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"A Research on: FORMULATION DEVELOPMENT OF PRIDINOL SUSTAINED-RELEASE TABLET FOR PARKINSON DISEASE"

Chavan Vishakha s. [1]
Student of Hon. Shri. Babanrao Pachpute Vichardhara Trust's
Group of Institutions, Faculty of Pharmacy, Kashti
Email: vishakhachavan29275@gmail.com

Abstract: Parkinson's disease (PD) is a progressive neurodegenerative complaint characterized by motor symptoms such as tremors, rigidity, and bradykinesia. Current pharmacological treatments aim to manage symptoms and ameliorate patients' quality of life. Pridinol, a centrally acting anticholinergic agent, has shown efficacy in easing Parkinsonian symptoms, but its short half-life necessitates frequent dosing, potentially reducing patient adherence. Sustained-release (SR) formulations offer a promising strategy to overcome this limitation by maintaining steady blood levels of medication over an extended period. This review explores the expression development of Pridinol sustained-release tablets, pressing the principles of SR medicine delivery systems, selection of applicable polymers and excipients, and colorful expression ways such as matrix systems, hydrophilic and hydrophobic medicine release modifiers, and in vitro evaluation styles. Also, it discusses the pharmacokinetic advantages, remedial eventuality, and challenges associated with developing SR formulations for neurological diseases. The review emphasizes the need for optimized delivery systems to enhance treatment issues and patient compliance in the operation of Parkinson's complaint

Keywords: Novel Drug Delivery System, hypertension, Novel drug delivery carriers, Novel drug delivery pathways

INTRODUCTION: Parkinson's disease affects millions encyclopedically and is primarily managed using dopamine-releasing agents and anticholinergic agents. Pridinol, a piperidine derivative, acts as a muscle relaxant and anticholinergic that helps palliate extrapyramidal symptoms. Although effective, Pridinol has limitations analogous to • Short natural half-life • Rapid systemic concurrence • Frequent dosing conditions, impacting patient adherence. Developing a sustained-release expression could overcome these downsides, offering continuous drug release, reducing dosing frequency, and improving patient compliance. Sustained-release systems are designed to release a drug at a fixed rate, extending its therapeutic effect and minimizing tube attention oscillations

❖ **For Pridinol:**

1. **Improved Bioavailability:** Sustained release helps maintain therapeutic levels for extended periods.
2. **Enhanced Patient Compliance:** Reduces the number of daily doses.
3. **Minimized Side Effects:** Avoids peak-trough fluctuations that can cause adverse effects.

❖ **Merits of Sustained-Release Tablets:**

a. Reduced Dosing frequency or smaller boluses per day ameliorate patient compliance, especially for habitual conditions.

b. Stable Blood medicine situations. Maintains harmonious tube medicine attention, reducing oscillations and side effects.

c. Bettered remedial effectiveness. Provides further controlled and dragged remedial action.

d. Reduced Side goods to avoid peak attention that can beget adverse goods.

e. More Case Compliance o Accessible dosing (e.g., formerly or doubly daily) enhances treatment adherence.

f. Lower overall cost of therapy, although unit cost may be advanced, reduced dosing and bettered issues can lower long-term costs.

❖ **Demerits of Sustained-Release Tablets**

a. Cure the jilting threat of Failure in the release medium can lead to unforeseen medicine release, leading to toxins.

b. Not Suitable for all medicines or medicines with very short half-lives or narrow remedial windows may not be suitable.

c. Delayed onset of action is not ideal when immediate medical action is needed (e.g., for acute pain or extremities).

d. Complex expression is more delicate and precious to design and manufacture compared to immediate-release tablets.

e. Variable release due to GI conditions, of differences in gastrointestinal pH, motility, or food input, can affect medicine release and absorption.

f. Cannot be split or crushed; doing so can compromise the sustained-release medium and increase side effects or reduce effectiveness.

❖ **Rationale for Sustained-Release Formulation:**

A) Selection of Pridinol as a medicine treatment, Sustained Release tablet:-

a. Pridinol is an oral medicine used for treating Characteristic treatment of muscle spasm. It belongs to a chemical class of piperidines.

b. The pharmacokinetic (PK) profile of Pridinol is characterized by rapid absorption and elimination, with a time to maximum plasma concentration (T_{max}) of 0.5 to 1 hour and a terminal half-life of approximately 3 hours

c. The natural half-life of Pridinol is 8.97 and 34.85 hours

d. The drug is rapidly absorbed from the gastrointestinal tract; bioavailability is found to be 42% due to its extensive first-pass effect.

B) Selection of Pridinol as a Sustained-Release tablet:-

a. Biopharmaceutics Classification System (BCS) Class II medicines are characterized by low solubility and high permeability. The poor solubility results in limited medicine immersion, challenging an advanced cure to achieve remedial situations, which may lead to implicit side effects and increased cost of remedy.

b. Despite their high permeability, these drugs often have low oral bioavailability because of their slow and limited release of the drug in gastrointestinal fluid

c. The primary issue is to enhance the solubility and dissolution rate of these drugs to ensure sufficient absorption in the gastrointestinal tract.

d. To overcome these problems, the formulation of sustain sustained-release dosage form can be a better option

e. Reported for use in treating muscle spasm.

f. Report to possess fewer side effects among the same category.

g. Report to have good safety, compatibility with other ingredients of formation.

❖ **DRUG PROFILE :-**

Name-Pridinol

Systematic (IUPAC) name: 1, 1-diphenyl-3-piperidin-1-ylpropan-1-ol

Structure:

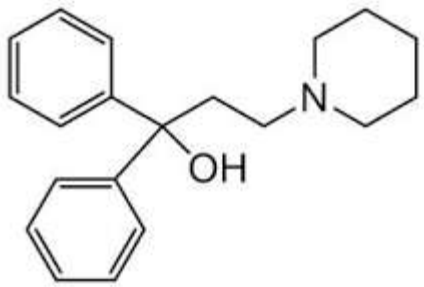


Figure. 1.1: Structure of Pridinol

Molecular formula: $C_{20}H_{25}NO$

Molecular weight: 295.426 g/mol

Description: white or almost white crystalline powder.

Solubility: it is slightly soluble in water and Methanesulfonate, soluble in acetone

Category: Anticholinergic drug.

Storage: Pridinol is protect from light and moisture.

Dose: 200mg, 400mg, 800mg and 1 gm tablet.

Therapeutic use: it is a muscle relaxant that an antiparkinsonian and anticholinergic drug.

