ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

ISSN 2277-7695

Vol. 1 No. 9 2012
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION

Formulation And Evaluation Of Sumatriptan Succinate Oral Disintegrating Tablets and Comparision of Disintegrating Property Between Superdisintegrants And Simpledisintegrants

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The main objective of this research work was to formulate and evaluate the oral disintegrating tablets of sumatrptan succinate of dose 25mg an anti-migraine drug. The tablets are prepared by direct compression method. The formulations was optimized by incorporating varying composition of Microcrystalline cellulose (Avicel PH 102), mannitol as diluent, crospovidone, croscaramellose and sodium starch glycollate as superdisintegrants, Other exipients like Carbomer (carbopol 940), Sodium CMC and Sodium Alginate were used, which acts as disintegrants when used at various concentrations, magnesium stearate as lubricant, talc as glidant. All the excipients are tested for compatability with model drug, which revealed that there was no physical and chemical interaction occurred. The preformulation parameters such as bulk density, tapped density, compressibility index and hausner ratio were analyzed for prepared tablet blend before compression. The thickness, hardness, friability, weight variation, disintegration time and drug content uniformity was evaluated for core tablets. The effect of these variables on drug release also studied. The In-Vitro drug release studied were Performed in the USP dissolution apparatus-II (paddle type) using phosphate buffer of pH 6.8 as dissolution media at 50rpm speed and temperature of 37oc ± 5oc. the sampling was done at periodic time intervals of 2,4,6,8 and 10 minutes and was replaced by equal volume of dissolution media after each withdrawal. The cumulative amount of drug release at different intervals is estimated using UV-method. Based on the evaluation result F-3 trial formulation (containing 6% crospovidone) was selected as best formulation among superdisintegrants and F-10 trial (containing 2% carbopol 940p) was selected as best formulation among simpledisintegrants.

Keyword: Sumatriptan Succinate, Oral Disintegrating, Migraine.

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INTRODUCTION: The most important drug delivery route is undoubtedly the oral route. It offers advantages of convenience of administration and potential manufacturing cost savings. Drugs that are administered orally, solid oral dosage forms in general and tablets in particular represent the preferred class of product. Today drug delivery companies are focusing on

solid oral drug delivery systems that offer greater patient compliance and effective dosages[1].

Over a decade, the demand for development of oral disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Oral disintegrating tablets offer an advantage for populations who have difficulty in swallowing. It has been reported that dysphagia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting and motion sickness complications. ODTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population.

Worldwide, migraines affect more than 10% of people. Rates of migraines are slightly lower in Asia than in Western countries. Chronic migraines occur in approximately 1.4 to 2.2% of the population. In each attack of migraine which lost for period of 15min to 180min. So it requires immediate relief. A fast dissolving tablet is one of best choice in such cases. sumatrptan succinate is one of the subclass of antimigraine drug. The main objective of this research work was to formulate and evaluate the oral disintegrating tablets of sumatrptan succinate.

Sumatriptan is used to treat migrainee. It helps to relieve headaches, pain and other symptoms of migrainee, including sensitivity to light/sound, nausea, and vomiting. Sumatriptan is a highly selective 5-HT1D receptor agonist that can contract intracranial artery and redistribute blood and improve cerebral blood flow.

Only 3% of the dose is excreted in the urine as unchanged sumatriptan, 42% of the dose excreted as the major metabolite, the indole acetic acid analogue of sumatriptan, bioavailability of drug is 15%. So there is a need to increase its bioavailability by formulating it into oral disintegrating dosage form and provide a better therapeutic profile than oral route.

MATERIALS AND METHOD:

Sumatriptan succinate was received from Natco pharma Ltd., Superdisintegrants like Crospovidone, Croscaramellose sodium and Sodium starch glycolate. Simpledisintegrants like Carbomer (carbopol 940), Sodium CMC and Sodium Alginate. Avicel 102(Microcystalline cellulose), aspartame, magnesium stearate, mannitol and talc were abtained from Drug India Pvt. Ltd.

INSTRUMENTS:

1. A rotary compression machine from CADMACH with 16 stations was used to prepare tablets.
2. An Electrolab Friabilator USP was used to check the friability of tablets.
3. CINTEX Mosanto hardness tester was used to check the hardness of the tablets.

