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Research Article

Formulation and Evaluation of Fast Dissolving Tablet of Silymarin

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ABSTRACT

In this investigation mouth dissolving tablets of Silymarin were prepared using different superdisintegrants by dry granulation method. Fast dissolving tablets were evaluated for physicochemical properties and in vitro dissolution. The preformulation studies and tablet evaluation test were performed and results were within the limit. The powder blend was evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner ratio. The powder blend show satisfactory flow properties. The silymarin tablet evaluated for tablet general appearance, hardness test, weight variation and drug content estimation. Oral route is the most preferred route for administration of various drugs because it is regarded as safest most convenient and economical route. Recently researchers develop the new dosage form fast dissolving tablet (FDT) with improve patient compliance and convenience. Fast dissolving tablets which dissolve rapidly in saliva without additional water and chewing. Fast dissolving tablets overcome the disadvantages of conventional dosage form especially dysphagia in pediatric and geriatric patients.

All the formulations shows uniform weight, hardness and friability data indicates good mechanical resistance of the tablet. All the tablets were disintegrated between min. The optimized (F6) formulation showed good disintegration time and release profile with maximum drug being released.

Keywords: Dysphagia, silymarin, superdisintegrants, Patient compliance

INTRODUCTION

In the world of pharmacy around 80% of the tablets manufactured are ingested orally. Administration of drugs through oral route is the most common and the easiest way to administer a drug. However, geriatric and bedridden pediatric, patient shows inconvenience swallowing conventional tablets or due to difficulties in swallowing with lesser amounts of water with the medication, because of large tablet size difficulties in swallowing, unable to tolerate the taste of many drugs when formulated as liquid dosage forms, resulting in poor patient compliance. The rationalized approach in case of medication leads to the development of dispersible tablet. These are manufactured so that they may be dispersible in the mouth producing a pleasant tasting residue in the oral cavity that is easily swallowed and does not leave a bitter a unpleasant taste. In recent decades a variety of pharmaceutical research has been conducted to develop new dosage forms. Recent advances aim to enhance safety and efficacy of drug molecules by formulating convenient dosage form for administration and to achieve better patient compliance. The various dosage forms develop to improve the ease of administration. Dysphagia, or difficulty in swelling, is common among all age groups. Dysphagia is common

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about 35% of the general population. tablet is most preferred dosage forms because of its ease of manufacturing, stability compared with oral liquids, convenience in administration, accurate dosing and it is more temper proof than other dosage forms. The bioavailability of drug is dependent on in vivo disintegration, dissolution and various physiological factors. The task of developing rapidly disintegrating is complished by using a suitable diluents and superdisintegrants.

PREFORMULATION STUDY

Identification of dispersible tablet of silymarin by HPLC

Identification of dispersible tablet of silymarin were Performed by HPLC. According to USP if the Retention time of standard and test products are same then they are said to be similar products.

The retention time of the peaks for silydianin, silybinA, silybin B, isosilybin A, and isosilybin B in the chromatogram of the test solution correspond to those in the chromatogram of milk thistle standard solution, as obtained in the test for content of silymarin.

Methodology & Procedure: In identification of APIs the column was C18 type, mobile phase was 7.8 gm disodium hydrogen Ortho Phosphate, the flow rate of mobile phase was 1.5 ml/ min, Sample injected volume was 20µl, and standard and test was prepared with the concentration of 100 mg in 100 ml water.

Mobile phase was prepared with 7.8 gm disodium hydrogen ortho phosphate. HPLC column was firstly wash with hot water and then with mobile phase for remove the previous solvents, then saturated the column to obtained the base line after that taken one trail to check retention time then run the standard and test product.

Evaluation of Granules: Bulk density was determined with 20 gm sample. Take 20 gm sample, after weighing sample was measured in measuring cylinder in ml and calculate the bulk density. After that Tap measuring cylinder for 100 times then note the volume of powder after tapping, by this determine the Tapped density. By the readings of bulk and tapped density determined the Carr's and Hausner's ratio.

Preformulation studies such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio were determined.

Angle of repose: Angle of repose was calculated to determine the flow properties of granules with the formula $\tan\theta=H/R$, where 'a' is the angle of repose and R is the radius of the conical pile.

