FORMULATION AND *IN VITRO* EVALUATION OF MUCOADHESIVE BUCCAL TABLET OF FEBUXOSTAT

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ABSTRACT:-
Mucoadhesive buccal tablets of febuxostat were prepared with an objective of Enhanced bioavailability using natural polymer in varying concentration of polymer like xanthan gum and Vigna mungo by direct compression method. The Preformulation study using FTIR spectroscopy revealed the compatibility of drug and polymer. The tablets were evaluated for hardness, thickness, weight variation friability and drug content concluded that all these parameters were in acceptable rang of pharmacopecial specification. The tablets were studied for surface pH, swelling index, *In vitro* drug release, bioadhesive strength. The surface pH of the tablet was from 6.85 to 6.95 which fall in the range of salivary pH and the entire tablets showed good bioadhesive strength from 0.0181±0.04to 0.1460±0.01gm. The buccal tablet showed good swelling index of >70 % up to 7 hr maintaining the integrity of polymers. The *In vitro* release of febuxostat was extended 4-6 hr. The *in vitro* release obeyed zero order kinetic with mechanism of release followed by Fickian diffusion. Therefore it was planned in this investigation to develop controlled release mucoadhesive buccal tablets containing Antigout, febuxostat to release the drug unidirectional in bioavailability to reduce the dosing frequency and improve the patient compliance.
Key words: Febuxostat, Xanthan Gum, Vigna mungo, Swelling Index, Drug Release

1. INTRODUCTION: [1, 2, 3]

Buccal systems are actually controlling the drug concentration in the body, not just the release of the drug from the dosage form, as is the case in a sustained-release system. The main objective of developing these systems is to increase the safety of a product to extend its duration of action and decrease the side effects of drugs. In buccal drug delivery systems Mucoadhesion is the key element so various mucoadhesive polymers have been utilized in different dosages form.

Gout is a rheumatic condition due to the deposition of monosodium urate crystals (tophi) in the joints or soft tissues and synovial fluid due to its saturation in blood. It is associated with increased serum uric acid levels. At high levels, uric acid crystallizes in surrounding tissues, resulting in an attack of gout. Gout occurs more commonly in those who eat a lot of meat, drink a lot of beer, or are overweight. Diagnosis of gout may be confirmed by seeing the crystals in joint fluid or tophus .The mucoadhesive polymers was selected for preparing buccal tablet such as xanthan gum and vigna mungo gum.
Febuxostat belongs to a BCS class Π of drugs. The drugs of this class have a high absorption number but a low dissolution number.

2. MATERIALS:-

Febuxostat was obtained from Pure Chem Pvt. Ltd. as a gift sample. Xanthan gum was obtained from Thermo Fisher Scientific India Ltd. Mumbai, Vigna mungo from Shree udid seed supplier, Avicel pH101, Mannitol, Magnesium stearate, Talc from Research lab fine Chem industries.

➢ Preparation of Seed Flour of Black Gram: [5]

The dehusked seed of black gram were properly washed with distilled water and dried in oven temperature less than 50 ºC. The dried seeds were powdered in mixer and passed through #120 sieve using sieve shaker and stored in desiccators until further use.

3. METHODOLOGY:

A. Preformulation study Identification and Characterization of the Drug: [4-8]

a) Oraganoleptic Properties: The Oraganoleptic properties of febuxostat such as colour, appearance, odor was observed visually

b) **Melting Point** The melting point was determined by melting point apparatus and the melting point was found

c) **Solubility :**
Solubility of Febuxostat was checked in various solvents.

d) **Determination of ʎmax of Drug in pH 6.8 phosphate buffer:**
UV spectrum of febuxostat was obtained by using 10 ppm solution of febuxostat. 10 ppm febuxostat solution was prepared by dissolving 10 mg of febuxostat in 100 ml of phosphate buffer pH 6.8 and from the above solution 1ml of solution is pipette out and the volume was made up to 100 ml with phosphate buffer pH 6.8, then this solution is scanned in the range of 200-400 nm by using UV visible spectrophotometer. The linearity was established by plotting calibration curve by using dilutions ranging from 2-12 ppm.

e) **FTIR Spectrum of febuxostat:**
The FTIR spectrum of febuxostat was obtained by scanning a powdered sample of febuxostat in the wave number range of 4000-200 cm^{-1}.

f) **Drug Polymer Compatibility Study:**
Drug polymer compatibility study was performed by fourier transform infrared spectroscopy. Drug polymer compatibility study was performed by mixing the drug with polymer in equal proportion and then the IR spectrum was recorded for a mixture. The spectra recorded over a frequency range 4000-200 cm^{-1}.

