Available online at www.abhipublications.org
Research Article
International Journal of Pharmacy and Engineering (IJPE)
ISSN 2320-849X

Studies on Mucoadhesive Properties of Some Natural Materials

Ranabir Chanda[*1], Saumya Samanta [2], Jyotishman Bhattacharya [2], Piyali Sanyal [2] and Pranabesh Chakraborty [2]

Bengal School of Technology, Chinsurah, West Bengal, India

*Corresponding author at: Bengal School of Technology, Chinsurah, West Bengal, India, *India.*
E. mail: ranabirchanda@yahoo.com (R.Chandra), Contact: +917278839102.

Abstract

Bioadhesive polymers that bind to the gastric mucin or epithelial cell surface are useful in drug delivery for the purpose of (a) retaining a dosage form in the G.I tract and (b) increasing the intimacy and duration of contact of drug with the absorbing membrane. In this investigation, natural mucoadhesive materials are isolated from different edible vegetables, fruits and seeds like *Aegle marmelos (Linn.) Cor.*, *Zizyphus mauritiana*, *Albelmoschus esculeatus* and *Tamarindus indica* by hot extraction method. Bioadhesive and mucoadhesive qualities of natural materials are evaluated individually by different *in vitro* testing methods such as Shear stress method, Wilhelmy plate method and Park and Robinson method and *in vivo* X-ray photograph method. It was observed that mucoadhesive materials isolated from *Zizyphus mauritiana* is the best mucoadhesive agent than any other natural mucoadhesive materials.

Key words: Natural mucoadhesive materials, *in vitro* and *in vivo* evaluation.

1. Introduction

Mucoadhesion, or the attachment of a natural or synthetic polymer to a biological substract, is a practical method of drug immobilization or localization and an important new aspect of controlled drug delivery [1]. While the subject of mucoadhesion is not new, there has been increased interest in recent years in using mucoadhesive polymers for drug delivery [2]. Substantial effort has recently been focused on placing a drug or a formulation in a particular region of the body for extended periods of time. This is needed not only for targeting of drugs but also to better control of systemic drug delivery [3]. Drugs that are absorbed through the mucosal lining of tissues can enter directly into the blood stream and not be inactivated by enzymatic degradation in the gastrointestinal tract [4]. Several synthetic bioadhesive drug delivery systems have been fabricated and studied in the past. Different types of bioadhesive synthetic polymers such as acrylic-based hydro gels [5] i.e., synthetic polymers such as carbopol 934, carbopol 937 and hydroxypropylmethylcellulose (HPMC) are also used to prepare oral mucoadhesive tablets [6]. However, the adhesiveness and drug delivery capabilities of these devices can continue to be improved as presently known bioadhesive materials are modified and more bioadhesive materials are discovered [7-11]. Science the biodegradability of the synthetic polymers is questionable, some natural mucoadhesive materials extracted from edible fruits and vegetables having good mucoadhesive properties are used for this purpose [12, 13].

2. Materials and Methods

2.1 Materials

Several chemicals like Methanol (Quest Chemicals, Kolkata- 41), Acetone, (E. Merck (India) Ltd. Mumbai-18), Gelatin, Radio Opaque Barium Sulphate (E. Merck (India) Ltd. Mumbai-18), were purchased. Fruits, vegetables and goat intestine were collected from local market.

2.2 Methods

2.2.1 Extraction of Natural Mucoadhesive Materials

The mucilage from the natural sources was extracted by hot extraction method [13]. In this method, 250 gm of natural material obtained from edible fruits, vegetables and starch were soaked in double distilled water and boiled for 5 hrs in a water bath until slurry was formed. The slurry was cooled and kept in refrigerator overnight so that most of the undissolved portion was settled out. The upper clear solution was decanted off and centrifuged at 500 rpm 20 min. The supernatant was concentrated at 60^0C on a water bath until the volume reduced to one third of its original volume. Solution was cooled down to the room temperature and was poured into thrice the volume of acetone by continuous stirring. The precipitate was washed repeatedly with acetone and dried at 50^0C under vacuum. The dried material was powdered and kept in a desiccator.

