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Refinement of solubility of Resperidone formulating as fast dissolving tablets using molecular dispersion technique

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ABSTRACT

The oral route is most common and preferred route for drug delivery system, it is convenient and easy ingestion. Solid dispersion techniques have been used to enhance the dissolution and oral bioavailability of many poorly soluble drugs .Hence the researchers focused on two areas i) To enhance solubility and dissolution ii) To increase the permeability of poorly water soluble drugs. Solid dispersion is containing at least two different components. Solid dispersion drug dissolves immediately to saturate the gastrointestinal tract (GIT) fluid, and excess drug precipitates as fine colloidal particles or oily globules of submicron to nano size Preparation of the soli dispersion can be done by the hot melt extrusion process and wet extrusion process. Various types of the materials are used in the preparation process they are carries, Emulsifiers, Cellulose Derivatives, Plasticizers and some other equipment's are used to determine the Risperidone's solubility and dissolution profile is expected to significantly improve its bioavailability and reduce its side effects.

Keywords: Risperidone, Emulsifiers, Carries, Hot extrusion, Wet extrusion process.

INTRODCTION

The oral route is most common and preferred route for drug delivery system, it is convenient and easy ingestion. Moreover patient compliance and drug treatment is more effective with oral administration than other routes of administration. Solid dispersion techniques have been used to enhance the dissolution and oral bioavailability of many poorly soluble drugs .Hence the researchers focused on two areas i) to enhance solubility and dissolution ii) to increase the permeability of poorly water soluble drugs. The main use of solid dispersion technique is to improve the dissolution rate and bioavailability of pooly water soluble drugs. About 40% of new chemical molecules are poorly water soluble. [1]

SOLID DISPERSION

Solid dispersion is containing at least two different components one is hydrophilic matrix and another is hydrophobic drug, the matrix may be either amorphous or crystalline, the drug can be dispersed either amorphous or crystalline particles. Solid dispersion system offers variety of formulations by using excipients to enhance dissolution of poorly water soluble drugs for oral administration. [2]

In solid dispersion drug dissolves immediately to saturate the gastrointestinal tract (GIT) fluid, and excess drug precipitates as fine colloidal particles or oily globules of submicron to nano size [3]

PREPARATION OF SOLID DISPERSIONS

Hot-Melt Extrusion

Extrusion is broadly elaborated as a technique to "press out", a process of forming a new material (the extrudate) by forcing it through an orifice or die, such as temperature, mixing, feed-rate and pressure.

The important parameter for this hot melt extrusion (HME) is the process temperature. The optimal process temperature is determined by the (*Tm)* of the drug, the *Tm* of the crystalline carrier, the (*Tg)* of the amorphous carrier and the thermoplastic properties of carrier. Commonly, the process temperature has to be higher than *Tm* or *Tg* of the carrier to soften and decrease the viscosity of the carrier allowing a sufficient flow through the extruder**.** [4]

Advantage of hot melt extrution technique over melting method is the use of low temperature and short residence time which prevents the drug-carrier mixture from thermal degradation. Another advantage is that production is continuous therefore fewer batches are required and efficient scale-up from laboratory to large-scale production.

The Hot-Melt Extrusion Process

The different zones of the barrel are pre-set to specific temperatures before the extrusion process. The feed stock is placed in the hopper and transferred into the heated barrel by the rotating screw. The feed stock must have good flow properties. This requirement is usually met by insuring that the angle of the feed hopper exceeds the angle of repose of the feed materials. When this prerequisite is not met, the feed stock tends to form a solid bridge at the throat of the hopper resulting in erratic flow. In these situations, a force feeding device can be used.

As the feed stock is moved along the length of the barrel, heat is generated by shearing imposed by the rotating screw in addition to conduction from the electrical heating bands. The efficiency of the feeding section is dependent upon the friction coefficient between the feed materials and the surface of the barrel and screw. High friction along the barrel and low friction at the screw interface contribute to efficient mass flow in the feed section. Obviously, the bulk density, particle shape, and compression properties of the raw materials impact the feeding efficiency. [5]

Wet Extrusion versus Dry Extrusion:

Based on the properties of the feed stock, extrusion processes can be classified as wet extrusion or dry extrusion. In wet extrusion, the feed stock is conditioned and softened with the addition of solvents prior to processing. Dry extrusion is a solvent free process. The feed stock is generally in solid form and heat is required to soften or melt the materials. In the dry extrusion process, materials are softened by the heated barrel, the shearing effect of a rotating screw and friction during transit. The extrudate solidifies after exiting the extruder. For obvious reasons, most of the extrusion processes use the dry technique.

