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Research Paper

"Formulation and Evaluation of Pharmaceutical Polyherbal Mucosal Gel for Treatment of Mouth Ulcers Containing Glycyrrhiza glabra, Aloe vera and Curcumin"

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ABSTRACT
The present study aimed to develop and evaluation of the pharmaceutical polyherbal mucosal gel containing Glycyrrhiza glabra, Aloe vera and Curcumin for the treatment of mouth ulcer. Causes of mouth ulcers include the deficiency of some nutrition's such as iron, vitamins especially B_{12} and vit. C, poor oral hygiene, infections, stress, indigestion, mechanical injury, food allergies, hormonal imbalance, skin disease etc. The mouth ulcers also known as Canker Sores.
The more acceptable remedies are natural that they are safer and lesser side- effects than the synthetic medicines. Herbalmedicinal plants which are widely used in the treatment of skin diseases and also known to possess wound healing, antifungal, antiviral and antimicrobial activities.
The present investigational formulations were prepared by using the different concentration of the carbopol 934, PEG 400, Methyl paraben used as a preservative. The formulation were characterized for pH, viscosity, spreadability, extrdability and mucoadhesion time and in-vitro drug release.
It was demonstrated that the developed herbal gel formulations of Glycyrrhiza glabra, Aloe vera and Curcumin possess significant, therapeutically efficacious. The results showed that due to combination dosage form developed new herbal gel formulation having good mucoadhesion activity so it is safe, stable and good for mouth ulcer treatment.
KEYWORDS: *Mouth Ulcer, Mucosal Gel, Carbopol 934, Mucoadhesion, Drug Delivery, Formulation, Evaluation, Glycyrrhiza glabra, Aloe vera, Curcumin.*

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I. INTRODUCTION

Mouth ulcer is one of the commonest disorders caused due to a variety of etiological factors. Mouth ulcers are painful round or oval sores that form in the mouth, most often on the inside of the cheeks or lips. Common causes of mouth ulcers include nutritional deficiencies such as iron, vitamins especially vitamin B_{12} and C, poor oral hygiene, infections, stress, indigestion, mechanical injury, food allergies, hormonal imbalance, skin diseases etc.

Although many formulations like solution, suspension and ointments are commercially available, no therapy can be said completely useful for the treatment of mouth ulcers. The efficacy of the therapy can be improved by the approach of polyherbal oral mucosal gel. The gel formulation of herbal extracts is developed with different gelling agents. The gels formulations base must have acceptable mucoadhesion so that the medication remains on the spot of application for a longer time. These drug systems form an intimate contact with the oral mucosal membrane and facilitate the rapid release of drug molecules at the site of absorption and hence the better bioavailability of drug.

Glycyrrhiza glabra, Aloe vera and Curcumin are known to have wound healing, anti-carcinogenic and anti-bacterial activities can be effective in treatment of mouth ulcers. The more acceptable remedies are natural

that they are safer and lesser side- effects than the synthetic medicines. Now-a- days the demand of the herbal remedies have increasing in the world market. The aim of the present investigation was to develop suitable formulation for the oral mucosal delivery of extract of Glycyrrhiza glabra, Aloe vera and Curcumin for the treatment ofmouth ulcer.

Gels are mainly semi-solid preparations having a liquid phase that has been thickened with some other components. Gels formulations formulations for skin application or to certain mucosal surfaces for local action or percutaneous penetration of medicament. The gels formulations base must have acceptable mucoadhesion so that the medication remains on the spot of application for a longer time. These drug systems form an intimate contact with the oral mucosal membrane and facilitate the rapid release of drug molecules at the site of absorption. Gels consists of two phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains.

The more acceptable remedies are natural that they are safer and lesser side- effects than the synthetic medicines. Now-a- days the demand of the herbal remedies have increasing in the world market. Over three forth of world population depends mainly on the plants and plant derived herbal medicines.The India offer a variety of plants having medicinal properties. Medicinal plants can be used to find out effective alternative to synthetic drugs.

Research on herbal medicinal plants is one of the leading areas of research globally. Moreover, allopathic medicine is too expensive and capital intensive for a developing country like India and has only limited success in the prevention and treatment of oral diseases. Hence, the plantextracts used in traditional medicine and alternative products continue are considered as good alternatives to synthetic and organic medicine.

II. METHODOLOGY:2.1 MATERIALS AND INSTRUMENTS:

The following chemicals, drug excipients, and instruments were used for the formulation and evaluation studies.

Table 1: Materials Used

Sr. no	CHEMICAL/DRUGS	COMPANY
1.	Carbopol 934	Central Drug House (P) Ltd.
2.	Propylene glycol 400	Central Drug House (P) Ltd.
3.	Glycerin	Central Drug House (P) Ltd.
4.	Honey	Dabur
5.	Methyl paraben	Central Drug House (P) Ltd.
6.	Pippermint oil	Central Drug House (P) Ltd.
7.	Aloe vera	Herbalife Nutrition Aloe Plus
8.	Curcumin	Dabur
9.	Glycyrrhiza glabra	H&C Herbal Ingredients Expert
10.	Di Sodium hydrogen orthophosphate	Central Drug House (P) Ltd.
11.	Pot. Dihydrogen orthophosphate	Central Drug House (P) Ltd.

Table 2. Instruments/ Equipment Used

Sr. No	INSTRUMENTS/EQUIPMENT	COMPANY
1.	UV Spectrophotometer	Systronic, india
2.	Electronic balance	Spruce enterprise ltd.
3.	Digital Ph meter	Systronic India
4.	FTIR	Agilent technologies
5.	Magnetic stirrer	Spruce Enterprise
6.	Franz Diffusion Cell Apparatus	Prepared from Journal
7.	Brookfield Viscometer	Ametek

2.2 PROCUREMENT OF API

Table 3: Selection of the Active ingredients and company

1.	Aloe vera	Herbalife Nutrition Aloe Plus
2.	Curcumin	Dabur
3.	Glycyrrhiza glabra	H&C Herbal Ingredients Expert

2.3 PREFORMULATION STUDIES:

1.Solubility: The solubility of herbal drug extracts in various solvents was measured. Solubility was determined by taking 10mg of drug sample in 10ml of solvent as water, Methanol and Ethanol. pH buffer 6.8 in small test tubes and well solubilized by shaking. Stability studies were performed to observe the effect of environmental conditions or storage conditions on formulations. The optimized formulations was kept in accelerated stability

condition at 25°C temperature 60 ± 5% relative humidity, 30°C temperature 65 ± 5% relative humidity and 40°C temperature 75 ± 5% for a period 3 months as per ICH guidelines.

2.Fourier Transfer Infrared Spectrophotometer (FTIR):

The FTIR studies were carried for the drug, the polymers and the drug-polymer physical mixture in the ratio 1:1 were mixed separately with IR grade KBr in the ratio of (100:1) and correspondings discs were prepared by applying 5.5 metric ton of pressure in a Hydraulic press using FTIR spectrophotometer. The discs were scanned over a wave number range (4000-400 cm).

