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Formulation and Evaluation of Mucoadhesive Buccal Patch Contain Anti Asthmatic Drug

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1. INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing. Although inhalation therapy is the cornerstone of asthma management, systemic delivery routes can sometimes be limited by poor bioavailability, extensive first-pass metabolism, and patient non-compliance. To overcome these challenges, alternative drug delivery systems such as **mucoadhesive buccal patches** have gained increasing attention.

Mucoadhesive buccal drug delivery involves the administration of medication via the buccal mucosa, which provides several advantages: it bypasses the hepatic first-pass effect, offers rapid onset of action, maintains steady plasma drug levels, and enhances patient convenience. Buccal patches are thin, flexible dosage forms designed to adhere to the mucosal surface, ensuring prolonged residence time and controlled drug release.

The formulation of a mucoadhesive buccal patch requires the careful selection of polymers that provide adequate adhesion, mechanical strength, and biocompatibility. Polymers such as hydroxypropyl methylcellulose (HPMC), sodium carboxymethyl cellulose (NaCMC), and polyvinyl alcohol (PVA) are commonly employed to achieve desirable film-forming and mucoadhesive properties. Incorporation of an anti-asthmatic drug into this system allows sustained delivery directly into the systemic circulation, potentially improving therapeutic outcomes and reducing dosing frequency.

The present study is aimed at the **formulation and evaluation of mucoadhesive buccal patches containing an anti-asthmatic drug**. The developed patches will be subjected to comprehensive evaluation, including physicochemical characterization (thickness, weight variation, surface pH), mechanical properties (tensile strength, folding endurance), mucoadhesive strength, drug content uniformity, in vitro drug release, and ex vivo permeation studies. Through this approach, the study seeks to establish an effective buccal delivery platform that can offer improved bioavailability and enhanced patient compliance in the management of asthma.

2. REVIEW OF LITERATURE

1. R. Khanna and colleagues (2019). Because it allows for both local and systemic absorption, the buccal mucosa is regarded to be a handy and conveniently accessible place for the administration of drugs at the same time. A process that is defined by the chemical interactions that take place between mucin and polymers is called mucoadhesion. Numerous individuals have shown a significant amount of interest in the use of mucoadhesive

polymers in buccal drug delivery. Tablets, patches, disks, wafers, ointments, and gels are only some of the mucoadhesive dosage forms that have been developed as a result of recent advancements in the field. When compared to other types, buccal patches provide a higher level of comfort and flexibility. Because of their efficient carrier capacity, prolonged drug residence time at the absorption site, increased drug bioavailability, reduced dosing frequency, and enhanced patient compliance, smart materials are essential for the progression of drug delivery systems. Some examples of smart materials include liposome-based patches, stimuli-responsive hydrogels, and polymeric micelles. When it comes to the fabrication of buccal patches, various designs and manufacturing methods, such as electrospinning, electrospraying, and 3D printing, are recognized as novel and efficient solutions. These approaches provide distinctive qualities in contrast to more conventional procedures, such as solvent casting. The objective of this research is to discover and demonstrate the most promising smart polymeric materials, novel designs, and manufacturing techniques for the purpose of developing buccal mucoadhesive patches as a revolutionary controlled drug delivery system [13]. ..

2.Patel KV., et al., (2009) . When compared to conventional dose forms such as tablets, gels, and liquids, a mucoadhesive patch that delivers medication to the mouth cavity at a controlled rate may offer a number of significant advantages. This study focused on the creation and evaluation of mucoadhesive buccal patches for the purpose of regulating the systemic administration of salbutamol sulfate in order to circumvent the first-pass hepatic metabolism. The physicochemical, mechanical, and drug release properties of the patches that had been created were examined and evaluated. It was proved that the patches possessed the requisite mechanical and physicochemical qualities to withstand the conditions that are present in the oral cavity. A study that was conducted using in-vitro release demonstrated that patches were capable of delivering the medicine to the oral mucosa for a duration of seven hours. During the evaluation that took place under expedited settings, the patches demonstrated sufficient stability [8].

