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Formulation and Evalution of Polyharbal Lozenges for the Treatment of Mouth Ulcers

Ms. Sharma Gayatri B., Dr. Nagoba S.N.,Mr. Sarnaik Shreyas S.
Department of Pharmaceutics,
Channabasweshwar Pharmacy College (Degree), Latur
Kava Road, Basweshwar Chowk, Latur-413512 (Maharashtra)

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ABSTRACT: The objectives of this study was to formulate and evaluate herbal lozenges containing vitex negundo leaves extract and Safed Musliroot extract to treat aphthous or mouth ulcer. Mouth ulcer is also known as canker sores or aphthous ulcer. More than half of the world's population accepting the herbal medicine and major role of the herbal medicine including the use of plant extract and their active constituents. Herbal medicines are getting increasing patient compliance as they are avoiding typical side effects. Herbal plants showed wide range of pharmacological activities including antiulcer, antimicrobial**,** antioxidant, anti-inflammatory, antiviral, and antifungal. The herbal plants are useful for healing as well as for curing of human diseases due to presence of phytochemical constituents. Cordia diachotoma showed some essential Phyto constitutions such as alkaloids, tannins, glycosides, starch, saponin, phenols, flavonoids, diterpenes, protein and amino acid. I was prepared herbal lozenges by using vitex negundo leaf extract and Musli root extract with sucrose, dextrose, Mannitol, HPMC, xanthan gum and required amount of distilled water. The triethanolamine was added to maintain the pH (6.7-7.3) of oral mucosa.The evaluation of lozenges such as weight variation, thickness, hardness, drug content, in-vitro drug release and stability study etc. Developed herbal lozenges formulation was stable, safe and effective for the treatment of Aphthous ulcer.
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KEYWORDS: Vitex negundo leaves extract, Chlorophytum borivilianum root extract, Poly-herbal lozenges; oral ulcer.

I. INTRODUCTION

Overview India is among the nations where several ancient medical systems are still in use. These systems rely heavily onplant resources for their raw components. About 75–80% of people worldwide (mostly in developing nations) still prefer herbal medications over other forms of primary healthcare because of their greater cultural acceptability, more compatibility with the human body, and lower side effects. Plant extracts or active compounds derived from or based on plant components are thought to be present in about 25% of prescription medications. [1.2] Indian spices have been utilized in Indian cooking for many centuries because of their therapeutic qualities. They are prescribed by Unani doctors, Ayurvedic doctors, and homeopathic doctors who are renowned for their ability to identify.

1.1 Mouth Ulcer;

An ulcer that develops on the mucous membrane of the oral cavity is known as a mouth ulcer (also known as an oral ulcer or a mucosal ulcer). These are painful oral sores, usually on the inside of the cheeks or lips, that are round or oval in shape. Although mouth ulcers are extremely prevalent and can be linked to a wide range of illnesses through a variety of pathways, there is typically no significant underlying cause. Mouth ulcers can arise from a number of typical nutritional deficits, including those in iron and vitamins, B12 and C, poor dental hygiene, infections, tension, constipation, injuries from machines, allergies to certain foods, imbalanced hormones, skin conditions, etc.

Mouth ulcers, also called pharyngeal ulcers, can cause excruciating pain during eating, drinking, or brushing your teeth. Mouth ulcer can be categorized as minor, large or herpetiform based on their size and quantity.

1.2. Causes of mouth ulcers

1. Mouth ulcers can be caused by a wide range of factors including:
2. Accidentally biting the inside of your cheek.
3. Injury from a toothbrush (such as slipping while brushing).

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4. Constant rubbing against misaligned or sharp/broken teeth.
5. Constant rubbing against dentures or braces.
6. Burns from eating hot food.
7. Irritation from strong antiseptics, such as a mouthwash.
8. Viral infections, such cold sores caused by the herpes simplex virus. Control over the non-adaptive type.

1.3. Sign & Symptoms

- A few days before to the appearance of an ulcer, some patients experience tingling or burning in their cheeks or within their lips. Poor dental hygiene, food, and drink can exacerbate the pain associated with ulcers. oral ulcers are;
- They manifest as very painful oral ulcers.
- They recur quickly, giving the impression that infections are growing larger all the time and eventually combining to produce a big, jagged ulcer.
- It takes ten days or longer to heal completely.
- Show up anyplace in the oral cavity
- They are more common in older persons and tend to be detected in more females than males.
- Appetite loss.

