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Scleroglucan Based Drug Deliveyr System

1varsha Baban Dhavale, 2akshata Anil Patil

1lecturer, 2lecturer

1shri Sayajinath Maharaj College Of Pharmacy Wadmukhwadi Pune,

2shri Sayajinath Maharaj College Of Pharmacy Wadmukhwadi Pune

Abstract:-

Scleroglucan can be used film forming polymer, along with 2% carbomer it gives good result, 1-2% glycerol use as plastizer, which give thin, elegant, transperants films.

Flurbiprofen (FP) is a nonsteroidal anti-inflammatory agent indicated for the acute or long-term treatment of the signs and symptoms of rheumatoid arthritis and osteoarthritis. FP is extensively metabolized in the liver. Serious gastrointestinal toxicity, such as bleeding, ulceration, and perforation.

The formulated mouth dissolving films were evaluated for physical characteristics such as uniformity of weight, thickness, folding endurance, drug content uniformity, surface pH, percentage elongation, tensile strength, disintegration time, *In-vitro* drug release tests and stability study and this entire test gave satisfactory results. The FTIR and DSC studies revealed that no physicochemical interaction between excipients and drug. All formulations exhibited essentially similar release patterns. The stability studies of the optimized formula were carried as per ICH guidelines.

So in these cases formulation of mouth dissolving films of flurbiprofen avoid above adverse effect to git system,.

Keywords: mouth dissolving films, scleroglucan, flurbiprofen. adverse effect on git system.

1. INTRODUCTION

formulation of mouth dissolving films of flurbiprofen avoid above adverse effect to git system, since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in side effects associated with the molecule. Flurbiprofen is BSC class-II drug, which have high permeability and low solubility, humic acid use as solubility enhancer which increases the solubility of drug. The results of this study indicate that flurbiprofen containing fast dissolving films is a promising approach therapy to provide relief for rheumatoid arthritis.

Scleroglucan can be use as film forming agent because of some ideal properties of scleroglucan as film forming polymer.such as the high stability a normal condition ,soluble in water.good fliming forming capacity.

2. MATERIALS AND METHODS:

2.1 Materials:

Flurbiprofen was obtained as gift sample from Plot no.19&20/2 M.I.D.C. Industrial area Dhatav , Roha, Dist-Raigad, Maharashtra**,** Methanol AR, from Loba Chemie Pvt. Ltd, Mumbai, Humic acid from Sigma-Aldrich co. Ethanol AR from ChangshuYangyuan Chemicals, China All chemicals were of analytical or technical grade and were used without further treatment.

2.2 Method

2.2.1 Analytical method

The absorbance of Flurbiprofen solutions (concentrations ranging between 10 and 50 µg/ml; in pH 6.8 phosphate buffer solution was determined at 247 nm (λmax of flurbiprofen) using UV spectrophotometer (Shimadzu UV-1800). The experiment was conducted in triplicate.(5,6)

2.2.2 Drug - Excipient Compatibility Study

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. Physical observation should be done at every week up to 1 month and FTIR studies and DSC Studies were carried out to determine the compatibility of excipients with the drug.(7,8)

2.2.2.1 DSC analysis

Samples of 2–8 mg of the pure drug and drug -excipients in 1:1 physical mixture were accurately weighed, encapsulated and hermetically sealed in flat bottomed aluminium pan with crimped on lid.

The pans were positioned on sample pan holder of a DSC 21e, (Mettler Toledo, Melbourne Australia).The samples were heated in an atmosphere of nitrogen over a temperature range from 30 to 300ºC with a constant heating rate of 10ºC/min. (12)

2.2.2.2 Fourier transforms infrared analysis

The physical mixture of drug with excipients was prepared in 1:1 ratio; the sample was kept at 40°C and was analyzed for any interaction in between the drug and polymer. The analysis was done as per the procedure described i.e. The FTIR spectra of flurbiprofen were recorded using Fourier transform infra-red spectrophotometer (Jasco, FT/IR-4100) with diffuse reflectance principle. The spectrum was scanned over a frequency range 4000 – 400 cm^{-1}. The resultant spectra were compared for any spectral changes.(25)

2.2.3 Preparation of mouth dissolving film by solvent Casting method

The preparation of FDFs of flurbiprofen was based on the solvent-casting method. Briefly, the method consisted of preparing an aqueous solution (Solution I) by adding appropriate amount of accurately weighted polymer in slightly less than 60% of the required volume of deionized water. The mixture was vigorously stirred at 85°C using a hot plate/magnetic stirrer (Remi 2 MLH, Mumbai.) with a dial setting of 400 r/min, until a uniform dispersion was obtained. The hot polymeric dispersion was cooled. This solution was stirred at 250 r/min for 20 min and then left undisturbed to remove air bubbles. The plasticizer was added into this solution and stirring was continued until it was thoroughly mixed.

A second solution (Solution II) was prepared by dissolving the required amount of accurately weighted flurbiprofen in slightly less than 40% of the required total volume of ethanol Solution II was mixed with Solution I stirred for 20 min and made up to 100% of the volume. The mixture was degassed and kept undisturbed to remove any remaining air bubbles. Accurately measured 60 ml of this solution was casted on a film former (VJ Instruments, Amravati) having a base area of 300 cm^2.(25)

2.2.4 Preparation of mouth dissolving film of flurbiprofen by using 23 full factorial designs

A 23 randomized full factorial design was utilized in the present study. In this design two factors were evaluated, each at three levels, and experimental trials were carried out at all n possible combinations. . The factors were selected based on preliminary study. The concentration of Polymer (X1) and concentration of Super disintegrant (X2) were selected as independent variables and were set at two levels ; low medium and high levels of each factor were coded as -1 , +1 ; respectively.

The independent variables were

X_1 = amount of scleroglucan (mg)

X_2 = amount of CCS (mg).

As per runs obtained in design total nine batches were prepared by solvent casting techniques.

2.2.5 Evaluation of oral film

2.2.5.1 Thickness Test

The thickness of the film can be measured by digital vernier calliper at different 5 strategic locations. This is helpful in determination of uniformity in the thickness of the film & this is directly related to the accuracy of dose in the film.(11)

2.2.5.2 Weight variation

Weight variation of the prepared films was studied by individually weighing 3 randomly selected patches. Such determination was performed for each formulation(11)

2.2.5.3 Folding endurance

Folding endurance of the film was determined by repeatedly folding the film at the same place until it break. The number of times the film could be folded at the same place without breaking was the folding endurance value.(11)

2.2.5.4. Tensile strength

Tensile strength of films was determined using an apparatus fabricated in laboratory. A small film strip (3 x 2 cm2) was cut and fixed to assembly. The weight required to break the film was noted and simultaneously film elongation was measured with the help of pointer mounted on the assembly. Measurements were done in triplicate for each batch. The mechanical properties tensile strength and % elongation were calculated for the mouth dissolving film from the above measurements.