2.2.2. Determination of Adhesiveness and Mucoadhesiveness Property of Natural Mucoadhesive Materials by *In-Vitro* Methods

2.2.3. Determination of Adhesiveness by Shear Stress Method

Two smooth, polished plexi glass blocks were selected. One block was fixed with adhesive 'Araldite' on a glass plate which fixed on a leveled table. To the upper block a thread was tied and the thread was passed down through a pully. At the end of the thread a beaker was fixed. The length of the thread from pully to the beaker was 7 cms. The weight of the beaker was counteracted. Different natural bioadhesive material solutions of 0.75% w/v were prepared using water as a solvent. A fixed volume (0.5 ml) of natural bioadhesive material solutions were kept on the centre of the fixed block with a pipette, and then second block was placed on the first block and pressed by applying 100 gm of weight, so that the drop of solutions spreads as a uniform film in between the two blocks. After keeping it for a fixed time intervals of 5, 10, 15, and 20 min, water was added into the beaker gradually, the weight of water just sufficient to pull the upper block or to make it slide down from the base block was recorded. This weight was considered as the adhesion strength, i.e. shear stress required to measure the adhesion [14]. Before every determination care was taken so that no air bubble form in between two blocks which may give erratic results, and the distance from pulley to glass slides was always same in all observations.

2.2.4. Preparation of Goat Intestinal Mucus Solution

Crude mucus was obtained by scraping goat intestine and was collected and diluted with twice of its volume with distilled water. The mixture was centrifuged for 30 min at 1200 r.p.m. The supernatant and sedimented portions were discarded, and the middle layer was collected for further use. The mucus was stored below -20^0 C until used. The pH of the collected mucus was 6.5 [15].

2.2.5. Determination of Mucoadhesiveness by Wilhelmy Plate Method

In this method small glass plates were coated uniformly by natural bioadhesive material solution to be tested and dried at 60^0 C. The prepared coated plates were immersed in goat intestinal mucus solution (pH6.5) for 5, 10, 15, and 20 min, at room temperature. The force required to pull the plate out of the solution was determined under constant experimental conditions [13].

2.2.6. Determination of Mucoadhesiveness by Park and Robinson Method

In this method [14], the force required to separate bio-adhesive sample from freshly excised goat intestine was determined using a modified tensiometer. A section of the tissue, having the mucus side exposed, was secured on a weighted glass vial placed in a beaker containing goat intestinal mucus solution (pH6.5). Another section of the same tissue was placed over a rubber stopper, again with the mucus side exposed, and secured with a vial cap. Then a small quantity of natural mucoadhesive agent was placed between the two mucosal tissues. The force used to detach the polymers and the nature mucoadhesive agents from the tissue was then recorded. The results of the study provided important information regarding the effects of charge density, hydrophobicity, and experimental conditions such as pH, ionic strength, mucolytic agents, and applied pressure on bio-adhesion. Experimentations were performed at room temperature.

2.2.7. Determination of Mucoadhesiveness of Natural Mucoadhesive Materials by *in-vivo* X-ray Study

The *in vivo* evaluation of the mucoadhesive property of the tablets formulated was performed in healthy rabbits by X-ray studies. For conducting the *in vivo* study, tablets containing 7.5 mg barium sulphate were prepared using 2% w/v solution of natural mucoadhesive materials as binding and coating agents [16]. A blank was prepared with same formulae but no mucoadhesive materials were incorporated. Here 2% w/v gelatin solution was used as binding agent. These tablets were orally administered to healthy rabbits with water after overnight fasting. X-ray photographs of different formulae were taken at different time intervals (1, 2, 3 and 4 h) to observe for the position of the tablets, in the GIT.

