ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research
Available Online at www.jbpr.in
CODEN: - JBPRAU (Source: - American Chemical Society)
Volume 4, Issue 2, 2015, 29-42

Research Article

ISOLATION AND EVALUATION OF DISINTEGRATING PROPERTIES OF *BASELLA ALBA* Linn. LEAF MUCILAGE IN TABLET FORMULATIONS

Vishnu Bhat[1], Ravikumar Nayak[1], Praveena M.B[2]

[1]Department of Pharmaceutics, Karavali College of Pharmacy, Vamanjoor, Manglore, Karnataka

[2]Department of QA Microlabs Ltd. Bangalore

Received 23 March 2014; Accepted 10 April 2015

ABSTRACT

There are number of synthetic polymers are available in market for pharmaceutical formulations, but these synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance. Because of these disadvantages natural polymers such as natural gums and mucilage are preferred to semi synthetic and synthetic excipients because of the following advantages: Low cost and natural origin, Free from side effects, Biocompatible and bio-acceptable, Renewable source, Environmental friendly processing, Local availability etc. Because of this demand for these substances are increasing and new sources are being developed *Basella alba* is a wildly cultivated, cool season vegetable with climbing growth habit. Malabar spinach is high in vitamin A, vitamin C, iron and calcium. It is low in calories by volume, but high in protein per calorie. The succulent mucilage is a particularly rich source of soluble fiber. Literature survey reveals that comprehensive physicochemical characterization and exploration of BAM as versatile pharmaceutical excipients in pharmaceutical formulations has not been done. Hence, the present study was aimed to enhance the use of BAM as a natural plant based excipients to develop various pharmaceutical formulations and it will encourage cultivation and use of this mucilage in the pharmaceutical industry. In the present work, an attempt was made to develop fast dissolving tablets of diclofenac using natural disintegrant isolated from *Basella alba* leaves and its efficiency was compared with other synthetic superdisintegrants like Crosscarmellose sodium and Crosspovidone.

Fast dissolving tablets of diclofenac were prepared by direct compression method comprising of three different superdisintegrants-BAM, Crosscarmellose sodium and Crosspovidone (1%, 2%, 3% and 4%). Fifteen formulations were prepared and evaluated for hardness, thickness, friability, weight variation, drug content, *in vitro* disintegration time, *in vitro* dispersion time, wetting time, water absorption ratio and *in vitro* dissolution studies. The results obtained in this study established for the first time, the fundamental characteristics of BAM. The present investigation was a primary platform to indicate the suitability of BAM as a pharmaceutical excipients Phytochemical tests carried out on BAM confirmed the absence of alkaloids, steroids, flavanoids, saponins, tannins, phenols and glycosides. On treatment of mucilage with ruthenium red, it showed red colour confirming the obtained product was mucilage and it confirmed the purity of the mucilage obtained. The toxicity studies of extracted mucilage revealed no behavioral changes, no changes in body weight, no mortality; no toxic syndromes were reported, indicating the safety of the mucilage. The results from the physicochemical parameters of the mucilage manifested all the characteristics of a good pharmaceutical excipient that can be used for the formulation of various pharmaceutical formulations. FTIR studies revealed that there was no chemical interaction between the drug and the excipients. Formulation F2 was found to be the best on the basis of wetting time, *in vitro* disintegration time and *in vitro* drug release the formulation F2 containing BAM (2%) was found to be the optimized combination. Stability studies were carried out at $25^0C \pm 2^0C$ / 60% ± 5% RH and $40^0C \pm 2^0C$ / 75% ± 5% RH for formulation F2 for 60 days. The results of stability studies indicated no significant changes with respect to physicochemical properties, *in vitro* disintegration time, wetting time and *in vitro* drug release.

Keywords: Fast dissolving tablets, diclofenac, *Basella alba* mucilage, Superdisintegrant, Direct compression, Crosscarmellose sodium, Crosspovidone.

INTRODUCTION:

Excipients were defined as 'the substance used as a medium for giving a medicament', that is to say with simply the functions of an inert support of the active principle or principles[1]. The specific application of natural polysaccharide polymers in pharmaceutical formulations include to aid in the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance any other attribute of the overall safety, effectiveness or delivery of the drug during storage or use[2]. Today we have several pharmaceutical excipients of plant origin, like starch, agar, alginates, carrageenan, guar gum, xanthan gum,

*Corresponding author: Vishnu Bhat |

gelatin, pectin, acacia, tragacanth, and cellulose. These natural excipients find applications in the pharmaceutical industry as binding agents, disintegrates, sustaining agents, protective's, colloids, thickening agents, gelling agents, bases in suppositories, stabilizers, and coating materials. The advantages of natural plant-based excipients include that they are of low cost, natural origin, fairly free from side effects, biocompatible, and bio-acceptable, with a renewable source, environmental friendly processing, local availability, better patient tolerance, as well as public acceptance[3].

Synthetic polymers have certain drawbacks viz high cost because they are prepared by different procedures or reactions by using costly instruments and equipments and it require a lot of time to form a synthetic polymer. Synthetic polymers are non renewable sources as they are not used again and again, they have more side effects as they are prepared by different reactions using different chemicals which can interact with the body components sometimes body can consider it as a foreign matter and cause allergic reactions in the body, they can cause toxicity in the body, synthetic polymer cause environmental pollution during their synthesis, synthetic polymers are non-biodegradable (biodegradable synthetic polymers are costlier) and patients generally do not prefer synthetic polymers because of the side effects so these are less patient compliant.

Excipients are also derived from natural sources, synthesized chemically, or prepared semi-synthetically starting from natural sourced materials. They range from simple, usually well-characterized, organic or inorganic molecules to highly complex materials that are difficult to fully characterize. Classification of excipients is based on their role in the pharmaceutical formulation, their interactions influencing drug delivery, or their chemical and physico-chemical properties[4]. Excipients are also sometimes used to bulk up formulations that contain very potent active ingredients, to allow for convenient and accurate dosage. Depending on the route of administration, and form of medication, different excipients may be used. To stabilize the active ingredient, excipients are added, ensuring that the active ingredient stays "active", and, just as importantly, stable for a sufficiently long period of time that the shelf-life of the product makes it competitive with other products. Excipients also can serve to mask an unpleasant taste or texture and help ensure that the right amount of the API makes it to the right spot in the body at the right time[5].

