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ISOLATION AND EVALUATION OF MUCOADHESIVE POLYMERS FROM *COLOCASIA ESCULENTA* AND *ZIZIPYS JUJUBE*

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ABSTRACT

Since Dr. Tsuneji Nagai of Hoshi University, Japan in the early 1980's used the concept of bio adhesion for the delivery of insulin across the buccal mucosa in beagle dogs; several researchers tried a large number of drugs for administration through buccal mucoadhesive dosage forms. The potential of these dosage forms have been found to be tremendous because of their ability to improve the bioavailability of many such drugs by bypassing the hepatic first pass metabolism. Because of the growing number of newer molecules in the form of peptides and proteins, the research in this field has gained the centre stage for the non-invasive drug delivery as an alternative to parenteral route. The novel design of the buccal delivery system can be achieved by the help of polymers of synthetic and natural polymers. The purpose of this review article to establish the developments and highlight the importance of mucoadhesive buccal delivery polymers which are isolated from colocasia esculenta and zizipys jujube and to compare the features for compatibility and stability studies with other synthetic polymers for developing the buccal delivery of low bio available drugs.

Key words *colocasia esculenta, zizipys jujube, bioadhesion, buccal delivery polymers, tensile strength, mucoadhesion.*

INTRODUCTION

Polymer is a generic term used to describe a very long molecule consisting of structural units and repeating units connected by covalent chemical bonds. The term is derived from the Greek words: *polys* meaning *many*, and *meros* meaning *parts*. The key feature that

distinguishes polymers from other molecules is the repetition of many identical, similar or complementary molecular subunits in these chains. These subunits, the monomers, are small molecules of low to moderate molecular weight, and are linked to each other during a chemical reaction called polymerization. Instead of being identical, similar monomers can have varying chemical substituents. The differences between monomers can affect properties such as solubility, flexibility, and strength. The term buccal adhesive polymer covers a large, diverse group of molecules, including substances from natural origin to biodegradable grafted copolymers and thiolated polymers.[1, 2, 3,4,5,6]

Bioadhesive formulations use polymers as the adhesive component. These formulations are often water soluble and when in a dry form attract water from the biological surface and this water transfer leads to a strong interaction. These polymers also form viscous liquids when hydrated with water that increases their retention time over mucosal surfaces and may lead to adhesive interactions. Bioadhesive polymers should possess certain physicochemical features including hydrophilicity, numerous hydrogen bond-forming groups, flexibility for interpenetration with mucus and epithelial tissue and visco-elastic properties.[7]

MATERIALS AND METHODS

Isolation of mucoadhesive material from C*olocasia esculenta* corms

Fresh corms of C*olocasia esculenta of Araceae* family were collected from Hyderabad district of Andhra Pradesh. It was collected from the local market and peeled. 500 gm of the peeled corms were cut into pieces was soaked in one liter of distilled water for 12 hrs. They were ground to a fine paste and added with 500 ml of water. Stirred vigorously for few minutes and kept for 12 hours. The slurry was filtered through a muslin cloth. The filtrate was collected and kept undisturbed in refrigerator for 12 hrs. Upper clear solution was collected by decantation. The filtrate was precipitated by the addition of 3 volumes of acetone. Stirred continuously for 15 min and the precipitated mucoadhesive material was washed thrice with acetone and dried in a vacuum drier and powdered. Powder was passed through the sieve no 120 and kept in a desicator for further studies.[8]

Isolation of mucoadhesive material from *Zizypus jujube* fruits

Tender fruits of Zizypus jujube belong to the Rhamnaceae family were collected from the tree and washed well with water. 500 grams of the fruits along with seeds were soaked with 1000 ml of distilled water for 2 hours. Heated at 60 ^{0}C for 4 hrs on water bath and set aside

for 12 hours. Then the liquid was filtered through muslin cloth and allowed to stand. By decantation the clear supernatant liquid was obtained and the sediments were rejected. The volume was reduced to half by heating on a rotary vacuum evaporator. The concentrated extract was precipitated with 3 volumes of acetone and purified by redispersing in water and precipitating with acetone. The precipitate was dried under vacuum desiccator, powdered and sieved (# 120) and kept in a desiccator for further studies.[9,10]

