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STEVIA LEAF POWDER AND CLOVE OIL AS TASTE MASKING SUBSTANCES IN THE FORMULATION OF CELECOXIB ORO-DISPERSIBLE TABLETS

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ABSTRACT

Taste masking of intensely bitter drugs became one of the most important pre-requisite to improve the patient compliance especially in the pediatric and geriatric population. In the present research work Celecoxib was selected as a model drug which is bitter in taste with high protein binding of 97%. Celecoxib is used as a non-steroidal anti-inflammatory drug (NSAID) to treat mild to moderate pain and inflammation, swelling, stiffness, and joint pains. So the main aim of the study was to mask the intensely bitter taste of Celecoxib drug using stevia leaf powder as taste masking agent and clove oil as a flavouring agent into orodispersible tablets to improve patient compliance, provide rapid onset of action and offer improved bioavailability. Five formulations (F1-F5) were formulated by using direct compression method and evaluated for different evaluation parameters. Among all the formulations, formulation F4 was found to be optimized with maximum *in-vitro* drug release of 100.1% within 20 minutes and with desired physico-chemical characteristics.

INTRODUCTION:

Solid dosage forms like tablets and capsules are most popularly preferred drug delivery system because they have high patient compliance, relatively easy to produce, easy to market, accurate dosing, good physical and chemical stability[1]. Pediatric and geriatric patients and patients who are mentally retarded, uncooperative, nauseated or on reduced liquid-intake/diet have difficulty in swallowing solid dosage forms. Those who are traveling or have little access to water are similarly affected[2]. For these reasons, tablets which can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Rapidly dissolving or disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[3]. The growing importance of mouth dissolving tablet was underlined recently when European Pharmacopoeia adopted the term "Orodispersible Tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing[4]. Scientists have developed innovative drug delivery system known as fast dissolving "melt in mouth" or mouth dissolving tablets. These are novel type of tablets that

disintegrate, dissolve / disperse in saliva[5]. Fast dissolving tablets can be prepared by direct compression, wet granulation, moulding, spray drying, and freeze drying or sublimation methods. Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) used to treat mild to moderate pain and helps to relieve symptoms of arthritis (e.g., osteoarthritis, rheumatoid arthritis, or juvenile rheumatoid arthritis), such as inflammation, swelling, stiffness, and joint pain. It is also used to treat ankylosing spondylitis, acute pain and menstrual cramps. Celecoxib was selected as a model drug which is bitter in taste with high protein binding of 97%. Taste masking of intensely bitter taste of Celecoxib was done by using stevia leaf powder as taste masking agent and clove oil as a flavouring agent into orodispersible tablets to improve patient compliance, provide rapid onset of action and offer improved bioavailability.

MATERIALS AND METHODS: Celecoxib was obtained as a gift sample from Mylan Laboratories Limited, Hyderabad. Stevia leaf powder was purchased from Herboveda, Noida, U.P. Clove oil was purchased from local market. Microcrystalline cellulose and Crosspovidone were purchased from Lab chemicals, Chennai. Magnesium stereate and Talc were procured from Loba chemie PVT. Ltd, Mumbai. All other chemicals and reagents used were of A.R. grade.

Method of preparation of taste masked orodispersible Celecoxib tablets by Direct Compression method: Disintegrating tablets of Celecoxib containing 100mg of drug were prepared by using crospovidone, micro crystalline cellulose, stevia leaf powder and clove oil by direct compression technique. The total weight of the single tablet was 200mg. Except magnesium stearate and talc, all the required quantities of materials as per the formulae given in Table 1 were weighed and passed through sieve no 60# separately and triturated in a mortar. Magnesium stearate and talc previously passed through sieve no 100# were also added and blended uniformly. The tablet mixture was then compressed using 10 station rotary tablet machine (Rimek, India) with 7mm round flat shaped punches.

EVALUATION STUDIES:

Preformulation Studies:

A. Compatibility Studies: Fourier Transform Infrared (FT-IR) spectrophotometer was used for infra-red analysis of samples to interpret the interactions of drug with polymers and other ingredients. The powder sample was used for FT-IR studies[6].

