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Formulation and evaluation of oral Disintegrating tablets of *Zingiber officinale*

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Abstract
Oral dissolving drug delivery system offers a solution for those patients having difficulty in swallowing. *Zingiber officinale*, has been used for medicinal purpose since antiquity to treat motion sickness, pregnancy, and cancer-chemotherapy-induced vomiting, mild stomach upset, cough, chronic bronchial problems, and low-grade infections of all kinds and anorexia condition. This work investigates the possibility of developing *Zingiber officinale* oral disintegrating tablets allowing fast, reproducible dissolution in oral cavity; thus bypassing first pass metabolism. The oral disintegrating tablets were prepared by Direct Compression method. Prepared tablets were evaluated for Pre and Post Compressional parameters like flow properties, hardness, Friability, Disintegration studies, Dissolution studies, accelerated stability studies. The different exciepients such as Lactose Anhydrous, MCC PH-102, Pregelatinized Starch, Cros Carmellose Sodium, Sodium Starch Glycolate, Cross Povidone, Sodium Sacharin, Aerosil, Magnesium Stearate were explored individually and in combination with each other for the formation of tablets. Among all the formulations the wetting time and disintegration time both are less for the formulation containing croscarmellose sodium (8%w/w) as super disintegrant (F6). The dissolution rate of the optimized formulations (F6) was found to be higher when compared to other formulations. Among the all the formulation F6 was found to be promising ODT formulation.

Keywords: *Zingiber officinale*, oral dissolving drug delivery systems, oral disintegrating tablets (ODTs), Direct Compression method

1. Introduction

1.1 Orally Disintegrating Tablets

The concept of Fast dissolving Drug Delivery, System emerged from the desire to provide patient with more conventional means of taking their medication [1-2]. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy [3-5]. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of Fast Dissolving Tablet. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. The center for drug Evaluation and Research states an ODT to be: "A solid dosage form containing medicinal substances, which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue [6-10]."

1.2 Mechanism of ODT drugs [11].

Generally, ODTs are formulated to disperse) rapidly in the mouth, enabling medication to be swallowed without water, thereby increasing convenience and compliance across a broad range of indications and patient types, including the young, elderly, and active patients. Following dispersion, the formulations are swallowed, and the drug is absorbed in the same way as conventional solid-oral dosage forms. "However, ODTs may also be used to deliver drugs to the oral cavity, for local action or, in some cases, absorption across the oral mucosa, thereby avoiding first-pass hepatic metabolism and potentially increasing the rate and extent of uptake, and reducing undesirable metabolites," The potential for such pregastric absorption rests largely in the physicochemical characteristics of the drug molecule [12-14].

2. Materials Used

Pre gelatinized Starch, MCC (PH-102), Lactose anhydrous, Crospovidone, Sodium starch Glycolate, Magnesium stearate, CrosCarmellose Sodium, Sodium Sacharin, Orange flavor, Aerosil.

3. Results & Discussion

3.1. Results

Table 1: Estimation of Zingiber Officinale Extract at 205 nm.

Concentration (µg\mL)	Absorbance
2	0.133
4	0.256
6	0.345
8	0.464
10	0.565
12	0.681
16	0.828
20	1.083

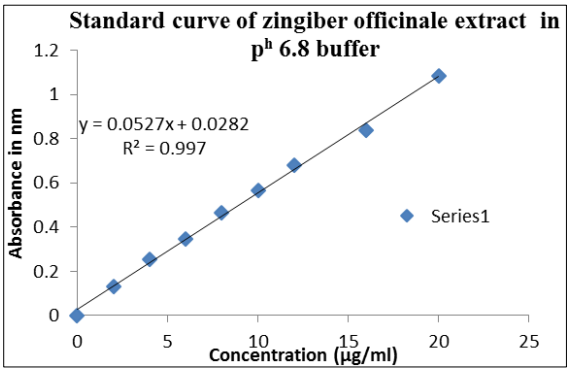

Fig 1: Calibration curve of Zingiber Officinale Extract in p^H 6.8 phosphate buffer at 205nm

