolution study of optimized tablet formulation

S .No	Time (min)%	Cumulative release
1.	5	80.12
2.	10	100.16

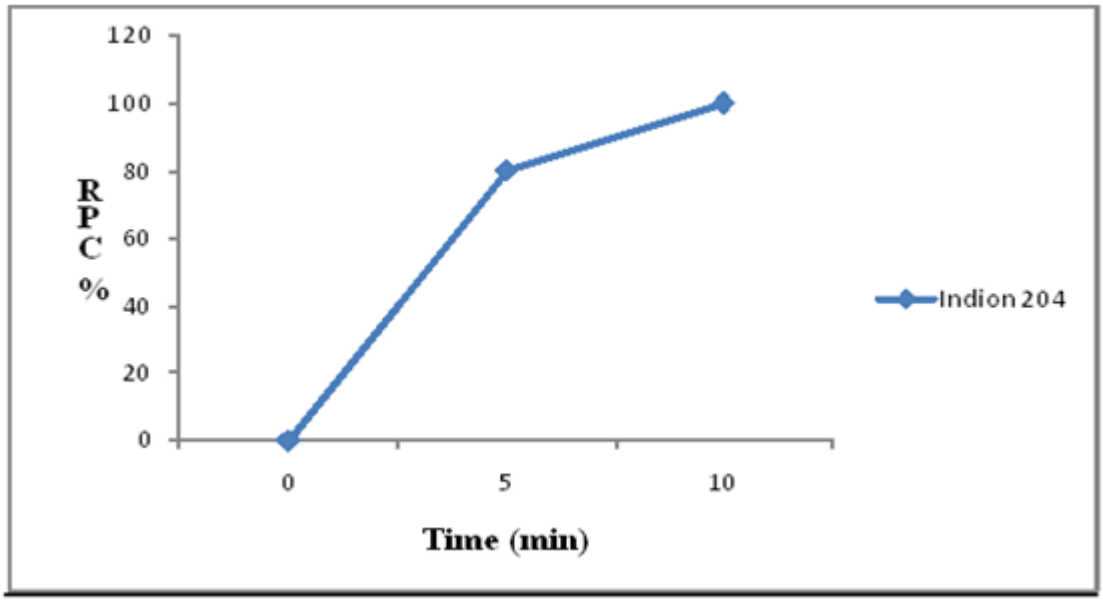

Figure No.10 In-Vitro drug release of taste masked Orodispersible tablet by Indiaon 204 resin

3.2I *Comparison of optimized formulation with conventional marketed tablet*

The In-Vitro drug release study of optimized formulation and marketed tablet was done and compare the drug release. Result was illustrated in table no. 20. comparative drug release pattern of conventional Risperidone tablet and optimized tablet represent in figure no. 11. Optimized tablet had more drug released compare to conventional marketed tablet.

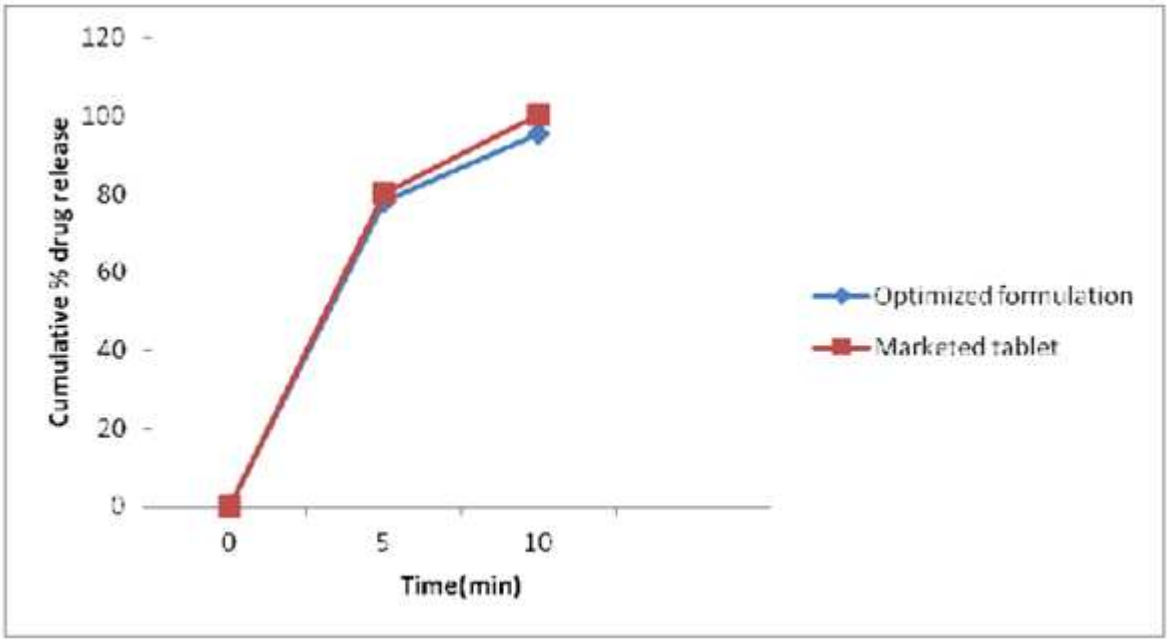

Figure No.11 Comparison of optimized formulation of taste masked Orodispersible tablet by Indiaon 204 with conventional marketed tablet of Risperidone

Table No. 20: Comparison of optimized with conventional marketed tablet

Sr.no	Time(min)	Cumulative % release from conventional marketed tablet	Cumulative % release from optimized batch
1.	5	78.12 ± 0.23	81.39 ± 0.15
2.	10	96.33 ± 0.18	100.04± 0.26

CONCLUSION

Use of cation exchange resin offers good method for preparing taste-masked substrate of Risperidone. While studying the effect of concentration of resin on drug loading, maximum drug loading were found in ratio 1:1 for drug: Kyron T-104 and 1:2 for drug- Indiaon 204 complex. Taste evaluation revealed that not only Kyron T-104 but also Indion 204 masks the bitter taste of the drug Resperidone completely. Results obtained in this work show that both drug-resin complex effectively masked bitter taste of Risperidone. Result of effect of concentration of resins (on drug loading), pH, temperature and time on maximum drug loading evaluated and optimization were done. Dissolution study of tablets revealed that more than 85 % of the drug was released within ten minutes in both tablets masked by Kyron T-104 and Indiaon 204. Thus, both complexation of Risperidone with Kyron T-104 and Risperidone- Indiaon 204 increases acceptability and palatability of formulated rapid disintegrating tablets. Comparison of optimized formulation with conventional marketed tablet was done and more drug release in less time from optimized tablet compare to marketed conventional tablet. Superdisintigrant play key role in immediate drug release. The results of this study can also be extrapolated to other intensely bitter drug by suitable selection of resin. So in this study successfully taste masking of Risperidone by two ion exchange resin Kyron T-104 and Indiaon 204 independently.

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