STRUCTURES OF MUCOADHESIVE POLYMERS WIDELY USED

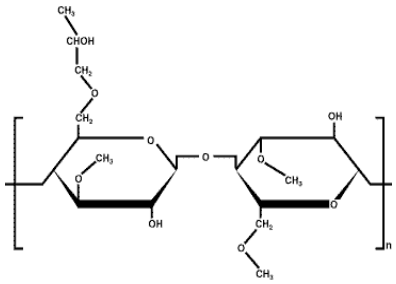

Fig. No.1. Hydoxypropyl methylcellulose

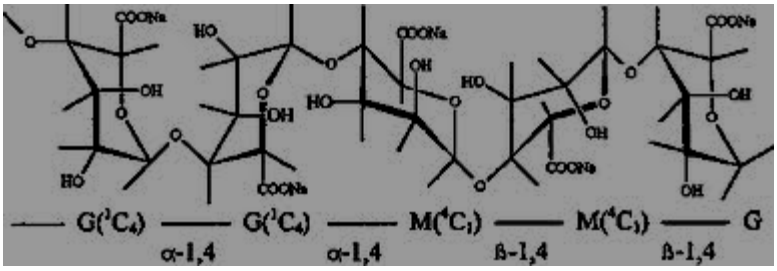

Fig No 2: Sodium alginate

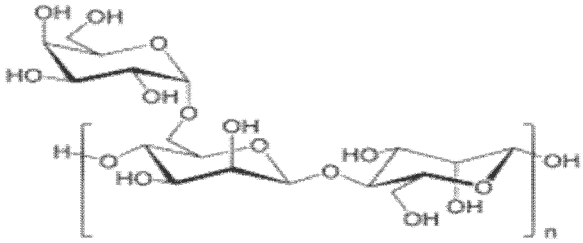

Figure 3 guar gum

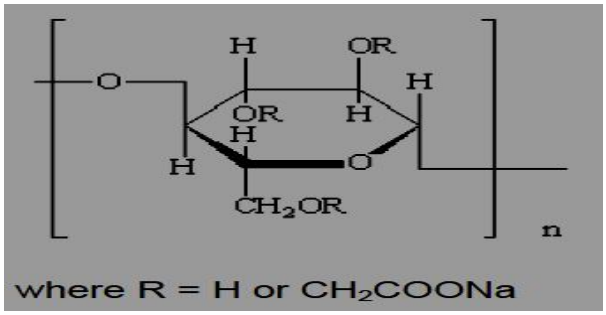

Figure 4 Sodium carboxy methyl cellulose

PREFORMULATION STUDIES

PH: pH of 1% w/v aqueous solutions of isolated mucoadhesive substances were measured by Toshniwal pH meter.

Determination of swollen volume*:* Swellability studies was done by dispersing 1 gm of mucoadhesive substance with a few drops of ethanol in a graduated measuring cylinder and were then made upto 50 ml with water. Swollen volume was noted after 24 hours. Swelling capacity was computed according to the following equation:

$S= (V_2 - V_1) / V_1 \times 100$ …… (1)

Where S is the % swelling capacity, V_2 is the volume of the hydrated or swollen material and V_1 is the tapped volume of the material prior to hydration.[11]

Moisture sorption capacity: 2 g of mucoadhesive substance was accurately weighed and evenly distributed over the surface of a 70 mm-tarred *Petri* dish. The sample was then placed in Thermolab Humidity chamber at room temperature and relative humidity of 100%. The weight gained by the exposed samples at the end of a five-day period was recorded and the amount of water sorbed was calculated from the weight difference.[12]

Loss on drying: The powder sample of mucoadhesive material (5 g) in a *Petri* dish was dried in an oven at 105^{o}C until a constant weight was obtained. The % moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage.[13]

MEASUREMENT OF MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS: THUMB'S TEST

Thumb's test is useful in initial screening test parameters. The test is being carried out by means of the force required or the difficulty to pull out the thumb from other finger, when kept in contact by the mucoadhesive material in specific concentration and volume, with respect to contact time.