Mass Flow during Hot-Melt Extrusion

Polymer melts behave as pseudoplastic fluids under typical processing conditions. The viscosity of a pseudoplastic fluid depends upon the shear rate. various types of the methods are Solvent Evaporation Method, Fusion method, Direct Capsule Filling, Kneading Technique, Co-Precipitation Method, Melting Method, Co-Grinding Method, Gel Entrapment Technique, Spray-Drying Method, Lyophilization Technique, Electro spinning Method, Dropping Method Solution and Melt Agglomeration Process [6]

MATERIALS USED IN HOT-MELT EXTRUSION

For a pharmaceutical material to be processed by hot-melt extrusion, it must be able to deform easily inside the extruder and solidify upon its exit.

Materials must meet the same levels of purity and safety as those prepared by traditional techniques. Most of the raw materials used in hot-melt extruded pharmaceuticals have been used in the production of other solid dosage forms such as tablets, pellets, granules and transdermal.

Hot-melt extruded dosage forms are complex mixtures of active medicaments and excipients. Excipients may be broadly classified as matrix carriers release modifying agents, bulking agents, antioxidants, thermal lubricants and miscellaneous additives. The selection and use of various excipients can impart specific properties to hot-melt extruded pharmaceuticals in a manner similar to those in traditional dosage forms. Oxidative or free radical degradation during the processing or storage the addition of an acid acceptors and light absorbers may be warranted.

Carriers

Carriers used in hot-melt extruded dosage forms have included water insoluble polymers and waxes such as ethyl cellulose or carnauba wax in which the rate of drug release are diffusion controlled. Those are **1 Poly** Ethylene Glycol (PEG) and 2 Polyvinylpyrrolidone (PVP) [7]

Emulsifiers

Emulsifying agents will influence the drug release rate, mainly two possible mechanisms are involved: 1.improvement of wetting properties and solubilization of the drug. 2. Owing to their potential toxicity problems of drugs, such as mucosal surface damage, emulsifying agents are usually in combination with another carrier.

Cellulose Derivatives

They are various types of the cellulose derivatives those areHydroxypropylmethylcellulose (HMPC), Hydroxypropylcellulose, Carboxymethylethylcellulose (CMEC), Hydroxypropylmethylcellulose phthalate (HPMCP), Polyacrylates and polymethacrylates, Urea, Sugar, polyols and their polymers, Organic acids and their derivatives and other carriers

Plasticizers

The use of polymeric carrier's usually low molecular weight compounds capable of softening polymers to make them more flexible. Incorporation of a plasticizer into the formulation in order to improve the processing of conditions during the manufacturing of the extruded dosage form or to improve the physical and mechanical properties of the final product. Recently, surfactants have also been shown to be promising plasticizers in producing solid dispersions by HME in addition to acting as solubilizers. Additionally, several drug substances have been reported to function as plasticizers in hot-melt extruded dosage forms TABLE 1: Plasticizers are Used in Pharmaceutical Dosage Forms

Type	Examples
Citrate esters	triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate
Fatty acid esters	butyl stearate, glycerol monostearate, stearyl alcohol
Sebacate esters	dibutyl sebacate
Phthalate esters	diethyl phthalate, dibutyl phthalate, dioctyl phosphate
Vitamin E TPGS	D-α-tocopheryl polyethylene glycol 1000 succinate
	Polyethylene glycol, propylene glycol
	Others triacetin, mineral oil, castor oil

Characterization of solid dispersions

Several methods have been used to characterize solid dispersions, such as differential scanning calorimetry (DSC), X-ray diffraction (XRD), infrared spectroscopy (IR), hot stage and electron microscopy, and dissolution testing. Among these, thermal and spectral methods (i.e. DSC, XRD and IR) are of special interest. The main purpose of using these methods is to differentiate between crystalline and non-crystalline structure of solid dispersions. [8, 9]

