ejpmr, 2022, 9(10), 513-518

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND EVALUATION OF POLYHERBAL LOZENGES FOR THE TREATMENT OF ORAL ULCERS

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Article Received on 17/08/2022 **Article Revised on 06/09/2022** **Article Accepted on 27/09/2022**

ABSTRACT

Herbal Medicines are still the mainstay of about 75-80% of the world's population, mainly in developing countries. They are found mainly in tropical and subtropical regions of the India for primary health care because of better compatibility with human body, cultural acceptability and lesser side effects. Herbal Formulations are derived from Herbal plant extracts and these are being increasingly utilized to treat a wide variety of diseases. The main objectives of present investigation were to formulate and evaluate polyherbal lozenges for the treatment of oral ulcers by using ethnolic extracts of guava, liquorice, neem, tulasi and different concentration of Hydroxypropyl Methylcellulose, Methylcellulose polymers. The prepared polyherbal lozenges formulations were characterized for various parameters like hardness, thickness, weight variation, friability and dissolution by standard pharmacopeia methods. However, that among all formulations, HF3 Polyherbal Lozenges was proved most promising formulation as it showed that 93.74 % drug release with in 30 minutes. The diameter, thickness and hardness of lozenges were found to be 16.11±0.08mm, 6.552±0.02mm and 5.5 ± 0.3 (kg/cm^2) respectively. The percentage of weight variation was found to be 3000.6 ± 2.65 mg. The friability of lozenges was found to be 0.92 ± 0.02 (%). Among all the Formulations HF3 with HPMC Polymer Polyherbal Lozenges showed best results because all the Evaluation parameters showed satisfactory results.

KEYWORDS: Guava, Liquorice Neem, Tulasi, Polyherbal formulation, Lozenges, Ulcer treatment.

I. INTRODUCTION

India is one of the countries where different traditional systems of medicines are practiced. These systems depend upon plant resources to a great extent for the raw materials. Herbal medicines are still the most preferred by about 75–80% of the world's population (mainly in developing countries) for primary healthcare due to better cultural acceptability, better compatibility with the human body, and lesser side-effects. It is estimated that approximately, one quarter of prescribed drugs contain plant extracts or active ingredients obtained from or modeled on plant substances.[1,2] Indian spices used in the kitchen until today are useful, and generations of Indians depend upon them for their curative properties. Unani doctors, Ayurvedic, prescribe them and Homeopathic doctors respected for their skills in weeding out the root cause of many diseases.

1.1. Mouth Ulcers

Mouth Ulcers usually develop on the inside of the lips and cheeks and on the underneath and edge of the tongue. Mouth ulcers can occur in any age group or population. Mouth ulcers can be the result of a mild condition, such as a canker sore or excessive or overly aggressive tooth brushing. Mouth ulcers can also be the result of a moderate condition, disorder or disease, such as gingivitis or a cold sore. Mouth ulcers can also occur due to some diseases, disorders and conditions that can be serious, even life-threatening. These include oral cancer and leukoplakia.

1.2. Causes of mouth ulcers

Mouth ulcers can be caused by a wide range of factors including:

- Accidentally biting the inside of your cheek.
- Injury from a toothbrush (such as slipping while brushing).
- Constant rubbing against misaligned or sharp/broken teeth.
- Constant rubbing against dentures or braces.
- Burns from eating hot food.
- Irritation from strong antiseptics, such as a mouthwash.
- Viral infections such as the herpes simplex viral infection (cold sore).

