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FORMULATION, DEVELOPMENT AND EVALUATION OF DELAYED RELEASE TABLETS OF ASPIRIN USP

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ABSTRACT

The investigation is undertaken with an aim to formulation, development and evaluation of delayed release tablet of Aspirin. The Assay and Impurity drug were carried out by HPLC method. The drug powders were subjected to Preformulation studies. The Preformulation characteristics are within the Pharmacopeial specifications. The drugs and excipients compatibility were carried out by FT-IR studies and DSC. The spectra showed that there was no interaction between them. The drugs and excipients compatibility were carried out by HPLC method and by physical observation showed that there was no interaction between them. For Aspirin DR tablets direct granulation was method of choice. Optimization was done and it was found that release profile was found to be best with disintegrant i.e. sodium starch glycolate. Enteric coating of Protectab HP-1 Sunset yellow Lake IPA coating 10%w/w was done on Aspirin tablets as to avoid any interaction gastric problems. Results found that release profile of batch no.AF4 matches with Innovator product . The Percentage cumulative drug release of batch. No. AF4 was found at 90 Minutes 104.21%. From results it can be inferred that release profile of Batch. No: AF4matches with that of innovator product, also f1&f2 (62) value are good enough to comply with the innovator's product INNOVATOR have reported similar kind of results for studies with Aspirin.

KEYWORDS: Aspirin, Coronary artery disease, Acute coronary syndrome, Delayed release.

INTRODUCTION

The convenient oral drug delivery has been known for decades is the most widely utilized route of administration among all the routes. It remains the preferred route of administration in the discovery and development of new drug candidates. The popularity of oral route is attributed to patient acceptance, ease of administration, accurate dosing, cost effective manufacturing methods and generally improve the shelf life of the product.[1]. These systems are based on pH dependent drug release mechanism of similar to conventional enteric-coated formulations, but they differ in target site for delivery and therefore type of enteric polymers. Most commonly used polymers are derivatives of acrylic acid and cellulose. These polymers have ability to withstand from low pH end several hours. In pharmaceutical practice several approaches exist for administration of drug to the patient. If the drug is given in conventional dosage form, it has to be administered several times to produce designed therapeutic effect. Because of frequent dosing fluctuation in plasma drug level occur. Fluctuation resulting from the conventional dosage form it minimize by delayed release dosage form. Drug concentration can be controlled within narrow therapeutic range by use delayed release system. The delayed release tablets of Aspirin were prepared by using direct compression method. Different formulations were prepared with varying concentration of disintegrating agent and lubricant and optimized formulation was to be found in this present study. This delayed release of the optimized formulation was expected to increase the bioavailability.

MATERIALS AND METHODS

Materials

Aspirin was received as a gift sample from Caplin Point Research Laboratory. MCC pH-102 was gifted by FMC Bio-polymer (India). Sodium Starch Glycolate was gifted by Chetan & Chetan (India). Purified Talc, Aerosil and Magnesium stearate was gifted by Cabot Sanmer (India).

IMPURITYPROFILE

Single and total impurities present in Active pharmaceutical ingredient (API) were measured by HPLC. The results are shown in Table. No: 10.

ASSAY

In house HPLC based method of assay was developed or both API's. The sample of drug solution was prepared and suitably diluted with mobile phase. Each sample was run and

chromatograms were obtained. The concentration of drug was calculated as

Concentration of sample=Peak area of sample x Concentration of reference standard
Peak area of reference standard

The results are shown in Table. No:10 & Figure. No:2

SPECTRAL IDENTIFICATION [2]

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, to promote the consistent release and bioavailability of the drug and protect it from degradation. Infra red spectroscopy is one of the most powerful analytical techniques to identify functional groups of a drug. In the present study, the potassium bromide disc (pellet) method was employed. Chemical stability was confirmed by IR spectrometry. The results are shown in Figure. No: 3-12.

DIFFERENTIAL SCANNING CALORIMETER STUDIES[3]

The sample of plain drug was scanned in beginning. Than physical mixtures of drug with excipients kept for one month, were scanned. Both the drug was scanned from50 $^{\circ}$C to 250 $^{\circ}$C. The results are shown in Figure. No: 13.

COMPATIBILITY STUDIES[4]

Drug–Excipients compatibility was performed using HPLC method and by physical observation. The results are shown in Table. No: 11-12.

Protocol for drug-excipients compatibility for Aspirin

Table. No: 1 Ratio of Aspirin to Excipients Taken For Compatibility Study

S.No.	Ingredient	Ratio
1	Aspirin	1
2	Aspirin : MCC pH-102	1:1
3	Aspirin : Sodium Starch Glycolate	1:1
4	Aspirin : Purified Talc	1:3
5	Aspirin : Colloidal Silicon Dioxide	1:3
6	Aspirin : Magnesium Stearate	1:3
7	Aspirin : Ethylcellulose	1:0.5
8	Aspirin : Kolicoat maaep-100	1:1
9	Aspirin : Titanium Dioxide	1:0.5
10	Aspirin : Sunset Yellow Lake	1:0.5
11	Aspirin : All Excipients	1:1

INNOVATOR TABLET CHARATERIZATION

Table.no:2 Innovator Tablet Parameters to be Evaluated (Aspirin)

S.NO.	PARAMETERSEVALUATEDFOR
1	Strength
2	Label Claim
3	Tablet Color
4	Tablet Shape
5	Description
6	Dimensions
7	Average Weight
8	Hardness
9	Dissolution Study
10	Uniformity Of Dosage Units
11	Impurity-A
12	Any Other Impurity
13	Total Impurities
14	Assay

The results are shown in Table. No:13-15 & Figure. No: 14

PREFORMULATION STUDIES OF PURE DRUG AND EXCIPIENTS[5-6]

Preformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance. Preformulation yields basic knowledge necessary to develop suitable formulation for the toxicological use. It gives information needed to define the nature of the drug substance and provide frame work for the drug combination with pharmaceutical recipients in the dosage form. Hence, the following Preformulation studies were performed on the obtained sample of drug. The results are shown in Table. No: 16-17.

Manufacturing Procedure

Manufacturing Procedure - Aspirin tablets using direct compression

The corresponding amount of drug (Aspirin) was screened using screen #40, and MCC pH-102 pass through #40, mix well for 3 minutes. Super disintegrant was pass through #80, mix well for 3 minutes. Aerosil was pass through #30 and Magnesium stearate was pass through #60, and then mixed in the poly bag or cage blender for 3 minutes. The mixture was compressed into tablets using an instrumented tablet press with 6mm punches for 100mg weight at 7-8kp hardness and tablets were collected during compression for in-process testing (weight, friability and hardness).

Table. No: 3 Formulation of Aspirin Tablets

Batch. No	AF1	AF2	AF3	AF4
Ingredients	**mg/tablet**			
Aspirin	75	75	75	75
MCC pH-102	20.5	18.5	16.5	14.5
Sodium Starch Glycolate	2	4	6	8
Talc	1	1	1	1
Aerosil	0.5	0.5	0.5	0.5
Magnesium Stearate	1	1	1	1
Total	100mg	100mg	100mg	100mg

Table. No:4 Sub Coating For Aspirin DR Tablets

S.NO	Ingredients	Quantity(mg)
Ingredients	**For One tablet**	
1	Ethylcellulose	2.0
2	Isopropyl Alcohol	Qs
3	Methylene Chloride	Qs

Table. No:5 Enteric Coating For Aspirin DR Tablets

S.NO	Ingredients	Quantity(mg)
Ingredients	**For One tablet**	
1	Kolicoat MAEP – 100	12.0
2	Sunset Yellow Lake	1.2
3	Purified Talc	1.0
4	Titanium Dioxide	1.0
5	Diethyl Phthalate	5.0
6	Isopropyl Alcohol	Qs
7	Methylene Chloride	Qs

Table. No:6 Optimized Parameters for Sub Coating for Aspirin DR Tablets

Conditions	Pre-heating	Coating	Drying
Inlet air temperature (°C)	55-60	60-65	50
Product temperature (°C)	55-60	50-55	55-60
Outlet air temperature (°C)	35-60	55-60	50-55
Spray rate (ml/min)	-	1-1.5	-
Atomizing air pressure (psi)	-	*20*	
Pan speed (rpm)	55-57	55-57	55-57

Table. No:7 Optimized Parameters for Enteric Coating for Aspirin DR Tablets

Conditions	Pre-heating	Coating	Drying
Inlet air temperature (°C)	55-60	60-65	50
Product temperature (°C)	55-60	50-55	55-60
Outlet air temperature (°C)	35-60	55-60	50-55
Spray rate (ml/min)	-	2-3	-
Atomizing air pressure (psi)	-	*30*	
Pan speed (rpm)	55-57	55-57	55-57

POST COMPRESSION PARAMETERS [7-10]

a) Weight Variation Test

Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in the weight of a tablet according to U.S. Pharmacopoeia. The following percentage deviation in weight variation was allowed.