$\text{Tan}\theta=h/r$

Therefore
$\theta=\text{Tan-1}h/r$
θ = Angle of repose
h = height of the cone
r =Radius of the cone base

If angle of repose less than 30º shows the free flowing the material

Bulk density: Bulk density of powder was determined by placing pre-sieved bulk powder into a graduated cylinder and measuring the volume and weight "as it is.

pb = m/v

Where pb= bulk density
M= Weight of sample in gm
V= Final volume of blend in cm^3

Tapped density: It was determined by placing known amount or weight of powder in a graduated cylinder and tapping it for fixed number of taps (around 250 taps) until the

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powder bed volume reached a minimum. Using the weight of the powder in the cylinder.

Compressibility index : By Carr's compressibility index the compressibility index of granules was determined.

%Carr index= (TBD-LBD)100/TBD

Where TBD=Tapped bulk density
LBD= Lowest bulk density

MATERIALS AND METHODS

Materials- Silymarin (Gift sample from Micro Labs.), Microcrystalline cellulose from Mingtai chem. Cells co. Ltd., Croscarmellose sodium from Base Chemicals, Magnesium stearate from Suzong Chemicals, Aspartame from Biocon Ltd and Aerosil from Wacker.

Calculation of API or Silymarin: The lable claim of silymarin tablet was 140mg the potency of silymarin was 80% according to calculation of API or Silymarin 175mg used for the preparation of fast dissolving tablet of silymarin.

Method:Dry Granulation

Raw material ➔ weighing ➔ screening ➔ mixing ➔ slugging ➔ milling ➔ screening ➔ mixing ➔ compression.

Procedure: Sifting is the first step of formulation of dispersible tablet. (Table 1) Then Dry Blending, In this step Load the sifted material of step first in the Octagonal blender & mix for 15 minutes. Then Compaction by roll compactor at the temperature of 20-25C. Then Granulation, Pass the compacted material through Oscillatory Granulator through 2.5 mm screen. Then Sifting, Sift the milled material of previous step through 18 # S.S. mesh. Then Drying, after sifting Dry the granular power in Vacuum Tray Dryer for Two hours at 60^0C temperature and vacuum at 710 ± 10 mm Hg. Then Blending, after sifting load the Drying material in the Octagonal blender and add Aerosil & Magnesium Stearate mix for 30 minutes. After that Compression, final step was compression of tablet of 27 stations D tooling machine is used to formulate dispersible tablet

Table 1: Sifting process of API & excipients

S.No.	NAME OF MATERIAL	SIEVE NO.
1.	Silymarin	30
2.	Cross povidone	30
3.	Micro crystalline Cellulose	30
4.	Croscarmellose sodium	30
5.	Aerosil	30
6.	Talcum	60
7.	Flavour strawberry	30
8.	Peppermint flavour	30
9.	Aspartame	30
10.	Magnesium stearate	60
11.	Sodium starch glycolate	30

Table No. 2: Composition of all formulations of dispersible tablet

FORMULATION	F1	F2	F3	F4	F5	F6
1.Silymarin	175mg	175mg	175mg	175mg	175mg	175mg

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2.Crosscarmilose sodium	25mg	30mg	35mg	--------	---------	---------
3.Colloidal silicon dioxide	6mg	6mg	6mg	6mg	6mg	6mg
4.Talcum	0.5mg	0.5mg	0.5mg	0.5mg	0.5mg	0.5mg
5.Magnesium striate	4.5mg	4.5mg	4.5mg	4.5mg	4.5mg	4.5mg
6.Cross povidone	35.5mg	30.5mg	25.5mg	35.5mg	30.5mg	25.5mg
7.Strawberry flavor	7.5mg	7.5mg	7.5mg	7.5mg	7.5mg	7.5mg
8.Aspartame	10.5mg	15.5mg	15.5mg	15.5mg	15.5mg	15.5mg
9.Peppermint flavor	1.5mg	1.5mg	1.5mg	1.5mg	1.5mg	1.5mg
10.Microcrystalline cellulose PH-112	34mg	34mg	34mg	34mg	34mg	34mg
11.Sodium starch glycolate	--------	---------	---------	25mg	30mg	35mg

EVALUATION OF TABLET

General Appearance: The general appearance of a tablet through visual identification is essential for consumer acceptance. Therefore tablets were evaluated for its organoleptic properties through visual inspection.