4. PREPARATION OF MUCOADHESIVE TABLETS: [3-8]

Mucoadhesive tablets were prepared by direct compression method. Febuxostat and all ingredients were individually passed through sieve no # 60. All the ingredients were mixed thoroughly by triturating up to 15 min. The drug is thoroughly mixed with mannitol on butter paper with the help of stainless still spatula. Then all the ingredients except lubricant mixed in the order of ascending weights and blended for 10 min. After uniform mixing of ingredients, lubricants was added and against for 2 min. Then tablets were prepared using drug and excipients mixture by direct compression .total weight tablet was considered as 200 mg. the compression of different formulation is given in table no.1

Table 1: ingredients used in formulation of buccal tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Febuxostat	40	40	40	40	40	40	40	40	40
Xanthan gum	40	60	80	40	60	80	40	60	80
Vigna mungo gum	10	20	30	10	20	30	10	20	30
Avicel pH101	98	78	58	88	68	48	78	58	38
Mannitol	8	8	8	8	8	8	8	8	8
Magnesium sterate	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200

5. EVALUATION PARAMETERS:

a. Bulk Density for Powder:

Bulk density is calculated by using the following formula:

Bulk density = m/v_0

Where, m =mass or weight of powder taken, v_0 = bulk volume.

b. Tapped Density:

Tapped density is calculated by using the following formula:

Tapped density = m/v_f

Where, m = mass or weight of powder taken, v_f = tapped volume.

c. Flow Properties:

- **Angle of Repose (ɵ):**

This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane .the powders were allowed to flow through the funnel fixed to a stand at definite height (h).the angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

T ɵ=$\tan^{-1}(h/r)$

Where, ɵ=angle of repose

h= height of heap

r= radius of the heap

The relationship between angle of repose and powder flow is as follows:

tan ɵ = h/r

- **Compressibility Index:**

The flow ability of powder can be evaluated by comparing the bulk density (do) and tapped density(df)of powder and the rate at which it packed compressibility index is calculated by –

$$\text{Compressibility Index (\%)} = \frac{\text{tapped density-bulk density} \times 100}{\text{Tapped density}}$$

- **Hausner's ratio:**

It is the ratio of tapped density to bulk density.

Hausner's ratio = tapped density/bulk density

d. Hardness:

Hardness was measured using incorporate hardness tester that measures the pressure required to break diametrically placed buccal tablets by applying pressure with coiled spring.

e. Friability:-

The friability of tablets was determined by using Roche friability. It is expressed in percentage (%). 6 tablets were initially weighed (W initial) and transferred into friability .the friability was operated at 25 rpm for 4 minutes or run up to100 revolutions. The tablets were weighed again (W final).the % friability was then calculated by-

%F=100(1-W initial/W final)

% friability of tablets less than 1% was considered acceptable.

f. **Weight variation: -**The causes for weight variation can be divided into granulation and mechanical problems. If the granule size is larger, the dies will not be uniformly filled. Similarly mechanical problems can be traced of lower punches of non- uniform length.

Method: Uncoated tablet complies with this test and the average weight was determined by weighing 20 tablets.

Not more than two tablets deviate from the average weight by a percentage greater than that given and no tablet deviates by more than double that percentage. Weight variation tolerances for uncoated tablet**:**

Table 2: Specification of % weight variation allowed in tablet as per USP

Average weight of tablet(mg)	Maximum difference allowed%
130or less	10
130-324	7.5
More than324	5

g. **Drug content:**

The drug content, 10tablet was crushed in glass mortar with pestle and powder containing 40mg of febuxostat was dissolved in 100 ml of phosphate buffer pH 6.8 .the solution was sonicated for 30 minutes and liquid was filtered through Whatman filter paper and the 10 ml of filtrate is taken into100 ml volumetric flask and made final volume with phosphate buffer 6.8 then absorbance is measured at 313.5 nm using UV visible spectrophotometry. The amount of drug present in one tablet is calculated using standard graph.

% Purity=absorbance of unknown (Au)/Absorbance of standard (As)*10

Where, C is concentration

h. ***In –vitro* dissolution studies:**

Detail of dissolution test:

The drug release profile was s studied using USP dissolution testing apparatus method II using a paddle at 50rpm.500 ml dissolution fluid , pH 6.8 phosphate buffer , was used and a temperature of 37±0.5°c was maintained. 5 ml aliquots at 0 min,15min,30min, 1h,2h,3h,4h,5h,6h,7h,8h,9h,10h,11h,12h,respectively were pipette out and same volume was replaced with pH6.8 phosphate buffer absorbance was measured at λmax 313.5nm and from which percentage of febuxostat was calculated using calibration curve. The procedure was repeated for three more tablets similarly and average was computed.

Drug release medium = Conc. of febuxostat × Dilution factor1000 × Dissolution

% of drug release = Drug release dose of drug ×100

Dissolution studies were performed for all formulation .the mean values and standard deviations were calculated**.**

Method:

The pure drug and its formulation were subjected to IR studies. In the present study, the potassium bromide disc (pellet) method was employed**.**

i. Swelling study:

The extent of swelling was measured in terms of percentage weight gain by the tablets. The swelling behavior of all the formulations was studied. One tablet from each formulation was kept in petri dish containing of phosphate buffer pH6.8 .at the end of 2,4,6,8,10,and 12 hr. tablet were withdrawn , soaked on tissue paper and weighed , and then percentage weight gain by the tablet was calculated using formula.

