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Research

Formulation And Evaluation Of Paliperidone Sustained Release Tablets

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Abstract

In the present work, an attempt has been made to develop Sustained release tablets of Paliperidone by selecting different types of Sodium alginate, Chitosan and HPMC K 15 M as retarding polymers. All the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F5 formulation showed maximum % drug release i.e., 99.68 % in 12 hours. hence it is considered as optimized formulation F5 which contains Chitosan (12 mg). Optimized formulation F5 was followed Zero order release mechanism.

Keywords: Paliperidone, Sodium alginate, Chitosan, HPMC K 15 M and Sustained release tablets.

INTRODUCTION

Administration of drugs, which is due in part to theease of administration and to the fact thatgastrointestinal physiology offers more flexibilityin dosage form design than most other routes.The terms Sustained release, prolonged release,modified release, extended release or depotformulations are used to identify drug deliverysystems that are designed to achieve or extendtherapeutic effect by continuously releasing medication over an extended period of time afteradministration of a single dose.The advantages of administering a singledose of a drug that is released over an extendedperiod of time, instead of numerous doses, havebeen obvious to the Pharmaceutical industry forsome time. The desire to maintain a near constantor uniform blood level of a drug often translatesinto better patient compliance, as well as enhancedclinical efficacy of the drug for its intended use. Because of increased complication and expenseinvolved in marketing of new drug entities, hasfocused greater attention on development ofsustained or controlled release drug deliverysystems . Matrix system is widely used for thepurpose of sustained release. It is the releasesystem which prolongs and controls the release ofthe drug that is dissolved or dispersed. In fact, amatrix is defined as a well-mixed composite of oneor more drugs with gelling agent i.e. hydrophilic polymers. The goal of an extended releasedosage form is to maintain therapeutic drug level inplasma for extended period of time.[1]

Now a day's conventional dosage forms of drugs arerapidly being replaced by the new and the novel drugdelivery systems. Amongst, these the controlledrelease/sustained release dosage forms have becomeextremely popular in modern therapeutics. Matrix system isthe release system which prolongs and controls the release ofthe drug, which is dissolved or dispersed. A matrix is definedas a well-mixed composite of one or more drugs with gellingagent i.e. hydrophilic polymers. Introduction of matrix tabletas sustained release (SR) has given a new breakthrough fornovel drug delivery system in the field of Pharmaceutical technology. Sustained release constitutes any dosage formthat provides medication over an extended time or denotesthat the system is able to provide some actual

therapeuticcontrol whether this is of a temporal nature, spatial nature orboth. Sustained release system generally do not attain zeroorder type release and usually try to mimic zero orderrelease by providing drug in a slow first order. Repeataction tablet are an alternative method of sustained releasein which multiple doses of drug are an alternative method ofsustained release, in which, multiple doses are containedwithin a dosage form and each dose is released at aperiodic interval.[2]

The goal in designing sustained or sustained delivery systems is toreduce the frequency of the dosing or to increase effectiveness of thedrug by localization at the site of action, reducing the dose requiredor providing uniform drug delivery. So, sustained release (SR) dosageform is a dosage form that release one or more drugs continuously in apredetermined pattern for a fixed period of time, either systemically or to a specified target organ. The goal of an SR dosage form is to maintain therapeutic blood or tissue levels of the drug for an extended period. This is usuallyaccomplished by attempting to obtained zero-order release from thedosage form. Zero-order release constitutes drug release from the dosage form that is independent of the amount of drug in the delivery system (i.e., a constant release rate). SR systems generally do not attain this type of release and usually try to mimic zero-order release by providing the drug in a slow first-order fashion (i.e., concentration dependent).[3]

Approaches of oralsustained/controlled release formulations

To achieve the rapid action, Bolourtchian et aldeveloped sublingual tablets of captopril which waseffective and safe method of lowering arterial bloodpressure in patient with hypertensive emergencies. More rapid attainment of plasma concentration andmore rapid onset of pharmacological effect havebeen observed after sublingual administration of captopril than oral route. Various pharmaceutical approaches have been madeto design long acting devices to administer once aday formulation as controlled and sustained releasesystems to deliver the drug. The differentmethodologies applied and their limitations aredescribed as follows.