Average weight of a tablet	Percentage deviation
130 mg or less	± 10
>130 mg and <324 mg	± 7.5
324mg or more	± 5

The results are shown in Table. No: 18-20.

b) Tablet Dimensions

Thickness and diameter were measured using calibrated Vernier calipers. Five tablets of each formulation were picked randomly and thickness and diameter was measured individually.
The results are shown in Table. No: 18-20.

c) Thickness

The thickness of the tablets was determined by Vernier calipers. Five tablets from each batch were used and the average values were calculated. The results are shown in Table. No: 18-20.

d) Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Five tablets were randomly picked and hardness of the tablets was determined. The results are shown in Table. No: 18-20.

e) Friability test

The friability of tablets was determined by using Roche friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed (Wt) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100revolutions. The tablets were weighed again (WF). The % friability was then calculated by-

$$\%F = \frac{W\ (initial)-W\ (final)}{W\ (initial)} \times 100$$

The results are shown in Table. No: 18-20.

f) Disintegration test

The disintegration time for immediate release layer was determined using the disintegration apparatus. One tablet was placed in each of six tubes placed in a beaker containing 1000 ml of purified water maintained at 37 ± 20 C and the apparatus was operated. The time taken for the tablets to disintegrate and pass through the mesh was noted. The results are shown in Table. No: 18-20.

METHOD OF ANALYSIS [11--15]

IN-VITRO DISSOLUTION STUDIES

Apparatus: Dissolution Apparatus USP Type II (Basket)

Medium: 0.1N Hydrochloric acid

Volume: 1000mL

Speed: 100 RPM

Time: 2 Hours.

Time intervals: 30 Minutes, 1 & 2 Hours.

Temperature: 37 ± 0.5°C.

Chromatographic Conditions

Apparatus: High Performance Liquid Chromatography system (HPLC)

Column: C18, 150 × 4.6, 5µ (Inertsil)

Wavelength: 265nm

Detector: UV/PDA

Injection volume: 20µl.

Flow rate: 1.0ml/min

Sample cooler temp. : 30°C

Run Time **:** 10 minutes

Elution **:** Isocratic

Calculations

From the Standard and Sample Chromatogram, calculated the percentage of the labeled amount of Aspirin (C9H8O4) percentage release of the Tablets taken by the following formula,

Dissolution of Aspirin in mg/tablet

$$= \frac{\text{SPL Area}}{\text{STD Area}} \times \frac{\text{STD wt in mg}}{100} \times \frac{5}{50} \times \frac{1000}{1\ \text{Tablet}} \times \frac{99.85}{100} \times \frac{1}{100} \times 100$$

The results are shown in Table. No:21 Figure. No: 17.

ASSAY

Apparatus : Dissolution Apparatus USP Type I (Paddle)

Medium : Buffer pH-6.8

Volume : 1000mL

Speed : 100 RPM

Time: 90 Minutes.

Time intervals: 15, 30, 45, 60 & 90 Minutes.

Temperature: 37 ± 0.5°C.

Chromatographic Conditions

Apparatus: High Performance Liquid Chromatography system (HPLC)

Column: C18, 150 × 4.6, 5µ (Inertsil)

Wavelength: 265nm

Detector: UV/PDA

Injection volume: 20µl.

Flow rate: 1.0ml/min

Sample cooler temp.: 30°C

Run Time: 15 minutes

Elution: Isocratic

Calculations

From the Standard and Sample Chromatogram, calculated the percentage of the labeled amount of Aspirin (C9H8O4) percentage release of the Tablets taken by the following formula,

Dissolution of Aspirin in mg/tablet

$$= \frac{\text{SPL Area}}{\text{STD Area}} \times \frac{\text{STD wt in mg}}{100} \times \frac{5}{50} \times \frac{1000}{1\ \text{Tablet}} \times \frac{99.75}{100} \times \frac{1.305}{100} \times 100$$

The results are shown in Table. No:22-25 &Figure. No: 18-19.

ASSAY

Chromatographic Conditions

Apparatus: High Performance Liquid Chromatography system (HPLC)

Column: C18, 150 × 4.6, 5µ (Inertsil)

Wavelength: 265nm

Detector: UV/PDA

Injection volume: 20µl.

Flow rate: 1.0ml/min

Sample cooler temp.: 30°C

Run Time**:** 10 minutes

Elution**:** Isocratic

Calculations

From the Standard and Sample Chromatogram, calculated the percentage of the labeled amount of Aspirin percentage release of the Tablets taken by the following formula,

Assay of Aspirin in mg/tablet

$$= \frac{\text{SPL Area}}{\text{STD Area}} \times \frac{\text{STD wt in mg}}{100} \times \frac{5}{50} \times \frac{100}{\text{SPLwt}} \times \frac{50}{5} \times \frac{99.76}{100} \times \frac{1}{100} \times 100$$

The results are shown in Table. No:24.

STABILITY STUDIES [16-18]

Stability testing forms an integral part of formulation development. It is important to assess the effect of temperature and humidity on stability of drug and in-vitro drug release rate. It helps to generate information for predicting the shelf life of the product and recommended storage conditions. Stability data is required to be submitted as part of the dossier submitted to the regulatory agencies.

Protocol For stability studies

Formulation was selected on the basis of in-vitro drug release profile which was comparable to that of the DR formulation under reference i.e. optimized formula for both Aspirin batches.

Optimized formula Batch.no:AT4for Aspirin DR(75mg),in Alu Blister Pack.

The conditions for stability are as mentioned in Table. No: 8

Table. No:8 Stability Condition for Aspirin Tablet

Study	Storage condition	Time Period Covered
Room Temperature (RT)	25℃ ± 2℃/60%RH± 5%RH	3months **Testing :**If accelerated condition tablet is passed
Accelerated	40℃ ± 2℃/75%RH± 5%RH	3 months Testing:1,2,3month

These were evaluated for their physicochemical characteristics, drug content, assay and in-vitro release profile of Aspirin Tablet. In–vitro release and content of active ingredients was estimated at one month interval during to rage period. The results are shown in Table. No:26-27 & Figure. No: 20-2

RESULT AND DISCUSSION

Table.no: 9 Standard Calibration Curve of Aspirin

S.No	Concentration in ppm	Area
1	10	25.8885
2	20	54.8114
3	50	140.4123
4	100	298.1254
5	120	375.2312
6	160	497.0895
7	200	607.1886

*Mean±SD n=3

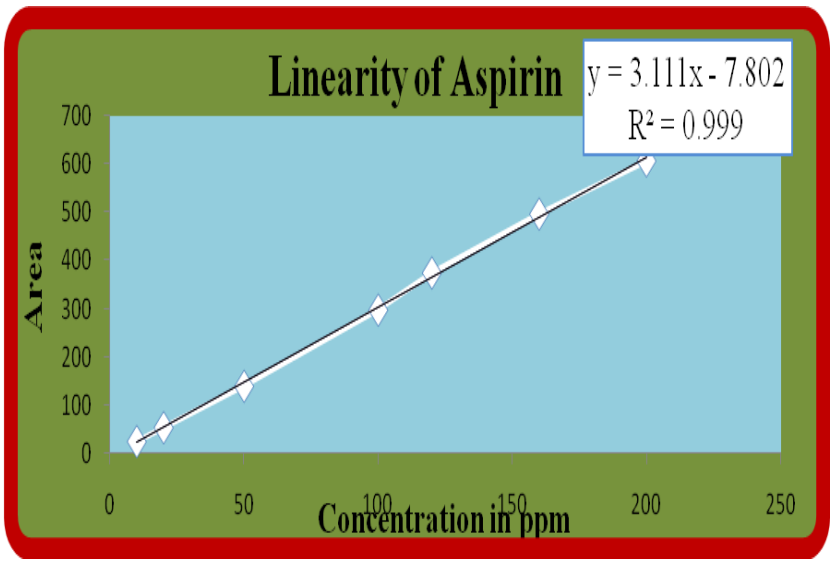

Figure.no: 1 Standard Calibration Curve of Aspirin

Table. No:10 Impurity Profile and Assay of Aspirin API

Impurity A	0.05%
Impurity B	Not Detected
Impurity C	Not Detected
Impurity D	0.06%
Any Other Impurity	Not Detected
Total Impurity	0.25%
Assay	99.85%
Conversional factor	1

