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Research Article

Formulation and Characterization of Montelukast Sodium Mouth Dissolving Film Using Cress Seed Mucilage

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Abstract

There is a rising interest in the development of orodispersible films (ODFs) as an alternative to fast dissolving tablets which is attributed to their faster dissolution rate, higher durability, and better patient compliance. Owing to its rheological and also various functional properties, many researchers tried to discover some of the pharmaceutical applications of L. sativum in the development of various dosage forms, in addition to its therapeutic studies, such as binding, dissolving, gelling and sustained release dosage form. The fast-dissolving oral film of the Montelukast sodium by using Cress seed mucilage (CSM) and HPMC (15cps) is prepared by solvent casting method. The fast-dissolving oral film evaluated for folding endurance, surface pH, in-vitro disintegration time, drug content and in-vitro drug release. The physical appearance and folding endurance properties were found to be reasonably good and electron microscopy shows that films are clear, colorless with smooth surface.The drug content of all the films was in the range suggesting that drug was uniformly dispersed throughout all films. The present study was an attempt to develop and evaluate an oral fast dissolving drug delivery system using cress seed mucilage as a film former.

Keywords: Orodispersible film, Montelukast sodium, Cress seed mucilage, HPMC

INTRODUCTION

Oral route of drug administration is the most important method of administration of drug for systemic effect despite of tremendous advancement in drug delivery. Dysphasia is a common problem associated with the tablets and capsule which results in high degree of noncompliance[1].Rapidly dissolving or quick dissolving dosage forms have acquired great importance in the pharmaceutical industry due to many advantages[2].There is a rising interest in the development of orodispersible films (ODFs) as an alternative to fast dissolving tablets which is attributed to their faster dissolution rate, higher durability, and better patient compliance. Recently, research work on the use of ODFs as promising carriers for multiple active pharmaceutical ingredients has emerged[3]. When placed on the tongue, they are postage-stamp-sized strips of thin polymeric films that crumble or dissolve practically instantly[4]. ODFs are good for travelers or patients who do not have constant access to water because they are thin and can be administered without water. Furthermore, ingestion is non-obtrusive[5,6].

Natural hydrocolloids are widely used in food systems as thickening and gelling agents, stabilizers and texture modifiers. Seed-plant polysaccharide exudates and mucilage's are a good source of such hydrocolloids[7].Owing to its rheological and also various functional properties, many researchers tried to discover some of the pharmaceutical applications of L. sativum in the development of various dosage forms, in addition to its therapeutic studies, such as binding, dissolving, gelling and sustained release dosage form[8]. Montelukast sodium is a leukotriene receptor antagonist (LTRA) that is used to treat asthma and alleviate seasonal allergy symptoms. It is commonly taken by mouth. Montelukast sodium is 63 percent bioavailable and is easily soluble in ethanol, methanol, and water[9,10]. The formulation of MLS as a strip film to be placed on the patient's tongue for dose administration, without the need to swallow, would significantly facilitate dose administration, with subsequent improvement in patient compliance.

Thus, the aim of this work was to design and characterize mouth dissolving films of Montelukast sodium formulated using HPMCas a polymer.

MATERIALS AND METHOD

Materials

Montelukast Sodium obtained as a as a gift sample from Unimark Remedies Ltd., Mumbai, HPMC, PEG-400, Tween 80 were obtained from SD Fine chem. Mumbai. All the chemicals were of analytical grade.

Methods

Extraction of CSG and preparation of Orodisperse film:

The fast-dissolving oral film of the Montelukast sodium by using Cress seed mucilage (CSM) and HPMC (15cps) is prepared by solvent casting method[11]. The oral fast dissolving strips were prepared by taking all the ingredients in different concentration as depicted in table 1.CSM and HPMC were dispersed in distilled water followed by continuous stirring up to 1hr on magnetic stirrer and kept for 30 min to remove all the air bubbles entrapped. To this tween 80 and plasticizer (glycerin/PEG 400) was added. Solution of aspartame was prepared in separate container. The solution was cast on a film former and the film was then peeled from the surface and cut into the necessary size (2x2) of a Montelukast sodium equivalent dose[12].Blank film without drug was also prepared using the same procedure.