Tensile strength is the ratio of maximum stress applied to a point at which the film specimen breaks and can be computed from the applied force at rupture to the cross sectional area of the fractured film as a mean of three measurements and described in the equation(11)

Tensile strength = Load at breakage/ (Strip thickness × Strip Width)

2.2.5.3 Percent elongation

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. (11)

Generally elongation of strip increases as the plasticizer content increases.[63]

% Elongation = (Increase in length ×100) / Original length

2.2.5.4 Surface pH measurement

The surface pH of Mouth dissolving film is determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to the oral mucosa, it is determined to keep the surface pH as close to neutral as possible. A combined pH electrode is used for this purpose. Film is slightly wet with the help of water. The pH is measured by bringing the electrode in contact with the surface of the oral film. This study is performed on three films of each formulation and mean ± S.D calculated. (12)

2.2.5.5 *In-vitro* disintegration studies

Disintegration time study was slightly modified to mimic the in-vitro and in-vivo conditions. For the study, film as per the dimensions (3 x 2 cm2) required for dose delivery were placed on a stainless steel wire mesh containing 10 mL distilled water. Time required for the film to break and disintegrate was noted as *in-vitro* disintegration time. Since, the film is expected to disintegrate in the mouth in presence of saliva; only 10 mL of medium was used. (26)

2.2.5.6 *In-vitro* dissolution studies

The *in-vitro* dissolution studies were conducted using simulated saliva (300 mL). The dissolution studies were carried out using USP dissolution apparatus XXIV (Electrolab, Mumbai, India) at 37 ± 0.5 °C and at 50 rpm using specified dissolution media. The film sample placed on the sieve was submerged into dissolution media.

Samples were withdrawn at 0, 15, 30, 60, 90, 120, 150, 180. Time intervals and filtered through 0.45µm whatman filter paper and were analyzed spectrophotometrically at 247 nm. The absorbance values were converted to concentration using standard calibration curve previously obtained by experiment. The dissolution testing studies were performed in triplicate for all the batches.(26)

2.2.5.11 DSC analysis:

The DSC thermograms of film were recorded using differential scanning calorimeter.

2.2.5.12 Powder X- ray diffraction :

The compatibility between the drug and excipients and stability of drug during storage is determined by using X-Ray diffractor (Bruker AXS D8 Advance).Max. The thermogram of pure drug and film was compared and checked for their compatibility and stability.(25)

2.2.5.12 *Infrared* spectroscopy:

The FTIR spectrum was obtained using FTIR spectrometer (Shimadzu-4100). The samples were mixed thoroughly with potassium bromide in 1:300 (sample: KBr) ratio in a glass mortar. These samples were then placed in a sample holder and scans were obtained at a resolution of 2 cm^{-1} from 4000 to 400 cm^{-1}.(25)

2.3 Accelerated Stability Study

Stability studies on the optimised formulation (batch F6) of oral fast dissolving film packed in aluminium foil were carried out to determine the effect of temperature and humidity on the stability of drug.

The formulation were assessed for their accelerated stability with respect to their appearance, *in-vitro* disintegration time, surface pH & drug release characteristics after storing them at 40 ± 2 ^{0}C / 75 ± 5 % RH for 45 days.(25)

3. RESULTS AND DISCUSSION

3.1 Analytical method

The sample of flurbiprofen was identified by UV spectroscopy. The stock solution 100 ug/ml after suitable dilution was scanned through 200-400 nm. Maximum absorption wavelength (λmax) was found to be at 247 nm. (40)

3.2 Drug-Excipient Compatibility Studies

3.2.1 DSC analysis:-

The DSC thermograms obtained reported that there was no polymer drug interaction as the pure drug Flurbiprofen displayed a single sharp endothermic peak at 119.93 oC corresponding to the melting point of the drug, and a similar peak was also observed in the formulation.(33)

3.3 EVALUAION OF FILM:-

3.3.1 Thickness(Table no-10)

Thickness of all formulation batches (F1 toF8) was observed in the range of 0.135-0.150 mm

3.3.2 Weight (Table no-11)

Weight of all formulations (F1 to F8) has been observed in the range of 63-66 mg

. **3.3.3 Drug content** *(Table no-11)*

Drug content of all F1-F9 formulation was observed in the range of 95 – 100 % . Highest % drug content was observed in F5 formulation.

From regression equation 8.2 indicates positive predominant effect of CCS (R=8928)

Drug content = $+518640+8928X_2$ ------8.2

3.3.4 Folding endurance (Table no-11)

Folding endurance of all formulations was observed in the range of 268 – 290. Folding endurance is the number of times the film could be folded at the same place without breaking. This is indicative of good plasticity of prepared films. The reduced model equation 8.3 indicates that X_1 factor have positive effects on folding endurance e. with increase in concentration of scleroglucan folding endurance increases. (R = 23680)

Folding endurance = $+2184000+23680X_1$ -----8.3

3.3.5 Tensile strength(Table no-15)

Tensile strength for all film was observed in the range of 0.50 to 0.70 $kg/mm^{2.}$.

Regression analysis equation exhibited predominant effect of scleroglucan concentration (R=39921.6)

The reduced model equation 8.4 is given as below

Tensile strength = $+720+39921.6X_1$ -------8.4

3.3.6 Percent elongation(Table no-14)

The % elongation was observed in the range of 42 – 63% for all batches. The reduced model equation 8.5 exhibited in % elongation increase of film with increase in scleroglucan concentration (R = 39408.8).

% elongation = $+373040+39408.8X_1$ ------8.5

3.3.7 Surface pH (Table no-11)

Surface pH of all mouth dissolving films prepared by using different polymers was found to be in the range of 6.5 to 7.2 pH, which was close to the neutral pH, which indicated that films may have less potential to irritate the sublingual mucosa, and hence, more acceptable by the patients.

3.3.8 In vitro disintegration time (Table no-11)

In vitro disintegrating time for mouth dissolving film ranges from 28 ± 0.58 to 38.00 ± 0.0171 sec . All the formulations found to gave minimum disintegration time as compared to other preparations, from reduced model equation 8.6 disintegration time decreases with increase in CCS concentration

3.3.9 In-vitro dissolution studies(Table no-12)

In vitro dissolution studies were carried out in phosphate buffer pH 6.8 and the per cent cumulative drug release was calculated. *In-vitro* drug release study results showed that as the concentration of polymer increases, drug release of mouth dissolving films decreases. From dissolution study, faster dissolution was shown by batch F6. This was attributed to increase in amount of CCS.