*Mean±SD (n=6)

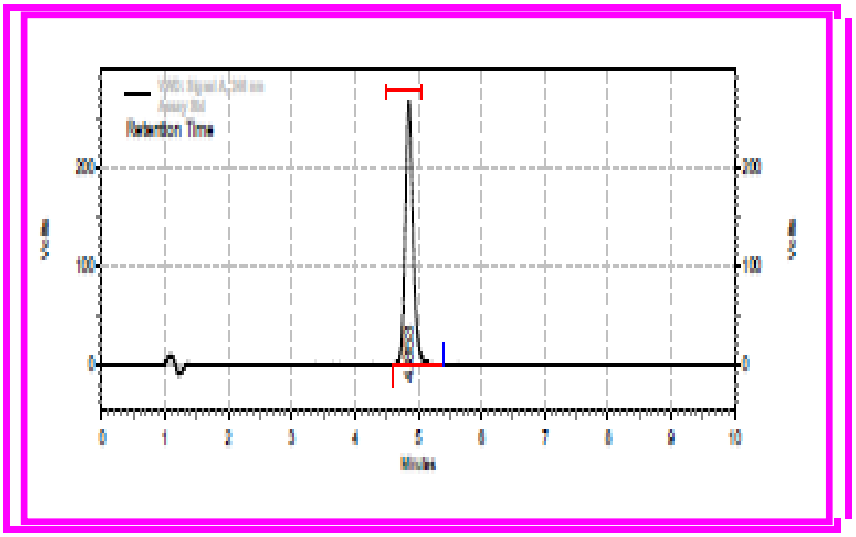

Figure. No: 2 Aspirin Assay Chromatogram

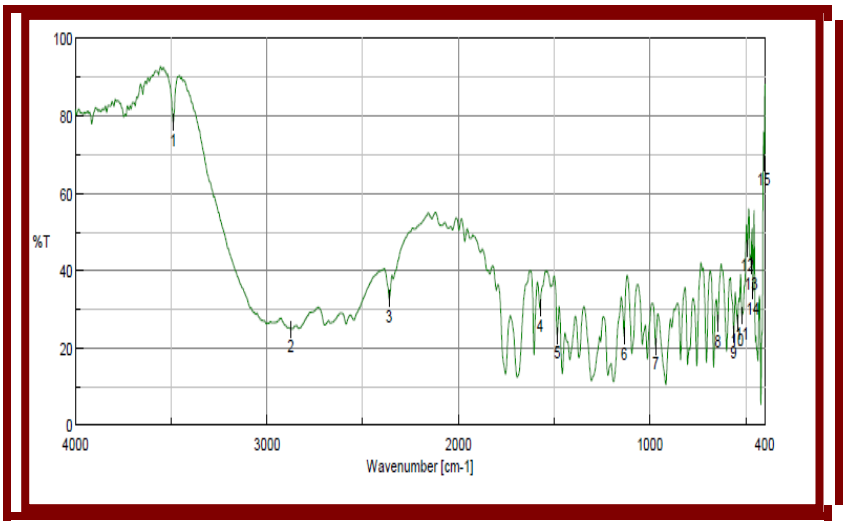

Figure.No:3 FTIR Spectrum of Aspirin Pure

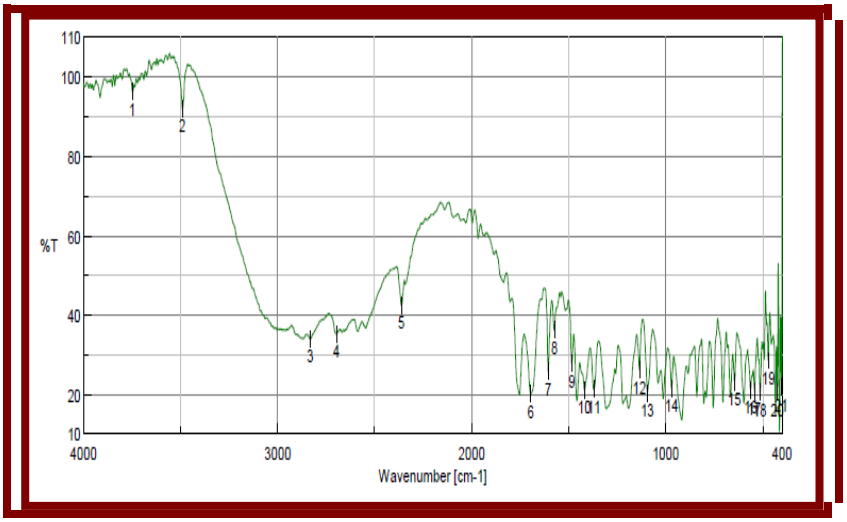

Figure. No:4 FTIR Spectrum of Aspirin + MCC pH-102

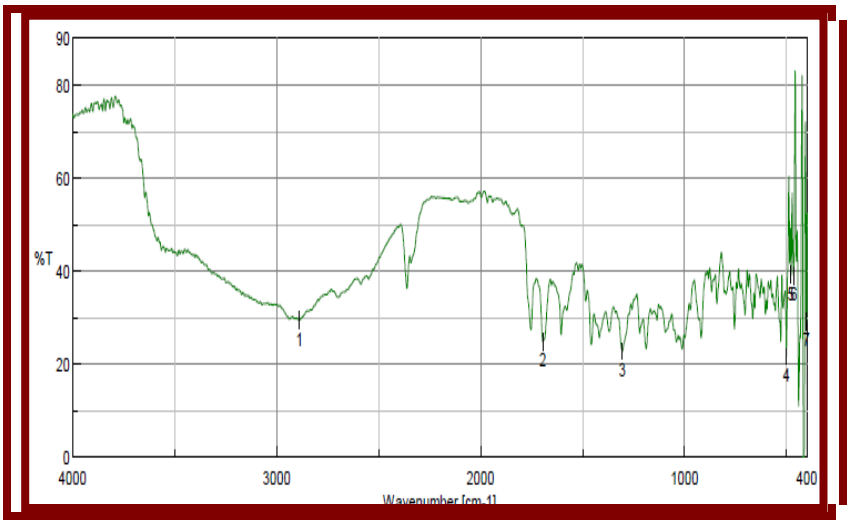

Figure.No: 5 FTIR Spectrum of Aspirin + Sodium Starch Glycolate

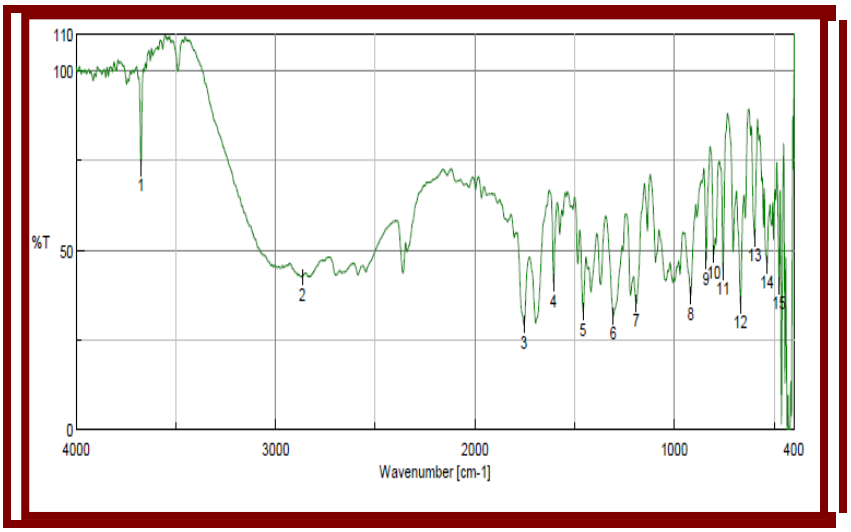

Figure.No:6 FTIR Spectrum of Aspirin + Purified Talc

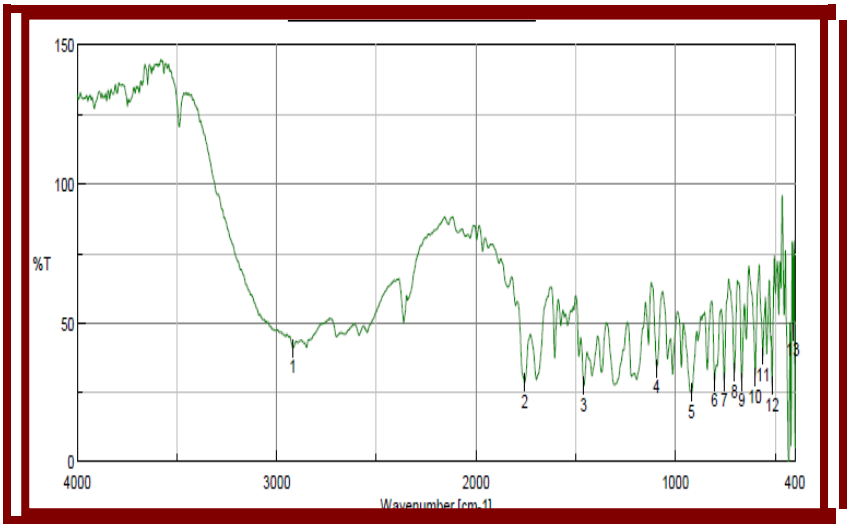

Figure.No:7 FTIR Spectrum of Aspirin + Aerosil

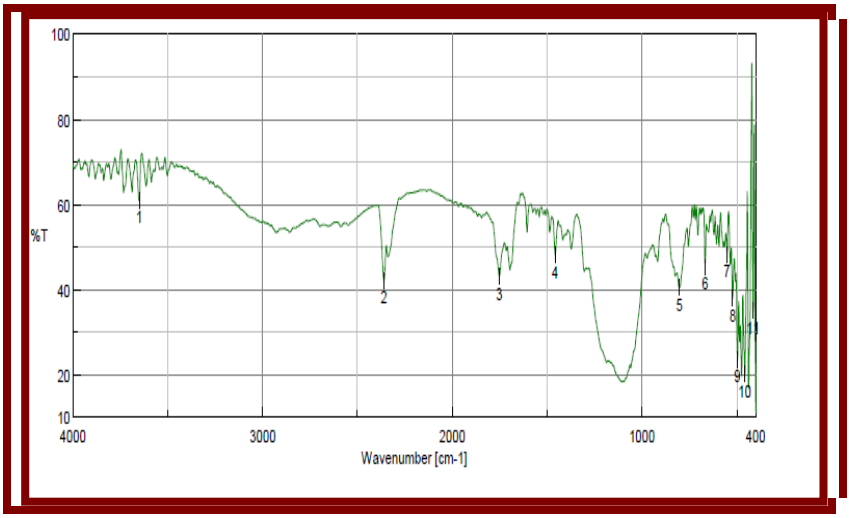

Figure.No:8 FTIR Spectrum of Aspirin + Magnesium Stearate

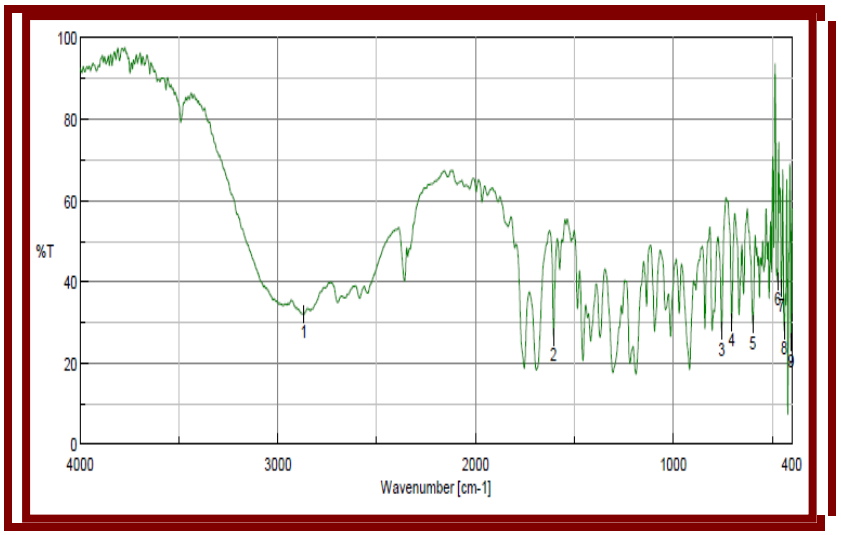

Figure.No:9 FTIR Spectrum of Aspirin + Ethyl Cellulose

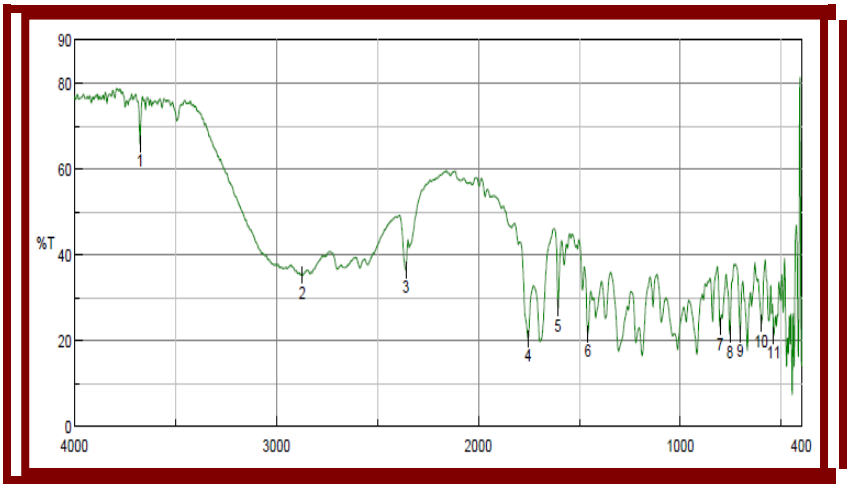

Figure.No:10 FTIR Spectrum of Aspirin + Enteric Coating polymer

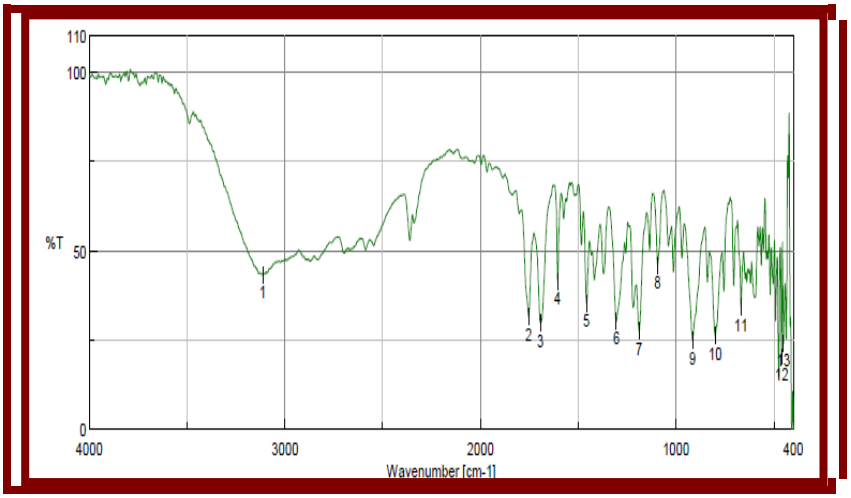

Figure.No:11 FTIR Spectrum of Aspirin + Colure

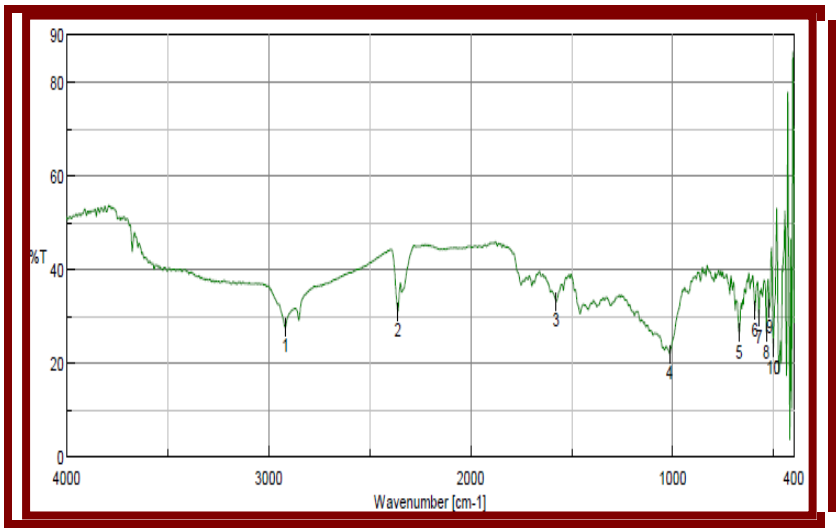

Figure.No:12 FTIR Spectrum of Aspirin + All excipients (Tablet)

DIFFERENTIAL SCANNINGCALORIMETERSTUDIES

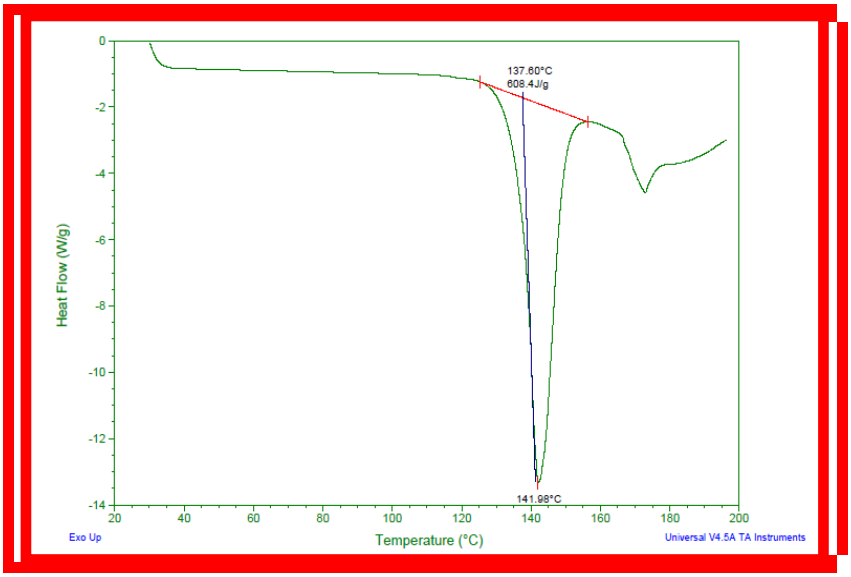

Figure.No: 13 DSC Graph of Aspirin

DISCUSSION: From this figure. No:13 it can be seen that peak value of Aspirin was found to be 141.98°C in DSC thermogram. This value matches with that given in the literature and confirm the purity of API.

