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Formulation and Evaluation of Mouth Dissolving Tablet of Azithromycin Using Natural Superdisintegrant

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ABSTRACT

The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of patient compliance. However, traditional tablets and capsules administered with a glass of water may be inconvenient or impractical for some geriatric patients because of changes in various physiological and neurological conditions. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as mouth dissolving tablets. Mouth dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology. Mouth dissolving tablets are fast disintegrating and/or dissolving rapidly in saliva before the need for water. Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Mucilage of Plant ago Ovate has various characteristics like binding, disintegrating and sustaining properties. Therefore mucilage can be used as superdisintegrant to formulate fast dissolving tablets because it has very high percentage of swelling index. The present work was aimed to formulate the mouth dissolving tablet of Azithromycin by using natural superdisintegrants plant ago mucilage. The results from in-vitro disintegration time, in-vitro dissolution study, wetting time and water absorption ratio showed that the plant ago mucilage is more beneficial. Thus it can be concluded that natural superdisintegrant based more cheap mouth dissolving tablets of Azithromycin would be quite effective in treatment, by providing quick onset of action.

Keywords: Natural Superdisintegrant, disintegration time, mouth dissolving tablet

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INTRODUCTION

The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of patient compliance. However, traditional tablets and capsules administered with a glass of water may be inconvenient or impractical for some geriatric patients because of changes in various physiological and neurological conditions associated with aging including difficulty in swallowing/dysphagia, hand tremors, deterioration in their eyesight, hearing, memory, risk of choking in addition to change in taste and smell. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as mouth dissolving tablets.[1]

Mouth dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology. Mouth dissolving tablets are fast disintegrating and/or dissolving rapidly in saliva before the need for water. The disintegration time for mouth dissolving tablets generally ranges from several seconds to about a minute. The basic approach in development of mouth dissolving tablets is the use of disintegrants which provide instantaneous disintegration of tablet after putting on tongue, there by release the drug in saliva. This accomplished by incorporating newer substances called superdisintegrants which are more effective at lower concentration with greater disintegrating efficiency and mechanical strength.[2]

Superdisintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs. [10, 11, 12,13]

.Mucilage of Plant ago Ovate has various characteristics like binding, disintegrating and sustaining properties. Therefore mucilage can be used as superdisintegrant to formulate fast dissolving tablets because it has very high percentage of swelling index. The rapid disintegration of the mouth dissolving tablets creates enough hydrodynamic pressure for quick and complete disintegration of the tablet. [3, 4]

The demand for development of mouth dissolving tablets has enormously increased as it has significant impact on the patient compliance Therefore in the present study mouth dissolving tablets of Azithromycin was developed using mucilage of Plant ago ovate as natural super disintegrant.[5,9]

MATERIALS AND METHOD

Drug Azithromycin obtained from the Sangrose Laboratories Pvt.LTD, Mavelikkara.Isapgol

obtained from nice chemicals.

Experimental Works

Isolation of mucilage

Mucilage was isolated by soaking seeds of Plant ago Ovate in water (20-30 times) for at least 48hrs, boiled for 2hrs subsequently mucilage was released into water completely. With the help of muslin cloth the mucilage was squeezed out and separated from seeds. The mucilage collected and precipitated using 3 times of 95% ethanol. Collected mucilage was dried in the oven at 50-55.Dried mucilage was scraped and powdered using pestle and mortar. Powder was sieves using mesh no.100 [6, 7]

Phyto chemical Evaluation

Preliminary test were performed to confirm the nature of mucilage obtained. Chemical tests that were conducted are ruthenium red test, molish test, test for proteins and alkaloids etc [8]

Preparation of Fast dissolving tablets

Azithromycin, mucilage, sodium lauryl sulphate, microcrystalline cellulose that is the intragranular substances were weighed accurately and are mixed and passed through the mesh 60.Then the extra granular components namely mannitol, magnesium stearate, kaolin, talc, sodium saccharine are weighed and mixed thoroughly and passed through mesh 60.Then the extra granular and intragranular were mixed and blended it thoroughly to get uniform mixture and kept aside. Then the powder blend was compressed using 9mm size tablet using rotary punching machine.

