Formulation and evaluation of anti-asthmatic drug montelukast in mucoadhesive buccal patches

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PEER REVIEW

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Comments
This is an interesting research which introduced a new way to treat patient with antiasmatic drug montelukast. In addition, the paper involved a lot of trial by using different polymers which added scientific fact to science.
Details on Page 913

ABSTRACT

Objective: To formulate and evaluate anti-asthmatic drug montelukast in mucoadhesive buccal patches.
Methods: Buccal patches were formulated by using different hydrophilic polymers by solvent casting technique. Buccal patches were evaluated by seven physical appearances, in addition to in vitro drug release study.
Results: All patches were uniform and translucent, and had smooth surface. In vitro release studies were conducted for montelukast buccal patches proved that release in the range of 75.26%–92.30% in 8 h. Emission of montelukast from all patches simulated zero order and diffusion mechanism. Finally it can be concluded that F3, F15 and F16 are the best formulation.
Conclusions: The investigation concluded that patch of 5 mg of montelukast sodium were formulated by using sodium alginate with sodium carboxy methyl cellulose, hydroxy propyl methyl cellulose K100M with sodium carboxy methyl cellulose, and hydroxy propyl methyl cellulose K100M with sodium alginate (F3, F15 and F16 formulations) were the best formulations.

KEYWORDS
Montelukast sodium, Gelatin, Hydroxy propyl methyl cellulose, Poly vinyl pyrrolidone, Buccal film, In–vitra release

1. Introduction

To increase bioavailability of montelukast sodium (MS), mucoadhesive buccal patches are used[1]. Problems such as high first pass metabolisms and drug degradation in the gastrointestinal tract can be circumvented by administrating the drug buccal routes[2]. Moreover, buccal drug delivery offers safe and easy method of drugs utilization, as drug absorption can be promptly terminated in case of toxicity by removing buccal dosage form from buccal cavity[3]. The buccal region offers an attractive route of administration for systemic drug delivery. Pharmaceutical aspects of mucoadhesion have been the subject of great interest during recent years, because it provides the possibility of avoiding either destruction by gastrointestinal contents or hepatic first-pass inactivation of drug[4]. Mucoadhesive drug delivery systems are delivery systems, which utilize the property of bioadhesion of certain polymers, which become adhesive on hydration and hence can be used for targeting of drug to particular region of the body[5]. The MS is a leukotriene receptor antagonist used for the maintenance treatment of asthma, chronic asthma attacks and to relive symptoms of seasonal allergies[6]. The main drawback of conventional...
MS formulation is that it undergoes hepatic first pass metabolism. Thus, it shows plasma or biological half-life 2.5 to 5.5 h, thereby decreasing bioavailability up to 64%[7]. The present work describes such delivery system, which will improve the biological half-life as well as bioavailability of montelukast. MS buccal patches were prepared using different mucoadhesive polymers such as sodium carboxymethyl cellulose (Na CMC), sodium alginate, poly vinyl pyrrolidone (PVP) K-30, gelatin and different grades of hydroxyl propyl methyl cellulose (HPMC K100M, and HPMC E5) by solvent casting technique. The prepared patches will be evaluated for seven physical appearances, in addition to in vitro drug release study. The buccal patches were used to enhance the bioavailability by avoiding first pass metabolism, greater therapeutic performance, and increase patient compliance.

2. Materials and methods

2.1. Chemicals

The montelukast was obtained from Global Napi Pharmaceuticals, Egypt. Hydroxypropyl methyl cellulose (HPMC) were kindly supplied by the Egyptian International Pharmaceutical Company (Egypt); sodium alginate and PVP were from Sigma Aldrich Co., USA; sodium carboxymethyl cellulose (SCMC), gelatin, propylene glycol, sodium chloride, disodium hydrogen phosphate and potassium dihydrogen phosphate were from El–Nasr Pharmaceutical Chemicals Co., (Cairo, Egypt). All other chemicals were of analytical grade, and water used in this assay was doubly distilled.

