Preliminary Evaluation of *Cassia auriculata* Seed Mucilage as Binding Agent

Singh S.K.*[1], Ushir Y.V.[2], Chidrawar R.V.[3], Vadalia K.R.[4], Sheth N.R.[5] and Singh S.[6]

[1, 2, 3, 4,] *Shree H. N. Shukla Institute of Pharmaceutical Education and Research, Rajkot, (Guj), India*
[5]*Dept. of Pharmaceutical sciences, Saurasrta University, Rajkot, (Guj), India*
[6]*C.P.S. Mahuda college of Pharmaceutical sciences, Bhermpur, (Oris), India*

ABSTRACT

Cassia auriculata is a tropical tree locally belonging to the family Caesalpiniaceae found widely in India. Seeds of plant contain gluco-mannose hence attempt to evaluate the seeds for suitability as tablet binder is considered and the present investigation reports the isolation of mucilage of *Cassia auriculata* seed. The DSC and FTIR thermograms of drug and gum indicated no chemical interaction. Phytochemical characteristics of mucilage, such as carbohydrate, protein and flavanoids etc. were studied. Physiochemical characteristics of mucilage, such as solubility, swelling index, loss on drying, viscosity, hydration capacity, powder porosity, microbiological properties and pH were studied. The mucilage was evaluated for its granulating and binding properties in compressed tablet, using Diclofenac sodium as model drug. Mucilage was used in four different concentration i.e. 0.25, 0.5, 0.75 and 1.0% w/v. The granules were prepared by wet granulation process. The prepared granules were evaluated for percentage of fines, average particle size, compressibility index and flow properties. The properties were compared with Guar gum, which was used as standard binder at 1.00% w/v concentration. The tablet were prepared and evaluated for content uniformity, hardness, friability, disintegration time and *in vitro* dissolution profile. The tablets had good physiochemical properties, and the drug release was more than 85% within 3 hour. It was observed that increasing the concentration of mucilage increases hardness and decreases the disintegration time. All the formulations (F1, F2, F3, F4 and F5) were subjected to stability studies for three months at 25°C/60% RH, 30°C/65% RH and 40°C/75% RH as per ICH guidelines, only F1 and F2 showed stability with respect to release pattern and other parameters which confirm the use of mucilage as excipient.

Keywords: *Cassia auriculata*, Mucilage, Hydrogel, Binder, Dicolfenac sodium.
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***Author for Correspondence:** +912813298393 ; +919978819269 ; sudarshansingh83@gmail.com

INTRODUCTION

The high cost of imitation polymer and ecological pollution by chemical diligence has made the scientist in budding country to enter into era, in which plant products serve as alternative to synthetic products because of local accessibility, environmental gracious nature, subordinate prices and nontoxic compared to imported synthetic products. Today we have number of plant based pharmaceutical excipients such as guar gum, starch, agar, alginate, acacia, cocoa butter, cellulose etc. These natural excipients are used as binder, disintegrants in tablet, protective colloids in suspensions, thickening agent in oral liquids, gelling agents in gels and based suppositories. Similarly many plants restrain mucilage, which provide high concentration of complex sugar and uronic acid unit.

Mucilage and gums have been known since ancient times for their medicinal uses. In the contemporary era also they are widely used in the pharmaceutical industries as thickeners, water retention agents, emulsifying agent, suspending agents, binders and film formers (1-2). Apart from its use in finished medicines, newer uses have been found in the preparation of cosmetics, textiles and paint paper, hence the demand for these substances is increasing and new sources are getting tapped (3-4). Though, India due to geographical and environmental positioning has traditionally been a good source for such products among the Asian countries, a large quantity of this is still being imported from the European countries to meet up the ever-increasing demand (5). Of all the orally administered dosage forms, tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of changes in

various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy.

Cassia auriculata is available locally belonging to the family Caesalpiniaceae and has not been explored as pharmaceutical excipients. The roots and seeds are astringent, cooling, depurative, alexateric, leprosy, tumors, asthma, urethrorrhoea, leaves are used in ulcers. Flowers are used in diabetes. The seed of *Cassia auriculata* swells and form gelatinous mass when it comes in contact with water due to its hydrophilic nature. Hence the present work was attempted to evaluate binding properties of seed mucilage of *Cassia auriculata*.

