INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN:2320-2831

IJPAR |Vol.8 | Issue 3 | Jul - Sep - 2019
Journal Home page: www.ijpar.com

Research article *Open Access*

Formulation and evaluation of mucoadhesive buccal tablets of nifedipine by using natural mucoadhesive polymers

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ABSTRACT

The objective of this study was to develop effective mucoadhesive buccal tablets of Montelukast sodium prepared by direct compression method using bioadhesive polymers like Xanthan gum, Tamarind gum and synthetic polymers like HPMC K15M,HPMC K100M and sodium CMC as a muco adhesive polymer. Buccal tablets were evaluated by different methods for parameters such as thickness, hardness, weight uniformity, content uniformity, swelling index, in vitro bioadhesive strength, in vitro drug release, stability studies in human saliva, in vivo mucoadhesive performance studies. Bioadhesion strength was increased with increase in the concentration of the polymer, higher bioadhesion strength was found in HPMC K100M. The tablets were evaluated for in vitro release in pH 6.8 phosphate buffer for 12 hr in standard dissolution apparatus. When compared with natural and synthetic polymers sustained drug release was found with synthetic polymer HPMC K100M (60mg) along with sodium CMC as a mucoadhesive polymer. The stability studies indicated that there was no significant change in drug release after 3months.

Keywords: Montelukast Sodium, Xanthan gum, Buccal tablets

INTRODUCTION

The concept of mucoadhesion was introduced in the field of controlled release drug delivery systems in the early 1980s [1,2] Thereafter, several researchers have focused on the investigations of the interfacial phenomena of mucoadhesive hydro gels with the mucus. For drug delivery purpose, the term bioadhesion implies attachment of a drug carrier system to a specific biological location. The biological surface can be epithelial tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion. Hence a bacterial attachment is to tissue surfaces, and mucoadhesion can be modelled after the adherence of mucus on epithelial tissue. Mucoadhesion is the relatively new and emerging concept in drug delivery. Mucoadhesion keeps the delivery system adhering to the mucus membrane. Oral delivery involves the administration of the desired drug through the Oral mucosal membrane lining of the oral cavity. Unlike oral drug delivery, which presents a hostile environment for drugs, especially proteins and polypeptides, due to acid hydrolysis and the hepatic first-pass effect, the mucosal lining of Oral tissues provides a much milder environment for drug absorption.[3] A number of relevant Mucoadhesive dosage forms have been developed for a variety of drugs. Several peptides, including thyrotropin releasing hormone (TRH), insulin, octreotide, leuprolide, and oxytocin, have been delivered via the mucosal route, albeit with relatively low bioavailability (0.1-5%), owing to their hydrophilicity and large molecular weight, as well as the inherent permeation and enzymatic barriers of the mucosa.[4]

MECHANISMS OF MUCOADHESION

The mechanism of adhesion of certain macromolecules to the surface of a mucous tissue is not well understood yet. The mucoadhesive must spread over the substrate to initiate close contact and increase surface contact, promoting the diffusion of its chains within the mucus. Attraction and repulsion forces arise and for a mucoadhesive to be successful, the attraction forces must dominate. Each step can be facilitated by the nature of the dosage form and how it is administered. For example, a partially hydrated polymer can be adsorbed by the substrate because of the attraction by the surface water.[5]

Thus, the mechanism of mucoadhesion is generally divided in two steps, the contact stage and the consolidation stage. The first stage is characterized by the contact between the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer.[6] In some cases, such as for ocular or vaginal formulations, the delivery system is mechanically attached over the membrane. In other cases, the deposition is promoted by the aerodynamics of the organ to which the system is administered, such as for the nasal route. On the other hand, in the gastrointestinal tract direct formulation attachment over the mucous membrane is not feasible. Peristaltic motions can contribute to this contact, but there is little evidence in the literature showing appropriate adhesion. Additionally, an undesirable adhesion in the oesophagus can occur. In these cases, mucoadhesion can be explained by peristalsis, the motion of organic fluids in the organ cavity, or by Brownian motion. If the particle approaches the mucous surface, it will come into contact with repulsive forces (osmotic pressure, electrostatic repulsion, etc.) and attractive forces (vander Waals forces and electrostatic attraction). Therefore, the particle must overcome this repulsive barrier.