3. Determination of Maximum Wavelength of extract and aloe vera and curcumin and Glycyrrhiza glabra:

Stock solution was prepared in 6.8 pH Phosphate buffer. This solution was diluted with same Solvent to obtain concentration of 100µg/ml. The resultant was plotted in chart in the range of 200-300nm.

2.4 Preparation of standard calibration curve

2.4.1 Method of preparation of standard calibration curve of Glycyrrhiza glabra:

Glycyrrhiza glabra extract (10mg) was dissolved in Phosphate Buffer (pH 6.8) and volume was made up to 100ml in 100ml volumetric flask. The solution (100g/ml) was further diluted with Phosphate buffer 6.8 pH to obtain solution of 25g/ml. Absorbance of each solution was measured at 282 nm using UV Spectrophotometer and phosphate buffer 6.8 pH as reference standard. The standard curve was generated for the entire range from 5 to 25 mcg/ml.

2.4.2 Method of preparation of standard calibration curve of Aloe vera:

Aloe vera extract (10mg) was dissolved in Phosphate Buffer (pH 6.8) and volume was made up to 100ml in 100ml volumetric flask. The solution (100g/ml) was further diluted with Phosphate buffer 6.8 pH to obtain solution of 25g/ml. Absorbance of each solution was measured at 286 using UV Spectrophotometer and phosphate buffer 6.8 pH as reference standard. The standard curve was generated for the entire range from 5 to 25 mcg/ml.

2.4.3 Method of preparation of standard calibration curve of Curcumin:

Curcumin (10mg) was dissolved in Phosphate Buffer (pH 6.8) and volume was made up to 100ml in 100ml volumetric flask. The solution (100g/ml) was further diluted with Phosphate buffer 6.8 pH to obtain solution of 25g/ml. Absorbance of each solution was measured at 280 nm using UV Spectrophotometer and phosphate buffer 6.8 pH as reference standard. The standard curve was generated for the entire range from 5 to 25 mcg/ml.

2.5 METHOD OF PREPARATION OF ORAL MUCOSAL GEL FORMULATIONS:

All ingredients were weighed accurately according to the required quantity. The gel base was prepared by Carbopol 934 in concentration 1gm was mixed with sufficient quantity of water in a beaker with constant stirring. Specified quantity of Polyethylene glycol 400 was added in the solution and honey was added with continuous stirring. The drugs extract was added in the solution with continuous stirring. Then the peppermint oil was added as a flavoring agent. Sufficient quantity of preservative is added and Triethanolamine is added in the solution to adjust the pH.

Table 4. Composition to Prepare Oral Mucosal gel

Ingredients	F1	F2	F3	F4
G.Glabra extract	0.05g	-	-	0.05g
Aloe vera extract	-	0.3g	-	0.3g
Curcumin	-	-	0.5g	0.5g
Carbopol 934	1g	1g	1g	1g
Polyethylene glycol 400	15.38ml	15.38ml	15.38ml	15.38ml
Glycrine	2ml	2ml	2ml	2ml
Honey	5ml	5ml	5ml	5ml
Methyl paraben	0.18ml	0.18ml	0.18ml	0.18ml
Pippermint oil	0.5ml	0.5ml	0.5ml	0.5ml
Triethanolamine	qs	qs	qs	qs
Water	18	18	18	18

2.6 EVALUATION OF GEL FORMULATIONS:

PHYSICAL EVALUATION

Physical parameters such as color, odour and consistency were checked visually.

Color: The color of the Formulation was checked by visual inspection.

Consistency: The consistency of Formulation was checked by applying on skin.

Odour: The odour of the Formulation was checked by mixing the gel in water and observing the smell.

MEASUREMENT OF pH:

The pH of various gel formulations was determined by using digital pH meter. 1g of gel was dissolved in 100ml of distilled water and kept aside for 2 hours. The measurement of pH of each formulation was done in triplicate and average values are calculated.

HOMOGENEITY:

All prepared gel formulation were tested for homogeneity by visual Inspection after the gels have been set in to the container. They were tested for their presence and appearance of any aggregates.

VISCOSITY TEST:

Viscosities were measured by Brookfield viscometer. Each gel was poured into the container and the proper spindle (no. 74) was attached. Then the viscosities were measured in 25^0C and 50-250 rpm.

EXTRUDABILITY STUDY:

The formulations were filled in the collapsible tubes after the gels were set in the container. The extrudability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of gel in 10 second. The percentage of gel extrude was calculated, recorded.

A grade were allotted +Poor, ++ Fair, +++ Good.

SPREADABILITY:

Spredability is expressed in terms of time in seconds taken by two slides to slip off from emulsified gel and placed in between the slides under the direction of certain load. Lesser the time taken for separation of two slides, better the spreadability. The spreadability of the gel formulation was determined, by measuring diameter of 1 gm gel between horizontal plates ($20\times20cm^2$) after 1 min. the standardization weight tied on the upper plate.

It is calculated by using the formula. S=M.L/T.

Where, M =wt. tied to upper slide

L= Length of glass slide

T=time taken to separate the slides.

DRUG CONTENT:

1gm of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of different concentration were prepared by suitable dilutions after the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve.

MUCOADHESIVE STUDIES:

The glass plates were coated with the polymer. The glass plate was immersed in a temperature controlled mucous solution. The Force required to pull the plate out of the solution is determined under constant experimental conditions.

Duration of mucosal adhesion i.e. time span required until the adhesive gel completely loses is adhesive contact with the mucosa was measured. The time span values were recorded.

IN-VITRO RELEASE STUDY:

The diffusion studies of the prepared gels were carried out using Franz diffusion cell through a cellophane membrane. Gel sample was taken in cellophane membrane and the diffusion studies were carried out at 37 ± 1^0using 250ml of phosphate buffer (6.8) as the dissolution medium. 5ml of each sample was withdrawn periodically at 1, 2, and 3 hours and each sample was placed with equal volume of fresh dissolution medium. Then the sample were analyzed for the drug content by using phosphate buffer as blank.

STABILITY:

The stability study was performed as per visual inspection for 90 days. The formulated gel was filled in collapsible tubes and stored at room temperature. The observation depicted in the tables at room temperature and with closed and open lid. Small change in pH, spreadability and extrudability studies was observed with the time.

III. RESULT & DISCUSSION

3.1 PREFORMULION RESULTS: The pre-formulation studies were carried out for the Glycyrrhiza glabra, Aloe vera and Curcumin.

