FABRICATION AND EVALUATION OF NOVEL MICROBEADS LOADED GEL FOR MOUTH ULCER

INTRODUCTION

Mouth ulcer is a sore that occurs on the mucous membrane of the oral cavity. Mouth ulcer is the loss or erosion of part of the delicate tissue that lines the inside of the mouth. Mouth ulcer is very common, occurring in association with many diseases and by different mechanism, but usually there is no serious underlying cause. (Vorvick LJ, 2012)

Gels are typically semi-solid formulations having a liquid phase that has been thickened with other components. Uses of topical gel preparations are for skin application or percutaneous penetration of medicament or local action to certain mucosal surfaces (Singh, 2014). A mouth ulcer is a break or breach in the mucous membrane, which is lines the inside of the mouth. It usually has yellow or white color and usually looks like a depression in mouth that is the mucous membrane. (Dosani, 2011)

Ascorbic acid (vitamin C) and its derivatives are known to perform various important physiological and metabolic functions in humans. In addition to dietary supplements, a number of topical formulations containing ascorbic acid and derivatives are now available that induce collagen synthesis, strengthening of skin tissues, reduction in pigmentation loss, and improved growth and health activities. It has shows antioxidant properties. (M. Sheraz, 2011)

OBJECTIVES:-

To prepare Mucoadhesive gel for mouth ulcer for localized healing effect to-

- Reduce irritation, inflammation, redness.
- To nourish the mucous membrane and promote healing.
- To provide cooling effect, to reduce irritation, pain, while chewing.
- To promote development of mucous layer.
- Such oral dosage form which are feasible in application & economical.

The objective of this work is to deal with the preparation of “Microbeads Loaded Menthol based Mucoadhesive Gel for Mouth Ulcer” using ascorbic acid as a drug and menthol as a cooling agent. This product imparts therapeutic effect at affected parts of oral cavity for treatment of mouth ulcer. Ascorbic acid used as an antioxidant and helps fighting bacterial infection and maintains blood pressure. It could treat mouth ulcer effectively with improved patient compliance and reduced side effect and toxic effect.

MATERIAL AND METHOD

Materials

Ascorbic acid and excipient received from college laboratory grade. Menthol purchased from Alpha Aromatica.

1. Preparation of microbeads

Ionotropic Gelation Method

1.1 Formulation of blank cross-linked sodium alginate microbeads

Procedure-

1.5 gm sodium alginate was mixed in the 20 ml of distilled water along with continuous stirring. The solution was dripped into 50 ml of 6% of calcium chloride solution until the microbeads were produced. The microbeads were stand in calcium chloride solution for 30 min, after that strain and wash with distilled water. The microbeads were store in the container with fresh 6% calcium chloride solution.

1.2 Formulation of L-ascorbic acid containing microbeads

Procedure-

1.5gm sodium alginate was dissolved in 20ml distilled water along with continuous stirring. The solution was dripped into the 50 ml of 6% of calcium chloride solution until the microbeads were produced. The microbeads were stand in calcium chloride solution for 30 min, after that strain and washed with distilled water. To create multilayer microbeads, the beads were then transferred into the 50 ml of 1.0% (w/w) ascorbic acid solution and stand there for 30 min, after that placed into the calcium chloride solution and left to stand for 30 min, and finally washed with distilled water. The microbeads were placed in a container with fresh 6% calcium chloride solution at 5 °C for 22 h until characterization.

Figure No. 1: Ascorbic acid containing microbeads

2. Evaluation of microbeads

2.1. Percentage yield

The percentage yield of microbeads of different batches were estimated by the mass of final product after preparation with respect to the initial weight of the drug and polymer used for preparation of microbeads and percentage yields were estimated as per the Formula followed below. : (Vinod Dhote, 2012)

$$\text{Percentage yield} = \left(\frac{\text{practical yield}}{\text{Theoretical yield}} \right) \times 100$$

2.2 .Measurement of beads size

The particle sizes of both blank and drug loaded preparation were measured by an Optical microscope fitted with an ocular and stage micrometer and particle size distribution was measured. In all measurements at least 50 microbeads in five different fields were examined. Each calculation was carried out in triplicate. (VM. Sherina, 2012)

2.3. Scanning electron microscopy

The shape and surface morphology of microbeads were examined by scanning electron microscopy (SEM) using gold sputter technique. The particles were Vacuum dried, coated to 200 Aº thicknesses with gold palladium using prior to microscopy. An operational distance of 20nm, a tilt of zero-degree and accelerating voltage of 15kv is the operating parameters. Photographs of microbeads were taken within a range of 50-500 magnifications. (Vinod Dhote, 2012)

2.4. Drying rate study of the microbeads

Prepared microbeads were placed in open glass bottles and stand in an incubator maintained at 50ºC. Initially, the microbeads were removed at short intervals of time (5, 10, and 15, up to obtain constant weight). These measurements were continued until attainment of constant weight and note down the temperature and time for the complete drying of the beads. (Dhote, 2015)

2.5. Evaluation of swelling ratio

Swelling ratio was estimated by measuring the percentage water uptake by the beads. For this study 50 mg of beads from prepared blank beads were accurately weighed and placed in 100 ml of phosphate buffer (pH 6.8 and 0.1 N HCl (pH 1.2). Beads were removed from their respective swelling media after 8 h and weighed after drying the surface water using filter paper. The water uptake was calculated as the ratio of the increase in weight of beads after swelling to the dry weight. (Shivhare, 2013)

$$\text{Swelling ratio} = \left(\frac{\text{swollen wt - initial wt}}{\text{Initial wt}} \right) \times 100$$