Table 1: Composition of Montelukast Sodium Mouth dissolving film

F. Code	*Ingredients*						
	CSM	*HPMC E15*	*PEG 400*	*SSG*	*Aspartame*	*Citric acid*	*Drug (mg)*
Blank Film	*100*	-	*0.2*	-	*30*	*5*	-
F1	*100*	-	*0.2*	*4*	*30*	*5*	*180*
F2	*150*	-	*0.2*	*6*	*30*	*5*	*180*
F3	*200*	-	*0.2*	*8*	*30*	*5*	*180*
F4		*150*	*0.2*	*6*	*30*	*5*	*180*

Evaluation of various excipients properties of cress seed mucilage

Film Weight and Thickness

The weight of prepared films was recorded. Film thickness was measured by means of a micrometer.

Drug Content

The drug content uniformity of each film was tested by dissolving the film in 10 ml of PBS, followed by filtering through 0.45 µm membrane filter. The filtrate was appropriately diluted, and the mean content of MOS was determined at 271 nm using UV spectroscopy

Moisture content

The prepared film samples of a 2cm average diameter were dried at 105 ◦C in an oven and their moisture content was carried out after 24 h of drying.

Folding endurance

The number of folds necessary to break the specimen or cause visible fissures is referred to as "folding endurance." The brittleness of the film is shown by this. It was manually measured for the produced film to have a surface area of 22 cm^2. This test was performed on a film with a defined area by folding it repeatedly in the same plane multiple times until obvious breaks appeared.

In vitro Disintegration of Films[13].

The film strip was placed in a glass Petri dish (6.5 cm in diameter) containing 25 ml of distilled water at37°C, with swirling every 10 s. The disintegration time was recorded as the time at which the film starts to break ordisintegrate.

The in vitro dissolution test

The in vitro dissolution test was carried out in a paddle dissolution apparatus**.**

Scanning electron microscopy

A scanning electron microscope (SEM) is a type of electron microscope that uses a concentrated beam of electrons to scan the surface of a sample to obtain images. The electrons interact with the atoms in the sample, resulting in a variety of signals that provide information on the sample's surface topography and composition. A raster scan pattern is used to scan the electron beam, and the position of the beam is coupled with the detected signal to create an image[14].

Mechanical strength

Tension testing with a LLOYD LS1 METRK and Nexygen PHS 3.0 Software were used to determine the mechanical properties of the film. First, films were cut into rectangular strips measuring 1 cm wide by 4 cm long and preconditioned for 48 hours at 25°C and 50% relative humidity in desiccators containing saturated calcium nitrate solutions. The CSG films were clamped between grips (starting distance, 1 cm) and force and deformation measurements were taken while the films were extended at 50 mm/min. All of Young's modulus (EM), tensile strength (TS), and elongation at break (EB) were computed[15].

Water Vapor Permeability

The quantity of water transmitted through a unit area of film in a unit of time is known as water vapor permeability. This water vapor permeation data is critical for establishing the film's permeation characteristics since it affects skin parameters such as stratum corneal moisture, blood flow, and skin temperature. On a Teflon plate, films are made using a solvent evaporation process and then dried for 72 hours at room temperature. Dry film sheets are sliced into circular samples. Glass vials with openings are filled with distilled water, coated with circular film samples and a silicone ring, then sealed tightly with an aluminum vial cap for sample processing.The vial's weight is measured, and it is then placed in a desiccator to create a 58 percent relative humidity or low relative humidity environment (approximately 0 percent). They are stored at a set temperature for 72 hours and weighed at regular intervals. The water vapor permeability is computed as the amount of water that permeates through the film in response to the surface area A (cm2) and the time t (h) from the weight loss of the vials W (g)[16].

$$WVP = W/A^* t$$

RESULT AND DISCUSSION

The formulated oral films were transparent, flexible, and showed no blooming. The weight and thickness values of prepared films are summarized in Table 2.

Table 2: Evaluation of Mouth Dissolving Film

F Code	Weight of Films (g)	Thickness of films (mm)	Folding Endurance	Disintegration Time (sec)	% Drug content
Blank Film	0.0146±0.007	0.15±0.06	22.43± 2	87± 2	-
F1	0.0318±0.006	0.19±0.06	33 ± 2	48 ± 1	99.47% ± 1.2
F2	0.0374±0.006	0.19±0.03	34 ± 1	41 ± 1	98.37% ± 1.2
F3	0.0414±0.024	0.20±0.01	38 ± 3	36 ± 1	98.49% ± 1.7
F4	0.0373±0.043	0.19±0.06	48 ± 1	51 ± 1	98.97% ± 1.1