1. Solubility: It was clear from the solubility studies that Glycyrrhiza glabra, Aloe vera and Curcumin are more soluble in distilled water in distilled water and slightly soluble in ethanol, methanol and phosphate buffer**.**

Table 5: Solubility of Glycyrrhiza glabra, Aloe vera and Curcumin in different Solutions

Sr. No.	Solution	Solubility		
		G. glabra	Aloe vera	Curcumin
1.	Distilled Water	Soluble	Soluble	Soluble
2.	Ethanol	Slightly soluble	Slightly soluble	Slightly soluble
3.	Methanol	Slightly soluble	Slightly soluble	Slightly soluble
4.	Phosphate Buffer	Slightly Soluble	Slightly Soluble	Slightly Soluble

Thus, from above solubility studies it was found that Glycyrrhiza glabra, Aloe vera and Curcumin found to be more soluble in distilled water.

Determination of Maximum Wavelength of extract and Glycyrhhiza glabra, Aloe vera and Curcumin: The λmax for Glycyrrhiza glabra, Aloe vera and curcumin was found to be at 282, 284 and 286nm which was in compliance with standard drug. The maximum absorbance and the corresponding graphs are shown in Fig. 1,2 and 3.

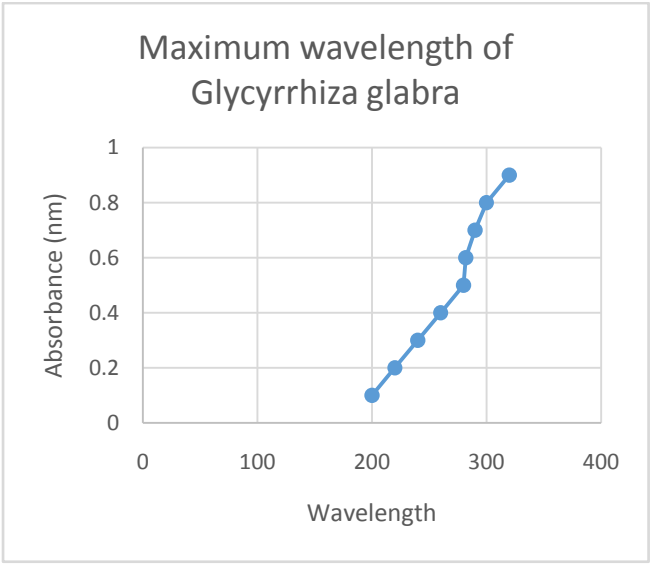

Fig. 1 Maximum wavelength of Glycyrrhiza glabra

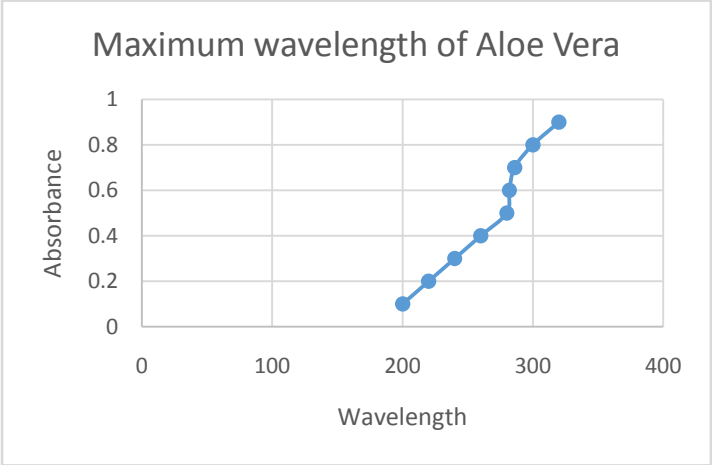

Fig.2 Maximum wavelength of Ale vera

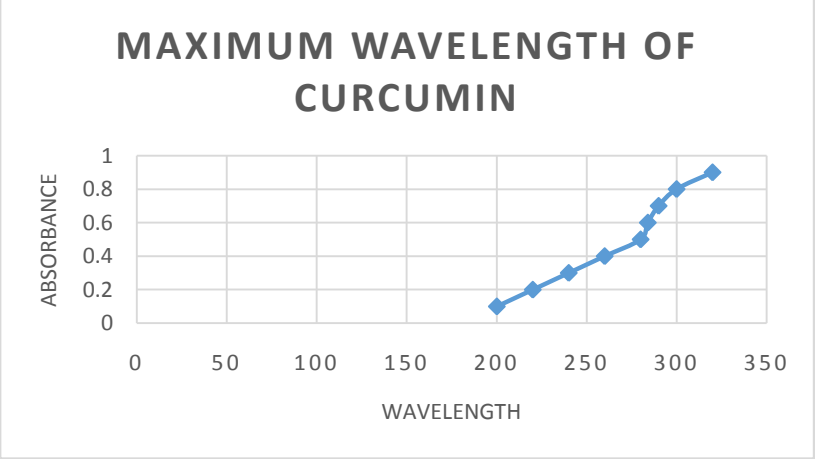

Fig. 3 Maximum wavelength of Curcumin

It was concluded that G. glabra showed maximum wavelength at 282nm and Curcumin 284nm and Aloe vera showed the maximum wavelength at 286nm.

3.2 Standard calibration curve:

3.2.1 Standard Calibration Curve of Glycyrrhiza glabra: Standard curve of Glycyrrhiza glabra by using of different concentration of Glycyrrhiza glabra in buffer solution with pH 6.8. The absorbance was recorded at different concentration 5, 10, 15, 20, 25µg/ml (Table 6). The regression coefficient also determined and found to be near unity and hence the standard graphs can be used for further analysis fig.

Table 6: Standard Calibration Curve of Glycyrrhiza glabra in 6.8 pH buffer reading

Concentration (mcg/ml)	Absorbance
5	0.120
10	0.196
15	0.256
20	0.355
25	0.427

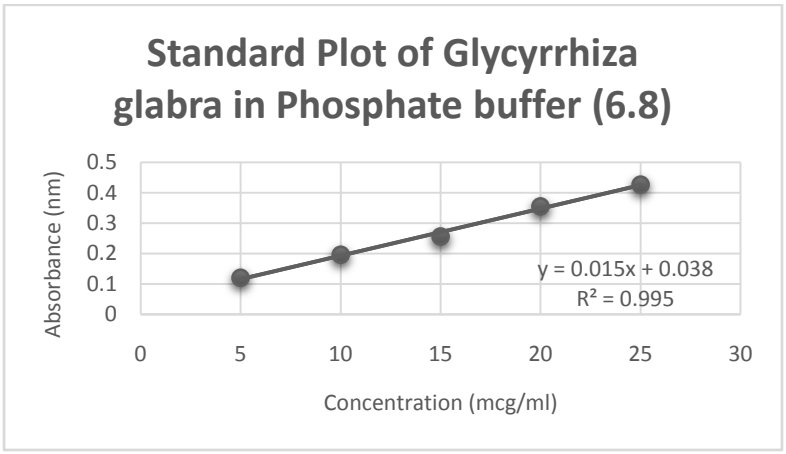

Fig.4

Standard calibration plot of Glycyrrhiza glabra

Standard curve of Glycyrrhiza glabra was obtained by using different concentration of Glycyrrhiza glabra in buffer solution with pH 6.8. The absorbance was recorded at different concentration that are 5, 10, 15, 20 and 25µg/ml. The regression coefficient also calculated and found to be near unity and hence the standard graphs can be used for further analysis.