Table 2: Formulation of oral disintegrating tablets of Zingiber Officinale Extract by using synthetic disintegrants

Ingredients(mg per tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Zingiber Officinale Extract	10	10	10	10	10	10	10	10	10	10	10	10
Lactose Anhydrous	80	80	80	80	80	80	80	80	80	80	80	80
MCC PH-102	47.5	43	40	47.5	43	40	47.5	43	40	47.5	43	40
Pregelatinized Starch	4.5	9	12	---	---	---	---	---	---	---	---	---
CrosCarmellose Sodium	---	---	---	4.5	9	12	---	---	---	---	---	---
Sodium Starch Glycolate	---	---	---	---	----	---	4.5	9	12	---	---	---
CrossPovidone	---	---	---	---	---	---	---	---	---	4.5	9	12
Sodium Sacharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Orange flover	1	1	1	1	1	1	1	1	1	1	1	1
Aerosil	3	3	3	3	3	3	3	3	3	3	3	3
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Glyceryl Behanate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total Weight	150	150	150	150	150	150	150	150	150	150	150	150

Table 3: Evaluation of flow properties of the blends of all formulations

Forimulations	Angle of repose	Bulk density	Tapped density	Carr's index	Hausner's ratio	Flowability
F1	33	0.56	0.65	13.84	1.16	Fair
F2	31	0.66	0.74	10.8	1.12	good
F3	29	0.69	0.75	8.12	1.08	good
F4	29	0.55	0.64	13.15	1.15	Excellent
F5	31	0.64	0.72	11.11	1.125	Good
F6	27	0.68	0.76	8.15	1.08	Good
F7	35	0.53	0.64	17.18	1.20	Good
F8	33	0.62	0.69	10.14	1.11	Excellent
F9	28	0.65	0.74	10.38	1.16	Excellent
F10	29	0.54	0.63	13.84	1.19	Excellent
F11	25	0.61	0.70	12.9	1.21	good
F12	23	0.67	0.75	10.6	1.119	Excellent

Table 4: Quality control tests for the oral disintegrating tablets of Zingiber Officinale Extract

Formulations*	Avarage Weight*	Hardness *Kg/cm^2	Friability *(%)	Wetting time*	Water absorbtion ratio*
F1	150±0.16	3.5±0.127	0.495±0.171	24.15±0.136	40±0.116
F2	148.6±0.16	3.7±0.132	0.42±0.165	21.56±0.156	42±0.256
F3	151.2±1.64	3.6±0.191	0.51±0.221	20.05±0.254	41±0.134
F4	152.5±0.99	3.6±0.131	0.48±0.187	11.56±0.190	28±0.146
F5	148.7±1.04	3.4±0.221	0.56±0.178	9.35±0.178	32±0.236
F6	150.3±1.96	3.5±0.329	0.59±0.166	8.25±0.147	35±0.214
F7	149±0.8789	3.9±0.129	0.30±0.157	15.67±0.168	37±0.166
F8	150±0.76	3.8±0.182	0.47±0.190	13.76±0.198	42±0.156
F9	151.2±1.64	3.7±0.178	0.40±0.256	13.22±0.210	39±0.188
F10	149.4±1.32	3.9±0.168	0.53±0.223	20.52±0.194	41±0.286
F11	147.9±1.22	3.8±0.134	0.52±0.229	18.46±0.186	44±0.194
F12	148.5±0.89	3.6±0.221	0.44±0.229	17.25±0.156	45±0.314

*Avarage of three determinants (n=3)

Table 5: Quality control tests for the oral disintegrating tablets of Zingiber Officinale Extract