Table. No:11 Compatibility study of Aspirin with Excipients The RS Data of Aspirin (By HPLC) of 1 month excipients Compatability @ 40°C-75% RH

S.No.	Ingredient	Ratio	Related substances %w/w
1	Aspirin	1	0.10
2	Aspirin : MCC pH-102	1:1	0.12
3	Aspirin : Sodium Starch Glycolate	1:1	0.14
4	Aspirin : Purified Talc	1:3	0.18
5	Aspirin : Colloidal Silicon Dioxide	1:3	0.19
6	Aspirin : Magnesium Stearate	1:3	0.18
7	Aspirin : Ethylcellulose	1:0.5	0.16
8	Aspirin : Kolicoat MAEP-100	1:1	0.17
9	Aspirin : Titanium Dioxide	1:0.5	0.14
10	Aspirin : Sunset Yellow Lake	1:0.5	0.13
11	Aspirin : All Excipients	1:1	0.19

*Mean±SD (n=6)

Discussion: From this table. No:11 it can be seen the Aspirin is compatible with all the excipients used in the study.

Table. No: 12 Compatibility study of Aspirin with Excipients The RS Data of Aspirin (By HPLC) of 1 month excipients Compatability @ 40°C-75% RH

Ingredient	Ratio	Description		
		Related substance %w/w	1 Month 25°C/60 %RH	1 Month 40°C/75 %RH
Aspirin	1	White to pale yellow, granular powder	*	*
Aspirin : MCC pH-102	1:1	White to pale yellow, granular powder	*	*
Aspirin : Sodium Starch Glycolate	1:1	White to Grayish white, granular FF powder	*	*