SHEAR STRESS METHOD

Several methods have been reported and in most of the cases, invitro models are based on the measurement of shear or tensile strength. Two smooth, polished plexi glass plates of 2.5×7.5 cm were fixed with the help of an adhesive (Araldite). A nylon thread was sandwiched in between the glasses. Another glass plate of same dimension has been taken and one end was

fixed with another nylon thread, which was then passed on a pulley and at the end, and provision was provided to add weight. The sandwiched plate was fixed on a flat table. Another glass plate fixed with nylon thread was kept in contact between the sandwiched plate by placing appropriate concentrations like 0.5%, 1.0% and 1.5% w/v of mucoadhesive material in specified volume of 0.5 ml and allowed at specified intervals of 5,10,15, 20 and 30 minutes. The force required to detach the plates were measured as a means of adhesive strength. This represents the adhesion strength i.e. shear stress required to measure the adhesion and repeated the same procedure for three times.[14]

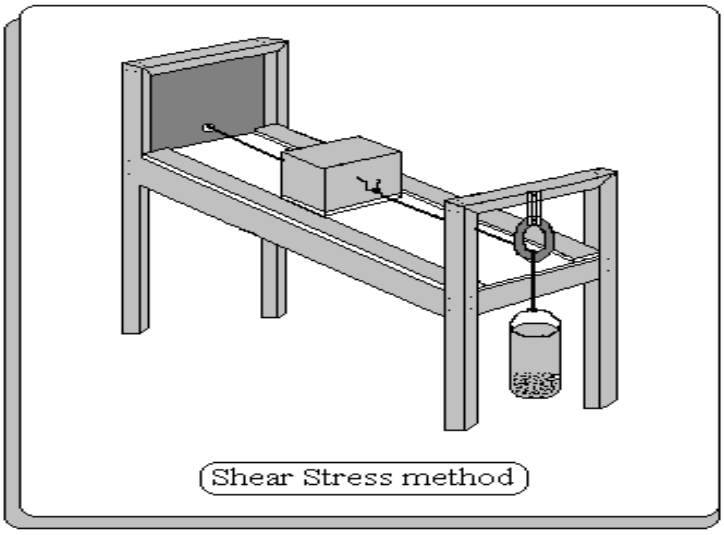

Fig. No 5. DESIGN OF MODEL FOR SHEAR STRESS METHOD

PARK AND ROBINSON METHOD

This method is based on the measurement of tensile strength. In this method, the force required to separate the bioadhesive sample from freshly excised buccal membrane of goat was determined using a modified instrument. A section of tissue having the mucus side exposed was secured on a glass vial placed in a beaker containing phosphate buffer of pH 6.6. Another section of the same tissue was placed over a rubber stopper, with the mucus side exposed, and secured with a vial cap. Small quantity of polymer solution (1.0%) was placed between two mucosal tissues. The force used to detach the polymer from mucosal tissue was then recorded The results of the study provided important experimental conditions such as pH, ionic strength, and applied pressure on bioadhesion.[15]

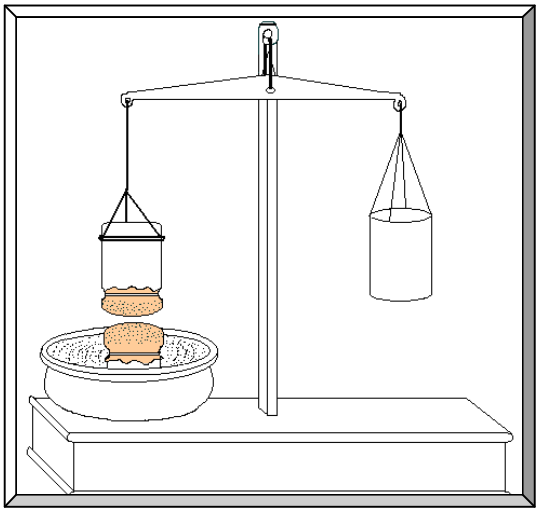

Fig. No.6. Instrument for measuring bioadhesiveness by Park & Robinson method

TABLE 1.PHYSICAL PROPERTIES OF THE MUCOADHESIVE POLYMERS

Mucoadhesive substance	Biological source	Part used	Organic solvent	Yield % w/w	pH	Swollen volume (ml)	Swelling Capacity (%)	Moisture sorption capacity (%)	Loss on drying (%)
CE	Colocasia esculenta	corms	Acetone	3.46	3.57	13.3 ± 0.7	167.3 ± 7.18	7.3	4.9
ZJ	Zizypus jujube	fruits	Acetone	3.87	4.08	18.3 ± 1.5	387.3 ± 13.78	18.2	5.4
HPMC	**	**	**	**	7.21	6.4 ± 0.7	87.3 ± 3.10	11.2	2.6
SCMC	**	**	**	**	2.86	27.4 ± 1.1	521.3 ± 10.08	24.1	7.2
SA	**	**	**	**	6.16	25.7 ± 1.6	512.4 ± 11.34	11.3	2.9
GG	**	**	**	**	6.54	31.2 ± 1.5	611.9 ± 18.51	8.7	1.4

