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Formulation and Evaluation of Mouth Dissolving Tablets of Celecoxib.

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ABSTRACT:

Mouth dissolving tablets (ODTs) are getting popularity over conventional tablets due to their convenience in administration and suitability for patients having dysphagia. There is an increasing demand for more patient compliant dosage form and a novel method is the development mouth dissolving tablets which dissolve or disintegrates instantly on the patient tongue or buccal mucosa. It is suited for tablets undergoing high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to minimize side effect and make it more cost effective. The main objective of the study was to formulate mouth dissolving tablets of Celecoxib to achieve a better dissolution rate and further improving the bioavailability of the drug. Mouth dissolving tablets prepared by direct compression and using Spray Dried Lactose, Avicel pH 102, Crospovidone XL-10, Croscarmellose Sodium, Sodium Starch Glycolate, Aspartame, Peppermint, Magnesium Stearate were prepared and evaluated for the preformulation parameters such as Organoleptic properties, bulk density, Tapped density, compressibility, Hausner's Ratio, angle of repose, Drug-Excipients compatibility study etc. The prepared batches of tablets were evaluated for Physical appearance, Thickness, hardness, weight variation, friability, disintegration time and in-vitro dissolution profile was found satisfactory. To achieve our goal, nine formulations of ODTs were prepared and optimized. Optimized formulation showed minimum disintegration time and maximum dissolution rate with drug release.

Keywords: Celecoxib, Superdisintegrant and mouth dissolving tablets.

INTRODUCTION

MOUTH DISSOLVINGTABLET:

Mouth dissolving Tablet Technology is an inventive innovation, which enables tablet to break down quickly, for the most part in a matter of seconds, without the requirement for water, giving ideal comfort to the patient. Numerous a times, an alternate wording is utilized for a similar significance like soften in-mouth, fast breaking down, quick dissolving, fast deteriorating, mouth crumbling, mouth dissolving, orodispersible (Honceau L., 2010) and so forth., in any case all terms wind up with a similar importance.

Advantages of Mouth dissolvingTablets:

- Enhanced consistence/included comfort.
- No water required.
- Better taste.
- Enhanced security.
- Reasonable for controlled/managed discharge actives.
- Capacity to give points of interest of fluid solution as strong readiness.
- Versatile and amiable to existing preparing and bundling apparatus.
- Permits high medication stacking.
- Financially savvy.
- Characteristics of Mouth dissolvingTablets:
- Ease of administrations

Material and Equipment Used

Name of materials
Celecoxib IP
Micro Crystalline Cellulose pH 102
Spray Dried Lactose
Lactose Anhydrous
Sodium Starch Glycolate
CrossPovidone XL-10
CrossCarmellose Sodium
Aspartame
Magnesium Stearate
Pineapple flavour
Colloidal silicon dioxide
Talc

Instruments used in the present investigation

Name of instrument
Digital weighing balance
UV Spectrophotometer
Hot air oven
Fourier Transform Infrared
Thermo stability chamber
Tablet Compression Machine
Disintegration test apparatus
Hardness tester
Friabilator
Dissolution test apparatus
Sonicator

Method of Analysis for Celecoxib determination:

Determination of absorption maxima by UV spectroscopy

Calibration Curve of Celecoxib in 0.1N HCl:

The working standard was analysed under Ultraviolet-

Visible spectrophotometer (Model: UV-1800; Make: Shimadzu Corporation, Japan) at 283nm in 0.1 N HCl and absorbance was recorded. Reading was represented in calibration plot of Celecoxib as depicted below

Table : Data for calibration curve of Celecoxib

Sr. No.	Concentration (µg/ml)	Absorbance (n=3)
1	0	0.000
2	5	0.201
3	10	0.368
4	15	0.521
5	20	0.698
6	25	0.895

Preformulation parameters:

- **Organoleptic properties**

Celecoxib is white, odourless crystalline powder.

- **Melting Point**

Melting point of Celecoxib found to be 142-146 ºC.