3.3.10. Solubilitystudy(Table no-16)

By taking different ratio of drug and humic acid absorbance was measured at 247 nm. by taking ratio as 1:1,1:2 and 1:3 there is increase in absorbance, but further increase in ratio of humic acid and drug such as 1:4, 2:1 there is decrease in absorbance. hence for solubility enhancement of flurbiprofen 1:3 ratio of flurbiprofen and humic acid give good release of drug from complex.

From phase solubility study with humic acid up to 2% ,w/v concentration of humic acid increase the solubility of flurbiprofen. above this concentration of humic acid there is no increase in solubility of drug.

3.4. Accelerated stability study(Table no-17)

Evaluation of formulation F6 kept for stability at 40 ºC /75 %RH for 15, 30 and 40 days. The samples were analyzed for *in vitro* disintegration time, surface pH, appearance, *in vitro* drug release studies, DSC, FTIR and PXRD. No appreciable difference was observed for the above parameters.

3.5Validation of 23 Full Factorial Design

Developed 23full factorial design was validated by setting targets for DT and dissolution. The experimental values and predicted values of each response are shown.The percentage relative error of each response was calculated using the following equation:

Percentage Relative Error = (| Predicted value – Experimental value | / Predicted value) ×100

4. CONCLUSION

Oral fast dissolving polymeric films of flurbiprofen were successfully formulated using solvent casting method. The process variables that could affect the film qualities were systematically investigated. Additionally, application of experimental design resulted into selection of significant factors that could affect the disintegration, dissolution and ultimate bioavailability of drug from film formulation. A film containing scleroglucan (film forming polymer) and Croscarmellose sodium (disintegrant) at higher amount is desirable for faster disintegration and dissolution of flurbiprofen . The results of this study indicate that flurbiprofen containing fast dissolving films is a promising approach therapy to provide relief for rheumatoid arthritis .

REFERENCES

REFERENCES:-

1. Gisel EG. Oral motor skills following sensori motor intervention in the moderately eating impaired child with cerebral palsy. Dysphasia. 1994; 9:180.192.

2. Anderson O. et al. Problems when swallowing tablets. Tidsskr NorLaegeforen. 1995; 115: 947- 949

3.Kahrilas P.J.Anatomy, physiology and pathophysiology of dysphagia. Acta. Otorhinolaryngol Belg. 1994; 48: 97.117.

4.Crama A, Breitkreutzb J, Desset-Brèthesc S, Nunnd T and Tuleuf C, Challenges of developing palatable oral pediatric formulations, Int J Pharm 2009; 365: 1-3.

5. Florence AT, Neglected diseases, neglected technologies, neglected patients? Int J Pharm. 2008; 350**:** 1-2.

6. Technology catalysts International Corporation, accessed on Jun. 15th 2011 Available from http://www.Technology catalysts. Com.

7.”Oral Thin **Films**,” in Orally Disintegrating Tablet and Film Technologies, 4th ed. (Technology Catalysts International, Falls Church, VA, 2006), pp: 18-31.

8.Orally Disintegrating Tablet and Film Technologies, Technology Catalysts 3rd Edition, 2006.

9.Kumar D, Rathi L, Tipathi A, Maddheshiya YP. A review of oral mucosal drug delivery system. International journal of pharmaceutical science and research 2010; 1(5): 50-56.

10. Slowson M, slowson, S. What do when patients cannot swallow their medications. Pharma Times.1985;51:90-96.

11. Doheny K. You really expect me to swallow those horse pills? Am Druggist. 1993; 208: 34-35.

15. Nishimura M, Matsuur K, Tsukioka T, Yamashita H. *In-vitro* and In vivo characterstics of prochlorperazine oral disintegrating film. International journal of pharmaceutics 2009; 368: 98-102.

16. Schimoda H, Taniguchi K, Nishimura M, Matsuura K. Preperation of a fast **dissolving** oral thin film containing dexamethasone: a possible application to antiemetic during cancer chemotherapy . European journal of pharmaceutics and Biopharmaceutics 2009; 73: 361-365.

17. Gisel EG. Oral motor skills following sensori motor intervention in the moderately eating impaired child with cerebral palsy. Dysphasia. 1994; 9:180.192.

18.Bayly ci, black wc, leger s, ouimet n, ouellet m, percival md: structure-based design of cox-2 selectivity into flurbiprofen. Bioorg med chem lett. 1999 feb 8;9(3):307-12.

19.Van haeringen nj, van sorge aa, carballosa core-bodelier vm: constitutive cyclooxygenase-1 and induced cyclooxygenase-2 in isolated human iris inhibited by s(+) flurbiprofen. J ocul pharmacol ther. 1, arnstein, h. R. V. (1962).

20.The preparation and use of isotopically labelledOrganic compounds. In c. Rodd (ed.), chemistry of carbon compounds.Elsevier, chapter 1.

21. Bardet, m., Rousseau, a., & vincendon, m. (1993). High-resolution solid-State 13c cp/mas nmr study of Scleroglucan hydration. Magnetic Resonance in chemistry, 31, 887–892.2000 aug;16(4):353-61.

22.anbar m. And neta p., a compilation of specific bimolecular rate constants for the reactions of hydrated electrons, hydrogen atoms and hydroxyl radicals with inorganic and organic compounds in aqueous solution, international journal of applied radiation and isotopes, 18: 493-523, 1967 (23)

23. Anderson r.c. et al., toxicological studies on synthetic glycerin, j. Of the am. Pharm. Ass. 39, 583-585, 1950 (30).

24.Indian Pharmacopoeia 1996, Vol. 2, The Indian Pharmacopoeia Commission. Ghaziabad, p. 734.

25.Jain SP, Shah S, Namita R, Singh PP, Punam A. Twice a day ocular inserts of acyclovir by melt extrusion technique. Indian J.Pharm. Sci. 2007; 5: 152-162.

26.UD. Shivhare. *et al.* / *International Journal of Biological & Pharmaceutical Research.* 2012; 3(1): 66-74.

27. Galey WR, Lonsdale HK and Nacht S. Clinical The in vitro permeability of skin and buccal mucosa to selected drugs and tritiated water. J. Investigative Dermatol. 1976: 67(6): 713-717.

28. Lindgren S, Janzon L. Dysphasia: Prevalence of swallowing complaints and clinical findings. Medical Clinics of North America, (1993); 77: 3 -5.