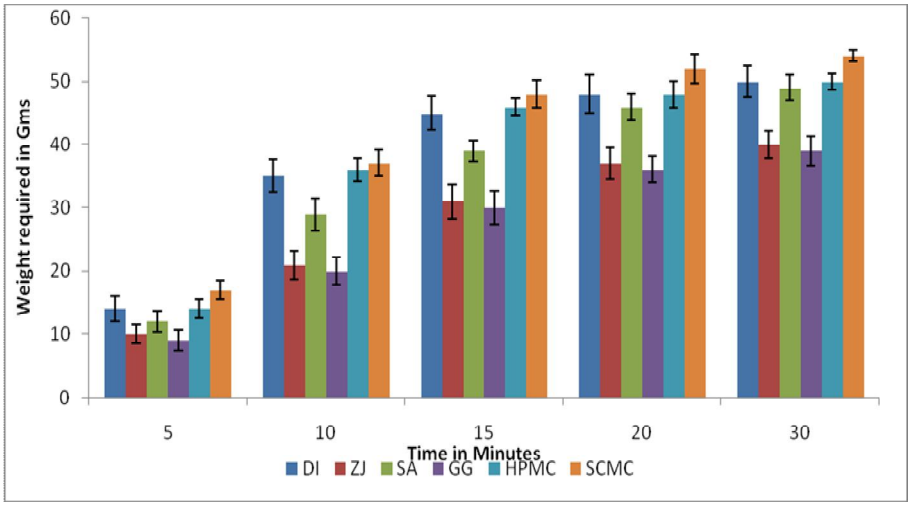

Fig 7 Mucoadhesive Strength of Polymer Solutions (0.5%) By Shear Stress Method

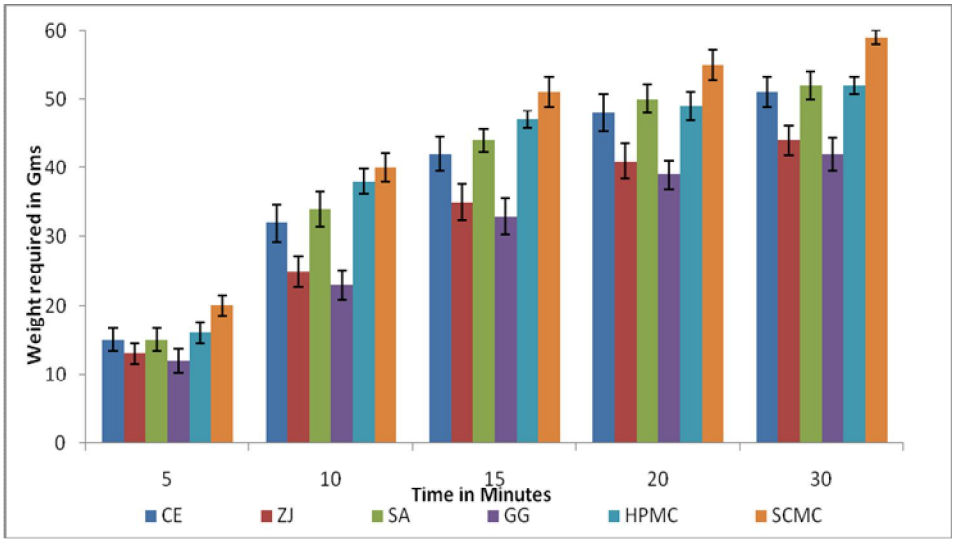

Fig 8 Mucoadhesive Strength Of Polymer Solutions (1.0%) By Shear Stress Method