Matrix tablets

Various methods are available to formulate watersoluble drugs into sustained release dosage forms byretarding the dissolution rate. One of the methodsused to control the drug release and therebyprolonging therapeutic activity is to use ofhydrophilic or lipophilic polymers.

Coated tablets

It is a classical technique to control the drug release. The drug has cross the barriers before it reaches thephysiological fluids. The type and composition ofthe barriers is the release determining step. Barriersare mainly composed of hydrophilic or hydrophobicpolymers and that is due to the compatibility ofthese substances beside their in vivo safety evenwhen used in large amounts.

Floating tablets

These systems were used to prolong the gastricresidence time of drug delivery systems. Theyremain buoyant in the stomach for prolonged periodof time without affecting the gastric emptying rateof other contents. A floating dosage form is usefulfor those drugs that act locally in the proximalgastro intestinal tract (GIT), are unstable in lowerparts of GIT, or are poorly absorbed in the intestine.

Slow release granules and Sustained release oilymatrix

Stulzer et al developed the captopril granules ofcontrolled release with different polymers as ethylcellulose, ethyl/methyl cellulose and immediaterelease with polyvinyl pyrrolidone by fluid bed driertechnique. The dissolution profile of granules coatedwith ethyl cellulose showed a median time releaseof 4hrs whereas for granules coated withethyl/methyl cellulose was 3.5hrs. The blockage ofangiotensin I-induced hypertensive effect lasted 8 hrin granules coated with PVP and of more than 12 hrin the granules coated with ethyl cellulose andethyl/methylcellulose.

Sustained release microparticles

Microparticles are small solid particulate carrierscontaining dispersed drug particles either in solutionor crystalline form. They are made from natural andsynthetic polymers. Dandagi et al worked onmicroparticles of Captopril using bovine serumalbumin as a drug carrier prepared byemulsification-heat stabilization technique. The invitro study of captopril loaded microparticlesshowed release of drug up to 24hrs. The invivoresult showed preferential drug targeting towardsliver, lungs, spleen and kidneys.

Mucoadhesive microcapsules

The adhesive properties of certain types of polymercould be used to increase the residence time oforally administered drugs. A fuller understanding ofthe molecular processes underpinning suchMucoadhesive phenomena will help in the optimaldesign of the delivery systems.[4]

Rational for developing of SRDDS

I. Formulation of SRDDS minimizes dosing frequencyand sustained release provides availability of a drug ataction site throughout the treatment to improve clinicalefficiency of a drug molecule.

II. To reduce cost of treatment by reducing number ofdosage requirement.

III. To minimize toxicity due to overdose which is often inconventional dosage from.

IV. To enhance the activity duration of a drug possessingshort half-life.

Principle of SRDDS

The conventional dosage forms release their active ingredientsinto an absorption pool immediately. This is illustrated in thefollowing simple kinetic scheme. The absorption poolrepresents a solution of the drug at the site of absorption, Kr, Ka and Ke - first order rate-constant for drug release,absorption and overall elimination respectively. Immediate drug release from a conventional dosage form implies that Kr>>>>Ka. For non-immediate release dosage forms, Kr<<<Ka i.e. the release of drug from the dosage form is the rate limiting step. The drug release from the dosage form should follows zero-order kinetics, as shown by the following equation:

Kr° = Rate In = Rate Out = Ke.Cd.Vd----------1

Where,

Kr°: Zero-order rate constant for drug release-Amount/time

Ke: First-order rate constant for overall drug elimination-time

Cd: Desired drug level in the body – Amount/volume

Vd: Volume space in which the drug is distributed in litter

Challenges for SRRDS

Dose dumping

This can greatly increase the concentration of a drug in thebody and there by produce adverse effects or even druginducedtoxicity. Dose dumping means the relatively largequantity of medication in a sustained release formulation isslowly released. If the dose dumping can leads to fatalities incase of potent drug, which have a narrow therapeutic, index e.g.Phenobarbital.