3. Results and Discussion

The results noted in Shear Stress Method, for various natural mucoadhesive materials with different contact time are shown in Table 1. From the results it was observed that among the natural materials, *Zizyphus mauritiana* exhibited highest adhesion and *Tamarindus indica* exhibited lowest adhesion property. The results noted in Wilhelmy Plate Method for various natural mucoadhesive materials with different contact time are shown in Table 2, using goat-intestinal mucus solution. From the results it was observed that among the natural materials, *Zizyphus mauritiana* exhibited highest muco-adhesion and *Tamarindus indica* exhibited lowest muco-adhesion property. The results noted in Park and Robinson Method for various natural mucoadhesive materials using goat-intestinal mucus solution with different contact time are shown in Table 3. From the results it was observed that among the natural materials, *Zizyphus mauritiana* exhibited highest muco-adhesion and *Tamarindus indica* exhibited lowest muco-adhesion property. From these results it was observed that increasing the contact time for adhesion and mucoadhesion increased the force required in terms of weights for of all the natural

Table 1 . Adhesiveness of Natural Mucoadhesive Materials by Shear Stress Method

Natural Mucadhesive Materials	Contact Time (min.)	Weight required (Grams)
Aegle marmelos (Linn.) Cor	05 10 15 20	11.6 13.0 15.3 17.6
Zizyphus mauritiana	05 10 15 20	13.0 13.6 15.6 18.0
Albelmoschus esculeatus	05 10 15 20	11.0 12.6 15.0 17.3
Tamarindus indica	05 10 15 20	4.3 5.3 6.6 8.6

materials. Therefore, increasing the time of contact increased the adhesion and mucoadhesion strength, allowing for greater adhesion and mucoadhesion. The results of the *in-vivo* X-ray studies on healthy rabbits are depicted in Figure 1-5. Mucoadhesive coated tablets were fed to rabbit and X-ray photographs were taken at one hour intervals. The X-ray studies in rabbits had shown that tablets prepared from mucoadhesive materials obtained from *Zizyphus mauritiana*, *Aegle marmelos (Linn.) Cor.*,and *Albelmoschus esculeatus* were present in rabbit intestine after four hours of feeding the tablet. In case of *Tamarindus indica*, it was only three hours. Tablets prepared by 2% w/v gelatin solution started disintegration within two hour.

Table 2 . Mucoadhesiveness of Natural Mucoadhesive Materials by Wilhelmy Plate Method, using Goat-intestinal Mucus Solution.

Natural Mucoadhesive Materials	Contact Time (min.)	Weight required (Grams)
Zizyphus mauritiana	05	12.6
	10	13.3
	15	14.3
	20	16.3
Aegle marmelos (Linn.) Cor	05	10.3
	10	11.6
	15	12.3
	20	15.6
Albelmoschus esculeatus	05	9.0
	10	11.0
	15	12.0
	20	14.6
Tamarindus indica	05	4.0
	10	5.0
	15	6.6
	20	7.0

Table 3. Mucoadhesiveness of Natural Mucoadhesive Materials by Park and Robinson Method, using Goat-intestinal Mucus Solution.

Natural Mucoadhesive Materials	Contact Time (min.)	Weight required (Grams)
Zizyphus mauritiana	05	19.6
	10	22.0
	15	24.3
	20	25.6
Aegle marmelos (Linn.) Cor	05	18.3
	10	21.3
	15	23.6
	20	25.3
Albelmoschus esculeatus	05	17.6
	10	20.6
	15	23.0
	20	24.6
Tamarindus indica	05	7.0
	10	8.6
	15	13.6
	20	15.6