Aspirin : Purified Talc	1:3	White to pale yellow, granular powder	*	*
Aspirin : Colloidal Silicon Dioxide	1:3	White to pale yellow, granular powder	*	*
Aspirin : Magnesium Stearate	1:3	White to pale yellow, granular powder	*	*
Aspirin : Ethylcellulose	1:0.5	White to pale yellow, granular powder	*	*
Aspirin : Kolicoat maaep-100	1:1	White to pale yellow, granular powder	*	*
Aspirin : Titanium Dioxide	1:0.5	White to pale yellow, granular powder	*	*
Aspirin : Sunset Yellow Lake	1:0.5	White to Grayish white, granular FF powder	*	*
Aspirin : All Excipients	1:1	White to pale yellow, granular powder	*	*

Result: * Indicated That No Change Was Observed

ASPIRIN INNOVATORTABLET CHARACTERIZATION

Table.no: 13Aspirin Innovator Tablet Characterization

Brand Name	INNOVATOR (75mg)
Strength	75mg TABLET
Label Claim	Each tablet contains Aspirin 75 mg
Tablet Color	Sunset Yellow Colour
Tablet Shape	Round Shape
Description	Debbosed with ‘z‘ on one side& ‘sz’ on other side, Enteric Coated Tablets
Dimensions	**DIAMETER:**5.69-5.72mm **THICKNESS**: 3.40- 4.48mm
Average Weight	122.23mg
Hardness	6-7kp
Uniformity of Dosage Unit	**MEAN: 102.12** **SD: 1.8** **RSD: 1.8**
Assay	102.14% (76.12mg/Tablet)

*Mean±SD (n=6)

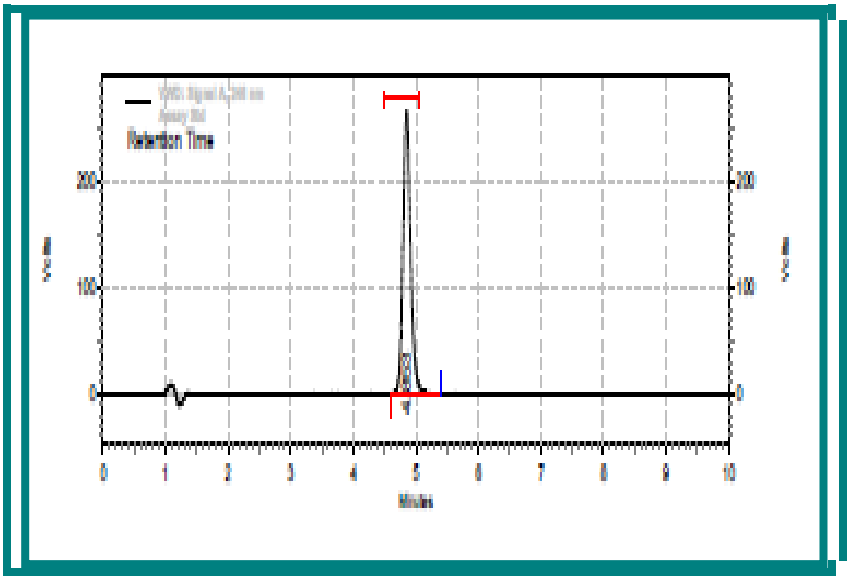

Figure. No:14 Assay chromatogram of the Aspirin Innovator (pH-6.8 Phosphate buffer)