B. Characterization of powder blends of formulations

a. Angle of repose[7]

The frictional force in a loose powder can be measured by the angle of repose. Angle of repose (θ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by fixed funnel method and is the measure of the flow ability of powder/granules. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The studies were done in triplicate. The angle of repose (θ) was calculated using the following formula:

$$\theta = \tan^{-1}(h/r)$$

b. Bulk Density[8]: The mass of powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density

(gm/cc) was determined by pouring gently 25 gm of sample (w) through a glass funnel into a 100mL graduate cylinder. After pouring the powder bed was made uniform without disturbing. The volume measured was called as the bulk volume and the studies were done in triplicate. Bulk density was calculated by following formula:

Bulk density (ρ_b) = weight of the powder (w) / Bulk volume (v_b) (g/cc)

c. Tapped Density[8]: It is the ratio of total mass of powder to tapped volume of powder. Tapped density was determined by pouring gently 25gm of sample (w) through a glass funnel into a 100mL graduated cylinder .The cylinder was tapped manually 100 times from a height of 2 inches initially followed by an additional tap of 100 times until the difference between succeeding measurements was less than 2%.Volume occupied by the sample after tapping were recorded (v_f) and the studies were done in triplicate. Tapped density was calculated using following formula:

Tapped density (ρ_t) = Weight of the powder (w) / Tapped volume (v_f) (g/cc)

d. Carr's Index (Compressibility Index)[9]: Compressibility is the ability of the powder to decrease in the volume under pressure. Compressibility is a measure that is obtained from density determinations. It is indirectly related to the relative flow rate, cohesiveness and particle size. It is also one of the simple methods to evaluate flow property of powder by comparing the bulk density and tapped density. High density powders tend to possess free flowing properties .Compressibility index can be calculated by the following formula:

Carr's index= (Tapped density- Bulk density/ Tapped density) ×100

e. Hasuner's Ratio[9]: Hausner's ratio provides an indication of the degree of the densification which could result from vibration of the feed hopper. A lower value of Hasuners' ratio indicates better flow and vice versa.

Hausner's Ratio = Tapped density /Bulk density

Post compression Evaluation Studies: Prepared orodispersible tablets were evaluated for the following tests.

A. **Physicochemical characterization of tablets:** The prepared tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content, wetting time and water absorption ratio, *In-vitro* disintegration time, *In-vitro* dispersion time, *In-vitro* drug release studies and *In-vivo* taste evaluation of celecoxib tablets

B. Weight variation[10]: Weight variation was calculated as per the method described in USP. Twenty tablets were weighed individually and the average weight is calculated. The percent weight variation was calculated by using the following formula.

% weight variation = Average weight- Individual weight/ Average weight ×100

The requirements are met if the weights of not more than two of tablets differ by more than the percentage listed in Table 5 and no tablets differ in weight by more than double that percentage.

C. Tablet thickness[11]: Tablet thickness was measured by vernier calipers. Tablet thickness should be controlled within a ± 5% of a standard value.

D. Hardness[11]: Five tablets from each batch were selected and hardness was measured using Monsanto hardness tester to find the average tablet hardness or crushing strength. The hardness was measured in terms of kg/cm^2.

E. Friability[12]: Twenty tablets from each batch were selected randomly and weighed. These pre weighed tablets were subjected to friability testing using Roche Friabilator for 100 revolutions. The tablets in the friabliator are subjected to both abrasion and shock in a

plastic chamber revolving at 25rpm, dropping the tablet at a height of 6 inches in each revolution. Tablets were removed, dusted and weighed again. Following formula was used to calculate the friability.

% Friability = Initial weight – Final weight / Initial weight × 100

F. Drug content uniformity[12]: Five tablets were selected randomly and powdered. A quantity of this powder equivalent to 100mg of celecoxib was dissolved in 100 mL of 0.1N HCl and stirred for 60 min and the solution was filtered and diluted suitably with 0.1N HCl. Absorbance of this solution was measured at 259nm using as blank and content of celecoxib was estimated.

G. Wetting time and water absorption ratio[13]: Five circular tissue papers of 12.5cm diameter are placed in petridish. Ten milliliters of water is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time. For measuring water absorption ratio the weight of the tablet before keeping in the petridish is noted (W_b). The wetted tablet from the petridish is taken and reweighed (W_a). The water absorption ratio, R can be determined by the following equation:

$$R = \frac{W_a - W_b}{W_b} \times 100$$

Where, W_b and W_a are weights before and after absorption respectively.