- **Partition Coefficient**

Partition Coefficient of Celecoxib was found to be 1.6 ±0.011.

- **Permeability Coefficient**

Permeability Coefficient of Celecoxib was found to be -6.91 ± 0.018.

- **Physical characterization**

Table: BD, TD, %CI, HR and Angle of Repose for Celecoxib& Excipients

Sr. No.	Ingredient	B.D. (gm/ml)	T.D. (gm/ml)	% CI	HR	Angle of Repose
1	Celecoxib IP	0.73	0.84	13.09	0.87	27.92
2	Lactose Anhydrous	0.73	0.82	10.97	1.12	29.62
3	MCC pH 102	0.33	0.37	10.81	1.12	22.25
4	Spray Dried Lactose	0.83	0.96	13.54	1.15	24.52
5	SSG	0.66	0.74	10.81	1.12	26.42
6	Crosspovidone XL-10	0.35	0.48	27.08	1.37	30.16
7	Croscarmellose sodium	0.71	0.90	21.11	1.26	27.14

8	Aspartame	0.75	0.87	13.79	1.16	25.62
9	Magnesium Stearate	0.56	0.62	09.68	1.10	21.89
10	Pineapple flavour	0.46	0.57	19.29	1.23	25.94

Compatibility Data Analysis for Drug and Excipients:

FTIR Study:

Fourier Transform Infrared Spectroscopy method is implied here to identify the chemical and/or physical reaction between Celecoxib and excipients. By exhibiting the test, no change in main peak of FTIR spectrum for mixture of Celecoxib and excipients was observed. The result is indicative of non-reactive nature of Celecoxib and excipients