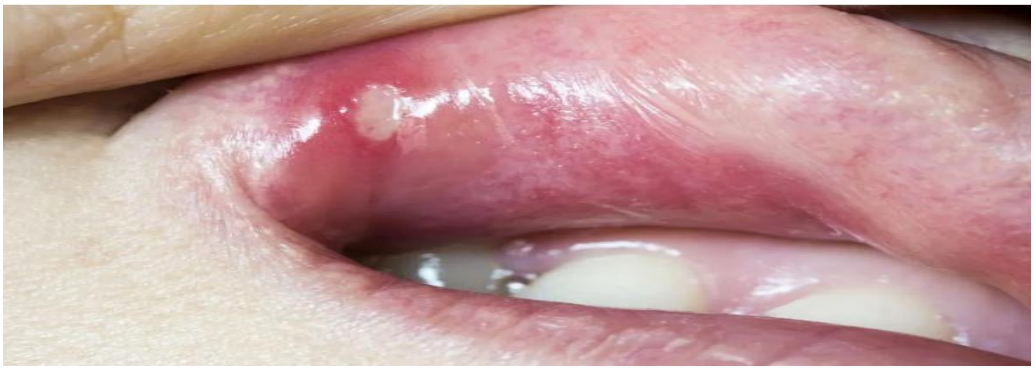
1.3. Sign & Symptoms

Some people feel a tingling or burning on the inside of the lips or cheeks, 1 -2 days before an ulcer

appears. Ulcers can be painful, and the pain can be made worse by food, drink, and poor oral hygiene.

Mouth ulcers are

- ❖ appear as extremely painful ulcers in the mouth
- ❖ recur very quickly, so infections seem continuous
- ❖ increase in size, eventually coming together to form a large, ragged ulcer
- ❖ Take 10 or more days to heal without scarring.
- ❖ appear anywhere in the mouth
- ❖ They tend to be found in more females than males and are more common in older adults.
- ❖ Loss of appetite.



Oral Mouth Ulcer

2. MATERIALS AND METHODS

2.1. Collection

The Fresh Plant Leaves of Guava, Neem, Tulasi were collected from a medicinal garden of our college and Liquorice powder were collected and purchased from herbal medical store. Other Polymers and chemicals used in present study were of analytical grade.

Table 2: 1.1 List of chemicals.

Sr.No	Chemicals	Name and address
1	Hydroxypropyl Methylcellulose	Qualikems fine chem. Pvt ltd, india
2	Methyl Cellulose	Qualikems fine chem. Pvt ltd, india
3	Sucrose	Isochem laboratory ,india
4	Dextrose	Labogens industries
5	Glycerin	Finar Chemicals limited, india
6	Propylene Glycol	Qualikems fine chem. Pvt ltd, india
7	Methyl Paraben	Oxford laboratory , india
8	Propyl Paraben	Oxford laboratory , india
9	Pepperment oil	Agrawal enterprises.Mumbai.

2.2. EXTRACTION

Preparation of Ethanolic Extract of Herbal Plant Materials

In the present study, the leaves and roots were carefully selected washed to remove impurities and shade dried. The dried material was reduced to fine powder in the mechanical grinder. The fine powder was passed through sieve no.43 and stored in an airtight container for further use. About 100 gm of powdered material was extracted with ethanol as a solvent by hot extraction method using Soxhlet apparatus. The extraction was continued until the solvent in the thimble became clear then few drops of solvent were collected in the test tube during the completion of the cycle and chemical test of the solvent was performed. After each extraction, the extract evaporation was done by using electronic water bath. Moreover, some part of the extract was preserved for preliminary Phytochemical screening for the detection of various plant constituents and rest extract was used for formulation of Polyherbal lozenges batches.

Table 2.2.1. Composition of extract.

S.No	Name of ingredients	Quantity
1	Extract of Liquorice	0.350 mg
1	Extract of Guava	0.350 mg
2	Extract of neem	0.150 mg
3	Extract of tulasi	0.150 mg

2.3. FORMULATION OF POLYHERBAL LOZENGES

2.3.1. PREFORMULATION STUDY

Preformulation studies are needed to ensure the development of a stable as well as effective and safe dosage form. It is a stage of development during which the pharmacist characterizes the physico –chemical properties of the drug substances and its interaction with various formulation components. Goals of Preformulation study: To determine the necessary physico- chemical parameter of a new drug substance.

2.3.2. Experimental design

During formulation two thinking agents used at different concentrations, resulting in six different batches of polyherbal lozenges for herbal extract, total six batches prepared. In this case Hydroxypropyl Methylcellulose (HPMC) and Methylcellulose these two types of thinking agents were taken.