Table. No:14 Dissolution profile of the Aspirin Innovator Tablet (0.1N Hydrochloric acid)

Dissolution Media (1000mL Media, at 100RPM)	Number of Units Used 6	Percentage of Drug Dissolved in Minutes		
		30	60	120
0.1 N Hydrochloric acid	Mean	0	0.75	1.2
	±SD	0	0	0
	±RSD	0	0	0

*Mean±SD (n=6)

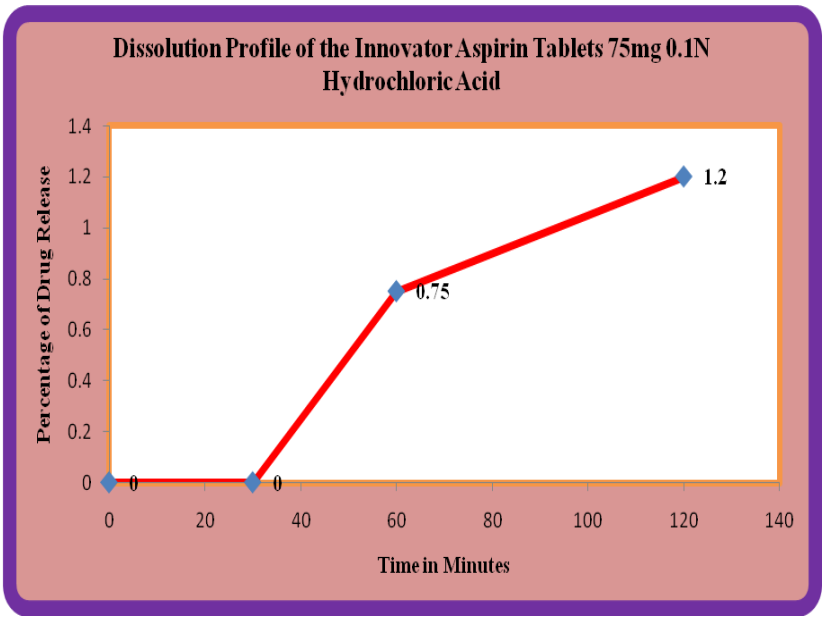

Figure. No: 15 Dissolution Profile of the Innovator Aspirin Tablets 75mg 0.1N Hydrochloric Acid

Table. No: 15 Dissolution Profile of the Aspirin Innovator Tablets 75mg (pH-6.8 Phosphate Buffer)

Dissolution Media (1000mL Media, at 100RPM)	Number of Units Used 6	Percentage of Drug Dissolved in Minutes				
		10	30	45	60	90
Phosphate Buffer pH-6.8	Mean	17.79	67.98	86.43	97.67	102.14
	±SD	1.6	1.7	1.6	1.7	1.8
	±RSD	1.6	1.7	1.6	1.7	1.8

*Mean±SD (n=6)

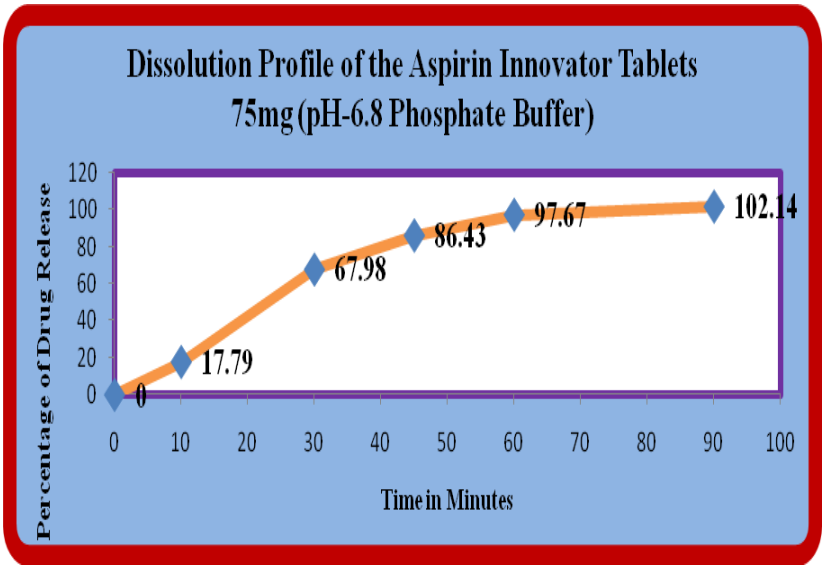

Figure. No: 16 Dissolution Profile of the Aspirin Innovator Tablets 75mg (pH-6.8 Phosphate Buffer)

Discussion: From this figure. No:16 it can be seen that amount of Aspirin DR dissolved in 10 & 90 Minutes is NLT 75% respectively. So, the above criteria as acceptance limit.

Table.No 16 Preformulation Study of Pure Drug (Aspirin).

S.NO.	Parameters	Result	Conclusion
1	Bulk Density*	0.765 gm/ml	------
2	Tapped Density*	0.675 gm/ml	-----
3	Angle of Repose*	18.61	Excellent
4	Carr's Index*	11 %	Excellent Flow
5	Hausner Ratio*	1.21	Better Flow
6	Melting Point*	135^0 C	----
7	Solubility*	Slightly soluble in water, freely soluble in ethanol	

*Mean±SD (n=6)

Table No 17 Preformulation Study of the blend (ASPIRIN)

Batch Code	Bulk Density*	Tapped Density*	Angle of repose*	% Compressibility*	Hausner Ratio*	Loss on Drying*
AF1	0.41	0.47	24.58	12.76	1.15	1.9
AF2	0.44	0.52	25.91	15.38	1.18	1.8
AF3	0.45	0.51	26.86	13.72	1.16	1.6
AF4	0.46	0.53	24.75	13.24	1.15	1.4

*Mean±SD (n=6); The physical parameters of drug as well as blends concluded that these were considerably good to formulate the tablet using direct compression technique.

Table No: 18 Evaluations of Aspirin Core-Tablets

Batch No	Weight variation (mm)**	Diameter (mm)*	Thickness (mm)*	Hardness (kg/cm^2)*	Friability (%)	Disintegration Time*
AF1	103±6.5	5.29±0.01	3.22±0.04	3.35±0.18	0.24	53 seconds
AF2	104±6.5	5.38±0.02	323±0.03	3.41±0.19	0.29	47 seconds
AT3	104±5.6	5.29±0.02	3.24±0.02	3.35±0.17	0.26	49 seconds
AT4	104±6.5	5.37±0.03	3.35±0.04	3.37±0.17	0.29	51 seconds

*Mean±SD (n=6) **Mean±SD (n=20)

Table No: 19 Evaluation of Aspirin Enteric Coated-Tablets (0.1 N Hydrochloric acid)

Batch No	Weight variation (mm)**	Diameter (mm)*	Thickness (mm)*	Hardness (kg/cm^2)*	Disintegration Time*
AF1	112±6.4	5.89±0.01	3.82±0.03	4.15±0.21	0 seconds
AF2	113±7.5	5.88±0.02	383±0.04	4.18±0.20	0 seconds
AT3	112±6.6	5.83±0.02	3.84±0.04	3.75±0.14	0 seconds
AT4	114±7.5	5.87±0.01	3.85±0.05	3.87±0.13	0 seconds

*Mean±SD (n=6) **Mean±SD (n=20)

Table No: 20 Evaluation of Aspirin Enteric Coated-Tablets (pH-6.8 phosphate buffer)

Batch No	Weight variation (mm)*	Diameter (mm)*	Thickness (mm)*	Hardness (kg/cm^2)*	Disintegration Time
AF1	112±6.4	5.89±0.01	3.82±0.03	4.15±0.21	2 mts 23 sec
AF2	113±7.6	5.88±0.02	383±0.04	4.18±0.20	2 mts 34 sec
AT3	112±6.6	5.83±0.02	3.84±0.04	3.75±0.14	2 mts 42 sec
AT4	114±7.5	5.87±0.01	3.85±0.05	3.87±0.13	2 mts 53 sec