Average weight: To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (Table no. 2)

Thickness: Tablet thickness is was recorded using Vernier caliper. Tablet thickness is important characteristic in reproducing appearance, counting using filling & packing equipment.

Weight Variation: Weight variation was calculated as per method described in Indian Pharmacopoeia. Take 20 tablets first weight 20 tablet then each tablet weight individually and calculate average weight.

Hardness: Tablet hardness was checked by using Monsanto Hardness Tester to ensure the hardness of tablet. Tablet hardness place important role during packaging process during handling and transportation.

Friability: The limit of friability is less then 1% (0.1-0.9%) for FDT is a challenge for a formulator since all methods of manufacturing of FDT are responsible for increase the % friability values. “Electro lab friabilator” ten tablets weight then rotated 25 rpm for 4 minutes or total 100 revolution then reweighed the tablets and calculate the percentage loss by the following equation.

F= (initial weight –final weight)/initial weight X 100

In-vitro dispersion time: One tablet was added to 10 ml of phosphate buffer solution, ph 6.8 at 37 ˚C and measured the time required for complete dispersion of a tablet.

Disintegration test: The time limit for the FDTs is generally less than 1 minutes and actual disintegration time that patient can experience ranges from 5 to 35 seconds. The disintegration test for FDT should mimic in mouth within sliva.

Disintegration in oral cavity: The time required for disintegration of tablet in mouth was obtained from six healthy volunteers, who were given tablets from the optimum formulation.

In-vitro dissolution: The in-vitro dissolution study of tablet was performed by using USP 2nd type dissolution apparatus (Temperature 37˚C±0.5˚C ,900 ml , at 50 rpm) in phosphate buffer ph 7.5 prepared by dissolve 27.6 gm of monobasic sodium phosphate and 6.08 gm of sodium hydroxide in water , and dilute with water to 4000 ml. Medium: pH 7.5 phosphate buffer containing 2% lauryl sulphate; 900 ml. Determine the amount of silymarin as silybin dissolved by employing the method in the test for content of silymarin, making any necessary modifications. The volume was analyzed by HPLC and cumulative percent drug release was calculated.

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RESULTS

Preformulation study: Solubility, identification and assay of Active pharmaceutical ingredients by HPLC, flow properties of granules were determined.

Identification: Identified successfully. It was performed by HPLC. The retention time of Standard curve and test curve were same. RT of standard silymarin was 2.060 and RT of test was also 2.06(fig.1&2), RT of standard silymarin was 1.924 and RT of test was also 1.928(fig.3&4).

Flow Properties: Evaluation of granules were determined successfully. The Results were in limits, The Carr's index of all batches was 9 to 13 it was in the limit and the Hausner's ratio was also in limit, it was 1.10-1.25.Angle of repose was also successfully determined, it was 22- 22.6(Table 3).

Evaluation of tablets: Tablets were evaluated for weight variation, hardness, friability, Disintegration time, Equivalent Relative Humidity, Assay and dissolution study. Tablets were having uniform weight, hardness and friability data indicates good mechanical resistance of the tablets.

In-vitro dissolution study:

Table no 3: In-vitro dissolution study

S.No.	Batch codes	After 5 min.	After 10 min.	After 20 min.	After 30 min.	After 40 min.
1	F1	92.56	93.05	93.25	93.44	93.76
2	F2	93.15	93.42	93.83	94.22	94.37
3	F3	93.56	94.05	94.35	94.62	94.79
4	F4	95.89	96.85	97.47	97.54	97.67
5	F5	97.97	98.68	99.72	99.18	99.28
6	F6	97.94	98.45	99.14	99.24	99.78