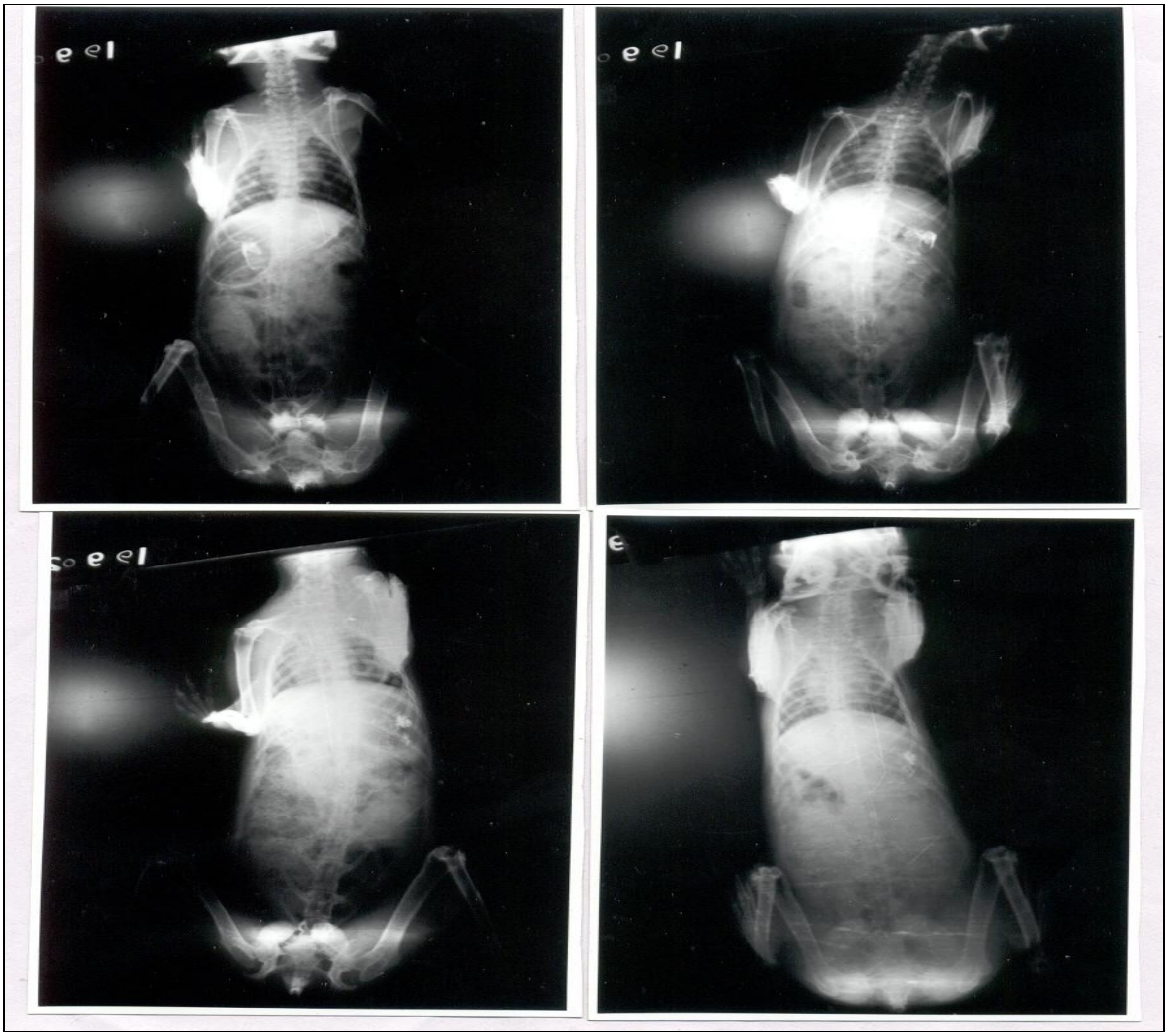

Figure 1. X-ray Photographs of Rabbit GIT after administration of Barium Sulphate Pellet Coated with materials extracted from *Aegle marmelos (Linn.) Cor*.

* 2% w/v solution of materials extracted from *Aegle marmelos (Linn.) Cor*.in water was used as binding and coating solution, for coating the tablets.