The prepared films were homogenous, colorless, smooth, and rough surface. The weight variation was found to be minimum which depicts the uniform distribution of the ingredients in MDF. The thickness shows a narrow range of 0.15 to 0.19 mm. All the polymers resulted in the formulations that have neutral surface pH. The surface pH of the strips was ranging from 6.8 to 7. The neutral values of surface pH of films assured that there will be no irritation to the mucosal lining of the oral cavity. The drug content was found to be uniform and ranged from 98.49% to 99.47%. The disintegration time was found to be in the range from 36 to 87 sec. The results indicated that the disintegration time is directly proportional to the concentration of super disintegrating agents. i.e., as the concentration of super disintegrants increases the films disintegrates at faster rate. Blank film showed higher disintegration time as compared to the film prepared with super disintegrating agent.

The folding endurance is expressed as the number of folds required for breaking the specimen or developing visible cracks. From the observation the film formed by using without drug (Blank Film) has least value of folding endurance while film prepared by different concentration of CSM and HPMC shows highest value of folding endurance. All the formulations are subjected for *in-vitro* dissolution study using USP type I apparatus (basket type) using a phosphate buffer of pH 6.8 solution. The prepared films released the 89.2 % ±0.48 to 95.66% ±0.24 as shown in Figure 1.

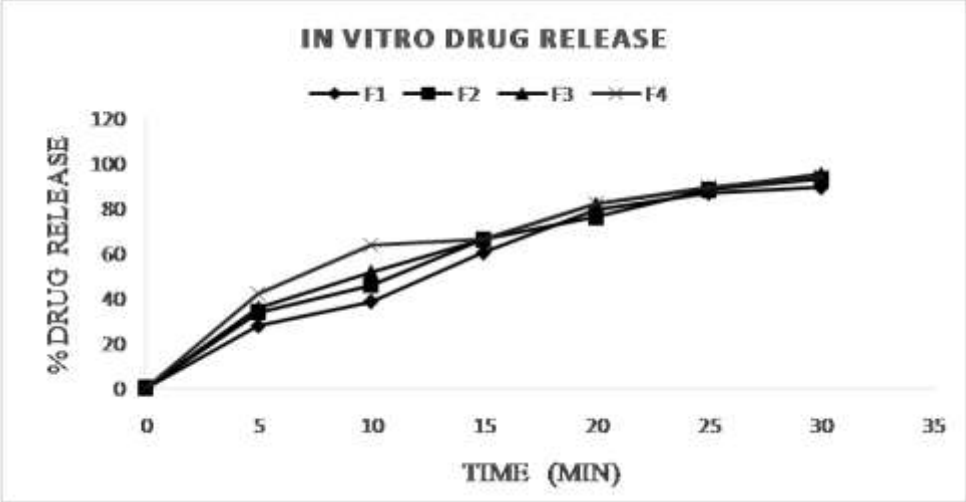

Figure 1: In vitro drug release of Batch F1-F4

The measurements of film mechanical properties for the different formulations are summarized in Table 3.

Table 3: Mechanical properties of Prepared film F1-F4

F. Code	Tensile strength	% Elongation	Water vapour permeability (g * cm2 * 24 h)
Placebo	21.12	2.0676	2.3.11
F1	35.55	4.5577	2. 201
F2	36.43	4.622	2.212
F3	36.89	4.676	2.231
F4	31.33	3.666	3.812

The tensile strength was performed on the placebo film and the drug loaded film. From the table it was observed that the drug loaded film was having high tensile strength as compared to placebo film also it required high compression strength. It was concluded that drug loaded film was better than placebo film. The films made of HPMC were hard in nature. In contrast, file prepared with CSG found to be more ductile. Tensile strength, % elongation, and folding endurance results indicate that prepared MDF is slightly elastic and breaks at low force which might be due to the presence of high solid content. Water vapor permeability is a measure of ease of the moisture to pass through a material. The high-water vapor permeability of MDF would have been due to the presence of pores in MDF which is also confirmed by SEM images.

SEM of cress seed film reveals a clean and even surface with circular pits and no particles, indicating the existence of extra-mucilaginous particles as shown in Figure 2.