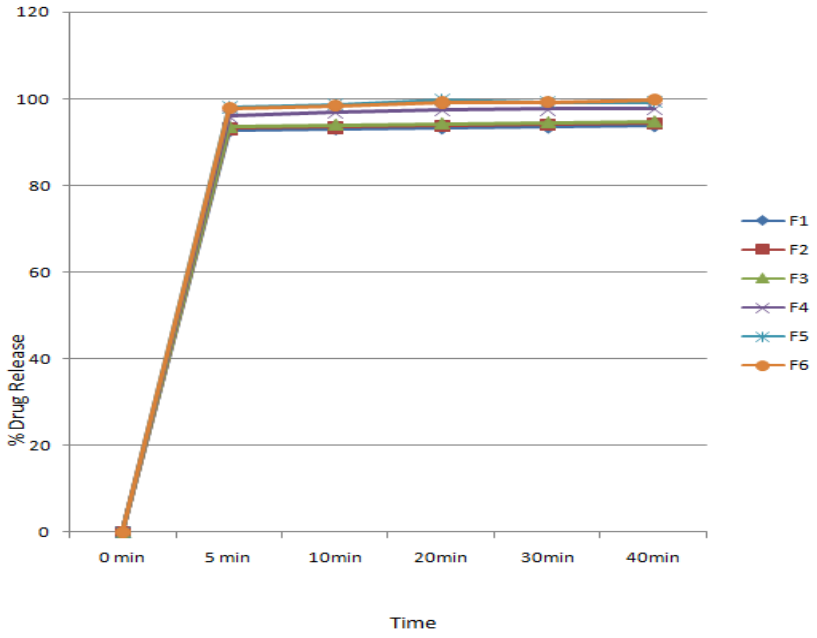

Fig 1: % Drug release of silymarin.

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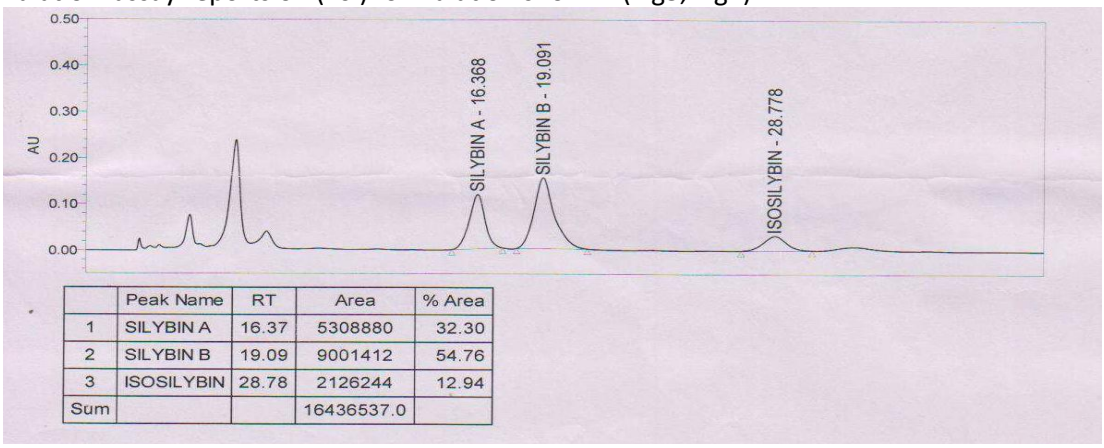
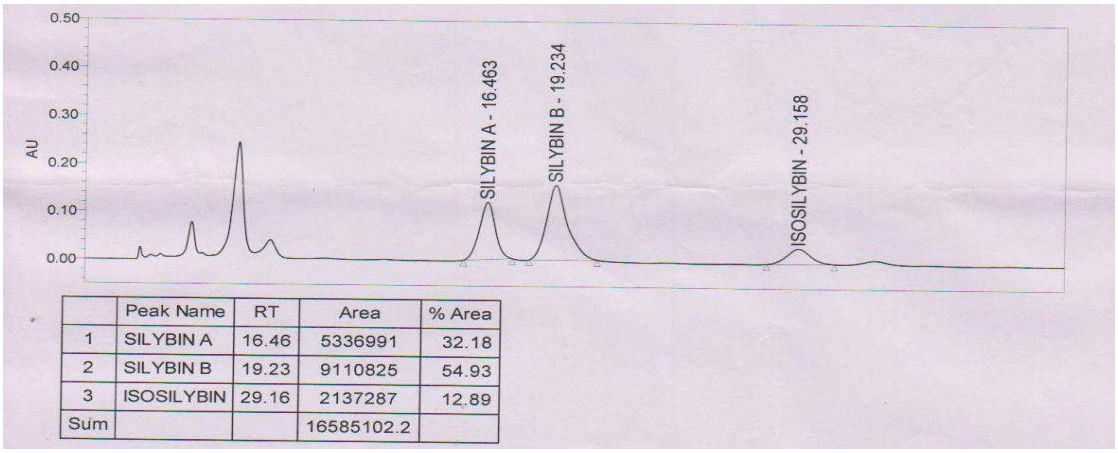
Assay of tablet by HPLC: Evaluation of tablet by HPLC successfully performed it was 93.48%to 99.90% of formulation assay reports of (F6) formulation show in (Fig3, Fig4)