*Mean±SD (n=6) **Mean±SD (n=20)

Table.No:21 Dissolution Profile of the Aspirin DR Tablet AT1-AT4 with Innovator (0.1N Hydrochloric acid)

% Cumulative Amount of Drug Release					
Time (Minutes)	**AF1**	**AF2**	**AF3**	**AF4**	**INNOVATOR**
30	0	0	0	0	0
60	0.58	0.56	0.55	0.54	0.72
90	0.96	0.97	0.98	0.96	1.2

*Mean±SD (n=6)

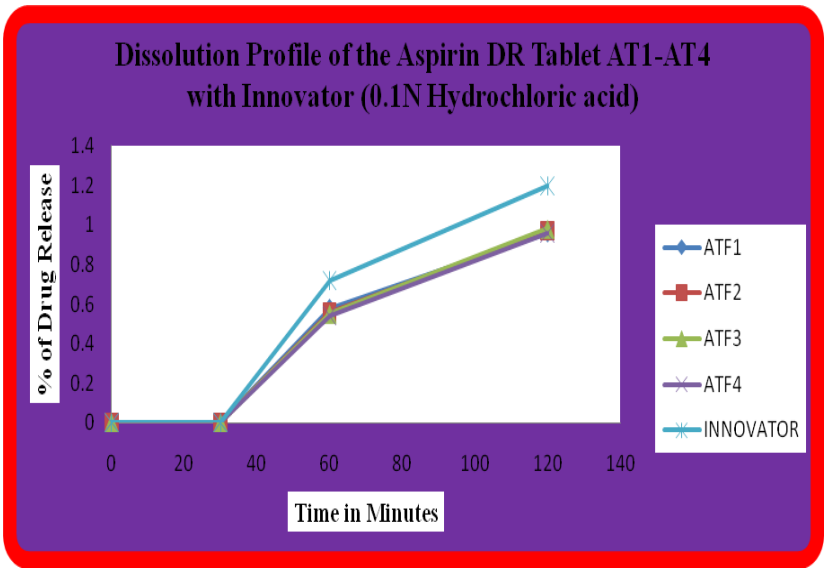

Figure. No :17 Dissolution Profile of the Aspirin DR Tablet AT1-AT4 with Innovator (0.1N Hydrochloric acid)

Table.No:22 Dissolution Profile of the Aspirin DR Tablet AT1-AT4 with Innovator (PHOSPHATE BUFFER pH-6.8)

% Cumulative Amount of Drug Release					
Time (Minutes)	**AF1**	**AF2**	**AF3**	**AF4**	**INNOVATOR**
10	14.13	14.36	14.78	15.12	17.79
30	50.45	52.34	54.67	69.12	67.98
45	72.35	74.67	77.78	89.13	86.43
60	91.87	93.87	95.57	99.89	97.67
90	93.89	95.98	98.43	104.21	102.14

*Mean±SD (n=6)

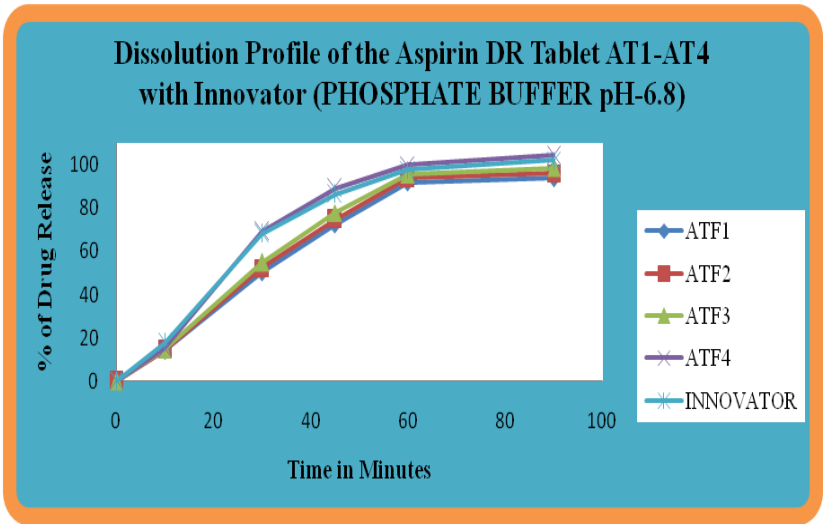

Figure. No: 18 Dissolution Profile of the Aspirin DR Tablet AT1-AT4 with Innovator (PHOSPHATE BUFFER pH-6.8)

Table.No:23 Dissolution Profile of the Aspirin DR Tablet Optimized Formulation of AT4 with Innovator (PHOSPHATE BUFFER pH-6.8)

% Cumulative Amount of Drug Release		
Time (Minutes)	**AF4**	**INNOVATOR**
10	15.12	17.79
30	69.12	67.98
45	89.13	86.43
60	99.89	97.67
90	104.21	102.14

*Mean±SD (n=6)

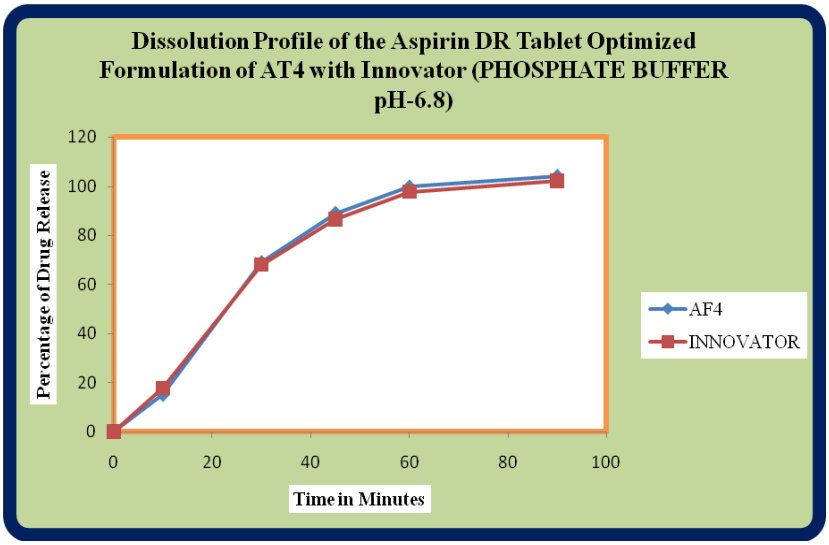

Figure. No:19 Dissolution Profile of the Aspirin DR Tablet Optimized Formulation of AT4 with Innovator (PHOSPHATE BUFFER pH-6.8)

Discussion: From table. No:22 & figure. No:18, it can be seen that the variation of concentration of Super disintegrant is affecting the release in same proportion. Different approaches were tried in batches AF4 it was found with single disintegrants at higher concentration showing good release pattern. AF4 shows a similar release profile to that of the Innovator with f2 value of 62. From the above results it is seen that Batch AT4 is showing best f2 & f1 value. From Fig.No:19 it can be inferred that release profile of Batch AF4 matches with that of innovator product, also f1&f2 values shown in Table.No:23 are good enough to comply with the innovator's product Deplatt have reported similar kind of results for studies with Aspirin.