Table 1 List of ingredients in the formulation

Sl no.	Ingredients	Quantity for 1 tablet
1.	Azithromycin	100
2.	Mucilage	015
3.	Sodium Lauryl Sulphate	015
4.	Talc	005
5.	Magnesium Stearate	005
6.	Kaolin	017.5
7.	Sodium saccharin	000.5
8.	mannitol	028.5
9.	Microcrystalline cellulose	073.5
	Total	260.0

Fourier Transferred Infrared Spectroscopy (FTIR)

The IR spectra were recorded for the mucilage extracted. The FTIR of drug alone and drug with its excipients are also recorded.

Pre-formulation studies

Pre-formulation studies are conducted. These includes tapped density, bulk density, and angle of repose, Car's index and Hausner ratio.

EVALUATION OF FAST DISSOLVING TABLETS

Weight Variation as per IP

20 tablets were selected randomly from the lot and weighed individually to check for weight variation. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method to determining the drug content uniformity.

Diameter and Thickness

Tablets from each formulation were selected and their diameter and crown thickness was measured by using screw gauge.

Hardness

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping. Monstanto hardness tester used for this purposes.

Wetting time & water absorption ratio

One circular tissue paper of 10cm diameter was placed in a Petridish with a 10cm diameter.10millilitres of water soluble dye eosin solution was added to petridish. Tablet placed on surface of tissue paper and time required for water to reach the upper surface of tablet was wetting time.

Water absorption ratio

Weight of tablet before keeping in petridish noted (Wa).Wetted tablet from Petridish is reweighed (Wb)

$$R=100(Wa-Wb)/Wb$$

Friability (F)

Tablets were tested for friability using Roche Friability. Ten tablets were weighed initially and transferred to the friability. The instrument was set at 25rpm for 4 minutes. The resulting tablets were reweighed and percentage loss was calculated using the formulae.

% Friability=loss of weight/Initial weight X 100

Disintegration Time

The disintegration test for tablets was carried out in disintegration test apparatus. The device contains 6 glass tubes that are 7.5 cm long, 2cm in internal diameter and a wall thickness of 2 mm. To test for disintegration time one tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker of water maintained at 37+-0.5C such that the tablet remained 2.5cm below the surface of the liquid on their upward movement and descended not closer than 2.5cm from the bottom of the beaker .A standard motor driven device was used to

move the basket assembly up and down through a distance 5 to 6 cm at a frequency of 28 to 32 cycles /minute. Time taken for tablet to disintegrate completely was noted.

In Vitro dissolution study [6]

900ml of 7.4 phosphate buffer was placed in the vessel of dissolution tester(paddle type) and temperature was maintained at 37+-0.5C.Azithromycin(100mg) was added to dissolution medium at 100rpm.2 ml sample was taken from the dissolution medium at regular time interval. After each sampling of 2 ml, 7.4 phosphate buffer was added to maintain sink condition. Further the sample were analyzed for the drug content at 209nm using U.V .visible spectrophotometer using 7.4 phosphate buffer as blank.

Standard calibration curve of Azithromycin

Took accurately measured 0.2ml, 0.4ml, 0.6ml, 0.8ml and 1ml quantity of stock solution into a series of 10ml volumetric flask and diluted to about 7 ml distilled water. A volume of 0.5ml 4X10-3Eosin Y solutions was added to each flask and the solution were mixed well before addition of 1ml of 0.4M acetate buffer (PH 3).The mixtures were diluted to 10ml with the distilled water the absorbance was measured at 540 against an appropriate blank prepared simultaneously.

RESULTS AND DISCUSSION

Isolation of mucilage

The mucilage was isolated and dried. The average yield of dried mucilage obtained from Plant ago ovate was 10gram.

Physico-chemical evaluation

The mucilage obtained was subjected to physicochemical characteristics. The results obtained are as follows.

Table 2.Physico-chemical evaluation of the mucilage

Parameters	observation
solubility	Soluble in water
pH	6.29
Loss on drying	1.67%
Ash value	5.34%

Phytochemical screening

Various Phytochemical tests were carried out on the mucilage so as to confirm the presence of alkaloids, glycosides and tannins. The observation and inference is given below.