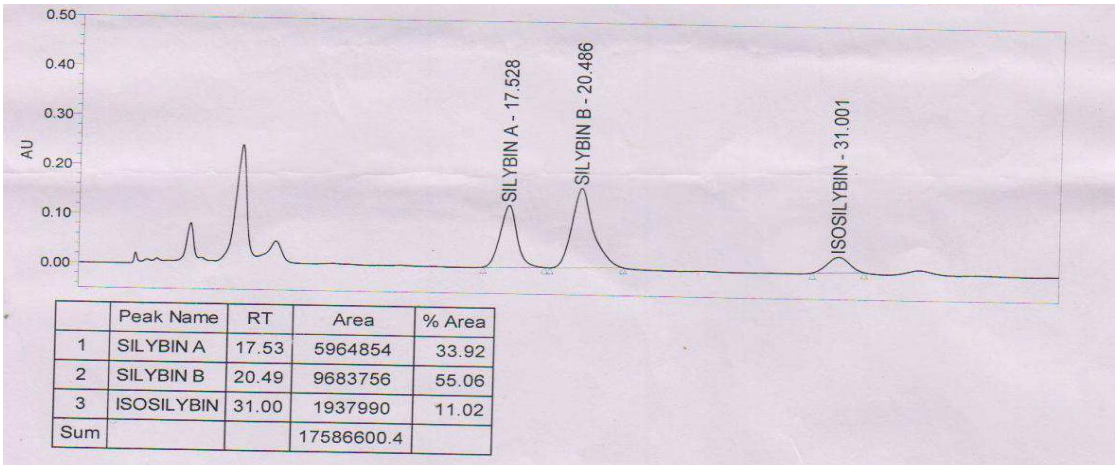
	Peak Name	RT	Area	% Area
1	SILYBIN A	16.37	5308880	32.30
2	SILYBIN B	19.09	9001412	54.76
3	ISOSILYBIN	28.78	2126244	12.94
Sum			16436537.0	

Fig 2: Standard graph (1) of silymarin by HPLC.



	Peak Name	RT	Area	% Area
1	SILYBIN A	16.46	5336991	32.18
2	SILYBIN B	19.23	9110825	54.93
3	ISOSILYBIN	29.16	2137287	12.89
Sum			16585102.2	

Fig. 3: Standard graph (2) of silymarin by HPLC.



	Peak Name	RT	Area	% Area
1	SILYBIN A	17.53	5964854	33.92
2	SILYBIN B	20.49	9683756	55.06
3	ISOSILYBIN	31.00	1937990	11.02
Sum			17586600.4	

Fig. 4: Sample graph (1) of silymarin by HPLC.

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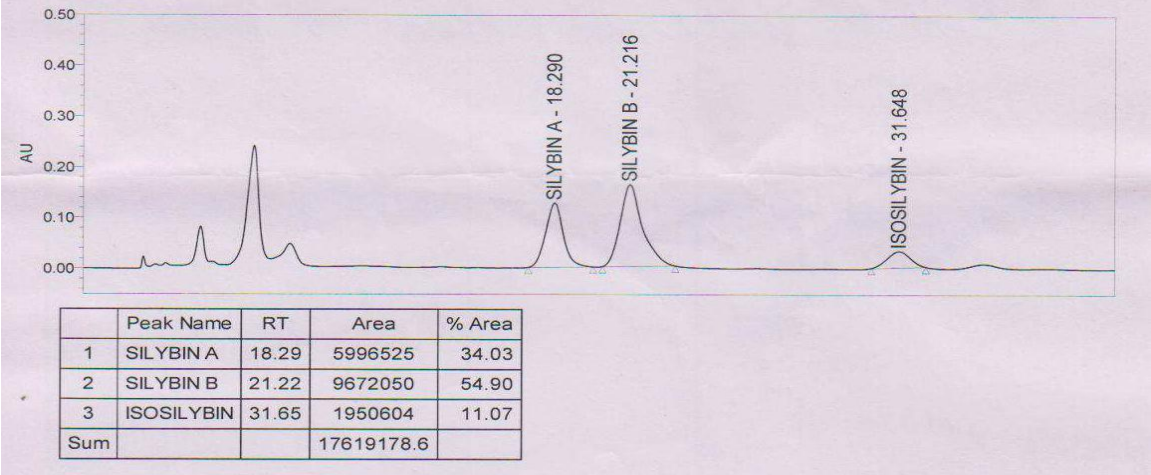

