INVITRO-EXVIVO STUDIES OF PREDNISOLONE MATRIX TABLETS FOR COLON TARGETED DRUG DELIVERY

Dr.M. Kishore Babu*, Selvam Devi Priya[1], Dr.K. Umasankar[2]
Principal, Dept. of Pharmaceutics, Krishna Teja Pharmacy College, Tirupati.
email: principal.af@jntua.ac.in
1. Krishna Teja Pharmacy College, Tirupati. dpbala79@gmail.com
2. Professor, Dept. of Pharmaceutics, Krishna Teja Pharmacy College, Tirupati.

Abstract

Prednisolone's standard formulation is regarded as having limited effectiveness, mainly because it is unable to produce and sustain therapeutically appropriate drug levels. This research focuses on the creation of a mucoadhesive buccal delivery system with the dual goals of providing prednisolone distribution that is both sustained and fast, along with improved therapeutic effectiveness. Prednisolone mucoadhesive films were created utilizing the solvent-casting technique, employing K100, Carbopol 940, and/or Eudragit NE 40 D. Drug loading was done on placebo films with the ideal physico mechaphysic mechanical tics. On film qualities, such as mucoadhesive strength, swelling and hydration, as well as in vitro drug release, the impact of polymer and its content was investigated.

Introduction

Due to its strong therapeutic potential, prednisolone is often used to treat a broad range of ailments, including inflammation, allergies, ulcerative colitis, psoriasis, skin conditions, etc. Asthma, rheumatoid arthritis, inflammatory bowel disease, and other chronic inflammatory illnesses are among the conditions for which this medication is most often used therapeutically. Prednisolone is often a synthetic corticosteroid having glucocorticoid action as its primary activity. Prednisolone has an anti-inflammatory impact principally because it has the ability to reduce the synthesis of prostaglandins and leukotrienes. In conditions where topical formulations may supply and maintain a greater drug concentration at the point of administration, local delivery of prednisolone is recommended. To achieve the highest level of therapeutic efficacy, prednisolone doses in systemic treatment are often customized based on the kind and severity of the condition. Prednisolone administration by oral medication is now regarded as the superior method, probably because to increased patient compliance. However, research indicates that this medication has a short biological half-life (2-4 h) after oral administration and that its bioavailability varies with dosage modification. Given the severity of acute inflammatory illness cases, it is conceivable that a dosage form that delivers prednisolone rapidly and continuously might be more beneficial than the traditional dose forms. A review of the literature shows that there have been few attempts to increase the therapeutic effectiveness of prednisolone in the treatment of inflammatory illnesses, but studies on animal models of rheumatoid arthritis have shown the potential of liposomes to do so. In a subsequent effort, long-circulating multifunctional, multimodal liposomes of prednisolone were created to treat the inflammation caused by atherosclerotic plaque, which improved the effectiveness and decreased the dosage. As an alternative, controlled, delayed, and extended-release prednisolone dosage forms were also created to increase the drug's effectiveness in the treatment of different inflammatory conditions. Despite all of these attempts, effective prednisolone therapy for the treatment of inflammatory disorders is still elusive. In this situation, our hypothesis is that delivering prednisolone through the buccal route might be a beneficial strategy. In addition to topical delivery, colon-targeted drug delivery systems can increase the bioavailability of medications that are susceptible to enzymatic and/or acidic destabilization in the upper gastrointestinal (GI) tract, particularly macromolecules like proteins and peptides because the colon has lower protease activity [6,7,8]. Though colonic delivery of macromolecules hasn't been studied as much as colonic delivery of small molecules, future study may show that colonic delivery of macromolecules has the potential to be an efficient oral delivery technique. Colon targeted drug delivery systems are made to only release a medication in reaction to the environment in the colon, preventing an untimely release of the drug into the upper GI tract. Therefore, it is crucial to take into account the microenvironment around the disease site(s) as well as the physiological characteristics of the colon in order to build colon-targeted drug delivery systems. From the stomach to the intestine, the GI tract generally experiences dynamic variations in motility, fluid contents, enzyme activity, and pH [9]. Additionally, a disease site's microenvironment in the colon differs noticeably from surrounding normal and healthy areas. Reactive oxygen species (ROS) and inflammatory cytokines are produced in considerable amounts by patients with colonic disorders. They also have an imbalance in key antioxidants and have mucosal damage [10]. Numerous formulation strategies, including pH-sensitive