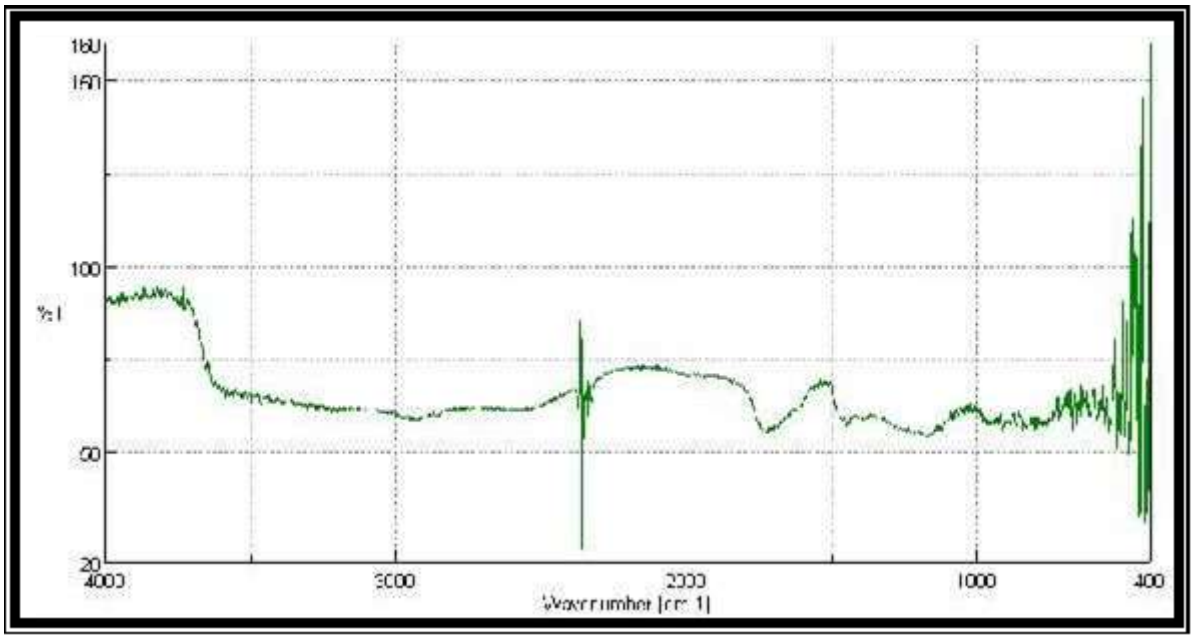

Figure : Celecoxib IR Spectra

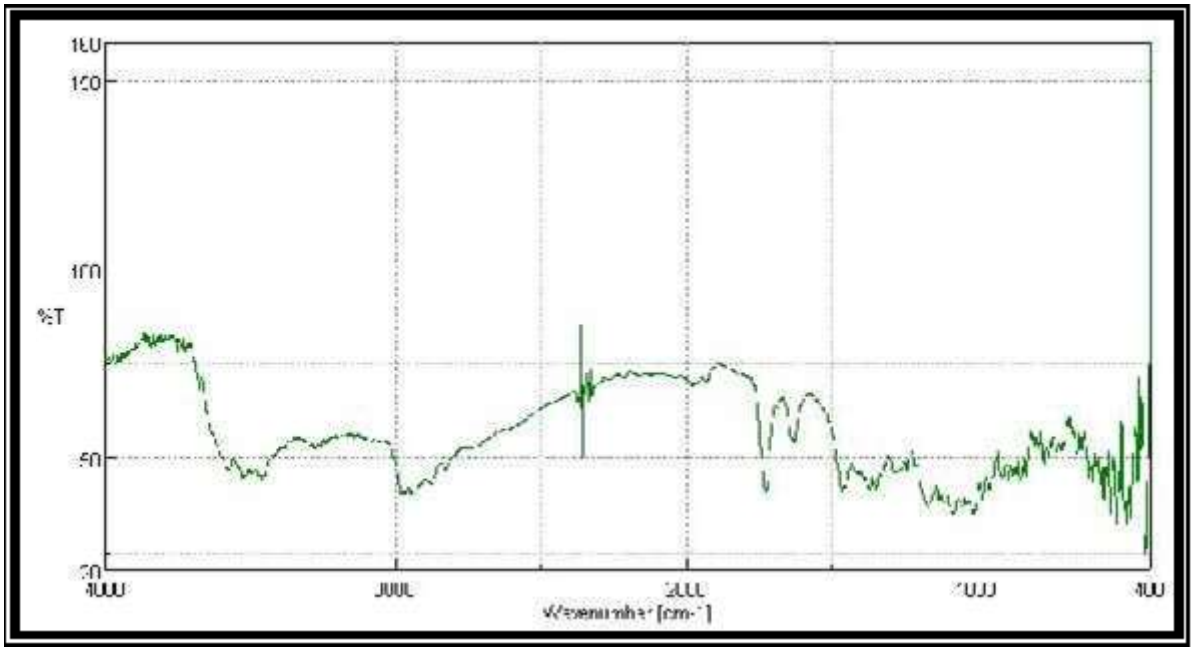

Figure : Celecoxib + Excipients IR Spectra

Formulation development

Below table indicates the formula of different optimization batches taken for mouth dissolvingtablets development of Celecoxib by using direct compression method.

Table: Formula of Mouth dissolving tablets of Celecoxib

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**
Celecoxib I.P.	5	5	5	5	5
Spray Dried Lactose	87	87	87	87	87
Lactose Anhydrous	-	-	-	-	-
MCC pH 102	19.9	18.7	17.5	19.9	18.7
Crospovidone XL-10	-	-	-	-	-
Croscarmellose Sodium	-	-	-	3.6	4.8
Sodium Starch Glycolate	3.6	4.8	6.0	-	-
Aspartame	2	2	2	2	2
Peppermint-Flavour	1	1	1	1	1
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5
Total weight (mg)	120	120	120	120	120

Characterization of mouth dissolving tablet of Celecoxib:

- **Physical appearance:**

White colored, Round, SC Tablet

- **Weight variation, Thickness, Hardness, % Friability and Disintegration time in below table.**

