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Comparison of lyophilization and compression technique of Risperidone oral disintegrating tablets

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Abstract

The aim of the present investigation was to develop oral disintegrating tablets (ODT) of insoluble and bitter drug like risperidone using taste masking agents, taste enhancers and flavors. ODT of risperidone were prepared using different process like lyophlization and compressed tablets technique. Amberlite was used a taste masking agent, Mannitol was used as a diluent and peppermint was used as a flavoring agent. The formulations were prepared and evaluated for weight variation, hardness, friability, dispersion time, disintegrating time, taste evaluation study and in vitro dissolution. All the formulation showed low weight variation with different disintegration time and rapid in vitro dissolution. The results revealed that the tablets containing taste masking had a good palatability for the patients. The drug content of all the formulations was within the acceptable limits of the United States Pharmacopoeia XXVII. The optimized formulation showed good taste masking, less disintegration time (<30seconds) and release profile with maximum drug being released at all time intervals. It was concluded that risperidone ODT's with improved taste masking and dissolution could be prepared by both lyophilization and compressed tablet technique with suitable taste masking agent like amberlite. This work helped in understanding the effect of formulation processing variables of lyophilization and compressed tablet technique, especially the disintegrating and taste masking agents on the drug taste masking, disintegration time and release profile. The present study demonstrated potentials for rapid disintegration in oral cavity with out water, improved taste masking and patient compliance.

Keywords: Oral disintegrating tablets (ODTs), Lyophilization process, compressed tablet technique, Risperidone and Amberlite IRP 64 Resin.

INTRODUCTION

Oral disintegrating tablets (ODT) are solid unit dosage forms which disintegrate or dissolve rapidly in the mouth without chewing and water. ODTs are also called as fast melt, fast disintegrating tablets. In April 2007, the FDA issued draft guidance, Guidance for Industry: Orally Disintegrating Tablets. It considers ODTs to be solid oral preparations that disintegrate rapidly in the oral cavity with an *in vivo* disintegration time of approximately 30 seconds or less, when based upon the USP disintegration test method or alternative [1].

ODT formulation containing ingredients which disintegrates rapidly, usually within matter of seconds, when placed upon the tongue, but which releases a drug (or drugs) at a time other than promptly after administration [2, 3]. The European Pharmacopeia however defines a similar term, orodispersible tablets, or tablets intended to be placed in the mouth where it disperses rapidly before swallowing [4]. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down in to the stomach. In such cases, bioavailability of drug is significantly grater than those observed from conventional tablet dosage form. ODTs are appreciated by a significant segment of population, particularly children and elderly, which have difficulty in swallowing conventional tablets or capsules [5-7].

The fundamental principle used in the development of the ODTs is to maximize its pore structure. Researchers have evaluated spray dried materials and soluble materials for development of such tablets. ODTs can be prepared by various techniques, mainly direct compression, lyophilization and moulding. The simplicity and cost effectiveness of the direct compression process have positioned this techniques as an attractive alternate to traditional granulation technologies. Usually super disintegrants are added to a drug formulation to facilitate the disintegration of tablet into smaller particles that can dissolve more rapidly than in absence of disintegrants [8].

The tablets prepared by lyophilization are very porous in nature and disintegrate or dissolve rapidly when come in contact with saliva. In this process, water is sublimated from the product after freezing. First of all, the material is frozen to bring it below its eutectic point. Then primary drying is carried out to reduce the moisture to around 4% w/w of dry product. Finally, secondary drying is done to reduce the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. A tablet that rapidly disintegrates in aqueous solution includes a partially collapsed matrix network that has been vacuum dried above the collapsed temperature of the matrix. The matrix is partially dried below the equilibrium freezing point of the matrix. Vacuum drying the tablet above its collapse temperature, instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva. However the use of freeze-drying is limited due to high cost of equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs [9-15].

Risperidone is a psychotropic agent belonging to the chemical class of benzisoxazole derivatives. The chemical designation is 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one. The absolute oral bioavailability

of risperidone is 70% (CV=25%). The relative oral bioavailability of risperidone from a tablet is 94% (CV=10%) when compared to a solution [16].

The objective of the present study was to develop orally disintegrating tablets of of risperidone with lyophilzation and compressed tablet technique and to investigate the effect of taste masking on the patient compliance and super disintegrating agent on the disintegration and release profile of the drug in the tablets.