MATERIAL AND METHOD

Cassia auriculata seeds were procured from the forest of KORBA, Chhattisgarh, India. Diclofenac sodium was obtained as gift sample from Active Pharmaceutical Ingredient. All other ingredient were of analytical grade and purchased from Loba Chemicals, Mumbai.

Isolation of Mucilage from Cassia auriculata Seeds

Cassia auriculata seeds Kernel's powder (20g) were soaked in cold distilled water (200 ml) and slurry was prepared. Then slurry was mixed with 800 ml of boil distilled water. The solution was boiled for 20 minutes under stirring condition in water bath. The resulting thin clean solution was kept overnight for settling protein and fibers. The solution is centrifuge at 5000 rpm for 20 minutes. The supernant was separated and poured in to twice the volume of absolute acetone by continues stirring to precipitate the polysaccharides. The precipitate was washed with absolute ethanol, diethyl ether and petroleum ether and then dried at 40–45°C and passed through sieve #120 and stored in desiccators until used for further studies (6–8).

Drug-Excipients Compatibility Studies

This study has been done to check whether there is any compatibility related problems are associated with drug and the excipients used for the formulation of tablet. The drug and excipients must be compatible with one another to produce a product that is stable, efficacious, attractive, and easy to administer and safe. If the excipients are new and not been used in formulations containing the active substance, the compatibility studies are of paramount importance. Thermal analysis and FTIR can be used to investigate and predict any physicochemical interactions between components in a formulation and can therefore be applied to the selection of suitable chemically compatible excipients.

FTIR Spectroscopy

The IR spectral analysis of a drug and other excipients were taken using Press pellet technique (using KBr). The IR spectra's were determined by using 1601 PC Shimadzu UV Spectrophotometer (9-12).

Differential Scanning Calorimeter Studies (DSC)

DSC was performed on a Shimadzu DSC-60 (Shimadzu Limited Japan). A 1:1 ratio of drug and excipient was weighed into aluminum crucible and sample was analyzed by heating at a scanning rate of 10°C/min over a temperature range 20°300°C under a nitrogen flow of 40ml/min. Reproducibility was checked by running the sample in triplicate (13-14).

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Preliminary Phytochemical Screening of Isolated Mucilage

The phytochemical properties such as presence of carbohydrate, protein, flavanoids, sterols, alkaloids, tannins, saponins and terpenoids determined (15).

Physicochemical Properties of Isolated Mucilage

The physicochemical properties such as solubility, pH and viscosity of dried mucilage were determined at 20°C. The loss on drying (LOD), ash values (total ash content, acid insoluble ash and water soluble ash) were determined according to Ayurvedic Pharmacopoeia of India (A.P.I) (16).

Microbiological properties

Microbial Load

Preparation of Inoculums

1g powder of *Cassia auriculata* mucilage was suspended in 10 ml of sterile water (inoculum). 1ml of inoculum was transferred to 99ml dilution blank (sterile water) which was diluted inoculum.

Plate Count Technique

Inoculum (1 ml) and diluted inoculum (1 ml) were transferred to separate petridishes 9 to 10 cm in diameter. After addition of both the inoculum to the plate, 20 ml of agar medium (40-45°C) was poured in to a each plate. Both the plates were gently rotated for through distribution of inoculum throughout the medium and solidified (17–19).

Preparation and Evaluation of Granules

Diclofenac sodium was used as model drug to formulate the granules. Lactose and aerosil was used as diluents and lubricant respectively. Binder solution was prepared by dissolving the mucilage of the *Cassia auriculata* in water at 0.25%, 0.50%, 0.75% and 1.0% w/v concentrations. The batch size was 100gm. The drug, lactose and aerosil were mixed thoroughly and sufficient volume of 20 ml of 0.25%, 0.50%, 0.75% and 1.0% w/v mucilage of *Cassia auriculata* (MCA) was added slowly to powder blend, and kneading was performed for near about 10 min until the formation of wet mass with enough cohesiveness. The wet mass forced through the sieve # 18 and dried at 40-45°C in hot air oven for 40 min the dried granules were received through sieve # 20. The prepared granules were then evaluated for percentage of fines, particles size and flow properties by measurement of angle of repose (20–21). The bulk and tapped densities of the granules were then assessed in accordance with the USP XXV tapped volume meter apparatus compressibility index of the granules was determined by Carr's compressibility index (22–23).