2.6 Encapsulation efficiency

Ascorbic acid content in the microbeads was measured by a UV- spectrophotometric method. Accurately weighed 50mg of microbeads were dissolved in 100ml of phosphate buffer pH 6.8.The solution was kept for 24hrs. After that next day it was stirred for 15min. The solution was filtered,

after prepared suitable dilution; ascorbic acid content in the filtrate was analyzed at 235nm using Shimadzu 1201 UV-Visible spectrophotometer. The obtained absorbance was plotted on the standard curve to find the accurate concentration of the drug. Calculating this concentration with dilution factor we find the percentage of actual drug content and entrapment efficiency. The drug entrapment efficiency was determined by the following formula; (Shivhare, 2013)

$$\% \text{ Drug entrapment efficiency} = \left(\frac{\text{Actual drug content}}{\text{Theoretical drug content}} \right) \times 100$$

2.7. In- vitro release studies

In-vitro release studies of prepared micro beads can be carried out with phosphate buffer (pH 6.8) using USP- basket type apparatus. Accurately weighed amount of 250 mg of prepared micro beads kept into the basket rotated at a constant speed at 100rpm and maintained temperature 37±5ºC in 900ml of the dissolution medium (phosphate buffer pH6.8).The sample was withdrawn at 0.25hrs, 0.5hrs, 1hrs, 2hrs, 3hrs, 4hrs, 5hrs, 6hrs, 7hrs, 8hrs, 9hrs, 10hrs, 11hrs, 12hrs, 14hrs, 18hrs and 24hrs. Every time interval 5 ml of sample was withdrawn, at the same time 5 ml of fresh dissolution media was replaced to maintain sink condition. The withdrawn samples were properly diluted and measure the absorbance at 235 nm spectrophotometrically. Then calculate the cumulative percentage drug release at regular time intervals. (Dhote, 2015)

3. Preparation of mucoadhesive gel

3.1 Preparation of blank gel

Procedure-

The required amount of distilled water was taken in the beaker. Specified amount if Carbopol 940 were dispersed in the distilled water with the continuous stirring. Menthol were added in carbopol mixture Required quantity of methyl paraben and propyl paraben were dissolved in 5 ml of distilled water by heating, then glycerine was added after cooling. In the above mixture varying concentration of Ascorbic acid was mixed. With continuous stirring finally to the carbopol 940 gel full mixed ingredients were mixed, there after 0.33 ml of triethanolamine was added to produce gel.

Figure No. 2: Blank gel

3.2 Preparation of microbeads loaded gel

Procedure-

The required amount of distilled water was taken in the beaker. Specified amount if Carbopol 940 were dispersed in the distilled water with the continuous stirring. Menthol was added in carbopol mixture. Required quantity of methyl paraben and propyl paraben were dissolved in 5 ml of distilled water by heating, and then glycerine was added after cooling. In the above mixture varying concentration of L-ascorbic acid was mixed. With continuous stirring finally to the carbopol 940 gel full mixed ingredients were mixed. There after 0.33 ml of triethanolamine was added to produce gel. Microbeads were added in the gel.

Figure No. 3: Microbeads containing mucoadhesive gel

4. Evaluation of gel

4.1. Physical appearance

Physical parameter such as appearance and color were checked. (Richa Singh, 2020)

4.2. Measurement of pH

The pH of ascorbic acid gel formulations were determined by using digital pH meter. 1 gm of gel was taken and dispersed in 10 ml of distilled water and keep aside for two hours. The measurement of pH of formulation was carried out in three times and the average values are reported. pH of gel formulation was reported in table no. 6 (Richa Singh, 2020)

4.3. Homogeneity

All developed gel formulations 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. Homogeneity of gel formulation was reported in table no. 6

4.4. Clarity

The clarity of all the three batches was examined by visual inspection.

4.5. Spreadability

To find out the Spreadability, 0.5 g of gel was kept within a circle of 1 cm diameter pre-marked on a glass plate, above which a second glass plate was placed. A weight of 1000g was acceptable to rest on the upper glass plate for 5 min. The raise in the diameter due to gel spreading was noted. Evaluations were conducted in triplicate with different samples of the gel. (R. Narayana, 2013)

4.6. Viscosity

Viscosity test Viscosities were measured by Brookfield (DV-III) viscometer. Each gel was poured into the container and the proper spindle (number 74) was attached. Then the viscosities were measured in 25°C and 50-250 rpm. (Aslani, 2016)

4.7. Extrudability

The mucoadhesive gel were filled in standard capped collapsible aluminum tubes and sealed to the end. The extrudability was examined by pressing of the thumb. (S. Shaikh, 2018)

4.8. Gel strength

Gel strength was determined by the time in seconds required by the weight to penetrate in the gel. A required quantity of 5 gm of each of the optimize batches were taken and 3.5 gm weight were placed on the surface of gel. The time is required by the weight to penetrate 0.5 cm in the gel were recorded.