Limitations of solid dispersions

Main problems limiting the commercial application of solid dispersion involve

a. The physical and chemical stability of drugs and vehicles
b. Method of preparation
c. Reproducibility of its physicochemical properties
d. Its formulation into dosage forms
e. The scale-up of manufacturing processes. [10]

Purpose of study

✓ According to the Biopharmaceutical Classification System (BCS), Respiridone belongs to class II drugs, that is, characterized by low solubility and high permeability therefore, the enhancement of its solubility and dissolution profile is expected to significantly improve its bioavailability and reduce its side effects.

Materials

Materials used in the work

S.No	Materials	Supplied by
1	Respiridone	SURA Labs
2	PEG 4000	Nihar traders pvt Ltd
3	PEG 6000	Nihar traders pvt Ltd
4	PolyplasdoneXL	Nihar traders pvt Ltd
5	Magnesium stearate	Himedia Laboratories
6	Mannitol	Nice chemicals Ltd
7	SSG	Nihar traders pvt Ltd
7	Microcrystalline Cellulose	Nihar traders pvt Ltd
8	Potassium dihydrogenortho phosphate	Finar chemicals Ltd
9	Sodium h ydroxide	Himedia Laboratories

Equipments

List equipment used in the work

S.NO	Equipments	Company
1	Ten station rotary tablet punching machine	Lab press
2	Electronic balance	Sartorious
3	Digital vernier calipers	Remi equipments Ltd
4	Rotary shaker	Remi equipments Ltd
5	UV/Visible-spectrophotometer	Lab india
6	Dissolution tester (USP)	Lab india
7	Franz diffusion cell	Borosil Glass Works Ltd
8	Modified 2- arm balance	Remi equipments Ltd
9	Digital pH meter	Elico
10	FT-IR spectrophotometer	Perkin elmer
11	Magnetic stirrer	Remi equipments Ltd
12	Roche Friabilator	Lab india

DRUG PROFILE

Resperidone

Proprietary Name: Risperdal, Risperdal Consta, Risperdal M-Tab.

Category: Antipsychotic, Dopamine antagonist, Serotonin antagonist

Solubility: practically insoluble in water, freely soluble in methylene chloride, and soluble in methanol and 0.1 N HCl.

Melting point: 170 ^{0}c

Absorption: Well absorbed. 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.

Half life: 20 hours (Oral), 2.9-6 days (IM).

Protein binding: ~88% bound.

Elimination: Urinary (70% [adults], 4.3% [children], 7.4% [adolescents]), faecal (14%).

Mechanism of action

Blockade of dopaminergic D2 receptors in the limbic system alleviates positive symptoms of schizophrenia such as hallucinations, delusions, and erratic behavior and speech. Blockade of serotonergic 5-HT_2 receptors in the mesocortical tract, causes an excess of dopamine and an increase in dopamine transmission, resulting in an increase in dopamine transmission and an elimination of core negative symptoms. Dopamine receptors in the nigrostriatal pathway are not affected by risperidone and extrapyramidal effects are avoided. Like other 5-HT_2 antagonists, risperidone also binds at alpha (1)-adrenergic receptors and, to a lesser extent, at histamine H1 and alpha(2)-adrenergic receptors.

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6	Dissolution tester (USP)	Lab india
7	Franz diffusion cell	Borosil Glass Works Ltd
8	Modified 2- arm balance	Remi equipments Ltd
9	Digital pH meter	Elico
10	FT-IR spectrophotometer	Perkin elmer
11	Magnetic stirrer	Remi equipments Ltd
12	Roche Friabilator	Lab india

METHODOLOGY

Preformulation Studies

Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

Drug-Excipients compatibility studies

Drug Excipients compatibility studies were carried out by mixing the drug with various excipients in different proportions (in 1:1 ratio

were prepared to have maximum likelihood interaction between them) was placed in a vial, and closed with rubber stopper and sealed properly.

Analytical method development for Risperidone

Determination of absorption maxima

The λmax was found to be 239nm. Hence all further investigations were carried out at the same wavelength.