2.2. Preparation of montelukast mucoadhesive buccal patches

Buccal patches of montelukast were prepared by solvent casting technique employing mercury as substrate[8]. The mucoadhesive patches were prepared using polymers such as HPMC K100M, HPMC E5, Na CMC, Na Alginate, Gelatin and PVP K–30. Propylene glycol was used as plasticizer. The calculated amount of polymer was dispersed in three fourth volume of water with continuous stirring using magnetic stirrer and the final volume was adjusted with distilled water. The calculated amount of MS was incorporated in the polymeric solutions after levitation with 0.1 mL of propylene glycol. The solution was casted onto mercury substrate then kept in hot air oven at 400 °C for 24 h. Compositions of circular cast patches of various formulations are shown in Table 1. All the patches were dried and cut into size 2 cm×2 cm, each film containing 5 mg of MS.

| Formulation Number | Na CMC | Na Alginate | Gelatin | HPMC K100M | HPMC E5 | PVP | PEG |
|--------------------|--------|-------------|---------|------------|---------|-----|-----|
| F1                 | 300    | –           | –       | –          | –       | –   | –   |
| F2                 | 200    | –           | –       | –          | –       | –   | –   |
| F3                 | 300    | 200         | –       | –          | –       | –   | –   |
| F4                 | 300    | –           | –       | –          | –       | –   | –   |
| F5                 | 300    | –           | –       | –          | 150     | –   | –   |
| F6                 | 300    | –           | 100     | –          | –       | –   | –   |
| F7                 | –      | 200         | –       | –          | –       | 150 | –   |
| F8                 | –      | 200         | 100     | –          | –       | –   | –   |
| F9                 | –      | 200         | –       | –          | 150     | –   | –   |
| F10                | 300    | 200         | 100     | –          | –       | –   | –   |
| F11                | 300    | –           | –       | 300        | –       | –   | –   |
| F12                | –      | 200         | –       | –          | 300     | –   | –   |
| F13                | –      | –           | –       | 300        | 150     | –   | –   |
| F14                | 300    | –           | –       | 300        | 150     | –   | –   |
| F15                | 300    | –           | –       | 100        | –       | –   | –   |
| F16                | –      | 200         | –       | 100        | –       | –   | –   |
| F17                | –      | –           | –       | 100        | 150     | –   | –   |
| F18                | 300    | –           | –       | 100        | 150     | –   | –   |
| F19                | –      | –           | –       | 100        | 300     | –   | –   |
| F20                | 300    | –           | –       | 100        | 300     | –   | –   |
| F21                | –      | 200         | –       | 100        | 300     | –   | –   |
| F22                | –      | –           | –       | 100        | 300     | 150 | –   |

2.3. Evaluation of mucoadhesive buccal patches

The prepared buccal patches were evaluated for different physical properties such as weight uniformity, thickness, folding endurance, swelling index, surface pH, mechanical properties like in vitro residence time of patches and evaluation of MS patches like drug content and in vitro release study. Appearance of the film was evaluated by observing the color, elegance, stickiness and texture.

2.3.1. Weight uniformity

Three patches of the size 2 cm×2 cm diameter were weighed individually using digital balance and the average weights were calculated[9]. The weight uniformity of all formulations was recorded (n=3).

2.3.2. Thickness of patches

Thickness of the patches was measured using screw gauge with a least count of 0.01 mm at different spots of the patches. The thickness was measured at three different spots of the patches and average was taken[10]. The thickness of all formulations was recorded (n=3).

2.3.3. Folding endurance

The flexibility of patches can be measured quantitatively in terms of folding endurance. Folding endurance of the patches was determined by repeatedly folding a small strip of the patches (approximately 2 cm×2 cm) at the same place until it
broke. The number of times patches could be folded at the same place, without breaking gives the value of folding endurance[11]. The folding endurance of patches are carried out for three times and average was taken.

