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EFFECT OF POLYMER RATIO AND EXCIPIENTS ON METOPROLOL TARTRATE RELEASE FROM CHITOSAN - SODIUM ALGINATE POLYMERIC IMPLANTS

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Keywords:

Biodegradable Polymeric Implant, Chitosan, Sodium Alginate, Glutaraldehyde, Metoprolol Tartrate

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ABSTRACT: Natural biodegradable chitosan-sodium alginate polymer combination is a promising candidate for preparing drug-loaded implants because of the availability and inexpensiveness of the polymers over the semi synthetic biodegradable ones. The main objective of this research was to prepare and evaluate a biodegradable implantable system of the drug metoprolol tartrate because it plays an important role in the treatment of high blood pressure, strokes, heart attacks and angina. 70:30 and 80:20 chitosan - sodium alginate combination implants of metoprolol tartrate with 15 and 30 minutes exposure time to glutaraldehyde for hardening were prepared. It was observed that loading efficiency and drug release could be influenced by varying polymer ratios, exposure times to glutaraldehyde and excipients. The implant formulated with 25 mg drug load in 70:30 chitosan - sodium alginate ratio with 15 minutes exposure produced the maximum sustained release for 15 days. Therefore, this formulation was chosen for preparing implants containing different excipients and the implants were evaluated for loading efficiency and *in-vitro* drug release. Morphological characteristics of the implants were analyzed using SEM. The release mechanism was explored and explained with zero order, first order, higuchi and korsmeyer-peppas models. Implants with excipients were found to follow first order model in most cases. also good co-relations were obtained with higuchi model. According to these models, the drug release from the implants was diffusion controlled, where the drug leaving the matrix through pores and channels formed by entry of dissolution medium.

INTRODUCTION: The concept of sustaining or prolonging the release of biologically active agents for extended periods of time has been well appreciated and rationalized for decades to overwhelm the drawbacks of fluctuating drug level associated with conventional dosage forms [1, 2]. Polymeric drug delivery system provides an attractive capability of releasing the drug from formulations in a synchronized manner and constant rate over extended periods [3].

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Patients suffering from some acute and chronic disease conditions often get benefits from such long-term drug delivery systems as they maintain the drug concentration in plasma above the minimum effective concentration and below the minimum toxic level for prolonged period of time [4]. Biodegradable polymers recently have gained much popularity in the development of several novel drug delivery systems [5]. As these polymers have either hydrolytically or proteolytically labile bond in their backbones, they are ruptured into biologically suitable molecules that are assimilated and discarded from the body through normal routes [6]. However, biodegradable materials do produce degradation byproducts that must be tolerated with little or no adverse reactions within the biological environment [7].

Thus biodegradable polymeric implant alleviates the need for surgical removal of the implant after the conclusion of therapy and increases patient acceptance and compliance [8]. We attempted formulating Chitosan - Sodium Alginate polymeric implant so that the drug could release over a prolonged period of time. Chitosan, a cationic natural biopolymer, produced by alkaline N-deacetylation of chitin, has attracted much attention over the past few years mainly because of its biodegradable, biocompatible, renewable, sustainable, non-toxic, film forming and antimicrobial properties [9, 10]. Chitosan and its derivatives can be used in implantable drug delivery systems as high molecular weight Chitosan is more viscous and delays the release of the active ingredient, prolongs the duration of drug activity, improves therapeutic efficiency as well as reduces the side effects [11].

Sodium Alginate, an anionic biodegradable polysaccharide, consists chiefly of the sodium salt of alginic acid, has received attention as a vehicle for controlled drug delivery due to its hydrogel-forming properties. When it comes in contact with aqueous media, forms viscous solutions and gels and thus prolongs the release of many drugs. Due to this property, Sodium Alginate is now widely used as a carrier in hydrophilic matrix controlled and sustained release dosage forms in many pharmaceutical industries [12].

The aim of the research was to explore the scope of sustaining the release of Metoprolol Tartrate, which is used in treatment of several diseases of the cardiovascular system, especially in hypertension, angina pectoris, cardiac arrhythmias and myocardial infarction [13], using Chitosan-Sodium Alginate biodegradable implants. Metoprolol Tartrate, available as immediate release tablets, is subjected to first-pass metabolism which reduces its systemic availability by about 50%. Therefore, entrapping it in sustained release implant formulations will improve its availability by avoiding first-pass metabolism and also patient compliance by reducing dosing frequency [14, 15].