29. Avery SW, Dellarosa DM. Approaches to treating dysphagia in patients with brain injury. Am. J.Occup.Ther. 1994; 48: 235.239.

30.Gisel EG. Oral motor skills following sensori motor intervention in the moderately eating impaired child with cerebral palsy. Dysphasia. 1994; 9:180.192.

31. Anderson O. et al. Problems when swallowing tablets. Tidsskr NorLaegeforen. 1995; 115: 947- 949

32.Kahrilas PJ. Anatomy, physiology and pathophysiology of dysphagia. Acta. Otorhinolaryngol Belg. 1994; 48:

33.Aggarwal J, Singh G, Saini S., Fast dissolving films: A novel approach to oral drug delivery. Int Res J of Pharm, 2011; 2(12): 69-74.

34.Arya A, Chandra A, Sharma V, Pathak K, Fast Dissolving Oral Films: An Innovative DrugDelivery System and Dosage Form, Int J of ChemTech Research, 2010; 2(1):576-583.

35.Choudhary D.R., Patel V.A. , Kundawala A.J., Formulation and evaluation of quick dissolving Film of levocetirizine dihydrochloride , Int J Pharma Tech ,2011;3 (1) :1740-1749

40.Cilurzo F., Minghetti P., Buratti S., Selmin F., Chiara G.. Gennari , Montanari L., Nicotine Fast Dissolving Films Made of Maltodextrins: A Feasibility Study, AAPS PharmSciTech,2010.

41.Dinge A and Nagarsenker M., Formulation and Evaluation of Fast Dissolving Films for Delivery of Triclosan to the Oral Cavity, Ame. Asso. of Pharma Scientists PharmSciTech. ,2008; 9(2): 349–356.

42.Dixit R.P.,Puthli S.P., Oral strip technology: Overview and future potential , J of Cont Release, 2009 ;139: 94–107

43.Kunte S., Tandale P., Fast dissolving strips: A novel approach for the delivery of verapamil , J Pharm Bioallied Sci. , 2010; 2(4): 325–328

44.Margareth R. C. , Raimar L., May A., Simulated biological fluids with possible application in dissolution testing, Dissolution Technologies 18(3):15–28

45.Reinhart M. , Pivotal Bioequivalence study for Drug Rapidfilm® successfully completed , Labtec Press Release Dummy.rtf dated on 01/14/08

46.Tripathi K.D. , Essentials of medical pharmacology, 5th ed., Jaypee Brothers Medical Publishers ,2009:84,337-340

47.www.accessdata.fda.gov/scripts/cder/dissolution/dsp_SearchResults_Dissolutions.cfmPrintAll=1

48.Rowe R., Sheskey P., Owen S., Handbook of Pharmaceutical Excipients, 5th ed. The Pharmaceutical Press, Grayslake, American Pharmacists Association, Washington 2006, 5th ed, 301-303 ,346-349, 592-593, 742-743.

49.Ozaki Y ,Nomoura T., Pullulan binder and its uses., U.S. Patent 5411945, May2, 1995.

50.Raju S., Reddy P., Kumar V., Flash release oral films of metoclopramide hydrochloride for pediatric use: formulation and in-vitro evaluation, j. Chem. Pharm. Res., 2011;3(4):636-646

51.Saini S., Nanda A., Dhari J., Formulation, development & evaluation of oral fast dissolving anti-allergic film of levocetrizine dihydrochloride , J. Pharm. Sci. & Res., 2011;3(7):1322-1325

52.Samita G., Kumar G., Fast dissolving drug delivery and its technologies. The Pharma Innovation ,2012; 1(2): 34-39.

53.Sapkal N., Kilor V., Daud A., Development of fast dissolving oral thin films of ambroxol hydrochloride: Effect of formulation variables., J of Adv Pharma Res, 2011; 2(2): 102-109

54.Gupta M, Patel M. Enhancement of Dissolution Rate of Rapidly Dissolving Film of Meclizine hydrochloride By Complexation of Meclizine Hydrochloride with beta Cyclodextrine.J of Applied Pharma Sci,2011;1(9):150-153.

55.Mashru R.C., Sutariya V.B., Sankalia M.G., Parikh P.P,. Development and evaluation of fast dissolving film of salbutamol sulphate, Drug Dev Ind Pharm 2005 ; 31 (1) : 25–34

56.Mishra R, Amin A. Formulation and characterization of rapidly dissolving films of cetirizine hydrochloride using pullulan as a film forming agent, Ind J Pharm Edu Res ,2011; 45(1): 71-77.

57.Prabhu P., Malli R., Koland M., Formulation and evaluation of fast dissolving films of levocitirizine

Table no-1.Organoleptic characteristic of drug:-

1	Colour	White
2	Taste	Tasteless
3	Melting point	117^0C
4	Solubility	Freely soluble in methanol and ethanol

Table no 2 .Properties of Scleroglucan (polymer):-

1	Appearance	Powder
2	Colour	Light cream
3	Form	Solid
4	Melting point	157°C
5	Solubility	Soluble in water
6	Chemical stability	Stable at normal condition

Table no 3. I.R.Ranges of flurbiprofen:-

Functional group	Standard value	Observed value
Aromatic	743	701.996
Fluorine	1217	1230
CH3 bend	1505	1414.53
Alkene	1596	16.05
Alkane stretch	3000	3000

Table no-4. Evaluation of trial batches

Sr.no	Evaluation parameters	T1	T2	T3
1	Weight of films	50 mg	51mg	50mg
2	Thickness of films	0.11mm	0.12mm	0.11mm
3	Folding endurance of films	200	225	220
4	PH of films	6.5	6.5	6.6
5	Disintegration time	90(sec)	75(sec)	80(sec)
6	% drug content	22.70%	34.22%	25.50%

Table no-5.Evaluation of films using different plastizier:-

Sr.no	polymer+superdisintegrating agent + plasticizer	Weight of films (mg)	Thickness (mm)	Folding endurance (no)
1	Scleroglucan+PEG400+SSG	40 ± 0.65	0.08 ± 0.04	240 ± 1.09
2	Scleroglucan+Propylene glycol+CCS	45 ± 0.43	0.1 ±0.065	250 ± 1.86
3	Scleroglucan+glycerol+ CCS	50 ± 0.67	0.1 ±0.027	360 ± 0.93
4	Scleroglucan+Sorbital+SSG	50 ± 0.43	0.14 ±0.048	340 ± 0.91

Table no-6. Composition of film :-

Composition of film	Concentration
Flurbiprofen	10%
Scleroglucan	45%
Mannitol	3-6%
Citric acid	2-6%
Na cross caramelllose	5%
Carbomer	2%
Glycerol	2%
Flavouring agent	q.s
Colouring agent	q.s
Ethanol	q.s
Water	q.s