3.2.2 Standard Calibration Curve of Aloe vera

Table 7: Standard Calibration Curve of Aloe vera reading

Concentration	Absorbance
5	0.067
10	0.069
15	0.106
20	0.124
25	0.132

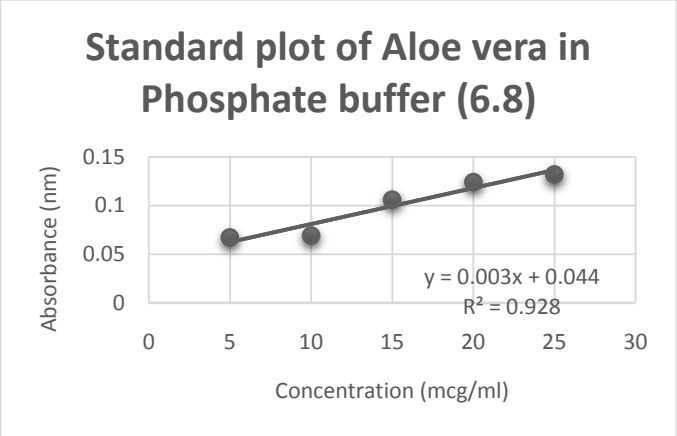

Fig. 5
Standard Calibration plot of Aloe vera

3.2.3 Standard Calibration Curve of Curcumin

Table 8: Standard Calibration Curve of Curcumin reading

Concentration	Absorbance
5	0.027
10	0.053
15	0.106
20	0.161
25	0.215

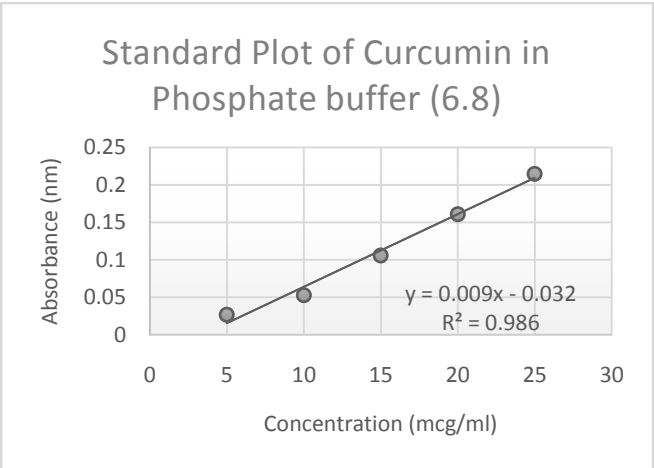

Fig. 6
Standard Calibration plot of Curcumin

3.Fourier Transfer Infrared Spectroscopic analysis:

Possible chemical interaction in a drug were investigated by performing FTIR of the individual drugs.

3.3.1 FTIR analysis of Glycyrrhiza glabra

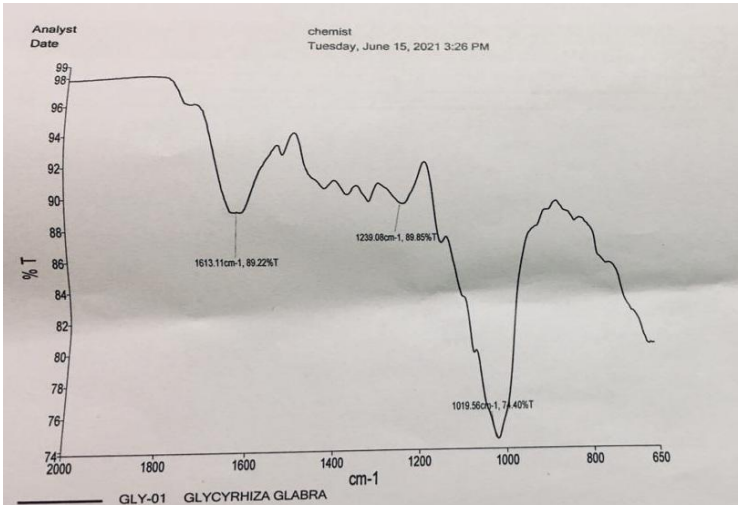

Fig. 7 FTIR of Glycyrrhiza glabra

Table:9 FTIR recorded peaks for Glycyrrhiza glabra

Procured sample of Glycyrrhiza glabra was observed under FTIR which depicts the peaks at following intensity 1613.11cm^{-1}, 1239.08cm^{-1}, 1019.56cm^{-1} for C=C aromatic, C-O-C and C-OH stretch respectively (Fig. 7). The peak data is further represented (Table 9).

Functional Group	Wavelength (cm^{-1})	Intensity (cm^{-1})
C=C	1680-1600	1613.11
C-O-C Stretch	1250-1050	1239.08
C-OH Stretch	1200-1000	1019.56

3.3.2 FTIR analysis of Aloe vera:

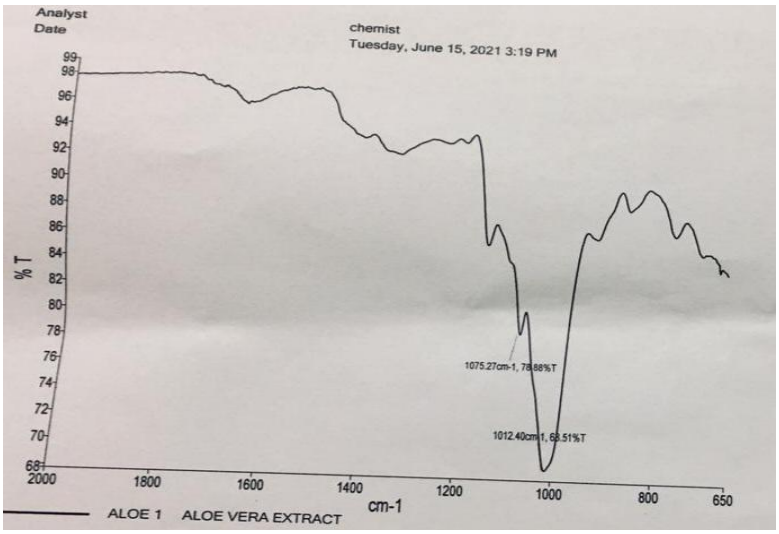

Fig. 8 FTIR of Aloe vera

Table:10 FTIR recorded peaks for Aloe vera

Procured sample of Aloe vera was observed under FTIR which depicts the peaks at following intensity 1075.27cm^{-1}, 1012.4cm^{-1} for C-O-C and C-OH stretch respectively (Fig.8). The peak data is further represented (Table 10).