4. TDT-08L (USP), Electro lab, USP to study the *In-vitro* dissolution profile.

5. Electrolab disintegration apparatus USP (Electro lab ED-2L) was used to check the disintegration time of tablets.

6. A Shimadzu Model No. UV-2450 double beam UV/Visible spectrophotometer with 1cm matched quartz cells was used to measure the absorbance of samples for testing Assay and Dissolution.

7. Microprocessor pH stat/Analyser, Digital pH meter was used to check the pH of the solution.

8. A shimadzu Affinity-1, FT-IR spectroscopy used for determining drug, excipient compatability studies.

9. Sartorious BSA 224S – CW, electronic weighing machine for weighing materials.

PREPARATION OF STANDARD GRAPH

Preparation of Stock solution with 6.8 P^H Phosphate Buffer

Stock I: 100mg of the drug was accurately weighed and transferred into the 100 ml volumetric flask. It was dissolved in sufficient quantity of phosphate buffer and volume was made up to the mark with phosphate buffer to get a 1000 µg/ml solution. This was the standard stock solution containing 1 mg/ml of model drug. (Stock I).

- **UV Absorption Maxima (λ_{max}) of drug sample in 6.8 P^H Phosphate Buffer**

Stock II: One ml of the above solution was then further diluted to 100 ml with phosphate buffer to get a stock solution of 10µg/ml. UV scanning was done for 10 µg/ml drug solution from 200-400 nm using 6.8pH phosphate buffer as a blank in schimadzu, UV 2450 spectrophotometer. The wavelength maximum was found to be at 226 nm.

- **Preparation of the calibration curve**

From the stock II solution 2, 4, 6, 8 and 10ml were transferred to 10 ml volumetric flasks and were diluted with the phosphate buffer, up to the mark to obtain concentration of 2, 4, 6, 8 and 10µg/ml respectively. Absorbance of each solution was measured at 226 nm. The Standard curve preparation was performed. The absorbances were plotted against the concentrations and the graph with the straight line equation and r^2 value were obtained 0.998 obeys Beer's Lamberts law.

Table. 3. Calibration curve of sumatriptan succinate

Concentration(µg/ ml)	Absorbance
0	0
2	0.206
4	0.398
6	0.656
8	0.842
10	1.044

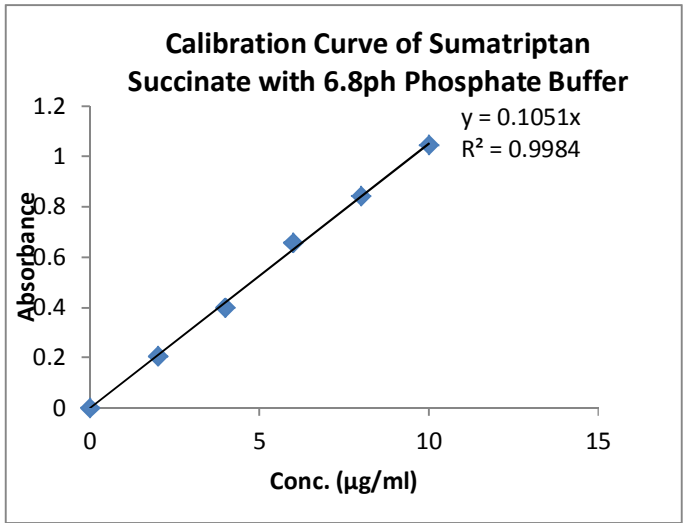


Figure. 1. Calibration Curve of Sumatriptan Succinate with 6.8ph Phosphate Buffer

FORMULATION OF DIFFERENT BATCHES

The main aim of the present study was to formulate different batches using three various superdisintegrants and other ingredients in varying concentrations. So, different batches of formulations were planned accordingly. According to that F1, F2, F3 (with Crospovidone-1.5%, 3%, 6%), F4, F5, F6 (with Crosscaramellose-1.5%, 3%, 6%), F7, F8, F9 (with Sodium starch glycollate-1.5%, 3%, 6%) and F10, F11, F12 (with carbopol 940 - 2%, 4%, 6%), F13, F14, F15 (with Sodium CMC-2%, 4%, 6%), F16, F17, F18 (with Sodium Alginate-2%, 4%, 6%) was formulated. The slight bitter taste of the drug was masked using aspartame (2.5% to 6%) as the sweetening agent.