$SI = Mt – Mo/ Mo \times 100$

Where, SI= Swelling index,

Mt=weight of tablet at time t'

And Mo= weight of tablet at time 0

j. Surface pH:-

For determination of surface pH of buccal tablet, a combined glass electrode is used. The tablet is allowed to swell by keeping it in contact with 10 ml of distilled water (pH 6.8±0.05) for 2h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing equilibrating for 1 min.

k. **Mucoadhesive strength:** [9, 10]

Mucoadhesive strength was conducted on modified physical balance .the equipment was fabricate by us in laboratory as polypropylene disc (A), also locally fabricated. The apparatus consist of modified double beam physical balance in which the right pan has been replaced by a glass slide with the copper wire and additional weight, to make the right side weight equal with left side pan. Teflon block of 3.8 cm diameter and 2 cm height was fabricate with an upward portion of 2 cm height was fabricated with an upward portion of 2 cm height and 1.5 cm diameter on one side. This was kept in beaker filled with buffer media pH6.75, which was then placed below right side of the balance. The right pan (D) was replaced with a lighter pan so that, the left pan weights more than the right pan. The lower polypropylene block was intended to hold the mucosal tissue (B) of goat cheek pouch and to be placed in a beaker containing simulated saliva solution pH6.75(C).goat cheek pouch was obtained commercially; the check pouch was collected into a sterile container containing sterile buffer solution of pH 6.75.the cheek pouch brought was stored in a refrigerator until use.

The following procedure was used for all the test formulations using the above equipment .the cheek pouch was removed from refrigerator and allowed to attain equilibrium with ambient conditions in the laboratory .the goat cheek pouch was carefully excised, without removing connective and adipose tissue and washed with simulated saliva solution .the tissue was stored in fresh simulated salvia solution. Immediately afterwards the membrane was placed over the surface of lower polypropylene cylinder

(B)and secured .this assembly was placed into beaker containing simulated saliva solution pH6.75at 37±2ºc.from each batch , one tablet at a time was taken and stuck to the lower surface of polypropylene cylinder with a standard cyanoacrylate adhesive. The beaker containing mucosal tissue secured upon lower cylinder (B), was manipulated over the base of the balance so that ,the mucosal tissue is exactly below the upper cylinder(A).the exposed part of the tablet was wetted with a drop of simulated saliva solution ,and then a weight of 20 minutes . After which the tablet binds with mucin. The weight was removed .then slowly and gradually separates from the mucosal surface/membrane. The weight required for complete detachment is noted (W1) (W1-5.25 gm.) gives force required for detachment expressed in weight in grams. Procedure was repeated for two more tablets .Average was computed and recorded.

l. Factorial Design:

A 3^2 factorial design was employed considering amount of MCC (A) and SSG (B) as two independent variables .by applying factorial, 9 batches were prepared for both the parts respectively. Analysis of variance (ANOVA) was performed to study the statistical were significance of independent variables and their interaction term. Polynomial equations were calculated for as responses. Design expert (Version) was used for the statistical and mathematical analysis**.**

Table 3: Investigating ranges of variable for Xanthan gum and vigna mungo

Sr.no	Factor	Low level (%)	High level (%)
A	Xanthan gum	20%	40%
B	Vigna mungo	5%	15%

The nine formulation of tablet were prepared by using 3^2 factorial design experts software as mentioned in table 7.10.xanthan gum as polymer (A), vigna mungo is secondary polymer were used as independent variable whereas % drug release, was dependent variable. Factor was tested at three levels designated as-1 ,0,and +1.the value of the factor was transformed to allow easy calculation of co-efficient in the polynomial equation to identify the effect of significant variables ,the reduced model was generated interactive multiple regression analysis and f statistics were utilized in order to evaluate the response.

m. Stability Study:

The detected formulations were packed in amber –colored bottles, which were tightly plugged with cotton and capped .they were then stored at 25ºC/60 %RH and 40ºC/75% RH for 3 months and evaluated for their physical appearance, drug content and drug excipients compatibility at specified intervals of time.

6. RESULT AND DISCUSSION:

A. Preformulation study of drug

- **Organoleptic properties:**

It is white to off-white, amorphous powder complying with the description given in the literature.

- **Melting point:**

Melting point of the drug matches with the melting point given in the literature, melting point of Drug is shown in the table 4.

Table 4: Melting point of Drug against reported value

Melting point		
Reported value	Practical value	
	Thiel's tube method	Capillary method

238-239^{0}C	214-216^{0}C	210-212^{0}C

- **Solubility**

Drug was found to be slightly soluble in water, sparingly soluble in ethanol and soluble in methanol, DMSO, pH 6.8, 7.4 phosphate buffers. The solubility details are given in table 5.