Functional Group	Wavelength (cm^{-1})	Intensity (cm^{-1})
C-O-C Stretch	1250-1050	1075.27
C-OH Stretch	1200-1000	1012.4

3.3.3 FTIR analysis of Curcumin:

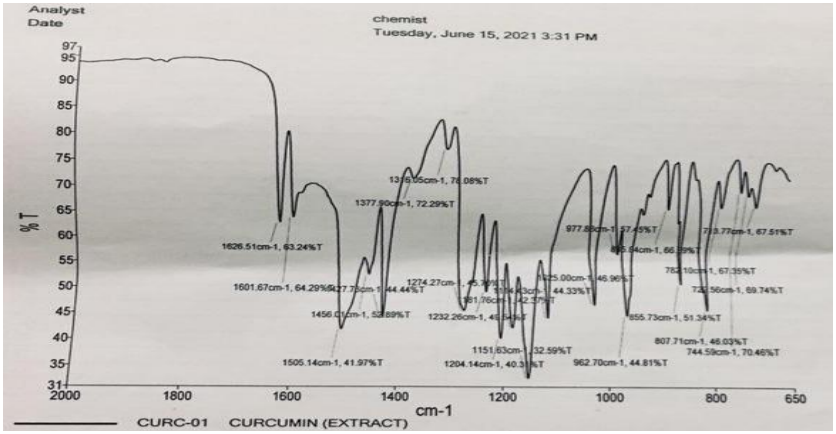

Fig. 9 FTIR of Curcumin

Table:11 FTIR recorded peaks for Curcumin

Procured sample of Curcumin was observed under FTIR which depicts the peaks at following intensity 1626.51cm^{-1}, 1601.67cm^{-1}, 1505.14cm$^{-1,}$ 1456.01 cm^{-1}, 1427.73 cm^{-1}, 1377.9 cm^{-1}, 1316.05 cm^{-1}, 1274.27 cm^{-1}, 1232.26 cm^{-1}, 1204.14 cm^{-1}, 1181.76 cm^{-1}, 1151.63 cm^{-1}, 1114.43 cm^{-1}, 1025 cm^{-1}, 977.88 cm^{-1}, 962.8 cm^{-1}, 885.84 cm^{-1}, 855.73 cm^{-1}, 807.71 cm^{-1}, 782.1 cm^{-1}, 744.59 cm^{-1},729.56 cm^{-1}, 713.77 cm^{-1} for C=O bend, C-O-C and C-OH Strecthing, CH_3 bend, C=C aromatic, Si-O and P-O Presence of organo silicon and Phosphorous compound, C-Br and C-Cl halogen compunds respectively (Fig. 9). The peak data is further represented (Table 11).

Functional Group	Wavelength (cm^{-1})	Intensity (cm^{-1})
C=O bend	1650-1550	1626.51
C=O bend	1625-1598	1601.67
C=O bend	1700-1500	1505.14
C=C aromatic	1600-1400	1456.01
C=C aromatic	1600-1400	1427.73
CH_3 bend	1390-1300	1377.9
CH_3 bend	1390-1300	1316.05
C-OH stretch	1300-1000	1274.27
C-O-C Stretch	1250-1050	1232.26
C-O-C stretch	1250-1050	1204.14
C-OH stretch	1200-1020	1181.76
C-OH stretch	1200-1020	1151.63
C-OH stretch	1200-1020	1114.43
C-OH stretch	1200-1020	1025
Si-O	1100-800	977.88
Si-O	1100-800	962.7
P-O	1100-800	885.84
P-O	1100-800	855.73
P-O	1100-800	807.71
C-Cl	800-600	782.1
C-Br	750-500	744.59
C-Br	750-500	729.56
C-Br	750-500	713.77

3.3 EVALUATION OF GEL FORMULATION:

3.3.1 Physical and Pharmaceutical parameters:

All the developed formulations were found to be smooth, adhesive and color with characteristic odour. The studies showed that F4 formulation complies with requirement of physical parameters and likewise found to be the best amongst all the formulations (Table 9).

From here onwards we used F4 formulation for further analysis.

Table 12: **Physical and Pharmaceutical Parameters of gel**

Parameters	F1	F2	F3	F4
Appearance	Pale yellow	Yellowish green	Orange Characteristic	Yellow
Consistency	Good	Good	Good	Good

Odour	Characteristic	Characteristic	Characteristic	Characteristic
Homogeneity	Good	Good	Good	Good
pH	6.8	6.82	6.87	7.0
Spreadability(gm.cm/sec)	29.12	24.51	31.90	33.20
Extrudability(%)	++	++	++	+++
Viscosity (cps)	1228	1831	2258	1069
Duration of mucosal adhesion (min)	20	25	27	30
Drug content(%) C.O	79	80	83.3	88.2
Drug content G.G	71	79	67	74

The above results, we can have concluded the color of the formulation F1, F2, F3 and F4 showed the characteristic odour and good consistency of the all formulations.

After analysis of all formulations for their evaluation parameter like pH, viscosity, spreadability, excrudability, homogeneity etc. It is observed that the formulation F4 (mixed) containing equal amount of Licorice, Aloe vera and Turmeric extract showed good results. The F4 optimized with good pH, viscosity, spreadability, extrudability, drug content and good mucoadhesive properties etc. Hence, this formulation is used for treatment of mouth ulcers.

3.4 IN-VITRO RELEASE OF GEL FORMULATION CONTAINING Glycyrrhiza glabra. Aloe vera and Curcumin: Franz diffusion cell was used to study drug release pattern. Graph was ploted in between %CDR and time.

It was observed from the graph that the free drug was releases within 4-5 minutes of time interval whereas the constant and slow release of drug was observed in formulated gel for 3 hours.