	Peak Name	RT	Area	% Area
1	SILYBIN A	18.29	5996525	34.03
2	SILYBIN B	21.22	9672050	54.90
3	ISOSILYBIN	31.65	1950604	11.07
Sum			17619178.6	

Fig. 5: Sample graph (2) of silymarin by HPLC

Table No 4: Pre compression Studies

S.No.	Test	F1	F2	F3	F4	F5	F6
1	Bulk density(gm/ml)	0.460	0.471	0.460	0.471	0.465	0.462
2	Tapped density(gm/ml)	0.532	0.522	0.532	0.522	0.536	0.538
3	Carr's index	13.53	9.77	13.53	9.77	13.24	13.26
4	Hausner's ratio	1.15	1.10	1.15	1.10	1.25	1.16
5	Angle of repose(degrees)	22.4	22.5	22	22.2	22.4	22.6

Table No.5: Post compression Studies of all formulations

S.No.	Batch codes	Average Weight of 20 tablets	Hardness (kg/cm^2)	% Friability	Average Disintegration Time(sec)	Average Wetting Time(sec)	% drug content
1	**F1**	6.10gm	4.5kg/cm²	0.24%	50 sec.	86sec.	93.48%
2	**F2**	6.05gm	5 kg/cm²	0.23%	47 sec	88sec.	94.58%
3	**F3**	6.05gm	4.5kg/cm²	0.22%	49 sec	90sec.	94.95%
4	**F4**	6.04gm	5.5kg/cm²	0.24%	44 sec	84sec.	98.78%
5	**F5**	6.08gm	4.5kg/cm²	0.21%	48 sec	85sec.	99.15%
6	**F6**	6.07gm	4.5kg/cm²	0.18%	41sec	75sec.	99.90%

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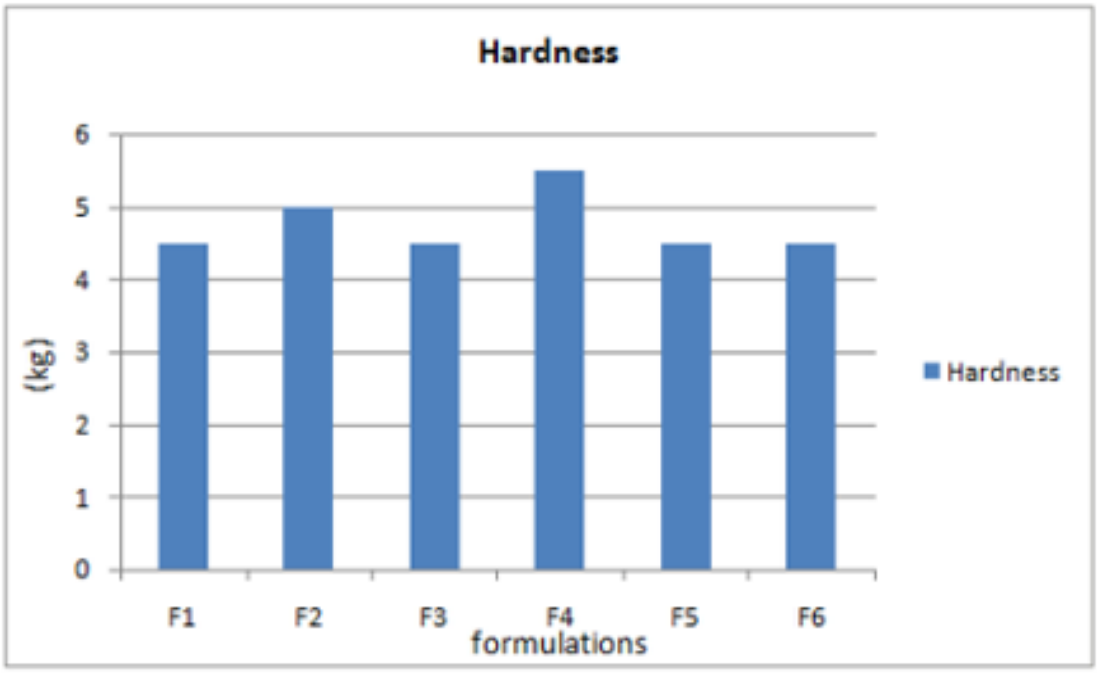

Fig 6: Hardness of all six formulations.