MATERIALS AND METHODS:

Materials: The active ingredient Metoprolol Tartrate was provided by Incepta Pharmaceuticals Ltd., Dhaka, Bangladesh. Other chemicals were of analytical grade. The research was performed in Department of Pharmacy, University of Asia Pacific, Dhaka, Bangladesh from May 2016 to October, 2016.

Preparation of Implants: Biodegradable implants of Metoprolol Tartrate were prepared by the use of two biodegradable polymers, Chitosan and Sodium Alginate. Implants were prepared using 25 mg drug with 2 different polymer ratios (70:30 and 80:20) as well as 25 mg drug load with 70:30 polymer ratio containing different excipients. 100 ml of 1% acetic acid solution was used to dissolve 4.167 g of Chitosan. 100 ml of distilled water was taken to dissolve 4.167 g of Sodium Alginate. The solutions were stirred until no large chunks remained and then blended until homogenous [16, 17]. Chitosan and Sodium Alginate solutions were then taken according to the respective ratios (70:30 and 80:20). Metoprolol Tartrate was then dispersed to the Chitosan and Sodium Alginate solutions. Excipient was added along with drug when implants were prepared using different excipients. After being mixed with ultrasonic, the mixture was poured into petridish. Then it was allowed to set by placing in a refrigerator at - 32 °C for 1 day. After 1 day, implants were cut into 1 cm width and 1 cm length square shape by NT cutter.

Hardening of Implants: Chemical cross linking can effectively guard the physicochemical stability of Chitosan applications since the gelation is irreversible. The higher stability of such modified Chitosan is based on the covalent bonds, but also other interactions (hydrogen or hydrophobic bonds) cannot be excluded. The most common chemical crosslinkers of Chitosan are dialdehydes (such as glutaraldehyde or glyoxal) and genipin [18]. The prepared implants were placed into a cross-linking solution of glutaraldehyde for 15 minutes and 30 minutes for hardening. Then they were washed with methanol and distilled water, respectively. After hardening they were placed in aseptic cabinet for air drying for few minutes. **Table 1** and **2** show different formulations that had been prepared.

Characterization of Implants:

Photographic Implant: Photographs of drug loaded implants were taken using SONY Cyber-shot, 14.1 Mega Pixel Camera. **Fig. 1** shows photo-graphic images of Metoprolol Tartrate implants.

TABLE 1: FORMULATION CHART OF IMPLANTS WITH DIFFERENT POLYMER RATIOS AND EXPOSURE TIMES

Name of Formulation	Polymer Ratio	Drug Loading	Glutaraldehyde Exposure
F1	70:30	25 mg	15 minutes
F2	70:30	25 mg	30 minutes
F3	80:20	25 mg	15 minutes
F4	80:20	25 mg	30 minutes

TABLE 2: FORMULATION CHART OF IMPLANTS WITH 15 MINUTES EXPOSURE TIME CONTAINING DIFFERENT EXCIPIENTS

Name of Formulation	Polymer Ratio	Drug Loading	Excipient Loading	Excipients
F5	70:30	25 mg	25 mg	Glyceryl Monostearate
F6	70:30	25 mg	25 mg	Cetyl Alcohol
F7	70:30	25 mg	25 mg	Guar Gum
F8	70:30	25 mg	25 mg	Stearic Acid
F9	70:30	25 mg	25 mg	Sesame Oil
F10	70:30	25 mg	25 mg	Glyceryl Behenate
F11	70:30	25 mg	25 mg	Kollidon SR
F12	70:30	25 mg	25 mg	Eudragit RS-100