MATERIALS AND METHODS

Materials

Risperidone API, Amberlite IRP 64 Resin, Gelatin, Glycine USP, Simethicone, Carbomer, Sodium hydroxide NF, Colloidal Silicon Dioxide NF (Aerosol 200), Mannitol NF (Pearlitol SD200), Microcrystalline cellulose NF (Avicel PH 101), Croscarmellose sodium NF (Ac-Di-Sol) Crospovidone NF (Polyplasdone XL 10), Peppermint Flavor Premium 501500 TP0504, Peppermint oil, Menthol, Acesulfame Potassium NF, Aspartame NF, L-Hydroxy Propyl cellulose Type 21, and Sodium Stearyl Fumarate NF (Pruv) were procured from Orchid Healthcare, Irungattikottai, Chennai. All other chemicals and reagent were of analytical grade.

Methods

1. Formulation of risperidone ODT by lyophilization process

The Oral disintegrating tablets of risperidone were prepared by lyophilization process, amberlite as a taste masking agent, mannitol as diluent, aspartame as a sweetening agent or taste enhancer, sodium hydroxide as a buffering agent, simethicon as an antifoaming agent, carbomer as a suspending agent, gelatin as a film forming or viscosity increasing agent and peppermint flavor as flavor enhancer. The composition of the each batch was shown in Table 1A.

Risperidone and amberlite were weighed and added in purified water with continuous stirring for an hour. Gelatin, glycine, sodium hydroxide, mannitol, peppermint flavor and simethicon were added to the above solution and subjected to stirring for an hour. Finally, carbomer was added to the above solution and stirred for 30 minutes or till the uniform dispersion was obtained. The above dispersion was weighed and distributed in tablet shaped PVDC foil and kept in the lyophilization chamber. The suspension was dried and the dried tablets were collected from the chamber and evaluated the physical and chemical characterization.

2. Formulation of Risperidone ODT by compression technique

The Oral disintegrating tablets of risperidone were prepared using the Croscarmellose sodium (Ac-d-sol) and crospovidone (polyplasdone XL 10) as super disintegrates, microcrystalline cellulose (Avicel PH 101) and mannitol as diluents, amberlite as taste masking agent, aspartame and acesulfame potassium as sweetening agents or taste enhancers, peppermint flavor and menthol as a flavor enhancers, L-Hydroxy Propyl cellulose Type 21 as binder, colloidal silicon dioxide and sodium stearyl fumarate (Pruv) as flow promoter. The composition of the each batch was shown in Table 1.

Initially development was started with dry granulation process since risperidone is a low dose molecule (maximum dose is 4mg). Commonly low strength dosage faces dose content

uniformity problem and to avoid this, wet granulation process was selected. The raw materials were passed through a #40mesh screen prior to mixing. The amberlite and risperidone dispersed in deionised water under stirring for 2hour and L-Hydroxy Propyl cellulose Type 21 was added to above drug solution under stirring for 20min. same suspension was used as a granulating fluid. Microcrystalline cellulose (Avicel PH 101), Croscarmellose sodium Ac-Di-Sol and L-Hydroxy Propyl cellulose Type 21 loaded in rapid mixer granulator and dry blend mixed for 10 min and granulated with above mentioned drug suspension. The wet mass was dried and passed through sieve no. 24. The dried granules were blend with Mannitol SD 200, crospovidone XL 10, peppermint flavor, acesulfame potassium, aspartame, L-Hydroxy Propyl cellulose Type 21, Menthol and Colloidal Silicon Dioxide NF (Aerosol 200) in octagonal blender for sufficient time and finally lubricated with sodium stearyl fumarate (ODTR009 to ODTR016) (Table 1B). The final blend was then compressed into tablets using flat face round 9.0mm tooling on a 16 station tablet machine and tablets were evaluated.

Table 1A: Composition of different batches of oral disintegrating tablets of risperidone for Physical and chemical characterization

Ingredients	001	002	003	004	005	006	007	008
Risperidone	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Amberlite IRP 64 Resin	0.0	2.0	4.0	6.0	8.0	6.0	6.0	6.0
Gelatin	4.0	4.0	4.0	2.0	4.0	4.0	4.0	4.0
Mannitol (fine grade)	59.7	57.7	55.7	55.7	51.7	52.5	54.7	53.7
Glycine	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
Simethicone (30%w/w)	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Aspartame (Fine grade)	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Carbomer	1.2	1.2	1.2	1.2	1.2	2.4	1.2	1.2
Sodium hydroxide	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Peppermint oil	2.0	2.0	2.0	2.0	2.0	2.0	1.0	2.0
Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total	80.0	80.0	80.0	80.0	80.0	80.0	80.0	80.0

Evaluation of formulated tablets

Hardness

The crushing strength of the tablets was measured using an Erweka hardness tester. Twenty tablets from each formulation batch were tested randomly and recorded the average reading.