4.9. Bioadhesive Strength

Bioadhesive strength was determined by using glass slide and wooden block apparatus. Bioadhesive strength used to measuring the force required to detach the gel formulation from cellophane membrane. Specified quantity that is 1 gm of prepared gel was taken on glass slide wrapped with cellophane membrane. Intimate contact was provided by the changeable glass slide was placed on fixed slide. Two minute contact time was given to ensure intimate contact between gel formulation and membrane. The weight was placed in the pan which is provided to apparatus until slides got detached. The bioadhesive force, expressed as the detachment stress in dyne/cm2 was determined by the formula (Jaiswal, 2012).

$$\text{Detachment stress} = (m \times g)/A$$

Where,

m = Weight required to detach two glass slides from each other (gm).

g = Acceleration due to gravity i.e. 980 cm/s^2.

A = Area of membrane exposed (cm^2).

4.10. Antifungal activity

The evaluation of antifungal activity of all developed ascorbic acid containing formulation and blank mucoadhesive gel were estimated by Cup-plate method in comparison with marketed antifungal

formulation (Daktarin oral gel).n which two different bacteria cultures used were Aspargilious Aureus & Candida Albicans.

For the antifungal evaluation test, prepared nutrient brought and poured in to sterile Petri plates and kept aside for drying and cooling. After that each bacterial culture were spread via micron wire loop. A sterile cork borer 6 mm diameter was used to drill holes 4 mm deep. Then 0.5 gm of mucoadhesive gel from each batches add in to this holes. Plates were then incubated at 270C for 48 hr. The zone of inhibition (diameter in mm) developed. Antifungal test studies were reported in table no. 8 (Richa Singh 2020)

4.11. *In vitro* diffusion study

Egg membrane were using for this diffusion study. In donor compartment of cell, 1 gm of gel was placed in modified Franz diffusion cell. The total surface of membrane was in contact with the receptor compartment used simulated salivary fluid. At normal body temperature i.e. 37 ± 10C, the receptor compartment was continuously stirred (100 rpm) using a magnetic stirrer with temperature maintained. At predetermined time interval the sample was withdrawn and same volume was placed with fresh simulated salivary fluid. After proper dilution at respective λmax to estimate drug concentration, the absorbance of withdrawn sample was measured. (Sabir Shaikh, 2018)

4.12 *In vivo* evaluation study

4.12.1. Experimental Animals

Healthy adult albino Wistar rats weighing between 200-250g were procured and boarded in ordinary cages at room temperature and were given food and water ad libitum. The experimental procedure was accepted by institutional animal ethics com-mittee and animals were sustained under ordinary conditions in an animal house permitted by (SRIP, Kumhari). (Lakshana S, 2020)

4.12.2. Experimental induction of ulcer

Paraffin wax heated to above 100 C and poured on the dorsal surface of the tongue as a drop to induced oral ulcer. The animals were divided into 6 groups with 6 rats in each group. The ulcer was induced to group II, III ,IV, V,VI rats.

Group I served as normal control. Group II served as ulcer induced ones. Group III and Group IV animals are given 0.5% and 1% of Ascorbic Acid gel respectively to the ulcer induced ones. Correspondingly, Group V and Group VI were given 1.5% and 2% of gel to the ulcer induced ones.

4.12.3. Administration of drug & duration

The animals in all subgroups were treated at the same time, twice daily. A cotton swab dunked in appropriate drug was applied topically to the ulcer from the second day for a period of 7days.

4.12.4. Observation of wound healing

Apart from observing the behavioral changes, the animals were also being examined for the size and appearance of the ulcer, pus formation, exudates release, weight gain or loss and behavioral changes from the day of infliction of the wound. At the end of 7 days, all the animals were sacrificed.

4.12.5. Gross lesion and oral ulcer size evaluation

The length (mm) and width (mm) of the ulcer was dignified by a sliding caliper and ruler. The inhibition percentage (1%) was measured by the following formula:

$$1\% = \frac{\text{UA control} - \text{UA treated}}{\text{UA control}}$$

UA: The sum of the areas of all lesions

4.12. Stability Studies:

Open and close container was used to perform stability studies, here, by for 1 month by subjecting the product to room temperature.

RESULT AND DISCUSSION

The aim of this investigation was to study the influence of varying drug concentration, polymer concentration, stirring rate, pH and other related parameters on fabrication and evaluation of novel microbeads loaded gel for mouth ulcers.

5. Preliminary study data

5.1. Drug- excipient compatibility studies by physical observation

Ascorbic acid was mixed with various proportion of excipient showed no color change at the end of two months, proving no drug- excipient interaction.

Table No. 1. Data of some physiochemical studies

Parameter	Result	Reported
Melting point	194±0.3ºC	191ºC
pH	2-3± 0.1	2-4
Solubility	Soluble in water, ethanol, glycerol, propylene glycol Insoluble in ether, chloroform, benzene, petroleum ether, oils, fats	Soluble in water, ethanol, glycerol, propylene glycol Insoluble in ether, chloroform, Benzene, petroleum ether, oils, fats.
pKa	4.3 ±0.4	4.7