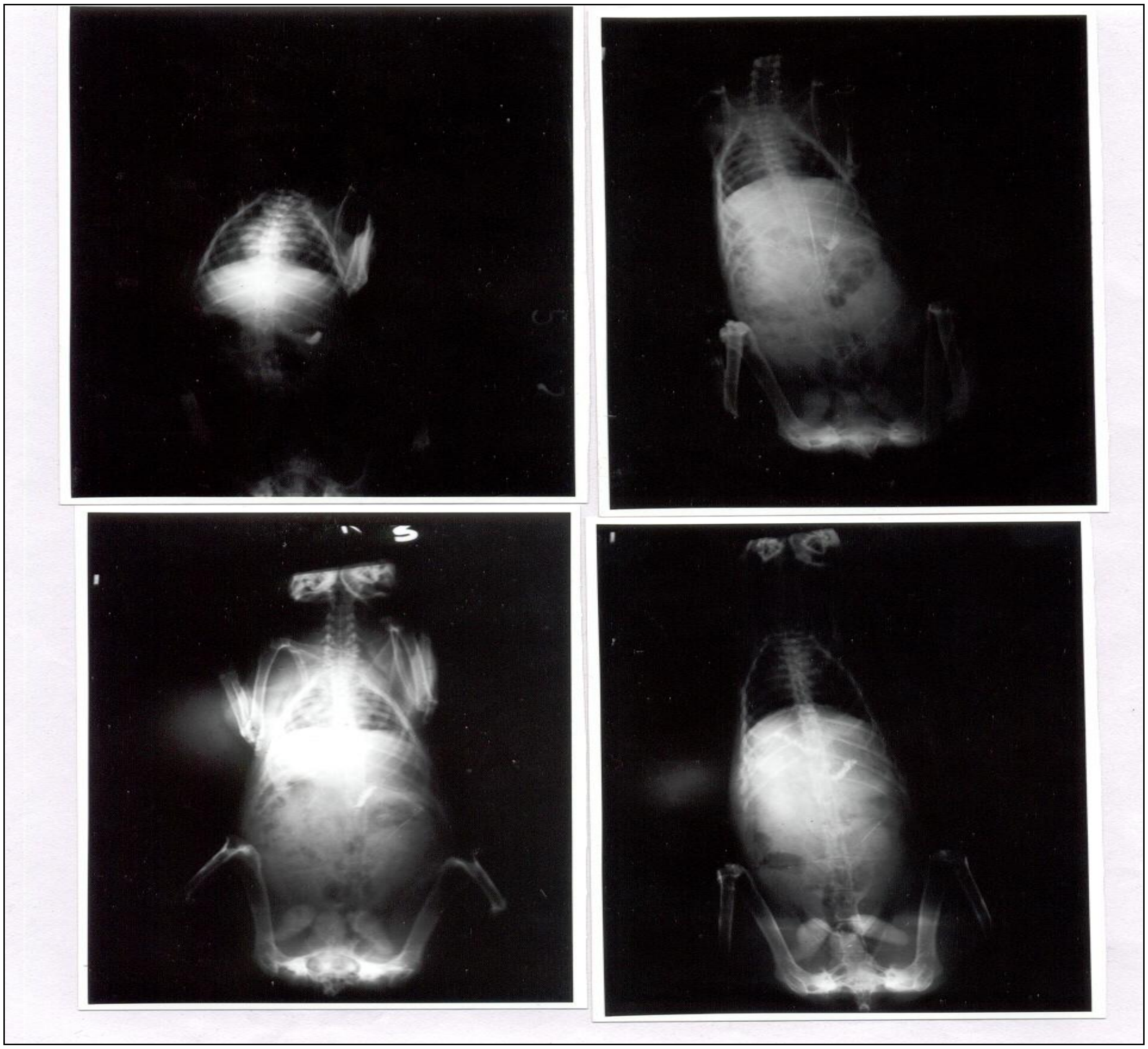

Figure 2. X-ray Photographs of Rabbit GIT after administration of Barium Sulphate Pellet Coated with materials extracted from *Zizyphus mauritiana*.

* 2% w/v solution of materials extracted from *Zizyphus mauritiana* in water was used as binding and coating solution, for coating the tablets.