Preparation and Evaluation of Tablet

Tablets were compressed by using single punch machine (Cadmach) using flat faced punches. Each tablet weighed 200mg (Table 1). The prepared tablets were evaluated for content uniformity, hardness, disintegration time and *in vitro* dissolution profile using method specified in Indian Pharmacopoeia (I.P) (17).

RESULT AND DISCUSSION

The dried and coarsely powdered seeds of *Cassia auriculata* yielded high percentage (14.6% w/v) of mucilage using acetone as mucilage precipitating solvent. The thermogarm of drug and mucilage shows that there is no change in melting point which confirms that there is neither change in crystallinty of the drug nor any interaction further it was confirmed by FTIR spectral analysis (Figure 1, 2). The phytochemical screening of natural mucilage confirmed polysaccharides in nature (Table 2). The physicochemical and microbiological properties of MCA were determined. The MCA completely soluble in warm water, swelling index, viscosity obtained 25% and 3.51cps. The pH of the mucilage was found to be 5.8 were very near to neutral it may be less irritating on gastrointestinal tract and hence gum is suitable for uncoated tablet (Table 3). The extracted and purified natural gum were evaluated for microbial load, MCA shows 120 CFU per gram of gum which shows mucilage were under microbial limit (Table 4). The prepared granules were evaluated for percentage of fines, flow Properties ((Table 5). It was observed that percentages of fines were reduced as the concentration of mucilage was increased. The percentage of fines was little higher in granules prepared using 0.25% of mucilage as binder. The flow properties of granules were determined by angle of repose which was found to be 28° to 32°. Hence all the granules exhibited good flow properties. Bulk densities of the prepared granules were found to decrease of prepared granules were found to decrease slightly by increasing the concentration of MCA. This result may be due to the formation of larger agglomerates and decrease in fines in the granules, as increasing MCA concentration. The result of compressibility index indicates decrease in flow ability with increasing MCA concentration. However, all formulation showed good flow properties. In general

Table 1: Composition of Tablet Formulation

Ingredient	Seed mucilage of *Cassia auriculata* as binder				Guar gum
	F1	*F2*	*F3*	*F4*	*F5*
Diclofenac sodium	50 mg	50 mg	50 mg	50 mg	50 mg
MCA	Q.S	Q.S	Q.S	Q.S	Q.S
Lactose	Q.S	Q.S	Q.S	Q.S	Q.S
Aerosil	4 mg	4 mg	4 mg	4 mg	4 mg
Total weight	200 mg	200 mg	200 mg	200 mg	200 mg