3.4.1 Table 13: In vitro release of F1 Gel Formulation Containing Glycyrrhiza glabra:

Time (Min.)	**Abs. (nm)**	**Conc. (µg/ml)**	**Drug Release (µ/ml)**	**Loss of Amt. (µg/ml)**	**CDR (µg/ml)**	**%CDR (%w/w)**
15	0.948	123.12	11.08	0	11.08	11.08
30	1.091	136.75	12.31	11.08	23.39	23.39
45	1.414	143.25	12.89	12.31	25.2	25.2
60	1.448	201.43	18.13	12.89	31.78	31.78
90	1.891	264.72	23.83	18.13	41.96	41.96
120	2.114	296.57	26.69	23.83	50.52	50.52
150	2.914	410.86	36.98	26.69	63.67	63.67
180	3.230	456	41.04	36.98	78.02	78.02
210	3.387	478.43	43.06	41.04	41.04	41.04

3.4.2 Table 14: In vitro release of F2 Gel Formulation Containing Aloe vera:

Time (Min.)	**Abs. (nm)**	**Conc. (µg/ml)**	**Drug Release (µg/ml)**	**Loss of Amt. (µ/ml)**	**CDR (µg/ml)**	**%CDR (%w/w)**
15	0.958	131.42	11.82	0	11.82	11.82
30	0.977	134.14	12.07	11.82	23.89	23.89
45	0.985	135.28	12.17	12.07	24.24	24.24
60	1.172	162	14.58	12.17	26.75	26.75
90	1.189	164.42	14.79.	14.58	29.37	29.37
120	2.123	297.85	26.80	14.79	41.59	41.59
150	2.919	411.57	37.04	26.80	63.08	63.08
180	3.397	479.85	43.18	37.04	80.22	80.22
210	3.788	535.71	48.21	43.18	43.18	43.18

3.4.3 Table 15. In vitro release of F3 Gel Formulation Containing Curcumin:

Time (Min.)	**Abs. (nm)**	**Conc. (µg/ml)**	**Drug Release (µg/ml)**	**Loss of Amt. (µg/ml)**	**CDR (µg/ml)**	**%CDR (%w/w)**
15	0.984	135.14	12.16	0	12.16	12.16
30	1.411	196.14	17.65	12.16	29.81	29.81
45	1.848	258.57	23.27	17.65	40.92	40.92
60	2.320	326	29.34	23.27	52.61	52.61
90	2.873	405	36.45	29.34	65.79	65.79
120	3.079	434.42	39.09	36.45	75.54	75.54
150	3.251	459	41.31	39.09	80.04	80.04
180	3.872	547.71	49.29	41.31	90.6	90.6
210	3.927	555.57	50.00	49.29	49.29	49.29

3.4.4 Table 16: In vitro release of F4 Gel Formulation Containing G. glabra, Aloe vera and Curcumin:

Time (Min.)	Abs. (nm)	Conc. (µg/ml)	Drug Release (µg/ml)	Loss of Amt. (µg/ml)	CDR (µg/ml)	%CDR (%w/w)
15	0.990	136	12.24	0	12.24	12.24
30	1.381	191.85	17.26	12.24	29.5	29.5
45	1.741	243.28	21.89	17.26	39.15	39.15
60	2.210	310.28	27.92	21.89	49.81	49.81
90	2.870	404.57	36.41	27.92	64.33	64.33
120	3.080	434.57	39.11	36.41	75.52	75.52
150	3.320	468.85	42.19	39.11	81.3	81.3
180	3.887	549.85	49.48	42.19	91.67	91.67
210	3.980	563.14	50.68	49.48	49.48	49.48

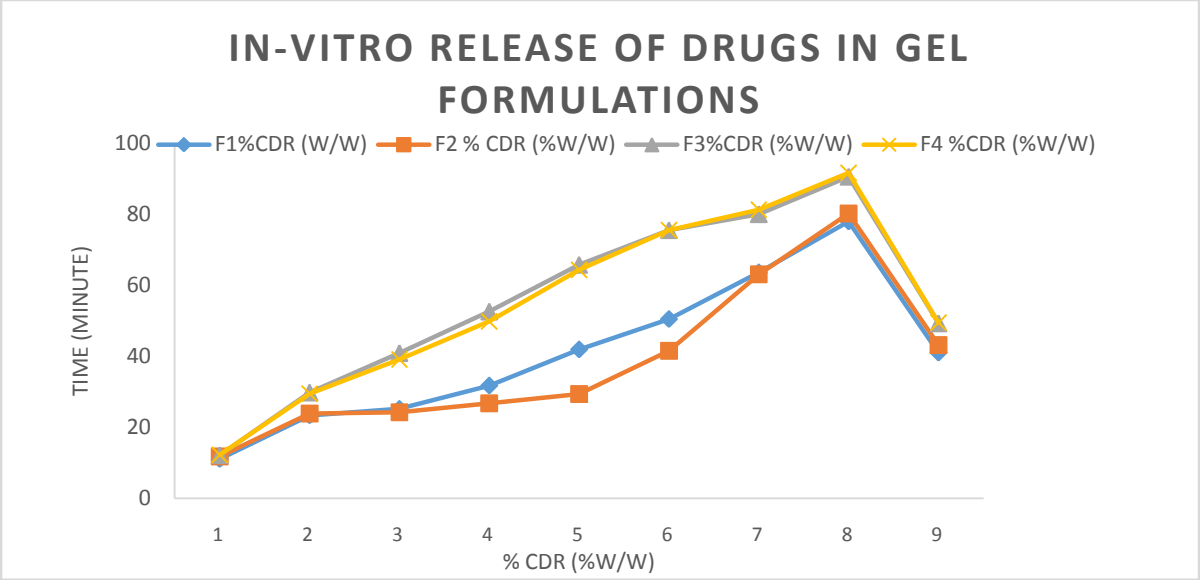

Fig 10: In-vitro release profile of drugs in gel in phosphate buffer (pH 6.8) at 284nm

3.5 Stability Studies: The stability studies were performed on the formulation at room temperature with open lid and closed lid for 90 days and various parameters were taken into consideration to check the stability of the gel. The observation depicted in the table at room temperature. No change in the pH was observed throughout the study.

Table17: **Stability data of F4 herbal gel formulation (Glycyrrhiza glabra, Aloe vera and Curcumin):**

Parameters	Optimized formulation (F4) mixed			
	Day 1	Day 30	Day 60	Day 90
Color	Yellow	Yellow	Yellow	Yellow
Odor	Characteristic	Characteristic	Characteristic	Characteristic
pH	7.0	7.0	7.0	7.0
Viscosity	1060	1060	1060	1060
Spreadability	33.20	33.20	33.20	33.20
Extrudability	+++	+++	+++	+++
Homogeneity	Good	Good	Good	Good
Mucoadhesive Time	30	30	30	30

Stabilities studies of all formulations showed that the Physical appearance, pH, extrudability, spreadability remain unchanged upon storage for 3 months. Therefore, it was concluded that herbal oral mucosal gel formulation F4 containing Glycyrrhiza glabra, Aloe vera and Curcumin could be very promising oral mucosal gel for the treatment of mouth ulcer.

IV. CONCLUSION

World's population still greatly depends upon traditional medicines for treatment of various diseases. In the recent years, The use of medicinal plants in developing countries has been a gradual revival of interest, as

herbal medicines have been reported to be safe with minimal side effects especially when compared with synthetic drugs. Herbal treatments applied topically have gained considerable attention due to their widespread use and ill-defined benefit/risk ratio.

There are numerous medicinal plants which are widely used in the treatment of skin diseases and also known to possess antimicrobial activity. Herbal application of gels at pathological sites offer great advantages in a faster release of a drug directly to site of action as compared to cream and ointment. Plants are considered to be a vital source of potentially useful constituents for the development of new therapeutic agents, as most of them are safe with less or no side effect.