Table 5: Solubility study:

Solvent	Amount soluble (febuxostat)in mg/ml
pH6.8	0.109
pH7.4	0.073
Distilled water	0.0034

- **Determination of λ_{max} of Drug in pH 6.8 phosphate buffer:**

After studying the UV spectra of Drug, it was found that drug shows maximum absorbance at 313.5nm when solution (100 µg/ml) is prepared in pH 6.8 phosphate buffer λ_{max} of Drug in pH 6.8 phosphate buffer is shown in Fig.1. Solutions of Drug prepared in pH 6.8 phosphate buffers and scanned between 200-400nm using UV Spectrometer which showed peak at 313.5 nm.

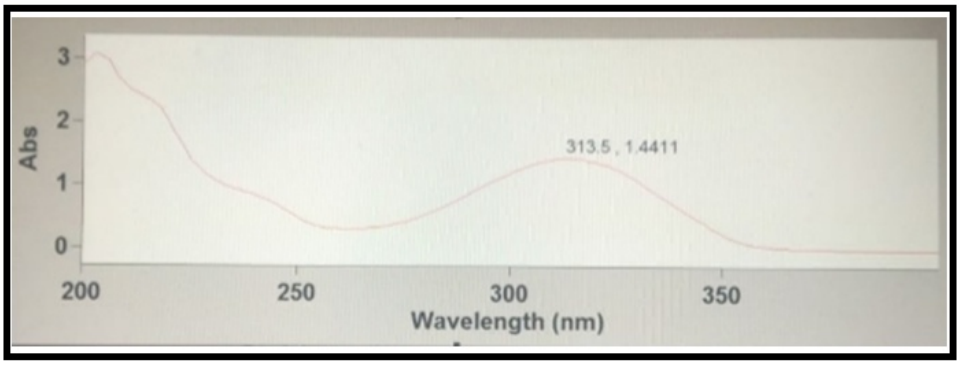

Fig. 1: UV-visible spectrum of Drug in pH 6.8 phosphate buffer

- **Calibration curve of Drug in pH 6.8 phosphate buffer-**

The calibration curve (Fig. 2) was found to be linear in the concentration range of 2-12µg/ml (Table 6) having coefficient of regression value R^2 =0.9996 and Slope y = 0.1143x +0.0023

Table 6: Absorbance's of different concentration of Drugin pH 6.8 phosphate buffer.

Sr.no.	Concentration (µg/ml)	Absorbance
1.	2	0.2342
2.	4	0.4540
3.	6	0.6789

4.	8	0.9331
5.	10	1.1422
6	12	1.337

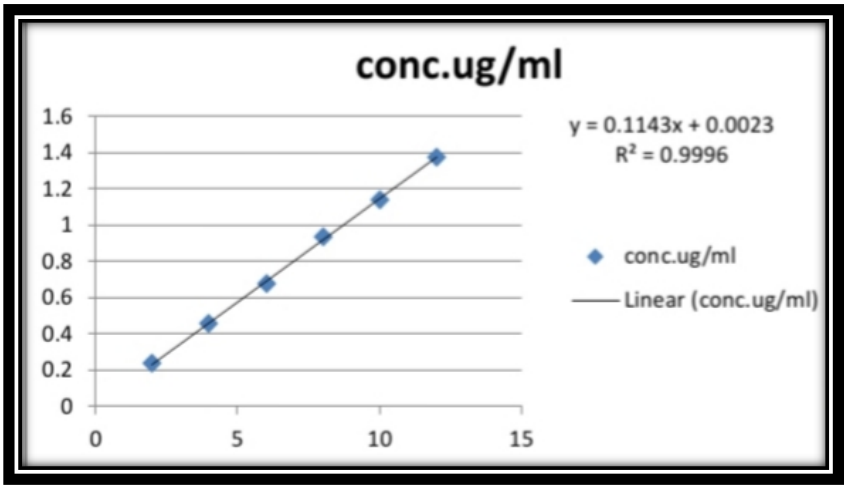

Fig.2: Calibration curve of Drug in pH 6.8 phosphate buffer

- **FTIR Spectrum of febuxostat:**

The FTIR spectrum of febuxostat shows the peaks at following values which are characteristics drug shown in table.

The FTIR spectrum of febuxostat is shown in fig. 3.

