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FORMULATION AND EVALUATION OF GLUCOSAMINE SULPHATE POTASSUIM CHLORIDE FILM COATED TABLET 1000 MG

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1. ABSTRACT:

Glucosamine is naturally hygroscopic is nature when exposed to air and moisture and degradable whether in the form of tablet or raw material. To overcome this problem Glucosamine needs to bond with suitable stabilizer. Glucosamine Sulphate in the form of Salt i.e. Sodium chloride and potassium chloride are stable. The normal dose of Glucosamine is 500-1500 mg TID. It is very difficult to compress the tablet at the label claim 1000 mg because some additives are also required in the formulation and the average weights are 1400 mg. As per the preformulation studies it is concluded that tablet average weight less than 70 mg are very difficult to compress and more than 1500 mg are difficult to swallow in adult patient.Glucosamine is a special formulation that prove the pharmacological value to nourish the joint health. Glucosamine stimulates the formation or manufacture of collagen, the protein portion of the fibrous substance that holds joints together and provides a shock-absorbing cushion, as a person ages, the cartilage that cushions the joints often loses its ability to support healthy cellular growth. In addition, the synovial fluid which lubricates these joints also deteriorates. This condition, called osteoarthritis, often leads to rough bones that rub together and cause distress with every twist or bend. In this condition patient regularly required the Glucosamine tablet in 1000 to 1500 mg three times a day.

But it's very difficult to compress the tablet at huge weight because D tooling compression machine have maximum limit is 1200 to 1500 mg. For such critical formulation weight cam is adjusted in lower direction

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to increase the weight and feeding of granules in feed frame through force feeder resolve the dissolution problem. This tablet is prepared by wet granulation method by using Non Aqueous binding showed good results physical evaluation parameters and chemical parameters such as Assay, and Dissolution values. The granules are lubricated using suitable lubricants / Glidant / Antiadhrants were good in their flow properties. Assay and dissolution studies were conducted by the HPLC method.

Keywords: Stable glucosamine So4 KCL tablets, solid formulation of glucosamine 1000 mg tablet, Force Feeder.

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2. INTRODUCTION:

Glucosamine Sulphate Potassium Chloride and Sodium chloride are generally used for joint health. Glucosamine support the collagen and protein portion of the fibrous substance that holds joints together and provides a shock-absorbing cushion. As the age of a person increases, the cartilage that cushions the joints often loses its ability to support healthy cellular growth. Also the synovial fluid which lubricates these joints also deteriorates as the age of a person increase or weight. This condition, called osteoarthritis, often leads to rough bones that rub together and cause distress with every twist or bend. In this condition to treat the patient Non-Steroidal anti-inflammatory drugs (NSAID) are used. NSAIDMay be COX1 or COX2 inhibitor destroyed cartilage. Other side effect in prolong used of NSAID are GIT damage, Haemorrhage.Medicinal science discovered a nutrients that help in preserving joint tissue and fluids. Glucosamine is a necessary nutrient in the production of cartilage and synovial fluid.

Pure Glucosamine is fully "hygroscopic" and degradable when it come in contact to moisture and air. To mask the hygroscopic nature of Glucosamine, it needs to be bound to a stabilizer to be sold commercially. The sulphate and the HCL forms are two of the most common "agents" that Glucosamine is bound and shows its stability. After Glucosamine is bound, it is stable and will not degrade. These are various difficulties and limitations in the formulation of Glucosamine formulation. For example, oral forms, such as tablets or capsules, require anti-oxidants, such as sodium hyposulphite to present in their formulations, which blocking the oxidation of the amino group.

3. MATERIALS:

3.1 API structure and Properties.

INN: No INN has been specifically assigns for glucosamine sulphate PotassiumChloride

Chemical name: Bis (D Glucose, 2 amino-2 deoxy), Sulphate potassium chloride complex

Appearance: White and almost white crystalline powder.

Solubility: Freely soluble in water, sparingly soluble in methanol and practically in soluble in acetone.