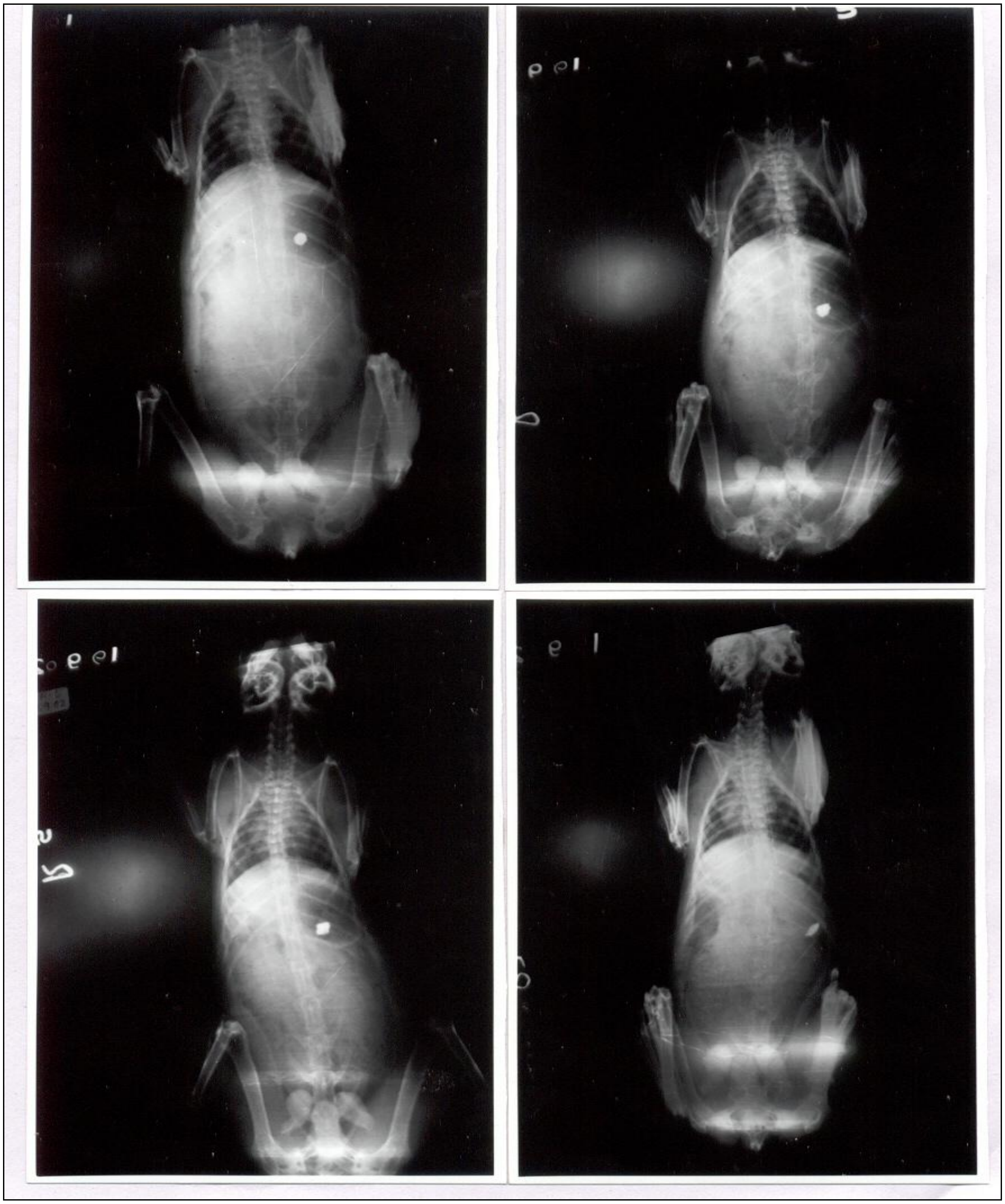

Figure 3. X-ray Photographs of Rabbit GIT after administration of Barium Sulphate Pellet Coated with materials extracted from *Albelmoschus esculeatus*

* 2% w/v solution of materials extracted from *Albelmoschus esculeatus* in water was used as binding and coating solution, for coating the tablets.

