IJMPR 2020, 4(4), 89-94

International Journal of Modern Pharmaceutical Research
www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Research Article
SJIF Impact Factor: 5.273

FORMULATION AND CHARACTERIZATION OF MOUTH DISSOLVING FILM OF LICORICE FOR THE TREATMENT OF MOUTH ULCER

Sheetal Parse* and Milind Umekar

Smt Kishoritai Bhoyar College of Pharmacy, Deparment of Pharmaceutics, Kamptee Nagpur Maharashtra.

Received on: 08/06/2020
Revised on: 29/06/2020
Accepted on: 19/07/2020

***Corresponding Author**
Sheetal Parse
Smt Kishoritai Bhoyar College of Pharmacy, Deparment of Pharmaceutics, Kamptee Nagpur Maharashtra.

ABSTRACT

Herbal medicine are important and good for action. Oral mouth dissolving drug delivery system is considered to be an important alternative to the peroral route for the systemic administration of drugs, as it considered the most convenient, easy, safest route of administration. Mouth dissolving film may be preferred over the mouth dissolving tablets in terms of flexibility and comfort. The aim of this study is to formulate and characterize oral mouth dissolving film of licorice. Oral films were prepared by Solvent casting method using HPMC-E 15, Propylene glycol, and other recipients. Films were evaluated for mechanical properties, disintegration time, and in-vitro drug release.

KEYWORDS: Mouth dissolving film, licorice, Solvent evaporation method, mouth ulcer.

INTRODUCTION

Fast dissolving drug delivery is rapidly gaining interest in the pharmaceutical industry because they are easy to administer and lead to better patient compliance. These systems either dissolve or disintegrate generally within a minute, without water or chewing. This system has emerged as a convenient way of taking unit dose of medication to normal as well as pediatric and geriatric patients who may face difficulty in swallowing conventional tablets or capsules and liquid orals or syrup. Fast dissolving dosage forms include tablets, films/strips and microspheres (Aggarwal J et. al 2011). It is also called as oral wafers or strips. Mouth dissolving film may be preferred over the mouth dissolving tablets in terms of flexibility and comfort. MDF are typically designed for oral administration, with the user placing the strip on or under the tongue (sublingual) or along the inside of the cheek (Buccal). These drug delivery options allow the medication to bypass the first pass metabolism, thereby increasing its bioavailability (Kulkarni PK, 2011; GavaskarB, 2010).

Glycyrrhiza glabra belonging to family Leguminoceae is well known for its expectorant and demulcent activity. liquorice is also effective in the reduction of pain and inflammation of stomatitis mouth ulcers. Applying of liquorice root extract to stomatitis mouth ulcers can reduce ulcer size and speed healing.

Liquorice is a hardy herb or under shrub, erect grows to about 2m height. The roots are long, cylindrical, thick and multibranched. the used part of the plant is the root and rhizomes. A number of components have been isolated from liquorice, including a water soluble, biologically active complex that accounts for 40-50 percent of total dry material weight. This complex is composed of triterpene saponins, flavonoids, polysaccharides, pectin, simple sugars, amino acids, mineral salts, and various other substances. Glycyrrhizin, a triterpenoid compound, accounts for the sweet taste of liquorice root. Among the natural saponins, glycyrrhizic acid is a molecule composed of a hydrophilic part, two molecules of glucuronic acid, and a hydrophobic fragment, glycyrrhetic acid. The yellow colour of Liquorice is due to the flavonoids content of the plant, which includes liquiritin, iso liquiritin (a chalcone), and other compounds. The isoflavones glabridin and hispaglabridins A and B have significant antioxidant activity, and both glabridin and glabrene possess estrogens-like activity. Glycyrrhiza has the following, clinically proved Pharmacological activities such as anti ulcer activity, anti-asthmatic activity, anti-diuretic activity and anti hepato toxic activity (Geetha R.V 2011).

AIM AND OBJECTIVE

Aim of the present investigation is to prepare and characterize oral mouth dissolving film. The objective is to extraction of active constituent from liquorice root, prepare a mouth dissolving film and study the effect of herbal drug licorice use for mouth ulcer anti bacterial activity.