2.3.3. Preparation of Polyherbal Lozenges

The polyherbal hard lozenges were prepared by heating and congealing technique. Using general principles a base formula was created to achieve desired weight per each lozenge usually of 1 to 3 grams. The quantity of each ingredient needed for compounding was calculated for 20 lozenges and the enough material for two extra lozenges were calculated and weighed. Syrup base was prepared in a copper vessel by dissolving the required amounts of sugar in water by heating and stirring for 2 hours by raising the temperature to 140 °C. Dextrose was dissolved in small quantity of water and heated it to 110 °C till dextrose dissolves completely forming as clear viscous syrup. Then the dextrose solution was poured into the sugar syrup. Heating and stirring were continued for 2 hours by raising the temperature to 160 °C till the colour changes to golden yellow. The temperature was brought down to 90 °C till a plastic mass was obtained. The Herbal drug formulation, polymer, colour, flavour were added and mixed for 30 min. The mixture was poured into the molds. Air drying was done for 2 hours. The prepared lozenges were wrapped in aluminium foil and stored in desiccators to prevent moisture uptake.

HEAT & CONGEALING METHOD

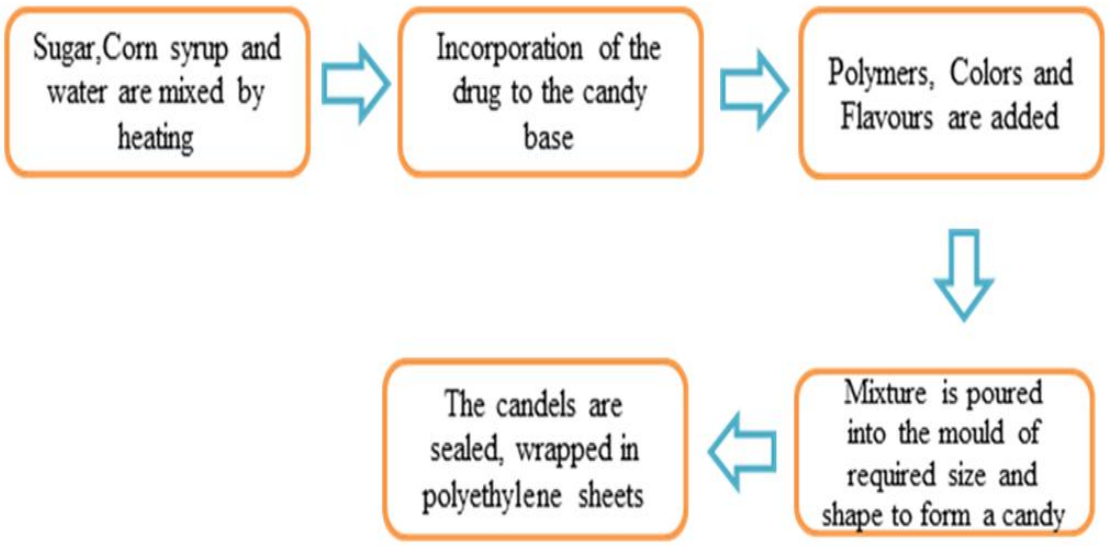


Table 2.3.4. Quantitative composition of polyherbal Lozenges.

INGRIDIENTS	HF1	HF2	HF3	HF4	HF5	HF6
Polyherbal Extract (gm)	1	1	1	1	1	1
Sucrose (gm)	1.5	1.5	1.5	1.5	1.5	1.5
Dextrose (mg)	300	200	100	300	200	100
Hydroxypropyl Methylcellulose (mg)	100	200	300	-	-	-
Methyl Cellulose (mg)	-	-	-	100	200	300
Glycerin(ml)	1	1	1	1	1	1
Propylene glycol(mg)	100	100	100	100	100	100
Methyl paraben(g)	0.2	0.2	0.2	0.2	0.2	0.2
Propyl paraben(g)	0.1	0.1	0.1	0.1	0.1	0.1
Flavouring Agents	q.s	q.s	q.s	q.s	q.s	q.s

Herbal Lozenges

3. PHYSICOCHEMICAL EVALUATIONS

A) Appearance/clarity

The Herbal Lozenges formulations were observed carefully by naked eye for appearance, colour, odour and presence of suspended particulate matter if any. It was further assessed by observing them against a dark and white background.

B) Diameter and thickness

Diameter of the lollipop is important for uniformity of lozenges size. It can be measured using Vernier Calipers. The extent to which thediameter of the lozenges deviated from ± 5% of the standard value.

Figure: 3.1.1. Measurement of Diameter and Thickness.