Category: Osteoarthritis, Muscle Injury Prevention, Osteochondritis; Rheumatoid Arthritis, tendonitis

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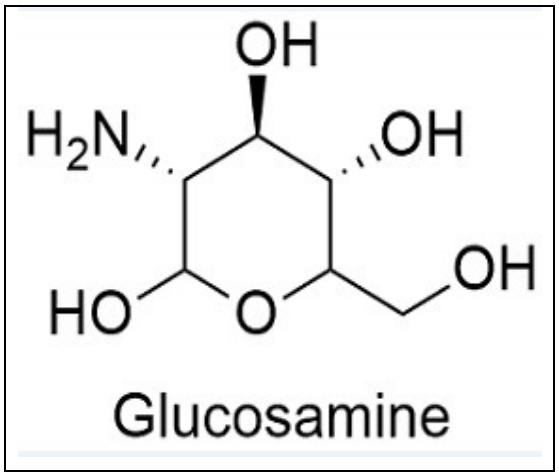
Structure:



Molecular formula:$(C_6H_{14}NO_5)_2SO_4$. 2KCL

Molecularweight:573.3 g/ mole

Glucosamine sulphate was obtained as gift samples from Zeon life science limited, Ponta sahib, and dist. Sirmour. H.P. (India).

(Manufactured by. Bio gene Extract Limited. Bangalore. Karnataka, and Costal Laboratories. India)

All the remaining Additives / binder/ preservatives/ solvent/ film former/ colouring agent/ plasticizer are the free sample from Tirupati Medicate limited, Ponta Sahib, Sirmour,H.P.(India)

3.2 List of Materials used in the Glucosamine 1000 mg Tablet.

S. No.	Ingredients	Role Of Ingredients	Supplier
1	Glucosamine SO4 KCL	Active Ingredient	Zeon life sciences
2	Lactose	Filler	Tirupati Medicare limited, Ponta sahib. Dist. Sirmour. H.P.
3	MCCP	Filler	
4	Methyl Paraben	Preservatives	
5	Propyl Paraben	Preservatives	
6	Iso Propyl alcohol	Solvents	
7	PVP-K 30	Binding agents	
8	Talcum Powder	Lubricants	
9	Magnesium Stearate	Antiadhrants	
10	Sodium Starch Glycolate	Disintegrants	
11	Aerosil	Glidant	

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12	Insta coat (White)	Film forming agent	
13	Iso Propyl alcohol	solvent	
14	Methylene Dichloride	Solvents	
15	Insta coat (Polish)	Polishing Agent	

3.3 Drug and Excipients Study.

S. No.	Drug+ Excipients	Duration (months)	Result
1	Glucosamine + Starch	6 Months	Stable
2	Glucosamine + Talcum	6 Months	Stable
3	Glucosamine + Mag. Stearate	6 Months	Stable
4	Glucosamine +MCCP	6 Months	Stable
5	Glucosamine +Lactose	6 Months	Stable
6	Glucosamine +CCS	6 Months	Stable
7	Glucosamine + PVP –K 30	6 Months	Stable
8	Glucosamine +DC starch	6 Months	Stable
9	Glucosamine + SSG	6 Months	Stable
10	Glucosamine + HPMC	6 Months	Stable

3.4 Formulation table.

Sr. no.	INGREDIENTS	C1 (mg)	C2 (mg)	C3 (mg)	C4 (mg)	C5 (mg)
1	Glucosamine SO_4 KCL	1000	1000	1000	1000	1000
2	Lactose	75	80	85	90	100
3	MCCP	75	80	85	90	95
4	Methyl Paraben	15	15	15	15	15
5	Propyl Paraben	03	03	03	03	03
6	Iso Propyl alcohol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
7	PVP-K 30	45	43	41	39	37
8	Talcum Powder	10	10	10	10	10