Mechanism of Action: Pridinol mesilate is a centrally acting muscle relaxant that is used in the symptomatic treatment of muscle spasm. It is also used as the hydrochloride salt for its antimuscarinic activity in the management of Parkinsonism.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, glaucoma, prostate hypertrophy, syndrome with urinary retention, gastrointestinal obstructions, arrhythmia, first trimester of pregnancy.

Side Effects

The following adverse effects may occur, particularly during concomitant administration with other anticholinergic medicinal products: dry mouth, thirst, transient visual disorder (mydriasis, difficulties with accommodation, photosensitivity, and slight increase in intraocular pressure), redness and dryness of the skin, bradycardia followed by tachycardia, micturition disorders, and constipation and, very rarely, vomiting, dizziness and unsteady gait.

❖ **MATERIAL:-**

Sr. No	Ingredient	Functions
1	Pridinol	Active ingredient
2	Lactose monohydrate	Binder
3	Microcrystalline cellulose	Diluent
4	Hypromellose	Rate Controling Polymer
5	Hydroxy Ethyl Cellulose	Rate Controling Polymer
6	Sodium lauryl sulfate	Solubility enhancer
7	Magnesium stearate	Lubricant
8	Opadry yellow	Colour

❖ PRE FORMULATION STUDIES:-

Pre-formulation testing is the first step in the rational development of dosage forms of the drug substance. It can be defined as an investigation of the physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of pre-formulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms.

1) Organoleptic properties: -

An organoleptic property such as color, odor, taste and appearance of API was observed.

2) Identification of pure drug: -

The identification of the API was carried out by melting point determination and UV spectroscopy.

3) Melting point determination: -

The melting point was determined by taking a small amount of API in a capillary tube closed at one end. The capillary tube was placed in an electrically operated melting point apparatus and the temperature at which the drug melts was recorded. This was performed thrice and average value was calculated.

4) Particle size determination: -

The particle size of API is determined by using a Malvern particle size analyzer.

5) Loss on drying: -

Loss on drying was carried out by using a halogen moisture analyzer at 105˚C.

6) Determination of λ max and calibration curve of API: -

A) Preparation of diluent

Mixed water and methanol in the ratio of 10:90 v/v mixed well.

B) Determination of λmax

Weigh and transfer Pridinol 40 mg API in a 100 ml dry and clean volumetric flask. Add 80 ml diluent, sonicated for 10 min to dissolve, make up to mark with diluent, and mixed well. Further 2 ml was pipetted out from the stock solution, and it was diluted to 50 ml to get the concentration of 16µg/ml. It was scanned for maximum absorbance by a UV-spectrophotometer (Shimadzu, Japan) in range of 200-400 nm using diluent as a blank

C) Preparation of standard calibration curve of Pridinol

Accurately weighed 40 mg of Pridinol was dissolved in 100 ml volumetric flask. This solution was used as a stock solution

Aliquots of 0.5 ml, 1 ml, 1.5 ml, 2 ml, 2.5 ml of working standards solution were transferred in to series of 50 ml volumetric flask. Then adjust volume up to 50 ml with diluent The concentration of these solution was 4 µg/ml, 8 µg/ml, 12 µg/ml, 16 µg/ml, 20µg/ml. Finally the absorbance of each sample was measured at 261 nm against blank. A standard curve of concentration vs. absorbance was plotted.

7) BCS solubility study: -

The solubility of drug in various solvent was determined by using shake flask method. Excess amount of API can be added into 250ml conical flask containing different types of media such as water, 0.1N HCl, pH 4.5 acetate buffers, pH 6.8 phosphate buffer, pH 7.5 phosphate buffer the shaking process was carried for 24 hours by keeping the conical flask on rotator shaker at 150 rpm. A portion drug dissolved was filtered through (0.45µm) and concentration of drug in the filtrate was determined by HPLC method.

8) IDENTIFICATION BY IR SPECTROSCOPY: -

Pridinol API, with a quantity of 20 mg, was individually mixed and thoroughly triturated in a mortar and pestle. The resulting mixture was then transferred onto a plate, and an infrared (IR) spectrum was obtained using the Diffused Attachment reflectance mode.

❖ **Drug excipients compatibility study:-**

The primary objective of this investigation was to identify a stable storage condition for drug in solid state and identification of compatible excipients for its formulation. In this method different excipients were selected and mixed separately with drug in proportion generally used for tablet formulation. The HPLC method was used to investigate any possible interactions between the drug and excipients utilized.

Procedure: - Drug: Excipients ratio Drug and excipients were taken in the ratios as mentioned in table

Table API/ excipients name with ratio

Sr.No.	**API/ Excipients Name with Grade**	**Drug: Excipients Ratio**
01	API	1
02	API + Lactose Monohydrate	1:25
03	API + Microcrystalline Cellulose	1:17
04	API + Hypromellose	1:3
05	API + Hydroxy ethyl cellulose	1:1.75
06	API + Sodium lauryl Sulphate	1:0.25
07	API + Magnesium stearate.	1:0.25
08	API + Opadry white	1:1
09	API + All excipient	Mixture

Pack details: Ambered color glass vial and aluminum seal.

API and excipients were thoroughly mixed in the predetermined ratio given in the table and passed through a 30# sieve. The blend was to be filled into amber-colored glass vials and was sealed with a perforated aluminum seal,

charged under the above conditions. Similarly API should be kept at all conditions as for the sample. Samples were withdrawn for analysis and physical observation should be done and HPLC studies were carried out to determine the compatibility of excipients with the drug.

❖ **Product Development:**

Objective of the project was to develop a stable product, which should be bio- equivalent to the sublingual drug product of Pridinol. Development of a new product starts with the evaluation of final product followed by compatibility studies, selection of process and equipment, optimization trials and evaluation. In order to develop bio-equivalent formulation of selected drug candidate, initial requirement was to choose a suitable manufacturing process.

❖ **Manufacturing process**:

Direct compression approach was development of pridinol sublingual tablet 4 mg. Based on target product profile, evaluation of physiochemical properties of the drug substances and other ingredients, literature search & scientific process below manufacturing process was carried out the development lab scale trial were performed to determine the manufacturing process parameters such as blending compression and coating. Ultimate goal of the experimentation was to obtained a product which will gives satisfactory in vitro The bulk density of the ingredients was measured using a graduated cylinder. It is the ratio of the total mass of powder to the bulk volume of powder. The measurement was done by pouring the weighed amount of powder into a graduated cylinder and recording the volume. It is expressed in g/ml and calculated using the following formula.rties of the inactive Excipients were selected accordingly. All the Excipients used in the development trials are suitable for direct compression. The results of the stability studies for the API, in conjunction with the API compatibility with the proposed inactive Excipients, justified the selection of the formulation composition.

