ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research

Available Online at www.jbpr.in

CODEN: - JBPRAU (Source: - American Chemical Society)

Index Copernicus Value: 72.80

PubMed (National Library of Medicine): ID: (101671502)

Volume 7, Issue 1: January-February: 2018, 55-67

Research Article

FORMULATIONS AND EVALUATION OF FILM COATED IMMEDIATE RELEASE TABLETS OF PIRACETAM

Anshul Jain [1], Dr. Manish Kumar Gupta[2], Vijay Sharma[3]

[1] M.Pharm. Research Scholar, Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur, Rajasthan, India

[2] Professor and Principal, Jaipur College of Pharmacy, Jaipur, Rajasthan, India

[3] Associate Professor, Jaipur College of Pharmacy, Jaipur, Rajasthan, India

Received 09 Dec. 2017; Accepted 20 Jan. 2018

ABSTRACT

An immediate release dosage form allows a manufacturer to extend market exclusivity, 100 mg of Piracetam was accurately weighed and transferred to previously dried 100 ml volumetric flask. Drug was dissolved in 0.01N sodium hydroxide solution. The solution was suitably diluted and scanned in the range of 230-380 nm using 0.01N sodium hydroxide solution as blank. The main objective of present work is to formulate safe and bioequivalent film coated immediate release tablet for treatment of cognitive and memory disorder. immediate release Piracetam tablets were prepared by Wet Granulation & Direct Compression. Coating by Ethyl cellulose and *Dibutyl sebacate* were dissolved in PEG-6000, HPMC-6cps, talc and titanium di oxide were dissolved in water, Both the solution were mixed together and stirred for 45 min to get a homogenous solution. Ten tablets were powdered in a mortar and powder equivalent to 5 mg of Piracetam was taken and extracted with 25 ml of 0.01N Sodium Hydroxide solution by shaking for 15 min. It was filtered and diluted to 50 ml with water. The scaled up formulations B10 and B11 were subjected to accelerated stability studies and parameters like hardness, disintegration time, drug content and in vitro drug release were analyzed after storing them at 40±20C / 75±5% RH for 2 months.

Keywords: Tablets, immediate release, Wet granulation, Dry granulation.

INTRODUCTION:

Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated. The excipients can include binders, glidants and lubricants to ensure efficient tabletting; disintegrants to promote tablet break-up in the digestive tract; sweeteners or flavors to enhance taste; and pigments to make the tablets visually attractive. These are included in the formulations to facilitate easy handling, enhance the physical appearance, and improve stability and aid in the delivery of the drug to the blood stream after administration. A polymer coating is often applied to make the tablet smoother and easier to swallow, to control the release rate of the active ingredient, to make it more resistant to the environment (extending its shelf life), or to enhance the tablet's appearance.

IMMEDIATE RELEASE TABLETS: The need for new oral drug delivery system continues, due to poor patient acceptance for invasive methods, need for exploration of new market for drugs and coupled with high cost of disease management. Developing new drug delivery techniques and utilizing them in product development is critical for pharma companies to survive this century.[2] An immediate release dosage form allows a manufacturer to extend market exclusivity, while offering patients a convenient dosage form or dosage regimen. Immediate Release Tablets are those tablets which are designed to disintegrate and release their medication with no special rate controlling features, such as special coatings and other techniques. Recently immediate release tablets have started gaining popularity and acceptance as

Corresponding author: Anshul Jain |

a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance. They are also a tool for expanding markets, extending product life cycles and generating opportunities.

DRUG PROFILE

PIRACETAM-

- **Chemical structure-**

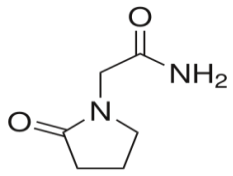

Fig. 1.1: Structure of Piracetam

- **Chemical name:** 2-oxo-1-pyrrolidine acetamide
- **Appearance-** White crystalline powder
- **Molecular formula-** $C_6H_{10}N_2O_2$
- **Molecular weight-** 142.16 g/mol
- **Category-** Central stimulant
- **Pka-** 5.24 – 7.69
- **Solubility-** Soluble in water (72 mg/ml at 25° C), methanol, *DMSO* (72 mg/ml at 25° C), and ethanol (<1 mg/ml at 25° C).
- **Melting point-** 147-157 C °
- **Mechanism of action-** The drug influences neuronal and vascular functions and influences cognitive function without acting as a sedative or stimulant.
- **Half-life-** 4-5 hours

MATERIAL & METHOD:

Thefollowing drugs, excipients/ polymer and chemicals were used for the formulation and evaluation of Piracetam tablet

Table 1: list of Materials used in formulation

Sr. No.	Drug/ Excipient/Polymer/solvents	Category	Vendor
1	Drug	Active	Pol. Pharma
2.	Ethyl cellulose	Binder	FMC
3.	Povidone k 30	Binder	ISP
4.	Magnesium stearate\	Lubricant	Dr.poallohman
5.	Ethyl cellulose dispersion\	Coating polymer	FMC
6.	Hypromellose	Coating polymer	Shin. Etsu.
7.	PEG 6000	Plasticizer	Clariant
8.	Talc	Glidant	Luzenac
9.	Titanium di oxide	Opacifier	Kronos
10.	Dibutylsebacate	Plasticizer	Vertellus
11.	Purified water	Vehicles	Plant

Table 2: List of equipment

Sr. No.	Equipment's / machine	Purpose	Description
1	Electronic weighing balance	Weighing of materials	Metterl Toledo
2	Mechanical sifter	Sifting of raw materials	Cadmach machinery co.
3	Rapid mixer granulator	Mixing and granulation	Saral RMG
4	Rapid dryer	Drying of granules	Cadmach machinery co.
5	Cage blender	Mixing and lubrication	Cadmach machinery co.
6	Compression machine	Compression of granules	Cadmach machinery co.
7	Coating machine	Coating of tablets	Gansons
8	Tablets hardness tester	Testing the hardness of tablets	Electrolab
9	Tablets disintegration appartus	Testing the disintegration time	Electrolab
10	Halogen moisture balance	Testing LOD of granules	Mettlertoledo