2.3.4. Surface pH

For determination of surface pH, three patches of each formulation were allowed in contact with 1 mL of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing equilibrate for 1 min[12]. A mean of three reading was recorded.

2.4. The percentage swelling index of patches

The swelling index of the patches was determined by immersing pre-weighed patch of size 2 cm x 2 cm in 50 mL water. The strip was taken out carefully at 5, 10 up to 30 min intervals, blotted with filter paper and weighed accurately[13]. The percent swelling index of patches was carried out for three times and average was recorded. The swelling index was calculated with the following equation:

\[
\% \text{ Swelling Index} = \frac{W_2 - W_1}{W_1} \times 100
\]

Where, \( W_1 \) is the initial patch weight at zero time; \( W_2 \) is the weight of the swollen patch after time \( t \).

2.5. Drug content uniformity study of patches

The patches were tested for drug content uniformity by UV–spectrophotometric method. Patches of 2 cm x 2 cm were cut from three different places from the casted patches. Each patch was placed in 100 mL volumetric flask and dissolved isotonic phosphate buffer (pH 6.8) for 8 h under occasional shaking, then 5 mL was taken and diluted with isotonic phosphate buffer pH 6.8 up to 10 mL, and the resulting solution was filtered through a 0.45 \( \mu \)m Whatman filter paper. The absorbance of the solution was measured at 282 nm using UV–vis spectrophotometer (Perkin Elmer Lambda 25). The percentage drug content was determined using the standard graph and the same procedure was repeated for three patches (\( n=3 \))[14].

2.6. In vitro mucoadhesion study

The mucoadhesive strength of different patches was measured using chicken pouch membrane (removed of its contents and surface fats) which was used as model mucosa for these studies[15]. The chicken pouch membrane was glued with cyanoacrylate adhesive on the ground surface of tissue holder made of plexiglas, and the film was glued to another holder of the same size. The surface of the mucosal membrane was first blotted with a filter paper and then moistened with 25 \( \mu \)L of phosphate buffer with pH 6.8. The two holders with mucosal membrane and film were put in contact with each other with uniform and constant pressure for 5 min (preload time) to facilitate adhesion bonding. The tissue holder with buccal mucosa was allowed to hang on an iron stand with the help of a piece of aluminum wire, a pre–weighted light weight polypropylene bag was attached to the hook on backside of the formulation holder with a piece of aluminum wire. After 5 min, water was added to the polypropylene bag through an intravenous infusion set at a constant rate of 1 drop/s until the film detached from the tissue. The water collected in the bag was measured and expressed as weight (g) required for detachment (bioadhesive strength). The average of three experiments was calculated.

Figure 1 shows a schematic presentation of the experiment design[16]. Force of adhesion for each patch was calculated according to the following equation:

\[
\text{Force of adhesion} (\text{N}) = \frac{\text{bioadhesive strength} \times 9.81}{1000}
\]

Figure 1. Modified apparatus for in vitro mucoadhesion test.

2.7. In vitro residence time of patches

The in vitro residence time was determined using a locally modified United States Pharmacopeia disintegration apparatus, based on the apparatus application[17]. The disintegration medium was composed of 500 mL phosphate buffer (pH 6.8) maintained at 37 °C. A chicken pouch membrane section was glued to the surface of a glass slab, vertically attached to the apparatus. The mucoadhesive patch was hydrated from drug loaded surface using 15 \( \mu \)L phosphate buffer and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down so that the patch was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the patch of each batch from the mucosal surface was recorded[18].
2.8. In vitro drug release of patches