Oral mouth ulcer

.II. MATERIALS AND METHOD

2.1 COLLECTION:

Vitex negundo and Safed Musli(Chlorophytum borivilianum) powder which can be purchased from Kshipra Biotech PVT LTD, Indoor, MP, IN. And other polymer and excipient and chemicals used in present study were of analytical grade

SR NO	CHEMICAL	SOURCES
1	Vitex Negundo Extract	Kshipra Biotech PVT.LTD
2	Safed MusliExtract	Kshipra Biotech PVT.LTD
3	Sucrose	DIPA Chemicals Industries, Mumbai.
4	Mannitol	Meher Chem, PVT, LTD Mumbai.
5	Dextrose	Meher Chem, PVT, LTD Mumbai.
6	Xanthan Gum	HI Media Lab PVT LTD Mumbai
7	HPMC	Meher Chem, PVT, LTD Mumbai.
8	Citric acid	HI Media Lab PVT LTD Mumbai
9	Mint flavor	Cosmo Chem, Pune
10	Amaranth	Meher Chem, PVT, LTD Mumbai.

III. EXTRACTION

PREPARATION OF ETHANOLIC EXTACT IF HARBAL PLANT MATERIALS.

In the present study, theleaves and root were carefully selected washed to remove impurities and shads dried. the dried materials were reduced to fine powder in the mechanicalgrinder the fine powder was passed through sieve no 43and stored in an airtight container for further use. About 100gm of powdered materials was extracted with ethanol as a solvent by hot extraction method using Soxhlet apparatus. Following the completion of the cycle and the chemical test of the solvent, a few drops of the solvent were collected in the test tube and the extraction process was repeated until the solvent in the thimble became clear. An electric water bath was used to evaporate the extract following each extraction. Moreover, some part of the extract was preserved for preliminary phytochemicals screening for the detection of various plant constituents screening forthe

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detection of various plant constituent and rest extract was used for formulation of poly herbal lozenges batch.

TABLE 2.2.1 COMPOSITION OF EXTRACT

SR.NO	NAME OF PLANT	QUANTITY
1	EXTRACT OF VITEX NERGUNDO	0.350mg
2	EXTRACT OF SAFED MUSLI	0.350mg

2.3 FORMULATION OF POLYHERBAL LOZENGES;

2.3.1 PREFORMULATION STUDY

To create a dosage form that is safe, effective, and stable, preformulation research is necessary. In this stage of development, the pharmacist provides a description of the physicochemical characteristics of medicinal substances and their interaction with various ingredients. Objectives of the preliminary preparatory study: To determine the necessary physio-chemical parameter of the new drug.

2.3.2 EXPERIMENTAL DESIGN

During formulation two thinking agent used at different concertation's, resulting in six different batch of polyherbal lozenges for herbal extract, total six batches prepared. In this case HPMC and xanthangum these two types of thinking agent were taken.

2.3.3PREPARATION OF POLYHERBAL LOZENGES

The polyherbal hard lozenges were prepared by heating and congealing technique. A foundation recipe was developed using general principles to attain the appropriate weight per lozenge, which is typically between one and three grams. Each ingredient's required amount for compounding was determined for 20 lozenges, and the amount of material needed for two more lozenges was also computed and weighed. In a copper kettle, the necessary amounts of sugar were dissolved in water and heated to 140 °C, stirring continuously for two hours. This process produced the syrup basis. A tiny amount of water was used to dissolve the dextrose, and the mixture was heated to 110°C untilthe dextrose entirely dissolved and formed a clear, viscous syrup. Afterthat, the sugar syrup was mixed with the dextrose solution. After two hours of heating and stirring, the temperature was raised to 160 °C until the color turned golden yellow. After lowering the temperature to 90 °C, a plastic mass was produced. The Herbal drug formulation, polymer, colour, flavour was added and mixed for 30 min. The mixture was poured into the moulds. Air drying was done for 2 hours. The prepared lozenges were wrapped in aluminium foil and stored in desiccators to prevent moisture uptake.