Limited choice of selecting desired dose in the unit

In case of conventional dosage forms, the dose adjustments aremuch simple e.g. tablet can be divided into two portions. Incase of sustained release dosage forms, this can appear to bemuch more complicated. Sustained release property may getlost, if dosage form is fractured.

Poor in-vitro – in-vivo correlation

In sustained release dosage form, the rate of drug release isslowly reduced to achieve drug release possibly over a largeregion of gastrointestinal tract. Hence it is so called as'Absorption window' becomes important and give rise tounsatisfactory drug absorption in-vivo despite excellent in-vitrorelease characteristics.

Patient variation

The time period required for absorption of drug released fromthe dosage form may vary among individuals. The coadministrationof other drugs, presence or absence of food andresidence time in gastrointestinal tract is different amongpatients. This also gives rise to variation in clinical responseamong the patient.[5]

Parameters for drug to be formulated in sustained release dosage form:

Physicochemical parameters for drug selection.

1. Molecular weight/size < 1000 Daltons.
2. Solubility > 0.1 mg/ml for pH 1 to pH 7.8.
3. Apparent partition coefficient High.
4. Absorption mechanism Diffusion.
5. General absorbability from all GI segments.
6. Release should not be influenced by pH and enzymes.

Pharmacokinetic parameters for drug selection

1. Elimination half-life preferably between 2 to 8 hrs
2. Total clearance should not be dose dependent
3. Elimination rate constant required for design
4. Apparent volume of distribution (Vd) The larger Vd and MEC, the larger will be the required dose size
5. Absolute bioavailability should be 75% or more
6. Intrinsic absorption rate must be greater than release rate
7. Therapeutic concentration Css The lower Css and smaller Vd, the loss among of drug required.
8. Toxic concentration Apart the values of MTC and MEC, safer the dosage form. Also suitable for drugs with very short half-life.[6]

The following are the rationale of developing SR

- ✓ To extend the duration of action of the drug
- ✓ To reduce the frequency of dosing
- ✓ To minimize the fluctuations in plasma level
- ✓ Improved drug utilization
- ✓ Less adverse effects

Advantages of sustained release dosage forms

1) The frequency of drug administration is reduced.
2) Patient compliance can be improved.
3) Drug administration can be made more convenient as well.
4) The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
5) Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduced.
6) The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.
7) The total amount of drug administered can be reduced, thus:
   - Maximizing availability with minimum dose;
   - Minimize or eliminate local side effects;
   - Minimize or eliminate systemic side effects;
   - Minimize drug accumulation with chronic dosing.
8) Safety margins of high potency drugs can be increased and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
9) Improve efficiency in treatment.
   - Cure or control condition more promptly
   - Improve control of condition
   - Improve bioavailability of some drugs
   - Make use of special effects; e.g. sustain release aspirin for morning relief of arthritis by dosing before bed-time.
10) Economy.

Disadvantages of sustained release dosage forms

1) Probability of dose dumping.
2) Reduced potential for dose adjustment.
3) Cost of single unit higher than conventional dosage forms.
4) Increase potential for first pass metabolism.
5) Requirement for additional patient education for proper medication.
6) Decreased systemic availability in comparison to immediate release conventional dosage forms.
7) Poor invitro and invivo correlations.[7]

Objectives of oral sustained released dosage form

- ✓ To maintain the concentration of drug at constant level for a desired period of time
- ✓ To reduce the frequency of doses administrated as compared to conventional dosage form
- ✓ It should deliver active entity directly to site of action, minimizing or eliminating side effects.
- ✓ This may necessitate delivery to specific receptors or to localization to cells or to specific areas of the body.
- ✓ The safety margin of potent drugs can be increased.
- ✓ Incidence of both local and systemic adverse side effects can be reduced in sensitive patient.

Challenges to sustained release drug delivery

- ✓ Biocompatibility
- ✓ Cost of formulation, preparation and processing
- ✓ Fate of controlled release system if not biodegradable
- ✓ Fate of polymer additives, e.g., plasticizers, stabilizers, antioxidants, fillers etc.