11	Friability test apparatus	Testing of friability	Electrolab
12	Vernier calliper	Tablets thickness and dimensions	Omega instruments ltd.
13	Dissolution test apparatus	Analysing the drug release	Electrolab
14	HPLC	Analysing the assay	Shimandzu
15	FTIR apparatus	Analysing the	Shimandzu
16	Bulk density apparatus		Electrolab
17	UV spectrophotometer	Testing of absorbance	Shimandzu

PRE-FORMULATION STUDIES

Characterization of Piracetam: -

1. Visual Examination- A small quantity of piracetam powder was taken in butter paper and viewed in well-illuminated place.
2. Taste and Odour- Very less quantity of Piracetam was used to get taste with the help of tongue as well as smelled to get the odour.
3. Solubility- The approximate solubility's of substances are indicated by the descriptive terms in the accompanying table. Solvents such as Methanol, water, hydrochloric acid and 0.01N sodium hydroxide solution were used for the solubility studies.

Table 3: Solubility Chart

Descriptive Term	Parts of Solvent Required for 1 part of Solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1,000
Very slightly soluble	From 1,000 to 10,000
Practically insoluble or Insoluble	Greater than or equal to 10,000

UV spectrum Analysis-

100 mg of Piracetam was accurately weighed and transferred to previously dried 100 ml volumetric flask. Drug was dissolved in 0.01N sodium hydroxide solution. The solution was suitably diluted and scanned in the range of 230-380 nm using 0.01N sodium hydroxide solution as blank.

PREPARATION OF CALIBARATION CURVE OF PIRACETAM

100 mg of Piracetam was accurately weighed and transferred to previously dried 100 ml volumetric flask. Drug was dissolved in 0.01N sodium hydroxide solution. The solution was suitably diluted with 0.01N sodium hydroxide solution to get standard concentration of 2, 4,6,8,10,12 and 14 µg/ml. Absorbance was measured at 283 nm using using UV-Visible Spectrophotometer.

Preparation of Piracetam by Wet Granulation:-

All the ingredients were accurately weighed as per batch 1st and 3nd dispense in clean polythene covers. Piracetam was sifted through sieve no-12. Ethyl Cellulose, Povidine K 30 were passed through sieve no-40. Magnesium stearate passed through sieve no-60. After sifting all the above ingredients were transferred into a big polythene cover and mixed for 30 min. Binder solution was prepared by dissolving weighed amount of PVP K 30 in required amount of distilled water.

The above blend was taken in a stainless steel container to which the earlier prepared binder solution was added slowly until a wet mass like substance was formed. The wet mass was passed through sieve no- 20 to get wet granules which were later dried in a Rapid drying Machine drier at

40 0 c for 1 hour. The dried granules were again passed through sieve no- 16and thoroughly mixed with magnesium stearate.

Preparation of Piracetam by Direct Compression:-

All the ingredients were accurately weighed as per Batch-2 and were dispensed in clean polythene covers. piracetam were sifted through sieve no-12. Ethyl Cellulose, Povidine K 30 were passed through sieve no-40. Magnesium stearate passed through sieve no-60. Piracetam, and Ethyl Cellulose were mixed in a polythene cover marked as PL-I. Povidine K 30 in polythene cover marked as PL-II.Magnesium stearate polythene cover marked as PL-III. The covers were mixed thoroughly for 5 min. Then PL -II and -PLIII were added to PL-I and again mixed thoroughly for 20 min.

Procedure for Scale up of Piracetam Tablets:- Scale up was done by following the same procedure as given Wet Granulation. Mixing was carried out in a Double cone blender for 15 min. This blend is then subjected to direct compression on a Double Rotary Compression Machine (20 station) at 40 rpm to yield Piracetam tablets.

FILM COATING OF IMMEDIATE RELEASE PIRACETAM TABLETS

Preparation of Coating Solution: All the ingredients were accurately weighed as per formula and dispensed. Ethyl cellulose and *Dibutyl sebacate* were dissolved in PEG-6000. HPMC-6cps , talc and titanium di oxide were dissolved in water. Both the solution were mixed together and stirred for 45 min to get a homogenous solution.

Coating Conditions:

Table 4: Coating conditions

Sr. No.	Parameters	Limits
1.	Pan speed	8 to 10 rpm
2.	Inlet air temperature	30 to 40°C
3.	Exhaust air temperature	30 to 35°C
4.	Bed temperature	30 to 35°C
5.	Atomizing air pressure	3.0 to 4.0 kg/cm²
6.	Spray gun nozzle diameter	1.0 mm
7.	Spray rate	6.0 ml to 8.0 ml/min

FORMULATION DESIGN

Table 5: Formula for Preparation of Immediate Release Piracetam Tablets

Sr. No.	INGREDIENTS	B1	B2	B3
1	Piracetam	800mg	800mg	800mg
2	Ethyl Cellulose	43mg	41mg	5mg
3	Povidine K 30	2mg	4mg	41mg
4	Magnesium stearate	5mg	5mg	5mg
5	Distilled water	q.s.	q.s.	q.s.
Total Tablet weight		850mg	850mg	850mg

Table 6: Formula for Preparation of Immediate Release Piracetam Tablets

Sr. No.	INGREDIENTS	B4	B5	B6	B7	B8	B9
1	Piracetam	800mg	800mg	800mg	800	800	800
2	Preglatinized starch	43mg	3	----	----	2	----
3	Collidol silicon dioxide	----	42	2mg	----		----
4	Macrogel 6000	3	----	43	2mg	3	----
5	Povidone k 90	----	----	----	43	40	-----
6	Glyceryl behenat	-----	----	----	----	----	45
7	Magnesium stearate	4mg	5mg	5mg	5	5	5

8	Distilled water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total Tablet weight		850mg	850mg	850mg	850mg	850mg	850mg

STABILITY STUDIES

Stability of a drug has been defined as the ability of a particular formulation in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability study is to provide evidence on the quality of a drug substance or drug product which varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. Recommended storage conditions, re-test periods and shelf-lives are to be established.