2.3.4HEAT AND CONGEALING METHOD:

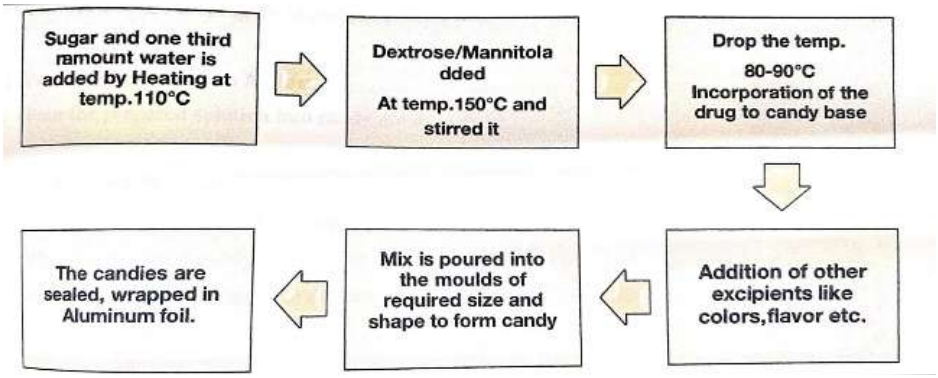

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Table 2.3.4 QUANITITIVE COMPOSITION OF POLY HERBAL LOZENGES

Ingredients(mg)	F_1	F_2	F_3	F_4	F_5	F_6
VN Extract	50	50	50	50	50	50
Safed MusliExtract	50	50	50	50	50	50
Sucrose	700	750	800	700	750	800
Mannitol	-	-	-	300	250	200
Dextrose	300	250	200	-	-	-
HPMC	-	-	-	377	377	377
Xanthan gum	377	377	377	-	-	-
Citric acid	23	23	23	23	23	23
Mint flavor	QS	QS	QS	QS	QS	QS
Amaranth color	QS	QS	QS	QS	QS	QS

IV. PHYSICOCHEMICAL EVALUTIONS

a. Weight variation:

Weight variation test: Twenty lozenges were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one lozenge was determined from the collective weight.

The percent deviation was calculated using the following formula;

% Deviation = (Individual weight – Average weight / Average weight) × 100

b. Thickness:

Thicknessis an important characteristic in reproducing appearance. Thickness was measured using Vernier Caliper's average thickness for Lozenges is calculated and presented with a standard deviation.

c.Hardness:

The force required to break the lozenge throughout its diameter is referred to as the lozenge's hardness. The hardness of the lozenge determines how resistant it is to chipping, abrasion, or breaking when stored, transported, and handled prior to use.

For each formulation, the hardness of tablets was determined using a Monsanto hardness tester and the average was calculated and presented with standard deviation. It is expressed in kg/cm^2. -

d. Assay%:

The drug content was estimated for all the formulations of Medicated lozenges. Lozenges from each batch were selected and weighed individually and crushed in a mortar. The resultant powder was dispersed in 5 ml methanol solvent and the final volume was then made to 50ml using pH 6.8 buffers. A UV-visible double-beam spectrophotometer was used to filter, dilute, and examine the volumetric flask solution spectrophotometrically at 306 nm.

e. Friability:

It is a gauge for tablets' mechanical strength. The following method was used to determine the friability using the Roche friabilator (Electro lab, Mumbai, India). Twenty pre-weighed lozenges were put into the friabilator. The lozenges were subjected to 4 minutes of 25 rpm spins. The lozenges were reweighed at the conclusion of the

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test, and the % change in the lozenge weight represents the degree of friability.

$F=W_I - W_F/W_I \times 100$

Were,

W_I = Initial weight of 20 tablets

W_F= Weight of the 20 tablets after testing

f. In-vitro drug release study:

In the present work, an in-vitro release study was carried out using dissolution apparatus. For different time intervals, the sample was withdrawn and cumulative drug release was calculated. The dissolution apparatus USP paddle-type Π was used. The temperaturewas maintained at 37±0.5°C and stirred at 50 rpm. The dissolution medium isa phosphate buffer of pH 6.8. The samples were withdrawn at predetermined time intervals with the same volume of the fresh medium being added after each withdrawal. The sample was suitably diluted and absorbance was measured at 306 nm for phosphate buffer of pH 6.8.