Preparation of standard graph in 0.1 Hcl medium

100 mg of Risperidone was dissolved in methanol 5 ml, volumetric flask make upto 100 ml of 0.1 Hcl , from this primary stock 10 ml was transferred to another volumetric flask made up to 100ml with 0.1 Hcl, from this secondary stock was taken separately and made up to 10 ml with 0.1 Hcl, to produce 10,20,30,40 and 50 µg/ml respectively. The absorbance was measured at 239 nm by using a UV spectophotometer.

Formulation Development

Solid dispersions were prepared by solvent evaporation method. Methanol was used as solvent. Rispiridone dose was taken as 50mg.Water soluble polymers such as PEG 4000 were selected as carriers. Drug and polymer were taken in different ratios 1:1,1:2,1:3,1:4,1:5 stated in the formulation chart (Table 2 Aand 2.1). The prepared solid dispersions were passed through the sieve no 20 to get uniform sized particles. The solid dipersions were mixed with required quantities of diluent, lubricant and glidant. The blend was evaluated for precompression parameters.(Rahman Z, 2010. Risperidone solid dispersion for orally disintegrating tablet: its formulation design and nondestructive methods of evaluation,Int J Pharm. Nov 15; 400(1-2):49-58.)

The tablets were prepared by using 6 mm flat surfaced punch. The hardness of the tablets was maintained as 4.5 kg/cm^2.

Formulation of fast dissolving tablet by using solid dispersion powder

Procedure

Solid dispersion were prepared by solvent evaporation method**.** methanol is a solvent .Risperidone drug taken by different ratios 1:1,1:2,1:3,1:4,1:5 the polymers about PEG 4000,polyplasdone and methyl crystalline cellulose were weigh individually according to below values by direct compression method.mix all the polymers ,drug and add magnesium stearate , talc then punch by compression machine using 6mm.

Table 2.1

	F1	F2	F3	F4	F5
Rispiridone	10	15	20	25	30
PolyplasdoneXL	24	24	24	24	24
Mg.stearate	1	1	1	1	1
Talc	1	1	1	1	1
MCC	QS	QS	QS	QS	QS
Total wt	80	80	80	80	80

EVALUATION OF TABLETS

Pre compression parameters

Measurement of Micromeritic Properties of Powders

Angle of repose

Table 3: Flow Properties and Corresponding Angle of Repose

Property	Angle of Repose (^{0})
Excellent	25-30
Good	31-35

Fair- aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, Vibrate	46-55
Very Poor	56-65
Very, very Poor	>66

Bulk density

Bulk density = M/V_0 …….. (2)
M = Powder mass
V_0 = apparent unstirred volume

Tapped density's

The tapped density is calculated in g/cm^3 by the formula. [57]
Tapped density=M/V_f ..... (3)
M =weight of sample power taken
V_f =tapped volume

Compressibility Index

The Compressibility Index of the powder blend is determined by Carr's compressibility index to know the flow character of a powder. The formula for Carr's Index is as below:
Carr's Index (%) = [(TD-BD) /TD] x100 …….. (4)

Hausner's ratio

The Hausner's ratio is a number that is correlated to the flow ability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hasner's ratio. It is calculated by the following equation. [58]
H = ρT / ρB …….. (5)
Where ρT = tapped density, ρB = bulk density

Post compression parameters

Thickness

The thicknes of tablets was determined by using Digital micrometer. Ten individual tablets from each batch were used and the results averaged.

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation three batches were calculated. It passes the test for weight variation test if not more than two of the individual tablet weights deviate from the average weight by more than the allowed percentage deviation and none deviate by more than twice the percentage shown. It was calculated on an electronic weighing balance.

Friability

The friability values of the tablets were determined using a Roche-type friabilator. Accurately weighed six tablets were placed in Roche friabilator and rotated at 25 rpm for 4 min. Percentage friability was calculated using the following equation.
Friability = [$w_O - w$] /w_O) × 100
Where; w_O = weight of the tablet at time zero before revolution.
w = weight of the tablet after 100 revolutions.

Assay

The content of drug in five randomly selected tablets of each formulation. The five tablets were grinded in mortar to get powder; this powder was dissolved in 0.1 N HCl by sonication for 30 min and filtered through filter paper. The drug content was analyzed spectrophotometrically at 239 nm using UV sectrophotometer. Each measurement was carried out in triplicate and the average drug content was calculated.