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9	Magnesium Stearate	05	05	05	05	05
10	SSG	15	12	09	06	03
11	Aerosil	15	10	05	00	00
	Film Coating Materials					
12	Insta coat (White)	35	35	35	35	35
13	Isopropyl alcohol	Q.S	Q.S	Q.S	Q.S	Q.S
14	MDC	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
15	Insta coat Polish	15	15	15	15	15
	Total Weight	1308 mg	1308 mg	1308 mg	1308 mg	1308 mg

4. METHOD OF PREPARATION OF GRANULES AND COMPRESSION OF TABLET.

4.1 Wet Granulation Method.

Generally the low weight tablet of Glucosamine Sulphate formulation in range of 500- 750 mg are prepared by direct compression method. But when the dose of Glucosamine are more than 1000 mg or 1500 mg, then it is very difficult to compress. In such case wet granulation method are used for preparation of Granulation. As glucosamine Sulphate are hygroscopic in nature then non aqueous solvent are used. For this the formulator used Acetone, Isopropyl Alcohol, or methylene dichloride.

Weigh accurately all the ingredient, Glucosamine pass through sieve 40, and Lactose starch and MCCP pass through sieve 60. Then active and filler mix together. After this the binding solution is prepared by dissolving the PVP-K 30 into Isopropyl alcohol. In the rapid Mixer Granulator the shifted active and filler are mixed for five minutes. Then binding solution added through opening duct of Granulator and mix till the smooth granules are obtained.

Remove the wet granules and finally dry in the tray dryer. Initially granules are dry on air drying and then start the heater and set the temperature at 40 ℃. The final dried granules contains the moisture not more than 1.5 %. By IR moisture balance.

Lubricants are mixed together and pass through sieve 60 and lubricate the granules for five minutes in Octagonal blander.

4.2 Compression of tablet.

Finally dried and lubricated granules are compressed at calculated weight by using the D Tooling 27 stationFluid Pack Accura (force feeder) at 12 RPM. The punches used for compression are buffed by using buffing machine. The finally compressed tablet are sorted by using tablet sorting machine. All the tablet which are used for in process quality control test viz DT, friability, Hardness are destroyed.

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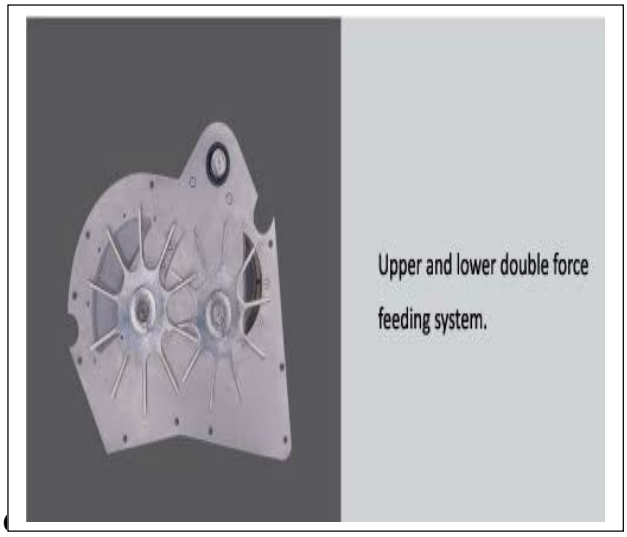
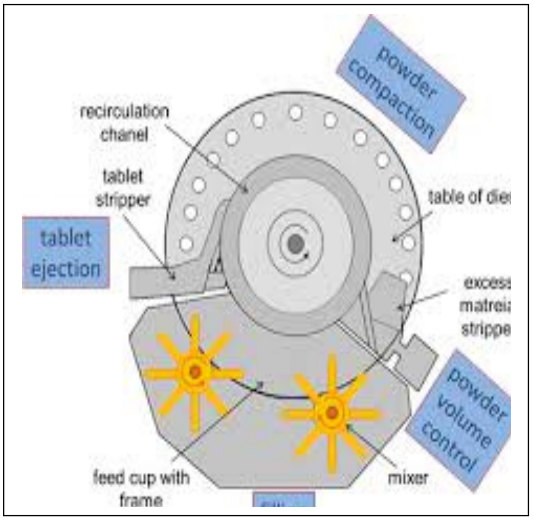
4.3 Tablet Coating.