Fast disintegrating tablets are very popular now-a- days as they get dissolved or easily disintegrated in mouth within few seconds of administration without the need of water[6]. Active drug is released immediately from the tablet when is placed on the tongue. This formulation is convenient for the patients suffering from Dysphagia. FDTs have several advantages over solid and liquid dosage form like these are very easy to handle as it is a solid dosage form it can be easily transported from one place to another, They are easily administered as it is a unit dosage form and do not need water to swallow they are taken anywhere at any time and also during travelling for motion sickness. In case of FDTs there is no risk of suffocation as it does not need water to swallow and there is no chance of sticking of tablet in the mouth, FDTs have more bioavailability than conventional tablets because when it is placed in the mouth it gets easily dissolved in the saliva, absorbed in the oral cavity and release the active drug within few seconds increasing the bioavailability of the tablet, FDTs have quick onset of action as its absorption is very fast within few seconds, FDTs are better in taste and hence the palatability of the tablet is improved, it also improve the patient compliance[11].

FAST DISOLVING TABLETS:

Fast dissolving tablets (FDTs) are the novel dosage form. These are the tablets that dissolve within few seconds in the mouth when come in contact with the saliva without the need of water. This dosage form improve patient compliance and mostly preferred by geriatric and pediatric patients with poor physiological and physical abilities and also by the travelling patients suffered from motion sickness FDTs are very effective in such situation as it dissolved rapidly in mouth and have quick action.

FDTs are also called fast disintegrated, mouth dissolving, fast melts, rapid melts and orodisperable tablets. It is mostly preferred by the patients who feel difficulty in swallowing (Dysphagia)

MATERIALS AND METHODS:

Diclofenac sodium and exepients are cross carmellose sodium,crosspovidone, microcrystalline cellulose aspartame, magnesium stearates ,and talc are collected from nimish pharma .Besella alba leaf collected from local market. all other solvents ,reagents and chemicals used wer of either pharmacopoeial grade or analytical grade. Different instruments viz; Vernier calipers, Monsanto hardness tester, Roche friabilator and disintegration apparatus were supplied by Campbell Electronics, Mumbai. USP XXIII dissolution apparatus-2 was from Tab-Machines, Mumbai and 1601 PC Shimadzu UV Spectrophotometer from Tokyo, Japan.

Methods:

Isolation and purification of mucilage from *Basella alba* leaves

The leaves of the *Basella alba* were brought from vegetable market of Mangalore (India). The collected leaves were sun dried for 10 days. The coarse powdered leaves were defatted using petroleum ether (60°-80°C) in a Soxhlet apparatus. The defatted material (60gm) was soaked in distilled water (1000ml) at room temperature for 6hr. After soaking material was reflux on water bath at 70 for 2 hr. The viscous solution was passed through eight fold of muslin cloth. Acetone was added slowly to filtrate till precipitation is completed. The precipitated mucilage was separated and washed thrice with acetone to remove the traces of water. The separated mucilage was spread on glass plates and dried at 40°C. The dried mucilage was tested for its phytochemical tests and physicochemical characterization.

Organoleptic Evaluation

The isolated mucilage was subjected for various organoleptic evaluations which included evaluation of color, odour, shape, taste and special features like touch and texture. The majority of information on the identity, purity and quality of the material can be drawn from these observations.

Physicochemical characterization of BAM

Solubility test

The separated mucilage was evaluated for solubility in water, acetone, chloroform, methanol, ether and ethanol in accordance with the British Pharmacopoeia specifications.Result obtained are shown in table 2

Loss on drying

The method adopted was that specified in the B.P.2004 for acacia. 1.0 g of the sample was transferred into each of several petri dishes and then dried in an oven at 105°C until a constant weight was obtained.

The percentage loss of moisture on drying was calculated using the formula and expressed as a percentage.

LOD (%) = (Weight of water in sample/Weight of dry sample) ×100

Swelling index

Swelling index of BAM was determined by using reported method. One gram of BAM powder (#100 mesh passed) was accurately weighed and transferred to a 100 mL stoppered measuring cylinder. The initial volume of the powder in the measuring cylinder was noted. The volume was made up to 100 mL mark with distilled water. The cylinder was stoppered, shaken gently and set aside for 24 h. The volume occupied by the mucilage sediment was noted after 24 h. □

Swelling index (SI) is expressed as a percentage and calculated according to the following equation.

$$\text{Swelling Index(SI)} = \frac{x_t - x_0}{x_0} \times 100$$

Where X_O is the initial height of the powder in graduated cylinder and X_t denotes the height occupied by swollen gum after 24 h. The content from the measuring cylinder from the above test were filtered through a muslin cloth and the water was allowed to drain completely into a dry 100 mL graduated cylinder. The volume of water collected was noted and the difference between the original volume of the mucilage and the volume drained was taken as water retained by sample and was referred to as water retention capacity or water absorption capacity. The same procedure was repeated using different media such as 0.1 N hydrochloric acid and pH 7.4 phosphate buffer. The data presented here is for triplicate determinations.

pH determination

This was done by shaking a 1% w/v dispersion of the mucilage in water for 5 min and the pH determined using a digital pH meter.

Determination of surface tension of mucilage

The surface tension of the isolated mucilage was determined by drop count method, using a stalagmometer. The stalagmometer was filled with purified water above the upper mark. Using the screw pinch cork, the flow rate was adjusted to 10-15 drops/min. Then, number of drops of water was counted between the marks of the stalagmometer (n_1). The water was removed and the stalagmometer was filled with the mucilage solution (0.1%w/v) and number of drops was counted (n_2). The surface tension of the polysaccharide was determined using formula given below.

Surface tension (γ_2) = $n_2\rho_1\gamma_1/n_1\rho_2$

Where, n_1=number of drops of water

n_2=number of drops of sample

ρ_1=density of water (0.9956 g/mL)

ρ_2=density of sample

γ_1=surface tension of water (71.18 dynes/cm)

Ash values

Ash values such as total ash, acid insoluble ash and water-soluble ash were determined according to Indian Pharmacopoeia. The following procedures were used for determination of ash values.

Total Ash

About 3 g of sample was accurately weighed and taken in a silica crucible, which was previously ignited and weighed. The powder was spread as a fine, even layer on the bottom of the crucible. The crucible was incinerated gradually by increasing temperature to make it dull red hot until free from carbon. The crucible was cooled and weighed. The procedure was repeated to get constant weight. The percentage of total ash was calculated with reference to air dried sample.

Acid Insoluble Ash

The ash obtained as described above was boiled with 25 mL of 2N HCl for five minutes. The insoluble ash was collected on an ash less filter paper and washed with hot water. The insoluble ash was transferred into a silica crucible, ignited and weighed. The procedure was repeated to get a constant weight. The percentage of acid insoluble ash was calculated with reference to the air-dried sample.

Water-soluble Ash

The ash obtained as described for the determination of total ash was boiled for 5 min with 25 mL of water. The insoluble matter was collected on ash less filter paper and washed with hot water. The insoluble ash was then transferred into silica crucible, ignited for 15 min, and weighed. The procedure was repeated to get a constant weight. The weight of insoluble matter was subtracted from the weight of the total ash. The difference of weight was considered as water-soluble ash. The percentage of water-soluble ash was calculated with reference to the air dried sample.