C) Hardness

The hardness of lozenges from all the batches was determined using the Pfizer or Monsanto hardness tester.

D) Friability

For each formulation, the friability of 20 Lozenges was determined using the Roche friabilator. In this test tablets were subject to the combined effect of shock and abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre weighted 20 Lozenges was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 min.

The tablets were then dusted and reweighed. Percent friability (%F) was calculated as follows,

$$\% F = loss\ in\ weight\ /\ Initial\ weight \times 100$$

E) Weight variation

Every individual tablet in a batch should be in uniform weight and weight variation within permissible limits. Twenty lozenges were randomly selected and accurately weighted using an electronic balance. The results are expressed as mean values of 20 determinations.

F) In-vitro drug release

Dissolution studies were performed on lozenge formulations in a calibrated 8 station dissolution test apparatus (LABINDIA) equipped with paddles (USP apparatus II method) employing 900 ml of 0.1 N Hcl as dissolution medium. The paddles were operated at 50 rpm and temperature was maintained at 37 ºC ± 1 ºC throughout the experiment. The samples were withdrawn at 5, 10, 15, 20, 30 and 45 minutes and replaced with equal volume of same dissolution medium to maintain the constant volume throughout the experiment and were estimated by ELICO double beam U.V spectrophotometer at 229 nm. The dissolution studies on each formulation were conducted in triplicate. From the dissolution profiles of % drug released versus time plots various in vitro dissolution parameters like T50, and DE30% were calculated as suggested by Khan.[8]

Dissolution Conditions

Medium Phosphate buffer Ph 6.8 at 37 ± 0.5 ^{0}c
Volume of medium in the jar: 900 ml
Apparatus : USP Apparatus type II (Paddle)
Rpm : 50
Time intervals : 5, 10, 15,20,25,30 Minutes.

4. RESULTS AND DISCUSSION

The present work aimed to increase anti ulcer activity of Polyherbal Lozenges formulation with using various polymers and excipients. The prepared formulations were characterized for Physical appearance, Diameter and thickness, Hardness, Friability, Weight variation, In-vitro drug release Studies.