H. *In-vitro* disintegration time[14]: Disintegration time is the time taken by the tablet to breakup into smaller particles. The tablet containing a basket rack assembly with two glass tubes of 7.75cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 minutes per minute in a medium of 900mL which is maintained at 37 ± 2^0C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh was considered as the disintegration time of the tablet.

I. *In-vitro* dispersion time[15,16]: *In vitro* disintegration time of orally disintegrating tablets was determined by placing 10 mL of water in a petridish of 12.5 cm diameter. The tablet was then carefully placed in the center of the petridish and the time required for the tablet to completely disintegrate into fine particles was noted.

J. *In-vitro* Drug Release studies[17]: The drug release from orodispersible tablets was studied by USP II (Paddle type) dissolution test apparatus. In this method, 900ml of buffer (0.1N HCl) was used as the dissolution media. The rate of stirring was 50rpm.The tablets were placed in buffer maintained at 37^0 C for a period of 45 minutes. At appropriate intervals (2, 4, 6, 8, 10, 12, 15 and 20 minutes) 5mL of each sample was taken. The dissolution medium was then replaced by 5mL of fresh dissolution fluid to maintain constant volume. The samples were analyzed spectrophotometrically by UV-Visible spectrophotometer at a wave length of 259nm (Lab India). The percentage drug release was calculated using calibration curve of the drug in buffer. Experiments were performed for three tablets for each formulation and standard deviation was calculated.

***In-vivo* taste evaluation of Celecoxib tablets:** Taste of tablets was evaluated by time intensity method. Six healthy human volunteers were selected. A tablet was held in mouth until the tablet disintegrated and volunteers were asked to evaluate for taste. Bitterness was recorded immediately, after disintegration of the tablet, after 1 min and after 2 min[18].

K. Release kinetics[19]: Data of *in vitro* release was fit into different equations to explain the release kinetics. The kinetic equations used were zero order and first

order equations. R^2 valves suggest that the release from the formulations may follow any one of these models.

a. Zero order release kinetics: It defines a linear relationship between the fractions of drug released versus time.

$$Q=k_o t$$

Where, Q is the fraction of drug released at time t. k_o is the zero order release rate constant. A plot of the fraction of the drug released against time will be linear if the release obeys zero order release kinetics.

b. First order release kinetics: Wagner assuming that the exposed surface area of a formulation decreased exponentially with time during dissolution process suggested that drug release most slow release formulation could be described adequately by apparently first-order kinetics. The equation is used to describe first-order release kinetics is

$$In\ (1-Q) = -kt$$

Where, Q is the fraction of drug release at time t. K is the first order release rate constant. Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

L. Characterization of drug in orodispersible tablets: FT-IR studies were conducted for characterization of drug in tablets of selected formulation. The IR spectra's were recorded using Fourier Transform Infrared spectrophotometer. The IR spectrum of pure drugs and best formulation were taken, interpreted and compared with each other.

M. Stability studies: Short term stability studies were conducted for best formulations of Celecoxib tablets at 4^0 C, at room temperature for 3 months and the % drug content of the formulations were estimated and compared.

RESULTS AND DISCUSSION

A. Compatibility studies: From the FTIR spectra of drug, the observed peaks were recorded in the following table 6 and the IR spectrum of physical mixture of drug with superdisintegrant, stevia leaf powder and clove oil revealed that there was no appreciable change in the position and intensity of peak with respect to IR spectrum of Celecoxib. This indicates that there were no chemical interactions between formulation ingredients.

B. Evaluation of pre-compressed powder blends for physical parameters:

All the prepared powdered blends were evaluated for Angle of repose, Bulk density, Tapped density, Compressibility index and Hausner's ratio. Angle of repose values ranged from 25.22-29.357 ^{0} (Table 6) indicates good flow property of powder blends. The values of Bulk density ranged from 0.455-0.490 gm/cc and the values of Tapped density ranged from 0.478– 0.588 gm/cc (Table 6). The free flowing properties of the powder blends were further confirmed by determining Carr's index and Hausner's ratio. The Carr's index values and Hausner's ratio were ranged from 16.03-16.89 and 1.111-1.26 respectively (Table 6), indicating all the powder blends show good flow.