Melting point determination

The powdered sample of BAM was transferred into a capillary tube and by using Besto melting point apparatus melting point was determined.

Viscosity determination

Rheological studies of dried mucilage were carried out using varying concentrations (1% w/v) prepared in distilled water. The viscosities were measured using a Brookfield viscometer.

Microbial Count

Specified amount (10 g) of the sample was dissolved in a suitable medium to have no antibacterial activity under conditions of test and the volume was adjusted to 100 mL with the same medium. The pH was adjusted to 7.

Examination for Bacteria and Fungi

To a petri dish of 10 cm diameter, 20 mL of nutrient agar was added at temperature not more than 45°C. The sample solution was spread on the surface of the solidified medium. The Petri dishes of required number were prepared and incubated at 37°C for 24 h. but, sabouraud dextrose agar medium was used for fungi and the plate was incubated at 28°C for 48 h. The number of colonies formed was counted.

Thermal stability

A sufficient quantity of the powdered mucilage was taken in a petridish and exposed to successive higher temperatures (30°C, 40°C, 50°C, etc.).The temperature at which the product showed a change in color was noted. For thermal stability under liquid conditions, 1% solution of mucilage was exposed to successive higher temperatures (30°C, 40°C, 50°C, etc...) and the temperature at which the product showed a change in viscosity was noted.

Differential scanning calorimetry study

Thermal properties of BAM were characterized using a differential scanning calorimetry (DSC- 60, Shimadzu limited, Japan). Nitrogen, at the rate of 20 mL/min, was used as purge gas; 2.7 mg of powdered material were sealed in aluminium pan and heated from 30°C up to 500°C at the rate of 10°C/min, followed by a cooling cycle back to 30°C at the same rate.

Fourier transform-infra red spectral study

The Fourier transform-infra red (FT-IR) spectrum of the sample was recorded in an IR spectrometer (FTIR 8300, Shimadzu, Japan), using potassium bromide (KBr) discs prepared from powdered samples mixed with dry KBr in the ratio 1:200. Triplicate measurements were made, and the spectrum with the clearest identifiable peaks was chosen.

X-ray powder diffraction study

X-ray diffraction (XRPD) patterns of the BAM were analyzed using a Siemens D5000 Xray diffractometer (Siemens, Munich, Germany). Powder sample, packed in rectangular aluminium cells, illuminated using CuKα radiation (λ = 1.54056 Å) at 45 kV and 40 mA. Samples were scanned between diffraction angles of 5° to 45°C 2θ. Scan steps of 0.1 were used and the dwell time was 15.0 Sec. A nickel filter was used to reduce the Kβ contribution to the X-ray signal. The'd' spacing was computed according to Bragg's law of diffraction. Triplicate measurements were made at ambient temperature.(figure 1)

Formulation of fast dissolving tablets of diclofenac sodium[81]

Fast dissolving tablets of diclofenac were prepared by the conventional direct compression technique using BAM powder, crosscarmellose sodium and crosspovidone at concentrations of 1,2,3,4 and 5% w/w. All the required

ingredients as per the formulation table were weighed and passed through Size 40# sieve. The Mixture was then blended in a double cone blender for 15 mins. The powder blend was evaluated for flow properties. The composition of each formulation is given in table 1

EVALUATION OF FAST DISSOLVING TABLETS

PRE-COMPRESSIONAL STUDIES

The prepared powder blend was evaluated for various parameters like bulkiness,bulk density,tapped density,angle of repose compressibility index,and hausner ratio.after the evaluation of the tablet blend tahe tablets were compressed with cadmach single punch machine using 12mm flate faced punches.

POST COMPRESSIONAL STUDIES

After tablet compression prepared tablet were tested for different parameters like thickness, hardness, friability, uniformity of weight, disintegration time ,water absorption ratio, wetting time, drug content, Invitro dissolution studies were carried out in USP dissolution test apparatus (Type2),using simulated intestinal fluid (pH6.8)(900ml,37±0.5)at 50 rpm.

Stability Studies:

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, and enables recommended storage conditions, re-test periods and shelf lives to be established.

ICH specifies the length of study and storage conditions:
Long term testing $25^0C±2^0C$/60% ±5% RH for 12 months
Accelerated testing $40^0C±2^0C$/75% ±5% RH for 6 months
In the present study, stability studies were carried out at $25^0C±2^0C$/60% ±5% RH and $40^0C±2^0C$/75%±5% RH for a period of 60 days for the selected formulations. The formulations were then evaluated for changes in the physicochemical properties, wetting time, *in vitro* disintegration time and *in vitro* drug release.

RESULTS AND DISCUSSION:

The powdered dry water soluble mucilage was extracted from leaves of *Basella alba* plant for pharmaceutical use. The standard procedure was used to isolate mucilage and where purified by using water as solvent and acetone as non-solvent. The total yield of mucilage by acetone precipitation method was found to be 14.5%. The extracted mucilage was characterized by various organoleptic, morphological and physical evaluatory studies such as colour, odour, taste, shape, nature, touch and texture. The results of organoleptic characteristics of the mucilage indicated that isolated mucilage was slight brownish white color, acceptable and characteristic odour, mucilaginous taste and amorphous in nature. The solubility behaviour of the mucilage indicated that it is quickly soluble and forms neutral, viscous colloidal solution in warm water, sparingly soluble in cold water, whereas insoluble in ethanol, methanol, acetone, chloroform and ether. Results of solubility behavior of the BAM are shown in Table 3 The moisture content of BAM was found to be 2.6% was found to be within official limit suggesting its suitability in formulations containing moisture sensitive drugs.

Various preformulation studies were carried out for diclofenac sodium which is found to comply with the specification of pharmacopoeia.

Drug-Excipients Compatibility Studies:

Fourier transform infrared (FTIR) analysis

Physical mixture of diclofenac and formulative ingredients were subjected for IR spectroscopic analysis to ascertain whether there was any interaction between drug and excipients used. The IR spectra's showed similar characteristic peaks at their respective wavelengths with minor differences.

The similarity in the peaks indicated the compatibility of drug with formulation excipients. IR spectra of the physical mixture of drug with formulative ingredients were depicted in figure 2,3 .

Differential Scanning Calorimetry (DSC)

The DSC thermograms for drug and physical mixture of drug and excipients are represented in figure 17 and 18 respectively. DSC analysis of Diclofenac sodium shows the exothermic peak at its melting point i.e. at 283.62^0C, which is in agreement of earlier observation and corresponds to the reported melting point of diclofenac. The DSC analysis of physical mixture of drug and excipients revealed negligible change in the melting point of diclofenac sodium in the presence excipients. This also indicated that there are no changes in its crystallinity of the drug and it may not affect the stability of formulation and it is confirmed that drug is compatible with excipients.figure 4.