MATERIALS

Paliperidone-Procured From Wockhardt Pharma, Aurangabad. Provided by SURA LABS, Dilsukhnagar, Hyderabad, Sodium alginate-Merck Specialities Pvt Ltd, Mumbai, India, Chitosan-Research Lab Fine Chem Industries, Mumbai, HPMC K 15 M-Yarrow Chem. Products, Mumbai, India, PVP K 30-Merck Specialities Pvt Ltd, Mumbai, India, Lactose-Shakti Chemicals, Mehsana, India, Magnesium sterate-Signet Chemical Corp., Mumbai, Talc-S. D. Fine Chemicals Ltd., Mumbai, India.

METHODOLOGY

Analytical method development

Determination of Wavelength

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

Determination of Calibration Curve:

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by thequality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel.

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as themass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting.

Tapped density

After carrying out the procedure as given in the measurement of bulk densitythe cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit.

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value.

Table 2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of Tablets

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 2. The tablets were prepared as per the procedure given below and aim is to prolong the release of Paliperidone. Total weight of the tablet was considered as 150mg.

Procedure

1) Paliperidone and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

Table 3: Formulation composition for tablets

INGREDIENTS	FORMULATION CODE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Paliperidone	3	3	3	3	3	3	3	3	3
Sodium alginate	6	12	24	-	-	-	-	-	-
Chitosan	-	-	-	6	12	24	-	-	-
HPMC K 15 M	-	-	-	-	-	-	6	12	24
PVP K 30	8	8	8	8	8	8	8	8	8
Lactose	126	120	108	126	120	108	126	120	108
Magnesium sterate	4	4	4	4	4	4	4	4	4
Talc	3	3	3	3	3	3	3	3	3
Total weight	150	150	150	150	150	150	150	150	150

All the quantities were in mg

RESULTS AND DISCUSSION

The present study was aimed to developing sustained release tablets of Paliperidone using various polymers. All the formulations were evaluated for physicochemical propertiesand *in vitro* drug release studies.

Analytical Method

Graphs of Paliperidone were taken in 0.1N HCL and in pH 6.8 phosphate buffer at 278 nm and 280 nm respectively.

Table 4: Observations for graph ofPaliperidone in 0.1N HCL

Copncentration (µg/ml)	Absorbance
0	0
10	0.139
20	0.251
30	0.356
40	0.478
50	0.596

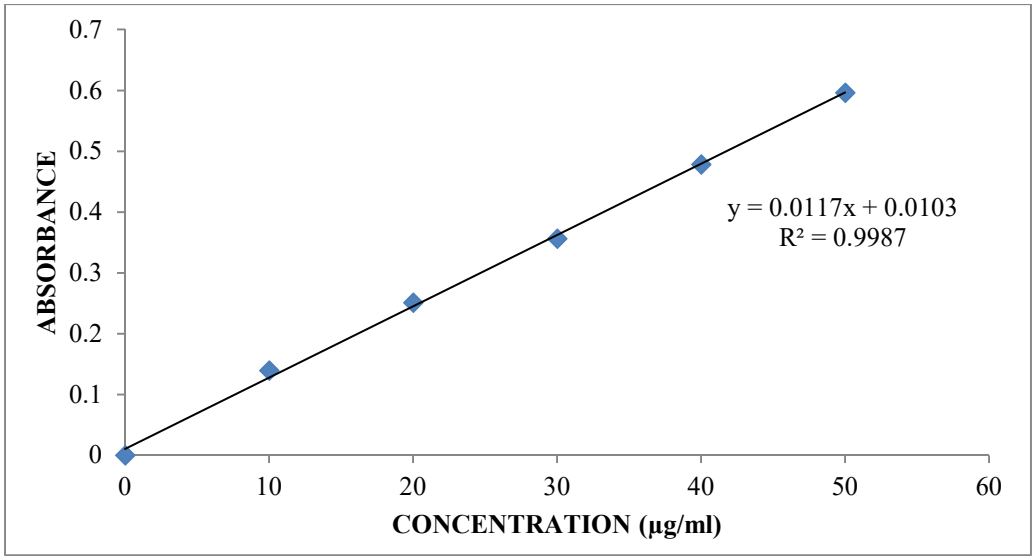

Fig 1: Standard curve of Paliperidone

Table 5: Standard graph values of Paliperidone at 280 nm in pH 6.8 phosphate buffer