Manufacturing process

1. Dispensing

1.1 Pridinol, Lactose Monohydrate, Hypromellose, Hydroxy Ethyl Cellulose, Sodium lauryl sulfate, and Magnesium Stearate were dispensed.

2. Sifting

2.1 Co-sift excipients Pridinol, Lactose Monohydrate, Hypromellose, Hydroxy Ethyl Cellulose, Sodium lauryl sulfate, Magnesium Stearate through mesh #50.

3. Dry mixing and granulation

3.1 Load the sifting material of step no 2.1 into rapid mixer granulator and dry mix for 15 min with impeller at slow speed and chopper off.

3.2 Take purified water in a container.

3.3 spray the purified water to the dry mix material of step 3.1 over a period of 10 to 15 min using peristatic pump while mixing with impeller at slow speed and chopper off

3.4 knead the wet mass step 3.3 for a period of 3 to 5 min at impeller slow speed and chopper slow speed

3.5 if required add additional quantity of purified water to the above wet mass of step 3.4 using peristaltic pump for a period of 1 to 8 min at impeller slow speed and chopper off.

3.6 if required knead the wet mass of step 3.5 for a period of 3 to 5 min at impeller slow speed and chopper slow speed

3.7 Discharge the wet mass of step 3.6 though co-mill fitted with 15 mm screen at impeller creep mode

4 drying

4.1 The wet mass of step 3.7 with air dry for about 15 min.

4.2 dry the wet mass of step 4.1 at an inlet temperature of NMT 45 °C in fluid bed dryer till to get LOD in the range of 1.0 -1.5 % w/w at 105°C by outmode using suitable IR moisture analyzer

5 sifting and milling

5.1 sift the dried granules of step no 4.2 though mesh #30

5.2 mill the retains of step 5.1 using co mill fitted with 1.5 mm grated screen at slow speed and shift the milled granules though mess #30

5.3 mill the retain of step 5.2 using co mill sifted with 1.0 mm grated screen at slow to medium speed and sift milled granules though mesh # 30

5.4 if required repeat the step 5.3 till the all granules passes though mess # 30

6.0 Extra granular material sifting

6.1 sift magnesium stearate though mess #50

7.0 blending of shifted granules

7.1 load the material of step 5.4 into suitable blender and blend for 5 min

8.0 Lubrication

8.1 Add sifted of material of step 6.1 to the material of step no 7.1 and lubricate for 3 min

9.0 Compression

The Lubrication from step 8.1 was compressed in to tablets by using suitable punch tooling using compression machine

10.0 Coating

2.0 % function coating has been given for all the formulation F1, F2, F3, F4, F5, F6, F7, F8, F9 To prevent direct interaction between Pridinol and Ethyl cellulose polymer

Sr. No	Ingredient	Quantity(gm)
1	Opadry yellow	4.5
2	Purified water	QS

Table: - Composition of ingredient function coating

Preparation of seal coating solution:

Weighed accurately a required quantity of HPMC Opadry White and soaked in water for 30 mins, and stirred until it swells. Finally, the volume was making up to the required quantity with purified water**.** Filtered the above solution with #100 mesh.

Weight built up calculation for function coating: [2.5 %]

195 x 2.5 % (5 gm 100 ml) = 5 mg

195 + 5 = 200 mg

The weight of Function function-coated tablet is 200 mg. Composition of ingredients for enteric coating

5% enteric coating has been given for the four formulations F5, F6, F7, F8, F9 to protect the drug from an acidic environment.

Table : Composition of ingredients for Enteric coating

Sr. No	Ingredient	Quality (gm)				
		F 5	F 6	F 7	F 8	F 9
1	Ethyl cellulose	4.00	4.00	4.00	4.00	4.00
2	PVP K 90	1.50	1.50	1.50	1.50	1.50
3	PEG 1450	0.70	0.70	0.70	0.70	0.70
4	Cross povidone	2.50	2.50	2.50	2.50	2.50
5	Polysorbate 80	2.50	2.50	2.50	2.50	2.50
7	Methyl alcohol	Q. S	Q. S	Q. S	Q. S	Q. S

❖ **Preparation of Enteric Coating Solution:**

A required quantity of Ethyl cellulose dispersion was weighed accurately and stirred until it swells. Meanwhile, PVP K 90, PEG 1450, Cross povidone, and Polysorbate 80 were triturated separately in a motor. and added to the solution and stirred. Finally, the volume that makes up to required quantity with methyl alcohol**.** Filtered the above solution with #100 mesh.

Weight Built up calculation for enteric coating: [5 %]

200 x 5 % (10 gm 100 ml) = 10 mg

210 + 10 = **220 mg**

The weight of the enteric-coated tablet = **220 mg.**

Coating parameter:

Process Parameter	**Limit**
Pan rpm	6-10 rpm
Inlet temp.	60-65ºC
Bed temp.	42ºC
Exhaust temp.	30-35ºC
Pan rpm	5-8 rpm
Atomization	1.3 bar
Spray rate	1gm/min

Table: Different formulation trial batches

Trials→	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Excipient		**Mg/Tablet**							
Pridinol	4	4	4	4	4	4	4	4	4
Lactose Monohydrate	101	100	100	100	100	97	100	99	102
Microcrystalline Cellulose	70	70	70	70	70	70	70	70	67
HPMC K100 LV	20	20	20	--	--	--	--	--	--
Hypromellose	--	--	--	20	15	15	15	15	12.5
Hydroxy Ethyl Cellulose	--	--	--	--	5	8	10	8	8
Sodium lauryl sulfate	--	0.5	1	1	1	1	1	2	1
Granulation									
Purified water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Lubrication									
Magnesium Stearate	1	1	1	1	1	1	1	1	1
Coating									
Opadry White	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Enteric Coating	--	--	--	--	10	10	10	10	10
Total weight	200	200.5	200	200	210	210	210.5	210.5	210

❖ **RESULT :**

Physiochemical properties of drug:-

1. Organoleptic properties:

Table: Organoleptic properties of API

Properties	Observation
Colour	White to off white powder
Taste	Bitter
Odour	Odourless
Appearance	White to off white crystaline

2. Melting point determination:-

Melting point of API was found to be, which is in range as given in literature (150- 153ºC). Hence the drug can be stated as pure.