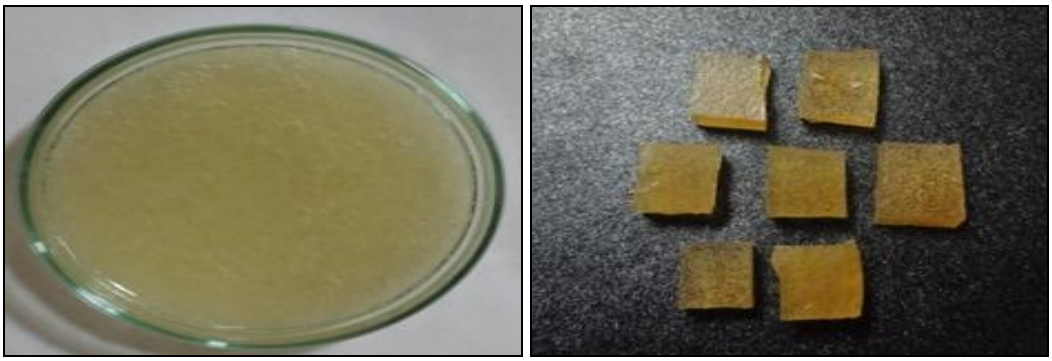

FIG. 1: PHOTOGRAPHIC IMAGES OF METOPROLOL TARTRATE IMPLANTS

Scanning Electron Microscope (SEM): Prepared implants were analyzed for their surface morphology by scanning electron microscope. The implants were initially spread on a carbon tape glued to an aluminium stub and coated with Au using a sputter coater under vacuum in a closed chamber. The Au layer was coated to make the implant surface conductive to electrons in the SEM. The implants were then observed under SEM in varying magnifications and micrographs were recorded. Scanning electron microscope (SEM) was used to observe interior morphology at cross section of hot-melt extrudates. Hot-melt extrudates were cut into approximately 3 - 5 mm pieces.

***In-vitro* Dissolution Studies:** The *in-vitro* release of Metoprolol Tartrate from implants was carried out in static conditions at 37 °C. The weighed implants (at least 3 implants) from each formulation and exposure time were kept in rubber capped glass vessels containing 100 ml of Phosphate Buffer, pH 7.4. 3 ml of the release medium was collected at predetermined time intervals and replaced with 3 ml of fresh buffer to maintain the sink condition [19, 20]. The withdrawn samples were then analyzed for determining the percentage of release of drugs by UV spectrophotometer at 273.5 nm (λmax of Metoprolol Tartrate in Phosphate Buffer, pH 7.4), after subsequent dilution of the samples. All data were used in statistical analysis for the determination of mean, standard deviation and release kinetics.

Statistical Analysis: Results were expressed as mean ± S.D. Statistical analysis was performed by linear regression analysis. Coefficients of determination (R^2) were utilized for comparison. *In-vitro* release studies were performed under the same conditions for each implant system. The means and standard deviations were calculated at each time interval. The means were graphed for each release profile with the standard deviations included as error bars. Linear regression was performed on cumulative drug release as a function of time and also on fitted curves to different kinetic models.

Determination of Drug Content (Loading Dose): The amount of drug that was actually loaded in implants during fabrication process was determined by spectrophotometric analysis. For determining the drug content of Metoprolol Tartrate loaded implants, first the implants were weighed and then crushed in a mortar and pestle. Then they were dissolved in 2 ml acetic acid by vigorous ultrasonication. Then 2 ml of acetronitrile, 4 ml hot buffer and 2 ml acetic acid were added for precipitating the polymer and extracting the drug in solvent. The total volume of acetic acid, acetonitrile and Phosphate Buffer (pH 7.4) ratio was 40:20:40. Then it was centrifuged at 4000 RPM for 30 minutes to separate the solid material. Clear supernatant was withdrawn and it was analyzed at 273.5 nm (λ_{max} of Metoprolol Tartrate) in UV spectrophotometer. The percentage of loading efficiency (% LE) of implants was determined with the formula:

$$\% LE = (LD/AD) \times 100$$

Where; LD is the amount of loaded drug in the implant and AD is the amount of added drug in the formulation [21].

RESULTS AND DISCUSSION:

Scanning Electron Microscope (SEM): Fig. 2 and **3** show SEM micrograph of Chitosan-Sodium Alginate polymeric implant surface containing Metoprolol Tartrate before drug release and after drug release.