Table 3: Phyto chemical screening of the mucilage

Tests	observations	Inference
Molish's test	Ring formed	Presence of carbohydrates
Ferric Chloride test	No deep blue black color	Absence of Tannins
Ninhydrin test	No purple coloration	Absence of proteins

Wagner's test	No reddish brown color	Absence of alkaloid
Keller-Killani test	No coloration at Junction	Absence of Glycoside
Ruthenium red test	Red coloration	Presence of mucilage

Characterization by FTIR

Characterization of mucilage of Plantago Ovate

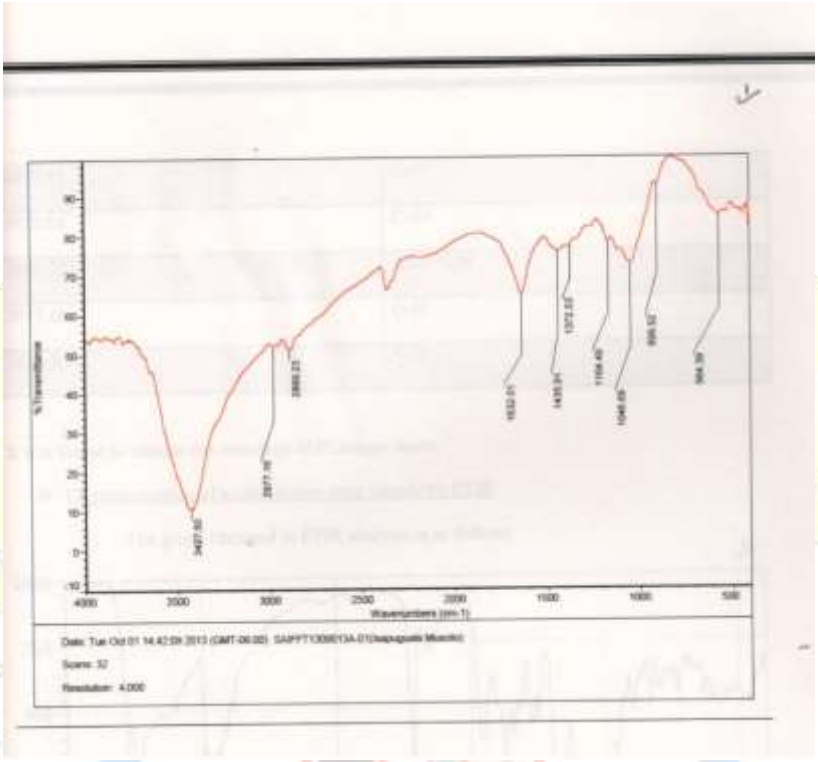

Figure 1: FTIR of Plantago Ovate

Interpretation Of FTIR Spectra

Table 4: IR interpretation of the mucilage

Wave number	Compound interpreted
898.52	C-H bending
1046.69	C-O stretching
1164.49	C-C stretching
1372.53	C-O
1435.91	C=C
1632.01	C=O
2889.23	AlkylC-H
2977.16	O-H
3427.5	N-H

Characterization of Azithromycin drug sample

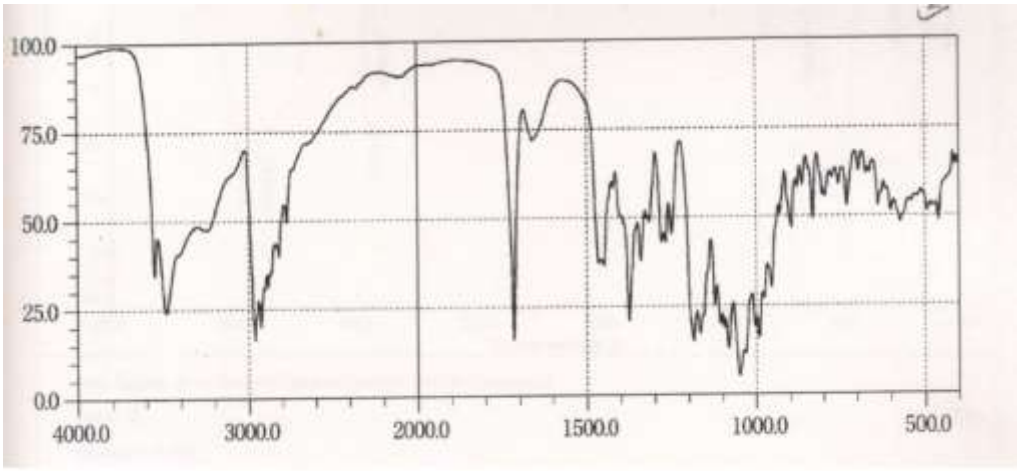

Figure 2: The graph obtained in FTIR of the drug sample

Table 5: Interpretation of drug sample

Wave Number	Interpretation
2973.8	C-H stretching presence of CH3 group
1469.3	C-H bending presence of methyl and methylene group
1050.8	C-N stretch presence of aliphatic amines