Forimulations*	Disintegration time * (sec)	Drug content* (%)	Percentage Drug Dissolved After 10 min*	Invitro dispertion time* (s)
F1	47.26±0.761	98.12±1.22	74.14±0.56	51±0.128
F2	46.56±0.821	97.56±1.01	79.56±0.92	49±0.55
F3	44.67±0.7898	98.7±0.91	83.22±0.47	48±0.46
F4	15.35±0.546	101.3±0.892	85.04±0.86	14±0.22
F5	12.54±0.678	96.57±1.71	90.43±0.47	12±0.56
F6	10.68±0.763	99.08±0.86	95.86±0.86	**11**±0.86
F7	58.57±0.890	96.56±0.611	84.30±0.45	61±0.11
F8	55.75±0.778	98.90±1.21	89.43±0.21	58±0.24
F9	54.56±0.890	97.35±1.39	92.91±0.46	58±0.481
F10	39.92±0.760	94.91±1.09	74.09±0.75	52±0.65
F11	37.69±0.886	97.16±0.86	79.31±0.64	49±0.67
F12	37.75±0.91	98.26±1.24	82.52±1.25	47±0.52

*Average of three determinants (n=3)

Table 6: Dissolution profile of the oral disintegrating tablets of Zingiber Officinale Extract

Batch code			Cumulative % drug dissolved (min)			
	0	**2.5**	**5**	**10**	**15**	**20**
F1	0	39.6±1.25	61.2±0.25	74.14±0.56	85.35±0.21	93.02±0.33
F2	0	42.8±1.48	64.8±0.56	79.56±0.92	92.6±0.35	98.51±0.16
F3	0	44.2±3.16	75.6±0.35	83.22±0.47	92.62±0.16	98.59±0.42
F4	0	46.4±0.98	79.2±0.49	85.04±0.86	98.11±0.85	102.2±0.96
F5	0	47.4±1.96	77.4±0.56	90.43±0.45	99.03±0.47	98.19±0.63
F6	0	51.4±1.46	82.6±0.65	95.86±0.21	101.3±0.85	100.59±0.57
F7	0	42.8±3.26	72±0.66	85±0.46	94.41±0.37	99.17±0.19
F8	0	44.6±1.74	73.8±0.25	90.41±0.75	95.41±0.19	100.43±0.69
F9	0	46.9±2.16	81±1.26	92.91±0.64	95.46±0.41	102.28±0.28
F10	0	38.2±0.91	68±0.95	74.6±1.26	82.0±0.49	88.0±0.17
F11	0	41.6±1.54	69.5±1.56	76±0.95	84.6±0.78	89.6±0.43
F12	0	43.6±2.84	71.8±0.89	80.49±0.55	88.91±0.51	92.56±0.32