X-ray powder diffraction analysis

The X-ray diffractogram of BAM is shown in figure 10. The Bragg reflection angle, 2θ, along with the interplanar spacing, d, and the relative intensity of the peaks were calculated and results are tabulated in table 28. The

interplanar spacing has been calculated using Bragg's equation given as; nλ = 2d sinθ, where θ is one half the angle read from the diffractogram. The sample shows peaks at approximately 20°, 19°, and 18°, 2θ. However, other peaks are very weak and unresolved. The result of XPRD corroborates that of the DSC which shows that, BAM is of low moisture and exhibit both amorphous and crystalline portions.figure 9

Toxicity Study

To determine the safety level of the extracted mucilage, acute and chronic toxicity studies were conducted according to OECD guidelines no.423. In both toxicity studies the extracted mucilage revealed no behavioral changes, no changes in body weight for first four hours and no mortality; no toxic syndromes were observed even at the dose level 4g/kg body weight after 24 hours, indicating the safety of the mucilage. To assess the suitability of mucilage for the oral delivery we have recorded the body weight profile for the animals during the chronic toxicities at regular intervals of 10 d. it was found that the body weight of both test and control and rate of increase were also comparable. Hence it is concluded that chronic administration of the mucilage might not influence either the food intake or growth. Hematological and biochemical parameters that were determined at the end of 30 d of continuous administration were also found to be comparable to that of control rat. The effect of mucilage on hematological and biochemical parameters is summarized in table 2respectively. Histological examination of the main organs like liver, kidney, heart and brain were carried out at the end of 30days of chronic toxicity study. From this study it was revealed that there was no sign of pathological changes in both control and in treatment group. The results are shown in figure 2.

Precompression parameters of powder blend

Since, the f;ow properties of the powder mixture are important for the uniformity of mass of tablets,the floe of the powder mixture was analyzed before compression to tablet .Low haunser ratio compressabilty index and angle of repose values indicated a fairly good flowability powder mixture.The vaue of precompression parameters evaluated were within the prescribed limits and indicated good free flowing properties results are shown n table 4.

Post compression parameters of fast dissolving tablets

a) All the tablet formulations were evaluated for parameters such as shape, colour, thickness, hardness, friability, weight variation, drug content, *in vitro* disintegration time, *in vitro* dispersion time, wetting time, water absorption ratio, *in vitro* dissolution studies, model fitting of release profile and stability studies. Thickness and diameter of all prepared fast dissolving tablets was measured by using calibrated vernier callipers. Tablet thickness should be controlled within ±0.1% variation of standard value to facilitate packaging and consumer acceptance. The tablets showed thickness and diameter in the range of 2.60 mm to 2.64 mm and 6.01 mm to 6.04 mm respectively. Tablets require certain amount of strength, hardness to withstand mechanical shocks during manufacture, packaging and shipping. The hardness was found to be in the range of 3.5 to 4.0 kg/cm^2. The obtained results revealed that the tablets were having good mechanical strength and compactness. % Friability of tablets less than 1% was considered acceptable. Percent friability ranged from 0.21 to 0.55%. The average weight of diclofenac sodium fast dissolving tablet was 200mg. the weight variation was found to be in the range of 199 mg to202 mg. The percentage drug content was found to be in the range of 98 % to 99.5 %. pH of the solution of all the tablets was found to be between 7.1 to 7.5, which suggest that the tablets can be conveniently administered orally and will not cause any discomfort.

b) Water Absorption Ratio:

Water absorption ratio, which is an important criterion for understanding the capacity of disintegrants to swell in presence of little amount of water, was calculated. It was found to be in the range of 53.21 to 61.23 in formulations containing BAM and 63.13 to 71.13 and 65.13 to 78.83 for formulations containing cross carmellose sodium and cross povidone respectively.

The Water absorption ratio increased with increase in the concentration of superdisintegrant from 1-5%. The water absorption ratio was found to be in the increasing order. This increase was due to the water up taking ability of the superdisintegrants. More the superdisintegrant concentration greater was water absorption. Water absorption ratios for all these formulation batches varied in the following decreasing order: Crosspovidone > Crosscarmellose sodium > BAM. Disintegration time was determined as per I.P. for all the formulations. The formulations contain BAM as disintegrant showed disintegration time less than 40 seconds (2%) and the formulation containing cross carmellose sodium and cross povidone as superdisintegrants showed disintegration time less than 50 seconds and 46 seconds respectively. Least *in vitro* disintegration time was shown by formulation containing BAM (F2). *In vitro* dispersion time was measured by the time taken to undergo uniform dispersion. All formulations showed rapid dispersion within seconds. Formulated fast dissolving tablets containing BAM as disintegrants showed

dispersion time less than 42 seconds and the formulation containing cross carmellose sodium and cross povidone as superdisintegrants showed dispersion time less than 52 seconds and 48 seconds respectively..The *in vitro* drug release characteristics were studied in phosphate buffer pH 6.8 using tablet dissolution apparatus USP XXIII. The samples were withdrawn at different time intervals and analyzed at 276 nm and the cumulative percentage drug released was determined.

The dissolution profiles of all formulations showed above 90% within 15 min. From drug release profile it was observed that increase in concentration of BAM increases the drug release upto 2% concentration in the tablet, but further increase in the concentration of BAM does not show any increase in the dissolution rate. In case of formulation F2, the 50% and 90% of drug release was found within 3 and 10 min respectively. Compared to crosscarmellose sodium and cross povidone formulations, BAM formulations showed faster release of drug, this is due to more swelling property of BAM .The results of *in vitro* dissolution studies obtained from these formulations were plotted in Zero order, First order, Higuchi and Korsmeyer-Peppas release model and Hixson-Crowell equation to study the mechanism of drug release. The correlation coefficient (r) for drug release kinetic models was tabulated in table 26 for various formulations of diclofenac fast dissolving tablets.

c) The formulations F2 and F8 showed first order and other formulations showed Peppas model. From the values obtained, it is proved that formulations F2,F8, F11, F12, F13, F14 and F15 dissolution (release) of the drugs follows first order may be due to rapid diffusion or the porous nature. The values of diffusion co-efficient (n) for formulations F1, F3, F4, F5, F6, F7, F9 and F10 are shown to be 0.3716, 0.3681, 0.3556, 0.3247, 0.2945, 0.2793, 0.3626 and 0.2924 respectively which indicates that the release of drug occurs by diffusion following Fickian transport mechanism, as all diffusion co-efficient values shows less than 0.5.