Characterization of drug, mucilage and other excipients

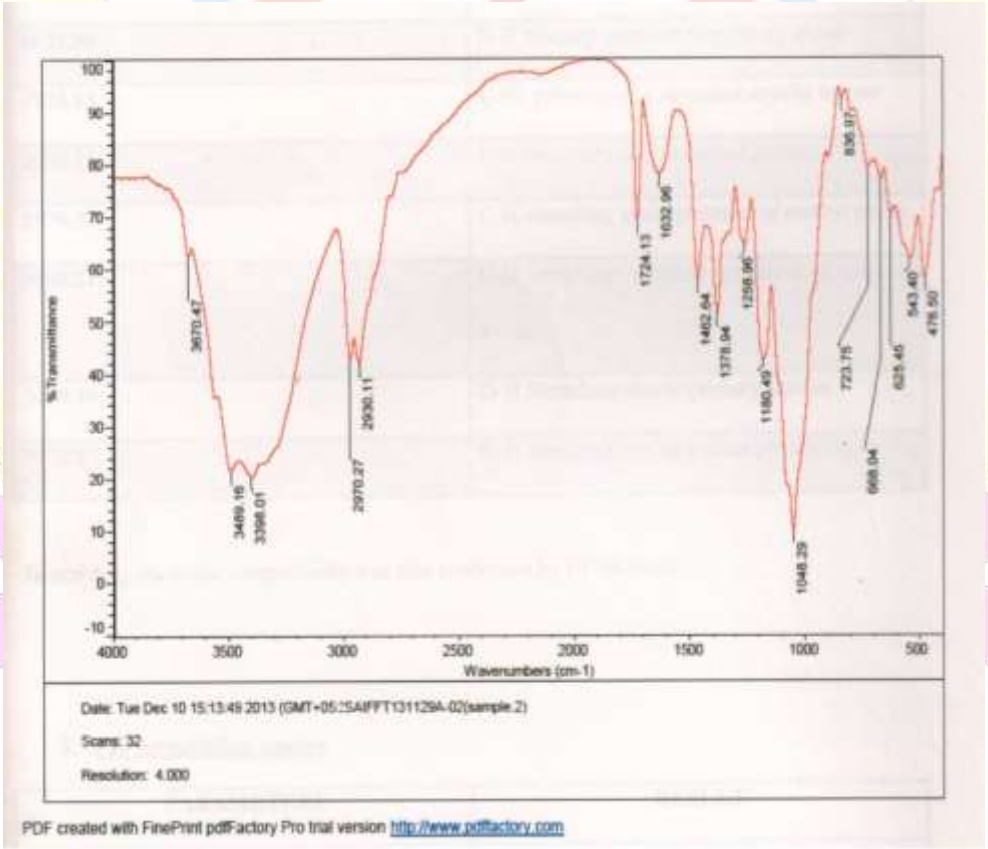

Figure 3: FTIR of drug, mucilage, excipients

Table 6: Interpretation of drug, mucilage and excipients

Wave number	Interpretation
668.04	N-H wagging presence of primary or secondary amines

723.75	C-H rock, presence of an alkane
1048.29	C-N stretch, presence of aliphatic amines
1180.49	C-N stretching of aromatic amines
1258.96	C-H wagging due to alkyl halide
1378.94	C-H bending due to primary amines
1632.96	N-H bending presence of primary amines
1724.13	C=O presence of a saturated acyclic ketone
2930.11	C-H stretching due to methyl group
2970.27	C-H stretching again presence of methyl group
3398.61	C-H stretching vibration presence of primary amines
3489.16	O-H stretching due to primary amines
3670.47	N-H stretching due to amines or amides

Hence drug excipient compatibility was also confirmed by FTIR study.

Pre-formulation studies

Table 7 preformulation studies

Parameters	Result
Bulk density	0.52±0.002
Tapped density	0.60±0.001
Angle of repose	29.25±1.70
Carr's index	15.87±1.51
Hausner's ratio	1.21±0.09

Preparation of Mouth dissolving tablets of Azithromycin

Azithromycin mouth dissolving tablets were prepared by direct compression. The formulations exhibit white color, odorless with smooth surface.