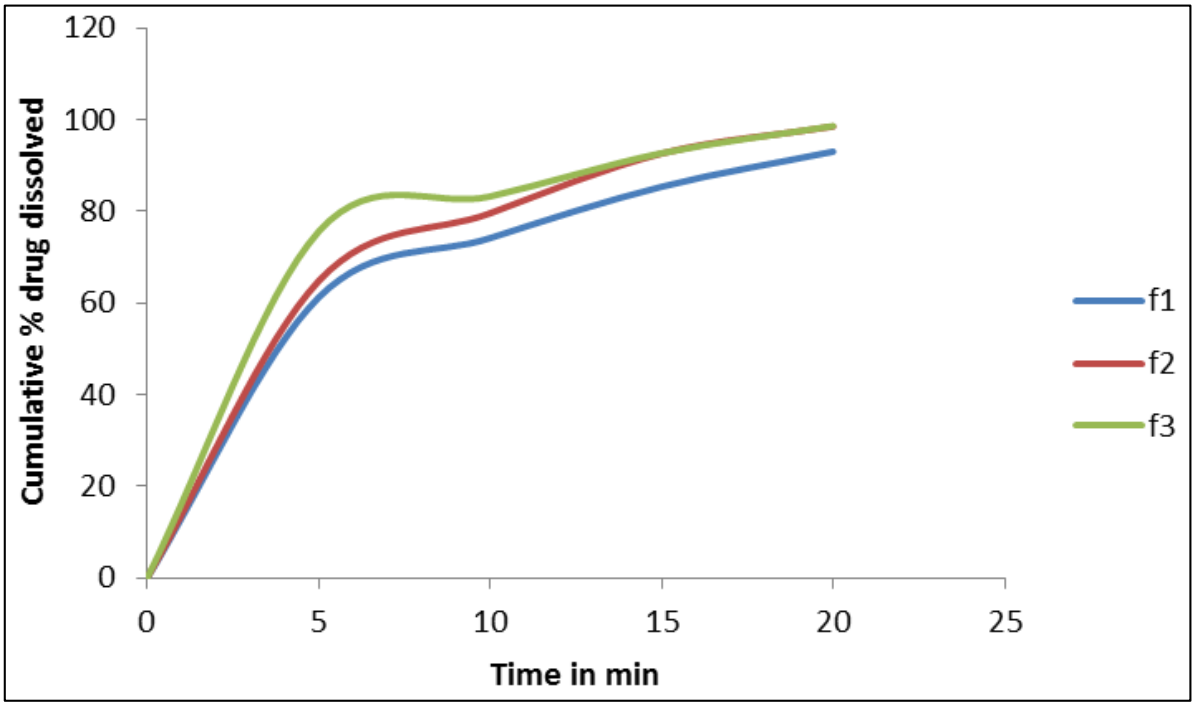

Fig 2: Comparative dissolution profiles of Zingiber Officinale Extract Oral Disintigation tablets containing different concentrations of pregelatinized starch as super disintegrant

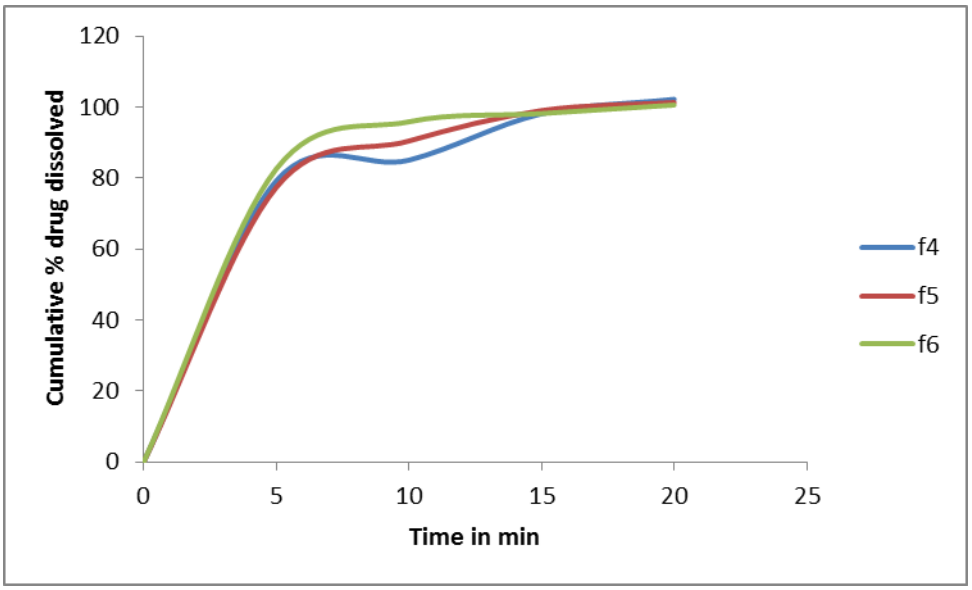

Fig 3: Comparative dissolution profile of Zingiber Officinale Extract Oral Disintigation tablets containing different concentrations of cros carmellose sodium as super disintegrant