Stability Studies:

Stability studies of formulation F2 was performed at 25^0C ± 2^0C / 60% ± 5% RH and 40^0C ± 2^0C / 75% ± 5% RH for a period up to 60 days. The formulations were selected for stability studies on the basis of their high percentage cumulative drug release and also results of *in vitro* disintegration time, wetting time and *in vitro* dispersion studies.

The samples were withdrawn for every 20 days interval and the tablets were analyzed for appearance, thickness, hardness, friability, weight variation, drug content uniformity, *in vitro* disintegration, wetting time and *in vitro* drug release up to 60 days.

The results obtained for physicochemical properties, wetting time, *in vitro* disintegration time and *in vitro* drug release of formulation F2 at 25^0C ± 2^0C / 60% ± 5% RH and 40^0C ± 2^0C / 75% ± 5% RH were shown in table 27, 28 and depicted graphically in figure 27. There was no change in color and shape of the tablets when stored at 25^0C ± 2^0C / 60% ± 5% RH and 40^0C ± 2^0C / 75% ± 5% RH and observed every 20 days interval upto 60 days. Formulations F2 showed not much variation in any parameter. From these results it was concluded that formulations were stable and retained its original properties.

CONCLUSION

Literature survey reveals that comprehensive physicochemical characterization and exploration of BAM as versatile pharmaceutical excipients in pharmaceutical formulations has not been done. Hence, the present study is aimed to enhance the use of BAM as a natural plant based excipients to develop various pharmaceutical formulations and it will encourage cultivation and use of this mucilage in the pharmaceutical industry.

In the present work, an attempt was made to develop fast dissolving tablets of diclofenac using natural disintegrant isolated from *Basella alba* leaves and its efficiency was compared with other synthetic superdisintegrants like Crosscarmellose sodium and Crosspovidone.

Table 1: Composition of different batches of diclofenac FDT's

Ingredients (mg/ tablet)	Formulation Code														
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Diclofenac sodium	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
BAM*	2	4	6	8	10	--	--	--	--	--	--	--	--	--	--
Cross Carmellose Sodium	--	--	--	--	--	2	4	6	8	10	--	--	--	--	--
Crospovidone	--	--	--	--	--	--	--	--	--	--	2	4	6	8	5
Aspartame	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Magnesium Stearate	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Talc	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Flavor Orange)	6	6	6	6	6	6	6	6	6	6	6	6	6	6	6
Avicel	124	122	120	118	116	124	122	120	118	116	124	122	120	118	116
Total weight of tablet	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200

Table 2: Results of Physicochemical characterization of BAM

Parameters	Result
pH (1%w/v)	6.5
Moisture content (%)	2.6
Ash value (%)	0.98± 0.21
Water-soluble ash (%)	0.55± 0.03
Acid insoluble ash (%)	0.35± 0.02
Sulphated ash (%)	1.34± 0.22
Swelling index	-
In distil water	23
In 0.1 N HCl	08
In Phosphate Buffer pH 7.4	17
Total bacterial count :Microbial Load Bacteria:(CFU/g) Fungi: (CFU/g)	 10 01
E.coli	Absent
Salmonella typhi	Absent
S.aureus	Absent
Pseudomonas aeruginosa	Absent
Water absorption capacity	13 ml
Surface tension (0.1%w/v)	82.22 ± 0.21
Average particle size (µm)	117.18±7.44µm
Test for foreign matter (%)	NMT 0.1
Test for Arsenic	<1 ppm
Test for heavy metal (lead)	15 ppm
Melting point (°C)	260±5.42°C
Viscosity (1% solution)	350 cps

Table 3: Results of phytochemical screening of BAM

	Tests	Observation
	Test for Carbohydrates(Molisch's test)	+
	Test with Corralin soda solution	Red (+)
	Powder+ Iodine sol.+ Zinc chloride	Violet (+)
	Mucilage +Methylene blue	Deep blue (+)
	Mucilage + Aq.KOH solution	Swell (+)
	Test for mucilage (Ruthenium red test)	+
	Test for flavanoids (Shinoda test)	-
	Test for reducing sugar (Felhing's test)	+
	Mounted in 95% alcohol	Transparent angular masses under microscope
	Mounting in the iodine	Particles stained blue
	Test with cupric –tartaric solution	Red precipitate is produced
	Warming with 5M sodium hydroxide	A brown color is produced
	Test for chlorides(silver nitrate test)	-
	Test for sulphates (barium chloride test)	-
	Test for Uronic acid	+
	Tests for saponins (Foam test)	-
	Tests for steroids (Salkowski test)	-
	Tests for triterpenoids (Salkowski test)	-
	Test for Tannins and phenolic compounds (Ferric chloride test)	-
	Test for proteins (Ninhydrin test)	+
	Test for alkaloids (Mayer's test)	-
	Test for glycosides(Keller– Killaini test)	-

*+ Present; - Absent

Table 4: Pre compression evaluation of diclofenac sodium powder blend

Formulation code	Angle of repose(°)*	Bulk density (gm/cm^3)*	Tapped density (gm/cm^3)*	Carr's index (%)*	Hausner ratio (H_R)*	Bulkiness (cc/g)*
F1	27.3±0.02	0.54±0.04	0.73±0.03	22.8±0.01	1.32±0.01	1.75±0.01
F2	27.9±0.03	0.55±0.02	0.72±0.01	18.7±0.02	1.24±0.01	1.75±0.01
F3	26.3±0.04	0.57±0.03	0.67±0.02	19.9±0.01	1.24±0.01	1.72±0.02
F4	26.3±0.02	0.55±0.03	0.67±0.02	16.9±0.03	1.22±0.03	1.79±0.03
F5	27.6±0.04	0.55±0.01	0.70±0.02	19.9±0.04	1.27±0.02	1.82±0.03
F6	26.9±0.05	0.54±0.03	0.73±0.03	21.5±0.02	1.35±0.04	1.72±0.01
F7	30±0.02	0.53±0.01	0.67±0.01	20.8±0.02	1.26±0.05	1.89±0.02
F8	28.0±0.03	0.57±0.01	0.74±0.02	23.1±0.01	1.29±0.02	1.75±0.04
F9	32.6±0.01	0.56±0.02	0.74±0.02	23.7±0.01	1.30±0.04	1.79±0.05
F10	28.1±0.01	0.57±0.02	0.71±0.03	19.0±0.01	1.24±0.02	1.75±0.02
F11	24.6 ±0.02	0.39±0.03	0.44±0.06	11.0±0.03	1.12±0.05	2.56±0.03
F12	23.9±0.08	0.26±0.02	0.30±0.03	11.2±0.02	1.12±0.03	3.74±0.05
F13	22.7±0.04	0.40±0.05	0.48±0.05	16.0±0.02	1.19±0.01	2.45±0.02
F14	21.8±0.03	0.31±0.02	0.36±0.01	14.2±0.01	1.16±0.01	3.20±0.04
F15	23.9±0.01	0.33±0.07	0.38±0.02	21.2±0.03	1.13±0.04	2.95±0.03

*All values are expressed as mean ± SD, n=3.