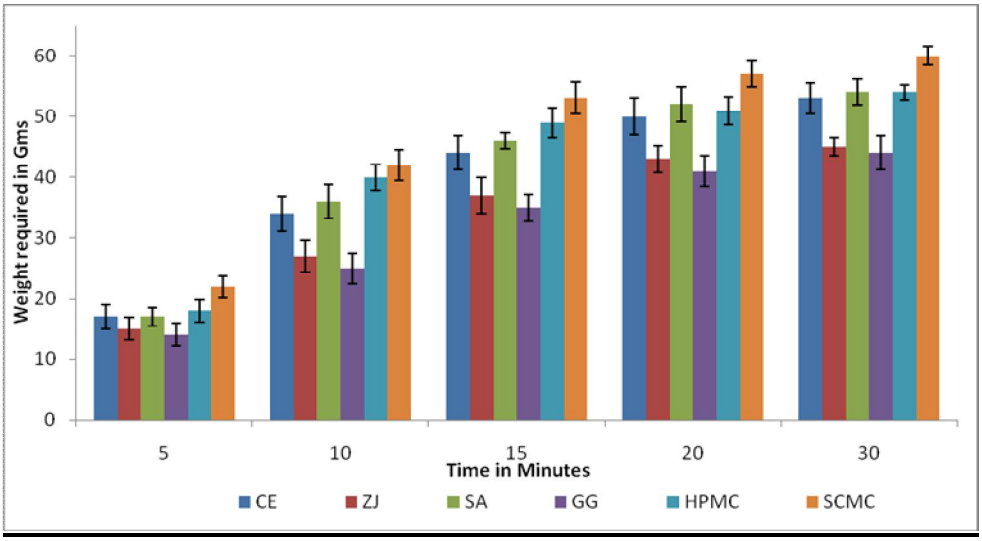

Fig 9 Mucoadhesive Strength Of Polymer Solutions (1.5%) By Shear Stress Method

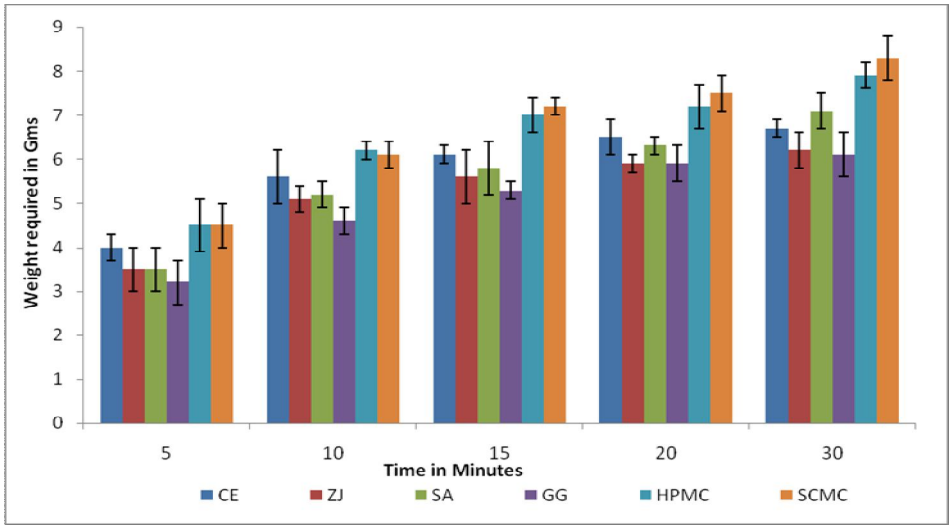

Fig 10. Mucoadhesive strength of polymer solutions (0.5%) by park & robinson method