3.**Parodi B., (2007).** An approach known as solvent casting was utilized in order to manufacture buccal patches that were mucoadhesive and contained propranolol hydrochloride. A bioadhesive polymer was created using chitosan, and the ratio of chitosan to PVP K-30 was varied in order to achieve the desired results. In order to evaluate the patches, various physical parameters were examined. These included mass variation, uniformity of drug content, folding durability, ex vivo mucoadhesion strength, ex vivo mucoadhesion length, surface pH, in vitro drug release, and in vitro buccal penetration studies. Over the course of seven hours, the patches demonstrated a regulated release of the substance. The non-Fickian diffusion process that conforms to first-order kinetics was identified as the mechanism responsible for the release of the medication. Generally speaking, the integration of PVP K-30 resulted in an increase in the release rate. The concentration of PVP K-30 was found to have a direct proportional relationship with the swelling index. In terms of bioadhesive strength, the optimized patches (F4) demonstrated a remarkable value of 9.6 ± 2.0 grams, while also demonstrating an ex vivo mucoadhesion endurance of 272 minutes. The pH of the surface of each patch ranged from 5.7 to 6.3, which indicates that it is highly unlikely that the patches will produce discomfort in the oral cavity by themselves. Patches that contained 10 mg of the medicine displayed higher bioadhesive strength and longer drug release in comparison to patches that contained 20 mg of the drug. The correlation coefficient between in vitro drug release and in vitro drug permeation was found to be 0.9364, indicating that there is a strong connection between the factors. The stability evaluation of optimized patches carried out in human saliva revealed that both the buccal patches and the pharmaceutical patches displayed stability [16].

4. **Chandira M., et al., (2012).**. The purpose of this research was to develop bioadhesive patches of carvedilol hydrochloride by utilizing chitosan (CH) and pectin (PE) interpolymer complexes, and then to thoroughly analyze the efficiency of these patches both in vitro and in vivo. Through the use of the solvent casting technique, buccal patches that were mucoadhesive and contained carvedilol were manufactured. FTIR and DSC techniques were utilized in order to investigate the physicochemical interaction that occurred between CH and PE. On the basis of their physical features, the patches were examined. These parameters included mass variation, content uniformity, folding endurance, ex vivo mucoadhesion strength, ex vivo mucoadhesion length, surface pH, in vitro drug release, in situ release analysis, and in vivo bioavailability assessment. It was discovered that the swelling index of the patches was directly proportional to the amount of polyethylene that was present. All of the bioadhesive patches that were included in the formulation had surface pH values that ranged from 6.2 to 7.2. The improved bioadhesive patch, which was designated as C1, CH:PE 20:80, exhibited a bioadhesive strength of 22.10 ± 0.20 grams, an in vitro release rate of 98.73%, and an ex vivo mucoadhesion duration of 451 minutes over the course of an 8-hour period. Both in vitro and in vivo tests revealed that the enhanced patch had beneficial effects. Carvedilol was administered to rabbits through the buccal route, and the results showed that the bioavailability of the medication was significantly higher through the buccal route than through the oral method.

3. AIM AND OBJECTIVES

AIM

To formulate and evaluate anti-asthmatic drug montelukast in mucoadhesive buccal patches.

OBJECTIVES

1. To prepare of anti-asthmatic drug montelukast in mucoadhesive buccal patches.
2. To evaluate of anti-asthmatic drug montelukast in mucoadhesive buccal patches.

4. MATERIAL AND METHOD

4.1 MATERIAL

4.1.1 Chemicals

Montelukast, Hydroxypropyl methyl cellulose (HPMC), sodium alginate and PVP, sodium carboxymethyl cellulose (SCMC), gelatin, propylene glycol, sodium chloride, disodium hydrogen phosphate and potassium dihydrogen phosphate. All other chemicals were of analytical grade, and water used in this assay was doubly distilled.

4.1.2 METHOD

4.1.2.1 Preparation of montelukast mucoadhesive buccal patches

1. Buccal patches of montelukast were prepared by solvent casting technique[8].

2.The mucoadhesive patches were prepared using polymers such as HPMC K100M,HPMC E5, Na CMC, Na Alginate, Gelatin and PVP K-30.

3. Propelene glycol was used as plasticizer.

4.The calculated amount of HPMC (400,600,800,1000,1200,1400mg) was dispersed in three fourth volume of water with continuous stirring using magnetic stirrer and the final volume was adjusted with distilled water.