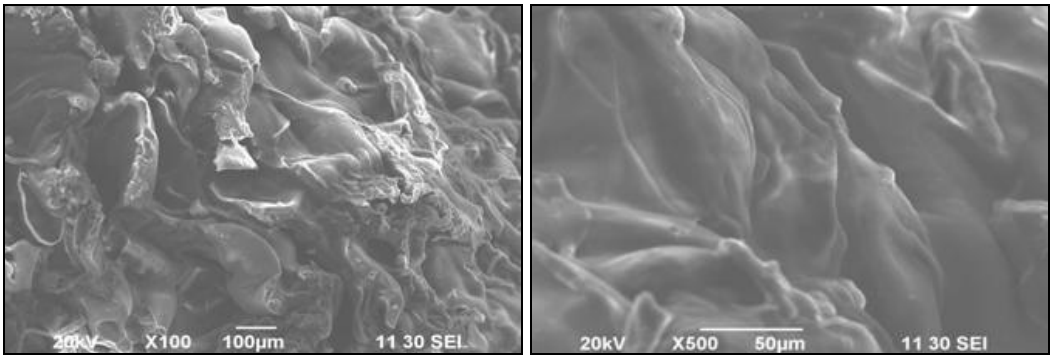

FIG. 2: SEM MICROGRAPH OF METOPROLOL TARTRATE POLYMERIC IMPLANT SURFACE BEFORE DRUG RELEASE (100 AND 500 TIMES MAGNIFIED)

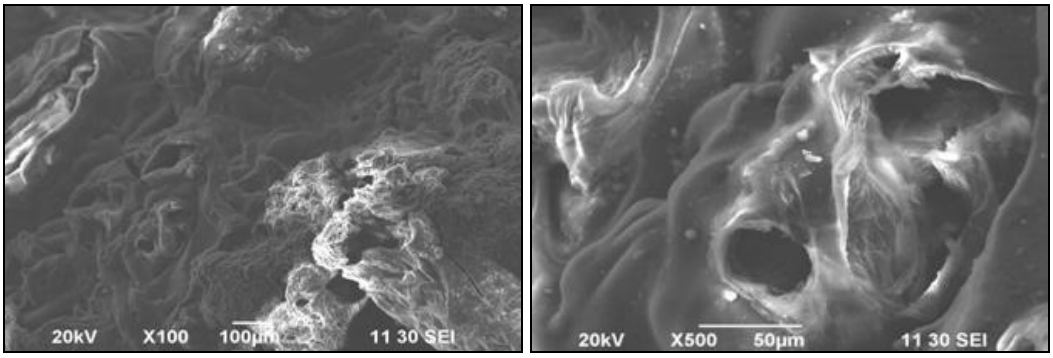

FIG. 3: SEM MICROGRAPH OF METOPROLOL TARTRATE POLYMERIC IMPLANT SURFACE AFTER DRUG RELEASE (100 AND 500 TIMES MAGNIFIED)

Fig. 2 and **3** display SEM micrograph of Metoprolol Tartrate Chitosan - Sodium Alginate polymeric implant surface before and after drug release (100 and 500 times magnified). Before drug release the implant surface is nonporous, smooth and the surface integrity is also found to be good.

But after drug release, the micrographs show the surface to be more porous and rough. It indicates that very low amount of drug was remaining after drug release which also complies with the findings of drug release studies.

Effect of Excipients on Loading Efficiency of Chitosan-Sodium Alginate Polymeric Implants: The changes in the loading efficiency of the implants were probably caused by the respective excipients. The data for different excipients with 25 mg load of Metoprolol Tartrate are presented in the **Table 3**.

TABLE 3: EFFECT OF EXCIPIENTS ON LOADING EFFICIENCY OF CHITOSAN-SODIUM ALGINATE POLYMERIC IMPLANTS OF METOPROLOL TARTRATE

Formulation	Excipient	Loading Efficiency (%)
F1	No Excieipent	65.69
F5	Glyceryl Monostearate	76.64 (maximum)
F6	Cetyl Alcohol	73.13
F7	Guar Gum	68.78
F8	Stearic Acid	67.37
F9	Sesame Oil	57.43 (minimum)
F10	Glyceryl Behenate	72.12
F11	Kollidon SR	68.97
F12	Eudragit RS-100	62.59

The highest loading efficiency was found with Glyceryl Monostearate (76.6%) and the lowest with Sesame Oil (57.4%). The loading efficiency was found to decrease in the following sequence:

Glyceryl Monostearate > Cetyl Alcohol > Glyceryl Behenate > Kollidon SR > Guar Gum > Stearic Acid > No Excipient > Eudragit RS-100 > Sesame Oil.

Effect of inclusion of excipients on loading efficiency (%) of Metoprolol Tartrate in Chitosan-Sodium Alginate polymeric implants is displayed in **Fig. 4**.