The International Conference of Harmonization (ICH) Guidelines titled, "stability testing of new drug substance and products" describes the stability test requirements for drug registration application in the European Union, Japan and the United States of America. ICH specifies the length of study and storage conditions Long-term testing: - 250C ± 20C / 60% RH ± 5% for 12 months. Accelerated testing: - 400C ± 20C/ 75% RH± 5% for 6 months. Accelerated Stability studies were carried out at 400C / 75% RH for the best formulations for 2 months.

RESULTS AND DISCUSSION

Organoleptic properties:

Table: Characterization of Piracetam tablets

Sr. No.	Test	Specification	Observation
1.	Colour	White crystalline powder	White to off white fine crystalline powder
2.	Odour	Odorless	Odorless or with a faint characteristic odors
3.	Appearance	Crystalline	Crystalline powder
4.	Hygroscopicity	Slightly hygroscopic	Slightly hygroscopic

Discussion: It was done on parameters like colour, odor, taste and loss on drying and the results were found to be within the limits.

Solubility of Piracetam

Quantity of Piracetam	Quantity of solvents	Inference
100 mg	30 ml of Water	Soluble
100 mg	100 ml of Methanol	Soluble
100 mg	100 ml Hydrochloric acid	Soluble
100 mg	100 ml 0.01N Sodium hydroxide solution	Soluble

Calibration curve of Piracetam in Methanol (λ_{max}= 230nm)

Sr. No.	Concentration (µg/ml)	Absorbance at 230nm
1	1	0.063±0.001
2	2	0.123±0.001
3	3	0.185±0.002
4	4	0.262±0.008
5	5	0.360±0.001
6	6	0.414±0.002
7	7	0.514±0.001
8	8	0.586±0.002
9	9	0.673±0.001
10	10	0.763±0.009
11	12	0.935±0.001

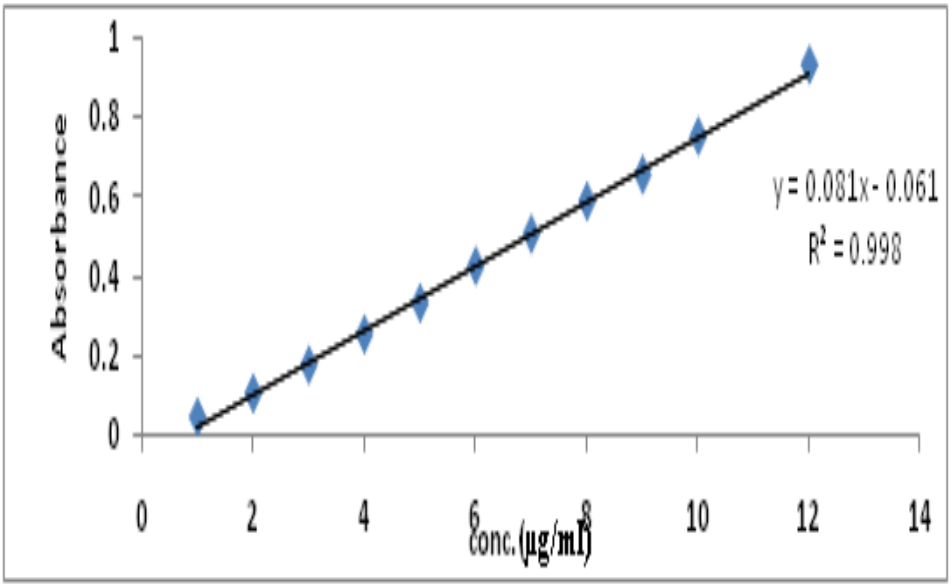

Figure: 1.2 Calibration curve of Piracetam in Methanol

Discussion: at 230 nm. The absorbance of the standard solution of Piracetam at 0-14µg/ml was plotted as absorbance versus concentration which gave a straight line passing from the origin with regression co-efficient 0.9982. So it followed Beer- Lambert's law at the concentration range of 0-14 µg/ml.

COMPATIBILITY

Table7: Compatibility (Drug: Excipient) Ratio

Sr. No.	Ingredients	Initial	1 week	2 week	3 week	4 week
1.	Drug	White fine powder	NC	NC	NC	NC
2.	Drug + Ethyl cellulose	White fine powder	NC	NC	NC	NC
3.	Drug + Povidone K 30	White fine powder	NC	NC	NC	NC
4.	Drug+Magnesium stearate	White fine powder	NC	NC	NC	NC
5.	Drug + + Ethyl cellulose dispersion	White fine powder	NC	NC	NC	NC

Note:-x = 1 if Piracetam

Storage condition: The samples were kept at:-

- 25 ± 3°C / 60 ± 5% RH
- 40 ± 2 °C /75 ± 5% RH
- 55°C

Observations:

The drug-excipient interaction study was carried out using FTIR. The spectral data obtained showed that Piracetam is compatible with all the excipients used in the formulation. Furthermore, no physical interaction with the active pharmaceutical ingredient was observed.

Observations were made after 7, 14, 21 and 28 days. No changes were observed in samples kept at 25 ± 3°C / 60 ± 5% RH and 40 ± 2 °C /75 ± 5% RH.

Evaluation of formulated batches:

Evaluation of blend – The blend prepared for compression of immediate release tablets were evaluated for their flow properties and were found to be as follows.