Weight variation

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±5%

Thickness

The thickness of the tablets was measured using Vernier Caliper (Mitu-tyo). Twenty tablets from each formulation batch were tested and the average reading was recorded.

Table 1B: Composition of different batches of oral disintegrating tablets of risperidone for Physical and chemical characterization

Ingredients	009	010	011	012	013	014	015	016
Risperidone	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Amberlite IRP 64 Resin	2.0	4.0	6.0	6.0	6.0	6.0	6.0	6.0
L HPC Type 21	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Deionised water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
MCC (Avicel PH 101)	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Ac-Di-Sol	6.0	6.0	6.0	3.0	6.0	6.0	6.0	6.0
L HPC Type 21	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Mannitol SD 200	119.1	117.1	115.1	118.1	119.1	117.1	111.1	115.1
Crospovidone XL 10	8.0	8.0	8.0	8.0	4.0	8.0	12.0	8.0
L HPC Type 21	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Aspartame	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Acesulfame Potassium	5.0	5.0	5.0	5.0	5.0	3.0	5.0	5.0
Peppermint Flavour	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Menthol	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Aerosol 200	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Sodium Stearyl Fumarate (Pruv)	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0
Total	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0

Friability

6.5g equivalent weight tablets were weighed and placed in a friabilator (Electrolab ET-2). Pre-weighed tablets were rotated at 25 rpm for 100 rotations. The tablets were then dedusted and re-weighed and the percentage of weight loss was calculated. The percentage friability of the tablets was measured as per the following formula:

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Disintegrating time

In vitro disintegration time was measured by using disintegration tester (Electrolab ED-2L) and tablet dropping in a 1000ml beaker containing 900ml of purified water which maintained at 37±0.5°C.

Dispersion time

In vitro dispersion time was measured by dropping a tablet in a 10 ml measuring cylinder containing 6 ml of buffer solution simulating saliva fluid (pH 6.8)

Wetting time

A piece of tissue paper folded twice was placed in a Petri dish (Internal Diameter = 9cm) containing 9ml of buffer solution simulating saliva pH 6.8. A tablet was placed on the paper and the time taken for complete wetting was noted. Five tablets from each formulation were randomly selected and the average wetting time was noted.

Dissolution

In-vitro dissolution study was performed by using USP Type II Apparatus (Paddle type) at 50rpm. 0.1 N HCl, 500ml was used as dissolution medium which maintained at 37±0.5°C[17]. 10ml dissolution medium was withdrawn at specific time intervals. The amount of drug dissolved was determined by HPLC [Photodiode array detector (Waters 996)] by measuring the sample.

Taste evaluation study

The objective of this study is to conduct and evaluate the Palatability of different formulations of risperidone oral disintegrating tablets. Risperidone ODT reference is risperdal tablets available in market for this product for comparison of the taste evaluation. Total nine formulations were selected for taste evaluation study, six test formulations, one reference formulation, one positive control (Placebo for risperidone) and one is negative control (Placebo for Taste masking agent like amberlite and taste enhancers like aspartame and acesulfame potassium and peppermint flavor). All formulations (formulation code) were randomized. Each randomization order was assigned with sequence code. For this study were selected ten healthy human male volunteers, and were assigned volunteer code.

Table 2A: Lyophilization process - Composition of different batches of oral disintegrating tablets of risperidone for taste evaluation study

Ingredients	ODTR003	ODTR007	ODTR008
Risperidone	2	2	2
Amberlite IRP 64 Resin	4	6	6
Gelatin	4	4	4
Mannitol	173.7	173.7	173.7
Glycine	8	8	8
Simethicone	0.4	0.4	0.4
Aspartame	0.7	0.7	0.7
Carbomer	1.2	1.2	1.2
Sodium hydroxide	2	2	2
Peppermint oil	2	1	2
Purified Water	Qs	Qs	Qs
Total	200	200	200