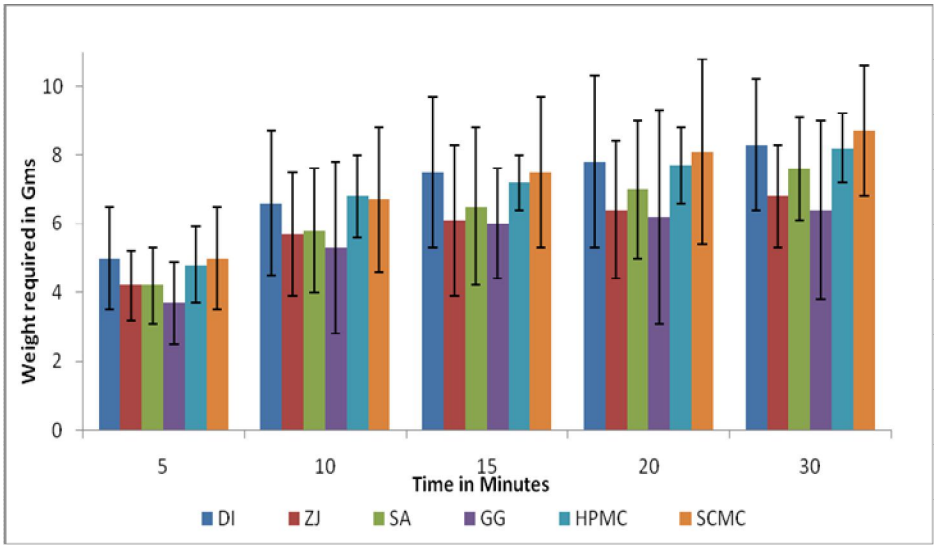

Fig 11 Mucoadhesive Strength Of Polymer Solutions (1.0%) By Park & Robinson Method

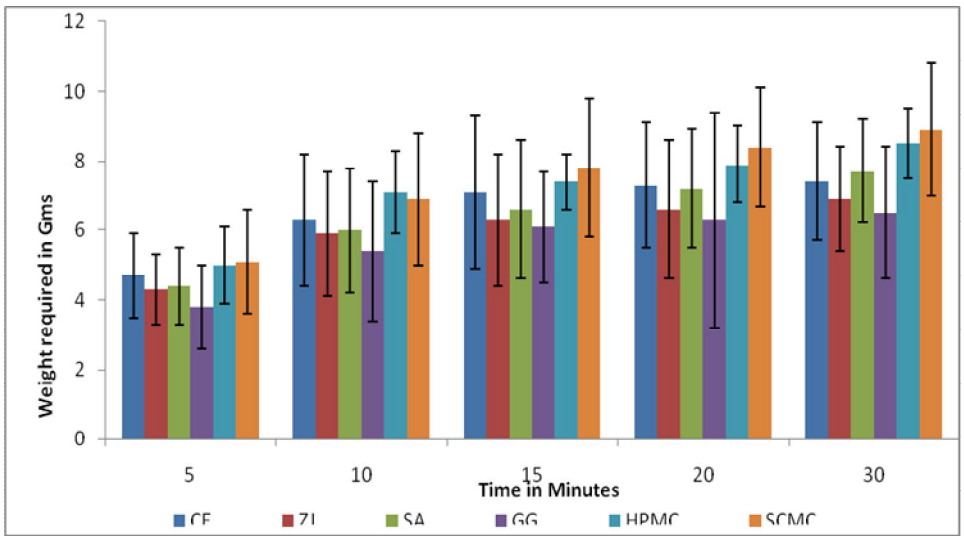

Fig 12.Mucoadhesive Strength Of Polymer Solutions (1.5%) By Park & Robinson Method

RESULTS AND DISCUSSION

Mucilages or mucopolysaccharides of plant origin have been used widely as demulcent because of their unique properties to bind with the mucus membrane. The selection of the materials for the current investigation was based on their edibility, blandness, availability, and the economics.

Isolation of water-soluble components from the natural edible sources was carried out by cold/hot aqueous extraction process followed by the organic solvent precipitation. The

selection of the process was based on previous literature giving utmost importance to preserve the components against thermal, enzymatic and hydrolytic degradation. The organic solvents used for precipitation can be recovered back by fractional distillation, making the process more economical. The processes used were found to be effective in selective isolation of the material and the yielded material possesses good handling properties.

Table 8 represents the details of the extraction process, respective yield, and their physical properties such as pH, swollen volume, swelling capacity, moisture sorption capacity, loss on drying etc. The yield of CE and ZJ was 3.46, 3.87 % w/w respectively to the initial weight. PH of 1% w/v solutions of CE 3.57 and ZE is 4.08. Swelling is the primary characteristic of any material to be a mucoadhesive substance, but over hydration causes slippery surface. Excessive swelling also causes loss of mechanical strength that is required to maintain the structural integrity of the solid dosage forms. Swollen volumes after 24 hours of hydration was found to be 13.3, and 18.3 indicating their moderate swellability compared to 25.7 of sodium alginate and 31.2 of guar gum. Swelling was also assessed by the determination of swelling capacity and moisture sorption profile.[9] Study of moisture sorption is also of considerable importance since it reflects the relative physical stability of dosage forms when stored under humid conditions. In all, this property showed that the CE & ZJ powders are sensitive to atmospheric moisture and should therefore be stored in airtight containers.. The loss on drying of CE & ZJ was less than the official limit of 6% stated in British Pharmacopoeia 2004.