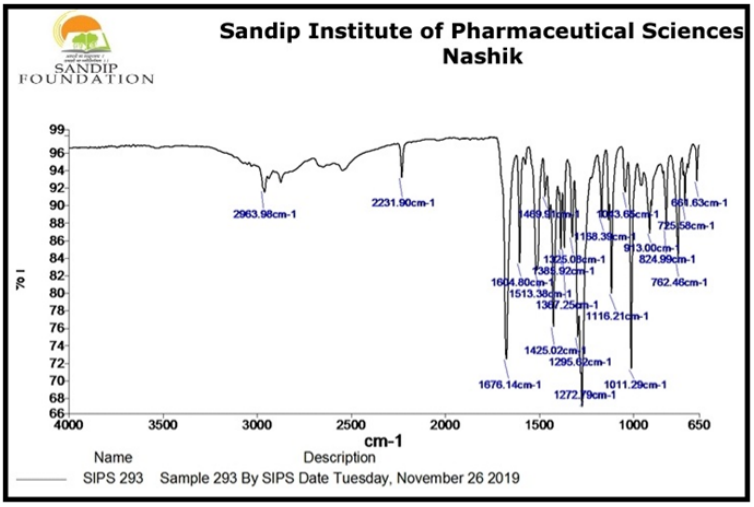

Fig. 3: IR of drug febuxostat

The IR spectra of drug shows the peak at wave number (cm^{-1}) which correspond to the functional group present in structure of drug. IR interpretation of drug is shown in table 7.

Table 7: IR Interpretation of Drug

Sr. no.	Functional group	Peak in cm-1	Peak observation
1	NH_2- Stretching	3462.95	3462.22
2	C=o Stretching	1670	1678.07
3	OH-C Stretching	1375.61	1385.92
4	N-C Bending	1603.25	1604.80

The absorption band show by Drug is characteristics of functional group present in its molecular structure above. The presence of absorption band corresponding to the functional group present in the structure of Drug conform identification and purity of the sample.

- **Drug Polymer Compatibility Study:**

FTIR spectra of drug polymer mixtures retained the characteristics functional peaks of the drug as shown in fig. 4 and 5.From the observation of the FTIR spectra of febuxostat and its interpretation data it was concluded that the polymer and drug did not interact with each other and are compatible.

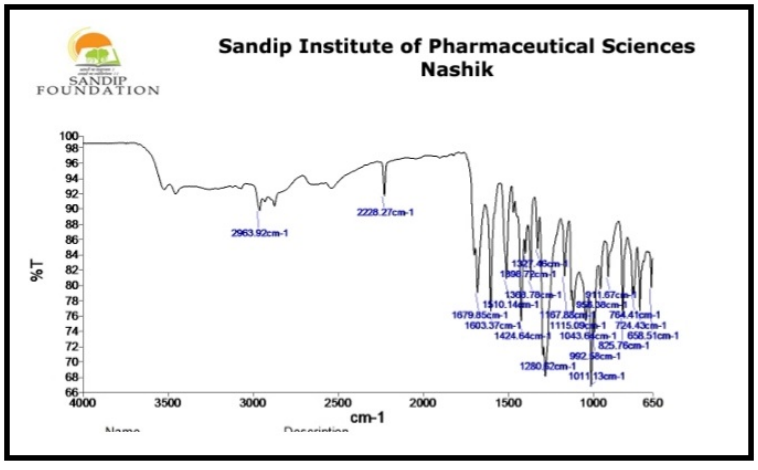

Fig. 4: physical mixture febuxostat and xanthan gum polymer

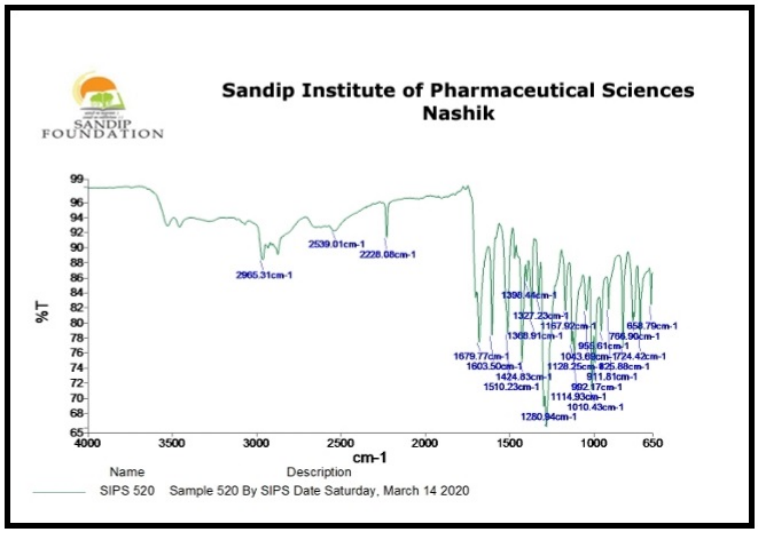

Fig. 5: IR spectra of physical mixture of drug and vigna mungo

B. Evaluation of Precompression characteristics of mucoadhesive tablet formulation: (Formulation code F1 to F9)

Precompression study:

The Drug mucoadhesive buccal tablets were prepared by direct compression. Ingredients were accurately weighed, grounded and passed through mesh # 120 and then thoroughly blended with talc and magnesium stearate before compression. The powder blend was studied for rheological characteristics. The uniformly blend of powder was then compressed in a 12 station tablet punching machine using 8 mm flat concave faced punches. Before compression powder bed of all formulations were studied for various rheological characteristics bulk density, true density, compressibility index, Hausner's ratio and angle of repose. The results of the studies indicated that the powder bed is easily compressible, and hence can be compressed into a compact mass of tablet. The angle of repose is an indicative parameter of powder flow ability from hopper to die cavity. Angle of repose between 25^0 to 30^0, indicates excellent flow ability of powder bed. In this work, the angle of repose was found to be varying between 21.85±0.5º and 26.34º ±0.6when glidants were incorporated. These studies indicated that, the powder beds of all formulations are easily flowable.