Table No. 2: DSC melting point of selected drug

Drug	DSC melting point in ºC
Ascorbic acid	194.6 ºC

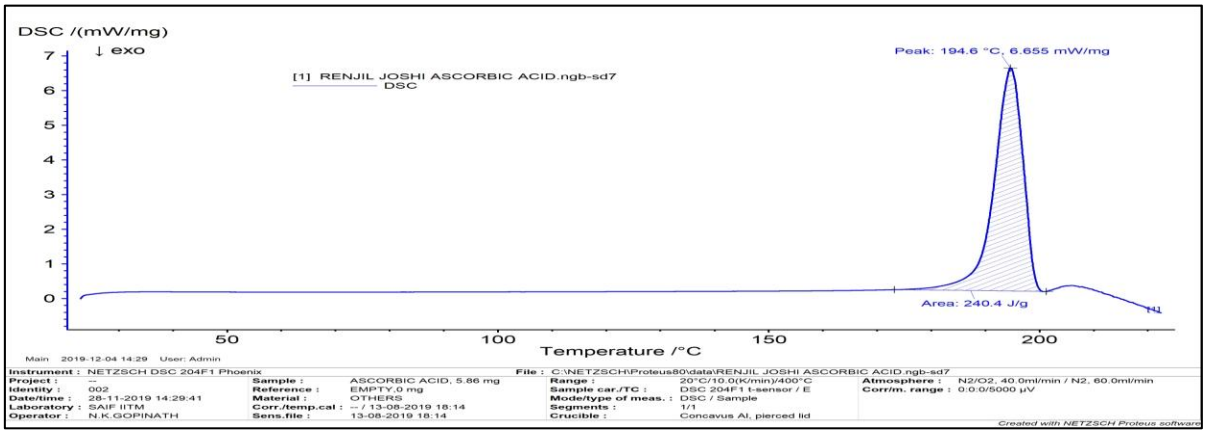

Figure No. 4: DSC curve of pure Ascorbic acid

5.2. <u>X-ray Diffraction:</u>-

X-ray powder diffraction is a scientific tool to elucidate structural characteristics in materials. X-rays that are directed at crystalline powders or polycrystalline materials will scatter in a pattern that is unique to that material. As such, a material can be identified by its scattered pattern.
Powder diffraction is a bulk sample procedure and can be employed to identify solids and heterogeneous samples and can be used to monitor solid-state reactions. Amorphous materials will also scatter X-rays and the amorphous patterns are useful information to the solid-state scientist.

The X-ray powder pattern for Vitamin C (ascorbic acid) is shown below.

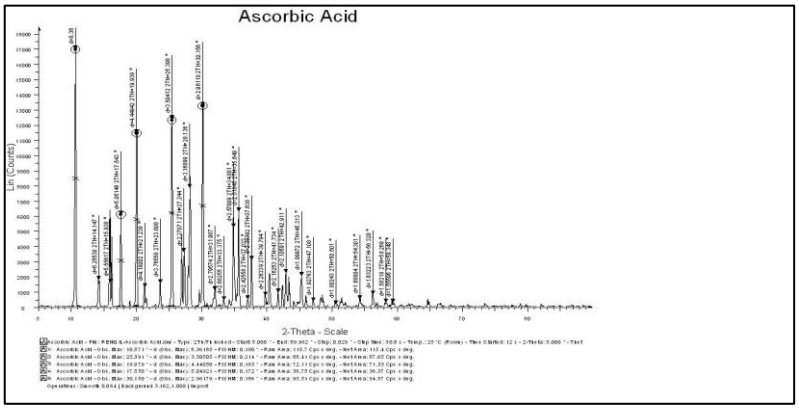

Figure No. 5: XRD peak of pure Ascorbic acid

6. Result of evaluated L- ascorbic containing microbeads

6.1. Percentage yield

The percentage yield ranged from 36.25% to 29-25%. it was observed that there was increase percentage yield with increase in sodium alginate concentration. Increase in drug concentration also had some significant effect. The percentage yield was decreasing with increase in drug concentration. However the effect of change in drug concentration was less as compared to the effect caused by

sodium alginate as the polymer to drug ratio increased, the percentage yield also increased, with maximum yield obtained for formulation 2.5% sodium alginate and 0.5% drug.

6.2. Measurement of beads size

The result concluded that the increasing the concentration of sodium alginate, the means particle size of microbeads increased. From results was seen that larger microbeads were obtained by increasing the concentration of sodium alginate. Therefore the concentration of the sodium alginate increase the particle size increases.