EVALUATION PARAMETERS FOR ODT

Drug Content Uniformity

Twenty tablets were selected randomly and powdered. A quantity of this powder corresponding to one tablet was dissolved in 100 ml of 6.8 pH phosphate buffer, stirred for 15 min and filtered. 1 ml of the filtrate was diluted to 100 ml with 6.8 pH phosphate buffer. Absorbance of this solution was measured at 226nm using 6.8 pH phosphate buffer as blank and content of drug was estimated.

Table 4: Formulations of Different Batches (F1 – F9)

Formulations Code									
Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Sumatriptan succinate	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**
Crospovidone	**3**	**6**	**12**	**------**	**------**	**-------**	**------**	**------**	**-----**
Croscarmellose sod.	**------**	**------**	**------**	**3**	**6**	**12**	**------**	**------**	**-----**
SSG	**------**	**-----**	**----**	**-------**	**------**	**-----**	**3**	**6**	**12**
MCC 101	**71**	**69**	**63**	**71**	**69**	**63**	**71**	**69**	**63**
Aspartame	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**	**10**
Mannitol	**80**	**80**	**80**	**80**	**80**	**80**	**80**	**80**	**80**
Magnesium stearate	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**
Talc	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**

Table 5: Formulations of Different Batches (F10 – F18)

	Formulation Code								
Ingredients (mg)	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**	**F17**	**F18**
Sumatriptan succinate	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**
Carbomer (Carbopol 940P)	**4**	**8**	**12**	**-----**	**-----**	**-----**	**-----**	**-----**	**-----**
Sodium CMC	**-----**	**-----**	**-----**	**4**	**8**	**12**	**-----**	**-----**	**-----**
Sodium Alginate	**-----**	**-----**	**-----**	**-----**	**-----**	**-----**	**4**	**8**	**12**
MCC	**50**	**50**	**50**	**50**	**50**	**50**	**50**	**50**	**50**
Aspartame	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**
Mannitol	**104**	**100**	**96**	**104**	**100**	**96**	**104**	**100**	**96**
Magnesium Stearate	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
Talc	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**

Assay calculation: The amount of drug present was calculated by given formula,

$$\text{Drug content} = \frac{\text{Spl abs. x Std. wt. x Std. dil. factor x std. purity}}{\text{Std. abs. x wt. of the tablet x Spl. dil. factor x 100}} \text{ x Avg. wt. of tablet}$$

Weight variation[26]

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

Table 6: Weight Variation

Average weight of Tablets(mg)	Maximum percentage different allowed
80 or less	10
80 - 120	7.5
250 or more	5

Friability[27, 28]

Friability is a crucial parameter for evaluation of ODT. Attempts for decreasing the disintegration time increase the friability of ODTs than the conventional tablets. Dosage forms like Zydis are very fragile. Friability is a measure of mechanical strength of the tablet. If a tablet has more friability it may not remain intact during packaging, transport or handling. Roche friabilator is used to determine the friability by following procedure. Pre weighed tablets are placed in the friabilator. Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least 4 minutes. At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

$$\% \textbf{ Friability} = \frac{\textbf{Loss in weight}}{\textbf{Initial weight}} \times \mathbf{100}$$

Hardness (Crushing load)[27, 28]

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. The hardness of ODTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. A good compromise between mechanical strength and disintegration time is achieved for a satisfactory mouth dissolving formulation.

Wetting time[28, 29]

The initial process in the disintegration of a ODT involves water uptake and wetting of the tablet. So determination of wetting time is also important. It also helps in studying the effect of various excipients in the disintegration of the tablet. A petridish containing 6 ml of distilled water is taken and a tissue paper folded twice is placed in it. A tablet containing a small quantity of amaranth color is placed on this. Time required for the upper surface of the tablet to become complete red is the wetting time.