EVALUATION OF CELECOXIB ORODISPERSIBLE TABLETS:

A. Physicochemical characterization: Celecoxib orodispersible tablets (F1-F5) prepared by direct compression method were subjected to many in-process evaluation parameters such as physical appearance, weight variation, thickness, friability, % drug content, wetting time, absorption time, *in-vitro* dispersion time, *in-vitro* disintegration time. All the tablets were round and flat in shape with no visible cracks having smooth appearance. The average percentage weight variation of twenty tablets was remained within ± 0.4%

.This weight variation test revealed that the tablets were within the range of pharmacopeial limit. All the tablets showed the thickness in the range of 2.26mm to 2.32mm. All the tablets reasonably showed good hardness values ranged from 2.4 to 2.9 kg/cm^2. Further to strengthen these values friability values were also considered. The percentage weight loss of all formulation was less than 1.0% as shown in the Table 7, this indicates that all the tablets can withstand the mechanical shocks during handling. The wetting time, water absorption ratio, *in-vitro* disintegration time and *in-vitro* dispersion time was found to be between 25.81sec to 29.57sec, 134.61% to 143.07%, 14.5 sec to 27.0 sec and 28.99 sec to 30.16 sec respectively as shown in Table 8. Percentage drug content of all batches of tablets was determined and it was within the range of 96.21% to 100.1% indicating good uniformity among different formulation of tablets.

B. *In-vitro* release studies: *In-vitro* drug release studies for the prepared Celecoxib orodispersible tablets (F1 –F5) were conducted for a period of 20 minutes using the USP type II dissolution apparatus. Dissolution of all the formulation was carried out using 0.1N HCl for 20 minutes at 37 ± 0.5^0 C with 50 rpm speed. At every interval, 5ml of sample was withdrawn, appropriate dilutions were done and the sample was analyzed at 259nm for Celecoxib by UV-Visible Spectrophotometer (Elico SL 244). The cumulative percentage drug released for formulations was shown in the Table 9. The formulations (F1 –F5) showed drug release of 96.21±0.1, 97.62±0.15, 98.22±0.17, 100.1±0.21 and 96.88±0.26% at 20 min respectively. Among all the formulations, formulation F4 was considered as best formulation based on wetting time, water absorption ratio, *in-vitro* disintegration time and *in-vivo* drug release and all other parameters.

C. Evaluation of Taste: Taste of all tablets formulations were evaluated by time intensity method by selecting six healthy human volunteers and the results were recorded and shown in table 10. The tablets of Formulation F1, which doesn't contain any taste masking substance, tasted bitter. F2 tablets, containing stevia leaf powder and clove oil, initially tasted bitter, but later tasted sweet. F3 tablets containing both stevia leaf powder and clove oil were initially tasted bitter followed by slightly bitter in taste and later tasted sweeter. Tablets of F4 containing both stevia leaf powder and clove oil, were initially tasted bitter, but tasted sweeter later on.

Table 1: Composition of Celecoxib tablets

Name of the ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)
Celecoxib	100	100	100	100	100
Micro crystalline cellulose	86	82	80	78	78
Crospovidone	8	8	8	8	8
Stevia leaf powder	--	4	6	8	8
Clove oil	q.s.	q.s.	q.s.	q.s.	--
Talc	4	4	4	4	4
Magnesium stearate	2	2	2	2	2
Total (mg)	200	200	200	200	200

Table 2: Relationship between Angle of Repose and Flow Property

Angle of Repose(θ)	Type of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Table 3: Carrs' index and corresponding flow properties as per USP30/NF25

Compressibility Index	Type of Flow
5-15	Fair to passable
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Table 4: Hasuner's Ratio and Corresponding flow properties

Hausner Ratio	Flow properties
<1.25	Good Flow (20% Carr's index)
1.25-1.5	Moderate flow (33%Car's index)
>1.5	Poor Flow

Table 5: Weight variation allowed as per USPXX-NF XV

Average weight of tablet (mg)	Percentage difference allowed
≤ 130	10
130-324	7.5
>324	5

Table 6: Functional group ranges for celecoxib pure drug

S.no.	Functional group	Range cm^{-1}	Pure drug (celecoxib) cm^{-1}
1	N-H	3300-3600	3321.11
2	S=O	1070-1030	1015.67
3	C-S	700-600	628.72
4	C-F	1350-1120	1225.11
5	C-H	3100-3000	3095.53
6	C-N	1250-1020	1096.59

Table 7: Micromeritic properties of the physical mixtures of formulations of Celecoxib