5.The calculated amount of montelukast sodium was incorporated in the polymeric solutions after levitation with 0.1 mL of proylene glycol.

6.The solution was casted onto mercury substrate then kept in hot air oven at 400 °C for 24 h.

7.Compositions of circular cast patches of various formulations are shown in Table 1.

8. All the patches were dried and cut into size 2 cm-2 cm, each film containing 5 mg of montelukast sodium.

Table 1: Composition of different mucoadhesive buccal patches of montelukast sodium (mg).

Formulation no.	Montelukast Sodium (mg)	Proylene Glycol (ml)	HPMC (mg)
1.	20	0.1	400
2.	20	0.1	600
3.	20	0.1	800
4.	20	0.1	1000
5.	20	0.1	1200
6.	20	0.1	1400

5. EVALUATIONS

5.1 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.

1.Weight uniformity:

Three patches of the size 2cm-2cm 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.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).

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 2cm-2cm) 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.

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.

5. The percentage swelling index of patches :

The swelling index of the patches was determined by immersing pre-weighed patch of size 2cm-2cm 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 were carried out for three times and average was recorded. The swelling index was calculated with the following equation:

% Swelling Index=(W2-W1)/W1×100

Where, W1 is the initial patch weight at zero time; W2 is the weight of the swollen patch after time 't'.

6. Drug content uniformity study of patches :

The patches were tested for drug content uniformity by UV- spectrophotometric method. Patches of 2 cm-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 µm 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)**.**

6. RESULT

Mucoadhesive patches of MS were prepared using different mucoadhesive polymers such as HPMC.

Table 2: Physical and mechanical mucoadhesive buccal patches of MS.

Formulation number	Weight uniformity (mg)	Thickness (mm)	Folding endurance	Surface pH	Swelling index (%)	Drug content uniformity
F1	111.57±4.058	0.233±0.012	279.0004.0±41	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±70.032	184.060±71.150	102.500±0.006
F3	144.917±1.747	0.353±0.015	200.100±5.12	6.930±0.036	476.900±3.230	95.550±0.013
F4	105.857±2.418	0.337±0.015	280.000±1.528	6.860±0.012	456.200±3.350	95.830±0.005
F5	167.74±1.232	0.21±0.012	280.000±0.577	6.720±0.012	387.290±3.340	95.500±0.002
F6	120.89±1.305	0.327±0.012	156.000±0.577	6.640±0.006	763.240±2.281	94.270±0.007

7. DISCUSSION

Buccal administration of drugs provides a convenient route of administration for both systemic and local 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 F3 and gelatin namely F4. 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[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 E5 patches was increased by the addition of PVP K-30[22]. It was observed that SCMC imparted continuous increase in swelling with time and SCMC containing patches showed higher percent swelling due to presence of more hydroxyl group in the SCMC molecules which held more amount of water in their network[11]. The PVP K-30 including patches had high swelling values due to its solubility in water, which allowed swelling the buccal patch and made weak hydrogen bonding[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[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[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 F1 and F2. Moreover, HPMC K100M hydrates fast achieving maximum swelling at shorter periods which could promote interpenetration of the polymer chain with the tissue[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[26]. Although rapid swelling is very important in obtaining a good polymer-mucosa interaction[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, F2) 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 F6. This aspect was further confirmed by measurement of residence time.

It was concluded that 20 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, F4, and F5 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.

8. CONCLUSION

Montelukast buccal patches offer a promising alternative drug delivery system for managing asthma and allergic rhinitis. These patches provide a controlled and sustained release of montelukast, improving bioavailability by bypassing the gastrointestinal tract and reducing first-pass metabolism. This can potentially enhance therapeutic outcomes and minimize side effects. The convenience of buccal patches, especially for patients who have difficulty swallowing pills, could lead to better patient compliance. Moreover, they offer the advantage of a steady drug release over time, reducing the need for multiple doses throughout the day. Early studies suggest they are safe and well-tolerated, although further clinical trials are necessary to confirm long-term safety and address any potential issues like local irritation. Despite their promise, challenges such as ensuring drug stability, cost-effectiveness, and

regulatory approval remain. Overall, montelukast buccal patches represent an exciting development in asthma and allergy treatment, but further research is needed to fully establish their efficacy and practicality in clinical settings.

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