systems, enzyme-triggered systems, and magnetically-driven systems, have been investigated to optimise the colonic drug delivery in light of the fact that the pathophysiological changes in the microenvironment surrounding disease sites should be taken into account during formulation development. Receptor-mediated systems, which selectively interact with certain receptors overexpressed at the site(s) of the illness, have also been researched to improve the specificity at disease sites. This study discusses current developments in diverse formulation strategies for creating colon-targeted drug delivery systems and their medical uses.

Materials and methods

Materials: Hydroxy propyl methyl cellulose (HPMC) K100, Carbopol940, EudragitÕNE 40 D, sodium carboxymethyl cellulose, ethyl cellulose and polyvinylpyrrolidone (PVP) K-30. Prednisolone was obtained as a gift sample from Ind Swift Laboratories Ltd.. Sodium lauryl sulfate (SLS) and propylene glycol (PG) were purchased from S.D Fine chemicals, Mumbai, India. Allother chemicals/reagents used in the study were of analytical grade.

Formulation of oral Muccoadhesive films

Bilayer Mucoadhesive tablets containing prednisolone were prepared by Wet Granulation method. Various batches were prepared by changing the ratio of pectin, PVP K 30 to identify the most effective formulation. The drug and polymer mixture was prepared by homogeneously mixing the drug with pectin, PVP K-30, CP-934 (mucoadhesive polymers), lactose (diluents) in a glass mortar for 15 minutes. Before direct compression, the powder were screened through a 60 µm sieve and thoroughly blended. The blend was lubricated with magnesium stearate for 3-5 min. The mixture (100 mg) was then compressed using an 8 mm diameter die in a 9-station rotary punching machine (Ahmadabad, India). The upper punch was raised and the backing layer of carbapol was placed on the above compact; the two layers were then compressed into a mucoadhesive bilayer tablet. Each tablet weighed 300 mg and the compositions of prednisolon bilayer tablets. After compression given by coating Eudragit polymer.

Mucoadhesion studies

In this area of the investigation, two separate parameters were noted. The mucoadhesive time or retention time was measured in minutes or hours, while the mucoadhesive strength was measured in grammes per square centimetre. The length of time the film stays in contact with the mucosal membrane without eroding or dissolving is determined by its mucoadhesive time. There is an increase in the amount of time available for the medicine to penetrate through the mucosa as the mucoadhesive time of the film rises. This might potentially make certain high-molecular-weight medications more permeable (Kamath & Park, 1994). The mucoadhesive strength is the second component of mucoadhesion. This affects how firmly the film adheres to the buccal mucosa.