Gels have been widely used as a vehicle for topical delivery of drugs. Medicinal properties of extracts of plants and herbs can be incorporated in this dosage form as active ingredients in order to therapeutical benefits. The gel formulations can provide better absorption characteristic and hence the bioavailability of drug. The formulation of solution to gel conversion can be useful due to its ease of administration compared to gel formulations. The Glycyrrhiza glabra, aloe vera and Curcumin to have wound healing, anti-carcinogenic and antibacterial activities can be effective in treatment of mouth ulcers. The developed formulations homogenous and the pH range 6.8-7.4. The work on the herbal drugs brings the traditional use of the medicinal plants and its extracts in the treatment of mouth ulcers.

And the polymer has significant effect on various parameters of formulations voz. Viscosity, spreadability, pH, drug content, stability etc. From this study it was revealed that the viscosity of the formulation was increased and spreadability decreased with increasing the concentration of polymers in the formulations. From the mucoadhesive studies it was concluded that as the concentration of the polymer increases, the adhesion time increases which result in better absorption of drug and hence improved bioavailability. The results of in-vitro drug release and its permeation studies showed that the highest value was from F4 formulation containing 0.05gm of Glycyrrhiza glabra, 0.3gm aloe vera and 0.5 gm of curcumin and drug released after 3 hours. In-vitro Relese study showed that the formulation F4 was better than the other formulations in respect to in vitro release profile.

FTIR studies were carried out of various drugs extracts.The stability studies of all formulation were carried out as per visual inspection for 3 months at different temperature and humidity conditions. The data presented in this study, it was demonstrated that the developed herbal gel formulations F4 (mixed) possess significant, therapeutically efficacious. The results showed that due to combination aosage form developed new herbal gel formulation having good mucoadhesion activity so it is safe, stable and good for mouth ulcer treatment.

REFERENCE

[1]. Senthil et al; The Erode collage of Pharmacy and Research Institute Tamilnadu, The Formulation and Evaluation of Buccal Patches., 2016.
[2]. Brazilian Journal of Pharmaceutical Sciences, Buccal Drug Delivery System, 2019.
[3]. Sanjana et al; Comparative Evaluation of In-situ Gels and Films; Rajiv Gandhi of Health Science Karnataka, 2016.
[4]. (International Journal of Pharmaceutical Science, Design and Characterization of trans buccal release of drug, 2013).
[5]. Journal of Current Pharma Research, Available online at www.jcpronline.in
[6]. Pranshu Tangri et al; Oral Mucoadhesive drug delivery systems, 2011;2(1):36-46 www.ijbonline.com.
[7]. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. Journal of Pharmaceutical Sciences and Research. 2013 Apr 1;5(4):80.
[8]. Paderni C, Compilato D et al; Oral local drug delivery and new perspectives in oral formulation. Oral Surg Oral Med Oral Pathol Oral Radiol. 2012; 114:e25-e34.
[9]. John D. Smart et al; Drug delivery using buccal adhesive systems, ScienceDirect. 1993, 253-270.
[10]. Irina M. Pelin & Dana M. Suflet et al; Mucoadhesive buccal drug delivery systems containing polysaccharides, Cellular Chemistry and Technology., 54 (9-10), 889-902 (2020).
[11]. Phanindra B. et al; The recent Advancement of Bioadhesion and Mucoadhesion Drug Delivery System: A Review., Int. J. Pharm. Med. & Bio. Sc. 2013.
[12]. R. Jagdeeshwer Reddy et al; A Review of Buccal Drug Delivery System, American Journal of Adance Drug Delivery., 2013.
[13]. Gawas SM. et al; Current approaches in buccal drug delivery system., Pharmaceutical and Biological Evaluations 2016; vol.3 (2): 165-177.
[14]. K.G. Bhutkar et al; Formulation and Evaluation of Herbal Buccal Patch., Journal of Current Pharma Research 5(1), 2014, 13-72-1377.
[15]. Y. Tian et al; Oromucosal Films: From patient centricity to production by printing technique., Expert Opinion on Drug Delivery, 2019, ISSN: 1742-5247.
[16]. Sachin Lokhande et al; Buccoadhesive Drug Delivery System: Need., Asian Journal of Biomedical and Pharmaceutical Sciences 2(14) 2012, 29-36.
[17]. Society of Pharmaceutical Sciences and Research; An overview on Buccal Drug Delivery system., International Journal of Pharmaceutical Sciences and Research; ISSN (online): 0975-8232, ISSN (Print) 2320.
[18]. Reena Sheoran et al; Buccal Drug Delivery System: A Review., Int. J. Pharm. Sci. Rev. Res., 50(1), May - June 2018; Article No. 07, Pages: 40-46.
[19]. Dena M. Sapanaro, DDS, MS et al. Transmucosal Drug Delivery in the Oral Cavity; The Journal of Multidisciplinary care of Decisions in Dentistry; 2018.
[20]. Radha Bhati & Raja K Nagrajan et al; A Detailed Review on Oral Mucosal Drug Delivery System., IJPSR, 2019.