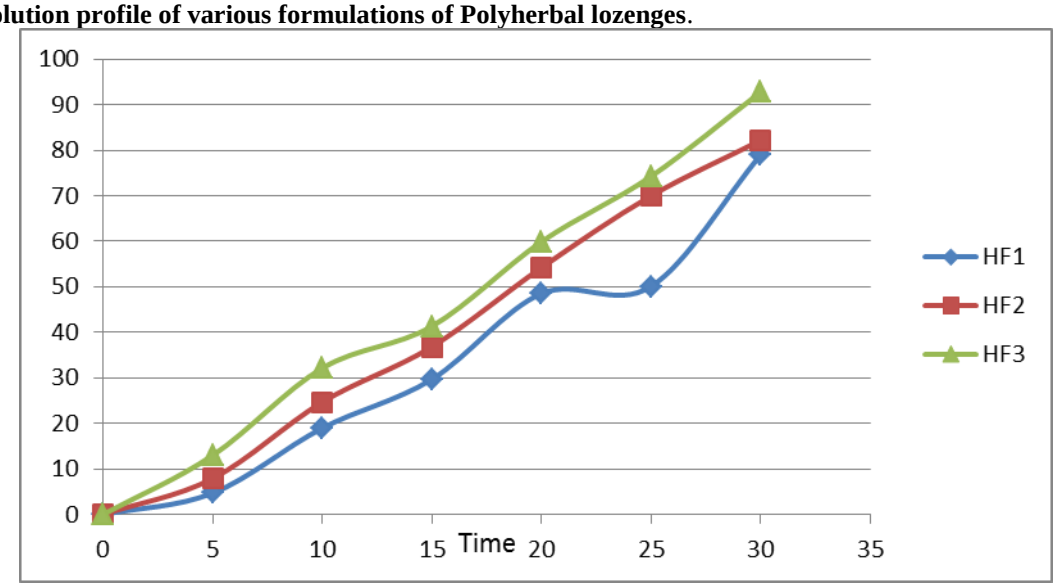
4.1. Evaluation Parameters Results

Formulations	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Diameter (mm)	Friability (%)	Moisture content %
HF1	2998.2 ±2.64	4.6 ±0.2	5.962±0.01	14.10 ± 0.05	0.54 ± 0.01	0.70 ± 0.02
HF2	3000.5 ±1.42	4.8 ±0.1	6.173±0.03	15.17±0.04	0.69 ± 0.03	0.80 ± 0.03
HF3	3000.6 ± 2.65	5.5 ± 0.3	6.552±0.02	16.11±0.08	0.92 ± 0.02	0.94 ± 0.01
HF4	3000.6 ±2.22	4.5 ± 0.1	5.150±0.01	14.15±0.06	0.49 ± 0.02	0.62 ± 0.02
HF5	2999.1 ±3.35	4.8 ±0.3	5.841±0.02	15.18±0.07	0.59 ± 0.05	0.70 ± 0.03
HF6	3000.7 ±2.42	5.1 ± 0.4	6.180±0.03	16.11±0.08	0.68 ± 0.02	0.84 ± 0.02

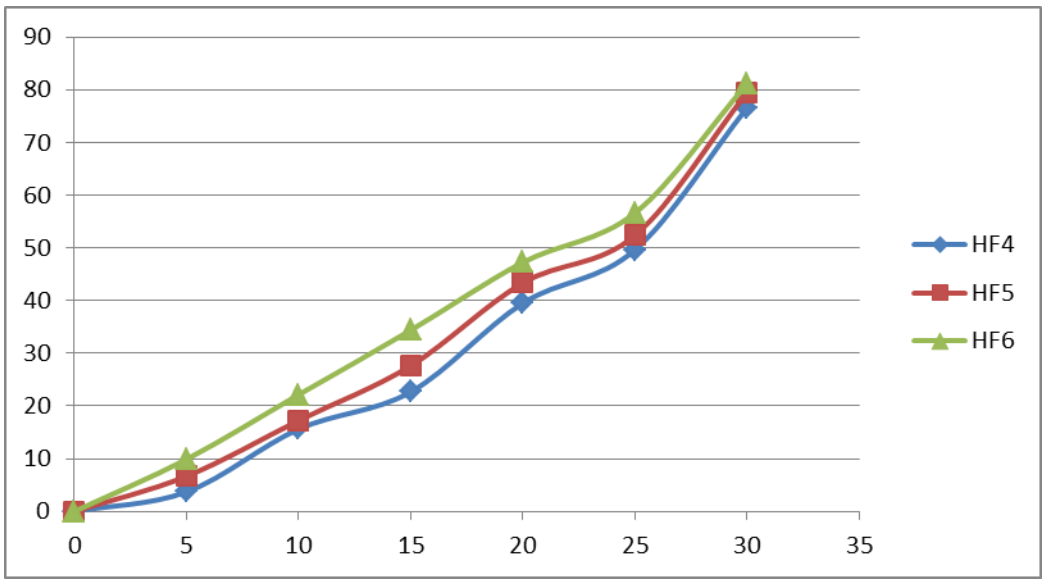
4.2. Cumulative Percent Release of Polyherbal Lozenges Containing Varying Concentration of Different Polymers.

Time(min)	HF1	HF2	HF3	HF4	HF5	HF6
0	0	0	0	0	0	0
5	4.68	7.88	12.96	3.71	6.68	9.91
10	18.96	24.66	32.12	15.62	17.25	22.16
15	29.68	36.81	41.32	22.68	27.63	34.38
20	48.51	54.19	59.89	39.52	43.36	47.26
25	50.07	69.95	74.23	49.63	52.36	56.63
30	78.94	82.14	93.74	76.62	79.49	81.14

4.3. Dissolution profile of various formulations of Polyherbal lozenges.



In-vitro release studies of HF1, HF2, HF3



In-vitro release studies of HF4, HF5, HF6

5. SUMMARY AND CONCLUSION

- Herbal Lozenges are more acceptable in the belief that they are safer than synthetic one. It is very good attempt to establish the Herbal Lozenges containing ethnolic extracts of Guava, Liquorice, Neem, Tulasi. These plants have been reported in literature having good anti-ulcers, anti-inflammatory, anti oxidant activity.
- It can be concluded from the present investigation that proper selection of polymers and drug is a prerequisite for designing and developing a oral drug delivery. The physical compatibility studies suggest that polymers selected i.e. Hydroxypropyl

Methylcellulose, Methylcellulose were found to be compatible with drug extract.