Disintegration test

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 10 minutes and the basket was lift from the fluid, observe whether all of the tablets have disintegrated.

Dissolution test of Rispiridone tablets

Drug releaase from Risperidone tablets was determined by using dissolution test United States Pharmacopoeia (USP) 24 type II (paddle). The parameters used for performing the dissolution were 0.1 N Hcl medium as the dissolution medium of quantity 900ml. The whole study is being carried out at a temperature of 37^0 C and at a speed of 50rpm.

5ml aliquots of dissolution media were withdrawn each time at suitable time intervals (5, 10, 20 mimutes.) and replaced with fresh medium. After withdrawing, samples were filtered and analyzed after appropriate dilution by UV spectrophotometer. The concentration was calculated using standard calibration curve.

RESULTS & DISCUSSION

Determination of λ max

The prepared stock solution was scanned between 200-400 nm to determine the absorption maxima. It was found to be 239 nm.

Calibration curve of Risperidone

The standard curve of Risperidone was obtained and good correlation was obtained with R^2 value 0f 0.999.the medium selected was 0.1 N Hcl. The standard graph values of Risperidone are tabulated as below-

Table5 : Standard Graph values of Risperidone at 239s nm in 0.1 N Hcl

Concentration (µg/ml)	Absorbance
0	0
10	0.198
20	0.396
30	0.601
40	0.804
50	0.998

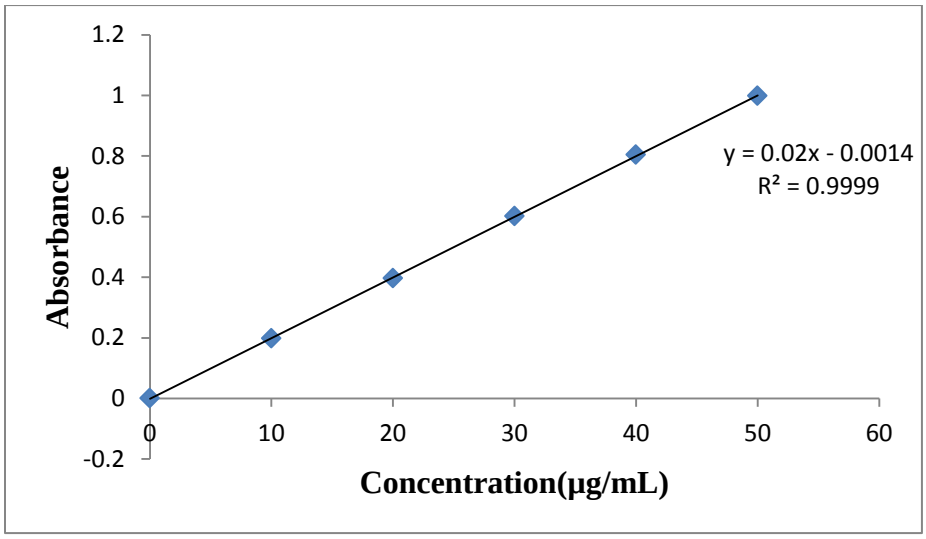

Fig no 7: STANDARD CURVE OF RISPERIDONE

Drug – Excipient Compatibility Studies By FTIR Studies

Risperidone was mixed with various proportions of excipients showed no colour change at the end of two months, proving no drug-excipient interactions.