The drug release rate from the buccal patches was studied using the United States Pharmacopeia type II dissolution test apparatus. Patches of 2 cm x 2 cm area were cut, and patches were meant to release the drug from only one side; therefore an impermeable backing membrane was placed on the other side of the patch. The assembly for release studies was prepared by sandwiching the patch in dialysis membrane (Hi Media molecular weight 5000). A piece of glass slide was placed as support to prevent the assembly from floating. The dialysis tubing with patch inside was secured from both ends using closure clips (Hi Media). Then it was placed in dissolution apparatus. The medium was 500 mL of isotonic phosphate buffer (pH 6.8) at 50 r/min at temperature of (37.0±0.5) °C. Samples of 5 mL were collected at different time intervals and analyzed by using UV−vis spectrophotometer at 282 nm. The experiment was performed in triplicates[19]. The release data were analyzed to study release kinetics using zero-order, first-order, Korsmeyer−Peppas, and Higuchi equations (n=3). The release studies were performed in six replicates and mean±SD values were calculated.

3. Results

Mucoadhesive patches of MS were prepared using different mucoadhesive polymers such as HPMC K100M, HPMC E5, Na CMC, Na Alginate, Gelatin, and PVP K−30 as drug delivery system.

3.1. Weight uniformity

Drug loaded patches (2 cm x 2 cm) were tested for uniformity of weight. The average weight of the patch was found in the range of (106.407±1.100) to (221.687±2.529) mg. Weight uniformity of the mucoadhesive patches are observed as given in Table 2.

3.2. Thickness uniformity

The thickness was observed to be in the range of (0.207±0.006) to (0.403±0.006) mm. The thickness of the mucoadhesive patches are observed as given in Table 2.

3.3. Folding endurance

Patches F3, F10−F11, F14−F16, F18−F20, F22 did not show any cracks even after folding for more than 300 times. Hence it was taken as the end point. All film formulations exhibited good folding endurance exceeding 300, indicating that they are tough and flexible. Other patches were found to be in the range of (122.000±2.000) to (285.000±1.000). Folding endurance did not vary when the comparison was made between plain patches and drug loaded patches. The folding endurance results are observed as given in Table 2.

Table 2

| Formulation number | Weight uniformity (mg) | Thickness (mm) | Folding endurance | Surface PH | Swelling index (%) | Drug content uniformity (%) |
|--------------------|------------------------|----------------|-------------------|------------|-------------------|-----------------------------|
| F1                 | 111.573±4.058          | 0.233±0.012    | 279.000±0.404     | 6.470±0.020| 480.600±6.210     | 98.170±0.007               |
| F2                 | 221.687±2.529          | 0.317±0.021    | 177.000±4.163     | 6.920±0.032| 184.060±1.150     | 102.500±0.006              |
| F3                 | 144.917±1.747          | 0.353±0.015    | >300              | 6.930±0.036| 476.900±3.230     | 100.800±0.013              |
| F4                 | 105.857±2.418          | 0.377±0.015    | 280.000±1.528     | 6.860±0.012| 456.200±3.350     | 95.800±0.005               |
| F5                 | 167.743±4.123          | 0.217±0.012    | 280.000±0.577     | 6.720±0.012| 387.290±3.340     | 95.500±0.002               |
| F6                 | 120.897±1.305          | 0.327±0.012    | 156.000±0.077     | 6.640±0.006| 763.240±2.821     | 94.270±0.007               |
| F7                 | 163.323±2.545          | 0.403±0.006    | 145.000±6.245     | 6.530±0.025| 160.147±5.574     | 95.700±0.006               |
| F8                 | 137.583±2.120          | 0.320±0.020    | 122.000±2.000     | 6.820±0.040| 729.303±4.360     | 102.100±0.006              |
| F9                 | 218.230±1.168          | 0.310±0.010    | 132.000±2.000     | 6.800±0.010| 43.290±2.747      | 95.320±0.005               |
| F10                | 202.870±2.380          | 0.387±0.015    | >300              | 6.630±0.012| 706.827±5.747     | 101.000±0.005              |
| F11                | 115.940±1.421          | 0.237±0.006    | >300              | 6.920±0.015| 255.767±1.855     | 98.930±0.006               |
| F12                | 124.270±2.028          | 0.315±0.003    | 265.000±2.000     | 6.530±0.046| 247.300±1.418     | 95.600±0.004               |
| F13                | 120.833±0.306          | 0.403±0.006    | 272.000±1.100     | 6.450±0.015| 244.233±0.833     | 101.170±0.003              |
| F14                | 106.407±1.100          | 0.403±0.006    | >300              | 6.440±0.012| 255.817±3.927     | 100.300±0.008              |
| F15                | 136.553±1.492          | 0.230±0.002    | >300              | 6.720±0.012| 688.277±9.347     | 100.500±0.010              |
| F16                | 146.250±2.375          | 0.333±0.021    | >300              | 6.710±0.015| 604.933±3.553     | 95.430±0.009               |
| F17                | 142.600±1.637          | 0.207±0.006    | 285.000±1.100     | 6.220±0.012| 659.900±1.908     | 97.970±0.007               |
| F18                | 126.333±0.896          | 0.397±0.006    | >300              | 6.310±0.015| 692.433±2.113     | 96.500±0.002               |
| F19                | 130.133±0.351          | 0.303±0.006    | >300              | 6.430±0.015| 251.533±1.106     | 100.970±0.006              |
| F20                | 133.433±0.723          | 0.220±0.010    | >300              | 6.430±0.021| 346.400±0.954     | 100.400±0.003              |
| F21                | 148.880±3.373          | 0.383±0.015    | 274.000±1.100     | 6.560±0.025| 300.173±8.981     | 98.370±0.008               |
| F22                | 97.230±0.001           | 97.230±0.002   | 97.230±0.003      | 97.230±0.004| 97.230±0.006      | 97.230±0.006               |
3.4. Surface pH