Table: Melting point determination

Sr.No.	Melting point [˚C] (observed)	Average [˚C]
1	152	153
2	153	
3	153	

3. Solubility:-

The solubility of the received sample of API was examined in various solvents (aqueous and organic). It is an only qualitative analysis. The results thus obtained were as follows-

Table: Details solubility of API

Sr.No.	Solvent	Solubility
1	Alcohol and Water	Freely soluble
2	Methylene chloride	Very slightly soluble

4. Particle size determination:-

Sample of API was analyzed by using Malvern particle size analyzer, particles were found in following size ranges

Table: Particle size determination

Sr.No.	Diameter	Particle size(µm)
1	D10	26.7
2	D50	61.4
3	D90	152.9

5. Loss on drying:-

Loss on drying was carried out by using halogen moisture analyzer and it was found to be 1.21% at 105ºC

❖ **Ultraviolet absorption spectroscopy:**

Wavelength Selection:

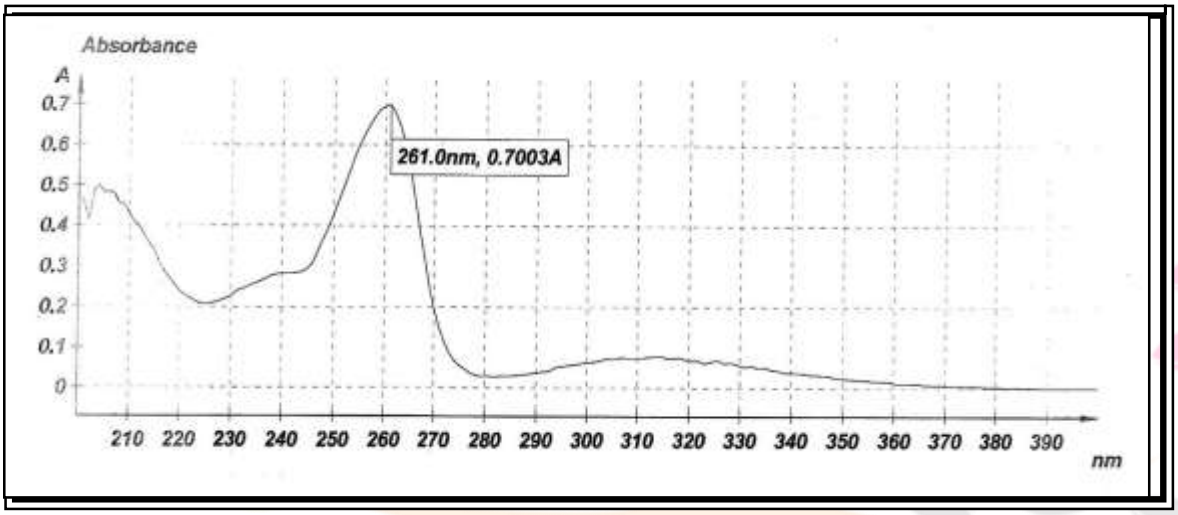


Figure: UV Spectrum of API

An absorption maximum was found to be at 261nm. Hence 261 nm was selected as λ max for further studies.

❖ **Calibration curve:**

The solution containing different concentration of pridinol was prepared and scanned at 261 nm by using UV spectrophotometer. Graph of absorbance vs. concentration was plotted and found to be linear over the range of 4-20 µg/ml indicating its compliance Lambert's-Beer's law.

Table: Absorbance at various conc. of API

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	4	0.1732
3	8	0.3512
4	12	0.5254
5	16	0.7020
6	20	0.8715

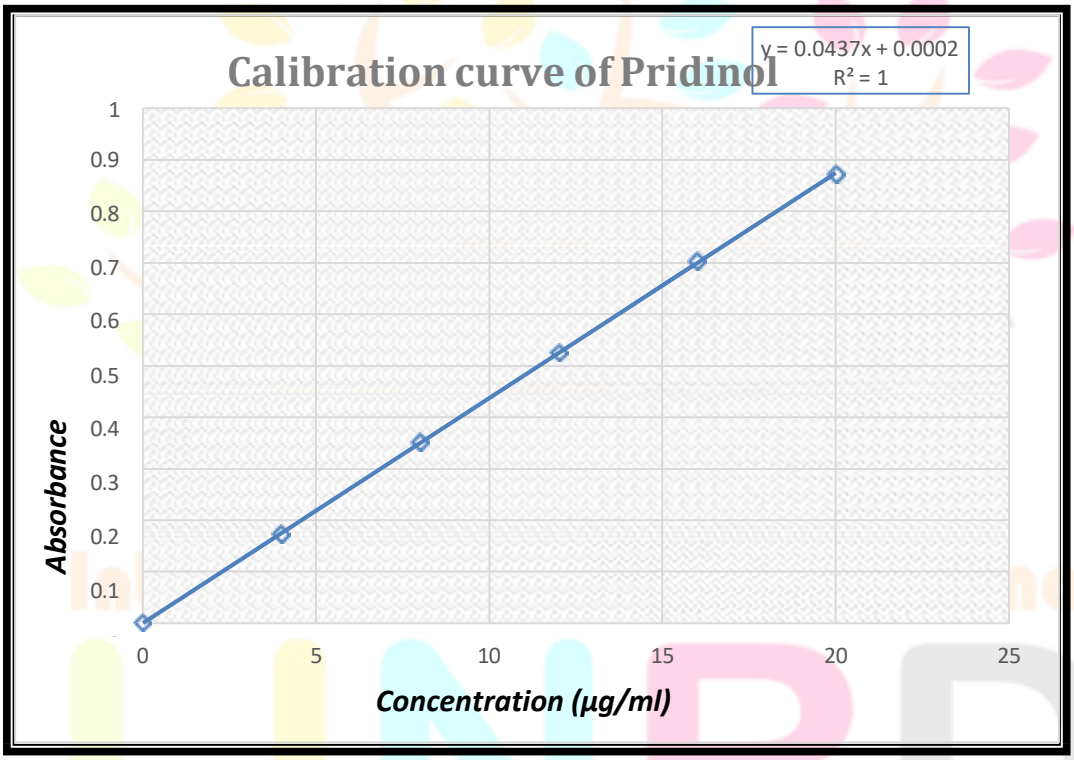


Figure: Calibration curve of Pridinol

Table: Parameters found in calibration curve

Sr.No.	Parameter	Finding
1	Wavelength detection	261 nm
2	Regression equation	y = 0.0437x + 0.0002
3	Correlation coefficient	R = 1