- **Dissolution Conditions:**
- Medium: Phosphate buffer Ph 6.8 at 37±0.5°C
- Vol.of medium in the jar: 900ml
- Apparatus: USP Apparatus type Π(Paddle)
- Rpm: 50
- Time intervals:

V. RESULTS AND DISSUSSION:

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, weightvariation, in -vitro drug release studies, stability studies.

4.1 Evaluation parameters Results

Batch code	Weight variation (mg)	Hardness (Kg/cm^2)	Thickness (mm)	Diameter (mm)	Friability (%)	moisture Content (%)
F1	1498.2±2.64	4.6±0.2	5.962±0.01	14.10±0.05	0.54±0.01	0.70±0.02
F2	1506.5±1.42	4.8±0.1	6.173±0.03	15.17±0.04	0.69±0.03	0.80±0.03
F3	1480.6±2.65	5.1±0.3	6.180±0.0.2	16.11±0.08	0.68±0.02	0.84±0.02
F4	1490.6±2.22	4.5±0.1	5.150±0.01	14.15±0.06	0.49±0.02	0.62±0.02
F5	1501.1±3.35	4.8±0.3	5.841±0.02	15.18±0.07	0.59±0.05	0.70±0.03
F6	1509.7±2.42	5.5±0.4	6.552±0.03	16.11±0.08	0.92±0.02	0.94±0.01

4.2 cumulative percent Release of poly herbal lozenges containing varying concentration of different polymers.

Time (min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	4.68	7.88	9.91	3.71	6.68	12.96
10	18.96	24.66	22.16	15.62	17.25	32.12
15	29.68	36.81	34.38	22.68	27.63	41.32
20	48.51	54.19	47.26	39.52	43.36	59.89
25	50.07	69.95	56.63	49.63	52.36	74.23
30	78.94	82.14	81.14	76.62	79.49	93.74

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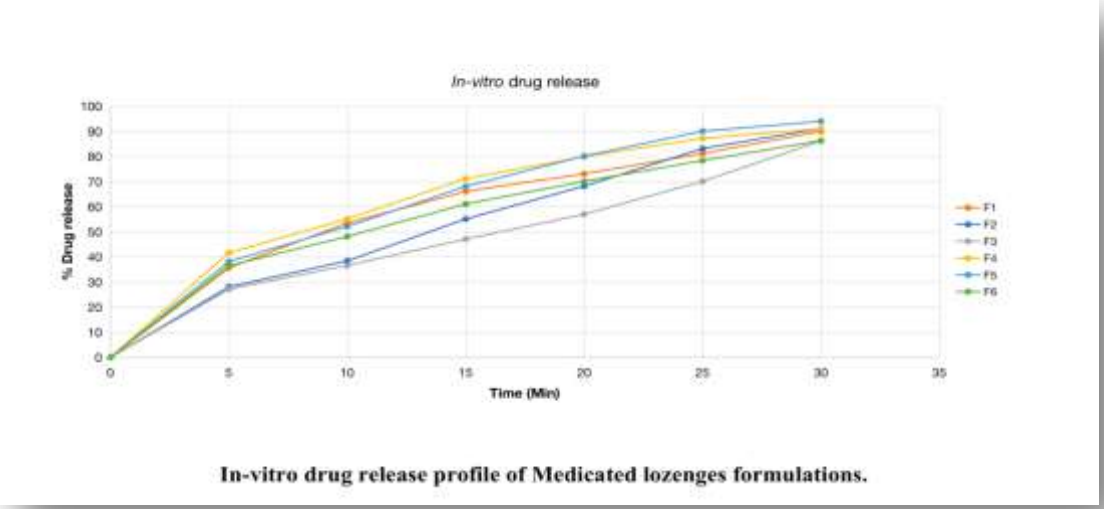
4.3 Dissolution profile of various formulations of poly herbal lozenges.



In-vitro drug release profile of Medicated lozenges formulations.

VI. 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 ethanolic extracts of vitex negundo, Safed Musli. 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 an oral drug delivery. The physical compatibility studies suggest that polymers selected i.e., Hydroxy propyl Methylcellulose, xanthan gum 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. The HF6 Polyherbal lozenges based on hydroxypropyl methylcellulose turned out to be the best formulation overall, with the highest percentage of drug release within 30 minutes (93.74%), making it the most promising formulation. The formulations HF6 with HPMC Polymer Polyherbal Lozenges produced the greatest results since they met all of the evaluation criteria.

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