Table 8: Flow properties of Blends

Formulation Code	Granules : fines	Bulk density	Tapped density	Hausner's Ratio	Angle of Repose (θ)	Carr's Index (%)
B1	70:30	0.555	0.714	1.22	28.56	18.31
B2	70:30	0.465	0.540	1.16	24.87	13.88
B3	80:20	0.571	0.740	1.21	29.49	18.84
B4	80:20	0.454	0.526	1.15	26.15	13.68
B5	80:20	0.465	0.540	1.16	28.13	13.88
B6	90:10	0.512	0.571	1.12	22.50	10.40
B7	60:40	0.434	0.526	1.22	31.02	17.50
B8	70:30	0.526	0.588	1.11	22.48	10.54
B9	75:25	0.526	0.588	1.11	22.45	10.54
B10	75:25	0.512	0.625	1.22	27.75	18.08
B11	80:20	0.488	0.571	1.17	26.38	14.54

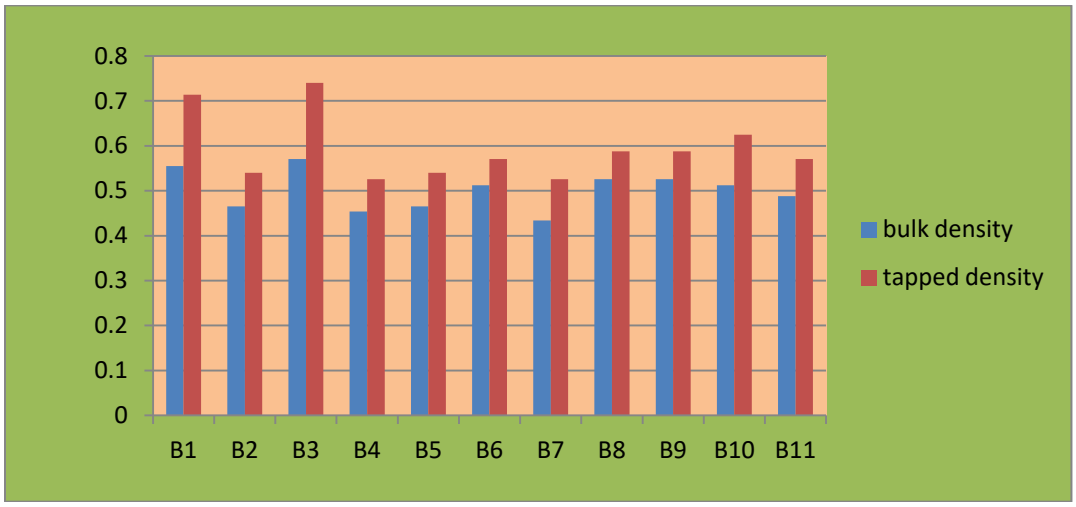

Figure: 1.3 Graph showing Bulk Density, Tapped Density of Various Formulations

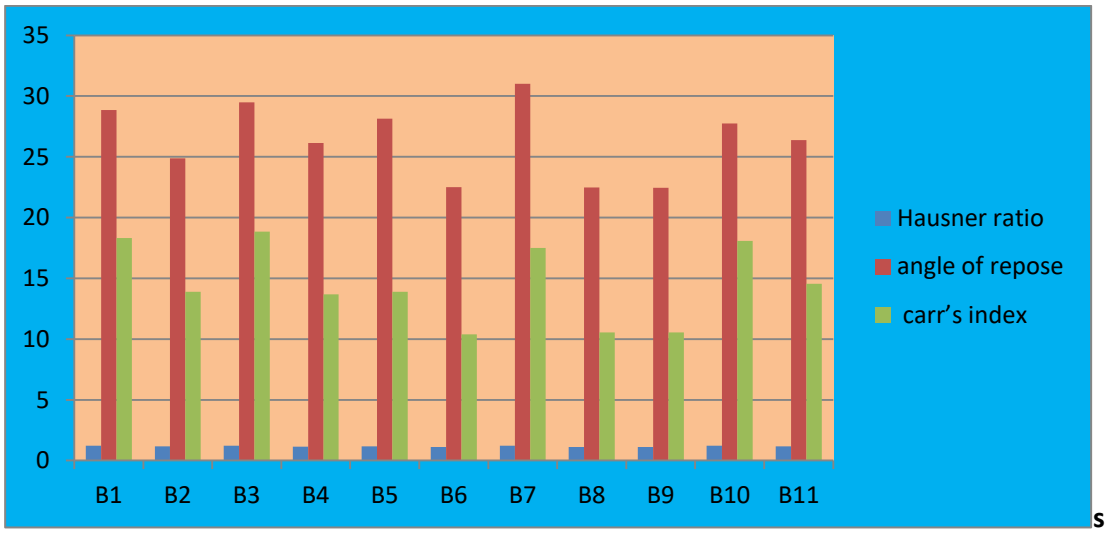

Figure 1.4: Graph showing Carrs's Index, Hausner's Ratio and Angle of

Reposeof Various Formulations

Table 9: Evaluation of Post-Compression Parameters

Formulation Code	Hardness Of tablets* (kg/c2)	Friability Of tablets*(%)	Weight variation (mg)	Percentage Drug content Per tablet*(%)	Thickness Of tablets* (mm)	Disintegration Time (min)*
B_1	12.1	0.65	3	76.70	6.13	11.21
B2	12.3	0.56	4	77.14	6.14	11.01
B3	12.6	0.43	3	80.06	6.21	10.54
B4	12.2	0.48	5	82.34	6.11	10.43
B5	13.0	0.32	2	111.92	6.14	10.42
B6	13.2	0.39	3	109.95	6.17	10.11
B7	12.9	0.41	4	111.02	6.13	9.43
B8	13.5	0.32	3	112.85	6.15	9.32
B9	13/1	0.34	5	107.69	6.14	10.1
B10	13.9	0.36	4	112.82	6.15	9.21
B11	14.0	0.31	3	112.93	6.14	9.31