Water absorption ratio[28, 29]

A pre weighed tablet (W_a) is placed in a petridish in the similar way as described in the wetting time test. When the tablet has absorbed water completely, it is removed and weight is noted (W_b). Water absorption ratio R is calculated as:

$$\mathbf{R} = \frac{\mathbf{Wa - Wb}}{\mathbf{Wb}} \times \mathbf{100}$$

Disintegration Time (DT)[30-33]

As described in pharmacopoeia, tablets are placed in the disintegration tubes and time is noted. According to the European pharmacopoeia the oral disintegrating/ Orodispersible tablets should disintegrate within 3 minutes without leaving any residue on the screen. However it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus the

disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth. To overcome these problems, several new methods have been proposed. One of these methods Disintegration of fast dissolving tablets is achieved by saliva in the mouth, however amount of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate *in vivo* conditions. A modified version of the simple but novel method was used to determine disintegration time of the tablets. A cylindrical vessel was used in which 10-mesh screen was placed in such way that only 4 ml of disintegrating medium would be placed below the sieve. To determine disintegration time, 6ml of Sorenson's buffer (pH 6.8), was placed inside the vessel in such way that 4ml of the media was below the sieve and 2ml above the sieve. Tablet was placed on the sieve and the whole assembly was then placed on a shaker. The time at which all the particles pass through the sieve was taken as a disintegration time of the tablet. Six tablets were chosen randomly from the composite samples and the average value was determined.

In vitro Dispersion Time[31-33]

Tablet was added to 10ml of buffer solution (pH 6.8) and time required for complete dispersion was measured. Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed.

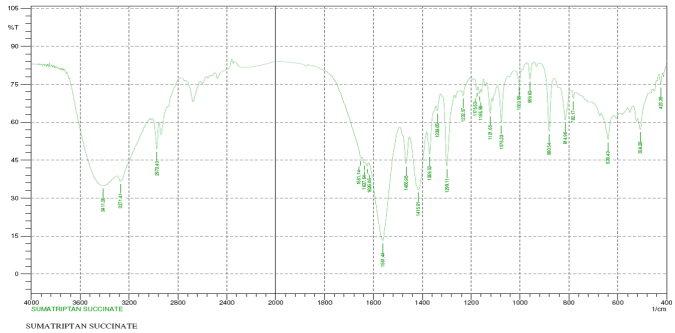
Dissolution test[31-33]

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP 2 paddle apparatus is most suitable and common choice for dissolution test of oral disintegrating tablets, where the paddle speed is 50 rpm is used. The USP 2 (Paddle) apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets. Specifically tablet fragments or disintegrating tablet masses become trapped on the inside top of the basket spindle where little or no effective stirring occurs, yielding irreproducible results in dissolution profiles.

RESULTS AND DISCUSSIONS

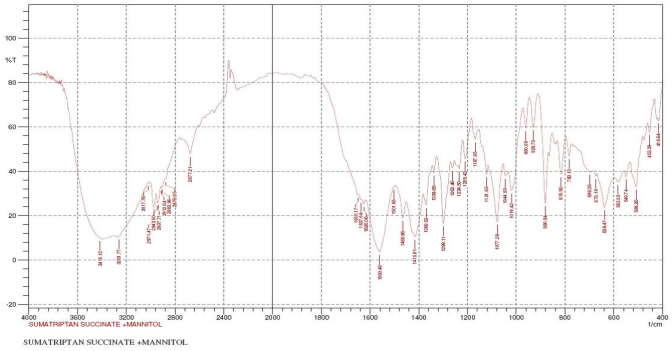
RESULTS:

Drug-excipients Compatibility studies



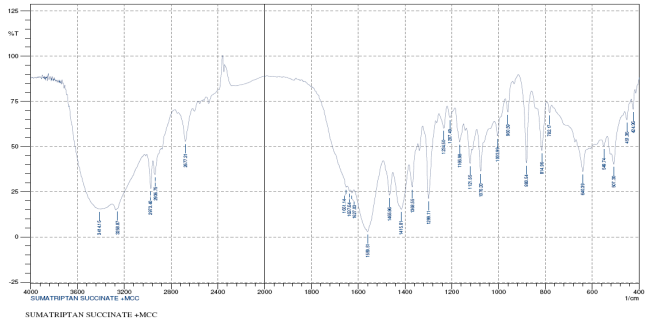
SUMATRIPTAN SUCCINATE

2. FT-IR spectra of sumatriptan succinate



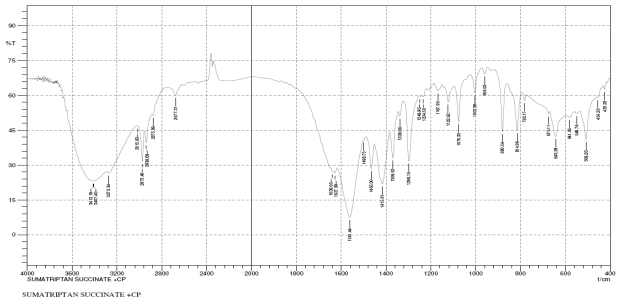
SUMATRIPTAN SUCCINATE +MANNITOL

3. FT-IR spectra of sumatriptan succinate + Mannitol



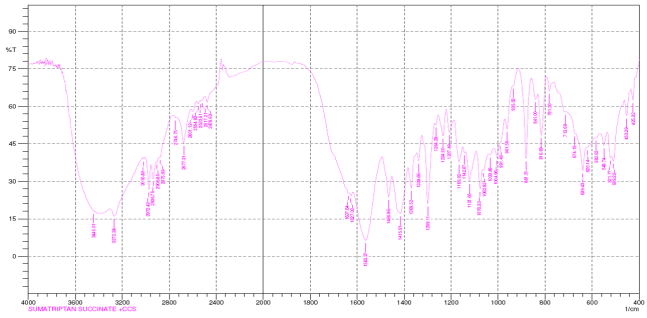
SUMATRIPTAN SUCCINATE +MCC

4. FT-IR spectra of sumatriptan succinate + MCC



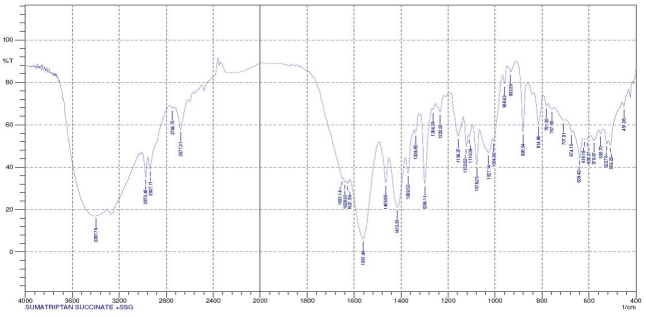
SUMATRIPTAN SUCCINATE +CP

5. FT-IR spectra of sumatriptan succinate + CP



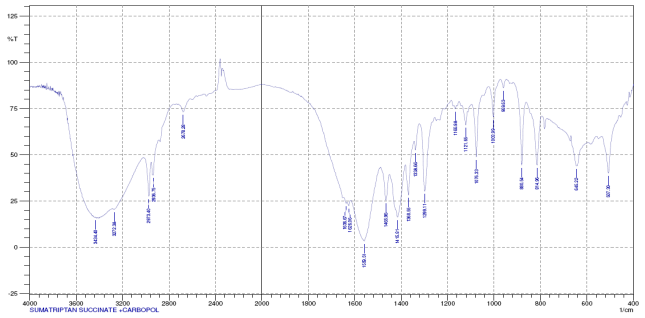
SUMATRIPTAN SUCCINATE +CCS

6. FT-IR spectra of sumatriptan succinate + CCS



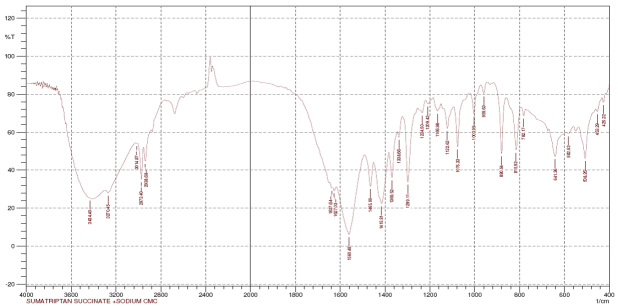
SUMATRIPTAN SUCCINATE +SSG

7. FT-IR spectra of sumatriptan succinate + SSG



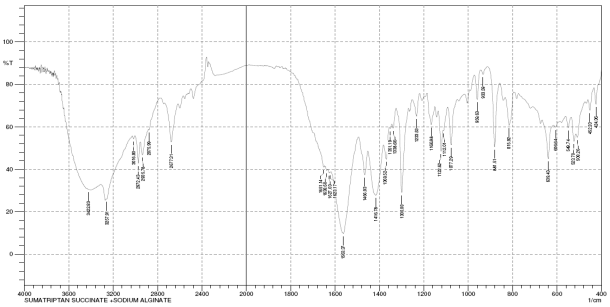
SUMATRIPTAN SUCCINATE +CARBOPOL

8. FT-IR spectra of sumatriptan succinate + Carbopol



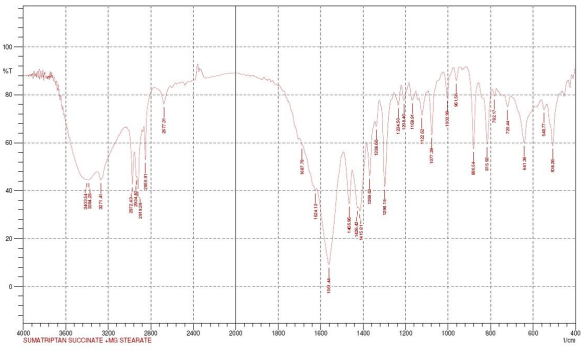
SUMATRIPTAN SUCCINATE +SODIUM CMC

8. 9. FT-IR spectra of sumatriptan succinate + Sodium CMC



SUMATRIPTAN SUCCINATE +SODIUM ALGINATE

10. FT-IR spectra of sumatriptan succinate + Sodium alginate



SUMATRIPTAN SUCCINATE +MG STEARATE

11. FT-IR spectra of sumatriptan succinate + Mg. stearate

Table 7: Wavelengths of functional groups

	Peaks of functional groups [wavelength (cm^{-1})]					
IR Spectra	**N-H_{def}**	**O-H_{str}**	**C-C_{str} alkanes**	**C-H_{def} alkenes**	**S=O**	**C-H_{def} aromatic**
Drug	1561-1651	1415	814-1299	959	1338	782-880
MCC	1559-1651	1415	814-1299	960	1338	782-880
CP	1561-1638	1415	814-1298	959	1338	782-880
CCS	1563-1637	1415	816-1299	935	1338	782-880