MATERIALS AND METHODS

Materials

Nifedipine was yarrow chemical, mumbai, Chitosan, tamarindgum, pectin are also procured from yarrow chemical, mumbai, and other excipients were procured from S.D Fine chemicals.

PREPARATION OF MUCOADHESIVE BUCCAL TABLETS [8]

Mucoadhesive Buccal tablets were prepared by a direct compression method, before going to direct compression all the ingredients were screened through sieve no.100. drug was mixed manually with different polymers along with tamarind gum,Chitosan,pectin mucoadhesive polymers and mannitol as diluent .The blend was mixed with Magnesium stearate and then compressed into tablets by the direct compression method using 8mm punche. The tablets were compressed using a cemach rotary tablet machine.

EVALUATION OF FORMULATIONS [9-13]

Pre compression parameters

It includes Angle of repose, Bulkdensity, Tappeddensity, Carsindex, Hausners ratio.

Post compression parameters

It includes Weight variation, Hardness, Friability, Thickness, Drug content, Swelling index and *In-vitro* dissolution studies, surfacePh, Mucoadhesive strength test.

RESULTS AND DISCUSSION

Mucoadhesive buccal tablets of Nifedipine were prepared by direct compression method, by using different natural like chitosan, Tamarindgum, pectin,. The prepared tablets were evaluated for various parameters such as compatibility studies, swelling studies, weight variation , hardness, drug content, thickness, friability, in vitro drug release studies, muco-adhesion strength and Release rate kinetics. From the results obtained from the FT-IR revealed that there was no chemical interaction between the drug and the polymer used. The prepared tablets had good mucoadhesiveness.

Based on the dissolution studies of the Nifedipine mucoadhesive buccal tablets formulated by using direct compression method i.e., from F1-F12 maximum drug release was found in the F10 formulation containing chitosan containing 70 mg .

So further drug release kinetics was performed for F10 formulation and the drug release was found to be zero order drug release with super case II mechanism.

Stability studies of the selected formulation was carried out to determine the effect of formulation additives on the stability of the drug and also to determine the physical stability of the formulation. The stability studies for formulations were carried out at 40 ºC/75% RH for 90 days. There was no significant change in the drug release of the opti during the study period.

Table 1: Formulation of nifedipine mucoadhesive buccal tablets by using natural polymer

Table 2: Pre Compression Evaluation Tests of Powder

Formulation code	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Hausner's ratio	Carr's Index (%)
F1	25.83±0.32	0.58±0.16	0.68±0.11	1.11±0.02	14.70±0.15
F2	23.47±0.23	0.56±0.18	0.67±0.26	1.10±0.01	15.24±0.21
F3	22.78±0.34	0.55±0.26	0.64±0.31	1.11±0.01	14.06±0.26
F4	25.47±0.25	0.53±0.21	0.62±0.26	1.10±0.02	14.52±0.16
F5	22.27±0.28	0.52±0.19	0.59±0.21	1.09±0.01	11.86±0.19
F6	21.68±0.31	0.50±0.23	0.57±0.19	1.11±0.01	12.28±0.25
F7	23.58±0.36	0.58±0.25	0.70±0.25	1.07±0.02	14.51±0.23
F8	26.58±0.32	0.59±0.28	0.71±0.28	1.12±0.02	11.34±0.19
F9	21.22±0.22	0.54±0.35	0.62±0.03	1.13±0.01	13.35±0.18
F10	22.21±0.24	0.55±0.31	0.61±0.38	1.08±0.02	10.54±0.14
F11	25.45±0.37	0.56±0.24	0.63±0.14	1.09±0.02	12.78±0.24
F12	23.43±0.34	0.54±0.31	0.65±0.28	1.10±0.01	13.16±0.11