Table no-7. Evaluation of film using different disintegrant:-

Sr.no	Conc. %	Disintegration time of CCN	Disintegration time of SSG
1	2	30	35
2	2	32	34
3	6	20	25
4	2	28	30
5	2	30	32
6	6	18	22
7	6	20	22
8	6	22	26

Table no-8 Disintegration time of film by using combination of different superdisintegrant and plastizer

Sr.no	Superdisintegrant+Plastizier	Disintegration time
1	PEG400+SSG	60
2	propylene glycol+CCS50	80
3	Glycerol+CCS	40
4	Sorbital+SSG	95
5	PEG400+CCS	60
6	Propylene glycol+SSG	50
7	Glycerol+SSG	45
8	Sorlbital+CCS	40

Table no 9. Evaluation based on concentration of polymer and plasticizer:-

Batch	Concentration of scleroglucan	Plastizer	Appearance
I	624 mg	PEG 400 (65 mg)	Sticky, transperants
II	156 mg	Propylene glycol(32.5mg)	Transperants but films is not dry
III	100 mg+carbomer 1%w/w	Glycerol (1 mg)	Smooth, transperants, non - sticky
IV	70 mg	PG (1mg)	Smooth , sticky
V	71mg	Glycerol 1mg	Smooth, transperants, but films is not dry in nature
VI	24.20mg	Sorbital	Films is not uniform it break

Table no 10.Optimization of batches with respect to dependent variables like DT, % drug content:-

Sr.no	Conc. of scleroglucan (%)	Conc. of glycerol (%)	Conc. of CCN (%)	Disintegration time(sec)	%drug content
1	40	6	2	30 ± 0.34	95 ± 0.67
2	45	6	2	32 ± 0.65	99 ± 0.84
3	40	1	6	28 ± 0.34	96 ± 0.56
4	40	1	2	20 ± 0.48	95 ± 0.93
5	45	1	2	20 ± 0.84	100 ± 1.07
6	40	6	6	15 ± 0.98	94 ± 0.54
7	45	6	6	20 ± 0.45	98 ± 0.87
8	45	1	6	18 ± 0.56	99 ± 0.34

Design Model:-

Model	0.000	0
Residual	300.88	7
Cor Total	300.88	7

Values of "Prob > F" less than 0.0500 indicate model terms are significant.

Table no 11.Folding endurance, PH ,disintegration time and drug content% of formulation F1 to F8:-

Batch	Folding endurance(n=3)	pH(n=3)	Disintegration time(sec)	% drug content
F1	220 ± 1.654	6.5 ± 0.6	30 ± 0.187	95 ± 0.066
F2	225 ± 2.03	6.4 ± 0.76	52 ± 0.195	99 ± 0.078
F3	220 ± 1.845	6.6 ± 1.04	20 ± 0.45	96 ± 0.198
F4	220 ± 2.067	6.5 ± 0.87	28 ± 0.78	95 ± 0.298
F5	230 ±1.598	6.5 ± 0.98	30± 0.65	99 ±1.09
F6	225 ± 1.498	6.4 ±1.04	15 ± 0.76	94 ± 0.98
F7	220 ± 2.059	6,6 ± 0.56	20 ± 0.56	98 ±0.96
F8	225 ± 1.78	6.5 ± 0.67	18 ± 0.34	99 ±1.03

Table 12. *In-vitro* dissolution studies for all batches

Time (secs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	**F6** (%)	F7 (%)	F8 (%)
15	20.07	21.61	29.32	19.3	23.92	**32.41**	24.7	21.61
30	24.70	27.78	31.64	27.79	38.59	**47.08**	40.9	39.36
60	30.01	34.73	39.36	30.01	56.34	**56.34**	52.48	45.53
90	33.19	48.63	48.62	37.04	79.49	**64.83**	57.11	52.48
120	45.53	60.98	58.65	43.22	84.13	**71.78**	68.69	56.34
150	47.85	84.13	70.23	54.80	87.21	**79.49**	74.86	65.6
180	79.5	87.21	77.95	84.13	77.95	**98.02**	77.95	71.78
210	81.81	82.58	89.53	85.67	82.58	**81.04**	81.04	80.27
240	78.73	79.5	91.07	82.58	79.5	**86.44**	74.09	81.04

Table13. *In vitro* dissolution kinetics

Batch code	$T_{50\%}$ (secs)	Best fit model	R	K	N
F1	128	Peppas	0.8410	0.0147	0.1810
F2	124	Peppas	0.9920	0.0124	0.2401
F3	132	Matrix	0.8821	0.0044	-
F4	127	Matrix	0.9103	0.0044	-
F5	139	Peppas	0.9814	0.0180	0.1727
F6	123	Matrix	0.9098	0.0042	-
F7	138	Matrix	0.9198	0.0041	-
F8	143	Peppas	0.9862	0.0162	0.1853

Table14.Average % Elongation of F1 to F 8 batches.

Batch	% Elongation
I	30..28 ± (0.635)
II	28.63 ± (0.613)
III	36.5 ±(0.634)
IV	46.53±(0.631)
V	35.6±(0.630)
VI	40.50±(0.628)
VII	44.44±(0.635)
VIII	35.30±(0.631)

Table 15. Average tensile strength (MDA):-

Batch	% Elongation
I	1.399±(0.03893)
II	1.689±(0.31312)
III	1.6767±(0.03121)
IV	1.480±(0.03252)
V	1.567±(0.03892)
VI	1.6767±(0.03123)
VII	1.382±(0.03823)
VIII	1.651±(0.03080)

Solubilitystudy

Table16Release of drug from complexes:-

Flurbiprofen:Humic acid	***Absorbance (247nm)***	***Concentration***
1:1	0.0010	0.075
1:2	0.0031	0.119
1:3	0.0031	0.119
1:4	0.0029	0.115
2:1	0.0019	0.094

Stability study:-

Table 17.