Experimental Work

Formulation of Fast Dissolving Films by Solvent casting method

In this method, firstly at the speed of 1,000 rpm the water soluble polymers are dissolved in water and heated up to 60^{o}C. All the other excipients like colors, flavouring

agent, sweetening agent, etc. are dissolved separately. Finally, both the solutions obtained are mixed thoroughly with stirring at the speed of 1000 rpm. The API dissolved in suitable solvent is incorporated in the above obtained solution. By using vacuum the entrapped air is removed. The resulting solution is cast as a film and allowed to dry and then it is cut into pieces of the desired size. (Rajni Bala, 2013).

METHODOLOGY

Extraction of drug

50 g Powder of licorice roots is used for the isolation of glycyrrhizin by the hyroalcoholic mesaration in ratio of 70:30 (alcohol: water) for 7 days alcoholic content are removed by evaporation on water bath. It contains about 7% of glycyrrhizin a sweet principle.

Preparation of film

The solvent casting method is used for the preparation of fast dissolving strip formulation. The oral fast dissolving strips were prepared by taking ingredients in different concentration of drug (licorice) and HPMC E15 and propylene glycol. HPMC was dispersed in distilled water followed by continuous stirring up to 1 hr on magnetic stirrer and kept for 30 min to remove all the air bubbles entrapped. To this plasticizer (propylene glycol) was added. Solution of aspartame was prepared in separate container.

Both the solutions were mixed together followed by keeping the solution mixture standing for 15-30 min to let the foams settle down. Then this solution was kept in sonicator for at least 15 min. The resulting solution was casted in specific amount(calculated according to the batch size) on a suitable inert platform of film former and the temperature of the film former was set to 40°c.After drying the film was scraped from the film former. Then the film was checked for any imperfections and cut according to the size required for testing(1×1inches). The samples were a glass container coated with aluminium foil maintained at appropriate temperature.

Composition of formulation of films

Formulation code	Ingredients				
	HPMC E15 (mg)	Propylene glycol (ml)	Glycyrrhiza (mg)	Aspartame (mg)	Distilled water in ml
F1	150	0.2	20	5	5
F2	150	0.2	50	5	5
F3	150	0.2	100	5	5
F4	150	0.2	150	5	5
F5	150	0.5	200	5	5

Drug characterization

A. Identification of glycyrrhizin

Glycyrrizin is basically triterpinoids and saponin glycoside which are conformed by foam test and hemolytic test.

B. TLC of glycyrrhizin

Silica gel G Plate activated in oven 105 degree for 20min
Solvent system-
Toluene: Ethyl acetate: Glacial acetic acid
12.5ml: 7.5ml: 0.5ml Detected by spraying anisaldehyde –sulphuric acid

C. % Practical Yeild

%Practical yield=Pratical yield/Therotical yield*100

D. Solubility Studies

Solubility Studies A solubility study was carried out to find out the solubility of drug in different solvents. According to this method, the pure drug was added to the solvent medium and shaken. The saturation was confirmed by observation of presence of un-dissolved material.

E. UV-Visible Spectrophotometric Analysis

Standard calibration curve of glycyrrhizin

10mg of glycyrrhizin was dissolved in 10 ml of distilled water and volume was made up to 100ml in a volumetric flask. And then pipette out this solution to prepared the serial dilution, solutions with concentration 10µg/ML, 20µg/ml, 30µg/ml, 40µg/ml and 50µg/ml were prepared as shown in table 2. was measured on a Shimadzu Double Beam Spectrophotometer(UV1601) at 254nm.

F. Antibacterial activity

Antimicrobial assay

Agar well-diffusion method: the agar diffusion method was to screen the antibacterial activity of all extracts of roots of Glycyrrhiza glabra used. Seeded broth containing test organism was inoculated on solidified agar and spread uniformly. The 3 wells were cut in the agar layer of each plate with an aluminum bore of 6 mm diameter. One for control and remaing two for test sample. In every plate extract of concentration 10mg/ml in ether. Then all plates were incubated at 370C ± 1for 24 hours. After the incubation period the mean diameter of the zone of inhibition in mm obtained around the well was measured.

Evaluation of Mouth Dissolving Film (khatoon et al, 2014)

Mouth dissolving film was evaluated for Visual appearance, weight variation, thickness of the film, folding endurance disintegration time as given in table.

Visual appearance

The fast dissolving films were evaluated by visual observation such as transparent and semi transparen t nature of film.