Fig 8: FTIR SPECTRA OF PURE DRUG

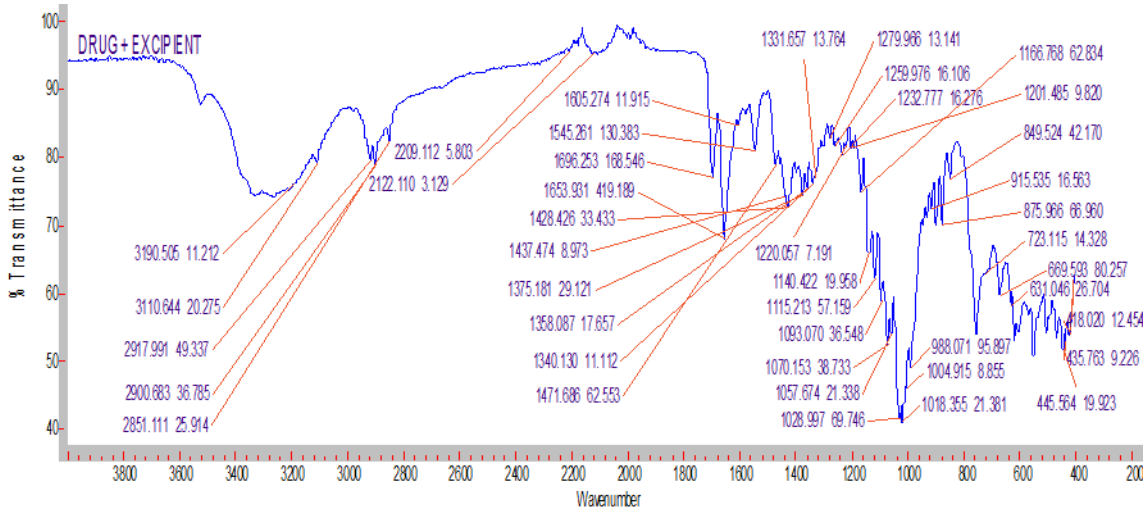

Fig 9: FTIR SPECTRA OF OPTIMISED FORMULA

EVALUATION

Characterization of Pre-compression Blend

The pre-compression blend of Etodalasc soild dispersions were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** Angle of repose was less than 28^0, Carr's index values were less than 11 for the pre compression blend of all the batches indicating good to fair flow ability and compressibility. Hausner's ratio was less than 1.25 for all the batches indicating good flow properties.

Table 6 . Physical properties of pre compression blend

Formulation Code	Angle of repose (Ɵ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's Index (%)	Hausner's ratio
F1	28.10	0.51	0.58	12.0	1.13
F2	25.43	0.54	0.61	11.47	1.12
F3	27.41	0.52	0.59	11.86	1.13
F4	22.40	0.56	0.62	9.67	1.10
F5	24.12	0.52	0.60	13.33	1.15
F6	23.31	0.53	0.62	11.29	1.17

F7	26.11	0.54	0.63	14.28	1.16
F8	28.13	0.52	0.59	11.86	1.11
F9	29.10	0.53	0.60	11.66	1.13
F10	25.11	0.56	0.64	12.52	1.07

All the values represent mean ± Standard deviation (SD), n=3

Evaluation of Tablets

Physical Evaluation of Risperidone solid dipersion tablets

The results of the weight variation, hardness, thickness, friability, and drug content of the tablets are given in Table 7.All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 4.6 to 5 kg/cm^2 and the friability values were less than 0.561% indicating that the tablets were compact and hard. The thickness of the tablets ranged from 4.71-4.91cm. All the formulations satisfied the content of the drug as they contained 98-100% of Risperidone and good uniformity in drug content was observed. Thus all the physical attributes of the prepared tablets were found to be practically within control limits.

Table7 .Physical Evaluation of Risperidone tablets

Formulation code	Weight variation (mg)	Thickness (cm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)
F1	79	3.3	2.5	0.44	96
F2	80	3.4	3.2	0.43	98
F3	78	3.1	2.6	0.41	101
F4	81	3.2	2.8	0.45	99
F5	84	3.4	2.8	0.42	98
F6	82	3.2	3.4	0.47	97
F7	79	3.0	3.2	0.51	100
F8	83	3.2	3.0	0.49	99
F9	79	3.1	2.9	0.50	101
F10	82	3.2	2.7	0.52	99

In vitro release studies

The drug release rate from buccal tablets was studied using the USP type II dissolution test apparatus. The dissolution medium was 900 ml of pH 0.1 Hcl at 50 rpm at a temperature of 37 ± 0.5 °C. Samples of 5 ml were collected at different time intervals up to 1 hrs and analysed after appropriate dilution by using UV Spectrophotometer at 239nm.

Table8 :Invitro dissolution data for formulations F1 – F5 by using PolyplasdoneXL Polymer.