1.Drug content:-

Batch	Initial	30 days	45 days
F81	93.98%	91.10%	90.32%

2. Disintegration time:-

Batch	Initial	30 Days	45 Days
F82	61.1 sec	60 sec	65 sec

3. t50(min)

Batch	Initial	30 days	45days
F83	6.0	7.5	7.8

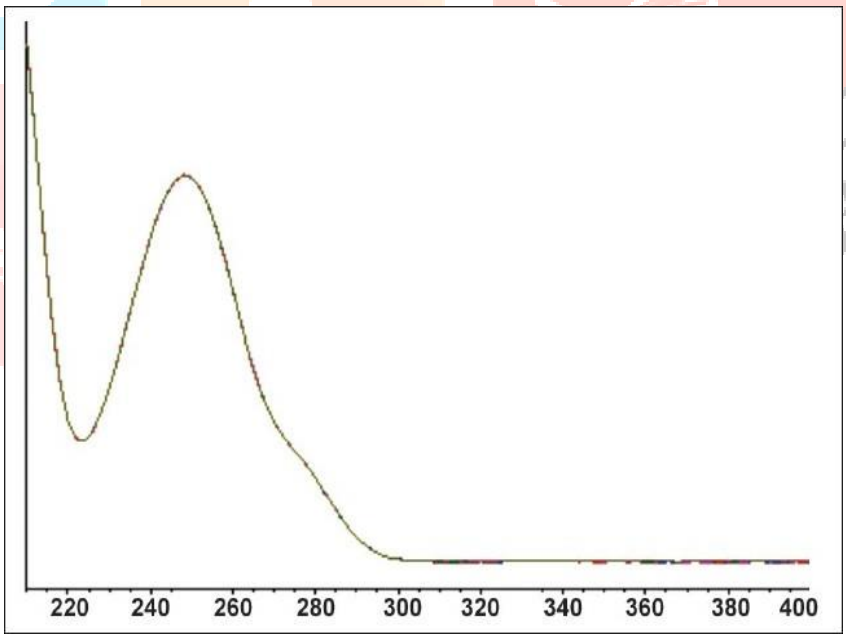

Fig-1. Maximum absorption of flurbiprofen at 247 nm (Wavelength in nm)

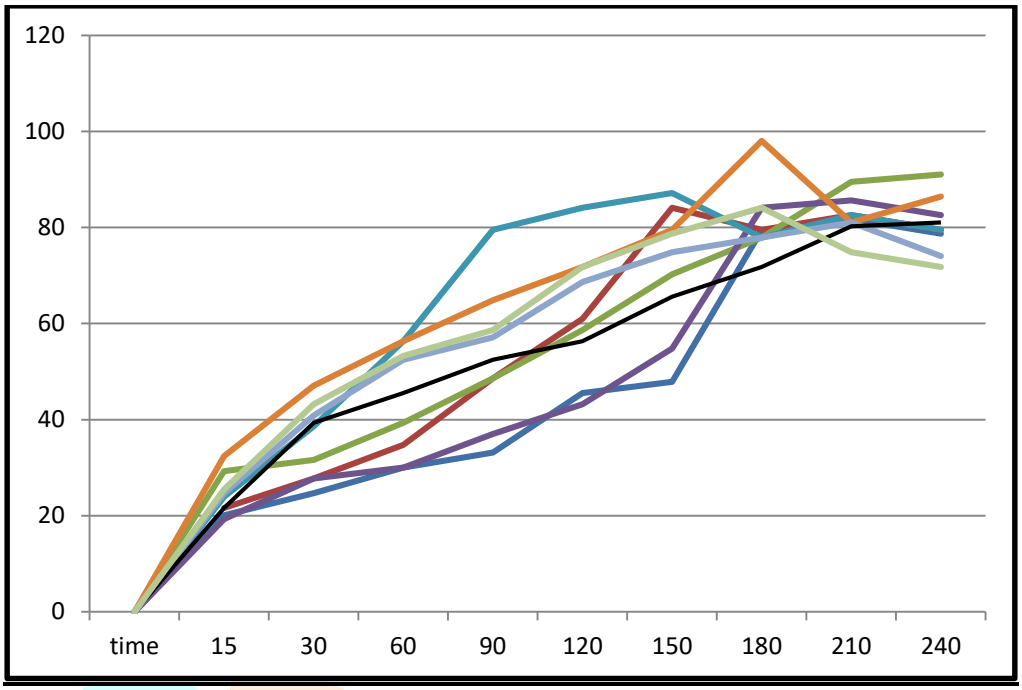

FIG. 2.Comparative *in* vitro dissolution profiles for all batches

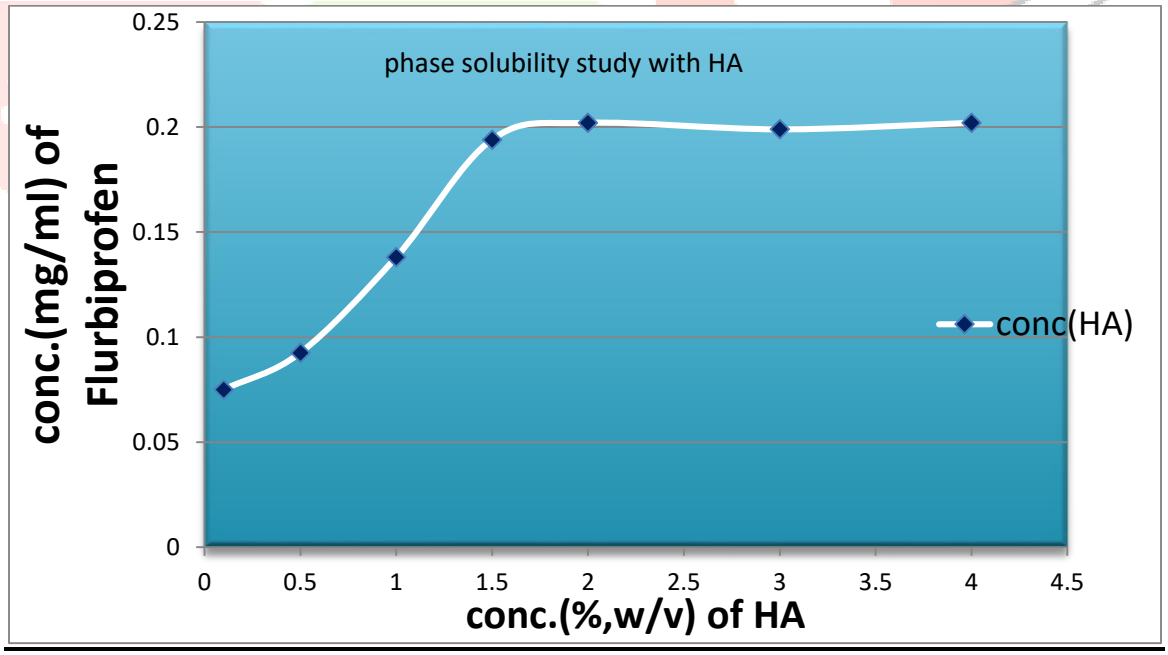

Fig.3- Phase solubility study of flurbiprofen with humic acid.