Table 2B: Compressed tablet process - Composition of different batches of oral disintegrating tablets of risperidone for taste evaluation study

Ingredients	ODTR010	ODTR014	ODTR016
Risperidone	2	2	2
Amberlite IRP 64 Resin	4	6	6
L-Hydroxy Propyl cellulose Type 21	1	1	1
Deionised Water	Qs	Qs	Qs
Microcrystalline cellulose (Avicel PH 101)	40	40	40
Croscarmellose sodium Ac-Di-Sol	6	6	6
L-Hydroxy Propyl cellulose Type 21	2	2	2
Mannitol SD 200	110.2	110.2	110.2
Crospovidone XL 10	8	8	8
L-Hydroxy Propyl cellulose Type 21	4	4	4
Aspartame	0.7	0.7	0.7
Acesulfame Potassium	5	3	5
Peppermint Flavour	2	2	2
Menthol	0.2	0.2	0.2
Colloidal Silicon Dioxide NF (Aerosol 200)	2	2	2
Sodium Stearyl Fumarate NF (Pruv)	6	6	6
Total	200	200	200

All the ten volunteers were evaluated all nine formulations as per the randomization order. Each of the nine formulations were transferred to HDPE bottles and labeled only with formulation code. Palatability evaluation feedback format prepared and submitted to each individual volunteer and were provided with instructions before starting study. One tablet of each formulation was given to volunteer for palatability study evaluation. The time interval between evaluations of each test formulation in the same volunteer was 30 min, at after evaluated each formulation, one half of a bread slice was given to each volunteer followed by half glass of water and coca powder for neutralizing the taste buds. After completion of the study, data was compiled and evaluated the formulations and allotted the rank for all formulation, based on the average value of the each formulation.

RESULTS AND DISSCUSSION

Water insoluble diluents such as microcrystalline cellulose and dicalcium phosphate were omitted from the study as they are expected to cause an unacceptable feeling of grittiness in the mouth, but wet granulation process small quantity of microcrystalline cellulose (20%) was used in the formulations. Among the soluble diluents considered its advantages in terms of easy availability and negative heat of dissolution. Table 3A and 3B shows that all the formulated tablets exhibited low weight variation. The drug content of all the formulations was found to be

between 99.6 – 101.2% which was within the acceptable limits as per USP XXVII. In Lyophilization process, addition of gelatin and carbomer at different concentrations as a film former and viscosity increasing agent had no pronounced effect on disintegration time of the tablets but process (drying time) time were observed significantly different. All batches disintegration time shown less than 20 seconds (ODTR001 & ODTR008). The in vitro dispersion time of the tablets were shown considerably increased in tablets containing carbomer and gelatin, because high viscosity of suspension and less porosity of tablet (Table 2A).

In compressed tablet process, addition of croscarmellose sodium and polyplasdone XL10 at different concentrations as a disintegrating agent had pronounced effect on disintegration time of the tablets. The in vitro dispersion time of the tablets were shown considerably increased in tablets containing less croscarmellose sodium and polyplasdone XL10, because less disintegrating agent (Table 2A). The batches ODTR013, ODTR014 and ODTR015 were prepared using polyplasdone XL 10 at different concentrations to study its effect on disintegration time. The disintegration time depended on the amount of polyplasdone XL 10 present in tablets (2%, 4% and 6%). Batch ODTR014 and ODTR015, containing 4% and 6% polyplasdone XL 10, showed the least and similar disintegration time. The results shown in Table 3A indicate that concentration dependent disintegration was observed in batches prepared using polyplasdone XL 10 as a disintegrating agent is responsible for faster water uptake; hence it facilitates wicking action and bringing about faster disintegration. It is worthwhile to note that as the concentration of polyplasdone XL 10 increased up to 4%.

Tablets with lyophilization process having higher friability (>2%) may break during administration of patients, handling on machines and/or shipping (ODTR001 to ODTR008). The use of a lyophilzation process resulted in increased friability due insufficient hardness and more porosity nature (Table 3A). The disintegration time was found to be more than 20 seconds (USP limits for ODT is NMT 30 seconds) which made us to try compressed tablet approach.