Evaluation Studies

Weight Variation

Table 8: Weight variation test for mouth dissolving tablets

No.of tablet	Total weight of tablet	Individual weight of tablet	Average weight	Weight differences	% deviation
20	5.23	0.2619	0.2615	0.0004	0.152
19	4.9681	0.2521	0.2615	0.0094	3.594
18	4.716	0.2611	0.2615	0.0004	0.152
17	4.4549	0.254	0.2615	0.0075	2.868
16	4.2009	0.2692	0.2615	0.0077	2.944
15	3.9317	0.2604	0.2615	0.0011	0.42
14	3.6173	0.2499	0.2615	0.0116	4.435
13	3.4214	0.2572	0.2615	0.0043	1.644
12	3.1642	0.2471	0.2615	0.0144	5.506
11	2.9171	0.2788	0.2615	0.0173	6.615
10	2.6833	0.2539	0.2615	0.0076	2.906
9	2.3944	0.2573	0.2615	0.0042	1.606
8	2.1371	0.2654	0.2615	0.0039	1.491
7	1.8717	0.2597	0.2615	0.0018	0.688
6	1.612	0.2532	0.2615	0.0083	3.173
5	1.3288	0.2548	0.2615	0.0067	2.567

4	1.074	0.2741	0.2615	0.0126	4.818
3	0.7999	0.2589	0.2615	0.0026	0.0994
2	0.521	0.2649	0.2615	0.0034	1.300
1	0.2561	0.2561	0.2615	0.0054	2.065

As per IP the weight variation test passes for the given tablets of Azithromycin. Weight variation was found within the specification of the IP limits. It was found to be ranging between 0.2499-0.2741 gm.

Hardness, wetting time, thickness of tablets

Table 9: Hardness, wetting time and thickness of mouth dissolving tablets

	Diameter(cm)	Thickness (cm)	Hardness(kg/cm)	Wetting Time(sec)	Water absorption (%)
Tablet	0.9033±0.0577	5.4±0.001	5	32	36

Friability test

Initial weight of 6 tablets=1.623gm

Weight of 6 tablets after friability=1.61gm

Loss in weight=0.013

Percentage Friability=0.8%

Disintegration time study

The disintegration time study was conducted. The disintegration time of the tablet was found to be 37 seconds, which is desired to be less than 60 seconds for mouth dissolving tablets. The rapid disintegration may be due to the rapid uptake of water from the medium, swelling, burst effect and thus promoting bioavailability.

Dissolution Study

Dissolution study was conducted. It was found that mouth dissolving tablets have better drug dissolution than conventional tablet. The values are given below

Table 10: Dissolution of mouth dissolving and conventional tablets

Time in minutes	Mouth dissolving tablets	Conventional tablets
0	0	0
5	7.12	7.29
10	25.67	23.6
15	40.6	44.7
20	65.46	56
25	88.75	64.1
30	96.15	73.4

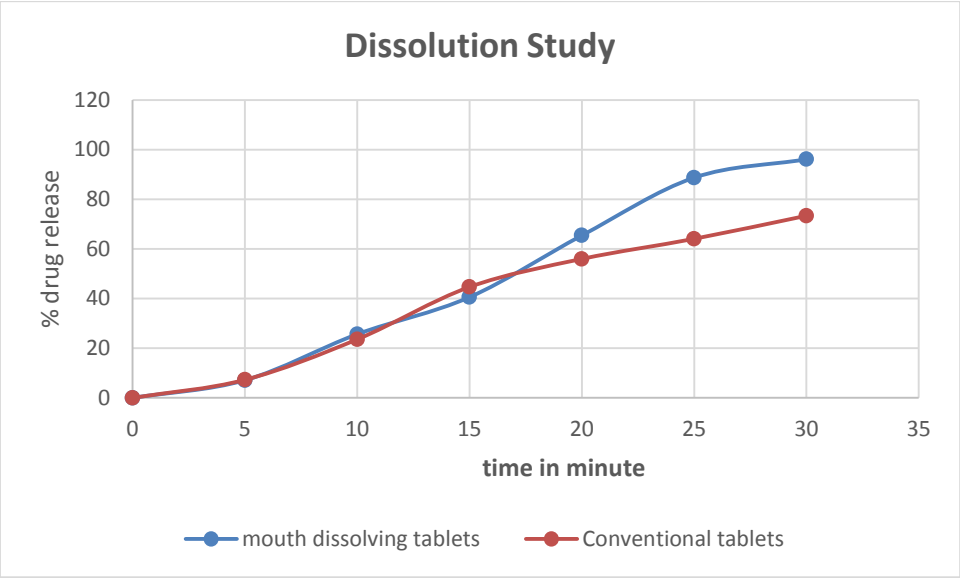

Figure 4: Graphical representation of dissolution of mouth dissolving and conventional tablets