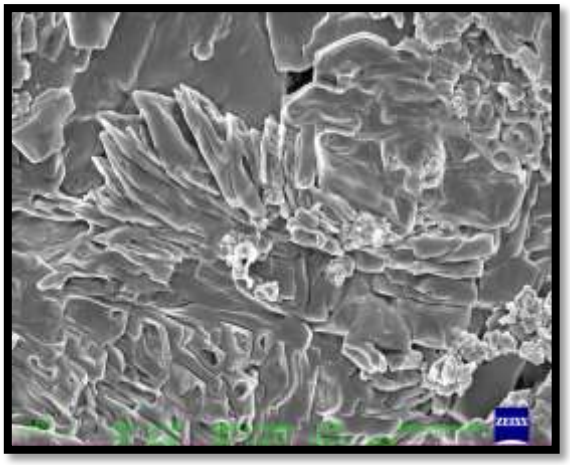

Figure 2: Scanning electron microscopy of cress seed mucilage-based film

The ease with which moisture can move through a substance is measured by its water vapour permeability. The presence of pores in the CSM film would have caused the film's high water vapour permeability, which is also supported by the SEM pictures detailed above. Cress seed water vapour permeability was computed as 2.201g * cm2 * 24 h. This demonstrates that water vapour can pass through cress seed film[16]. The physical parameters of the film were used to determine its stability and the results reveal that the color and surface characteristics of the film did not change, indicating that it was stable.

CONCLUSION

The fast-dissolving films of montelukast sodium were prepared by solvent casting technique using film forming polymer Cress seed mucilage and HPMC. The effect of super disintegrants such as sodium starch Glycolate was also observed. The film prepared with Cress seed mucilage found to be more ductile than film prepared with HPMC. Tensile strength, % elongation, and folding endurance results indicate that prepared MDF is slightly elastic and breaks at low force which might be due to the presence of high solid content.

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Competing interests

Authors have declared that no competing interests exist.

REFERENCES

1) Mahore JG, Wadher KJ, Umekar MJ. Formulation and in-vitro evaluation of taste masked orodispersible tablet of metoclopramide hydrochloride.International Journal of PharmTech Research, 2010; 2(3):1827-1835

2) Kamlesh Wadher, Kunal Dhote, Monika Mane, Ajit Khapne, Anjali Gaidhane Milind Umekar. Orodispersible Dosage Form: Advancement and Challenges.Int J Pharma Res Health Sci. 2019; 7(4):3013-3019 https://doi.org/10.21276/ijprhs.2019.04.01

3) Cilurzo F, Cupone IE, Minghetti P, Selmin F, Montanari L. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm. 2008; 70:895-900.6. Cilurzo F, Cupone IE, Minghetti P, Buratti S, Selmin F, Gennari CG, et al. Nicotine fast dissolving films made of maltodextrins: a feasibility study. AAPS PharmSciTech. 2010; 11:1511-7. https://doi.org/10.1208/s12249-010-9525-6

4) Hariharan M, Bogue A. Orally dissolving film strips (ODFS): the final evolution of orally dissolving dosage forms. Drug DelivTechnol 2009;9(2):24-9.

5) Liang AC, Chen LH. Fast-dissolving intraoral drug delivery systems. Expert OpinTher Patents2001; 11(6):981-6. https://doi.org/10.1517/13543776.11.6.981

6) Borsadia SB, O'Halloran D, Osborne JL. Quick-dissolving films - a novel approach to drug delivery. Drug DelivTechnol 2003; 3(3):63-6.

7) Avachat, M. K., and A. G. Dhamne. "Method of manufacturing of husk from Lepidium sativum seeds." The Patent Cooperation Treaty (PCT), WO 2.102856 (2002): A1.

8) V.B. Divekar, M.G. Kalaskar, P.D. Chougule, V.K. Redasani, D.G. Baheti, Int. J.Pharm. Res. Dev. 2010; 2:1-5.

9) VijaykumarGhorwade, AjaykumarPatil, SatishkumarPatil, KarunasriSrikonda, RaghavenderKotagiri and Priya Patel.Development and Evaluation of Fast-Dissolving Film of Montelukast Sodium.WJMPBS. 2011; 1(1):06-12.

10) Dr. RaghavendraRao N. G and UpendraKulkarni.Formulation and Design of Fast Dissolving Tablets of Felodipine Using Novel Co-Processed Superdisintegrants.IJPRD. 2010; 2(9):113-121.