Compressed Tablet are coated in the conventional coating pan / auto coater. In Auto coater the appearance of the tablet are not the desired quality. All the compressed tablet are coated in the conventional coating pan at 6-7 RPM, and spay rate is 1000 ml / 40 minutes. Insta coat readymade coating material are used containing Titanium dioxide, HPMC, PEG, Talcum. Finally coated tablet are polished by using Insta coat polishing agent in polishing pan.

5. EQUIPMENTS AND INSTRUMENTS:

Tablet Compression Machine by Fluid Pack Accura (force feeder), Tablet dissolution apparatus Type II by Electro lab. Limited., Electronic Balance Model, Sansui; pH meter by Hanna Instrument, Italy; Pfizer Hardness Tester, Roche Friability test apparatus; Hot Air Oven by Metalab Scientific Industries, Mumbai. Try dryer, rapid mixer granulator, Conventional coating pan, Polishing pan.





6.1 Thickness of compressed tablet.

The thickness of the compress tablets of Glucosamine 1000 mg was determined using a Digital Vernier calliper. Ten tablets from each type of formulation were used and average values were calculated. It is expressed in mm.

6.2 Hardness

The resistance of tablets during passing through hopper, Blister Cartooning, breakage, under conditions of storage, transportation and Handling before usage are directly proportional to its hardness. For each formulation, the hardness of 6 tablets was determined using the Pfizer Hardener Tester and Monsanto

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hardness tester. The tablet was held along its oblong axis in Between the two jaws of the tester. At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob in Monsanto tester and in case of Pfizer directly force applied until the tablet breakdown in the pieces. The reading in the both cases at this point are noted.

6.3 Friability Test:

Friability Test is generally used the measure of tablet strength. Roche Friability tester was used for testing the friability using. In This test subjects a number of compressed tablets to the combined effect of shock abrasion by utilizing a circular plastic chamber which revolves at a speed of 25 revolution per minutes for 4 minutes i.e. 100 rpm, dropping the compressed tablets of glucosamine to a distance of 6 inches in each revolution. A sample of compressed 20 tablets of was placed in Roche friability chamber which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then de-dusted, and broken tablet are removed and reweighed. A loss of less than 1 % in weight in generally considered acceptable according to Pharmacopeia. Percentage friability (% F) was calculated as follows:

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Initial Weight}} \times 100$$

6.4 Weight variation test:

As per the limitation of Pharmacopeia to find out weight variation test, 20 tablets of each type of formulation were weighed individually using single pan balance or an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight.

Specifications for tablets as per Indian Pharmacopeia. 1996.

S. No.	Percentage Deviation	Average Weight of Tablet(mg)
1	10	80 mg or less
2	7.5	More than 80 mg but less that 250 mg
3	5	250 or more

6.5 Uniformity of drug content:

As per the official pharmacopeia's the randomly sampled tablet from the all five compression batches should contained the Glucosamine sulphate KCL NLT 90 % and NMT 110 % of labelled amount. If from

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the 20 sample tablet at least 18 tablet passed and 2 tablet fail in the assay calculation then the tablet passed in uniformity of drug content.

6.6 In vitro disintegration time:

The process of breakdown or convert the tablet into pieces or into smaller particles is called as disintegration. The in vitro Disintegration time of a tablet was determined using disintegration test apparatus as per Indian Pharmacopeia specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using distilled water maintained at 37° ± 2°C which is similar to body temperature. The assembly should be raised and lowered between 30 cycles per minute in the 0.1 N HCL or Distilled water maintained at 37° ± 2°C. The time in seconds taken for complete disintegration of the tablet.