Table 3: Post Compression Evaluation Tests Of Powder

Formulation code	Weight variation test (mg)	Thickness test (mm)	Hardness test (Kg/cm^2).	Friability test (%)	Drug content (%)
F1	200±0.12	4.32±0.45	4.4±0.45	0.81±0.01	98.51±1.25
F2	198.9±0.38	4.41±0.04	4.5±0.60	0.78±0.03	99.56±1.37
F3	200±0.14	4.27±0.10	4.6±0.51	0.77±0.06	99.45±2.47
F4	199.9±0.19	4.25±0.08	4.8±0.42	0.69±0.07	99.49±0.88
F5	200±0.12	4.29±0.03	4.0±0.25	0.72±0.05	99.85±0.80
F6	200±0.27	4.30±0.04	4.2±0.15	0.69±0.04	99.61±1.87
F7	200±0.23	4.31±0.04	4.2±0.18	0.74±0.02	98.51±1.99
F8	200±0.19	4.27±0.03	4.5±0.35	0.77±0.02	99.87±1.14
F9	199.8±0.37	4.28±0.05	4.3±0.27	0.75±0.06	99.56±2.18
F10	200±0.18	4.30±0.02	4.4±0.36	0.68±0.04	99.81±0.98
F11	200±0.15	4.31±0.03	4.5±0.44	0.69±0.05	99.12±0.95
F12	199.9±0.44	4.32±0.05	4.5±0.26	0.70±0.04	98.75±1.25