[21]. Shaikh Rahamatullah, Thakur Raghu Raj Singh et al; Mucoadhesive drug delivery systems., J Pharma bio allied Sci., 2011 Jan-Mar; 3(1): 89–100.
[22]. Hussain et al; A Comprehensive Review of Buccal Drug Delivery System., American Journal of Advance Drug Delivery., 2013.
[23]. Larson R.G.; The Structure and Rheology of Complex Fluid., Oxford university Press, New York; 1999, 8(3), 8-95.
[24]. Carter S. J. et al.; Cooper and Gunn's Tutorial Pharmacy, 6th edition; New Delhi; CBS Publishers and Distributors; 2000; 7(4); 68-72.
[25]. Wikipedia the free encyclopedia; Mucoadhesion
[26]. Aslani et al; Treatment of Recurrent Aphthous stomatitis, Advanced Pharmaceutical bulletin., 2016: 6(3), 391-398.
[27]. Shaikh Sabir et al; Formulation and Evaluation of herbal gel for mouth Ulcers,SAC collage of Pharmacy, Karnataka; Pharma Tutor; 2018, 6(4); 32-38.
[28]. Nautiyal et al; Herbal remedies Used for Mouth Ulcers, International Journal of Health and Clinical Research, 2019; 2(1); 17-23.
[29]. Jenna Fletcher et al; Mouth Ulceration, Medical News Today., 2019.
[30]. , Formulation and evaluations of semi-solid gels for treatment of mouth ulcers International Journal of Pharm Tech Research
[31]. http://ulcertreatmentinfo4u.Com/Causes-of-Mouth-Ulcers.php.
[32]. Joseph E.P. et al; Text book of Natural Medicine, Volume 2, 2nd edition, 1085.
[33]. Nem Kumar et al; Formulation of Polyherbal aquous gel, Research Journal of Pharmacognosy and Phytochemistry, Year: 2020, Volume : 12.
[34]. Ashwini A. Bachhav et al; Formulation and evaluation of Metronidazole Mouth Ulcer Gel, J. Global Trends Pharm Sci, 2018; 9(4): 5992-5997.
[35]. R. Rezvaninejad et al; Herbal Medicine in Treatment of Recurrent Aphthous Stomatitis: A Literature Review., http://jidai.ir. Article.
[36]. Gupta et al; Aloe vera: A Natural Perquisite to Dental Therapy, Cent. Euro. J. Exp. Bio., 2017, 5(2): 24-30.
[37]. Adil et al; Aloe vera Gel Mucilage IPC based mucoadhesion buccal films of Tramadol HCl., Asian Journal of Pharmaceutics, Jan-Mar 2016, 9(5)/S43.
[38]. Indian Herbal Pharmacoepia, Indian Drug Manufacturers Association, Numbai 2002, 5(2); 89-97.
[39]. Mostafa, Ammar et al; New Herbal Formulations For Oral Ulcer Remedy., Medical Journal of Islamic World Academy of Sciences 21:2, 69-76, 2013.
[40]. Haley et al; Licorice Root Extract Oral Patch For Treating Canker Sores, United State Patent., US 7,201,930 B2, Apr. 10, 2007.
[41]. Salehi Bahare et al; Plant-Derived Bioactives In Oral Mucosal Lesions., Biomolecules 2019, 9, 106; www.mdpi.com/journal/biomolecules.
[42]. Gnnars Kris et al; Health Benefits of Turmeric and Curcumin., July 13, 2018. https://www.healthline.com.
[43]. Florence A. et al; Novel Oral-Drug Formulations., Their Potential in Modulating Adverse-Effects Drug Saf. 1994, 410(3), 225-231.
[44]. Aggarwal Geeta et al; Pharmaceutical Polymer Gels in Drug Delivery., Research gate; Feb, 2018.
[45]. B.F. Goodrich Company Technical Literature; Carbopol Resin handbook, 1991.
[46]. Kaur Darshan et al; Formulation and Evaluation of carbopol 934 based Transdermal Gel., International journal of Pharmacy and Pharmaceutical Sciences., vol. 6, 2014.
[47]. S. Roy et al; Polymers in Mucoadhesive Drug-Delivery Systems: A Brief Note, Designed Monomers and Polymers, 2009, 12:6, 483-495.
[48]. Zolfaghari Behzad et al; Design, Formulation and evaluation of oral Gel., Adv Pharm Bull. 2016 Sep; 6(3): 391–398.
[49]. https://en.wikipedia.org The free encyclopedia.
[50]. https://www.researchgate.net Glycerol in Pharmaceutical Preparations.
[51]. https://go.drugbank.com
[52]. https://pubmed.ncbi.nim.nih.gov.
[53]. https://www.sciencedirect.com
[54]. https://www.healthline.com
[55]. Viny Dave & Ashwani Mishra et al; Formulation of Buccal Strips using PEG400 and Honey as a Plasticizers., Current Research in Pharmaceutical Sciences (2018). Available online at www.crpsonline.com.
[56]. Nergis Yilmaz et al; Biochemical Evaluations of the Therapeutic Effectiveness of Honey in Oral Mucosal Ulcers., Journal of the association of Basic Medical Sciences; 2009 Nov; 9(4): 290–295.
[57]. Jeffrey T. Haley et al; Licorice root extract oral patch for treating canker sores, Google Patent., 2007.
[58]. Dixit et al; Recent Approaches of Herbal Drugs Standardization., International Journal of Integrative Biology; 2008 vol. 2,195.
[59]. Jeff Burgess et al; The Journal of Contemporary Dental Practices., Mar 2008, 2(2), 108-119.
[60]. Nikunjana A. et al; Formulation and Evaluation pf Polyherbal Gel for Wound Healing., 2011, 1(1), 23-29.
[61]. K. Purushtham et al; Formulation of Topical Oral Gel for the treatment of Oral Submucous Fibrosis (OSMF); 2011, 3(1), 103-112.
[62]. Patil et al; Development and Validation of UV Spectrophotometric Method or Estimation of Glycyrrhetinic acid in Hydroalcoholic Extract of Glycyrrhiza glabra, IJPCBS, 2012, 2(4), 617-621.
[63]. Bhasha et al; Recent trends of Usage of Polymers in the Formulations of Dermatological Gels., IJRPB; 2013, vol. 1(2), 161.
[64]. YS Throat et al; Treatment of mouth Ulcers by Curcumin loaded Thermoreversible Mucoadhesive Gel., IJPPS; 2015, vol. 7, no. 11. Pp 399-405.
[65]. Sabirm shaikh et al; Traditional Herbal Remedies., World Health Organization., Institution Repository for Information Sharing 2020.
[66]. Dwivedi et al; Important Medicinal Plants of India., Labert Academy Publishing; Germany., Pages 132.
[67]. Thombre et al; Formulations and Evaluations of Pharmaceutical Aqueous Gel of Cordia Dichotoma and Gauva Leaves., Am J. Pharm research 2018; 8(2).
[68]. Thombre et al; Formulations and Evaluations of Pharmaceutical Aqueous Gel of Cordia Dichotoma and Gauva Leaves., Am J. Pharm research 2018; 8(2).
[69]. Aggarwal and M. Nagpal et al; Polymers Gels in Drug Delivery., 2018; In books: Polymer Gels, Page no. 249-284.
[70]. Reddy et al; Current Situation of Bioadhesive Drug Delivery Systems., 2018 source Pubmed., DARU Jornal of Pharmaceutical Sciences, 19(6): 385-403.
[71]. Mittal & Nautiyal et al; Ayurvedic Preparations for the Management of RAS., IJPPS; 2020, 7(9).
[72]. Uma Maheshweri T et al; In-situ Gel Treatment for Mucosal Lesions., 2020, vol. 12, pages 499-503.
[73]. Richa & Bansal et al; Formulation and Evaluation of Herbal Oral Gel Containing Extracts of Powdered Psidium guajava Linn Leaves with Curcuma longa Linn Rhizomes to Treat Mouth Ulcer., International Journal of Drug Development and Research; imedpub Journal; 2020; vol.12, 2:150.
[74]. Sharma V et al; Glycyrrhizaglabra- A Plant For the Future., MJPM; 2012, 15(2), 2320-3315.
[75]. Goyel S et al; Novel Anti- Inflammatory Topical Herbal Gels Containing Withania somnifera and Boswellia serrata 2011; 2(4): 1087-1094.

[76]. Bhardwaj et al; Herbal Medicines., International research of Medical and Health Sciences; Sep 2018; Vol. 1, Issue 1.