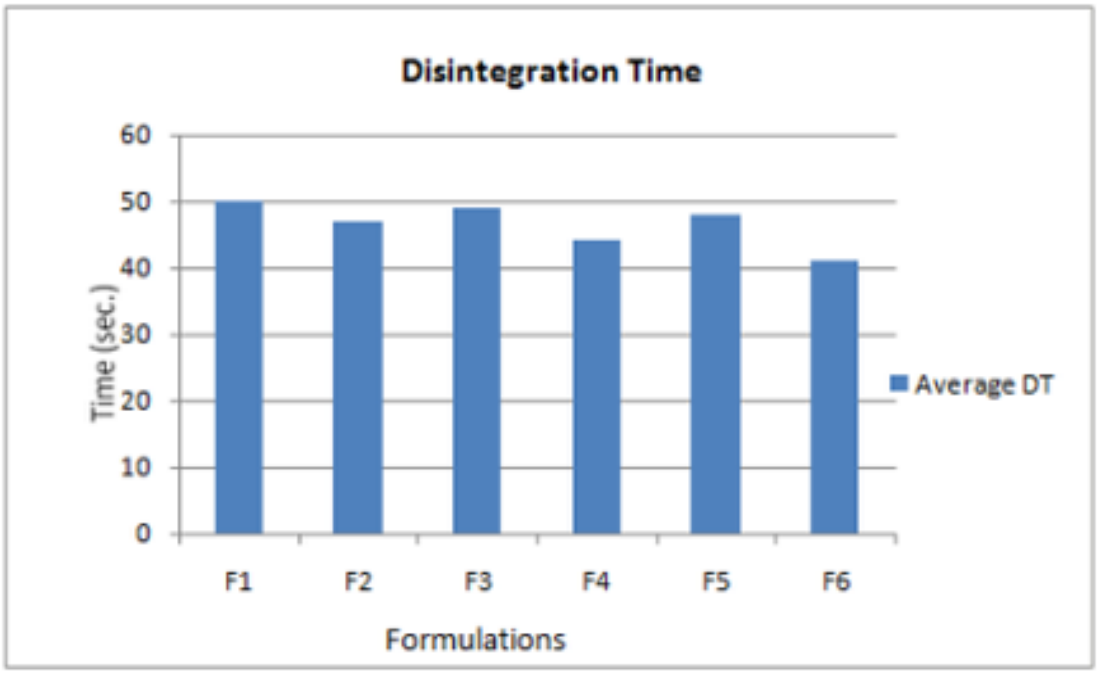

Fig 7: Disintegration time of all six formulations.

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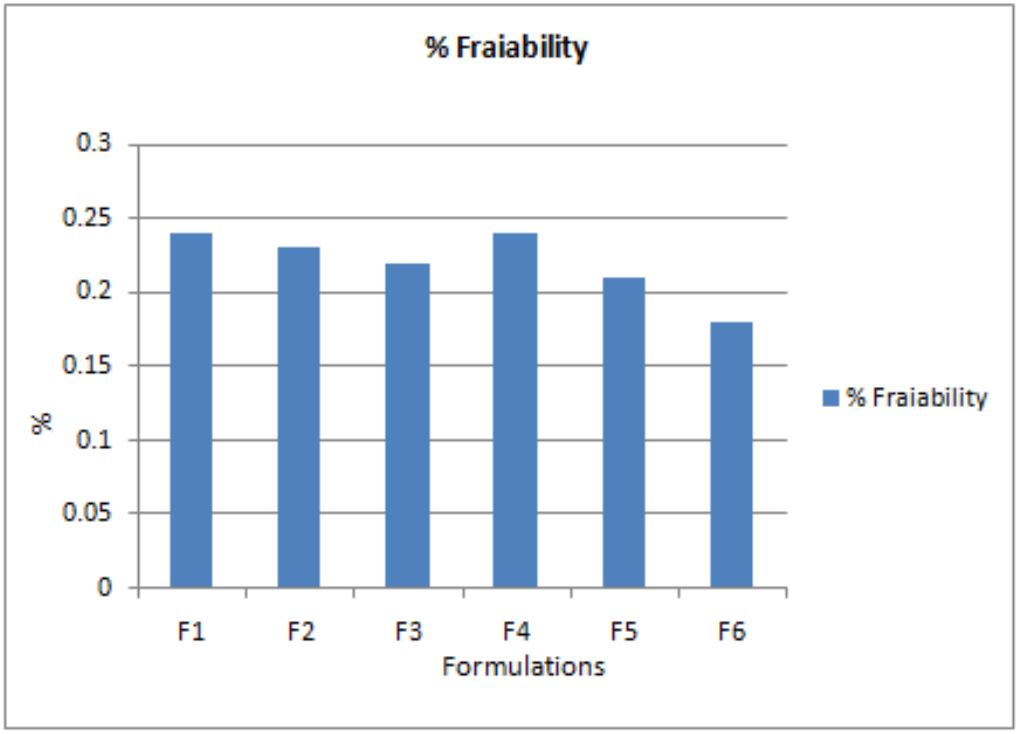