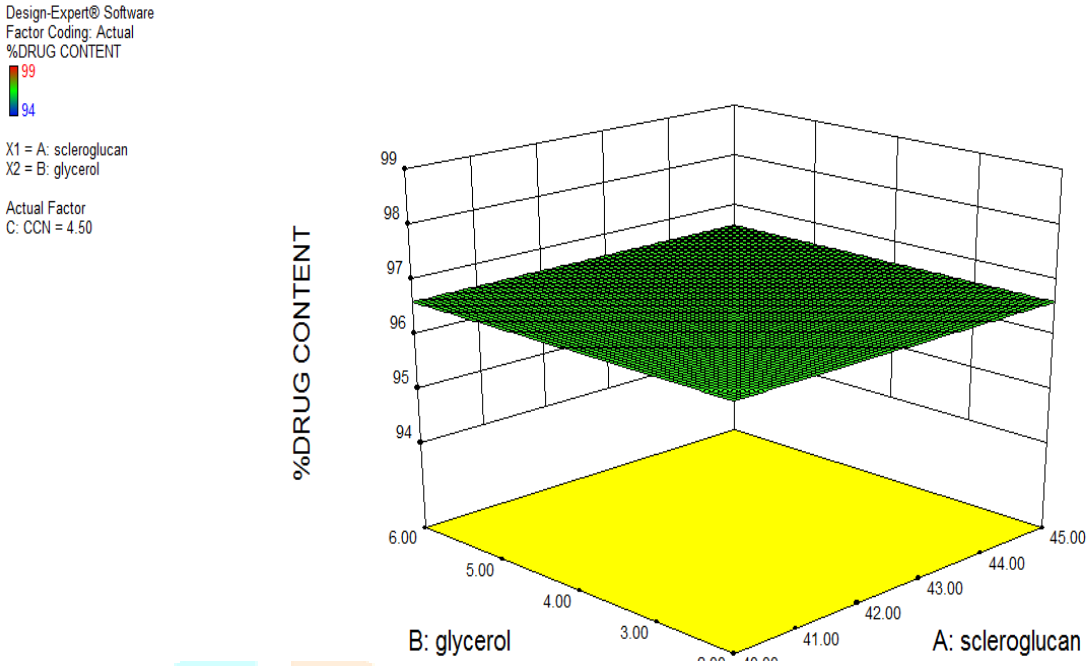

Fig 4 :-Response surface plot of % drug content

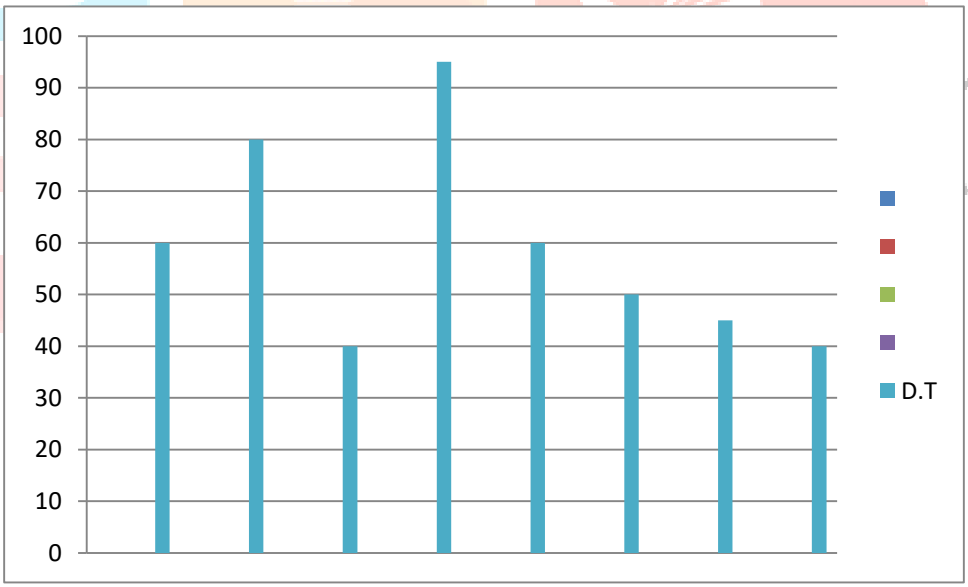

Fig-5.-Disintegration time of film by using combination of different superdisintegrant and plastizer