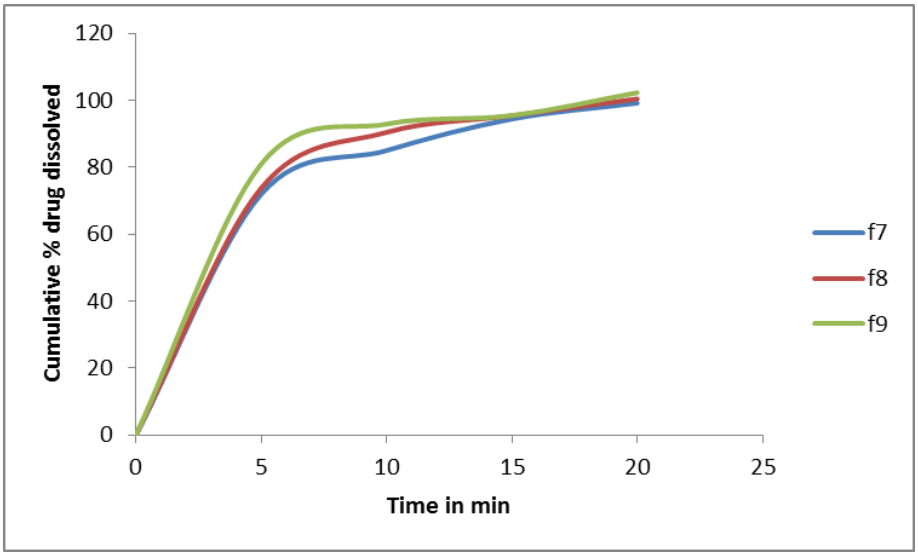

Fig 4: Comparative dissolution profile of Zingiber Officinale Extract Oral Disintigation tablets containing different concentrations of sodium starch glycollate as super disintegrant.

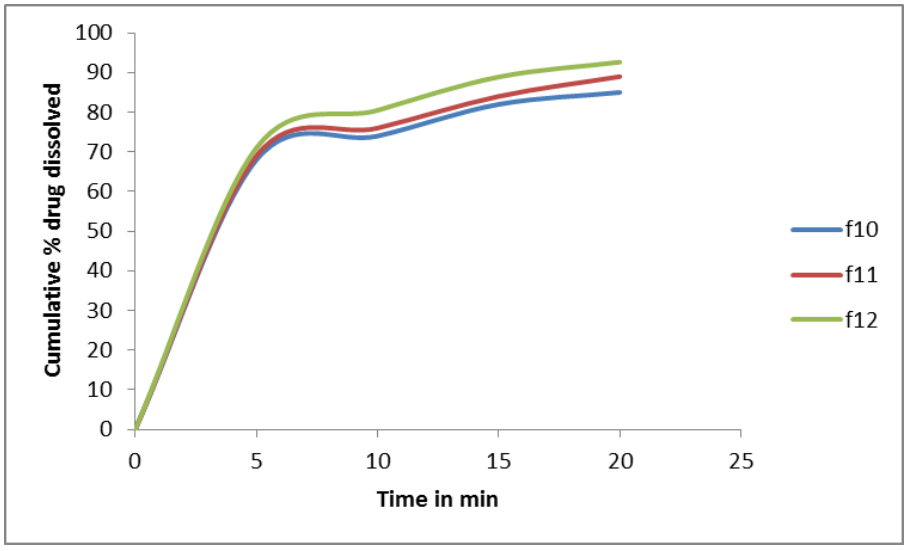

Fig 5: Comparative dissolution profile of Zingiber Officinale Extract Oral Disintigation tablets containing different concentrations of cross povidone as super disintegrant.