Drug Release Profile of Implants Based on Varying Chitosan-Sodium Alginate Polymer Ratios and Different Exposure Times: Drug release profile of implants in combination of 70:30 and 80:20 Chitosan-Sodium Alginate polymeric ratios with 15 minutes and 30 minutes exposure time (F1, F2, F3 and F4) is shown in **Fig. 5**. From **Fig. 5**, it can be said that time taken for F1, F2, F3 and F4 formulations to release nearly 100% of the drug was 15 days, 10 days, 10 days and 8 days respectively. As F1 formulation released the drug for more days compared to other formulations, this formulation was chosen for further development of implants with incorporation of different excipients.

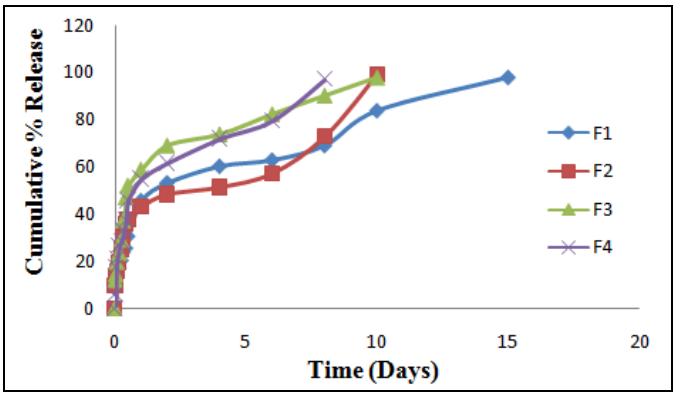

FIG. 4: EFFECT OF INCLUSION OF EXCIPIENTS ON LOADING EFFICIENCY (%) OF METOPROLOL TARTRATE CHITOSAN - SODIUM ALGINATE POLYMERIC IMPLANTS

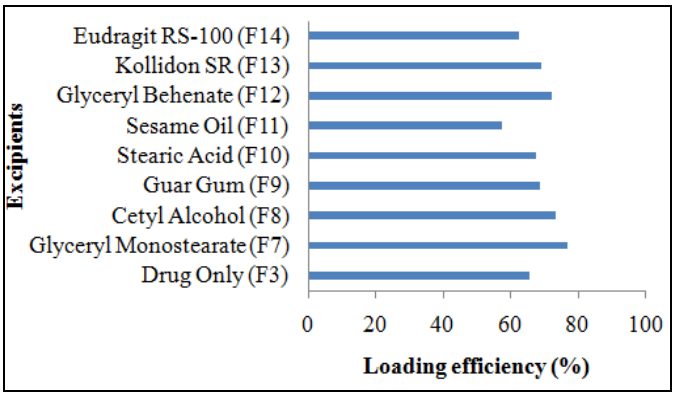

FIG. 5: DRUG RELEASE PROFILE OF 70:30 AND 80:20 CHITOSAN-SODIUM ALGINATE POLYMERIC IMPLANTS WITH 15 AND 30 MINUTES EXPOSURE TIMES (F1, F2, F3 AND F4)

Effect of Excipients on Drug Release from 70:30 Chitosan-Sodium Alginate Polymeric implants with 15 minutes Exposure Time: Excipients have various effects on drug release profile. The rate and extent of drug release from implants can be controlled by the use of excipients in the formulation. These agents can act as rate modifier by increasing or retarding the rate of release depending upon the nature of the agent. They probably extent their effects by influencing the way of formulation formed and therefore on the release characteristics of the sustained release implants [22]. Comparison of drug release profile of implants containing different excipients with F1 (70:30 polymer ratio with 15 minutes exposure time) is graphically represented in **Fig. 6** and **7**.

From **Fig. 6** and **7**, it is observed that among all excipients, F5 (Glyceryl Monostearate) showed the maximum sustain release effect and F12 (Eudragit RS-100) showed the minimum sustain release effect when compared to F1 (No Excipient). Glyceryl Monostearate has a HLB value of 3.8 which indicates its hydrophobic nature and it is practically insoluble in water. It is used as a matrix ingredient for a biodegradable, implantable, controlled release dosage form [23]. Eudragit RS-100 is practically insoluble in water and is used in

delayed and sustained drug release [24]. But it failed to give the expected sustained release effect which should be more than 15 days. So, further investigation is needed in this regard. Time taken for all formulations containing excipients to release nearly 100% of the drug is displayed in **Table 4**.