Weight variation of the film
2.5×2.5 cm film was cut from different locations in the caste film. The weight of each film strip was taken and the weight variation was calculated.

Thickness
The thickness of the film was measured by the micrometer and the average thickness was calculated and shown in table 3.

Folding endurance
The folding endurance is expressed as the number of folds required for breaking the specimen or developing visible cracks. This gives an indication of brittleness of the film. A small strip of 2.5×2.5 cm was subjected to this test by folding the film at the same point repeatedly several times until a visible crack was observed.

Disintegration time
Disintegration time study was slightly modified to mimic the in-vitro and in-vivo conditions. For the study, film as per the dimension (2.5×2.5cm) required for dose delivery was placed in a basket containing 900 mL distilled water. Time required for the film to break and disintegrate was noted as in-vitro disintegration time.

Drug content
A film of 1.5×1.5cm was cut and dissolved in 100ml of 0.5% SLS and filtered. From this solution 1mL of solution was pipette out and the volume was made upto 10mL. The drug is determined spectroscopically at 254nm.

RESULTS AND DISCUSSION

Test for glycrri hizin.

Test	Observation	Inference
Saponin glycoside		
Foam test	foam was produced	Saponin glycoside confirmed
Heomolytic test	break down of rbc observed.	Saponin glycoside confirmed

- %Practical yield=Pratical yield/Therotical yield*100
- % practical yeild =6.3/7*100 = 90%

Rf = distance travelled by solute from origin/ Distance travelled by solvent from origin
=2.5/6
Rf =0.41

Fig. 1: TLC of Glycyrrhizin.

Rf value	0.40cm
%Practical yield	90%

Concentration(µg/mL)	Absorbance
0	0
10	0.2099
20	0.5470
30	0.9258
40	1.1047
50	1.2858

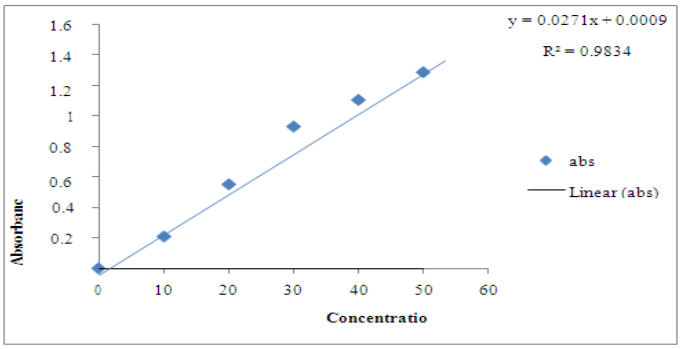
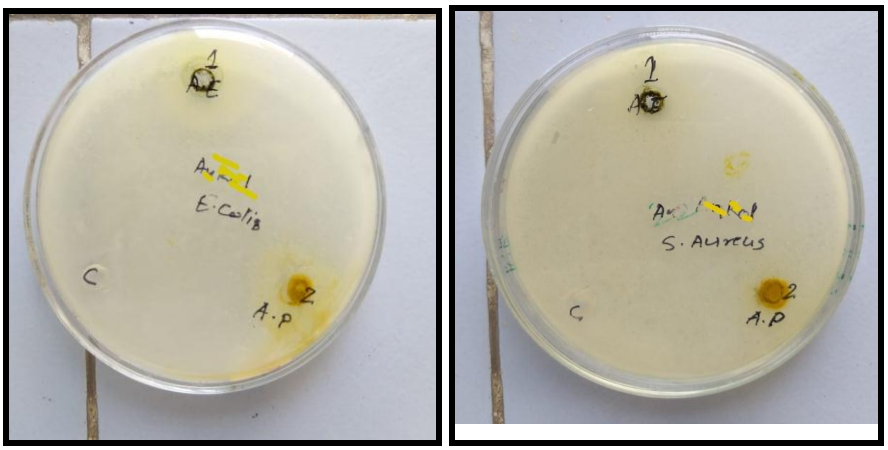


Fig. 2: Standard Calibration Curv.

Antibacterial activity

Zone of inhibition shows antibacterial action againt micro organism.



Zone of inhibition againt E.coli **Zone of inhibition againt S.aureu**

Fig. 3: Biological Activity of Glycyrrizin.

Evaluation of Mouth Dissolving Film

The evaluation of mouth dissolving film was carried out by using following parameters given follows

A. Visual Appearance

On visual appearance it was observed that all the film formed by using propylene glycol was transparent in appearance as given in figure no 1.