SSG	1561-1651	1415	814-1299	959	1338	782-880
Carbopol	1559-1636	1415	814-1299	959	1338	782-880
Sod. CMC	1560-1637	1415	815-1299	959	1338	782-880
Sod. Alginate	1563-1651	1416	815-1300	959	1338	782-881
Mannitol	1560-1650	1415	815-1299	960	1338	783-880
Mg. Stearate	1561-1687	1415	815-1298	961	1338	782-880
SSG	1561-1651	1415	814-1299	959	1338	782-880

Table 8: Evaluation of ODT for formulations (F1 – F9)

Formulation	Hardness[a] (kg/cm2)	Friability[b] (%)	Weight[c] (mg)	Thickness[a] (mm)	Drug content[d] (%)
F1	3.0±0.17	0.25	201±0.59	3.9±0.05	97.2±0.62
F2	3.1±0.20	0.23	198±0.63	4±0.02	97.72±0.23
F3	3.2±0.18	0.26	201±0.45	3.7±0.07	98.4±0.34
F4	3.0±0.15	0.24	202±0.88	3.8±0.10	97±0.56
F5	3.2±0.16	0.28	203±0.56	3.9±0.03	98.44±0.49
F6	3.1±0.22	0.32	198±0.74	3.9±0.06	100.8±0.27
F7	3.2±0.24	0.27	201±0.67	3.8±0.15	97.2±0.63
F8	3.0±0.22	0.29	201±0.77	3.9±0.03	98.4±0.56
F9	3.1±0.16	0.24	203±0.86	4±0.01	99.32±0.37

a = 6 tablets, b = 33, c = 20, d=10

Table 9: Evaluation of ODT for formulations (F10 – F18)

Formulation	Hardness[a] (kg/cm2)	Friability[b] (%)	Weight[c] (mg)	Thickness[a] (mm)	Drug content[d] (%)
F10	3.1±0.14	0.31	200±0.91	3.8±0.11	97.08±0.36
F11	3.0±0.16	0.33	201±0.58	3.6±0.04	98.4±0.52
F12	3.2±0.21	0.27	199±0.62	3.6±0.08	99.08±0.48
F13	3.1±0.17	0.29	202±0.84	3.6±0.07	99.4±0.49
F14	3.2±0.23	0.26	203±0.90	3.7±0.05	101.92±0.27
F15	3.0±0.22	0.28	201±0.73	3.6±0.05	97.20±0.47
F16	3.3±0.15	0.30	200±0.75	3.9±0.06	96.76±0.38
F17	3.2±0.15	0.25	201±0.56	3.7±0.12	98.82±0.43
F18	3.2±0.18	0.27	200±0.78	3.9±0.08	100.72±0.61

a = 6 tablets, b = 33, c = 20, d=10

Table 10: Evaluation of ODT for formulations (F1 – F9)