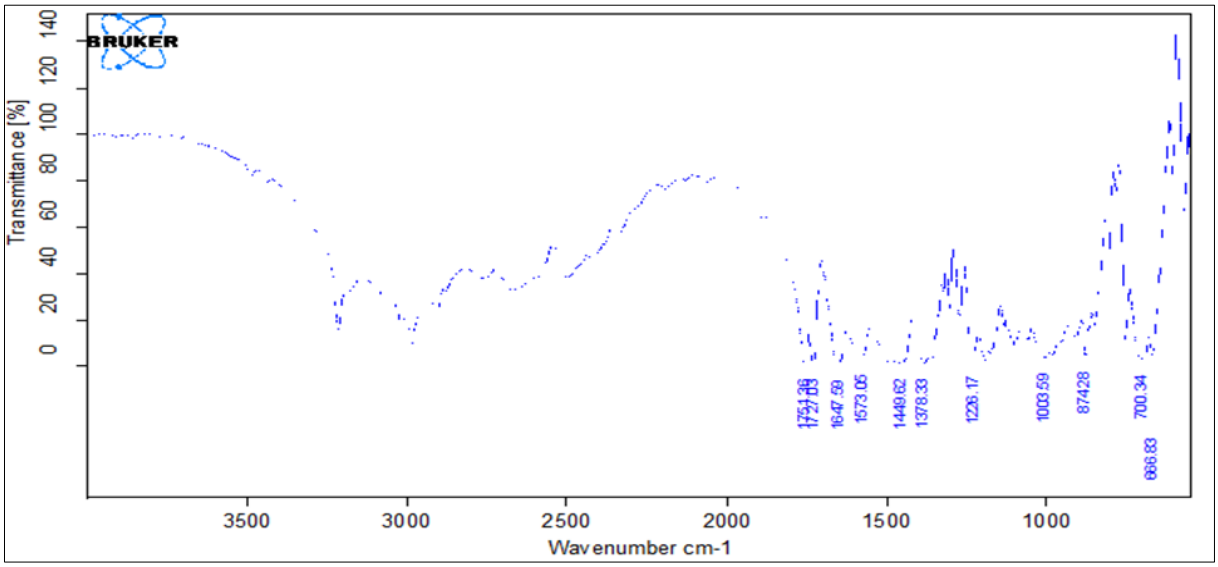

Fig 6: FTIR of Zingiber Officinale Extract (pure drug)