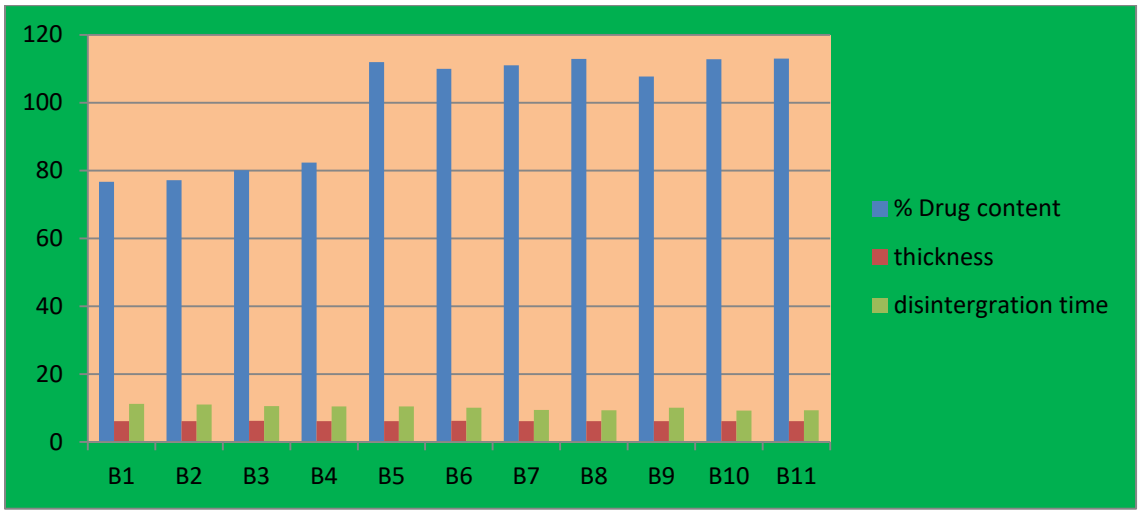

Figure: 1.5 Graph showing Thickness, Drug content and Disintegration time of Various Formulations.

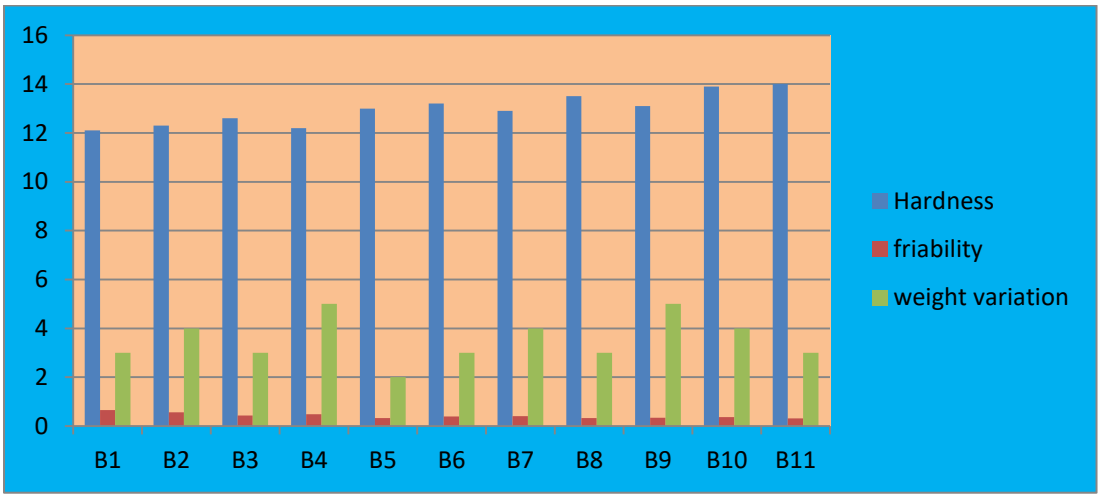

Figure: 1.6 Graph showing Hardness, Friability and Weight Variation of Various Formulations.

Table 10: *In-Vitro* Drug Release Study of Various Formulations.

Formulations	5 Min	10 min	15 Min	20 Min	25 Min	30 Min	35 Min	40 Min	45 Min
B1	40.12	42.45	48.6	53.64	57.32	60.54	64.26	68.04	69.45
B2	42.48	43.69	48.21	55.60	57.05	59.11	64.87	67.88	70.10
B3	53.97	54.30	59.92	61.77	65.23	68.19	70.05	72.44	74.69
B4	50.97	54.36	57.29	61.66	65.08	68.27	70.12	72.21	73.57
B5	54.35	58.96	65.11	72.80	76.00	82.61	87.37	89.03	91.85
B6	56.04	58.41	64.98	72.16	78.80	82.88	87.51	90.81	92.79
B7	57.18	59.99	65.00	74.31	78.19	81.95	87.87	89.01	91.09
B8	55.28	59.03	66.25	73.42	80.17	84.67	88.79	91.77	93.20
B9	52.04	54.41	63.98	68.16	74.80	80.88	84.51	89.81	90.79
B10	55.93	60.10	66.01	73.39	81.27	85.00	89.00	91.76	93.24
B11	54.81	62.37	67.56	72.82	79.92	82.01	84.15	89.70	91.45