An acidic or alkaline pH of administered dosage forms could irritate the buccal mucosa. The prepared formulations provided an acceptable pH range that was compatible with normal buccal mucosa pH (6.780±0.040) in healthy people[20], consequently these patches can be considered non irritant to the buccal cavity. The surface pH of the mucoadhesive patches are observed as given in Table 2.

3.5. Swelling index

Appropriate swelling behavior of a buccal adhesive system was an essential property for uniform and prolonged release of drug and effective mucoadhesion. The percentage of swelling of MS mucoadhesive patches are observed as given in Table 2.

3.6. Drug content uniformity

The results of content uniformity indicated that the drug was uniformly dispersed. Recovery was possible to the tune of 94.27% to 102.50%. The drug content uniformity of the mucoadhesive patches are observed as given in Table 2.

3.7. In vitro mucoadhesion measurement

Bioadhesion is a very important aspect for maintaining high drug levels at the site of administration and prevents expulsion of formulation. Bioadhesion strength and bioadhesion force of the prepared MS mucoadhesive buccal patches on chicken pouch mucosa have been shown in Table 3.

### Table 3

**In vitro mucoadhesion measurement of mucoadhesive buccal patches of MS.**

| Formulation code | In vitro mucoadhesion measurements | In vitro residence time (h) |
|------------------|------------------------------------|-----------------------------|
|                  | Bioadhesion strength (Gm) | Force of bioadhesion (N) | |
| F1               | 34.57±4.221 | 0.339±0.0022 | 4.35±0.03 |
| F2               | 33.35±2.040 | 0.327±0.0020 | 4.14±0.03 |
| F3               | 35.46±3.000 | 0.348±0.0020 | 4.55±0.02 |
| F7               | 30.73±1.176 | 0.302±0.0017 | 3.43±0.02 |
| F10              | 3.28±1.112 | 0.032±0.0011 | 1.23±0.02 |
| F14              | 24.62±0.089 | 0.242±0.0009 | 4.36±0.02 |
| F15              | 22.57±0.195 | 0.221±0.0019 | 5.24±0.03 |
| F16              | 34.31±0.058 | 0.338±0.0006 | 5.13±0.03 |
| F20              | 24.51±0.072 | 0.240±0.0007 | 5.07±0.02 |
| F21              | 64.32±0.089 | 0.631±0.0009 | 5.04±0.01 |
| F22              | 8.68±0.047 | 0.085±0.0005 | 4.51±0.01 |

Data are expressed as mean±SD.