Time(MIN)	% Drug release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
2	25.89	24.67	41.45	66.12	20.45
4	32.12	34.76	53.67	78.98	32.56
6	43.34	42.89	72.45	99.32	44.67
8	56.67	52.12	87.21		59.23
10	62.11	62.45	95.45		71.67
15	69.12	70.34	98.12		80.67
20	72.23	86.13			88.23

25	88.45	97.34	97.45
30	99.34		

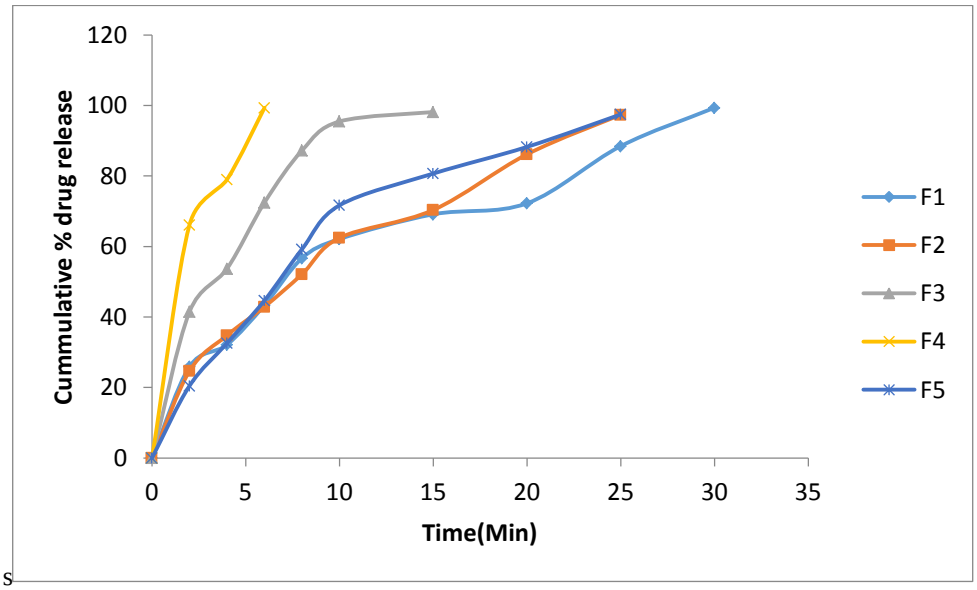

Fig10: Invitro dissolution data for formulations F1 – F5 by using PolyplasdoneXLs Polymer

Table9: Invitro dissolution data for formulations F6– F10 by using SSG Polymer.

Time(MIN)	% Drug release				
	F6	F7	F8	F9	F10
0	0	0	0	0	0
2	21.86	28.18	19.21	37.51	44.67
4	39.01	31.86	31.60	50.90	67.34
6	46.16	46.06	46.43	65.55	75.89
8	58.22	51.44	54.83	73.80	87.54
10	66.99	69.62	61.32	80.29	97.09
15	78.81	79.77	77.95	91.98	
20	83.55	85.59	80.90	97.58	
25	92.12	99.23	89.45		
30	98.56		91.34		