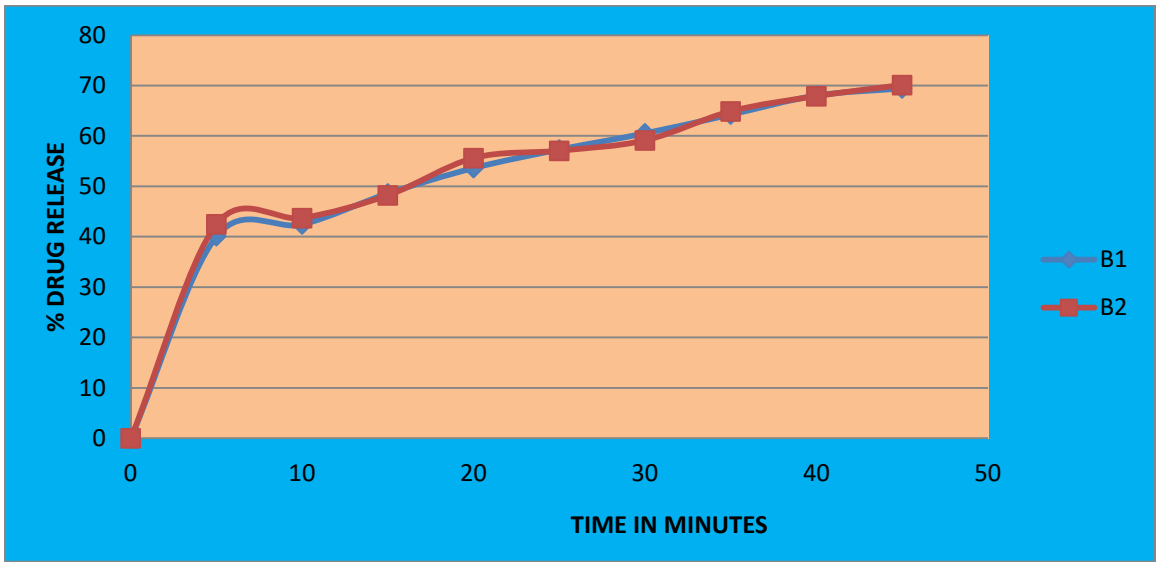

Figure1.7: Dissolution profiles of batchesB1 andB2

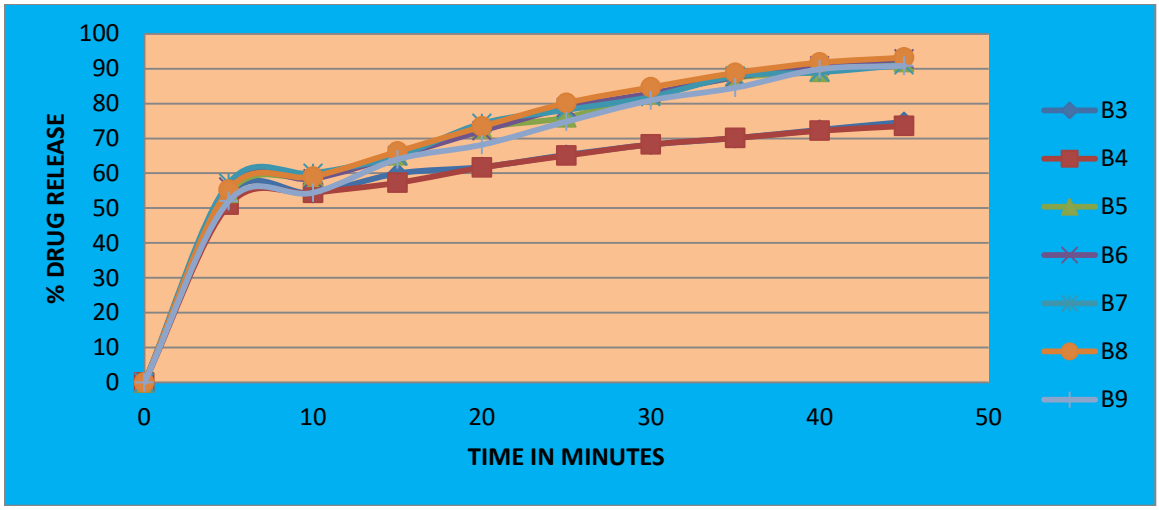

Figure 1.8: Dissolution profiles of batchesB3, B4, B5, B6, B7, B8 and B9.

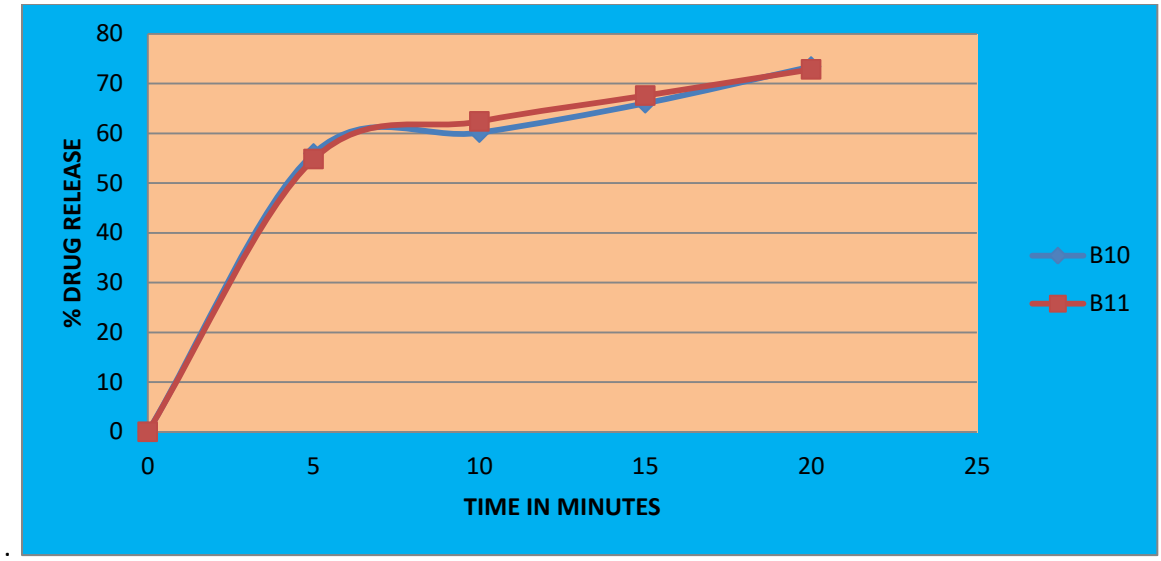

Figure 1.9: Dissolution profiles of scale up batchesG10 and G11

Table 11: Results of Stability Studies of Selected Formulations (B10 and B11).