In this disintegration test if the tablet are adhere to the 10 # sieve then continue the test till all tablet are completely disintegrated.

6.7 In vitro dissolution test:

Rate of dissolution are studied by using USP type-II apparatus having 50 rpm, using 900ml of 0.1 N Hydrochloric acid as dissolution solvent. Temperature of the dissolution medium was maintained at 37 ± 0.5°C. The sample of dissolution medium was withdrawn at every 5 min interval and first filtered. The absorbance of filtered solution was measured by using Ultra Violet spectrophotometric method at mentioned nm specified in official pharmacopeia and concentration of the drug was determined from standard calibration curve.

In vitro drug release studies details:

1. Dissolution test apparatus
2. 0.1 N HCL as Dissolution medium
3. 900 ml Dissolution medium volume
4. 37 ± 0.5°C as std. Temperature
5. 50 rpm Speed of basket paddle
6. 5 min sampling intervals
7. 10 ml volume Sample withdraw
8. Absorbance measured as specified in the official books

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7. RESULT AND DISCUSSION:

7.1 Pre compression Parameter and studies

S. No.	Formulation code	Angle of Repose	Bulk density (weight/ml)	Taped Density (weight/ml)
1	C1	34.32±0.70	0.53±0.02	0.45±0.04
2	C2	33.10±0.56	0.49±0.03	0.41±0.02
3	C3	31.86±0.63	0.47±0.03	0.38±0.04
4	C4	29.44±0.45	0.46±0.02	0.38±0.02
5	C5	28.40±0.69	0.44±0.03	0.35±0.02

7.2 Post compression Parameter Studies.

Formulacode	Hardness (KG/cm2)	Friability (%)	Thickness (mm)	Length (mm)	Wt. of Uncoated Tablet (mg)	Wt. of film coated Tablet (mg)
C1	7.2	0.85	7.56	20.02	1255	1305
C2	7.4	0.78	7.54	20.00	1248	1298
C3	7.2	0.75	7.52	20.03	1262	1315
C4	6.8	0.70	7.48	20.00	1245	1310
C5	7.0	0.80	7.50	20.04	1252	1305

7.3 Post compression Studies:

Formulation code	Assay of Drugs (%)	Disintegration time (minutes) Uncoated	Disintegration time (minutes) Film coated	Dissolution (%)
C1	99.52	4.3 to 5.4	7.4 to11.2	95.45
C2	98.80	5.5 to 7.3	9.4 to 13.4	93.50
C3	98.35	6.2 to 8.4	10.5 to 14.3	88.32
C4	98.90	6.4 to 9.2	10.4 to 15.3	86.08
C5	98.72	7.2 to 10.2	11.2 to 16.3	83.65

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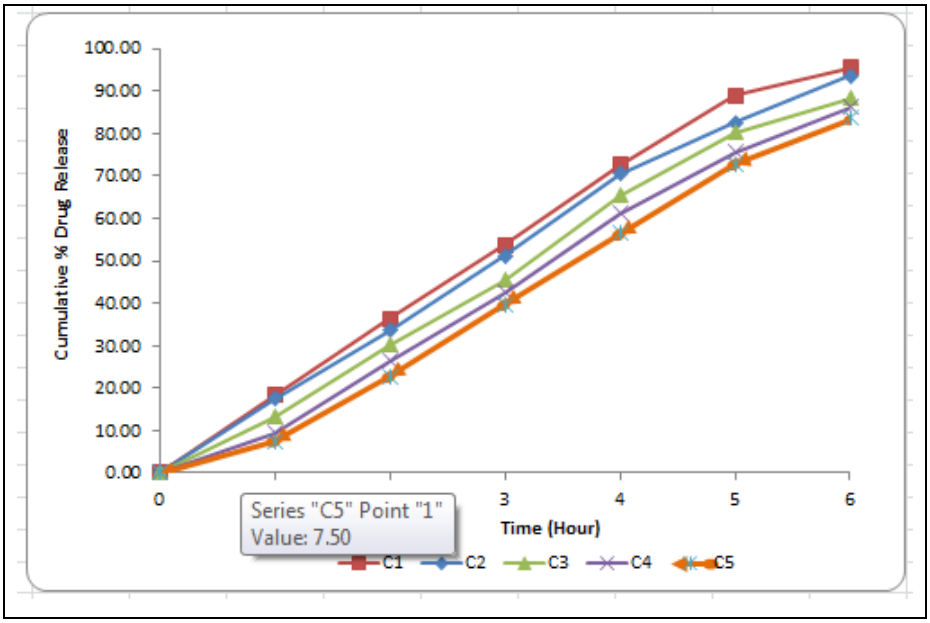
8. GRAPHS:

Time (months)	Cumulative % Drug Release				
	C1	C2	C3	C4	C5
0	0.00	0.00	0.00	0.00	0.00
1	18.32	17.56	13.28	9.45	7.50
2	36.45	33.65	30.25	26.48	22.59
3	53.65	51.26	45.56	42.57	39.78
4	72.58	70.45	65.48	61.25	56.48
5	88.89	82.56	80.15	75.59	72.89
6	95.45	93.50	88.32	86.08	83.65



8.1 Glucosamine SO4 KCL 1000 mg Tab. Drug Dissolution

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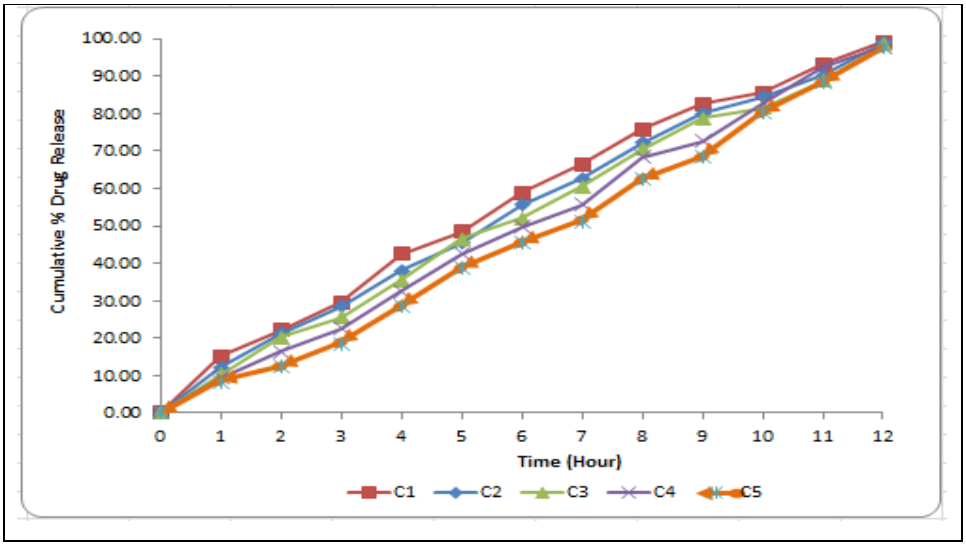
Time (months)	Cumulative % Drug Release				
	C1	C2	C3	C4	C5
0	0.00	0.00	0.00	0.00	0.00
1	15.13	12.13	10.25	9.45	8.45
2	22.18	21.25	20.15	16.48	12.45
3	29.45	28.45	25.46	22.56	18.56
4	42.59	38.12	35.56	32.45	28.45
5	48.46	45.56	46.59	42.56	38.87
6	58.89	55.63	52.13	49.78	45.56
7	66.45	62.56	60.45	55.56	51.25
8	75.78	72.13	70.48	68.45	62.58
9	82.56	80.12	78.74	72.59	68.45
10	85.56	84.56	81.45	82.88	80.45
11	93.25	90.12	88.78	92.58	88.25
12	99.12	98.85	98.56	97.85	97.85