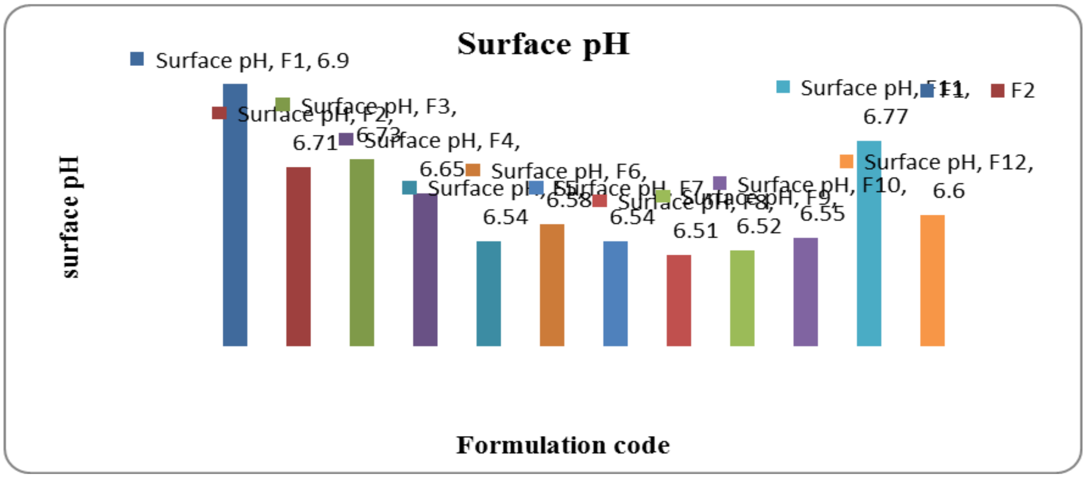

Figure 1:Surface pH

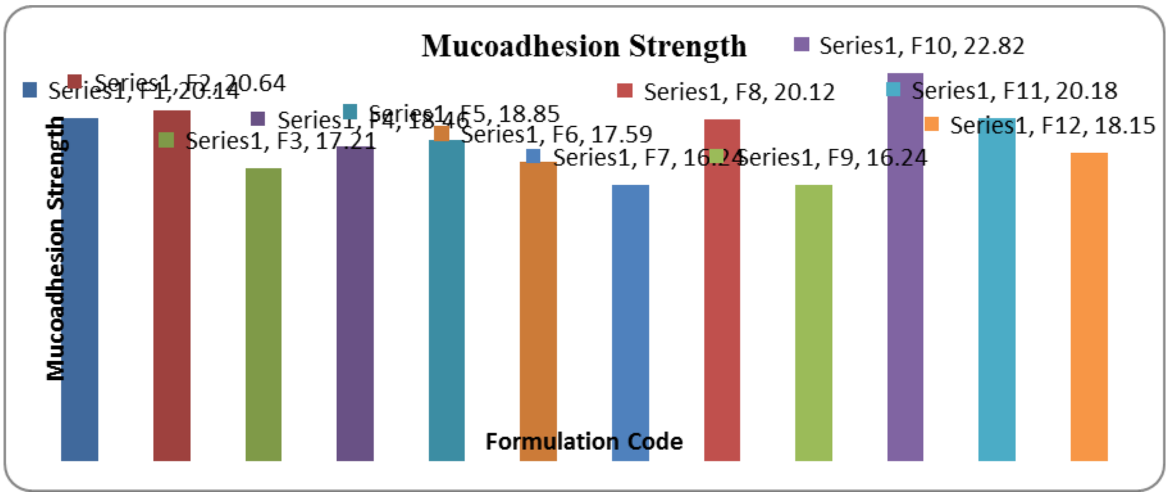

Figure 2: Mucoadhesion Strength

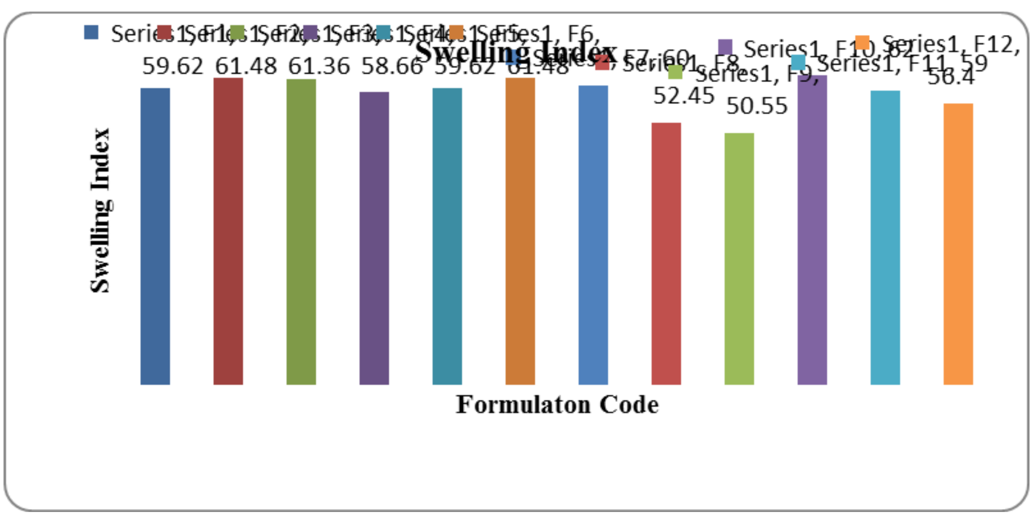

Figure 3: Swelling index (%)