Figure 4. X-ray Photographs of Rabbit GIT after administration of Barium Sulphate Pellet Coated with materials extracted from *Tamarindus indica*

* 2% w/v solution of materials extracted from *Tamarindus indica* in water was used as binding and coating solution, for coating the tablets.

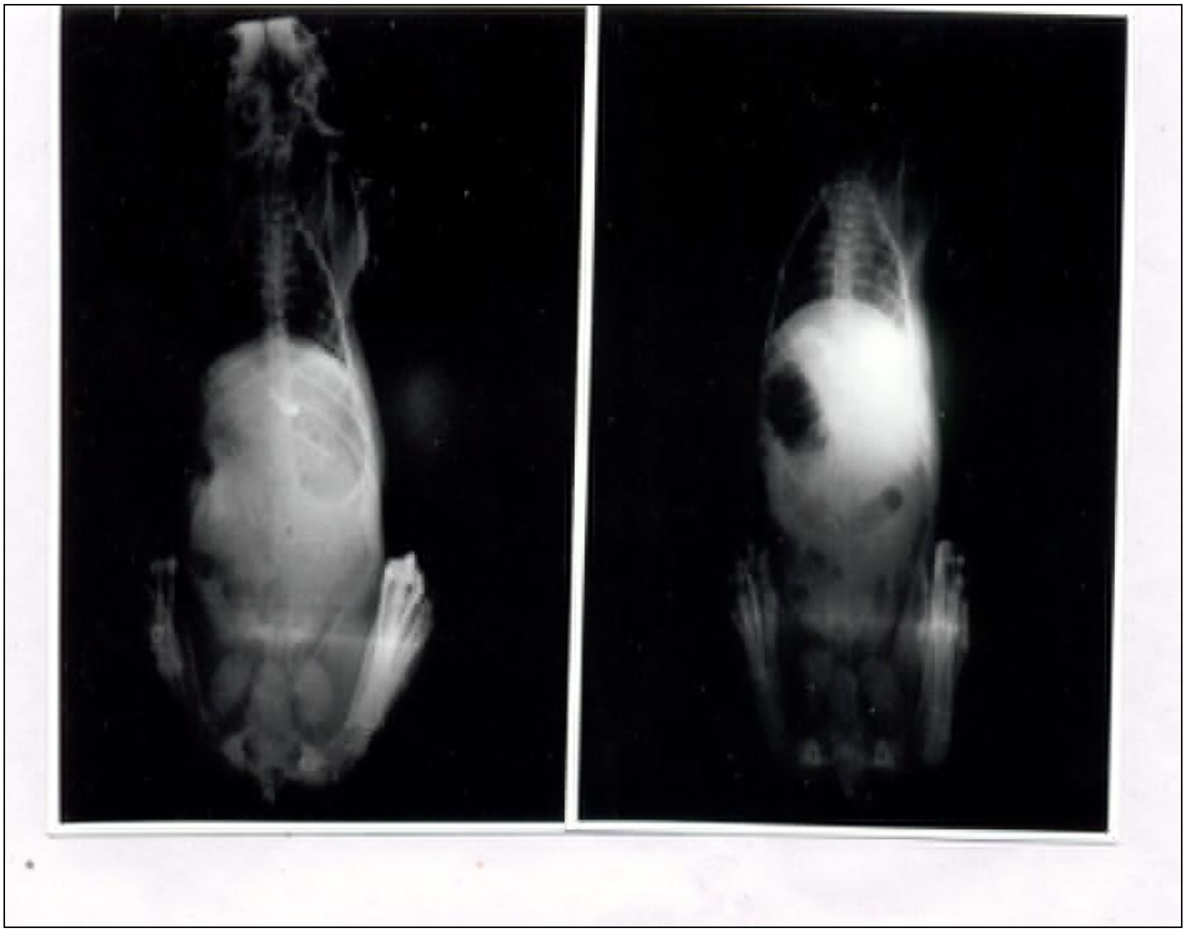

Figure 5. X-ray Photographs of Rabbit GIT after administration of Barium Sulphate Pellet Control Pellet.