Formulation B10				Formulation B10		
Time(days)	Hardness	Disintegration Time	% Drug Content	Hardness	Disintegration Time	% Drug Content
0	12.2	11.15	112.85	12.2	11.16	112.95
15	12.2	11.15	112.85	12.2	11.16	112.95
30	12.2	11.15	112.82	12.2	11.16	112.93
45	12.2	11.14	112.82	12.2	11.15	112.93
60	12.2	11.14	112.81	12.2	11.15	112.92

Table 12: In-Vitro Drug Release Study of B10

DAYS	5 Min	10 min	15 Min	20 Min	25 Min	30 Min	35 Min	40 Min	45 Min
0	55.93	59.89	65.91	72.61	80.35	84.55	88.77	92.65	94.20
15	55.65	60.10	66.01	73.39	81.27	85.00	89.00	92.76	94.24
30	55.76	59.06	66.10	71.69	78.99	81.07	86.19	92.04	93.88
45	55.61	58.77	65.34	71.77	79.26	86.19	89.01	90.87	91.91
60	54.87	58.50	64.88	70.84	80.12	83.50	87.20	91.66	93.85

Table 13: In-Vitro Drug Release Study of B11

DAYS	5 Min	10 min	15 Min	20 Min	25 Min	30 Min	35 Min	40 Min	45 Min
0	54.77	61.19	65.97	70.50	76.88	80.80	83.64	88.04	90.40
15	54.81	61.37	66.56	70.82	76.99	81.01	84.15	87.70	90.45
30	53.89	59.79	64.85	67.89	75.30	80.66	84.54	86.03	89.50
45	53.91	60.64	64.70	68.55	75.20	81.12	83.50	86.15	89.88
60	52.77	58.69	63.44	67.10	74.45	81.21	85.09	87.48	89.48

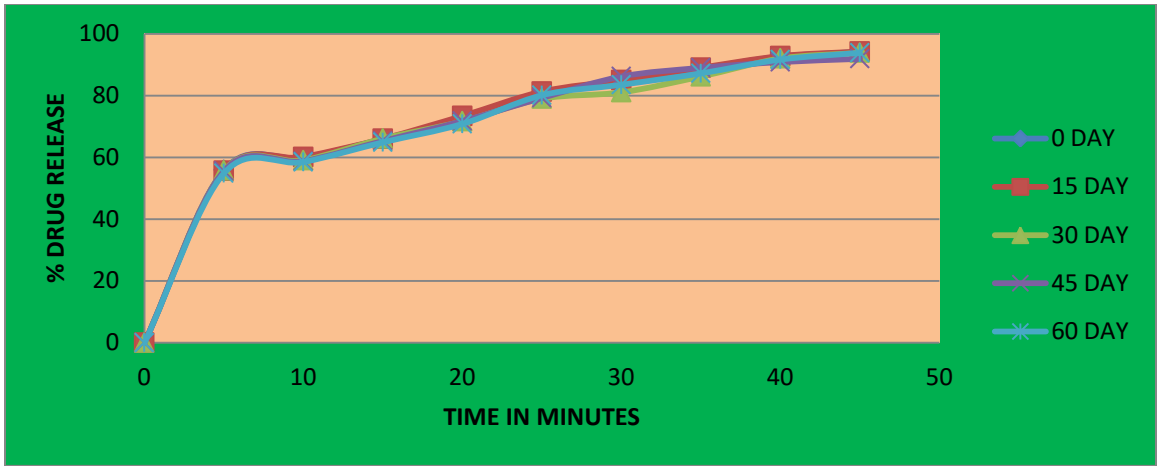

Figure 1.10: In-Vitro Drug Release Study of B10

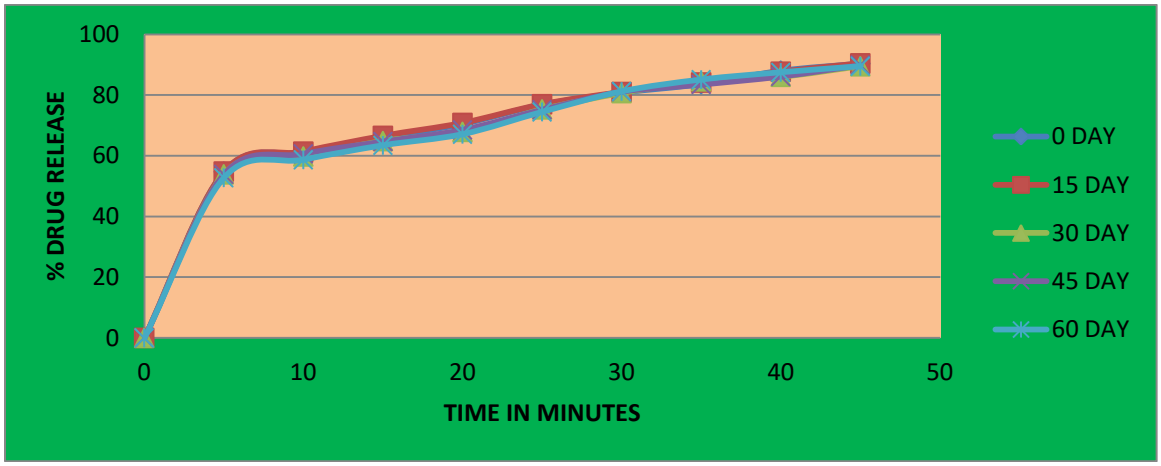

Figure 1.11: In-Vitro Drug Release Study of B11

Discussion:

***In-Vitro* Drug Release: -** B5 to B11 to which was added showed a drug release of more than 89% at the end of 45 min which confirms within the limits given by USP which states that not less than 75% of labeled amount of Piracetam was dissolved within 45 min. B1, B2 showed an in- vitro drug release of 55 to 70% at the end of 45 min which were not acceptable.B10 showed maximum drug release of 93.24%. On considering some important parameters like disintegration time (9.21 min), percentage drug content per tablet (112.85%) ,in vitro drug release (93.24%) and cost factor B10 containing glyceryl behenat as disintegrant was selected as the best formulation.