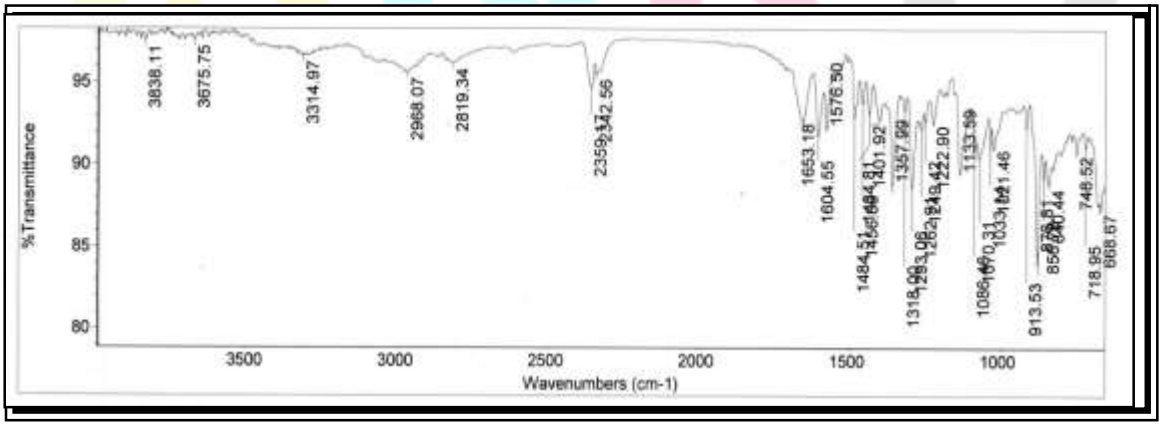
❖ BCS solubility study:-

Table: BCS solubility data of API in different media

Sr.No	Media	mg/250ml
1	Purified Water	4.2
2	0.1N HCl	3.1
3	pH 4.5 Acetate buffer	2.5
4	pH 6.8 phosphate buffer	4.6
5	pH 7.5 phosphate buffer	4.3

❖ IDENTIFICATION BY IR SPECTROSCOPY: -

Pridinol API, with a quantity of 20 mg, was individually mixed and thoroughly triturated in a mortar and pestle. The resulting mixture was then transferred onto a plate, and an infrared (IR) spectrum was obtained using the diffused attachment reflectance mode.



IR peak Assignment value of Pridinol

Standard IR Ranges (cm^{-1})	IR Ranges (cm^{-1})	Functional Group
3333-3267	3314.97	**C-H Stretching**
3000-2800	2968.07	**N-H Stretching**
3200-2700	2819.34	**O-H Stretching**
1658-1648	1653.18	**C=C Bending**

❖ **Drug-excipients compatibility result:**

The objective of this Drug-excipients compatibility study to identify a stable storage condition for drug in solid state and identification of compatible excipients for its formulation. The excipients mixed separately with drug in proportion generally used for tablet formulation. The HPLC method was used to investigate any possible interactions between the drug and excipients utilized by assay method.

1 Physical and chemical compatibility:

Table: Result of physical compatibility of Drug

Sr.No.	API/ Excipients Name with Grade	Drug:Excipients Ratio	Observation on appearance	Assay (%)
01	API	1	Off White powder	99.8
02	API + Lactose Monohydrate	1:25	Off White powder	99.4
03	API + Microcrystalline Cellulose 102	1:17	Off White powder	98.7
04	API + Hypromellose	1:3	Off White off white	98.9
05	API + Hydroxy ethyl cellulose	1:1.75	Off White powder	100.0
06	API + Sodium lauryl Sulphate	1:0.25	Off White powder	100.1
07	API + Magnesium stearate.	1:0.25	Off White powder	99.8
08	API + Opadry white	1:1	Off White powder	100.0

09	API + All excipient	Mixture	Off White powder	99.5

Conclusion:

The appearance of mixture of excipient and drug was observed There is no loss in assay was observed in any of these mixtures at assay of API. There is no incompatibility with the selected excipients. Hence selected excipients are the correct.

❖ **Pre compression parameter: -**

The wet granulation blend were evaluated for the characteristics before compression into the tablet, the density, compressibility index and Hausner ratio were performed to check the blend parameter

Table: Evaluation of lubricated blend

Formulation. no	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility index (%)	Hausner ratio
F1	0.483	0.614	19	1.25
F2	0.528	0.624	18	1.21
F3	0.520	0.637	16	1.23
F4	0.498	0.687	18	1.21
F5	0.510	0.634	13	1.22
F6	0.488	0.598	13	1.23
F7	0.531	0.654	15	1.16
F8	0.520	0.637	12	1.13
F9	0.527	0.657	14	1.16

Conclusion:

In the above table characteristic of the powder blend from F1 to F9 is given. From values of Compressibility index and Hauser's ratio we can conclude that blend of the above formulation have passable flow properties and compressibility index. The all obtained values has acceptable for further characteristics of blend. The blend has prepared by wet granulation method for convenient characteristics of blend

❖ **Post compression Parameter:**

The accepted percentage deviation ±7.5% for more than 250 mg weight tablets since weight variation of tablet was within range the thickness of the tablets was found to be in the range. The result showed that the thickness of all formulates tablets is found to be uniform. The hardness of the all tablet formulation was found to be in range. It indicates all the tablets have adequate mechanical strength. In friability test the maximum weight loss should not be more than 1%. The result revealed that the tablets passed the friability test. Initial feasibility trials were taken with direct compression and wet granulation approaches. With wet granulation approach, significant drop in assay was observed. Hence the direct compression approach was considered for formulation development.

Table: Evaluation of Post compression Parameter.

F. No	Weight Variation (mg)	Hardness (KP)	Thickness (mm)	Friability (%)	Assay (%)
F1	199.3	10	4.0	0.6	97.3
F2	201.5	10	4.2	0.7	98.6
F3	200.6	9	4.1	0.5	98.5
F4	200.1	10	4.1	0.8	97.3
F5	220.3	11	4.5	0.6	98.5
F6	220.5	12	4.5	0.5	99.2
F7	221.2	13	4.7	0.6	98.3
F8	221.8	11	4.8	0.7	99.8
F9	220.6	12	4.6	0.4	99.5

Conclusion:

Among the eight comparison batches, batch no. F9 was found to be satisfactory compared to the other formulations. In this, the thickness, hardness, and of the prepared tablet were found to be adequate as that of the reference Formulation tablet. In the friability test, the maximum weight loss should not exceed 1%. The result revealed that the tablets passed the friability test.