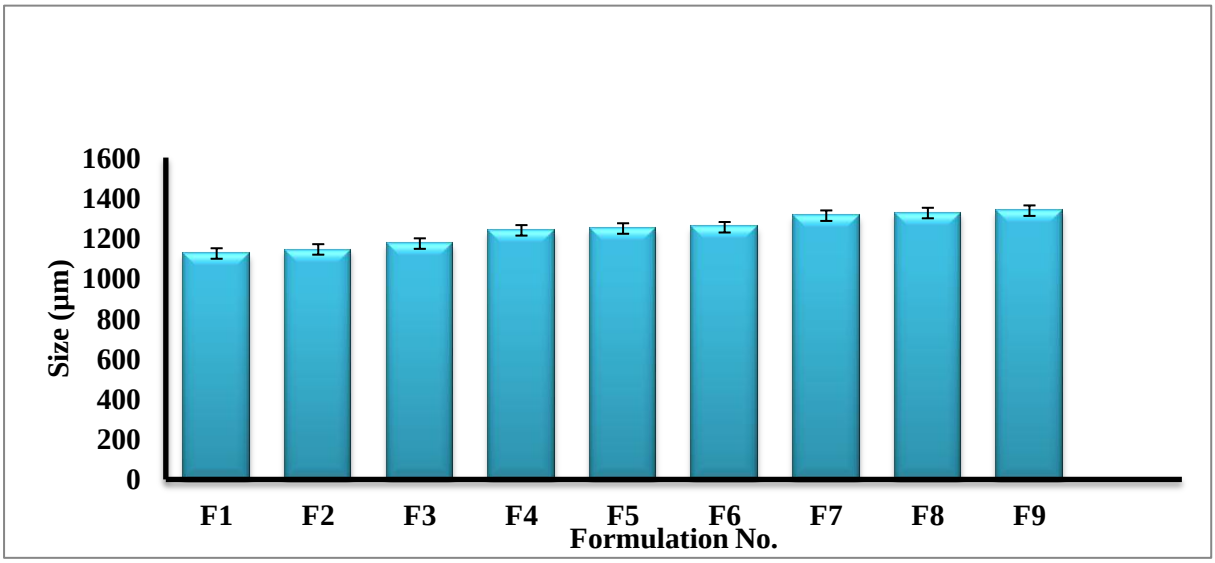

Figure No. 6: Beads size of different formulation

6.3. Drying rate study of the beads

Table No. 3: Drying rate of various formulations

Formulation No.	Drying rate/hr. at 50 ºC
F1	1.34 ± 0.32
F2	1.28 ± 0.12
F3	2.14 ± 0.9
F4	1.50 ± 0.12
F5	1.71 ± 0.23
F6	2.39 ± 0.12
F7	2.90 ± 0.31
F8	2.87 ± 0.93
F9	1.49 ± 1.1

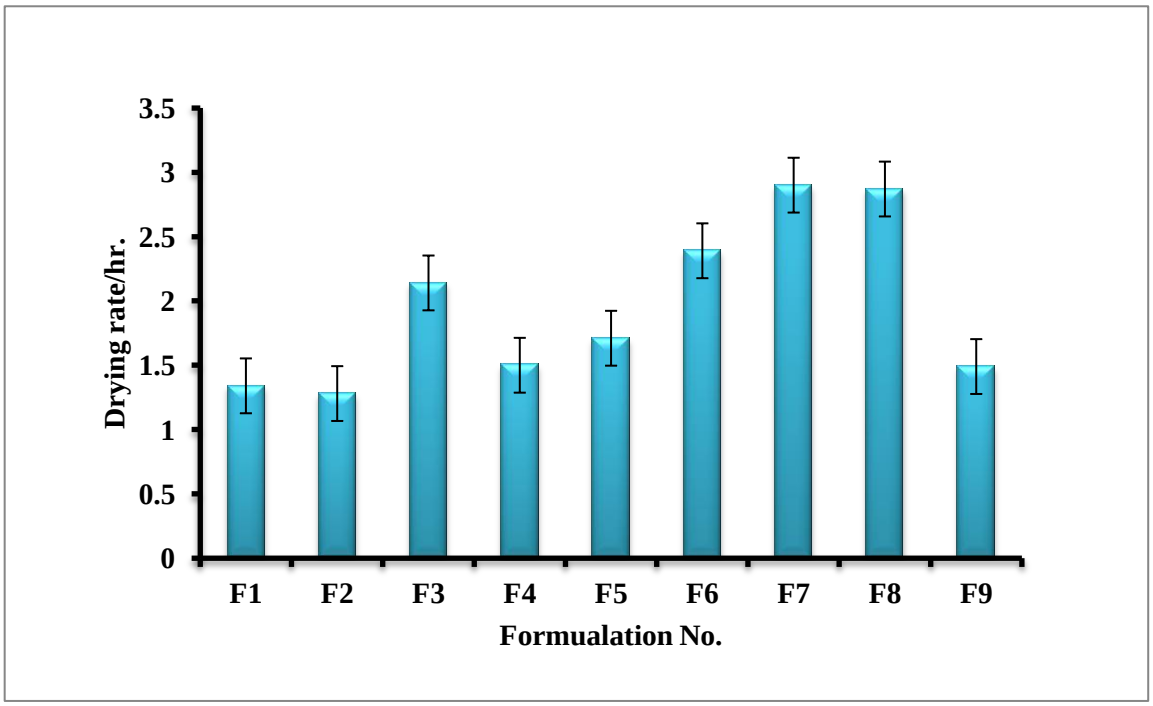

Figure No. 7: Effect of drying rate of various formulations

6.4. Evaluation of swelling ratio

Table No. 4: Swelling index of different formulation of ascorbic acid loaded microbeads

Formulation No.	Swelling Index	
	pH 1.2	pH 7.4
F1	234.45± 2.67	510.54±1.34
F2	280.67 ±5.03	554.66±2.66
F3	298.53 ±4.31	597.12±1.45
F4	310.34 ±3.21	642.57±3.34
F5	354.56 ±4.13	688.98±2.37
F6	388.34± 2.45	702.65±4.06
F7	401.41 ±6.23	755.34±5.10
F8	467.21 ±3.01	798.24±3.30
F9	491.46 ±2.22	814.45±4.03