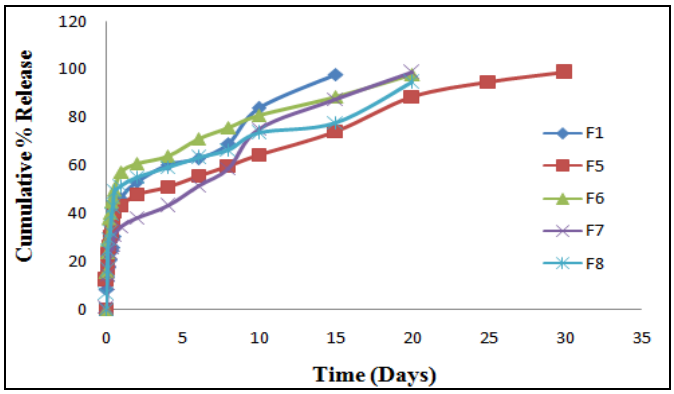

FIG. 6: COMPARISON OF METOPROLOL TARTRATE RELEASE PROFILE OF FORMULATIONS F1, F5, F6, F7 AND F8

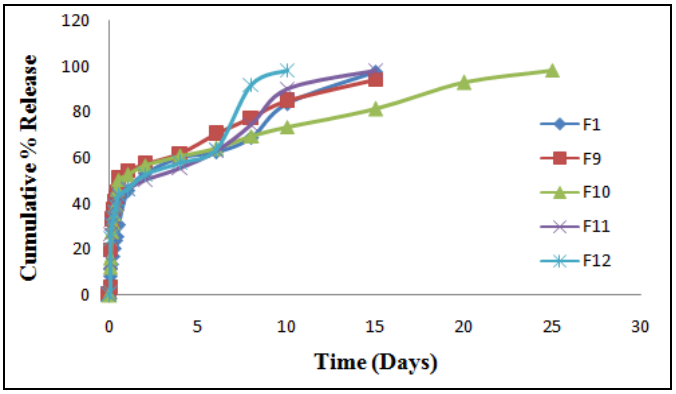

FIG. 7: COMPARISON OF METOPROLOL TARTRATE RELEASE PROFILE OF FORMULATIONS F1, F9, F10, F11 AND F12

TABLE 4: TIME TAKEN FOR ALL FORMULATIONS CONTAINING EXCIPIENTS TO RELEASE NEARLY 100% OF THE DRUG

Formulation	Calculated time (Days) for drug release
F1 (No Excipient)	15
F5 (Glyceryl Monostearate)	30
F6 (Cetyl Alcohol)	20
F7 (Guar Gum)	20
F8 (Stearic Acid)	20
F9 (Sesame Oil)	15
F10 (Glyceryl Behenate)	25
F11 (Kollidon SR)	15
F12 (Eudragit RS-100)	10

Kinetics of Drug Release Study: The release profile and kinetics of drug release are important because they correlate the *in-vitro* and *in-vivo* drug responses by comparing result of dissolution profile and pharmacokinetic patterns [25]. The kinetics of Metoprolol Tartrate from 70:30 Chitosan-Sodium Alginate polymeric ratio containing different excipients with 15 min exposure time were determined by finding the best fit of the release data to Higuchi, Korsmeyer-peppas, Zero order and First order plots.

TABLE 5: FITTING COMPARISON OF EQUATION OF KINETIC MODELS

	Kinetic Model			
Formulations	Higuchi	Korsmeyer-peppas	Zero order	First order
	R^2	R^2	R^2	R^2
F1	0.960	0.884	0.840	0.915
F5	0.938	0.848	0.837	0.939
F6	0.858	0.849	0.692	0.923
F7	0.961	0.723	0.887	0.898
F8	0.846	0.775	0.688	0.884
F9	0.835	0.674	0.680	0.931
F10	0.869	0.829	0.712	0.918
F11	0.908	0.808	0.815	0.907
F12	0.873	0.584	0.786	0.851