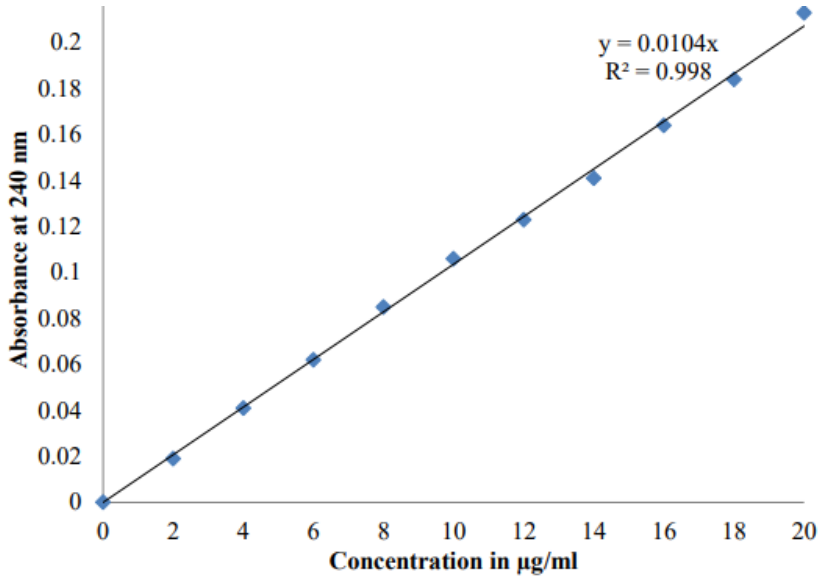
In-Vitro Drug Release Study

The USP type II rotating paddle method was used to study the drug release from the muco adhesive Tablet. The dissolution medium consisted of 900 ml of phosphate buffer pH 1.2 The release study was performed at 37 ± 0.5° C, with a rotation speed of 50 rpm. Then samples

were collected at regular intervals of time and absorbance was measured at 250 nm. Then medium was replaced with pH6.2 than samples were collected at regular intervals of time and absorbance was measured at 250nm. The USP type II rotating paddle method was used to study the drug release from the muco adhesive Tablet. The dissolution medium consisted of 900 ml of phosphate buffer pH 6.8. The release study was performed at 37 ± 0.5° C, with a rotation speed of 50 rpm. The backing layer of the muco adhesive Tablet was attached to the glass slide with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. Aliquots (5ml each) were withdrawn at regular time intervals and replaced with fresh medium to maintain sink conditions. The samples were filtered, with appropriate dilutions with phosphate buffer pH 6.8 and were analyzed spectrophotometrically at 250 nm.

Results and Discussion

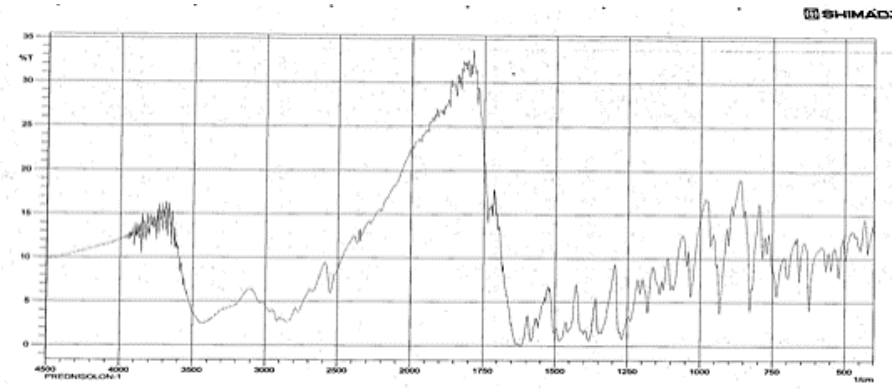
100 mg of the drug (Prednisolon) was dissolved in 6.8 pH Phosphate buffer and made up to 100 ml with the same to give a concentration of 1000 µg/ml. From this stock solution, 10 ml was taken and diluted to 100 ml with the same buffer to give the concentration of 100 µg/ml, from this 0.2, 0.4, 0.6…2ml of the solution was transferred to 10 ml volumetric flasks and made up to the volume with 6.8 phosphate buffer to give the concentrations of 2, 4, 6, ……20 µg/ml. then the absorbance was measured at 250 nm against a blank using UV Spectrophotometer. Using these absorbance values the standard graph was plotted by taking concentration on X-axis and absorbance on Y-axis.