8.2 Glucosamine SO4 1000 mg Tab. Drug Assay

Time (months)	Cumulative % Drug Release				
	C1	C2	C3	C4	C5
0	95.45	93.50	88.32	86.08	83.65
1	94.52	93.20	87.85	85.92	82.52
2	93.80	92.50	86.52	84.59	82.25
3	91.56	91.52	85.96	83.62	82.12
4	88.90	88.40	85.69	82.59	81.96
5	87.69	87.69	84.96	81.88	81.56
6	85.69	85.00	85.00	80.59	81.21

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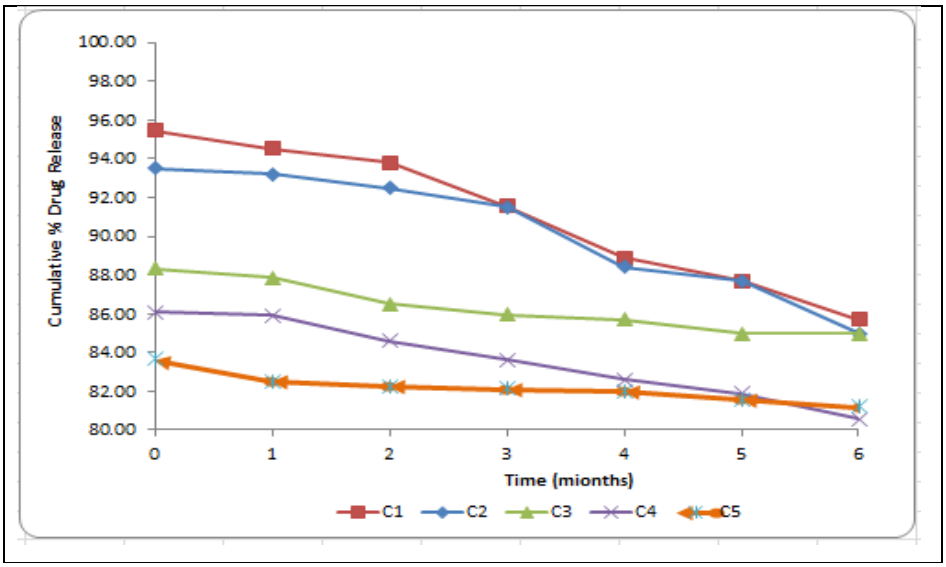
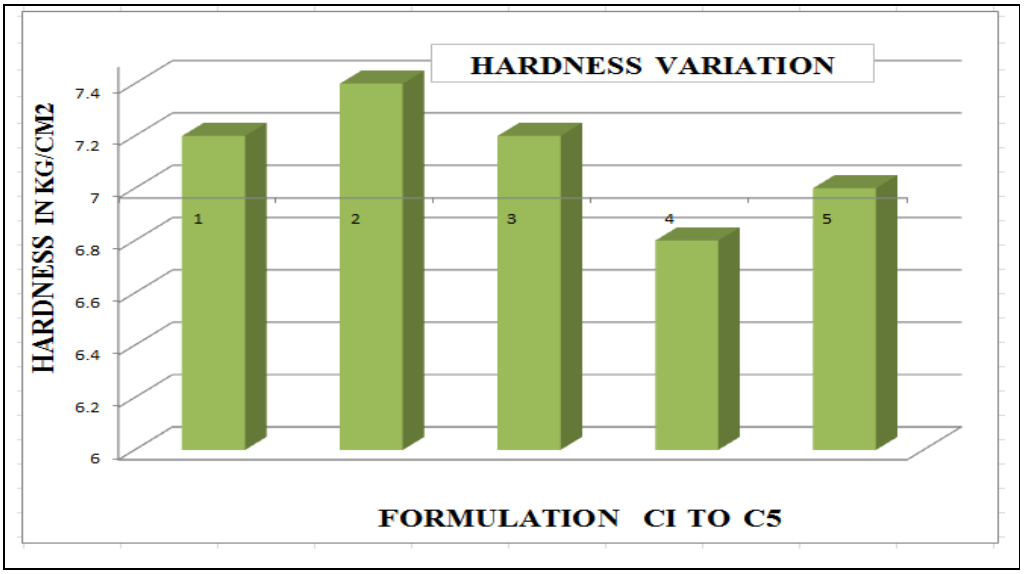