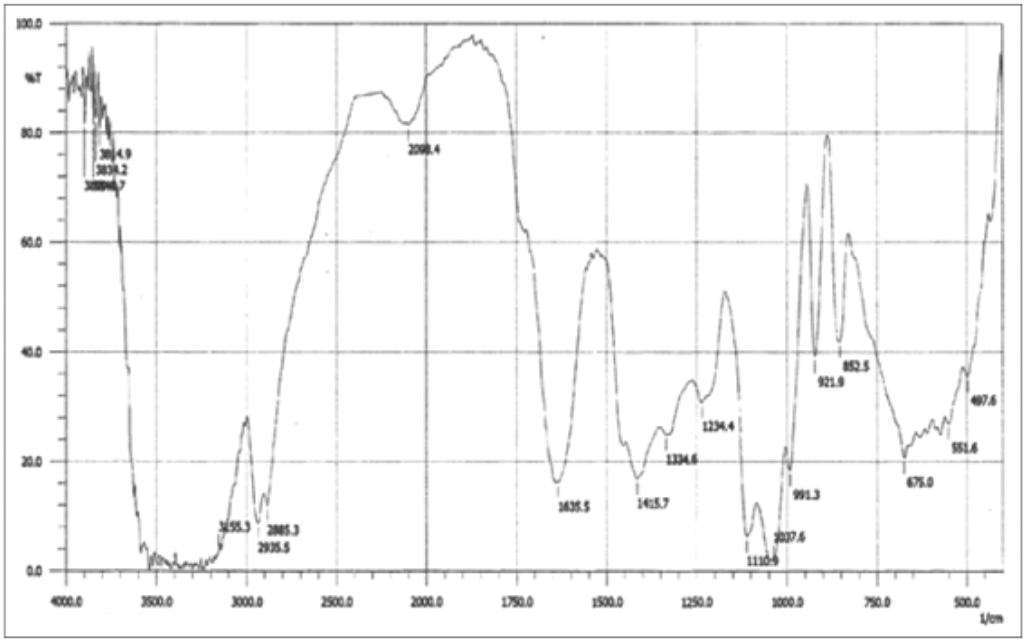

Figure1: FTIR spectrum of BAM(between852 and 1415 per cm)

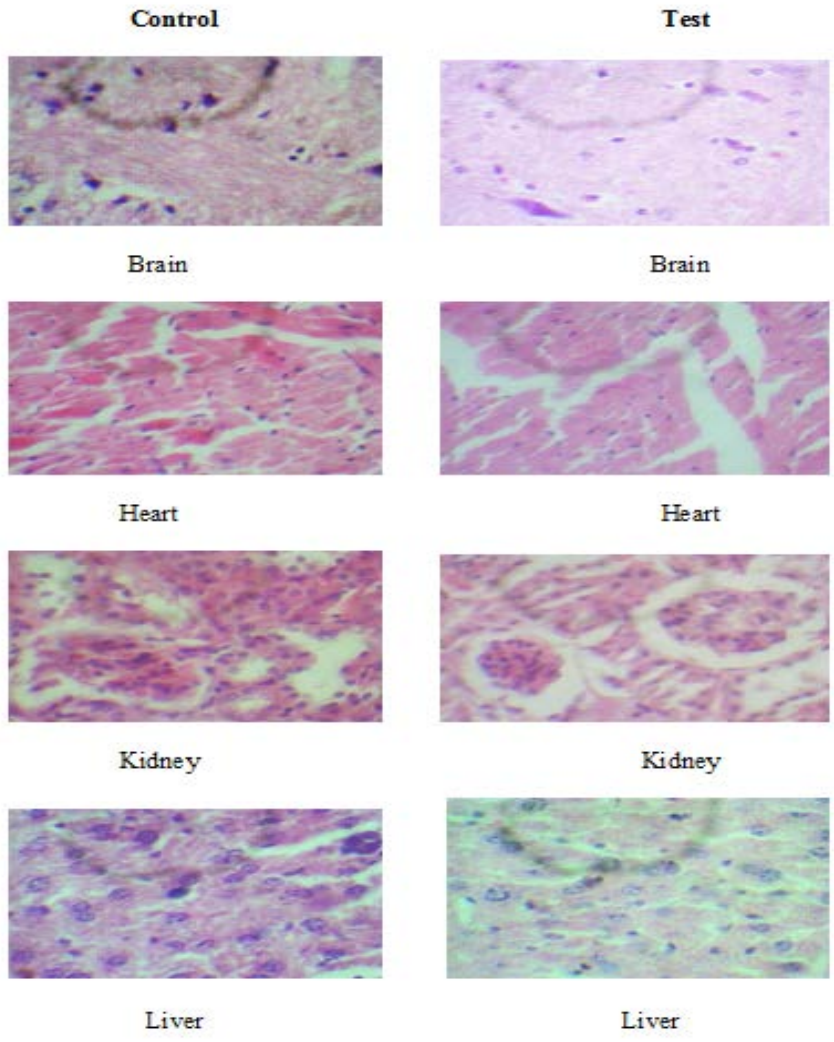

Figure 2: Histological sections of vital organs after treatment of BAM for 30 days