Precompression characteristics of all tablet formulations are shown in table 8.

Table 8: Precompression characteristics of all tablet formulations

Formulation code	Bulk density (gm./ml) Mean± S.D	Tapped density (gm./ml) Mean± S.D	Angle of repose (⁰)	Compressibility index (%) Mean± S.D	Hausner's ratio Mean± S.D
F1	0.47±0.008	0.55±0.001	25.45±0.4	14.54±0.6	1.17±0.02
F2	0.45±0.003	0.52±0.009	23.49±0.7	13.64±0.7	1.14±0.01
F3	0.46±0.005	0.57±0.001	24.19±0.5	15.20±0.4	1.12±0.02
F4	0.44±0.001	0.58±0.002	25.72±0.6	12.74±0.6	1.15±0.01
F5	0.50±0.002	0.54±0.005	21.99±0.4	13.94±0.3	1.16±0.03
F6	0.46±0.001	0.57±0.009	26.00±0.3	16.50±0.6	1.20±0.03

F7	0.42±0.007	0.55±0.003	24.19±0.4	13.57±0.6	1.14±0.02
F8	0.46±0.003	0.57±0.002	21.85±0.5	15.27±0.3	1.11±0.03
F9	0.45±0.006	0.54±0.001	26.34±0.6	14.98±0.4	1.18±0.02

C. Evaluation of compressional characteristics of all mucoadhesive formulations:

Hardness of the tablets varied between 3.2 ± 0.7 Kg/cm^2 and 4.4± 0.6Kg/cm^2 indicating good binding and satisfactory strength of tablets to withstand stresses during transportation and also may offer good adhesion to mucosa. %. The drug content of the formulations F1 to F9 was found to be in between 96.4±0.52 and 99. 8±0.58%.The surface pH of all the mucoadhesive tablet formulations was found to be uniform, consistent and in the range of 6.85 to 6.95. It is indicating that all the formulations provide an acceptable pH in the range of salivary pH (5.5 to 7.0).

Table 9: Evaluation of Physical Characteristics of mucoadhesive tablets containing Drug

Formulation code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation (mg)	%Drug content	Surface pH
F1	4.4±0.2	2.70±0.02	0.52±0.05	198.05±	99.2±0.48	6.94
F2	4.4±0.5	2.77±0.07	0.56±0.01	198.12±	98.5±0.33	6.93
F3	3.2±0.7	2.69±0.04	0.56±0.05	199.34±	96.4±0.52	6.87
F4	4.4±0.2	2.72±0.01	0.53±0.05	197.2±	99.7±0.71	6.89
F5	3.4±0.5	2.75±0.01	0.57±0.02	199.2±	98.5±0.79	6.93
F6	3.9±0.3	2.71±0.05	0.51±0.01	199.8±	99.5±0.18	6.85
F7	4.5±0.2	2.73±0.05	0.54±0.03	198.5±	99.3±0.14	6.95

F8	4.4±0.2	2.76±0.02	0.51±0.01	199.5±	99.8±0.58	6.94
F9	4.4±0.6	2.77±0.04	0.55±0.02	198.5±	99.3±0.30	6.93s

D. Swelling study:

The % swelling index of Drug mucoadhesive buccal tablet for a period of12 h is shown in table .8.12the water uptake nature of the polymer is one of the important properties that affect the onset of swelling. Swelling has been increases with increase in amount of xanthan gum or Vigna mungo. Maximum swelling was attained at12 h.

Table 10: Swelling study for Drug

Time(hr.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	16.34±0 .29	17.47±0 .42	20.43±0 .07	23.06±0 .05	25.95±0 .48	27.05±0 .25	29.64±0 .16	34.21±0 .05	29.05±0 .32
2	21.65±0 .23	22.37±0 .82	27.38±0 .05	36.45±0 .77	37.41±0 .86	39.35±0 .38	34.41±0 .38	44.85±0 .18	36.45±1 .77
3	26.27±0 .23	26.30±0 .67	33.53±0 .61	36.88±0 .90	42.95±0 .27	45.32±0 .31	46.65±0 .24	53.84±0 .49	45.32±0 .78
4	30.12±0 .18	30.19±0 .27	37.25±0 .21	41.01±0 .65	47.69±0 .33	53.03±1 .95	57.13±1 .59	59.62±0 .27	60.33±0 .78
5	34.33±0 .84	34.65±0 .68	42.57±0 .92	46.49±0 .52	51.53±0 .49	60.33±0 .79	60.85±0 .43	65.05±0 .09	62.12±0 .98
6	37.18±0 .64	38.61±0 .53	45.42±0 .30	49.29±0 .44	54.41±0 .90	65.97±1 .22	65.89±0 .19	70.87±0 .27	66.49±0 .34
7	40.10±0 .93	41.23±0 .26	47.31±0 .49	52.16±0 .27	57.45±0 .8	66.49±. 3	67.12±0 .97	75.53±0 .53	69.76±0 .67
8	42.76±0 .16	44.20±0 .19	49.21±0 .34	54.42±0 .11	60.45±0 .18	71.44±0 .38	70.43±0 .32	78.06±0 .17	74.06±0 .17