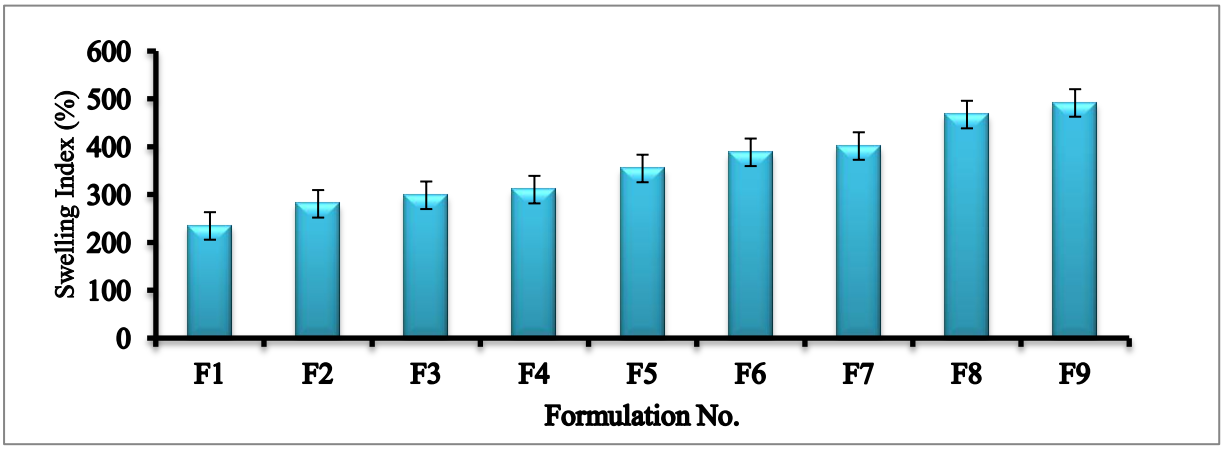

Figure No. 8: Effect of swelling index of microbeads at pH 1.2

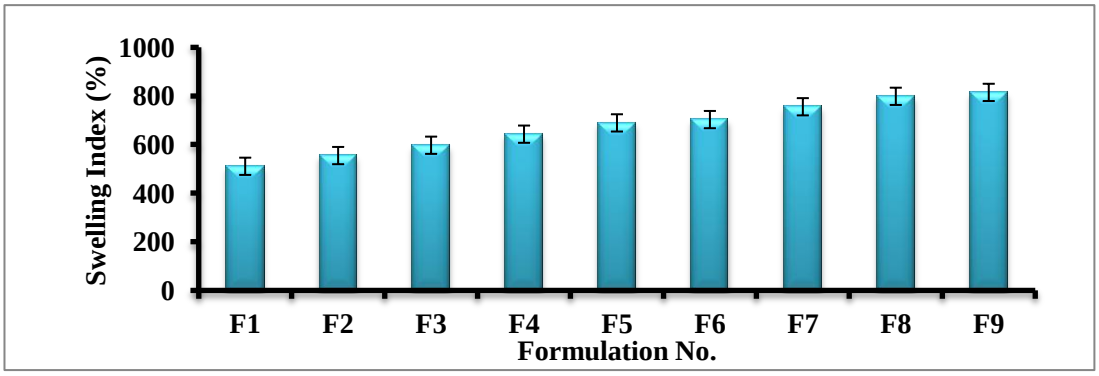

Figure No. 9: Effect of swelling index of microbeads at pH 7.4

The % swelling ratio of pH 1.2 and pH 7.4 ranges from 234.45 to 491.46 and 510.54 to 814.45 respectively. It was determined from the swelling study that alginate beads had swollen in phosphate buffer pH 7.4 more than in 0.1 N HCl (pH 1.2). The release will depend on diffusion of L- ascorbic acid through the insoluble matrix of alginate polymer in pH 1.2 HCl buffer. On the other hand, rapid swelling and erosion of beads prepared form alginate were examined at pH 7.4 because at this pH exchange of Na+ ion and Ca2+ takes place and Ca-alginate is converted into Na-alginate which is more soluble.

6.5. Drug entrapment efficiency

The % drug encapsulation efficiency for formulation (F1-F9) ranges from 43.24% to 81.12%. The higher encapsulation efficiency was observed as the concentration of alginate increased. This is due to the greater availability of active calcium binding sites in the polymeric chains and consequently the greater degree of cross linking.

6.6. Drug Content Estimation

Table No 5: Drug content estimation of prepared formulation

S.No.	Formulation No.	% Drug content
1.	F1	18.47 ± 0.21
2.	F2	22.38 ± 0.11
3.	F3	16.01 ± 0.51
4.	F4	21.56 ± 1.01
5.	F5	18.67 ± 0.32
6.	F6	17.1 ± 0.24
7.	F7	21.62 ± 0.13
8.	F8	16.30 ± 0.10
9.	F9	20.13 ± 0.24

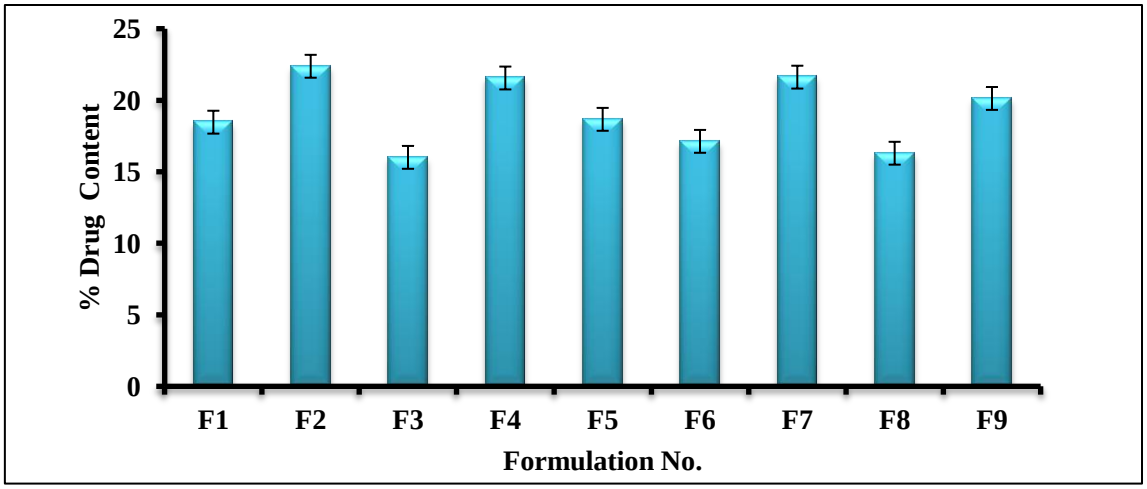

Figure No. 10: Graph of % Drug content

Drug content of formulation F1 to F9 ranges from 18.47 to 20.13%. Drug content is lower, because no external medium present for the prevention diffusion of the drug.