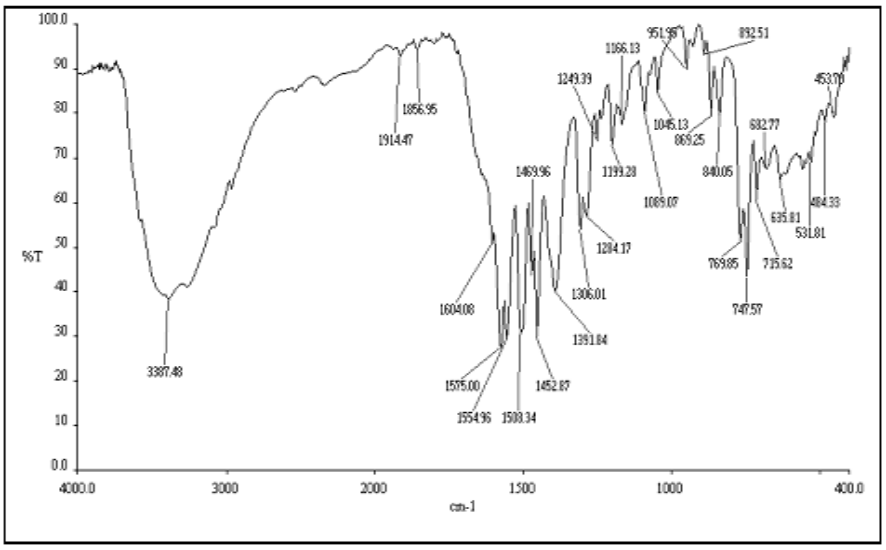

Figure 3: FTIR spectra of diclofenac sodium pure drug

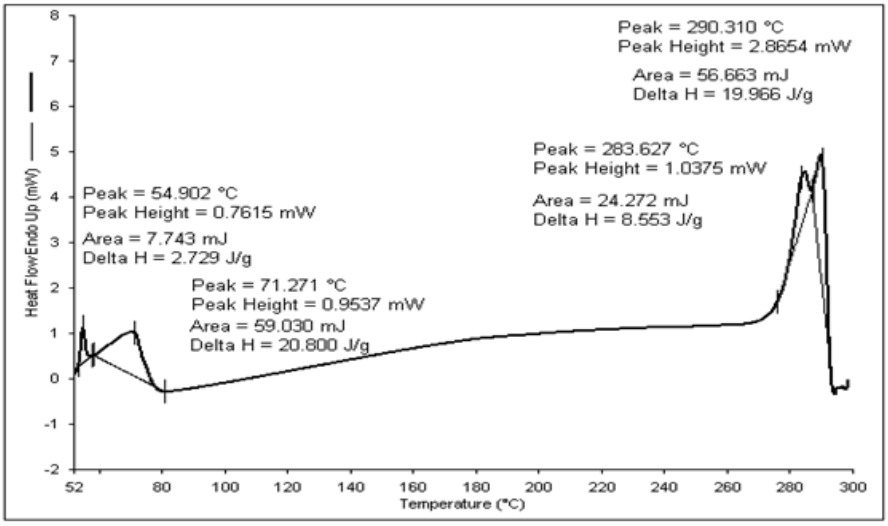

Figure 4: DSC thermogram of diclofenac sodium

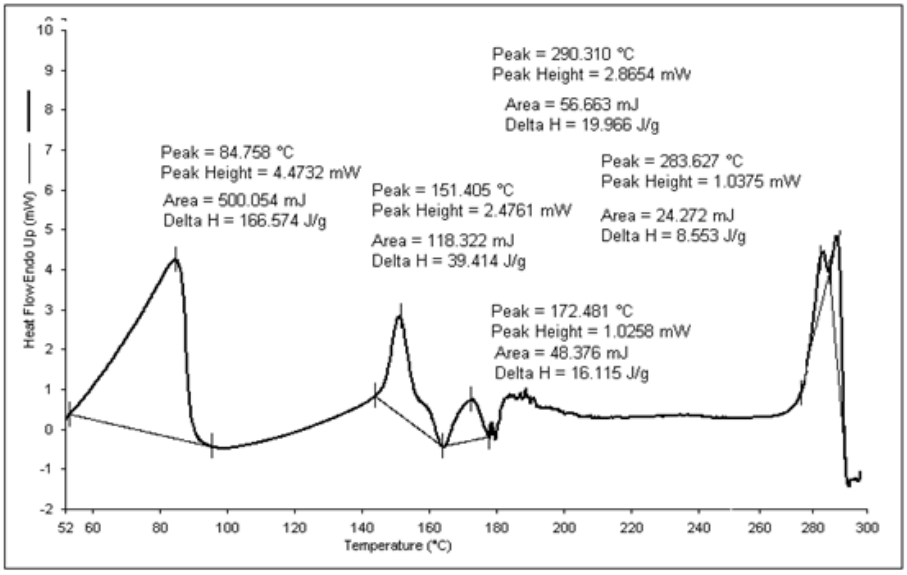

Figure5: DSC thermogram of diclofenac sodium and different excipients

Figure 6: Comparison between wetting time and water absorption ratio of formulated diclofenac fast dissolving tablets

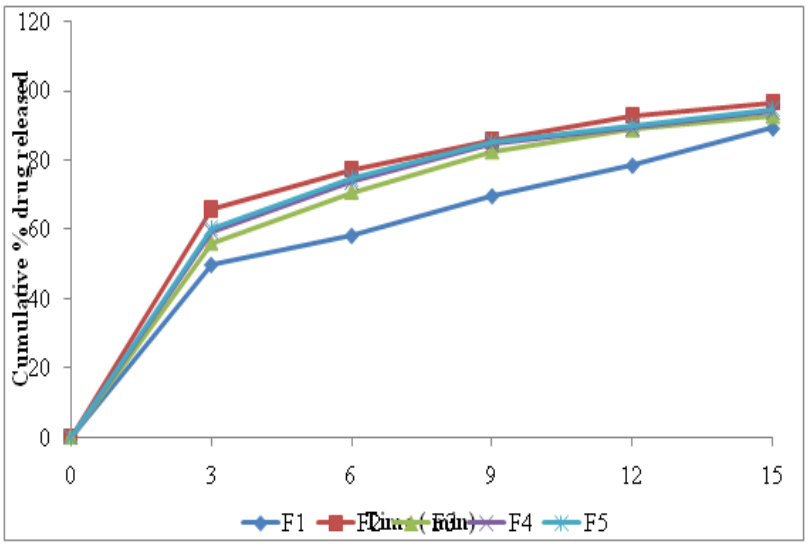

Figure7: *In vitro* dissolution profiles for formulated diclofenac fast dissolving tablets containing BAM

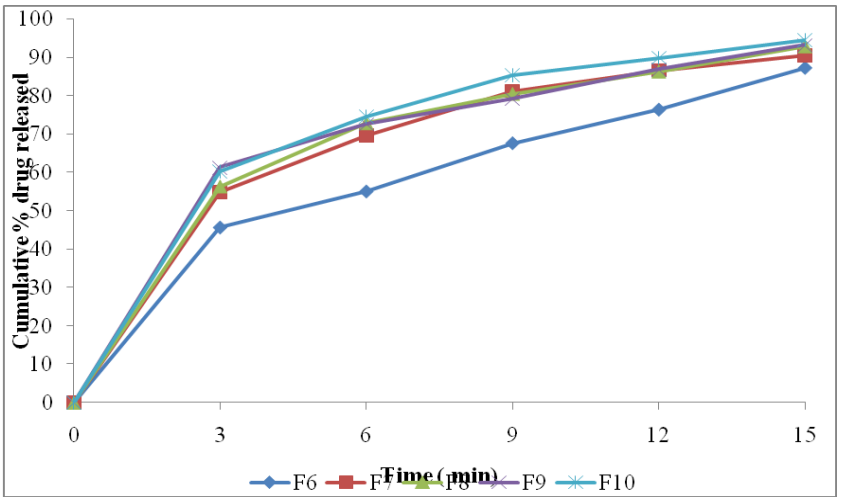

Figure8: *In vitro* dissolution profiles for formulated diclofenac fast dissolving tablets containing cross carmellose sodium