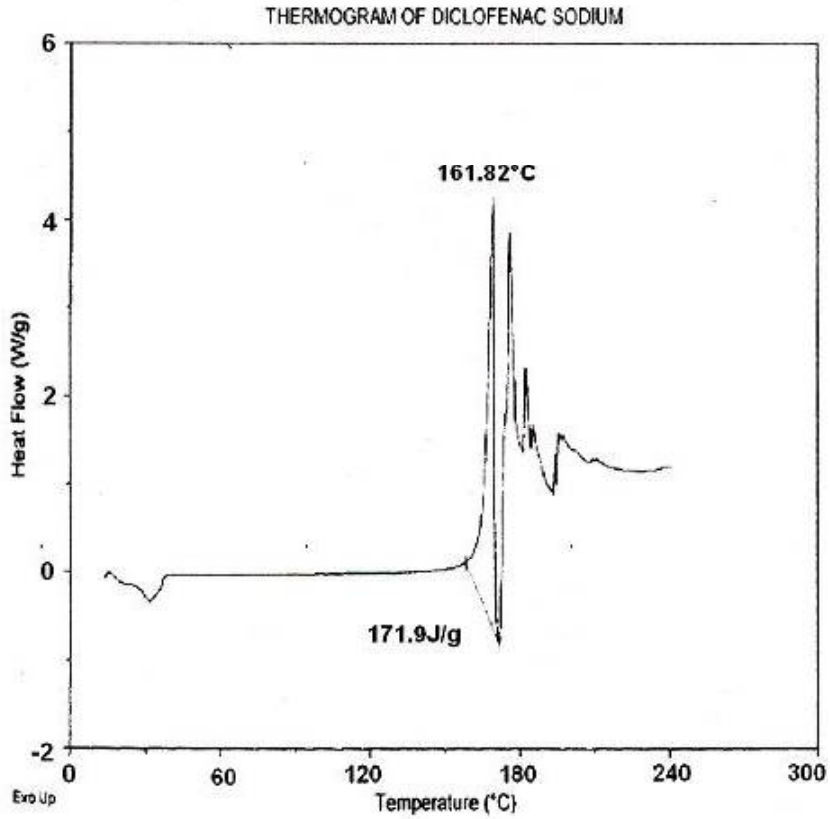

Figure 1: *DSC Thermogram of Diclofenac sodium*

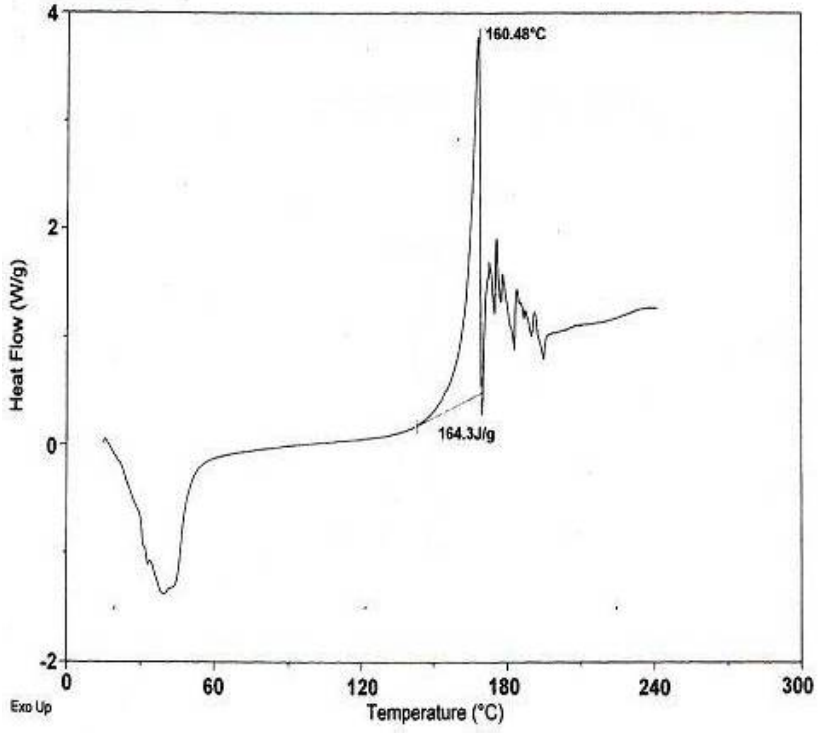

Figure 2: *DSC Thermogram of Diclofenac Sodium and MCA Physical Mixture*

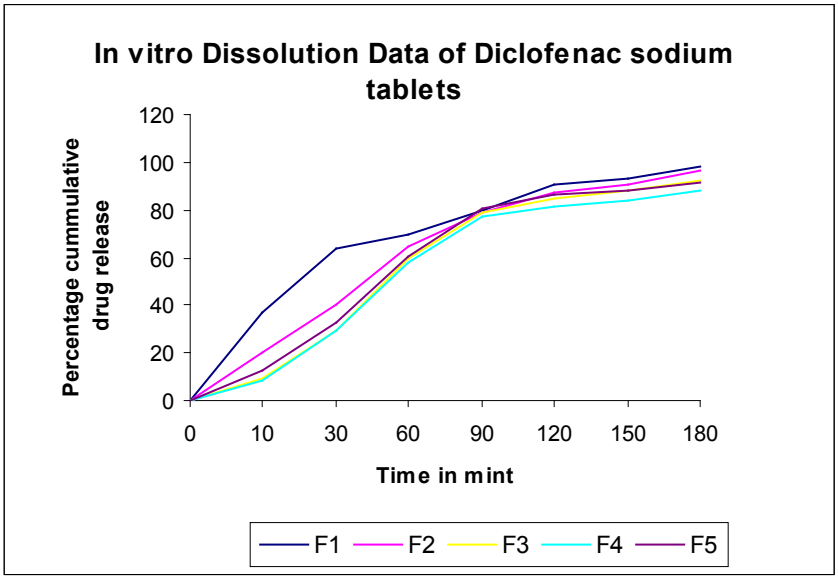

Figure 3: *in vitro dissolution profile of Diclofenac sodium tablets prepared with seed mucilage of Cassia auriculata as binding agent.*