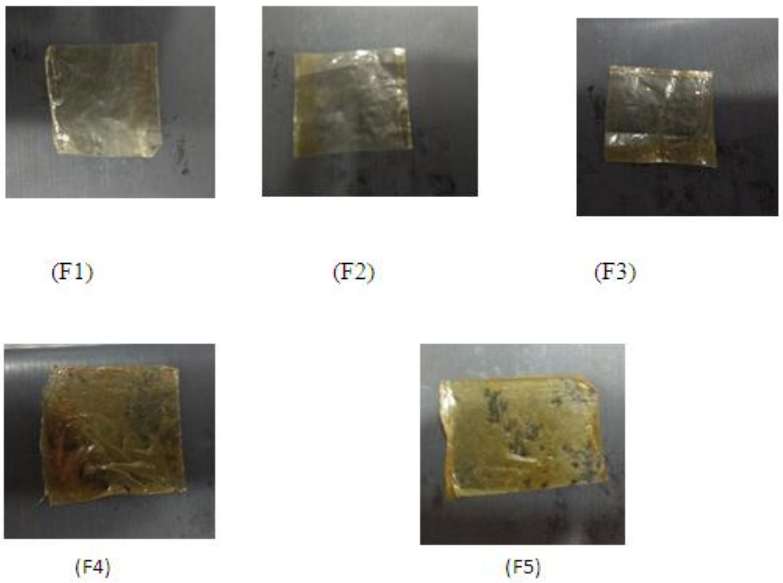


Fig. 4: Visual Appearance of Flims.

B. Weight variation of the film

The weight of the prepared films was determined by using digital balance. The films showed weight variation ranging from 12 to 32.66 ± 1.33 mg for the films.

C. Thickness of the film

The thickness of the film was measured by Vernier Callipers and the average thickness was calculated. All the films have uniform thickness throughout. The thickness of all the formulations ranged between 0.15 ± 0.05 to 0.26 ± 0.05mm.

D. Folding endurance

The film formed by using 0.1ml (F3) of PEG-400 have least value of folding endurance while film of 0.1ml (F4) show height value of folding endurance.

E. Disintegration time

The In-vitro disintegration time of films prepared with HPMC was in the range of 35±1.18 to 41±1.14 sec. Based on the *in-vitro* disintegration time, formulation F7, F8 and F9 were found to be promising and showed a disintegration time of 39, 34 and 30 sec respectively.

F. Drug content

The drug content of all the films was in the range of 96.27 to 99.68 % suggesting that drug was uniformly dispersed throughout all films.

Table 1:

F. Code	Visual Appearance	Weight of films in mg±SD	Thickness in µm ±SD
F1	Transparent Pale yellow colour	12±0.57	0.20±0.05
F2	Transparent Pale yellow colour	15.33±0.33	0.15±0.05
F3	Transparent Pale yellow colour	13.33±0.88	0.21±0.02
F4	Transparent Pale yellow colour	31.33±0.88	0.26±0.06
F5	Transparent Pale yellow colour	32.66±1.33	0.25±0.05

Table 2:

F.Code	Folding endurance	Disintegration time in sec±SD	Drug content in%
F1	71±0.23	39±0.10	96.27
F2	78±0.15	41±0.21	97.11
F3	85.5±0.25	41±0.15	96.85
F4	92±0.12	35±0.20	99.68
F5	84±0.18	38±1.25	98.46

SUMMARY AND CONCLUSION

Summary

Glycyrrhizin used for the treatment of expectorant and demulsant and to relieve symptoms of mouth ulcer In present research work an attempt has been made to prepare mouth dissolving films of glycyrrhizin were prepared using different concentration of glyctrrhizin. The fast dissolving oral film evaluated for folding endurance, Thickness surface pH, in-vitro disintegration time, drug content,. The physical appearance and folding endurance properties were found to be good.

In the present study, each mouth dissolving film was 2.5×2.5 cm in size and contained 20 ,50, 100,150,200 mg repectively. The thickness of the films was approximately 0.02-0.04 mm. The film disintegrated completely within 1 minutes.