6.7. *In vitro* release studies

After evaluation of microbeads F3, F6, F9 formulations was optimized for the In-vitro drug release studies.

The *In-vitro* drug release studies of different formulations of microbeads cumulative percentage drug release was determined in the range of 90.24%-97.30%.The formulations F3, F6, F9 containing 1.5%, 2.0%, 2.5% sodium alginate respectively showed a release of drug 90.24%, 93.56% and 97.30% after

12 hours. This shows that more sustained release was examined with the increase in percentage of sodium alginate. The excellent formulation was observed as F9, by the observation of all results of the three formulations of L-ascorbic acid microbeads.

"After the optimization of all formulations, F9 showed 81.12% encapsulation efficiency and 97.30% drug release in 12 h, hence considered as optimized batch."

7. Result of Evaluated microbeads loaded gel

Table No. 6: Evaluation of prepared gel formulation

Formulation	Physical appearance	pH	Clarity	Homogeneity
F1	Transparent	7.2 ±0.08	Good	Good
F2	Transparent	6.7 ±0.04	Good	Good
F3	Transparent	7.1 ±0.08	Good	Good

Table No. 7: Evaluation parameter of prepared gel formulation

Formulation	Spreadability (gm.cm/sec)	Viscosity (Pa·S)	Extrudability	Gel strength	Bioadhesive Strength (dyne/cm$^{2)}$
F1	5.36 ± 0.040	2.145± 0.031	Good	32 ±1.34	2324 ±0.04
F2	6.32 ±0.030	3.205 ±0.033	Good	26 ± 1.41	3591 ±13.24
F3	6.42 ±0.020	3.431± 0.012	Good	41 ±0.26	4276 ±34.80

7.1 Anti- Fungal studies

Table No. 8: Anti- fungal studies of gel formulation

Formulation	Anti- Fungal study	
	Aspergillus aureus	Candida albicans (mm)
Blank	13	14
F1	16± 0.7	18± 0.7
F2	19± 0.5	20±0.8
F3	21± 0.6	22± 0.3
Marketed Formulation	27±0.1	29± 0.4

7.2. *Invitro* diffusion study

Table No. 9: In-vitro drug diffusion study of prepared gel formulation

S.No	Time (hours)	% CDR		
		F1	F2	F3
1.	30 min	8.345± 0.03	7.435± 0.01	9.304 ± 0.56
2.	1	15.345 ±0.36	13.997± 0.57	19.982 ±0.92
3.	1:30	18.786± 0.45	19.223± 0.23	24.349 ±0.45
4.	2	19.345± 0.34	25.289 ±0.38	30.275± 0.39
5.	2:30	21.981± 0.20	29.201± 0.18	48.295 ±0.93
6.	3	34.789 ±0.02	32.789± 0.92	58.719± 0.30
7.	3:30	39.503 ±0.78	38.203± 0.28	64.205 ±0.58
8.	4	41.891± 0.34	43.456 ± 0.56	73.897 ±0.67

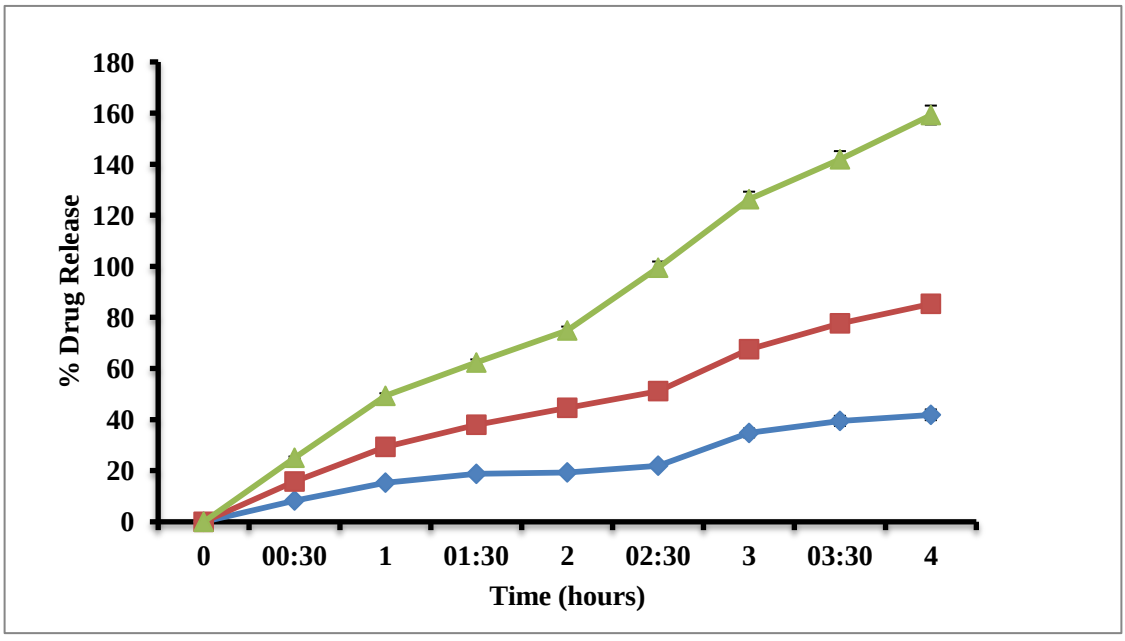

Figure No. 11: Graph of In-vitro drug diffusion study of prepared gel formulation