compressibility index values up to 15% result in good to excellent flow properties. All these result indicates that the granules possessed satisfactory flow properties and compressibility. Four batch of tablet were prepared using MCA at four different concentration (0.25, 0.5, 0.75, 1.0%w/v) Guar gum mucilage (1.0 %w/v) was used as standard binder for comparison. The prepared tablets were evaluated for content uniformity, hardness, friability, disintegration time, dissolution profile. All the batches of tablet exhibited good uniformity in content. Hardness of tablet increased with increase in concentration of mucilage. The tablet prepared with 1.0% mucilage of MCA showed the hardness nearly equal to the tablet prepared by using 1.0% w/v of Guar gum mucilage. The percentage friability values were slightly decreased as increase in concentration of mucilage. Through increase in hardness of tablet, increase in concentration interestingly showed decreased in disintegration time of tablet. However this may be due to disintegrant property of such type of mucilage. In vitro dissolution study showed that drug release from the tablets prepared by using mucilage at four different concentrations was more than 85% in 3h (Figure 3).

Table 2: Data Showing, Preliminary Phytochemical Screening of Isolated Mucilage

Active constituent	"NG" Mucilage
Carbohydrate	+
Protein	-
Flavanoids	-
Tannins	-
Saponins	-
Sterols	-
Alkaloids	-
Terpenoids	-

+ Present, - Absent.

Table 3: Physicochemical Properties of MCA

Parameter	Result*
Solubility	Soluble in cold water and warm water; forming viscous colloidal solution, Insoluble in Alcohol, Chloroform, Ethyl acetate & Diethyl ether.
Swelling index (%)\	25.0± 0.15
pH	5.8
Viscosity (0.15%w/v solution)	3.51 cps
Specific gravity (g/ml of 0.15%w/v solution)	0.9975
Loss on drying (%)	8.1 ± 0.02
Total ash (%)	7.72± 0.13
Acid insoluble ash (%)	0.57± 0.05
Water soluble ash (%)	6.532± 0.08

*All values are mean ± S.D. for n=3

Table 5: Technological Characterization of Granules and Tablet, Using MCA as Binder.

Properties	Seed mucilage of *Cassia auriculata* as binder				Guar gum
Concentration	0.25%	0.50%	0.75%	1.00%	1.00%
Percentage of fines (%)	21.50	20.40	19.10	17.40	18.06
Angle of repose	32.56°	30.40°	28.64°	29.42°	25.84°
Mean particle size (mm)	0.34	0.31	0.33	0.32	0.34
Percentage friability (%)	0.75	0.62	0.54	0.46	0.35
Disintegration time in min	8	9	11	14	13
Loose Bulk density (g/cm^2) ± SD	0.576±0.05	0.553±0.03	0.530±0.06	0.513±0.01	0.522±0.04
Tapped bulk density (g/cm^2) ± SD	0.620±0.04	0.607±0.01	0.588±0.02	0.582±0.01	0.580±0.02
Compressibility index (%)	7.09±0.78	7.02±0.24	7.062±0.05	7.01±0.04	7.08±0.07
Content uniformity (%) ± SEM	99.6±0.44	100.2±0.54	100.1±0.52	101.4±0.51	101.0±0.70
Hardness (kg/cm^2) ± SEM	4.90±0.44	5.80±0.04	6.20±0.08	7.10±0.07	6.8±0.10

*All values are mean ± S.D. for n=3

Table 4: Technological Characterization of Microbial load

Natural gum	No. CFU/ ml	Microbial load (No. of CFU / gm of gum)
MCA	12	120

CONCLUSION

The exhausted literature survey conclude before the present work that there is no binding property study on record of this much valued traditional drug. From the above study, it was conclude that Cassia auriculata mucilage can be used as a binder in formulation of uncoated tablets as increase in concentration of mucilage increases the hardness and decrease the disintegration time. This property of mucilage can overcome the friability problems of orodispersible tablets. Moreover it may prove economical as binding property of 1.0% MCA is almost equivalent to 1.0% Guar gum mucilage.