Formulation code	Angle of repose (0)*	Bulk density*(g/cc)	Tapped density (g/cc)*	Carr's index (%)*	Hausner's ratio *
F1	26.811±0.03	0.475±0.047	0.569±0.048	16.52±0.370	1.26±0.043
F2	29.357±0.05	0.455±0.134	0.478±0.01	16.11±0.278	1.111±0.08
F3	25.22±0.143	0.487±0.053	0.580±0.067	16.03±0.28	1.12±0.183
F4	25.115±0.07	0.490±0.122	0.588±0.035	16.89±0.268	1.19±0.049
F5	29.357±0.05	0.455±0.134	0.478±0.01	16.11±0.278	1.111±0.08

*****all values represent mean ± standard deviation (SD), n=3

Table 8: Post Compression Evaluation parameters

Formulation code	%Weight* Variation	Thickness* (mm)	Hardness* (Kg/cm^2)	Friability * (%)
F1	0.28±0.24	2.26±0.03	2.9±0.21	0.72±0.022
F2	0.34±0.36	2.28±0.02	2.6±0.31	0.79±0.011
F3	0.33±0.27	2.32±0.01	2.6±0.10	0.68±0.023
F4	0.34±0.16	2.31±0.03	2.4±0.23	0.67±0.019
F5	0.36±0.18	2.32±0.02	2.5±0.34	0.69±0.011

*****all values represent mean ± standard deviation (SD), n=3

Table 9: Post Compression Evaluation parameters

Formulation code	Wetting time* (sec)	Water absorption ratio	*In-vitro* disintegration time* (sec)	*In-vitro* dispersion time* (sec)	% Drug content*
F1	26.89±1.44	140±1.56	27±0.48	30.11±0.67	99.86±0.083
F2	26.54±0.90	134.61±0.84	23.0±0.96	29.09±0.24	100.19±0.063
F3	27.90±1.31	135.00±0.46	16.3±0.79	29.00±0.63	99.48±0.012
F4	25.81±0.61	143.07±0.75	14.5±0.73	28.99±0.41	100.16±0.032
F5	29.45±1.23	142.49±0.98	16.5±0.29	30.16±0.33	99.38±0.082

*****all values represent mean ± standard deviation (SD), n=3

Fig 1: Cumulative percentage Drug Release profiles of Celecoxib orodispersible tablets (F1-F5)

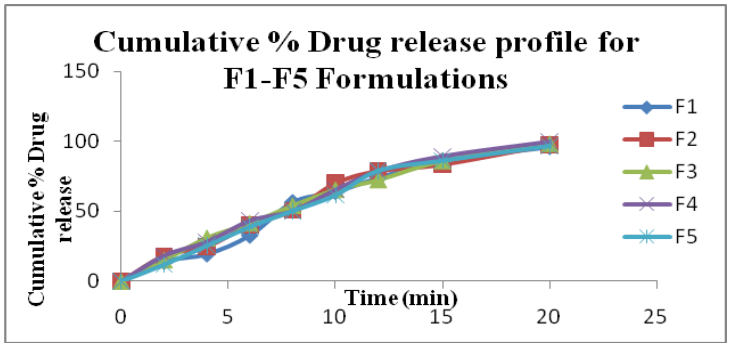

Table 10: Cumulative % drug release for celecoxib

TIME (min)	Cumulative % drug release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
2	14.23±0.14	18.35±0.21	15.25±0.15	18.45±0.18	12.05±0.23
4	19.54±0.15	25.02±0.16	31.04±0.17	28.4±0.20	25.56±0.45
6	32.97±0.17	40.28±0.23	41.51±0.16	43.45±0.18	39.08±0.11
8	56.62±0.16	50.74±0.14	54.05±0.18	50.4±0.20	50.4±0.14
10	64.02±0.17	70.2±0.23	65.4±0.17	65.57±0.23	61.7±0.15
12	74.07±0.15	78.85±0.14	72.4±0.15	78.94±0.26	79.2±0.22
15	86.5±0.14	83.57±0.14	85.88±0.14	89.62±0.21	86.4±0.17
20	96.21±0.13	97.62±0.15	98.22±0.17	100.1±0.21	96.88±0.26