8.3 Glucosamine SO4 1000 mg Tab. Drug Dissolution stability



8.3 Glucosamine SO4 1000 mg Tab. Hardness Variation

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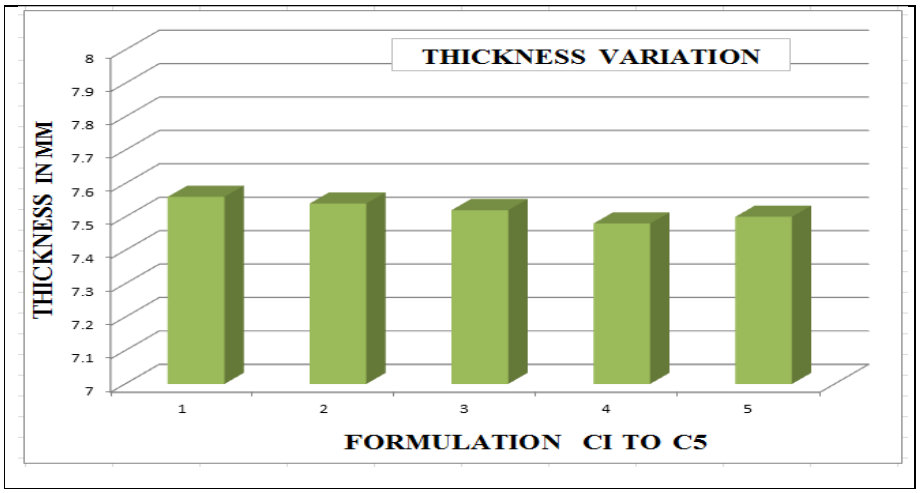

8.3 Glucosamine SO4 1000 mg Tab. Thickness Variation

9. CONCLUSION:

After the completion of this experiments the result obtained and we conclude that development of Glucosamine Sulphate KCL Tablet formulation by using PVP k 30 as Binder and cross carmillose as disintegrate are given the result of stable tablet having good hardness, required dissolution and well film coated tablet. Some result are mentioned below:

1. Active drug Glucosamine sulphate are stable with different excipient are stable viz Starch,Talcum, MCCP, Lactose, Magnesium stearate, cross carmillose sodium and PVP K 30.

2.Film coated tablet of Glucosamine sulphate 1000 mg FC tablet are successfully prepared.

3. The flow property of the granules and uniformity of the compressed tablet are better in

Non Aqueous binding with PVP K 30 as compare the granules prepared by Aqueous

binding with starch Paste.

4. The angle of repose of prepared granules are less than 30º which show the good quality

of granules.

5. The hardness of compressed tablet by Non Aqueous PVP K 30 binding in the rage of

6.8 to 7.4 kg/cm2.

6.The Thickness of the prepared tablets by all three methods was found between 7.48 mm.

to7.56 mm.

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7.The Friability of the compressed tablet are within the range i.e. less than 1%.

8. The in vitro disintegration studies are found to be in 4.3to 10.2 minutes for uncoated tablet and 7.4 to 16.3 minutes. Formulation C1 showed in vitro disintegration time is 4 to 6 minutesfor uncoated tablet and 7.4 to 11.2 minutesfor film coated tablet.

On the basis of disintegration time formulation C1 which facilitate the faster disintegration, sufficient hardness, well dissolution, good stability data, and assay, it is better formulation and stable during its shelf life. We conclude that film coated tablet are prepared by this Method is stable and pass all the test mentioned in the pharmacopeia.

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