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REFERENCES:

1. Monif T, Mahlhotra AK and Kapoor VP. *Cassiafustula* seed galactomannan: Potential binding agent for pharmaceutical formulation. *Indian J Pharm Sci*. **54**:234–240 (1992).
2. Kapoor VP, Banerji R and Prakash D. Leguminous seeds: Potential industrial sources for gum, fat and protein. *J. Sci Ind Res*. **51**:1–22 (1992).
3. Kakrani HK and Jain NK. A study on binding properties of guggul gum. *Indian J Hosp Pharm*. 100–102 (1981).
4. Bhunvara NS and Khorana ML. Studies on suspending property of mucilages of *hyprophilaspinosa*, *Indian Drugs*. **22**:500–502 (1985).
5. Whistler RL, *Polysaccharides and their Derivatives Industrial gums*, 2nd edition. (Academic Press, New York, 1973) 807.
6. Nandi RC, A Process for preparation of polyose from the seeds of Tamarindus indica, *Ind. Pat*, 142092 (1975).
7. Rao PS and Srivastav HC, *Tamarind Indusrtial gums* In: Whistler R.L., 2nd Edition, (Academic Press, New York, 1973) 369–411.
8. Rao PS. Extraction and purification of tamarind seed polysaccharide. *J Sci Ind Research*. **4**:705 (1946).
9. Willard, Meritt, Dean and Settle, *Instrumental method of analysis*, 7th edition, (CBS Publication New Delhi, 1988) 201–209.
10. Sharma YR, *Element organic Spectroscopy*, 4th edition. (S.Chand Publication, New Delhi, 2009) 132–133.
11. Beckett AH and Stenlake JK, *Practcal Pharmaceutical chemistry, Part 2*. (CBS Publication New Delhi, 2004) 383–389.
12. Tayed PT and Vavia PR. Inclusion complexes of ketoprofen with -cyclodextrin: oral pharmacokinetics of ketoprofen in human *Indian J. Pharm. Sciences*. 408–412 (2005).
13. Murli Mohan GV, Controlled release of diclofenac sodium by gum karaya-chitosan complex coacervate *in vivo* Evaluation. *Indian J. Pharm. Sciences*. 408–412 (2001).
14. Ministry of health and family welfare, *Indian pharmacopeia* 3rd edition. (New Delhi, 1985) A73, A-88.
15. Kokate CK, *Practical Pharmacognosy*, 4th Edition. Vallabh Publication, Delhi; 123 (2006).
16. Michael J and Pelezar JR, *Microbiology*, 5th edition. (Tata, McGraw-Hill Publication, New Delhi, 1993) 126–127.
17. Ministry of health and family welfare, *Indian Pharmacopeia*, (New Delhi, 1996) 2, 710, 711, A-89, A-95, A-114–115, A-80.
18. Gordon RE, Rashanka TW, Fonner DE, Anderson NR and Bankar GS. In: Lachman L., Liberman H.A., and Schwartz J.B. ed. *Pharmaceutical Dosage Forms: Tablets*. Vol. **2**, Marcel Decker, New York; 245 (1999).
19. Banker GS and Neil RA. In; Lachman L., Liberman H.A. and Joseph L.K., ed. *Theory and practices of industrial pharmacy*, 3rd Edition. Varghese publication, mumbai; 297 (1987).
20. Shah D, Shah Y and Rampradhan M. Development and Evaluation of Controlled-Release Diltiazem HCl Microparticles Using Cross-Linked Poly(Vinyl Alcohol). *Drug Develop. Ind. Pharm*. **23**:567 (1997).

21. Aulton ME. Powder flow. In: *Pharmaceutics-The design and manufacture of medicines*. Churchil Livingstone, London New York; 176 (2007).
22. Martin A, Swarbrick J and Cammarata A. Micromeritics. In: *Physical pharmacy and pharmaceutical sciences*, 5th Edition. Wolters Kluwer publication, New Delhi; 492 (2008).
23. Reddy KR, Mutalik S and Reddy S. Once-daily sustained-release matrix tablet of Nicorandil: formulation and *in vitro* Evaluation. *APPS Pharm. Sci. Tech*. **4**(4): (2003).

Figure 1: DSC Thermogram of Diclofenac sodium

Figure 2: DSC Thermogram of NG

Figure 3: in vitro dissolution profile of Diclofenac sodium tablets prepared with seed mucilage of Cassia auriculata as binding agent.