11) Karazhiyan, Razavi, and Phillips (2011)/Karazhiyan, H., Razavi, S. M. A., Phillips, G. O., Fang, Y., Al-Assaf, S., & Nishinari, K. Physicochemical aspects of hydrocolloid extract from the seeds of Lepidiumsativum. International Journal of Food Science and Technology, 2011; 46:1066-1072. https://doi.org/10.1111/j.1365-2621.2011.02583.x

12) Mashru RC, Sutariya VVB, Snkalia MMG, Parikh PP. Development and evaluation of fast-dissolving film of salbutamol sulphate. Drug DevInd Pharm. 2005; 31:25-34. https://doi.org/10.1081/DDC-43947

13) Wadher Kamlesh J, Umekar Milind J, Sheikh Ghousiya Bano*, Mohd Younus, Sapate Ruchika P, Ansari Namuna Fatima. Formulation and characterization of pediatric paracetamol oral mouth dissolving film. Int. J. Res. Pharm. Sci., 2017, 8(3):393-398

14) Senthilkumar, K., Grozema, F. C., Bickelhaupt, F. M., &Siebbeles, L. D. A. Charge transport in columnar stacked triphenylenes: Effects of conformational fluctuations on charge transfer integrals and site energies. The Journal of chemical physics, 2003; 119(18):9809-9817. https://doi.org/10.1063/1.1615476

15) S. Karaki et al/Karki, S., Kim, H., Na, S. J., Shin, D., Jo, K., & Lee, J. Thin films as an emerging platform for drug delivery. asian journal of pharmaceutical sciences, 2016; 11(5):559-574. https://doi.org/10.1016/j.ajps.2016.05.004

16) Kathe, K et al/Kathe, K., &Kathpalia, H. Film forming systems for topical and transdermal drug delivery. Asian journal of pharmaceutical sciences, 2017; 12(6):487-497. https://doi.org/10.1016/j.ajps.2017.07.004

17) El-Setouhy D, El-Malak NSA. Formulation of a novel tinapetine sodium orodispersiblefilm.AAPSPharmSciTech. 2010; 11:1018-25. https://doi.org/10.1208/s12249-010-9464-2

18) Malke S, Shidhaye S, Desai J,KadamV. Oral films-patient compliant dosage form for pediatrics.Internet J PedNeonatol. 2010; 11. https://doi.org/10.5580/44e

19) Martineau B. A look at fast-dissolving drug delivery systems. Drug Deliv Technol. 2009; 9:36-8.

20) Shimoda H, Taniguchi K, Nishimura M, Matsuura K, Tsukioka T, Yamashita H, et al. Preparation of a fast-dissolving oral thin film containing dexamethasone: a possible application to antiemesis during cancer chemotherapy. Eur J Pharm Biopharm. 2009; 73:361-5. https://doi.org/10.1016/j.ejpb.2009.08.010

21) 1Osés, J., Niza, S., Ziani, K., &Maté, J. I. Potato starch edible films to control oxidative rancidity of polyunsaturated lipids: Effects of film composition, thicknessand water activity. International Journal of Food Science and Technology, 2009; 44. https://doi.org/10.1111/j.1365-2621.2009.01965.x

22) Pérez, C. D., Flores, S. K., Marangoni, A. G., Gerschenson, L. N., & Rojas, A. M. Development of a high methoxyl pectin edible film for retention of l- (+)-ascorbic acid. Journal of Agricultural and Food Chemistry, 2009; 576:844-6855. https://doi.org/10.1021/jf804019x

23) Abdorreza, Cheng, &Karim, 2011; Ahmadi, 2011)/ Abdorreza, M. N., Cheng, L. H., &Karim, A. A. Effects of plasticizers on thermal properties and heat sealability of sago starch films. Food Hydrocolloids, 2011; 25:56-60. https://doi.org/10.1016/j.foodhyd.2010.05.005

24) Aliheidari, N., Fazaeli, M., Ahmadi, R., Ghasemlou, M., &Emam-Djomeh, Z. Comparative evaluation on fatty acid and Matricariarecutita essential oil incorporated into casein-based film. International journal of biological macromolecules, 2013; 56:69-75. https://doi.org/10.1016/j.ijbiomac.2013.02.007

25) Khatoon, N et al/ Khatoon, N., Alam, H., Khan, A., Raza, K., &Sardar, M. Ampicillin silver nanoformulations against multidrug resistant bacteria. Scientific Reports, 2019; 9(1):1-10. https://doi.org/10.1038/s41598-019-43309-0

26) Behrouzian.F et al/ Behrouzian, F., Razavi, S. M., &Karazhiyan, H. Intrinsic viscosity of cress (Lepidium sativum) seed gum: Effect of salts and sugars. Food Hydrocolloids, 2014; 35:100-105. https://doi.org/10.1016/j.foodhyd.2013.04.019