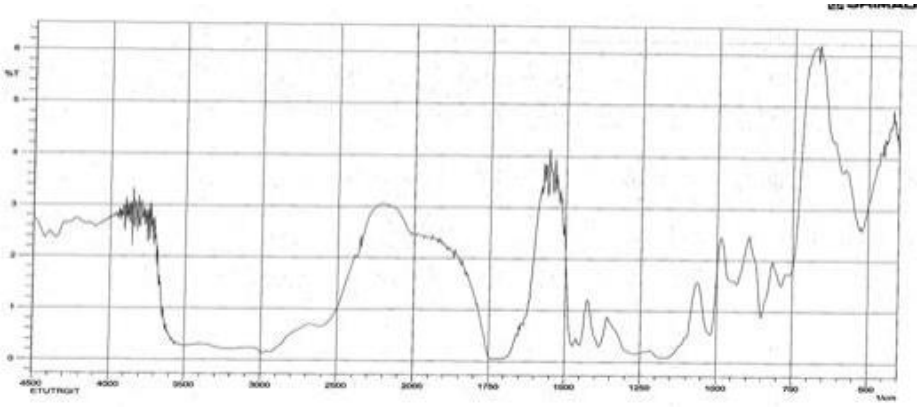
Standard Calibration Curve for prednisolone using acidic buffer6.8 pH at 250 nm

Drug –Polymer Compatibility Studies By FTIR

Infrared (IR) spectra were obtained on a Perkin Elmer 2000 IR system (Perkin Elmer, Norwalk, CT) using the KBr disk method (2 mg sample in 200 mg KBr). The scanning range was 400 to 4000 cm-1 and the resolution was 1 cm-1 . FTIR absorption spectra ofpure drugand all the polymers used like pectin, Eudragit, PVP, Crabapple and the combination of drug and polymers were shows no significant interaction between drug and polymers.