Table 3A. Lyophilization process: Evaluation of physicochemical parameters of oral disintegrating tablets of risperidone

Formulation	Weight variation (mg)	Hardness (Kp)	Friability (%)	Drug content (%)	In vitro dispersion time	Disintegration time (Sec)	Dissolution (%w/w) (15min)
ODTR001	200±1	<1.0	Failed	101±1	6	6	98
ODTR002	200±1	<1.0	Failed	99±1	9	7	96
ODTR003	200±1	<1.0	Failed	100±1	13	9	95
ODTR004	200±1	<1.0	Failed	101±1	21	15	94
ODTR005	200±1	<1.0	Failed	100±1	25	19	89
ODTR006	200±1	<1.0	Failed	101±1	23	18	85
ODTR007	200±1	<1.0	Failed	99±1	13	11	92
ODTR008	200±1	<1.0	Failed	99±1	11	10	93
Reference	57.8	<1.0	Failed	99±1	9	8	94

Tablets with compressed tablet process having lower friability (<0.7%w/w) may not break during administration of patients, handling on machines and/or shipping (ODTR009 to ODTR016). The use of a compressed tablet process resulted in decreased friability due sufficient

hardness (Table 3B). Tablets with compressed tablet process were shown less porosity than lyophilization process. Batch no. ODTR016 were shown faster disintegration and dissolution similar with reference product and lyophilization process tablets.

In the first few attempts (ODTR001 to ODTR008), lyophilization process was performed for drug taste masking and for drug suspension prior to dry into lyophilization chamber. Batches ODTR001 to ODTR008 showed good porous nature, fast disintegrating, good dispersion in water and low mechanical integrity, but the hardness was very low and friability was failed. For Compressed tablet process (ODTR009 to ODT016) tablets were showed good hardness, friability and less disintegration time but less porous nature when compare with lyophilzation process.

Table 3B. Compressed tablet process: Evaluation of physicochemical parameters of oral disintegrating tablets of risperidone

Formulation	Weight variation (mg)	Hardness (Kp)	Friability (%)	Drug content (%)	In vitro dispersion time	Disintegration time (Sec)	Dissolution (%w/w) (15min)
ODTR009	200±2	2.5 – 3.5	0.5±2	101.5	21-25	11-14	95
ODTR010	200±2	2.5 – 3.5	0.5±2	100.3	26-29	14-17	92
ODTR011	200±2	2.5 – 3.5	0.5±2	100.1	31-35	20-23	91
ODTR012	200±2	2.5 – 3.5	0.5±2	99.8	42-46	31-34	89
ODTR013	200±2	2.5 – 3.5	0.5±2	101.1	51-55	36-39	90
ODTR014	200±2	2.5 – 3.5	0.5±2	101.6	23-25	13-16	92
ODTR015	200±2	2.5 – 3.5	0.5±2	99.5	36-41	28-33	87
ODTR016	200±2	2.5 – 3.5	0.5±2	100.8	29-33	17-21	92
Reference	57.8	<1.0	Failed	99±1	9	8	94

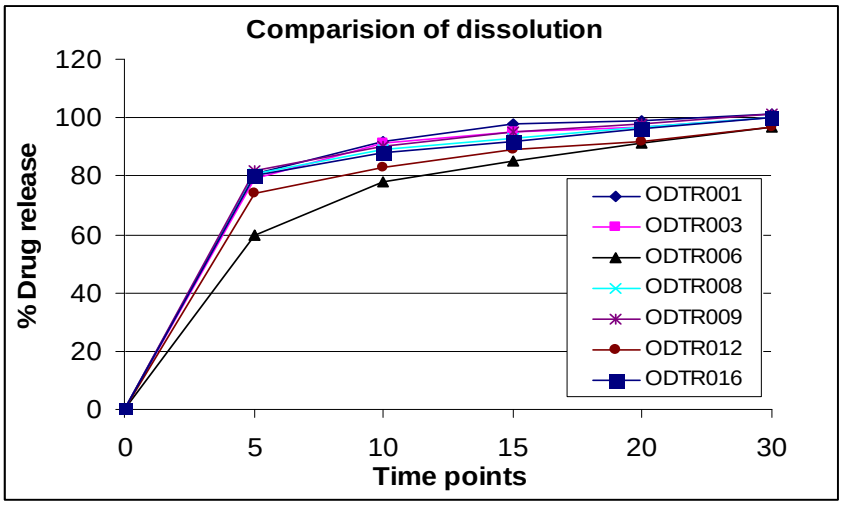

Fig. 1: In vitro drug release of risperidone

In vitro release studies were carried out using USP XXVII tablet dissolution test apparatus paddle method at 37±0.5°C, taking 500ml of 0.1 N HCl as dissolution medium. Speed of rotation of the paddle was set at 50 rpm. 10 ml dissolution sample were withdrawn after 5, 10, 15, 20 and

30 min and analyzed HPLC. The in vitro dissolution profile (Fig. 1) indicated slower and lesser drug release from formulation ODTR006, and remaining batches shown similar drug release.