Copncentration (µg/ml)	Absorbance
0	0
10	0.139
20	0.254
30	0.381
40	0.492
50	0.611

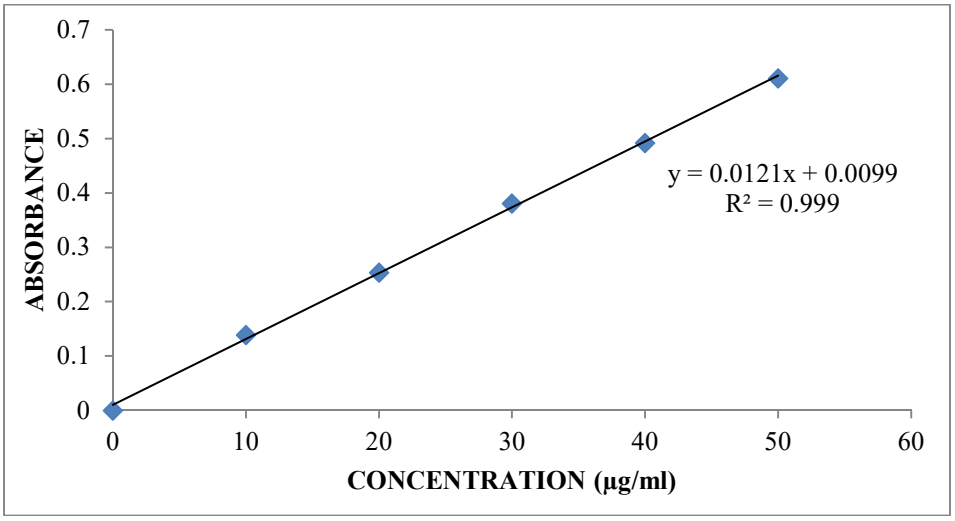

Fig 2: Standard curve of Paliperidone

Preformulation parameters of powder blend

Table 6: Pre-formulation parameters of Core blend

Formulation code	Angle of repose (Ɵ)	Bulk density (gm/cm^3	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	25.11	0.52	0.50	9.32	1.21
F2	24.41	0.53	0.69	9.45	1.12
F3	25.43	0.51	0.51	10.05	1.07
F4	26.42	0.56	0.68	10.14	1.15
F5	27.10	0.52	0.64	10.30	1.02
F6	25.12	0.58	0.63	10.18	1.15
F7	26.13	0.53	0.68	9.96	1.10
F8	26.25	0.56	0.53	10.12	1.06
F9	26.10	0.52	0.62	10.5	1.16

All the values represent n=3

Tablet powder blend was subject edtovarious pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range showing that the powder has good flow properties. The tapped density of all the formulations powders has good flow properties.The compressibility index of all the formulations was found to be below 10.30 which show that the powder has good flow properties.All the formulations has shown the hausner ratio below 1.21 indicating the powder has good flow properties.

Quality Control Parameters For tablets

Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression tablet.

Table 7: *Invitro* quality control parameters for tablets

Formulation codes	Average Weight (mg)	Hardness	Friability (%loss)	Thickness (mm)	Drug content (%)

		(kg/cm2)			
F1	148.30	4.8	0.18	3.14	98.79
F2	146.59	5.6	0.30	3.29	99.45
F3	150.02	5.2	0.42	3.65	98.90
F4	149.75	4.7	0.75	3.21	97.42
F5	148.92	4.9	0.65	3.57	96.86
F6	147.50	5.3	0.82	3.46	99.10
F7	148.12	4.8	0.49	3.21	98.62
F8	149.39	5.0	0.27	3.82	97.81
F9	148.47	5.9	0.36	3.91	99.47

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet. The average weight of the tablet is approximately in range of 146.59to 150.02mg, so the permissible limit is ±7.5% (>150 mg). The results of the test showed that, the tablet weights were within limit.