Fig 8: average friability of all formulations.

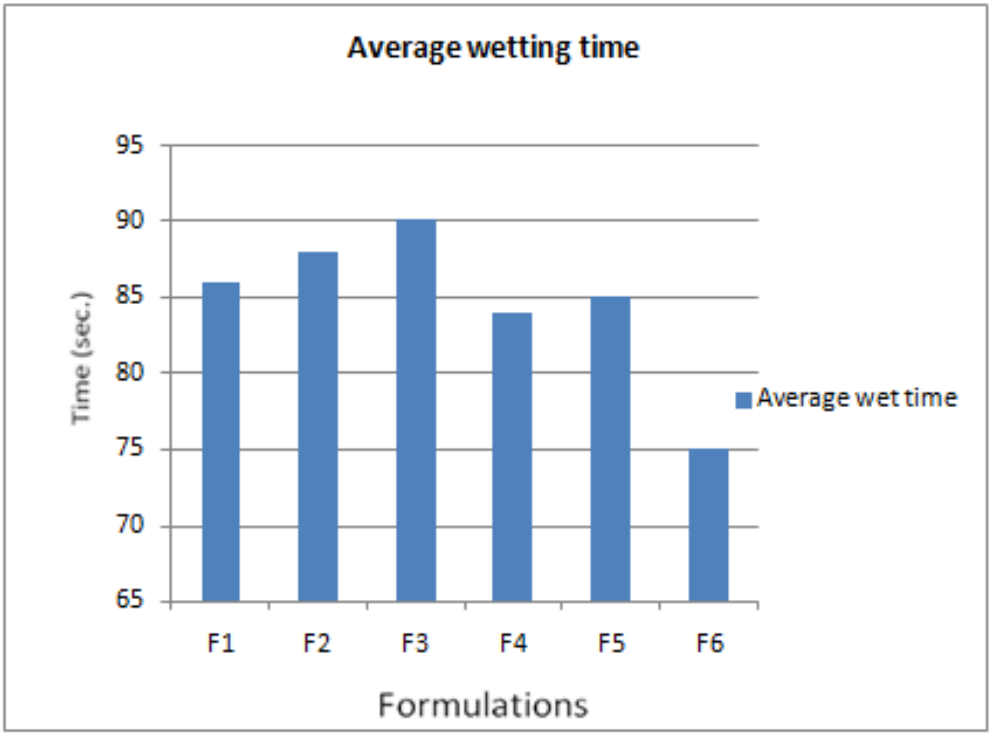

Fig 9: average wet time of all six formulations.

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CONCLUSION

In the present work dispersible tablets of silymarin were prepared by dry granulation method using superdisintegrants such as sodium starch glycolate, croscarmellose sodium, crospovidone. Total six formulations were prepared, these all the tablets formulations of silymarin were subjected to weight variation, hardness, friability, in-vitro disintegration, drug polymer interaction, drug content uniformity, wetting time, disintegration time and in-vitro drug release. All formulations were found to be good and were free from chipping and capping. The drug content of tablets was uniform in all the batches and was between 95to 100%.Formulation F6 have found best formulation compare to other formulations so it was concluded that fast dissolving tablet of silymarin can be prepared and in this research work it was successfully prepared with less than 1 minute disintegration time.

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