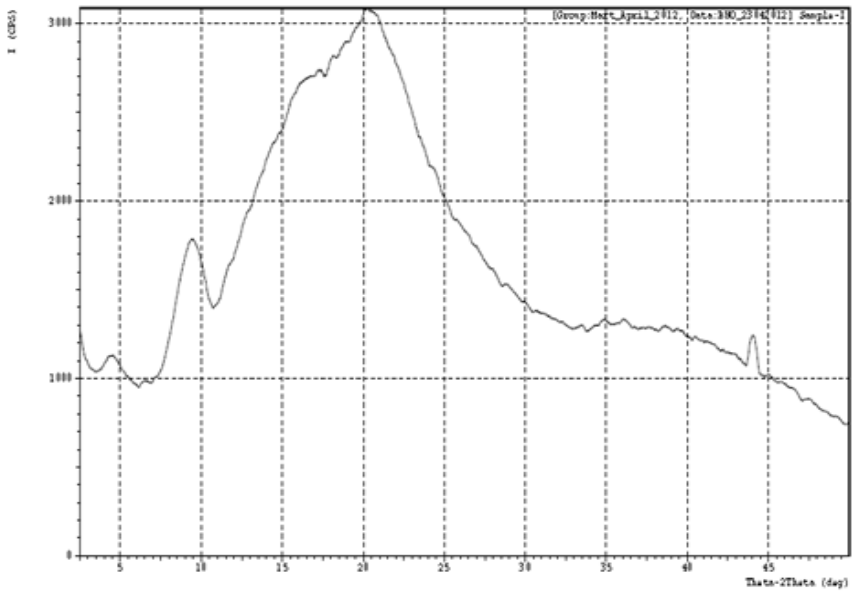

Figure 9: XRD pattern of BAM

BIBLIOGRAPHY:

1. Morton's. The Nurse Dictionary. 24th ed. Faber & Faber: London, 1957.
2. The Joint IPEC–PQG Good Manufacturing Practices Guide for Pharmaceutical Excipients, 2006.
3. Wade A, Weller PJ. Handbook of Pharmaceutical Excipients. 11th ed. The Pharmaceutical Press: London, 1994; 426-8.
4. http://www.bccresearch.com/pharmaceuticals/accessed (30 Dec. 2011).
5. Guidance for Industry, Drug Product. Chemistry, Manufacturing and Controls Information, U.S Dept. of Health and Human Services, FDA, CDER, CBER, 2003: 3-9.
6. Kawtikwar PS, Zade PS, Sakarakar DM. Formulation, Evaluation and optimization of fast dissolving tablet containing Tizanidine Hydrochloride. Int J pharm Tech Res 2009; 1(1): 34-42.
7. Kaur T, Bhawandep G, Sandeep K, Gupta G D. Mouth Dissolving tablets: A novel approach to Drug delivery. Int J curr Pharm Res 2011; 01(01): 1-7.
8. Hirani J J, Rathode DA, Vadalia KR. Orally Disintegrating Tablets: A review. Tropical J Pharm Res 2009; 8(2): 161-172.
9. Sharma S, Garg R, Naruka PS, Gupta GD. Fast dissolving tablet: The future of compaction. Pharmainfo.net 2007.
10. Panigrahi D, Baghel S, Mishra B. Mouth Dissolving tablets: An overview of prepration techniques, evaluation and patented technologies. J Pharm Res 2005; 4:33-8.
11. Bhandari S, Mittapalli RK, Ramesh G, Rao YM. Orodispersable tablets: An overview. Asian J Pharm 2008; 2(1): 2-11.
12. Rani TR, Mridul K. An unlimited scope for novel formulations as orally disintegrating system: present and future prospects. J Applied Pharm Sci 01(01); 2011: 13-19.
13. Ratanaparkhi P M, Mohanta GP, Upadhyay L. Review on fast dissolving tablets, J Pharm Res 2009; 2(1):5-12.
14. Pahwa R, Piplani M, Sharma PC, Kaushik D and Nanda S. Orally Disintegrating tablets- friendly to pediatrics and geriatrics. Archives of Applied Sci and Res 2010; 2(2):35-48.
15. Pahwa R, Gupta N. Superdisintegrants in the development of orally Disintegrating Tablets: A Review. Int J Pharm Sci Res 2011; 2(11):2767-2780.
16. Vaibhav S, Mahaveer PK, Gupta MK, Agarwal D and Sharma N. Orally disintegrating tablet: friendly dosage form. Int J Res in Ayurveda and Pharmacy 2010;1(2): 399-407.
17. Ghosh T, Ghosh A and Prasad D. A review on new generation orodispersable tablets and its future prospective. Int J pharm and pharm Sci 2011; 1(2):399-407.
18. Velmurugan S and Vinushitha S. Oral disintegrating tablets: an Overview. Int J chemical and Pharm Sci 2010; 1(2):1-12.
19. Khan T, Nazim S, Shaikh S, Shaikh A, Khairnar A and Ahmed A. An Approach for rapid disintegrating tablet: a review. Int J Pharma Res and development 2011; 3(3): 170-183.

20. Deshmukh KR, Vidyanand P, Shekhar V, Kumar PA and Dewangan P. A review on mouth dissolving tablet techniques. Int J Res in Ayurveda and Pharmacy 2011; 2(1):66-74.

21. Biradar SS, Bhagavati ST, Kuppasad IJ. Fast Dissolving Drug Delivery Systems: A Brief Overview. The Internet Journal of Pharmacology 2006; 4(2).

22. Mohanachandran PS, Sindhumol PG & Kiran TS. Superdisintegrants: An Overview. Int J Pharm Sci Rev Res 2011; 6: 105-109.

23. Kaur T, Gill B, Kumar S, Gupta GD. Mouth Dissolving Tablets: A Novel Approach to Drug Delivery. Int J Curr Pharm Res 2010; 3: 1-7.

24. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. Journal of Chemical and Pharmaceutical Research 2009; 1(1): 163-177.

25. Hirani JJ, Rathod DA, Vadalia KR. Orally disintegrating tablets: A review. Tropical J Pharm Res 2009; 8(2): 161-172.

26. Saxena V, Khinchi MP, Gupta MK, Agarwal D, Sharma N. Orally disintegrating tablet: friendly dosage form. IJRAP 2010; 1(2): 399-407

27. Facciola S. Cornucopia: A source book of edible plants. Kampong Publications; vol. 2, 1990. p. 183-7 Duke JA, Ayensu ES. Medicinal Plants of China Reference Publications, Inc; 1985

CODEN (USA): JBPRAU