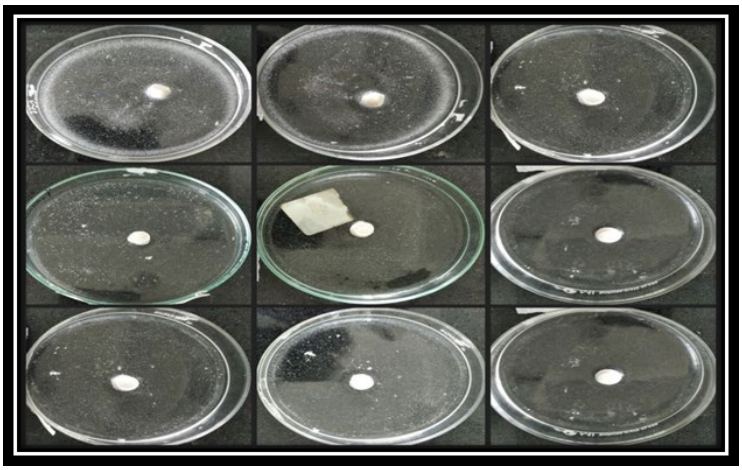

Fig. 1: Swelling study at 12 hour

E. Mucoadhesive strength:

The bioadhesive property of mucoadhesive tablets of Drugcontaining varying proportions of polymers was determined with an insight to develop the tablets with adequate bioadhesion. It was found that, all the tablet formulations possess adequate bioadhesion. Xanthan gum and vigna mungo influences the bioadhesion strength irrespective of the polymer used. Also, bioadhesion is found to be increasing with increase in amount of polymers used. The result is shown in table 11.

Table 11: Mucoadhesive strength

Sr. no	Formulation code	Mucoadhesive strength (N)
1	F1	0.0181±0.04
2	F2	0.0252±0.05
3	F3	0.0312±0.03
4	F4	0.0521±0.01
5	F5	0.0751±0.05
6	F6	0.0916±0.13
7	F7	0.1191±0.07
8	F8	0.1211±0.01
9	F9	0.1460±0.01

F. *In-vitro* Dissolution Study % Cumulative Drug Release:

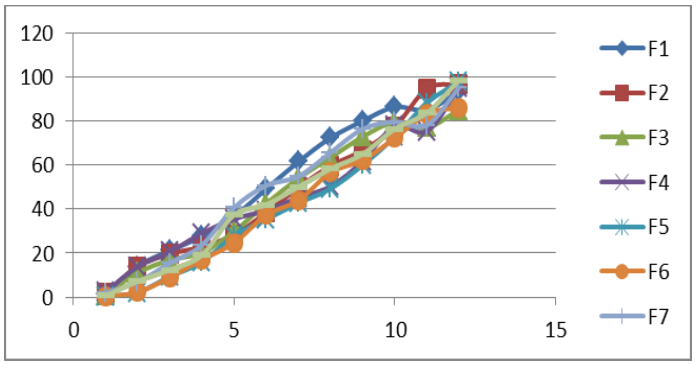

Fig. 2: % Cumulative Drug Release of F1 to F9 batches.

G. Kinetic study: [11-12]

In the present study, the drug released was analyzed to study the kinetics of drug release mechanism. The result shows that the factorial design batches followed zero order, first order model kinetics, Higuchi and Connor's model kinetics and Korsemeyer's Peppas model kinetics. The kinetic study is described in table 12.

Table 12: Kinetic Study

Formulations	F1	F2	F3	F4	F5	F6	F7	F8	F9
R^2 value for Zero order	0.979	0.9829	0.9773	0.9765	0.9806	0.991	0.9778	0.9916	0.9894
R^2 value for First order	0.9412	0.7795	0.9567	0.7501	0.7027	0.9196	0.8557	0.6906	0.9097
R^2 value for Higuchi order	0.9253	0.9688	0.9357	0.9457	0.9795	0.9667	0.9296	0.9568	0.9718
R^2 value for Korsemayer order	0.7232	0.7368	0.7368	0.7881	0.7465	0.997	0.765	0.7927	0.7847

H. Optimization:

A 3^2 full factorial design was selected and the 2 factor were evaluated at 3 levels, respectively. The percentage of xanthan gum (X1) and vigna mungo (X2) were selected as independent variables and the dependent variable was % drug release. The data obtain were treated using design expert version DX7 software and analyzed statistically using analysis of variance (ANOVA).