Formulations ODTR008 and ODTR016 were prepared by lyophilzation process and compressed tablet process with 3.0% amberlite. The final tablets were showed release 92% and 93% drug at the end of 15 min and 100% at the end of 30 min when compared to other batches tablets. The rapid drug dissolution might be due to easy breakdown of particles due to porous structure formation and rapid absorption of drugs into the dissolution medium. Based on below (Fig 2) results, it clear that both lyophilization process and compressed tablet process shown similar drug release. Hence drug release wise no different for both the process.

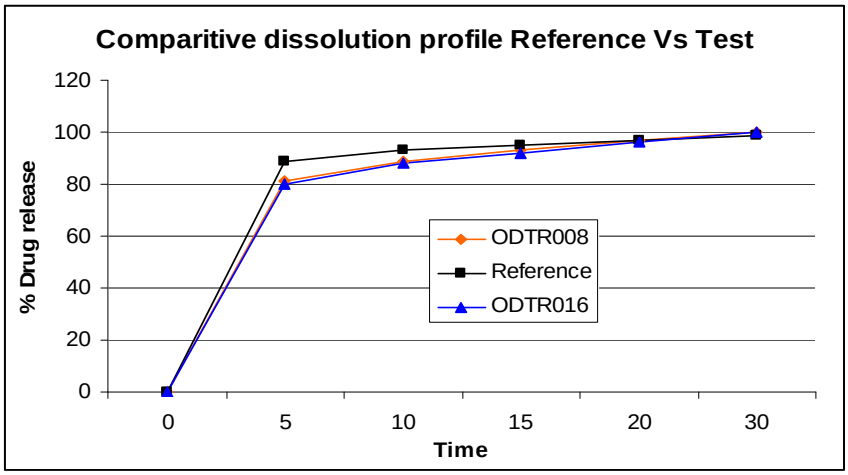

Fig. 2: Dissolution comparison of Reference (Risperdal 2 mg) Vs ODT test product

Reference product was available for this ODT formulation, but reference product was available for risperidone (Brand name is Risperdal 0.5, 1, 2, 3 & 4 mg) as a Lyophilized product form. The ODT in house tablets and Reference tablets were shown similar % drug release in invitro dissolution study. Based on the above data, the ODT formulation of in house product shown similar dissolution profile with reference product (Fig. 2).

Total nine batches were prepared and conducted for taste evaluation study, in that one was positive control (which contain all ingredients except drug), three formulations (ODTR003, ODTR007, ODTR008) were lyophilized test products, three formulations (ODTR010, ODTR014, ODTR016) were compressed method test products and one formula was negative control (which contain all ingredients except taste masking agent and flavor enhancers like amberlite aspartame, acesulfame potassium and peppermint flavor).

The batches ODTR007 and ODTR008 were prepared using liquid peppermint flavor at different concentration to study its effect on patient acceptability in terms of flavor. The flavor concentration depended on the amount Peppermint Flavor present in tablets (0.5%, or 1.0%). The batches ODTR003 and ODTR008 were prepared using amberlite at different concentration to study its effect on patient acceptability in terms of taste masking. The batches ODTR014 and ODTR016 were prepared using powder peppermint flavor at different concentration to study its

effect on patient acceptability in terms of flavor. The flavor concentration depended on the amount peppermint flavor present in tablets (1.5%, or 2.5%). The batches ODTR010 and ODTR016 were prepared using amberlite at different concentration to study its effect on patient acceptability in terms of taste masking.

Formulation ODTR008 (Lyophilized process) and ODTR016 (Compressed tablets process) were prepared with 3.0% amberlite and volunteers acceptability of this formulation were significantly similar with positive control in terms of mouth feel, taste, flavor and disintegration. Formulation ODTR010 and ODTR003 were prepared with 2.0% amberlite and volunteer's acceptability was significantly different with positive control in terms of mouth feel and taste. Formulation ODTR007 was prepared with 0.5% liquid peppermint flavor and acceptability was significantly different with positive control in terms of mouth feel, and flavor. Formulation ODTR014 was prepared with 1.5% powder peppermint flavor and acceptability was significantly different with positive control in terms of mouth feel and flavor. Based on the patient evaluation study, taste masking agent and flavor enhancers were not sufficient in formulation ODTR003, ODTR007, ODTR10 and ODTR014, the quantities were sufficient for formulation ODTR008 and ODTR016 (Table 4 and Fig. 3). Hence for risperidone ODT, formulation ODTR008 (lyophilization process) and ODTR016 (Compression tablet process) were finalized.