❖ **Dissolution study:**

In vitro Dissolution Study in release media:

An in vitro dissolution study was carried out for the optimized formulation of pridinol Tablets and the reference standard in a pH 6.8 phosphate buffer. The dissolution apparatus (USP Type II, Paddle) operated at 50 RPM. The temperature of the dissolution medium was maintained at 37 ± 0.5°C. Time points of 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 20, and 24 hours were followed, and the drug concentration was determined by the HPLC method.

Table: %Comparative dissolution profile of all Formulation batches in pH 6.8 phosphate buffer

Media	**900ml of pH 6.8 phosphate at 50 rpm in USP Type II apparatus (Paddle)**								
Time	**% Drug Release**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
0.5	2	3	12	10	7	10	5	8	6
1	7	13	24	21	18	16	7	15	10
2	12	22	38	34	27	28	15	31	24
3	19	35	53	48	43	41	24	51	32
4	24	49	68	66	65	58	35	69	44
6	33	62	80	76	74	68	48	82	60
8	42	70	88	82	84	73	62	91	79
12	57	76	96	88	89	85	73	98	86
16	69	83	99	93	92	91	82	91	93
20	75	89	90	97	95	96	90	85	96
24	81	93	84	99	89	99	94	77	100

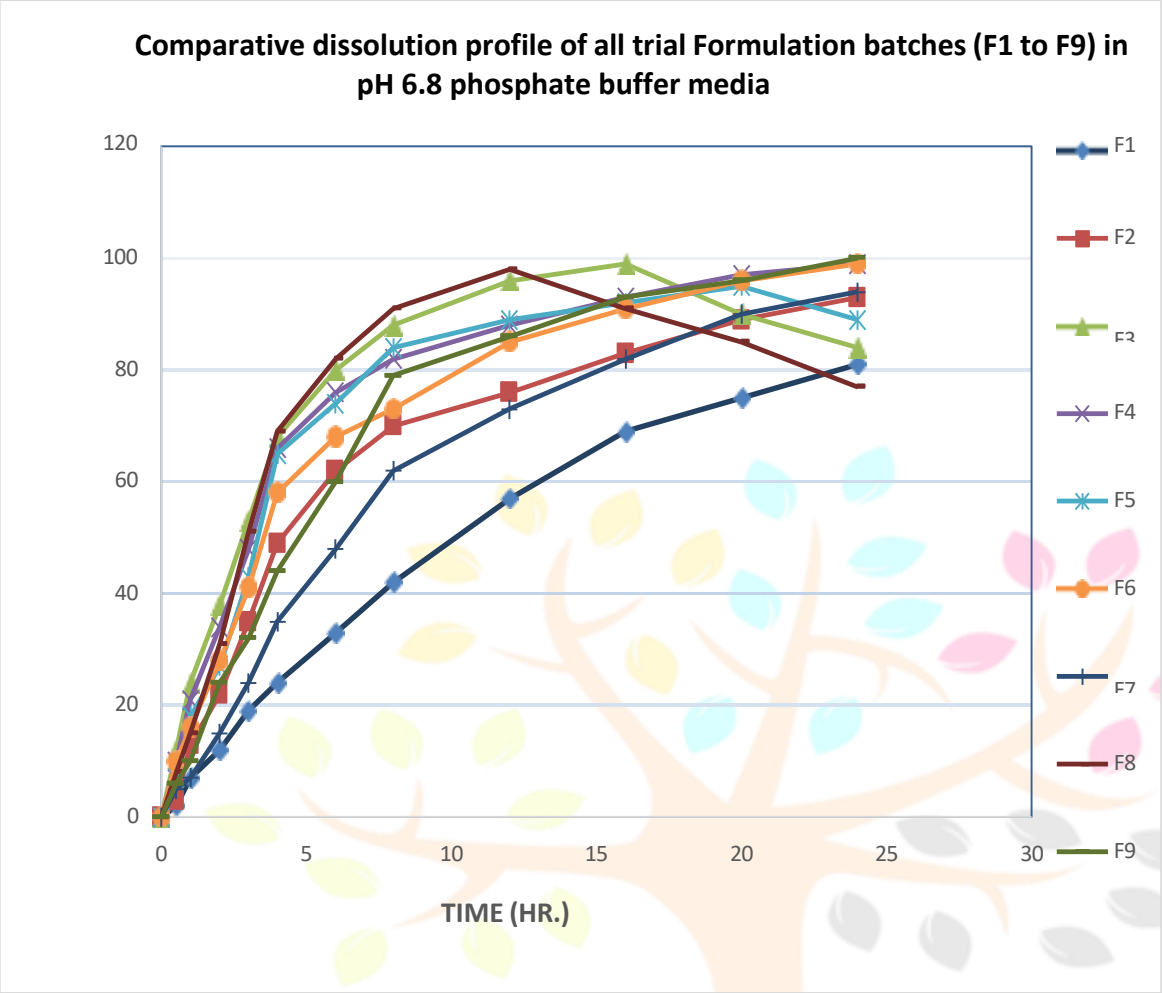


Figure: **In vitro Dissolution Study in Multi-Media**

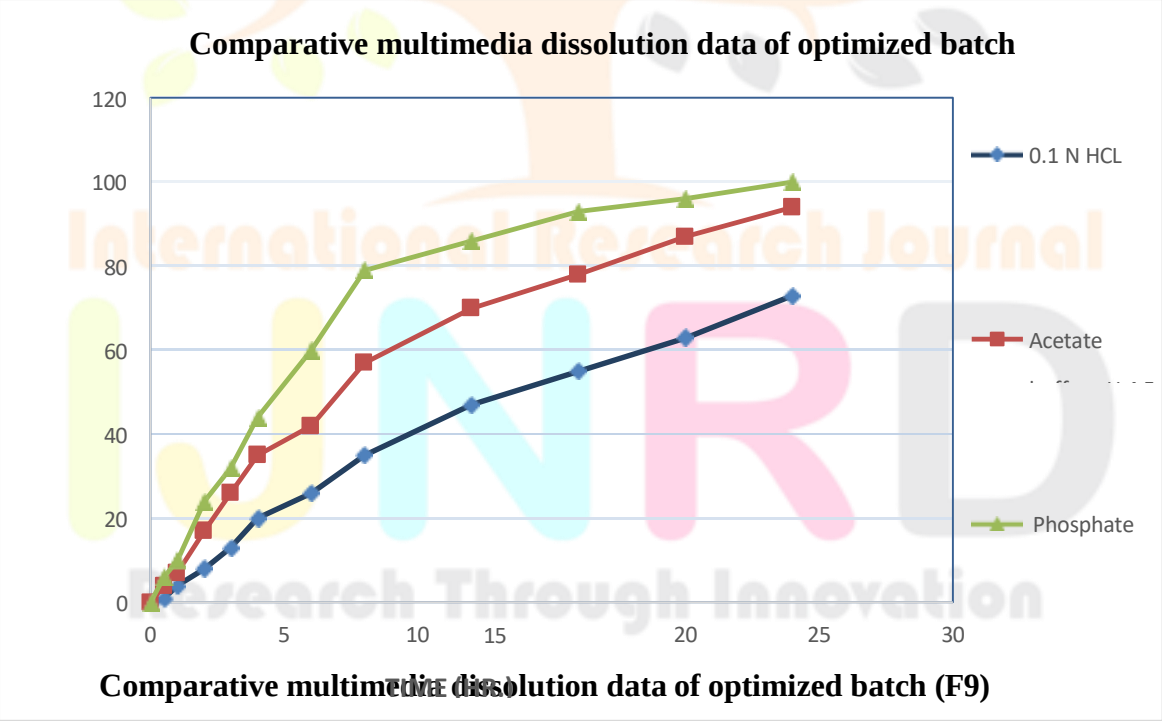
An in vitro dissolution study was carried out for the optimized formulation of pridinol Tablets and the reference standard in 0.1 N HCl and a pH 4.5 acetate buffer. The dissolution apparatus (USP TYPE II Paddle) operated at 50 RPM. The temperature of the dissolution medium was maintained at 37 ± 0.5°C. Time points

of 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 20, and 24 hours were followed, and the drug concentration was determined by the HPLC method.

➢ **Comparative dissolution profile of optimized batch (F9) in 0.1N HCl, pH 4.5 acetate buffer and pH 6.8 phosphate buffer.**

Table: Comparative multimedia dissolution data

Apparatus: USP II		**Speed:** 50 RPM	
Volume: 900 ml		**Temperature:** 37 °C	
Time(Hr)	**% Drug release**		
	0.1 N HCL	pH 4.5 Acetate	pH 6.8 Phosphate buffer
0	0	0	0
0.5	1	4	6
1	4	7	10
2	8	17	24
3	13	26	32
4	20	35	44
6	26	42	60
8	35	57	79
12	47	70	86
16	55	78	93
20	63	87	96
24	73	94	100



Comparative multimedia dissolution data of optimized batch (F9)

❖ **CONCLUSION**

The present study aimed to design and evaluate a novel drug delivery system for the poorly water-soluble drug Pridinol. This study aimed to improve the solubility of Pridinol by using a novel solubility enhancer and to formulate

a sustained-release tablet using Hypromellose and Hydroxy Ethyl Cellulose as controlled-release polymers. A compatibility study shows compatibility between the drug and its excipients. Preformulation studies have been conducted to investigate the nature of the API and its compatibility with excipients through physical observation. The results showed that there was no interaction between the API and any of the selected excipients. Sustained-release tablets of Pridinol were successfully formulated by the wet granulation method using the selected excipient quantities. The formulated tablets were evaluated for both pre-compression and post-compression parameters in accordance with the