*****all values represent mean ± standard deviation (SD), n=3

Table 11: Evaluation of Taste

Formulation	Immediately	After disintegration	After 1 min	After 2 min
F1	Bitter	Bitter	Bitter	Bitter
F2	Bitter	Bitter	Sweet	Sweet
F3	Bitter	Slightly bitter	Sweet	Sweet
F4	Bitter	Sweet	Sweet	Sweet
F5	Bitter	Bitter	Sweet	Sweet

Table 12: Regression values of Celecoxib formulations(F1-F3)

Formulation code	Zero Order (R^2)	First order (R^2)
1	0.905	0.943
2	0.850	0.938
3	0.840	0.936
4	0.937	0.950
5	0.895	0.947

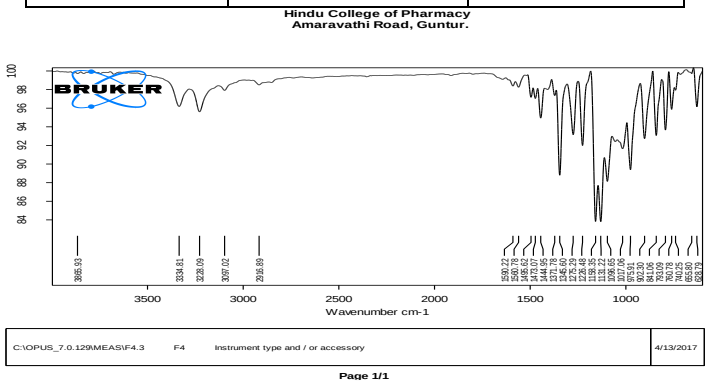

Fig.2: IR Spectrum of F4 (Celecoxib+ Crospovidone + Stevia leaf powder+ MCC + Magnesium stearate + Talc)

Table 13: Short time stability studies of F4 formulation

S.NO	Time (weeks)	% Drug content		
		4^0C	Room Temperature	45^0 C
1	0	100.16±0.032	100.16±0.032	100.16±0.032
2	1	100.15±0.032	100.14±0.032	100.15±0.032
3	2	100.14±0.032	100.13±0.032	100.14±0.032
4	3	100.13±0.032	100.12±0.032	100.13±0.032

*****all values represent mean ± standard deviation (SD), n=3

Tablets of F5 contain only stevia leaf powder, were initially tasted bitter, but tasted sweeter later. Among all the formulations, formulation F4 tasted good. Even though F4 tasted bitter initially but after disintegration it immediately tasted sweeter and retained its sweetness until tablet completely disintegrates. It can be concluded that as the concentration of stevia leaf powder increases, the bitterness of the drug was effectively masked leading to enhanced patient compliance.

***D. In-vitro* Drug Release Kinetics:**

In order to elucidate the mode and mechanism of drug release , the *in-vitro* release data obtained for orodispersible formulations was fitted into various kinetic models. The results were shown in Table 11. The kinetics and release mechanism was estimated by the regression plots for zero order and first order. When R^2 values of regression plots for first order and zero order were considered, R^2 values for first order were found to be more than zero order. Hence it was confirmed that the drug release from Celecoxib orodispersible formulations F1 – F5 followed first order release kinetics. Therefore the rate of drug release is dependent on concentration or amount of drug incorporated in the dosage form.

E. Characterization of drug in orodispersible tablets:

The best formulation F4 was examined for drug-polymer interactions by FTIR studies. IR analysis (fig. 2) revealed that there were no chemical interactions of drug with superdisintegrant and other ingredients in prepared orodispersible tablet formulations

F. Stability studies: Short term Stability studies were conducted for best formulation F4 of Celecoxib orodispersible tablets at 4^0C, at room temperature and 45^0 C for 3 months. There was no significant change in the % drug content after 8 weeks. The results were given in Table 12.

CONCLUSION

In the present study an attempt was made to mask the intensely bitter taste of celecoxib drug using stevia leaf powder as taste masking agent and clove oil as a flavouring agent into orodispersible tablets to improve patient compliance, provide rapid onset of action and offer improved bioavailability. Five different formulations were formulated by direct compression method and evaluated for different evaluation parameters and promising results were obtained. From the study, it can be concluded that F4 was the best formulation with maximum *in-vitro* drug release achieved at 20 minutes and the bitter taste of the drug was effectively masked along with desired physico-chemical characteristics. This study can be further extended for assessment of pharmacokinetic and pharmacodynamic properties of the drug and for *In-vitro/In-vivo* correlation studies.

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