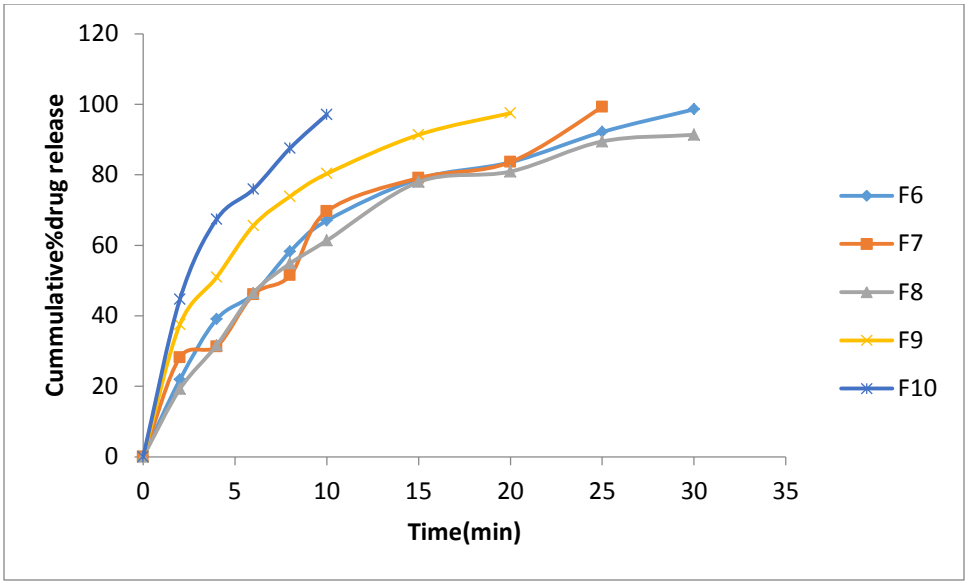

Fig11: Invitro dissolution data for formulations F6– F10 by using SSG

Table10: Invitro dissolution data for formulations F4 by using PEG 4000.

Time(MIN)	% Drug release
	F4
0	0
2	
4	
6	
8	
10	
15	
20	
25	
30	

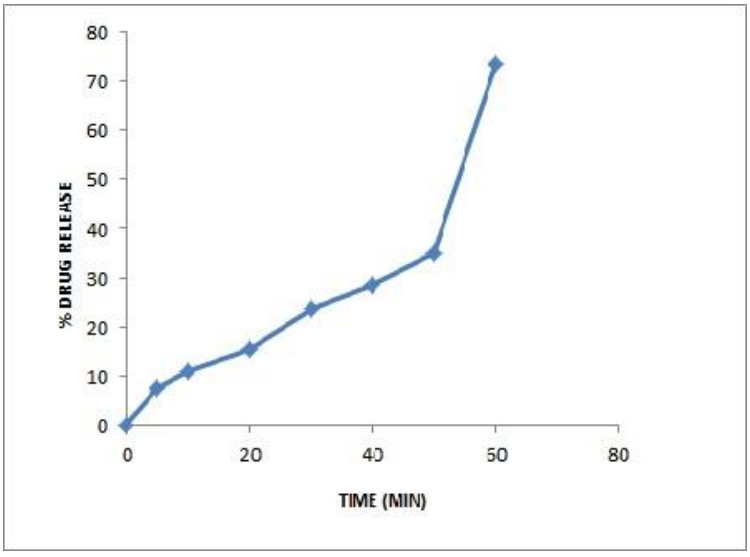

Fig12: Invitro dissolution data for formulations F9 by using PEG 4000 & 6000 Polymer.

Among all the formulations F1 formulation containing, Drug and Peg 4000 in the ratio of 1:4 showed good result that is 99.32 % in 6 minutes. As the concentration of polymer increases the drug release was decreased. While the formulations containing Polyplasdone XL showed less release. Hence from the dissolution data it was evident that F4 formulation is the better formulation. The formulation containing combination of SSG was also not producing desired percentage drug release. The formulation is following zero order release kinetics.

SUMMARY & CONCLUSION

- ✓ Risperidone belongs to class II drugs, that is, characterized by low solubility and high permeability therefore, the enhancement of its solubility and dissolution profile is expected to significantly improve its bioavailability and reduce its side effects.
- ✓ Risperidone was mixed with various proportions of excipients showed no colour change at the end of two months, proving no drug-excipient interactions.
- ✓ The pre-compression blend of Risperidone solid dispersions were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** The precompression blend of all the batches indicating good to fair flowability and compressibility.
- ✓ Solid dispersions were prepared with various concentrations of carriers, the prepared solid dispersions were compressed into tablets by using rotary tablet punching machine, and 6 mm punch, with the hardness of 4.5kg /cm^2.
- ✓ The formulated tablets were evaluated for various quality control parameters. The tablets were passed all the tests.
- ✓ Among all the formulations F4 formulation containing, Drug and Peg 4000 in the ratio of 1:4 showed good result that is 99.32 % in 6 minutes. As the concentration of polymer increases the drug release was decreased. While the formulations containing PEG 4000 showed less release. Hence from the dissolution data it was evident that F4 formulation is the better formulation.
- ✓ By conducting further studies like In vivo studies, preclinical and clinical studies we can commercialize the product.

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