Table: Formulation Parameters

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Percentage Friability (%)	Disintegration Time (sec)
F1	121.3±0.072	3.51±0.054	3.8±0.016	0.63±0.010	80±0.088
F2	119.1+0.023	3.50+0.023	4.0+0.052	0.72+0.025	71+0.095
F3	119.8±0.075	3.51±0.038	4.0±0.016	0.80±0.035	65±0.089
F4	120.2+0.091	3.52+0.061	4.0+0.019	0.78+0.065	59+0.096
F5	121.3±0.053	3.52±0.012	3.8±0.075	0.90±0.042	54±0.097

Dissolution Parameters

Different parameters selected in dissolution study was mentioned below:

- ✓ USP Type II Apparatus (Paddle Type) was used as a dissolution test apparatus.
- ✓ 0.1M Hcl was used as a dissolution medium and 500ml volume was taken.

- ✓ Temperature condition is set to be as 37±2° C and speed as 50 RPM.
- ✓ Sampling were made at time intervals of 5 mins, 10 mins, 15 mins, 20 mins and 30 mins.

Table : Cumulative % Drug Release of Celecoxib ODT (F1, F2, F3)

Time (min)	Formulations		
	F1	F2	F3
0	0	0	0
5	91.1 ⊥ 0.025	91.8 ⊥ 0.033	92.3 ⊥ 0.064
10	91.3 ± 0.083	93.1 ± 0.045	94.5 ± 0.046
15	92.6 ± 0.065	95.0 ± 0.086	97.0 ± 0.081
20	92.8 ± 0.052	96.3 ± 0.075	98.6 ± 0.074
30	93.4 + 0.045	97.1 − 0.061	99.9 + 0.054

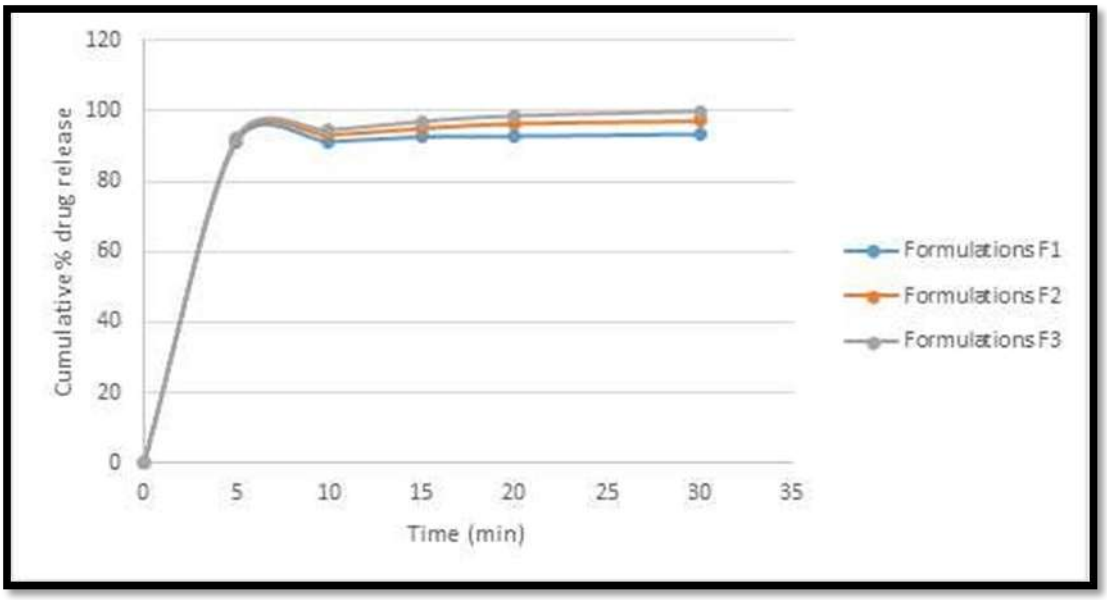

Figure : Dissolution profile of formulation F1, F2, F3

Conclusion

By evaluating all different formulation parameters, it can be concluded that formulation F5 with Lactose Anhydrous and MCC pH 102 as a diluent, Crospovidone XL-10 as superdisintegrant shows excellent results than other trails in terms of tablet disintegration time, hardness, friability, drug release study etc

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