Standard graph of Azithromycin

Table 11: standard curve of Azithromycin

Sl no.	Concentration(microgram/ml	Absorbance
1	0	0
2	2	0.102
3	4	0.222
4	6	0.338
5	8	0.448
6	10	0.590

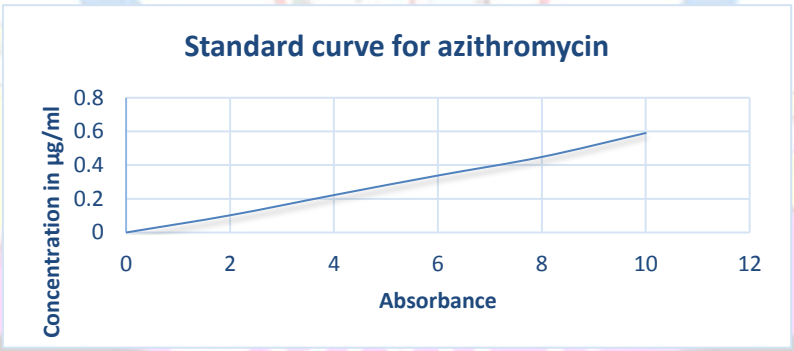

Figure 4: Graphical representation of Azithromycin

CONCLUSION

The present work was aimed to formulate the mouth dissolving tablet of Azithromycin by using natural superdisintegrants plant ago mucilage. The results from invitro disintegration time, in-vitro dissolution study, wetting time and water absorption ratio showed that the plant ago mucilage is more beneficial. Thus it can be concluded that natural superdisintegrant based more cheap mouth dissolving tablets of Azithromycin would be quite effective in treatment, by providing quick onset of action.

REFERENCE

1. Azithromycin Dihydrate-Product Data Sheet".TOKU-E. December 1,2010
2. Augsburger L L,Stephen W H;oral disintegrating tablets. Pharmaceutical dosage forms:Tablets.Informa Healthcare Publication.3(2):293-3.
3. R. Deveswaran, S. Bharath,S. Furtado. B. V. Basavaraj, S. Abraham& V. madhavan. Studies on the disintegrant properties of mucilage and seed powder of Plantago ovate. International Journal of chem Tech Research. 1(2009)621-626.
4. Seager H. Drug-delivery products and Zydis fast dissolving dosage forms. Journal Of Pharmacy and Pharmacology.1998;50(4):375-82.
5. Pratical Pharmacognosy ,Khandawal K R,page no.149-153.
6. Kumaresan C,orally Disintegrating Tablet-Rapid Disintegration. Sweet Taste, and Target Release Profile ,Pharmainfo.net sep9,2008.
7. Anderson,J.R.,K.Bukhave,L.Hojgaard,J.Rasmussen,N.Hermensen,H.Worning and E.Krag 1988.Decomposition of wheat bran and isabgol husk in the stomach and small intestine of healthy men. J.Nutur. 118(3):326-331.
8. Anderson,J.W., D Deakins,T.Floore,B.Smith,S.Whitis.1990.Dietary fiber and coronary heart disease .Crit.Rev.Food Sci.Nutr.29(2):95-147.
9. Auwaerter, Paul (Nov 17,2011).Haemophilis Species .Johns Hopkins ABX Guide. Retrieved September 19,2013.
10. Chisholm,S.A;Neal,T.J;Alawattegama,A.B;Birley,H.D.L;Howe,R.A;Ison,C.A(2009). "Emergence of high-level azithromycin resistance in Neisseria gonorrhea in England and Wales". Journal of Antimicrobial Chemotherapy 64(2):353-8
11. G. Jyothi & P. K. Lakshmi. Comparative evaluation of natural and synthetic superdisintegrants with newer superdisintegrant Kyron T-314.ActaPharmaceuticaSciencia.(2011)35-44.
12. Kauri T, Bhawandeep G, Sandeep K, Gupta G D. Mouth Dissolving tablets: a novel approach to drug delivery. Int J Curr Pharm Res.2011;3(1):1-7.
13. Banic Tomisic, Z.(2011)."The Story of Azithromycin".Kemija u industry 60 (12):603-617.