Later scale up of this formula was done in two batches, out of which one was film coated. B10 showed 93.24% release which was slightly higher than B11 which was film coated. All other parameters of scaled up batches were found to be satisfactory.

CONCLUSION AND SUMMARY:

The formulation of piracetam tablets 800 mg was developed using glyceryl behenate as binder and magnesium stearate as a lubricating agent. The batch was prepared by wet granulation method using RMG. The tablets were film coated for patient compliance. Piracetam tablets was comparable to the reference product for all the physical and chemical parameter. The product was found stable at every stage when hold for the period of 60 day, at controlled room temperature. So, form the above conclusion, the formulation of the piracetam tablets was stable. The present work involves the formulation development,

optimization and in-vitro evaluation of immediate release Piracetam tablets. To minimize critical process parameters and since piracetam is moisture and heat sensitive,wet granulation compression method was selected for the formulation of Immediate release Piracetam tablets. Under the pre formulation studies API characterization and drug excipient compatibility studies were carried out. The API characterization s howed compliance with the drug characteristics. The polymers and other excipients were selected based on the satisfying results produced during drug- excipient compatibility studies to develop the final formulation. The final suitable formulation (B10) was achieved fruitfully by thewet granulation compression technique using glyceryl behenate as binder which exhibited acceptable disintegration time (9,21 min), percentage drug content per tablet (112.85%) and in vitro drug release (93.24%). The best formulation was later subjected to scale up in two batches containing 30,000 tablets each (B10 and B11) which were later subjected to stability studies after packing in amber colored PVC-PVDC blister packing. One batch of scale up was film coated for following reasons. Considering the results of scaled up batches containing pre gelatinized starch as disintegrant it can be concluded that the formulation B10 and B11were meeting the desired in vivo and in vitrocorrelation limits provided by the company.The formula B10 and B11were subjected for cost evaluation and marketing department approval for costing and patient compliance respectively, and a positive feedback was received for formulation B10 and B11. It was also observed that wet granulation method compression was the best suitable method used for producing immediate release tablets Piracetam tablets.

Based on all the above considerations these formulas will be subjected for bio availability studies and if it complies to all the requirement of those studies the same formula will be commercialized. Further improvement in these formulation scan be achieved by optimizing the film coating given to Piracetam tablets.

REFERENCE:

1. Banker GS, Anderson SN. “Modern Pharmaceutics”. 4rd Ed. New York: Taylor & Francis Group; 2005.
2. Allen LV, Nicholas GP, Howard CA. Ansel’s “Pharmaceutical Dosage Forms & Drug Delivery Systems”. 8th Ed. New Delhi: Lippincott Williams & Wilkins; 2005.
3. Rudman A., “Guidance for Industry-Immediate Release Solid Dosage Forms”. CDER 1995 Nov; 59(83): 48754-59.
4. Hayder M. Alkuraishy, Ali I. Algareeb, Ali K. Albuhadilly, Basim M. ALmgoter. “Modulation Effects of Piracetam and Ginkgo biloba on the Cognitive and Working Memory Functions: Psychometric Study” VOLUME: 3 ISSUE: 2Year: 2014Page: [87 - 92]Mansal Denton “Nootropidea” 2017.
5. Kulkarni RS and Behera AL, “Formulation and Evaluation of Immediate Release Tablet of Valsartan”. Int J Pharm Sci Res 2015; 6(2): 808-15.doi: 10.13040/IJPSR.0975-8232.6 (2).808-15.
6. Bhandari Neeraj*, Kumar Abhishek, Choudhary Abhilash, ChoudharyRubia, BalaRajni , “A Review On Immediate Release Drug Delivery System” International Research Journal of Pharmaceutical and Applied Sciences (IRJPAS) 2014; 4(1):78-87
7. Mohalkar Rahul et al, “A Review on Immediate Release Drug Delivery Systems” pharma tutor 2014 2(8); 95-109.
8. Jadhav Santosh B, “Formulation and evaluation of immediate release tablets of Imipramine hydrochloride” International Journal of Biomedical And Advance Research, (2014) 05 (11) page no. 559-564
9. Sonje Abhijit , Yadav Arun “Formulation And Evaluation Of Immediate Release Tablet Of Antihypertensive Drugs According To Bcs System” International Journal of Therapeutic Applications, Volume 7, 2012, 18-
10. Atram SC, Shahi SR, Udavant YK, Salunke RJ, Neb GB, Gulecha BS, “.Formulation of bilayer tablet conatiningmetoprolol succinate and amlodipine besylate as a model drug for antihypertensive therapy”. J Pharmacy Res 2009;2: 1335-47.

11. Kyriacos S, Dimassi H, "Formulation optimization study for an immediate-release tablet". Int J Pharm Compd. 2009 May-Jun;13(3):259-61.

12. Abhay Gupta, Robert L. Hunt, Rakhi B. Shah, Vilayat A. Sayeed, and Mansoor A. Khan "Disintegration of Highly Soluble Immediate Release Tablets: A Surrogate for Dissolution" AAPS Pharm SciTech. 2009 Jun; 10(2): 495–499

13. Daniel Cohen et al "compositions for improving memory performance" WO 2014037412 Shirsand SP, Suresh S, Swamy PV, Kumar DN, Rampure MV. "Design and evaluation of fast dissolving tablets of clonazepam". Int J of Pharm Sci 2008; 17(6): 791-95.