standards' requirements. And the results complied with the pharmacopoeia specification. Different concentration of polymer was used to control the drug release from the dosage form. This sustained-release tablet is based on a polymer selected for its ability to sustain drug release. Different polymers were used to achieve the desired release profile over 12 hours. Different batches of extended-release formulations were prepared using the wet granulation method, respectively. All the formulations were evaluated for physical characteristics, disintegration, in vitro dissolution study, and stability. The following conclusions have been made from the present study. The physical characteristics of all the blended formulations were satisfactory. The prepared tablets evaluated for Assay, weight variation, hardness, thickness, and friability, and Disintegration time were found to be within the official limits. The *in vitro* dissolution studies were performed for all the SR formulations. *In Vitro* Dissolution study of SR formulations F9 showed a release profile were complies with the USP concentration of HPC with respect to the drug compared with the other 6 formulations. Among the entire coated optimized batches, formulation F9 has been selected for a comparative dissolution profile study against the reference Product.

❖ REFERENCES

1. Andrade, C. (2015). Sustained-release, extended-release, and other time-release formulations in neuropsychiatry. The Journal of Clinical Psychiatry, 76(8), 20558.

2. Banker, Gilbert S., Juergen Siepmann, and Christopher Rhodes. "Sustained-and Controlled-Release Drug-Delivery Systems." In Modern Pharmaceutics, pp. 768-810. CRC Press, 2002.

3. Remington, The Science and Pharmacy Practice of Pharmacy, 21st edition, volume I, II, 869870.

4. Reddy, K. R., Mutalik, S., & Reddy, S. (2003). Once-daily sustained- release matrix tablets of nicorandil: formulation and in vitro evaluation. AAPS pharmscitech, 4(4), 61

5. Hebert A. Liberman. Leon Lachman, Joseph B. Schwartz. Pharmaceutical dosage forms tablet- Vol-1, Vol-2, 112.220.

6. Anisul Quardir, Karl Kolter, A comparative study of current Super disintegrates, Pharmaceutical Technology, Oct 1, 2006.

7. Karna, Sudhir, Shashank Chaturvedi, Vipin Agrawal, and Mohammad Alim. "Formulation approaches for sustained release dosage forms: a review." Asian J Pharm Clin Res 8, no. 5 (2015): 46-53.

8. Leon Lachman, Joseph B.Schwartz, compression coated and layered Tablets, Pharmaceutical Dosage forms: Tablets, 1989, Vol II, 273-274.

9. R.S. Sathoskar, S. D, Bhandarkar, Nimala N. Rege, Pharmacology and pharmacotherapeutics, Ninth edition,884-891.

10. Silverstone, T., Jill Fincham, and Jill Plumley. "An evaluation of the anorectic activity in man of a sustained release formulation of tiflorex." British journal of clinical pharmacology 7, no. 4 (1979): 353.

11. Andrade, C. (2015). Sustained-release, extended-release, and other time- release formulations in neuropsychiatry. The Journal of clinical psychiatry, 76(8), 20558.

12. Jantzen, Gwen M., and Joseph R. Robinson. "Sustained-and controlled-release drug delivery systems." Drugs and The Pharmaceutical Sciences 121 (2002): 501- 528.

13. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, 4th Edition, 121, 2005, Marcel Dekker, Inc, 501-514.

14. Thomas Wait-Yip Lee and Joseph R Robinson, Controlled Release Drug Delivery System, In the Science and Practice of Pharmacy, Volume 1, 20th edition, 2001, 903.

15. Mamidala, R. K., Ramana, V., Sandeep, G., Lingam, M., Gannu, R., & Yamsani, M. R. (2009). Factors influencing the design and performance of oral sustained/controlled release dosage forms. Int. J. Pharm. Sci. and Nanotech, 2(3), 583-594.

16. Yei W. Chein, Oral Drug Delivery System, Novel drug delivery Systems, volume 50, 2nd Edition, Marcel Dekker, Inc., 139-157.

17. Narwate, B. M. "Sustained release dosage form: a concise review." International journal of pharmaceutics and drug analysis 5, no. 5 (2017): 153-160.

18. Donald L. Wise, Handbook of Pharmaceutical Controlled Release Technology, 2005, Marcel Dekker, Inc, 435-440.

19. Gwen M. Jantzen and Joseph R. Robinson, Sustained and controlled Release Drug Delivery System, In Modern Pharmaceutics, Marcel Dekker, Inc., 3rd edition, 1996, 582-593.

20. Ankit, Bhargava, R. P. S. Rathore, and Y. S. Tanwar. "Oral sustained release dosage form: an opportunity to prolong the release of drug." International Journal of Advanced Research in Pharmaceutical & Bio Sciences 2, no. 2 (2013): 7-15.

21. Li VHK, Robinson JR, Lee VHL, Design and Fabrication of oral Controlled Drug Delivery System, In Controlled Drug Delivery, Marcel Dekkar 1987, 2nd edition, 412.

22. Agis Kydonieus, Treatise on Controlled Drug Delivery, Marcel Dekker 1st Edition, 1992, 43-93.

23.S.P. Vyas, Roop. K. Khar, Controlled Drug Delivery Concept and Advances, 1st edition, 2002, 54.

24. Dixit, Navin, Sheo Dutt Maurya, and Bhanu PS Sagar. "Sustained release drug delivery system." Indian Journal of Research in Pharmacy and Biotechnology 1, no. 3 (2013): 305.

25. British Pharmacopoeia. The Stationary office, MHRA, British Pharmacopoeia Commission office, Vol. 1, London, 2004.

26. Raymond C Rowe, Paul J Sheskey and Sian C Owen, Hand Book Of Pharmaceutical Excipients, 5th edition, 2006, 553-560.

27. Sharma, Ashish, and Vikas Bhatt. "Sustained Release Matrix Type Drug Delivery System A Review." World Journal of Pharmacy And Pharmaceutical Science 2 (2015).

28. Raymond C Rowe, Paul J Sheskey and Sian C Owen, Hand Book Of Pharmaceutical Excipients, 5th edition, 2006, 278-282.

29.P. Lindborg et al. Pharmacokinetics and pharmacodynamics of metoprolol after conventional and controlled-release administration in combination with hydrochlorothiazide in healthy volunteers, European Journal of Clinical Pharmacology, 45(2)1993, 161-163.

30. Hema Ravishankar et al. Modulated release metoprolol succinate formulation based on ionic interactions: In vivo proof of concept, Journal of Controlled Release, Volume 111, Issues 1-2, 2006, 65-72.

31. James W Hainer et al. Metoprolol succinate extended release/hydrochlorothiazide combination tablets, Am J Hypertens.19 (12), 2003, 117-25.

32. Kumar, KP Sampath, Debjit Bhowmik, Shweta Srivastava, Shravan Paswan, and Amit Sankar Dutta. "Sustained release drug delivery system potential." The pharma innovation 1, no. 2 (2012).

33. Papademetriou V. Factorial antihypertensive study of an extended-release metoprolol and hydrochlorothiazide combination, Am J Hypertens.19 (12), 2006, 1217-25.

34. Pareek, Shraddha Pawan, Sunil Kumawat, Vijay Sharma, Devender Sharma, Devendra Singh Rathore, and Mahadev Agarwal. "Review on sustained release technology." Int. J. Pharm. Biol. Sci. Arch 7 (2019): 29-38.

35. Papadopoulos DP et al. Metoprolol succinate combination in the treatment of

hypertension. Angiology. 60(5), 2009, 608-13.

36. Plosker GL et al. Controlled release metoprolol formulations. A review of their pharmacodynamics and pharmacokinetic properties, and therapeutic use in hypertension and ischaemic heart disease, Drugs. 1999; 43(3):382-414.

37. Nagaraju et al. Core-in-Cup Tablet Design of Metoprolol Succinate and its Evaluation for Controlled Release, Current Drug Discovery Technologies, Volume 6, Number 4, 2009, 299- 305.

38. Tilak R. Bhardwaj et al. Natural Gums and Modified Natural Gums as Sustained-Release Carriers, Drug Development and Industrial Pharmacy, Vol. 26, No. 10, 2000, 1025-1038.

39. Rajesh, Asija, Rathi Harish, and Asija Sangeeta. "Sustained Released Drug Technology: A Review." International Journal of Research in Pharmacy & Science 2, no. 4 (2012).

40.F. Siepmann et al. Polymer blends for controlled release coatings, Indian Journal of Pharmaceutical Sciences, 61(6), 1996, 42-5.

41. Udaya S. Toti et al., Modified guar gum matrix tablet for controlled release of diltiazem hydrochloride, Indian Journal of Pharmaceutical Sciences, 61(6), 1998, 212-5.

42. Khullar P et al., Guar Gum as a hydrophilic matrix for preparation of Theophylline Controlled Release dosage form, Indian Journal of Pharmaceutical Sciences, 61(6), 1999, and 342-5.

43. Praveen Khullar et al. Evaluation of Guar Gum in the Preparation of Sustained- Release Matrix Tablets,1998, Vol. 24, No. 11, 1998, 1095-1099.

44. James W Hainer and Jennifer Sugg; Vascular Health and Risk management, 2007, 3(3), 279–288.

45. Wani, Manish Shivadas, S. A. Polshettiwar, V. V. Chopade, R. N. Joshi, M.
H. G. Dehghan, A. A. Gadkari, S. Chepurwar, and V. Mute. "Controlled Release System A Review." Pharmaceutical Reviews 6, no. 1 (2008): 41-46.

46. Yie Chein; Novel drug delivery system" 2nd. Marcel jekkerinc. New York. 1992, 1-3.