* No coating material was used. 2% w/v gelatin was used as binder.

4. Conclusion

From these experiments it was confirmed that the material obtained from *Zizyphus mauritiana* had shown the best adhesive and mucoadhesive property among all natural materials followed by the materials obtained from *Aegle marmelos (Linn.) Cor.*

5. Acknowledgement

We are very pleased to acknowledge the Faculty and the Librarian of Bengal School of Technology (W.B, India) for technical support. We would like to thank the institution for providing the apparatus, chemicals and animals.

6. References

[1]. Peppas NA, Moniga NK, Hung Y, Dekker M., Handbook of pharmaceutical controlled release technology., New York., Marcel Dekker INC, 2005, pp. 236-247.
[2].Marriott C, Gregiry NP., Mucus physiology and pathology. In: Enaerts V, Gurny R. (Editors). Bioadhesive drug delivery system. Boca Ratan: CRC Press, 1990; pp. 1-24.
[3].Gandhi BR, Robinson JR. Bioadhesion in drug delivery, Ind J Pharm Sci., 1988, 50: 145-152.
[4].Langer RS, Peppas NA., New drug delivery system. BMES Bull., 1992, 16: 3-7.
[5].Duchene D, Touchard F, Peppas NA., Pharmaceutical and medical aspects of bioadhesion systems for drug administration. Drug Dev Ind Pharm, 1988, 14: 283-318.
[6].Khanna R, Agrawal SP, AHuja A., Mucoadhesive buccal drug delivery: A potential alternative to conventional therapy. Indian J Pharm Sci., 1998, 60: 1-11.
[7].Gurny R, Meyer JM, Peppas NA., Bioadhesive intraoral release systems: Design, testing and analysis. Biomaterials, 1984. 5: 336-340.
[8].Achar L, Peppas NA. Preparation, characterization, and mucoadhesive interactions of poly (methacrylic acid) copolymers with rat mucosa. J Control Release, 1994, 31: 271-296.
[9].Peppas NA, Moniga NK. Ultrapure poly (vinyl alcohol) hydrogels with mucoadhesive drug delivery characteristics. Eur J Pharm Biopharm, 1997, 43: 51-58.
[10].Ascentiis DA, Colombo P, Peppas NA., Scening of potentially mucoadhesive polymer microparticles in contact with rat intestinal mucosa. Eur J Pharm Biopharm., 1995, 41: 229-234.
[11].Hoffman AS, Chen G, Wu X, Ding Z, Kabra B, Randeri K, Schiller M, Ron E, Peppas NA., Graft copolymers of PEO-PPO-PEO triblock polyethers on bioadhesive polymer backbones: Synthetisis and properties. Polym Prepr, 1997, 38: 524-555.
[12].Khullar P, Khar RK, Agarwal SP., Evaluation of guar gum in the preparation of sustained-release matrix tablets. Drug Dev Ind Pharm., 1998, 24: 1095-1109.
[13].Ranabir Chanda, Lila Kanta Nath, Sontosh Mahapatra., Formulation Development of Oral Mucoadhesive Coated Terbutaline Sulphate Tablets Using Some Natural Materials Extracted from Edible Fruits Available in India., Iranian J Pharm Sci., 2009, 5: 3-12.
[14].Ranabir Chanda, S.K. Mahapatra, Tutun Mitra Amit Roy, Sanjib Bahadur., Development of Oral Mucoadhesive Tablets of Terbutaline Sulphate Using Some Natural Materials Extracted from *Albelmoschus esculentus* and *Tamarindus indic. Research Pharm Tech 2008 ,Jan-Mar, 46-52.*
[15].Chanda, R., Design and Development of Mucoadhesive Drug Delivery Systems, M. Pharm Thesis, Jadavpur University, 2000, pp 45.
[16].Chowdary, K.P.R and Sundari, B., Design and evaluation of muco adhesive controlled release oral tablets of glipizide, *Indian J. Pharm. Sci*, **65**:591-594, 2003.