Fig 5 & 6 represents the schematic diagrams of the apparatus used for preliminary screening of mucoadhesive strengths. Fig 7-12 represents the weight required to detach the blocks/tissues attached together by the mucoadhesive solutions after specified contact times. The results suggest that the isolated mucoadhesive material possessed comparable shear and tensile strengths to the commercially available GRAS (generally regarded as safe) category polymers and higher than the other natural polymers such as sodium alginate and guar gum. Further, these strengths were increased with the increase in concentration but no considerable increase was observed after 15 minutes of contact time, irrespective of polymers studied. Strengthening of bioadhesion may be due to the formation of more number of secondary bonds as time progresses.

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REFERENCES

1. Chien YW, Concepts and system design for rate-controlled drug delivery, in: Y.W. Chien (Ed.), Novel Drug Delivery Systems, Marcel Decker, Inc; New York, (1992): 1-42.
2. The Drug Delivery Arena – In Brief; An Authoritative Round-up of Trends, Statistics and clinical Research. Touch briefings, *Future Drug Delivery* (2006): 12-13.
3. Prescot LF, Nimmo WS.The need for improved drug delivery in clinical practice, in: L.F. Prescott (Ed.), Novel Drug Delivery, John Wiley and Sons Ltd, Chichester, West Sussex, England (1988) :1-11.
4. Rathbone MJ, Ponchel G, Ghazali FA.Systemic oral mucosal drug delivery and delivery systems, in: M.J. Rathbone (Ed.), Oral Mucosal Drug Delivery.Vol. 74, Marcel Decker, New York, 1996: 241-284.
5. DeGrande G, Benes L, Horriere F,Karsenty H, Lacoste C. Specialized oral mucosal drug delivery systems: patches, in: M.J. Rathbone (Ed.), Oral Mucosal Drug Delivery, Vol. 74, Marcel Decker, New York, 1996, :241-284.
6. SudhakarY,Kuotsu K Bandyopadhyay AK, Buccal bioadhesive drug delivery-A promising option for orally less efficient drugs, *Journal of controlled Release.* (2006); 114(6): 15-40.
7. H. Batchelor, Novel bioadhesive formulations in drug delivery. The drug delivery companies report Autumn / Winter, PharmaVentures Ltd, 2004.
8. *The Morton Arboretum Quarterly*, Morton Arboretum/University of California, 1965,. 36.
9. Clarke,D.L,1988. *W. J. Bean Trees and Shrubs Hardy in the British Isles*, Supplement. John Murray ISBN 0-7195-4443-2.

10. Mahajan RT, Chopda MZ., Phyto-pharmacology of Ziziphus jujuba mill – Aplant review" Mahajan R.T., Chopda M.Z. *Pharmacognosy Reviews*, 2009 ;3:6:320–329
11. S.A. Mortazavi, J.D. Smart, An investigation of some factors influencing the in vitro assessment of mucoadhesion. *International Journal of Pharmcy*,1995; 116 : 223–230.
12. H. Park, J.R. Robinson, Bioadhesive polymers as platforms for oral controlled drug delivery, Method to study bioadhesion, *International Journal of Pharmacy*,1984: 107-127.
13. D. Train, Some aspects of the property of angle of repose of powders, *Journal of Pharmacy and Pharmacology*, 1958, 10: 127T-134T.
14. M. Ishida, Y. Machida, N. Nambu, T. Nagai, *Chemical Pharma Bulletin*. (Tokyo), 1981; 29(3) : 810-816
15. T.A. Barber, Pharmaceutical Particulate Matter, Analysis and Control. Interpharm Press, Buffalo Grove, IL, 1993:266-349.
16. J.W. Lee, J.H. Park, J.R. Robinson, Bioadhesive based dosage forms: the next generation, *Journal of Pharmaceutical Sciences 2000;* 89: 850-866.