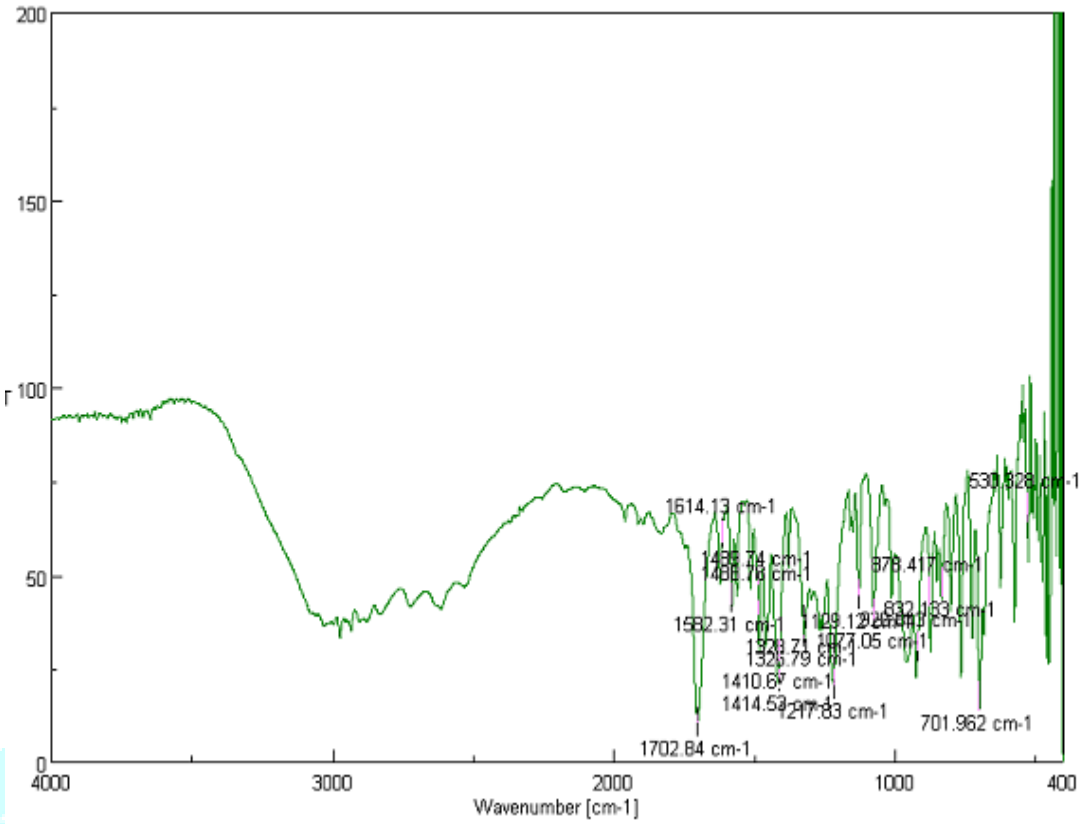

Fig -6 I.R GRAPH OF FLURBIPROFEN

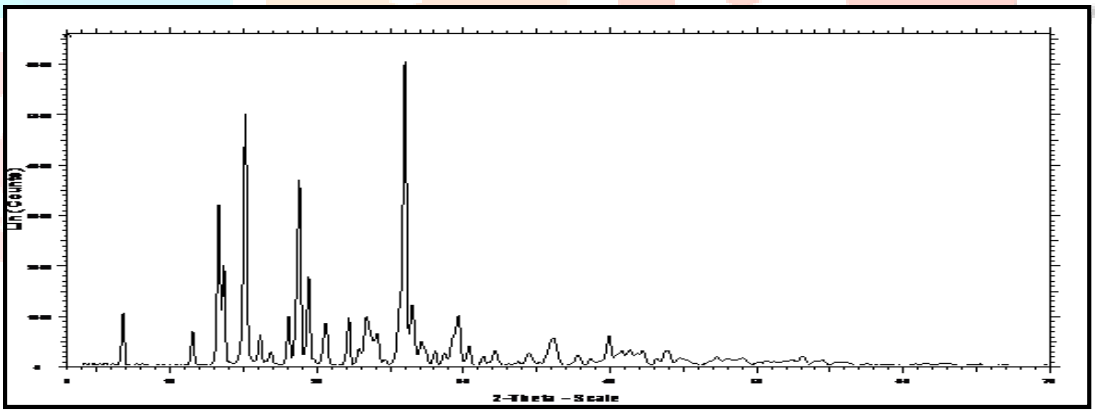

Fig 7 XRD graph of flurbiprofen

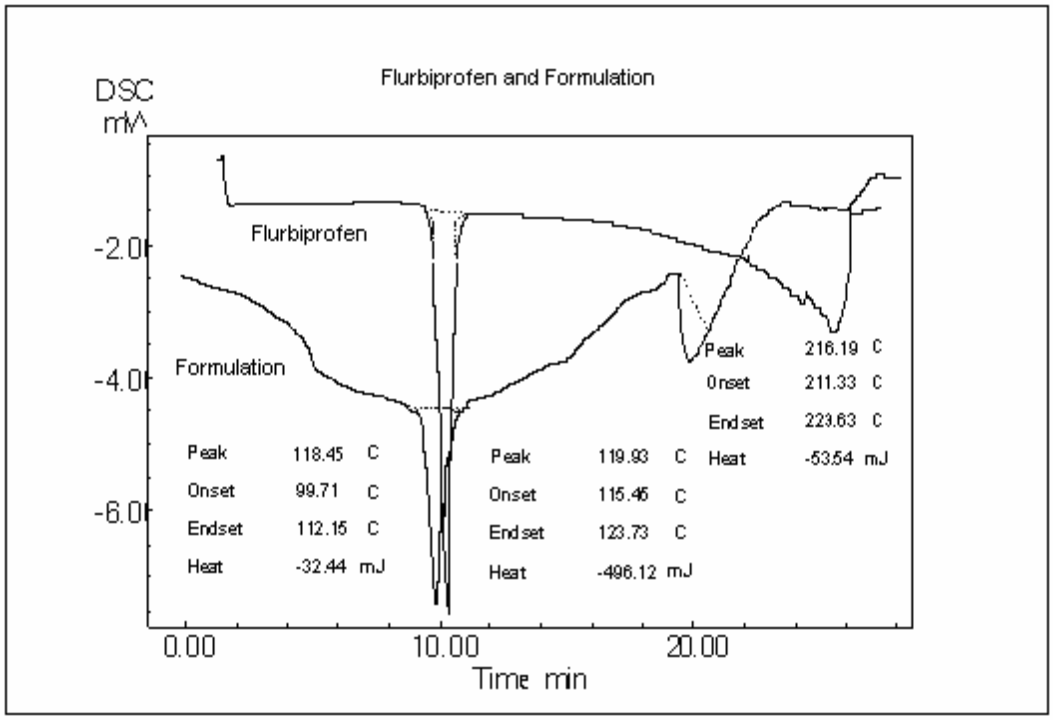

Fig 7 DSCgraph of formulation and flurbiprofen

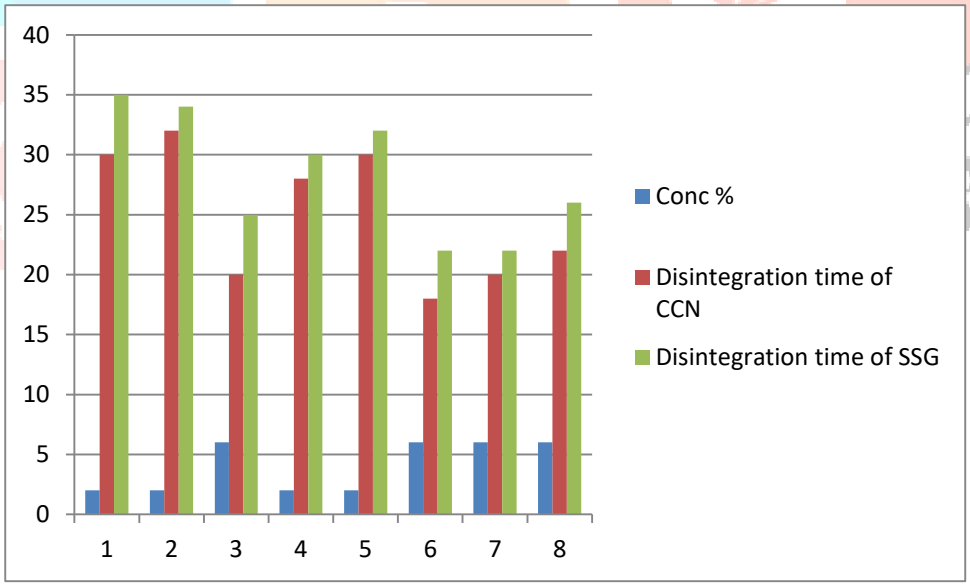

Fig 8 comparative study of disintegration time of CCS and SSG