The results shown in Table 4, Fig. 3A & 3B indicate that concentration dependent acceptability was observed in batches prepared using peppermint flavor as a flavor enhancing agent and Amberlite as a taste masking agents are responsible for good acceptability by volunteers. It is worthwhile to note that as the concentration of Amberlite increased up to 3%, the acceptability also increased. Lyophilization process showed better acceptability than compared with Compressed tablets process because less DT and contain more porous nature, but significantly not much effect.

Table 4: Overall summary report of taste evolution study

Sr. No.	Formulations	Average points by volunteers	Acceptability	Rank
1	Positive control	99	Very Good	1
2	ODTR003	59	Poor	7
3	ODTR007	70	Acceptable	6
4	ODTR008	87	Poor	2
5	Reference	82	Good	3
6	ODTR010	47	Poor	8
7	ODTR014	74	Acceptable	5
8	ODTR016	81	Good	4
9	Negative control	10	Worst	9

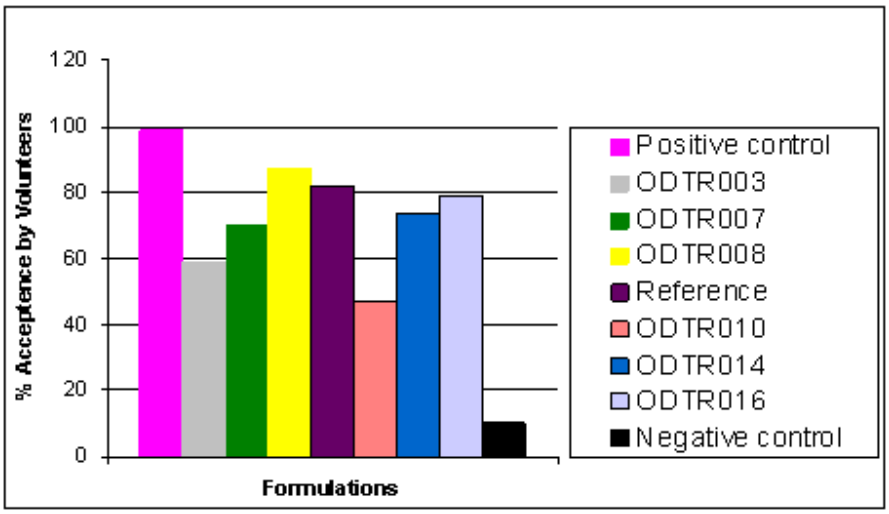

Fig 3: Graphical representation of taste evaluation study report

CONCLUSION

Oral disintegrating tablets (ODT) of risperidone were successfully prepared by using both lyophilization and compressed tablet process. Undoubtedly the availability of various technologies and the manifold advantages of ODT will surely enhance the patient compliance, low dosing, and rapid onset of action, fast disintegration, low side effect, good stability and its popularity in the near future. The prepared tablets disintegrate within few seconds without need of water; thereby enhance the patient compliance and the absorption leading to its increased bioavailability. Based on the above data lyophilization process final tablets and compressed tablet process final tablets were similar with the reference product in terms of drug release, disintegration time and taste masking. From the study, it can be concluded that the compressed tablet process was similar with lyophilization process in terms of taste and disintegration. In terms of hardness, compressed tablet process were showed higher side and friability also passed than lyophilzation process, but lyophilization process showed slightly better disintegration than compressed tablet process. Compressed method process is very cheap, effective, easy to pack the tablets, easy to take the tablet from the pack, easy to transport, more stable and normal storage conditions are sufficient. Tablets manufactured using lyophilzation exhibited low hardness, difficulty in packing, required special storage and transportation condition, and difficult to take tablet from the pack. Compressed tablet process would be an effective, low cost and simple alternative approach compared with the use of more expensive process like lyophilization and adjuvant in the formulation of oral disintegrating tablets.

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