CONCLUSION

According to the results of this study, liquorice is effective in the reduction of pain and inflammation of stomatitis mouth ulcers. The results of this study confirmed that applying of liquorice root extract to stomatitis mouth ulcers can reduce ulcer size and speed healing

Antimicrobial study shows effective zone of inhibition againt the Glycyrrhiza glabra belonging to family Leguminoceae is well known for its expectorant and demulcent activity. From the above study we can also conclude that it also exhibits good antimicrobial activity against various bacterial strains microorganism.

REFERENCES

1. Aggarwal J, Singh G, Saini S et al. “Fast dissolving films: A novel approach to oral drug delivery”. International Research Journal of Pharmacy, 2011; 2: 69-74.
2. BhuraN,Sanghivi K, Patel U, Parmar B. “A Review on Fast Dissolving Film”.Int J Res Bio Sci, 2012; 3: 66-9.
3. Squier CA, Lesch CA et al. “The permeability of human oral mucosa and skin to water. Journal of Dental research, 1989; 68: 1345-9.
4. Collins LM and Dawes C. The surface area of the adult Human mouth and thickness of salivary film covering the teeth and oral mucosa. J Dent Res., 1987; 66(8): 1300-2.
5. Delivery System, International Journal of Pharmaceutical Research & Allied Sciences, 2013; 2(1): 14-24.
6. Gavaskar B, Vijay K, Sharan G. Overview on “Fast

Dissolving Films". International Journal of Pharmacy and Pharmaceutical Science, 2010; 2: 29-33.
7. Harris D, Robinson JR., "Drug delivery via the mucous membranes of the oral cavity" J Pharm Sci., 1992; 81(1): 1-10.
8. Kaur Mandeep, Rana AC, Seth N, "Fast Dissolving Films: An Innovative Drug". Int J Pharm Res Allied Sci., 2013; 2(1): 14-24
9. Kulkarni PK, Dixit M, GunashekaraK, Kulkarni "A Formulation and Evaluation of Mouth Dissolving Film containing Rofecoxib". International Research Journal of Pharmacy, 2011; 2: 273-278.
10. Preis MK. an Oromucosal film preparations for pharmaceutical use "Formulation development and analytical characterization", February 2014.
11. Naziya Khatoon, N.G. Raghavendra Rao*, B. Mahipal Reddy - Formulation and Evaluation of Oral Fast Dissolving Film of Montelukast Sodium International Journal of Pharmaceutical Sciences and Research. IJPSR, 2014; 5.
12. Rajni Bala, Pravin Pawar, Sushil Khanna, Sandeep Arora "Orally Dissolving strips: A New Approach To Oral Drug Delivery System", International J. Pharm Investigation, 2013; 3(2): 67-76.
13. Vijaykumar Ghorwade, Ajaykumar Patil et. al., "Development and Evaluation of Fast Dissolving Film of Montelukast Sodium" World Journal of Medical Pharmaceutical and Biological Sciences, 2011; 1(1): 06-12.
14. Wertz and Squier et al., "Comparison of Lipids from Epidermal and palatal stratum corneum" Journal of investigative Dermatology, 1992; 98(3).
15. Fan Y. G.; Shi Z. Q.; He B. L.; Extraction separation and application for glycyrrhizic and glycyrrhetic acid. Natural Product Research and Development, 1996; 8: 93-99.
16. Salwa Khalil and Khidir A.M. Hassan., Liquorice Mouth Washes As Treatment for Mouth Ulcer, Indo Am. J. P. Sci, 2018; 05(02).
17. Manoj M. Nitalikar et al/Int.J Antimicrobial assay of glycyrrhizin (licorice). PharmTech Res., 2010; 2(1).
18. M.Akram, Shahab-uddin, Afzal Ahmed, Khan Usmanghani, Abdul Hannan, E. Mohiuddin, M. Asif and S. M. Ali Shah Glycyrrhiza glabra L. Medicinal uses, Medicinal Plants Research, 2011; 5(25): 5658-5661.
19. Lakshmi T, Geetha R.V. Glycyrrhiza glabra Linn commonly known as licorice: a therapeutic review, Pharmacy and Pharmaceutical Science, 2011; 3(4): 1-6.
20. Vijay S. J Santosh K S , Pankaj Khatri and Ashish K Sharma Recent Pharmacological Trends of Glycyrrhiza glabra Linn, International Joournal of Pharmaceutical Frontier research, 2011; 1(1): 170-185.