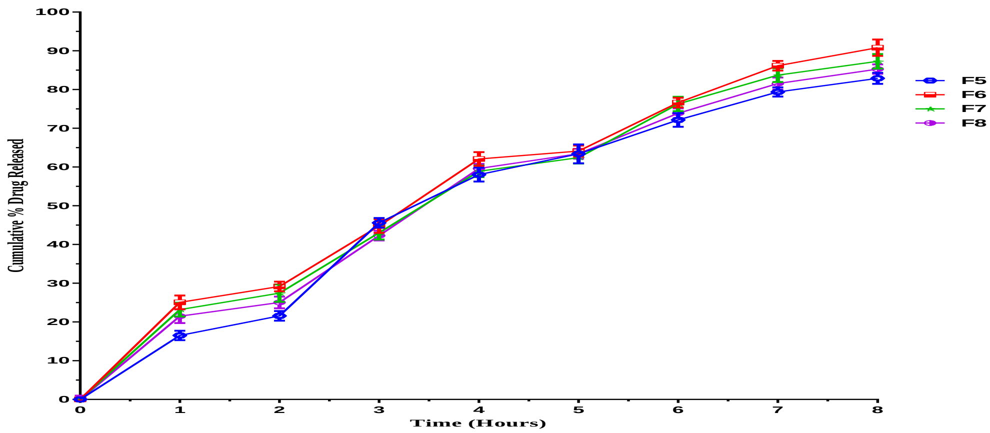

Figure 4: Comparison of % cumulative drug release of F1, F2, F3,&F4 formulation

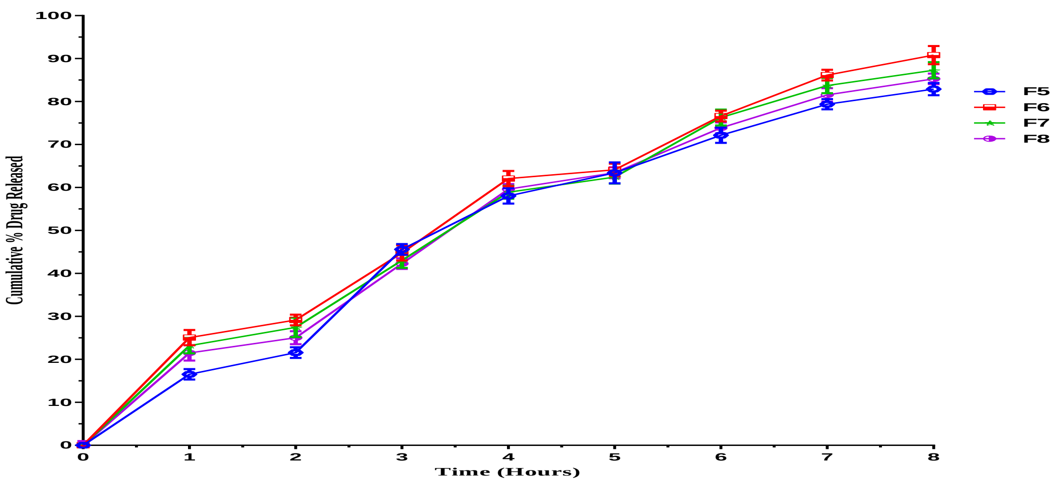

Figure 5: Comparison of % cumulative drug release of F5, F6, F7,&F9 formulation

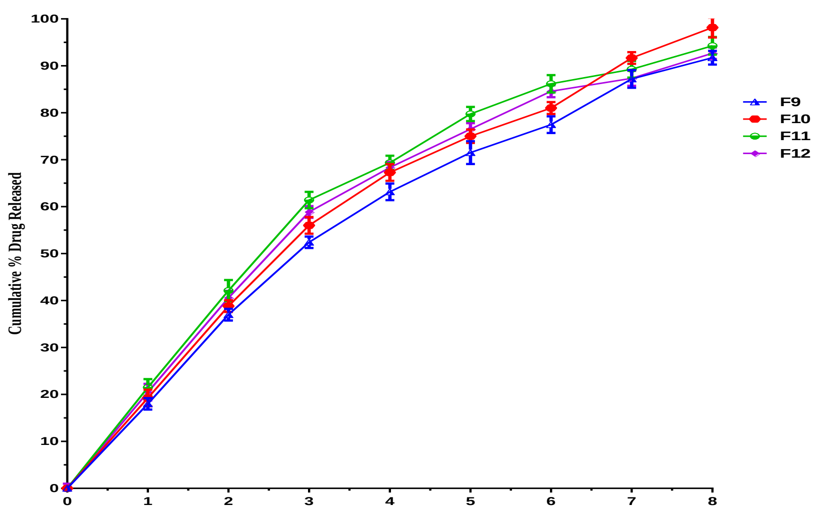

Figure 6: Comparison of %cumulative drug release of F9, F10, F11 & F12formulations.

CONCLUSION

In this work an attempt was made to design mucoadhesive buccal tablet delivery system containing a Nifedipine. The main objective of the present research work was to bypass the first pass metabolism and prolong the drug release at the site of absorption. FTIR analysis revealed that there was no interaction between drug and polymer. Mucoadhesive buccal tablets were prepared by direct compression method of nifedipine by using different polymers like tamarind seed polysaccharide, pectin, chitosan. The prepared tablets were evaluated for various parameters such as compatibility studies, surface pH, *in vitro* drug release studies, *in vitro* mucoadhesion strength.

Further the analysis of release mechanism was carried out by fitting the drug release data to various kinetic equations like zero order, first order, higuchi's and korsmeyerpeppas equation and from the values so obtained, the fit model were arrived at. From the above the results formulation F10 was found to best formulation for the mucoadhesive buccal delivery of nifedipine that complied with all the parameters. Nifedipine mucoadhesive buccal tablets could be formulated using the tamarind seed polysaccharide, pectin, chitosan with their proportion. It can be seen that by increasing the concentration of polymer in the formulation, the drug release rate from the tablets was found to be decreased. But when the concentration of polymer increased, the drug release rate was found to be increased and with in the concentration mucoadhesion strength was also increased. The in vitro release kinetics studies reveal that all formulations fits well higuchi's model, followed by korsmeyerpeppas, zero order kinetics and the mechanism of drug release is Non-fickian diffusion.

From the all formulations F1-F12 the formulations F10 was selected as optimized formulation because it showed maximum release and the other properties such as mucoadhesion strength shown good, whereas other formulation showed good release but the mucoadhesion strength was less.

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