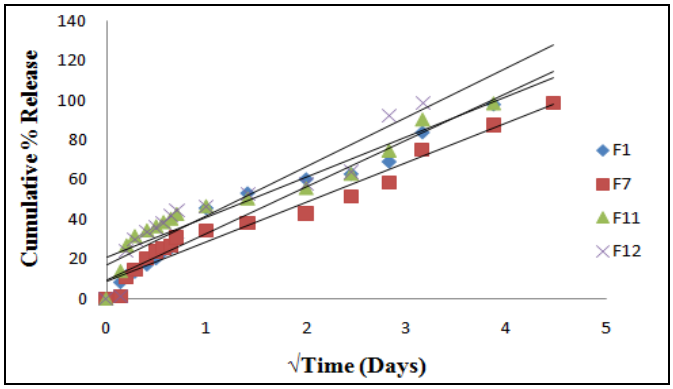

FIG. 8: HIGUCHI PLOT OF METOPROLOL TARTRATE RELEASE FROM FORMULATIONS F1, F7, F11 AND F12

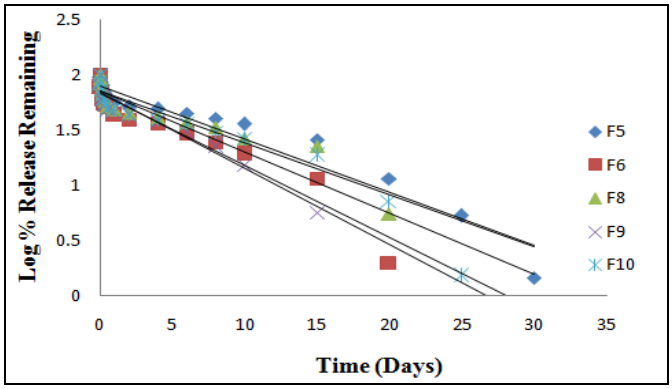

FIG. 9: FIRST ORDER PLOT OF METOPROLOL TARTRATE RELEASE FROM FORMULATIONS F5, F6, F8, F9 AND F10

From **Table 5**, it can be said that implants with excipients were found to follow First order model in most cases. Also good co-relations were obtained with Higuchi model which are shown in **Fig. 8** and **9**.

Higuchi model describes drug release as a square root time dependent diffusion process based on Fick's law [26] and First order model describes drug release from the system where release rate is concentration dependent [27]. According to these models, the drug release from the implants was diffusion controlled, where the drug leaving the matrix through pores and channels formed by entry of dissolution medium.

CONCLUSION: Metoprolol Tartrate, a cardio selective beta-blocker, used in management of high blood pressure, irregular heart rhythm, strokes, heart attacks and angina pectoris, is available as immediate release dosage forms which require frequent dose administration. Dosage forms that release the drug over a prolonged length of time can be prepared by incorporating drug into biodegradable polymeric implants. Biodegradable polymeric implants will improve the patience compliance by reducing the dosing frequency and there will be no need of surgical removal of the implants as the polymers will be degraded and cleared by the body.

The effects of different polymer ratios and excipients were studied on loading efficiency and drug release profile of Chitosan-Sodium Alginate polymeric implants of Metoprolol Tartrate. The implants exhibited high drug loading efficiency and long term drug release under *in-vitro* conditions with most of the excipients. Thus biodegradable polymers offer a novel approach for sustained release drug delivery systems that are simple and convenient to the patients.

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CONFLICT OF INTEREST: The authors declare no conflict of interest.

REFERENCES:

1. Gavasane AJ and Pawar HA: Synthetic biodegradable polymers used in controlled drug delivery system: An overview. Clinical Pharmacology & Biopharmaceutics 2014; 3(2): 1-7.
2. Karna S, Chaturvedi S, Agrawal V and Alim M: Formulation approaches for sustained release dosage forms: A review. Asian Journal of Pharmaceutical and Clinical Research 2015; 8(5): 46-53.
3. Priya VSV, Roy HK, Jyothi N and Prasanthi NL: Polymers in drug delivery technology, types of polymers and applications. Scholars Academic Journal of Pharmacy 2016; 5(7): 305-308.
4. Gandhi A and Kumar SLH: Recent trends in sustained release drug delivery system. International Journal of Interdisciplinary and Multidisciplinary Studies 2014; 1(6): 122-134.
5. Joshi JR and Patel RP: Role of biodegradable polymers in drug delivery. International Journal of Current Pharmaceutical Research 2012; 4(4): 74-81.
6. Srivastava A, Yadav T, Sharma S, Nayak A, Kumari A and Mishra N: Polymers in drug delivery. Journal of Biosciences and Medicines 2016; 4: 69-84.
7. Shaik MR, Korsapati M and Panati D: Polymers in controlled drug delivery systems. International Journal of Pharma Sciences 2012; 2(4): 112-116.
8. Phale T, Agnihotri J and Khale A: Technical advancement in biodegradable polymers and their recent patents. International Journal of Research and Development in Pharmacy and Life Sciences 2013; 3(1): 766-774.
9. Kammoun M, Haddar M, Kallel TK, Dammak M and Sayari A: Biological properties and biodegradation studies of chitosan biofilms plasticized with PEG and glycerol. International Journal of Biological Macromolecules 2013; 62: 433-438.
10. Elieh-Ali-Komi D and Hamblin MR: Chitin and chitosan: Production and application of versatile biomedical nanomaterials. International Journal of Advanced Research 2016; 4(3): 411-427.
11. Cheung RCF, Ng TB, Wong JH and Chan WY: Chitosan: An update on potential biomedical and pharmaceutical applications. Marine Drugs 2015; 13: 5156-5186.
12. Patel HV, Vaza SS, Mishra A, Raj MM and Patel NK: Evaluation of oral sustained drug delivery of ciprofloxacin hydrochloride loaded sodium alginate microspheres prepared by ionotropic gelation technique. World Journal of Pharmacy and Pharmaceutical Sciences 2014; 3(3): 916-925.
13. Ela AESFA, Allam AA and Ibrahim EH: Pharmacokinetics and anti-hypertensive effect of metoprolol tartrate rectal delivery system. Drug Delivery 2016; 23(1): 69-78.
14. Regardh C and Johnsson G: Clinical pharmacokinetics of metoprolol. Clinical Pharmacokinetics 1980; 5(6): 557-569.
15. Chien YW: Novel Drug Delivery Systems. CRC Press, Second Edition 1991.
16. Balasubramanian V, Malathy VV, Balasubramanian E, Joseph A and Girija R: Chitosan-alginate drug loaded polymer network for accelerated wound healing. BioMedRx 2013; 1(1): 97-101.
17. He B, Leung M and Zhang M: Optimizing creation and degradation of chitosan-alginate scaffolds for *in vitro* cell culture. Journal of Undergradutae Research in Bioengineering 2010: 31-35.

18. Szymańska E and Winnicka K: Stability of chitosan- A challenge for pharmaceutical and biomedical applications. Marine Drugs 2015; 13: 1819-1846.
19. Jaybhaye SJ, Kamble R, Raju A, Bhandari A and Sreenivas SA: *In vivo* studies of chitosan based meloxicam drug implants. Journal of Pharmacy Research 2012; 5(4): 2178-2180.
20. Chaus WN, Shrivastava B, Rao KP, Jadge DR and Satpute KL: Characterization and *in-vitro* evaluation of drug implants. International Journal of Pharmaceutical and Chemical Sciences 2014; 3(3): 676-681.
21. Saha M, Debnath A, Afrose F and Islam S: Effect of excipients on the release of tramadol hydrochloride from biodegradable polymeric implants. International Journal of Pharmaceutical Sciences and Research 2014; 5(9): 3802-3809.
22. Islam S: Study of steroidal drug delivery from biodegradable polymeric systems using *in situ* formation of implants for parenteral administration [PhD Thesis]. University of Dhaka 2008.
23. Taylor AK: Handbook of Pharmaceutical Excipients. Pharmaceutical Press, London, Edition 6, 2009: 290-293.
24. Joshi M: Role of eudragit in targeted drug delivery. International Journal of Current Pharmaceutical Research 2013; 5(2): 58-62.
25. Gunjal PT, Shinde MB, Gharge VS, Pimple SV, Gurjar MK and Shah MN: Design, development and optimization of s(-) atenolol floating sustained release matrix tablets using surface response methodology. Indian Journal of Pharmaceutical Sciences 2015; 77(5): 563-572.
26. Mathew ST, Devi SG and Sandhya KV: Formulation and evaluation of ketorolac tromethamine-loaded albumin microspheres for potential intramuscular injection. AAPS Pharm Sci Tech 2007; 8(1): 1-9.
27. Shaikh HK, Kshirsagar RV and Patil SG: Mathematical models for drug release characterization: A review. World Journal of Pharmacy and Pharmaceutical Sciences 2015; 4(4): 324-338.

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