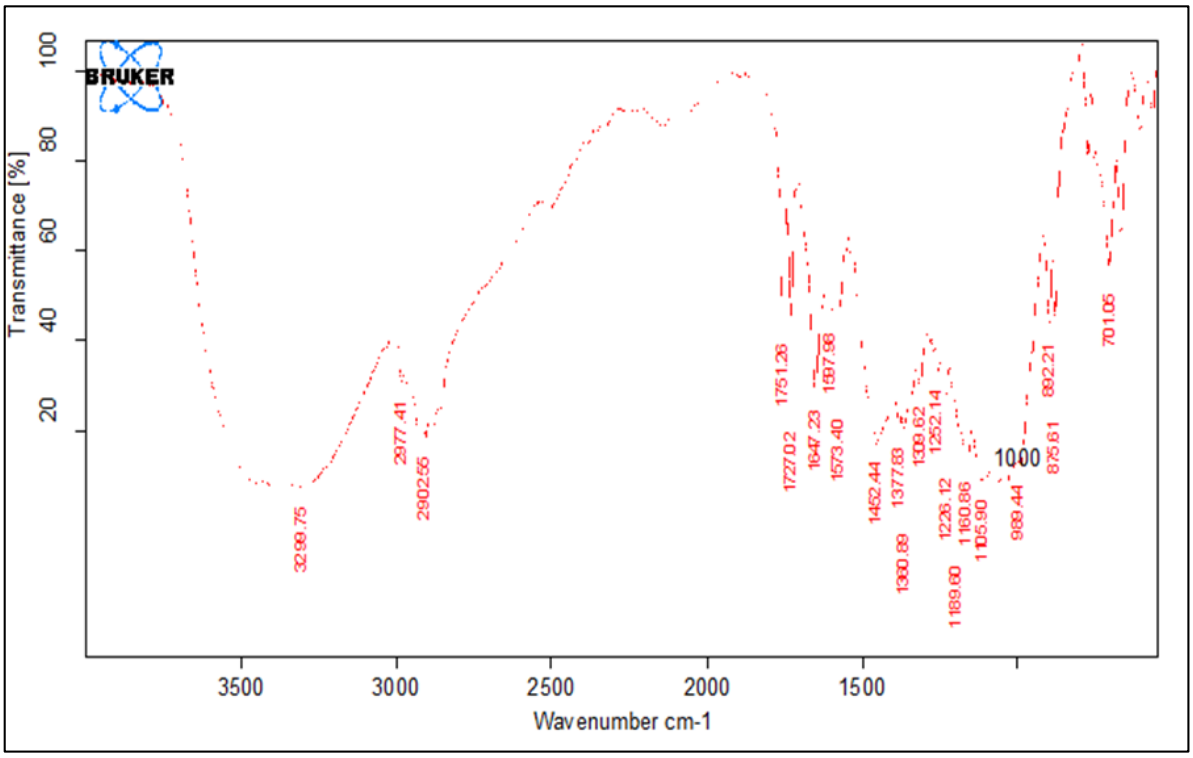

Fig 7: FTIR of Optimized Formulation (F6)

Table 7: Stability analysis for Optimized Formulation (F6)

Formulation	No of days	25˚C & 60%RH		40˚C &75% RH	
		Wetting time(s)	Disintegration time(s)	Wetting time (s)	Disintegration time (s)
F6	0	8.47±0.124	10.68±0.226	8.47±0.225	10.68±0.146
	15	8.45±0.148	10.65±0.446	8.45±0.256	10.61±0.228
	30	8.48±0.346	10.66±0.424	8.46±0.154	10.59±0.446
	45	8.43±0.146	10.64±0.568	8.44±0.654	10.62±0.356
	60	8.44±0.214	10.62±0.146	8.43±0.168	10.64±0.186

Table 8: Drug content for Optimized Formulation (F6)

Formulation	No of days	25˚C / 60%RH	40˚C / 75% RH
F6	0	99.08±0.86	99.08±0.86
	15	98.12±0.56	98.75±0.23
	30	98.74±0,24	98.06±0.36
	45	98.38±0.328	97.86±0.28
	60	98.25±0.156	97.54±0.442

4. Discussion

The 12 formulations of Zingiber Officinale Extract (F1-F12) were formulated with different Concentrations (3%, 6% and 8%) of four super disintegrants namely, pregelatinized starch, croscarmellose sodium, sodium starch glycollate and crospovidone.

Microcrystaline cellulose was used as directly compressible vehicle. Colloidal silicon dioxide used as glidant to improve the flow property of the formulation. Magnesium stearate and glyceryl behanate are used as lubricants and glidant respectively.

FTIR studies reveled that there is no drug –excipients interaction.

For each formulation blend of drug and excipients were prepared and evaluated for various pre compressional parameters like angle of repose, bulk density, tapped density, Carr's index and hausner's ratio. The powder blend of all the formulations had hausner's ratio of 1.16 indicating good flowability. The carr;s index was found to be between 8.12-13.84% indicating fairly good flow ability of the blend. The good flowabiliy of blend was also made evident with angle of repose values (23˚-35˚) which is below 40˚ indicating good flowability. Since the powder material was free flowing, tablets were prepared by direct compression technique. The drug content was found to be in the range of 97.56-101.3 (with in the acceptable limit) and the hardness of the tablets between 3.4-4.0 Kg./cm^2. The wetting time of the formulations was found to be 11.56-24.15 sec. and the disintegration time was ranging from 9.21-58.75 seconds. The wetting time and disintegration time both are less for the formulation containing croscarmellose sodium (8%w/w) as super disintegrant (F6).

The order of enhancement of dissolution rate with various super disintegrants was found to be croscarmellose sodium > cross povidone > pregelatinized starch > sodium starch glycollate.

The stability studies for the optimized formulations F6 was performed for about 2 months at 40˚C / 75% RH AND 25˚C /60%RH. The samples were analyzed at intervals of 0, 15, 30, 45 and 60 days. There were no significant change in the physical appearance of the tablets, disintegration time and wetting time.

5. Conclusion

The prepared oral disintegrating tablets of Zingiber Officinale Extract were found to be good in appearance without cracking, lamination and chipping. The promising formula (F6) have showed fast disintegration and displayed *in vitro* dispersion time of 11 s. The dissolution rate of the optimized formulations (F6) was found to be higher when compared to other formulations. Among the all the formulation F6 was found to be promising ODT formulation.

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