3.8. In vitro residence time of patches

The time required for the complete removal of the buccal film from the buccal mucosa varied with the composition of the film. The in vitro residence time is observed to be in the range of (1.23±0.02) to (5.24±0.03) h in Table 3.

3.9. In vitro drug release of patches

The in vitro release studies of various formulations were performed in isotonic phosphate buffer (pH 6.8) at 282 nm. Distinguishable difference was observed in the release pattern of MS film in graph plotted between the cumulative percent drug released from the formulation and time (Figure 2). After 8 h, the release was found in the range of 75.26%–92.3% in all formulations. Kinetics drug release results were given in Figures 2–5 and Table 4. Mechanism of drug release pattern, i.e. diffusion and swelling, was confirmed by Higuchi plots.

### Figure 2

Comparison in vitro drug release profiles of formulations F1–F3, F7, F10, F14–F16, F20–F22.

### Figure 3

Log cumulative drug remaining of different formulations.

### Figure 4

Higuchi plot of different formulations.

### Figure 5

Peppas plot of different formulations.
Drug actions. From the results of the tests for physical characterization of MS buccal patches with different polymers, it conducted that the all the patches were shown smooth surface, elegant texture, translucent and flexible depending on the type of polymer.

The measurement of swelling index indicates that maximum swelling takes place in the formulations containing higher proportions of HPMC K100M namely F15–18 and gelatin namely F6, F8 and F9. It was also observed that patches containing the hydrophilic polymers disintegrated very fast. Presence of soluble excipients such as PVP K-30 and gelatin make swelling of patches started within 5 min\cite{21}. The presence of the hydrophilic polymer, HPMC K100M seems to increase the surface wettability and swelling of the patches. The percentage swelling of HPMC K100M was increased by the addition of PVP K-30\cite{22}. The bioadhesive force measured was found to be higher for those film formulations containing higher proportions of the mucoadhesive polymer, HPMC K100M as in the case of F16 and F21. Moreover, HPMC K100M hydrates fast achieving maximum swelling at shorter periods which could promote interpenetration of the polymer chain with the tissue\cite{25}. Also, polymers having high molecular weight and high viscosity exhibited higher adhesion. HPMC K100M was found to be having good mucoadhesive strength. HPMC possesses hydroxy and carboxy groups respectively required for bioadhesion\cite{26}. Although rapid swelling is very important in obtaining a good polymer–mucosa interaction\cite{27}, the extent of water uptake should not be very large so as to start dissolving the polymer and disintegrate the mucoadhesive dosage form rapidly. It was observed that patches which retained their integrity for the longest times (F1, F14 and F21) in the swelling study showed the highest adhesion times. It could be concluded from the swelling and mucoadhesion studies that a moderate water uptake was beneficial in keeping the integrity and mucoadhesion of the patches for longer times, or in other words, formulations showing slower swelling rate achieved higher values of adhesion times. The in vitro mucoadhesive strength exhibited by MS patches was satisfactory for maintaining them in oral cavity except for F10. This aspect was further confirmed by measurement of residence time.

Main difference in vitro residence time depends on many factors that affect the efficacy of such formulations. First of all, solubility in water and hydration where polymers of high water solubility are less effective as mucoadhesive polymers. Another important factor to be considered is the homogeneity of the polymer solution mixtures. Using of PVP K-30 makes reduction of in vitro residence time of the formulation, due to the increase in swelling behavior\cite{2,10}.