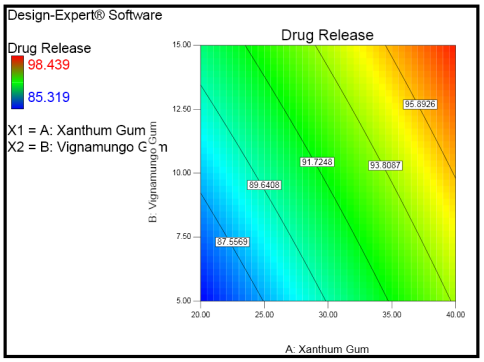

Fig. 3: Counter plot showing Effect of xanthan gum and vigna mungo on drug release

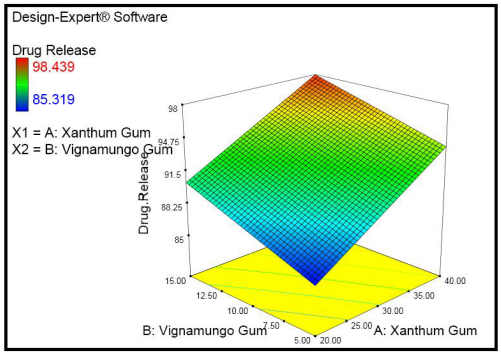

Fig. 4: Surface response plot showing Effect of xanthan gum and vigna mungo on % drug release.

From design expert optimum batch of Xanthan Gum and vigna mungo gum was found to be optimized. From this data F8was selected as optimized formulation. Design summary is given in table 13.

I. Design Summary:

Table 13: Design Summary

factor	Name	Unit	Type	Min	Max.	-1 Actual	+1 Actual	mean	Std. Dev.
A	Xanthan gum	mg	Numeric	20	60	-1.00	1.00	40	20
B	Vigna mungo	mg	Numeric	5	15	-1.00	1.00	5	5

J. Stability study: [13-15]

The stability study for optimized formulation F8 was conducted at 400 C, 75% RH as per ICH guideline. The % drug content, appearance and hardness were studied after 8 days, 15 days, 1 and 2 months is shown in Table 14. From the data obtained it can be inferred that there was no change in physical parameters of the buccal tablets. Also, the tablets did not show any significant loss in their drug content, hardness and percent appearance. Therefore it was ascertained that, the mucoadhesive buccal tablets of Drug could be stored for a period of at least 2 years.

Table 14: Stability Study

Frequency of testing	Appearance	Hardness (%± S.D)	% Drug content (% ± S.D.)
Formulation F8			
0	White color circular concave faced bevel edge	4.4±0.8	99.33±0.48
8 days	White color circular concave faced bevel edge	4.4±0.3	99.20±0.99
15 days	White color circular concave faced bevel edge	4.4±0.2	99.04±0.5
1 month	White color circular concave faced bevel edge	4.4±0.3	99.05±0.2
2 months	White color circular concave faced bevel edge	4.4±0.2	99.06±0.2

7. CONCLUSION:

Febuxostat is an Anti-gout agent useful in the treatment of gout disorder. The aim of this work was to develop a mucoadhesive buccal tablet for the buccal delivery of the febuxostat via buccal mucosa. Buccal tablets of febuxostat are designed to release drug at mucosal site in unidirectional pattern for extended period of time without wash out of drug by saliva xanthan gum, vigna mungo are used as mucoadhesive polymers.

In present study, an attempt was made to design mucoadhesive buccal tablets containing febuxostat using xanthan gum and vigna mungo polymers. the tablets were prepared by direct compression method .nine formulations were designed in which the amount of xanthan gum and amount vigna mungo is selected as low , medium, and high concentration. The nine formulations were evaluated for hardness, thickness, weight variation, drug content estimation, and surface pH determination swelling index, *in- vitro* mucoadhesive strength, in vitro drug release, and stability study.

Majority of designed mucoadhesive buccal tablets containing febuxostat with xanthan gum and vigna mungo displayed drug release in the 8 hrs. *In vitro* release data was fitted into various release kinetics models to study the release mechanism. The entire prepared tablets were stable at room temperature. Overall evaluations of the mucoadhesive tablets show good mucoadhesive properties. Based on the in vitro dissolution studies, it was found that formulation F8 showed maximum drug release in 12 hours. Stability study was performed for optimized formulation F8 as per ICH guidelines, for appearance,

hardness and drug content and it was stable for specified period of time. Hence, the mucoadhesive buccal tablets of febuxostat can be prepared with enhanced bioavailability and prolonged therapeutic effect for the better management of gout.

8. ACKNOWLEDGEMENT:

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9. CONFLICTS OF INTEREST:

All authors have no conflicts of interest in the publication.

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