- All the formulations were evaluated by determining various parameters like hardness, thickness, weight variation, friability and dissolution by standard pharmacopeia methods.
- However, the Hydroxypropyl Methylcellulose based HF3 Polyherbal lozenges proved to the formula of choice, since it showed the highest percentage of proved most promising formulation as it showed that 93.74% drug release within 30 minutes. Formulations HF3 with HPMC Polymer Polyherbal Lozenges showed best results because all the Evaluation parameters showed satisfactory results.

6. ACKNOWLEDGEMENT

We thank our Principal Dr. N.M.Vageesh sir, Mrs. Sowjanya madam and Mr U.P. Veeresh sir and SJCPS Staff of st johns college of pharmaceutical sciences, Yemmiganur, Andhrapradesh for providing all the facilities to conduct this work.

REFERENCES

1. Zain R "Classification, epidemiology and aetiology of oral recurrent aphthous ulceration stomatitis". Annal Dent Univ Malaya, 1999; 6: 34-37.
2. Jurge S, Kuffer R. "Recurrent aphthous stomatitis". Mucosal disease series, 12: 1–21.
3. Crispian S, Meir G "The diagnosis and management of recurrent of aphthous stomatitis" American Dental Association, 2003; 134: 200-207.
4. Cohen ML. Epidemiology of resistance: Implicationfor a post- antimicrobial era. Science, 1992; 257: 1050-1055.
5. Barrons RW. Treatment strategies for recurrent oral aphthous ulcers. Am J Health Syst Pharm, 2001; 58(1): 41-50.
6. Stanley HR. Aphthous lesions. Oral Surg Oral Med Oral Pathol, 1972; 33(3): 40716.
7. Bafna, P.A. and Balaraman, R "Anti-ulcer and antioxidant activity of DHC-1*, a herbal formulation", J. of Ethno. pharmacology, 2004; 90: 123-127.
8. Sircus W, Church R, Kelleher J. Recurrent aphthous ulceration of the mouth; a study of the natural history, aetiology, and treatment. Q J Med, 1957; 26(102): 235-49.
9. Hoogstraate, A.J. and P.W. Wertz. Drug delivery via the buccal mucosa, 1998.
10. Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, Häyrinen-Immonen R. Recurrent aphthous ulcers today: A review of the growing knowledge. Int J Oral Maxillofac Surg, 2004; 33(3): 221-234.
11. Boldo A. Major recurrent aphthous ulceration: Case report and review of the literature. Conn Med, 2008; 72(5): 271-273.
12. Kini, R., Rathnanand, M. and Kamath, D. 2011. Investigating the suitability of isomalt and liquid glucose as sugar substitute in the formulation of Salbutamol sufate hard candy lozenge. J. Chem. Pharm. Res.
13. Bhowmik D, Pankaj C, Tripathi KK, Chandira MR, Kumar KPS. Zingiber officinale the herbal and traditional medicine and its therapeutically importance. ResJ Pharmacognos Phytochem, 2010.
14. Aulton ME. Pharmaceutics: the science of dosage form design. Churchill Livingstone, 2000.
15. Esimone CO, Onuh PU, Egege MK, Ugoeze KC, Obitte NC. In vitro evaluation of lozenges containing extracts of roots of Zapoteca portoricensis (FAM: Fabaceae). J Pharmacol Toxicol, 2009.
16. Raymond, C Rowe., Paul, J Sheskey., Sian, C Owen., Handbook of pharmaceutical excipients. Pharmaceutical press. Great Britain, 2006; 5.
17. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier JP, et al. (2004) Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disinte-gration. Int J Pharm, 2004.
18. Benbassat N, Kostova B, Nikolova I, Rachev D. Development and evaluation of novel lozenges containing marshmallow root extract. Pakistan Journal of Pharmaceutical Science, 2013.
19. Dharmajit Pattanayak., Saumya Das., Formulation Development and Optimization of Medicated Lozenges for Pediatric Use. IJPSR, 2012; 3(1): 138-140.
20. Irwin, R S., Curley, F J., Bennett, F M., Appropriate use of antitussive and protussives. A practical review, 1993; 46: 80-91.