ASSAY AND CONTENT UNIFORMITY FOR ASPIRIN

Content Uniformity	Aspirin Optimized AF4 (ALU BLISTER PACK)		
	Mean	SD	RSD
	102.46	1.6	1.6

*Mean±SD (n=6)

Table. No:24 Assay of the Aspirin

Tablet (Batch No)	% of Drug Release*	Content uniformity**
AF4	104.21	101.177±0.478
INNOVATOR	102.14	100.674±0.453

*Mean±SD (n=6) ***Mean=Not less than 75% ; **Mean = Not less than 80%**

Table. No:25 Dissolution Profile of the Aspirin DR Innovator with AT4

Dissolution Media (1000mL Media, at 100RPM)	Number of Units Used 6	Percentage of Drug Dissolved in Minutes				
		10	30	45	60	90
INNOVATOR Phosphate Buffer pH-6.8	Mean	17.79	67.98	86.43	97.67	102.14
	±SD	1.6	1.7	1.6	1.7	1.8
	±RSD	1.6	1.7	1.6	1.7	1.8
AT4 Phosphate Buffer pH-6.8	Mean	15.12	69.12	89.12	99.89	104.21
	±SD	1.7	1.7	1.8	1.8	1.9
	±RSD	1.7	1.6	1.8	1.8	1.9

*Mean±SD (n=6)

STABILITY STUDIES

Table. No:26 Stability Studies Data of the Aspirin Optimized Formulations (AF4) (ALU BLISTER PACK)

Parameters	Initial	1st Month		2nd Month		3rd Month	
		RT	40°C	RT	40°C	RT	40°C
Weight variation (mm)**	114±7.5	113.5±7.3	113.5±7.2	113.5±7.3	113.5±7.1	113.5±7.3	113.5±6.9
Diameter (mm)*	5.87±0.01	5.85±0.26	5.85±0.24	5.85±0.26	5.85±0.23	5.85±0.26	5.85±0.21
Thickness (mm)*	3.85±0.05	3.83±0.21	3.83±0.18	3.83±0.21	3.83±0.18	3.83±0.21	3.83±0.18
Hardness (kg/cm2)*	3.87±0.13	3.84±0.11	3.84±0.08	3.84±0.11	3.84±0.08	3.84±0.11	3.84±0.04
Disintegration Time*	2 mts 53 sec	2 mts 47 sec	2 mts 34 sec	2 mts 47 sec	2 mts 30 sec	2 mts 47 sec	2 mts 25 sec

*Mean±SD (n=6) **Mean±SD(n=20)

Table. No:27 Stability Studies Data Assay & Dissolution of the Aspirin Optimized Formulations (AF4) With INNOVATOR (ALU BLISTER PACK) &

Parameters	Initial	1st Month		2nd Month		3rd Month	
		RT	40°C	RT	40°C	RT	40°C
*Assay	101.177 ±0.478	101.128 ±0.468	101.101 ±0.418	101.128 ±0.453	101.091 ±0.418	101.128 ±0.447	101.065 ±0.389
*INNOVATOR (Assay)	100.674 ±0.453	100.556±0.454		100.574±0.483		100.574±0.453	
*% of Cumulative Release	104.21	103.89	103.29	103.65	102.79	103.56	102.49
*INNOVATOR (% of Cumulative Release)	102.14	102.22		101.98		102.09	

*Mean±SD (n=6)

Discussion: Assay*Mean=Not less than 75% ; DissolutionMean = Not less than 80%.** The results indicated that the, optimized formulated tablets were within the Pharmacopeial specifications.

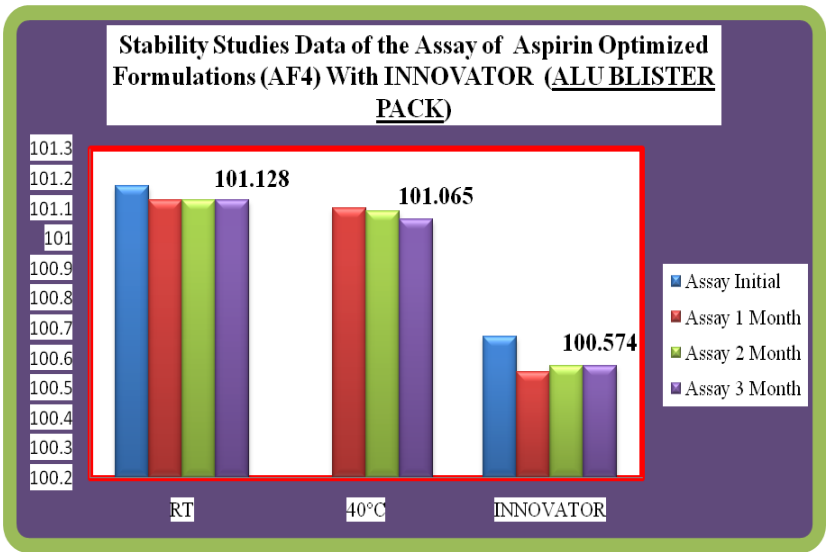

Figure. No:20 Stability Studies Data of the Assay of Aspirin Optimized Formulations (ATF7) With INNOVATOR

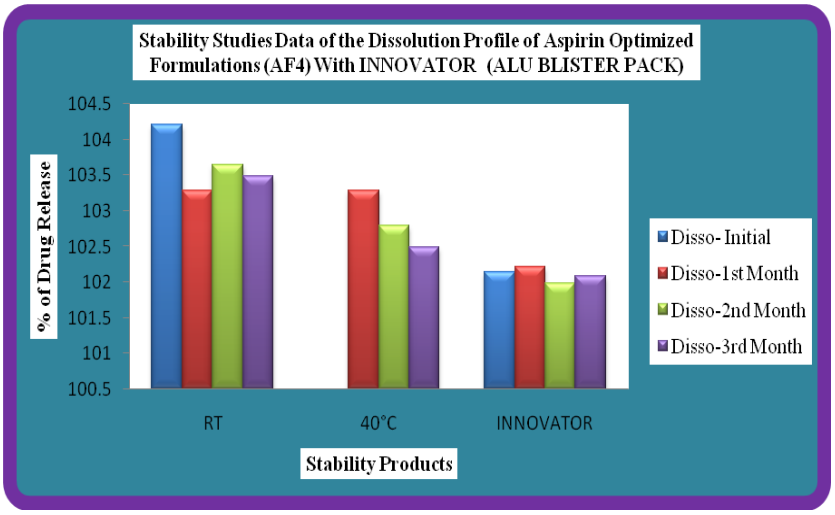

Table. No:21 Stability Studies Data of the Dissolution Profile of Aspirin Optimized Formulations (AF4) With INNOVATOR (ALU BLISTER PACK)

Discussion: From Table and Figure , it was seen that Aspirin DR Tablets Batch. No: AT4, was showing good stability for three months accelerated condition @ 40°C &75%RH. It was found that dissolution and assay value are not affected for the batch, and total impurity is also less than 1%.

SUMMARY AND CONCLUSION

The research work was aimed with formulation, development and evaluation of delayed release tablet of Aspirin. The Assay and Impurity drug were carried out by HPLC method.The drug powders were subjected to Preformulation studies. The Preformulation characteristics are within the Pharmacopeial specifications. The Preformulation studies were carried out and the results were found to be satisfactory. The drugs and excipients compatibility were carried out by FT-IR studies and DSC. The spectra showed that there was no interaction between them. The drugs and excipients compatibility were carried out by HPLC method and by physical observation showed that there was no interaction between them. The drugs Assay and impurity were carried out by HPLC method. The bulk density of the powdered blend was found to be 0.41 - 0.46gm/cm^3, tapped density between 0.47 – 0.53gm/cm^3 for all formulations. % Compressibility, Hausner ratio to be found between USP limit. Angle of Repose was found in the range of (28) º. Hardness was found to be (3-4) kg/cm^2. The flow properties of the powdered blend for all the batches were found to be good and free flowing. The weight variation, hardness and friability of all the formulated tablets within the specified requirements. The disintegration times for the formulated tablets are within the range of USP. For Aspirin DR tablets direct granulation was method of choice.

Optimization was done and it was found that release profile was found to be best with disintegrant i.e. sodium starch glycolate. Enteric coating of Protectab HP-1 Sunset yellow Lake IPA coating 10%w/w was done on Aspirin tablets as to avoid gastric irritations. Results found that release profile of batch no.AF4 matches with Innovator product DR Tablet. The Percentage cumulative drug release of batch. No. AF4 was found at 90 Minutes 104.21%. From results it can be inferred that release profile of Batch. No: AF4matches with that of innovator product, also f1&f2 values are good enough to comply with the innovator's product have reported similar kind of results for studies with Aspirin. Finally, the optimized formulations were subjected to accelerated stability studies and at room temperature (RT) as per ICH guidelines. The result obtained showed that there were no significant changes in tablet parameters such as appearance, hardness, friability, weight variation, drug content uniformity, and in-vitro drug release profile.

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