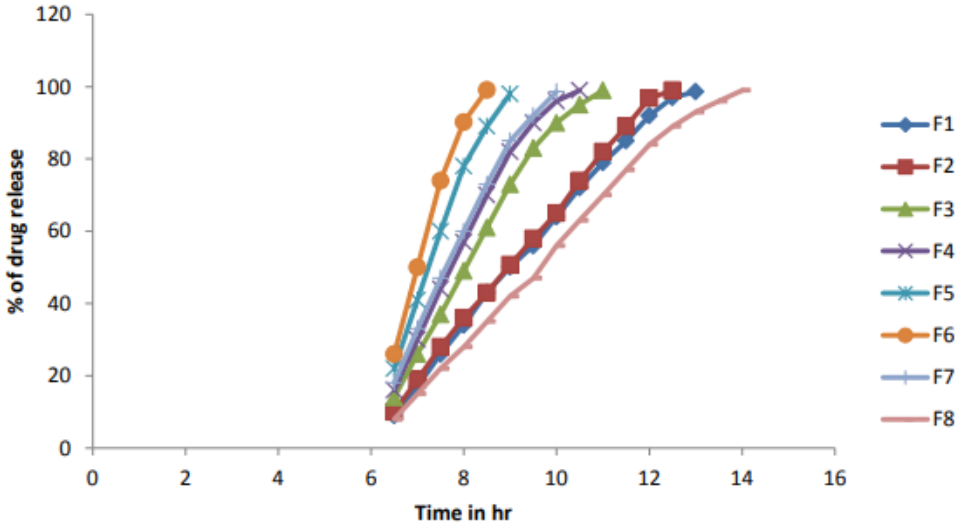


FTIR studies for prednisolone



FTIR studies for polymer Eudragit

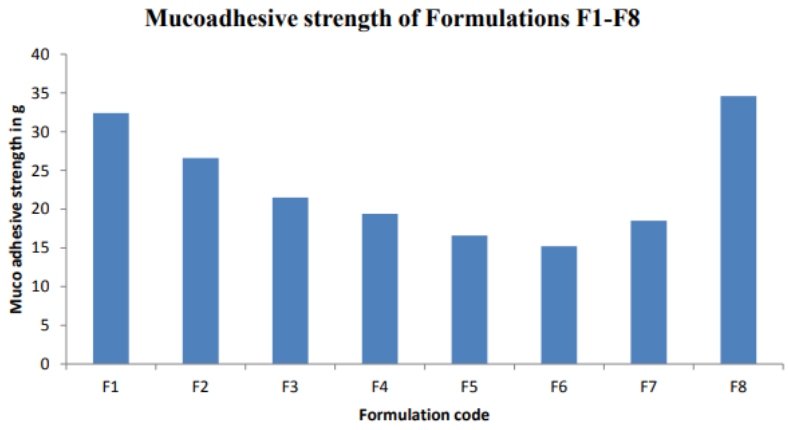
In-Vitro Drug Release Study



Ex-Vivo Mucoadhesive Strength

A modified physical balance method66, 67was used for determining the ex vivo mucoadhesive strength. Fresh sheep colon mucosa was obtained from a local slaughterhouse and used within 2 h of slaughter .The mucosal membrane was separated by removing underlying fat and loose tissues. The membrane was washed with distilled water and then with phosphate buffer pH 6.8. The two sides of the balance were made equal before the study, by keeping a 6.8 buffer solution

at 37 o C. The Sheep colon mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of colon mucosa was tied to the glass vial, which was filled with phosphate buffer. The glass vial was tightly fitted into a glass beaker (filled with phosphate buffer pH6.8 at 37 o c+1 0 c) so that it just touched the mucosal surface. The mucoadhesive tablet was stuck to the lower side of a rubber stopper with cyanocarylate adhesive and adds weight on the right-hand pan. A weight of 5 g was removed from the right hand pan. This lowered the pan along with the Tablet over the mucosa. The balance was kept in this position for 8 hr contact time. To the right-hand pan until the Tablet detached from the mucosal surface. This detachment force gave the mucoadhesive strength of then Mucoadhesive tablet in grams. Force of adhesion (N) = (Mucoadhesive strength (g) ×9.8)/1000 Bond strength (N m–2) = Force of adhesion / surface area.



Conclusion

Mucoadhesive films for transmucosal buccal delivery of prednisolone were designed. Films were prepared making use of a combination of mucoadhesive polymers, i.e. hydroxypropyl methyl cellulose, Carbopol with Euregion 40 Placebo films exhibited adequate mucoadhesive strength, time and possessing good mechanical strength were selected for drug loading. Physicochemical tests were performed on drug-loaded films. Drug-loaded films with adequate mucoadhesive time and strength were selected for further

References

1. Salunkhe KS, Kulakarni MV, Journal Of Pharmaceutical Research., oct 2015, vol 6, No 4, Pg No:248-250.
2. V.Ravi,T.M. Pramod Kumar and siddaramaiah, Indian Journal Of Pharmaceutical Sciences., 201,6 70(1), Pg No:111-113.
3. O.Munjeri, J.H.Collett and J.T.Fell, “Hydrogel beads based on amidated pectins for colon specific drug delivery : the role of chitosan in modifying drug release”, Journal of Controlled Release, 46 (2013) 273-278.
4. Nirav V. Patel et al. Design, development and in vitro evaluation of Mesalamine Tablets containing Pectin and Chitosan for colon-specific drug delivery Int. J. Res Pharm. Sci. Vol-1, Issue-2, 94-102, 2019.

5. Nath, B. S., Venkatesh and Hiremath, D, “Formulation and evaluation of Sustained Release Dosage form of Theophylline Using combined Hydrophobic and Hydrophilic Matrix”, Ind. J. Pharma. Sci. , 62 (1), 33, 2020.
6. V.S.Mastiholimath, P.M.Dandagi, S.Samata Jain, A.P.Gadad and A.R. Kulakarni, “Time and PH dependent colon specific, pulsatile delivery of theophylline for nocturnal asthma”, International Journal of Pharmaceutics, 328 (2016) 49-56.
7. F. J Ahmed and R. K Khar, “Development of colon specific drug delivery system of 5-Amino salicylicacid”, Indian Journal of Pharmaceutical Sciences, 2010, 527.