Hardness test

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 8.47. The results showed that the hardness of the tablets is in range of 4.7 to 5.9 kg/cm^2, which was within IP limits.

Thickness

Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-7. The result showed that thickness of the tablet is raging from 3.14to 3.91 mm.

Friability

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 7. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Drug content

Drug content studies were performed for the prepared formulations. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 96.86 -99.47 %. All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

TIME	% Cumulative Drug Release								
(hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
				In dissolution media 0.1 N HCL					
0	0	0	0	0	0	0	0	0	0
0.5	14.14	13.10	16.14	12.10	10.85	15.52	15.14	12.32	14.55
1	18.25	21.15	20.56	18.64	20.92	19.41	18.12	17.45	17.47
2	22.68	26.22	28.15	28.22	22.61	23.35	20.32	26.62	26.62
				In dissolution media 6.8 Phosphate Buffer					
3	26.98	34.49	32.15	36.78	30.56	28.12	28.16	31.85	31.47
4	31.75	40.12	39.55	40.81	36.85	37.67	33.47	42.71	39.12
5	36.41	47.84	49.31	47.49	57.42	43.51	47.62	49.15	42.85
6	45.82	59.17	54.25	58.93	64.98	57.19	59.45	53.78	48.41
7	52.36	63.50	60.55	61.62	70.34	68.67	67.63	65.32	56.65
8	59.50	69.48	65.63	66.87	79.87	76.45	73.74	70.41	58.12
9	62.27	76.72	73.52	69.17	87.50	80.87	79.85	75.23	62.56
10	71.10	81.65	81.41	74.82	92.33	83.30	85.70	80.14	67.14
11	76.97	84.41	86.82	77.79	96.45	87.71	89.09	86.49	74.81
12	78.34	89.59	92.63	82.73	99.68	90.18	93.45	90.75	78.32

***In Vitro* Drug Release Studies**

From the dissolution data it was evident that the formulations prepared with Sodium alginate gumas polymer were retard the good drug release up to desired time period i.e., 12 hours. Formulations prepared with Chitosan retarded the drug release in the concentration of 12 mg (F5 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.68% in 12 hours with good retardation. Whereas the formulations prepared with HPMC K 15 M retarded the drug

release in the concentration of 6 mg (F7 Formulation) retarded the drug release (93.45%) up to 12 hours(Required Time). Finally Concluded that F5 formulation was considered as optimized formulation.

Table 8: Release Kinetics

Cumulative (%) Release Q	Time (T)	Root (T)	Log(%) Release	Log (T)	Log (%) Remain	Release Rate (Cumulative % Release / T)	1/Cum% Release	Peppas Log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
10.85	0.5	0.707	1.035	-0.301	1.950	21.700	0.0922	-0.965	89.15	4.642	4.467	0.174
20.92	1	1.000	1.321	0.000	1.898	20.920	0.0478	-0.679	79.08	4.642	4.292	0.349
22.61	2	1.414	1.354	0.301	1.889	11.305	0.0442	-0.646	77.39	4.642	4.261	0.380
30.56	3	1.732	1.485	0.477	1.842	10.187	0.0327	-0.515	69.44	4.642	4.110	0.531
36.85	4	2.000	1.566	0.602	1.800	9.213	0.0271	-0.434	63.15	4.642	3.982	0.659
57.42	5	2.236	1.759	0.699	1.629	11.484	0.0174	-0.241	42.58	4.642	3.492	1.150
64.98	6	2.449	1.813	0.778	1.544	10.830	0.0154	-0.187	35.02	4.642	3.272	1.370
70.34	7	2.646	1.847	0.845	1.472	10.049	0.0142	-0.153	29.66	4.642	3.095	1.546
79.87	8	2.828	1.902	0.903	1.304	9.984	0.0125	-0.098	20.13	4.642	2.720	1.921
87.5	9	3.000	1.942	0.954	1.097	9.722	0.0114	-0.058	12.5	4.642	2.321	2.321
92.33	10	3.162	1.965	1.000	0.885	9.233	0.0108	-0.035	7.67	4.642	1.972	2.669
96.45	11	3.317	1.984	1.041	0.550	8.768	0.0104	-0.016	3.55	4.642	1.525	3.116
99.68	12	3.464	1.999	1.079	-0.495	8.307	0.0100	-0.001	0.32	4.642	0.684	3.958

From the above graphs it was evident that the formulation F5 was followed Zero order release mechanism.