7.3. *In vivo* evaluation studies

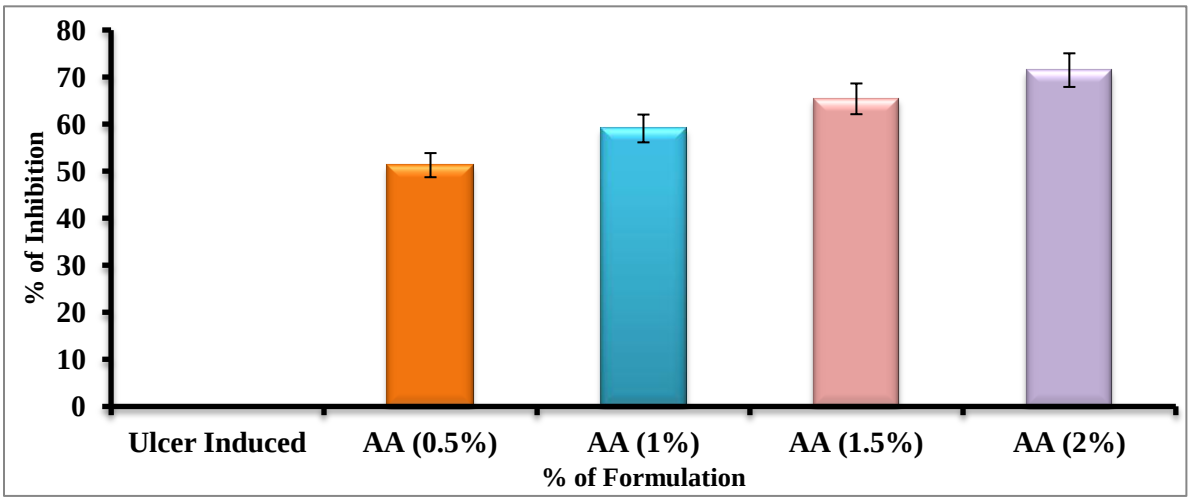

Figure No. 12: Percentage of ulcer inhibition by Ascorbic Acid Gel treatment on ulcer induced rats.

Results were expressed as Mean ± SEM (n=6). *p<0.05 statistically significant as compared with ulcer induced control group.

Table No. 10: Ulcer size of control and experimental rats

Variables	Ulcer induced	AA (0.5%)	AA (1%)	AA (1.5%)	AA (2%)
Ulcer size	13.47 ±1.2	10.01± 0.5*	6.02± 0.3*	4.05± 0.2*	3.25 ±0.1*
Inhibition %	-	51.3 ±1.3	59.1± 2.1	65.4 ±3.5	71.5± 4.0

Results were expressed as Mean ± SEM (n=6). *p<0.05 statistically significant as compared with ulcer induced control group. AA= Ascorbic acid percentage of composition

7.3.1. Statistical Analysis

The results were measured as the Mean± SEM for each group. Statistical differences were evaluated using a one-way analysis of variance (ANOVA). Results were measured to be statistically significant at p<0.05.

In the present study, Ascorbic acid gel was evaluated for its oral antiulcer activity. The results of study are tabulated in (Table No. 10). Among the ulcer induced rat model, Ascorbic acid (2%) showed more oral ulcer protective activity. This research proved that the Ascorbic acid gel possess also highly significant beneficial action on oral ulcer. Oral ulcer size measurement and percentage of inhibition in the oral cavity were observed and tabulated under (Table No.10).

7.4. Stability Studies:

Table No. 11: Stability study of prepared gel formulation

Formulation	Stability study for 1 month	
	Open container	Closed container
F1	Not stable	Stable
F2		
F3		

CONCLUSION

L-ascorbic acid containing microbeads loaded mucoadhesive gel was prepared for the treatment of mouth ulcer. In which the L- ascorbic acid loaded sodium alginate microbeads with calcium chloride as a cross-linking agent were prepared by Ionic Gelation method. Mucoadhesive gel was prepared by using different concentration of ascorbic acid and Carbopol 934, menthol, glycerine as a gel base.

It was demonstrated that the developed gel formulation have significant, therapeutically efficacious, appropriate vehicle for drug delivery in low cost but definitely with high potential. Developed new gel formulation is suitable for mouth ulcer treatment, because after the absorption of ascorbic acid through the mucosal membrane drug treat the stomach problem like constipation, acidity etc. Generally the mouth ulcer can arise by the improper digestion. Ascorbic acid also recovers the canker sore and provides nourishment and development of the mucus membrane. In the mouth ulcer treatment menthol has also provide cooling effect so minimize the effect of pain.

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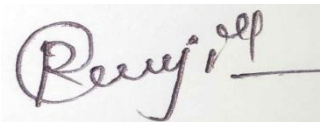

(Signature of the Candidate)

Miss Renjil Joshi