The formulation F2 containing sodium alginate yielded a faster initial burst effect. This indicates that the formulation F2 did not control the drug release and it released the drug as immediate release\cite{28}. MS release was which allowed swelling the buccal patch and made weak hydrogen bonding\cite{23}.

Sodium alginate is one of the polysaccharides that possesses a mucoadhesive property because it contains numerous hydrogen bond forming groups, i.e., carboxyl and hydroxyl groups\cite{24}. It has been proposed that the interaction between the mucus and hydrophilic polymers occurs by physical entanglement and chemical interactions, such as hydrogen bonding as reported by Pongjanyakul and Suksri\cite{24}. The bioadhesive force measured was found to be higher for those film formulations containing higher proportions of the mucoadhesive polymer, HPMC K100M as in the case of F16 and F21. Moreover, HPMC K100M hydrates fast achieving maximum swelling at shorter periods which could promote interpenetration of the polymer chain with the tissue\cite{25}.

Table 4. Kinetics data of montelukast buccal patches.

| Formulation code | Zero order \(N^1\) | First order \(N^2\) | Higuchi plot \(N^3\) | Peppas plot \(N^4\) |
|------------------|---------------------|---------------------|---------------------|---------------------|
| F1               | 0.9928              | 0.9180              | 0.9595              | 0.9960              |
| F2               | 0.9909              | 0.9740              | 0.9646              | 0.9978              |
| F3               | 0.9925              | 0.8849              | 0.9775              | 0.9862              |
| F7               | 0.9868              | 0.9104              | 0.9485              | 0.9892              |
| F10              | 0.9938              | 0.9364              | 0.9562              | 0.9978              |
| F14              | 0.9922              | 0.9486              | 0.9552              | 0.9762              |
| F15              | 0.9924              | 0.9337              | 0.9603              | 0.9919              |
| F16              | 0.9903              | 0.9633              | 0.9548              | 0.9847              |
| F20              | 0.9661              | 0.9654              | 0.9169              | 0.9042              |
| F21              | 0.9818              | 0.9108              | 0.9735              | 0.9927              |
| F22              | 0.9914              | 0.9667              | 0.9627              | 0.9652              |
slower from patches containing SCMC (F1, F3, F10, F14, F15, F20). This may be due to the higher swelling profile and slower erosion rate of SCMC based patches, which created a thick gel barrier, resulting in an increase in diffusional path length of drug and the consequent reduction of drug release[29,30]. During diffusion inside the patches, PVP k-30 containing patches swelled forming a gel layer on the exposed film surfaces. The loosely bound polymer molecules in these patches were readily eroded, allowing the easy release of MS as in formulations (F4, F6, F13, F14, F17, F18, F22)[2]. Formulations F15–F22 show good release characteristics, where as polymer of lower water solubility such as HPMC K100M which if the viscosity increases, the entrapment of drug is tightly bound in between the cross–links of the polymer; thereby the drug will take time to release from the film[31]. As HPMC K100M has a very high viscosity of 100 000 cP as compared to HPMC E5 (5 cP). These results were consistent with the literature in which many authors have generally observed that increasing the amount of hydrophilic polymer in the patches produces a water–swollen gel–like state that can substantially reduce the permeation of the dissolution medium into the patches and thus retard the drug release[32].

It was concluded that 5 mg of montelukast formulated by using sodium alginate with sodium carboxy methyl cellulose, HPMC K100M with sodium carboxy methyl cellulose, and HPMC K100M with sodium alginate (F3, F15, and F16 formulations) were the preferable formulations. Hence these formulations of MS mucoadhesive buccal patches showed promising results with respect to controlled drug delivery, moderate swelling and convenient resident time, leading to greater therapeutic efficacy and improving the drug bioavailability, thereby buccal administration of drugs provides a convenient route of administration for both systemic and local drug actions.

**Conflict of interest statement**

We declare that we have no conflict of interest.

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