Drug – Excipient compatability studies

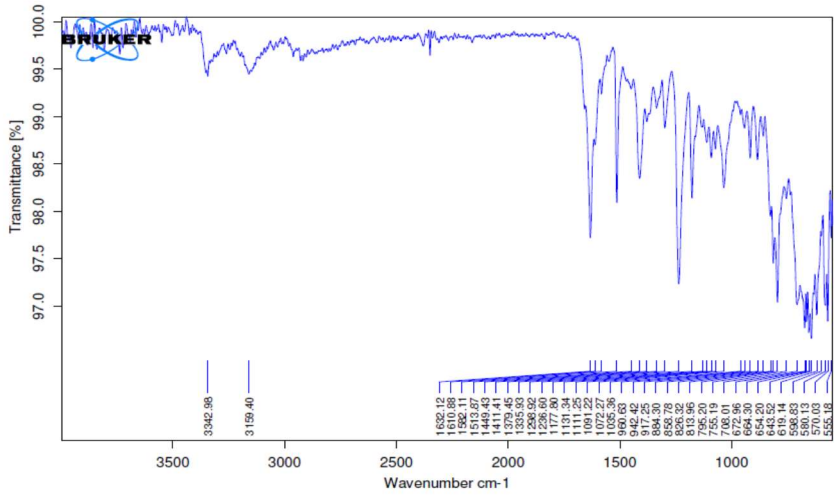

Fig 3: FT-TR Spectrum of Paliperidone pure drug

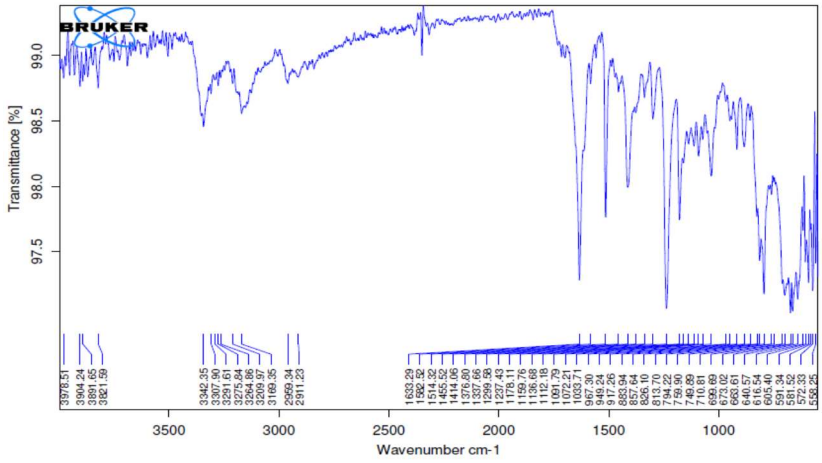

Fig 4: FT-IR Spectrum of Optimised Formulation

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions. Paliperidone are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

CONCLUSION

The present study was carried out to evaluate the natural and synthetic polymers for its matrix forming ability due to formation of thick gel structure, so we concluded that Sodium alginate, Chitosan and HPMC K 15 M formulated tablets were found to be effective in sustaining the drug release up to 12 hrs. Drug release was found to be diffusion coupled with erosion. During this study, it was also found that polymer concentration influences the drug release behaviour. Drug Excipient Compatibility studies revealed that there was no considerable change. FT-IR studies resulted that all peaks corresponding to different functional groups of pure drug were present in the drug-exicipient mixture no interaction between the drug and excipients. Whereas from the dissolution studies it was evident that the formulation (F5) showed better and desired drug release pattern i.e., 99.68 % in 12 hours. It contains the polymer Chitosan as sustained release material. It followed Zero order release kinetics mechanism.

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