Formulation	Disintegration time[a] (sec)	Wetting time[a] (sec)	Water absorption ratio[a] (%)	*In vitro* dispersion time[a] (sec)
F1	19±0.54	15±0.23	52±0.42	17±0.79
F2	16±0.63	12±0.47	56±0.47	15±0.82
F3	12±0.48	10±0.35	59±0.78	11±0.64
F4	28±0.57	19±0.32	49±0.13	23±0.63
F5	23±0.72	14±0.49	55±0.27	19±0.71
F6	18±0.41	16±0.28	50±0.17	16±0.92
F7	34±0.68	25±0.16	47±0.32	28±0.87
F8	26±0.43	20±0.25	51±0.47	21±0.83
F9	22±0.60	17±0.51	53±0.92	19±0.75

a = 6 tablets, b = 33, c = 20, d=10

Table 11: Evaluation of ODT for formulations (F10 – F18)

Formulation	Disintegration time[a] (sec)	Wettingtime[a] (sec)	Water absorption ratio[a] (%)	*In vitro* dispersion time[a] (sec)
F10	25±0.33	48±0.46	45±0.21	24±0.40
F11	34±0.49	54±0.48	42±0.30	28±0.64
F12	45±0.51	52±0.35	40±0.76	41±0.61
F13	58±0.27	58±0.43	34±0.15	53±0.52
F14	43±0.32	46±0.54	38±0.37	42±0.43
F15	39±0.29	33±0.32	41±0.74	30±0.45
F16	48±0.47	36±0.29	33±0.48	38±0.33
F17	52±0.30	40±0.38	36±0.35	46±0.67
F18	59±0.37	44±0.28	42±0.27	48±0.58

a = 6 tablets, b = 33, c = 20, d=10

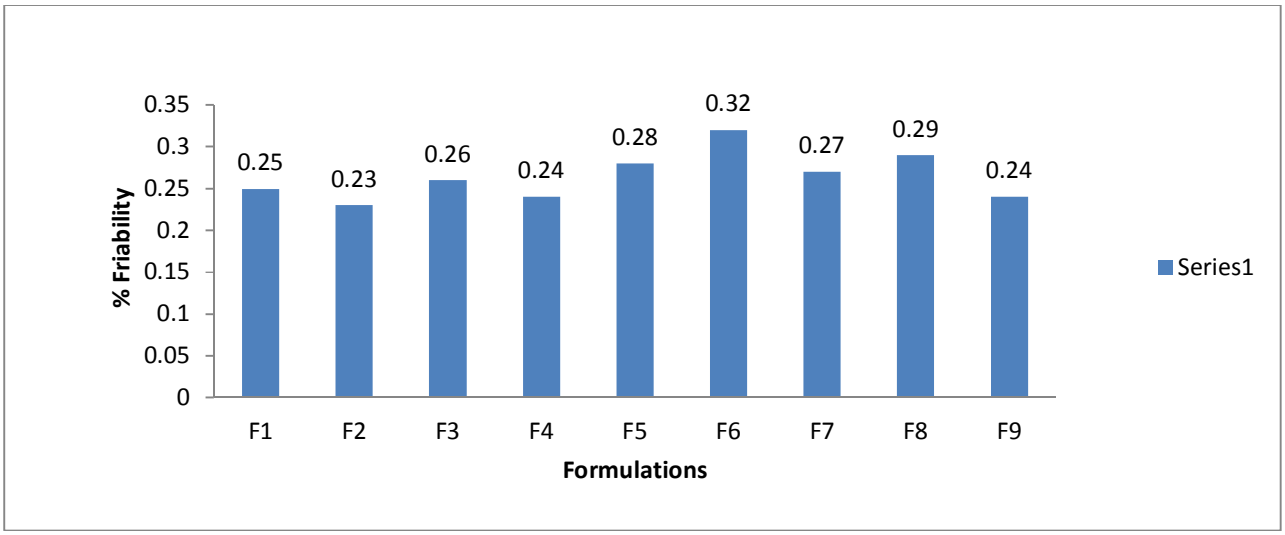


Figure 12: Bar graph comparison friability for formulations (F1- F9)

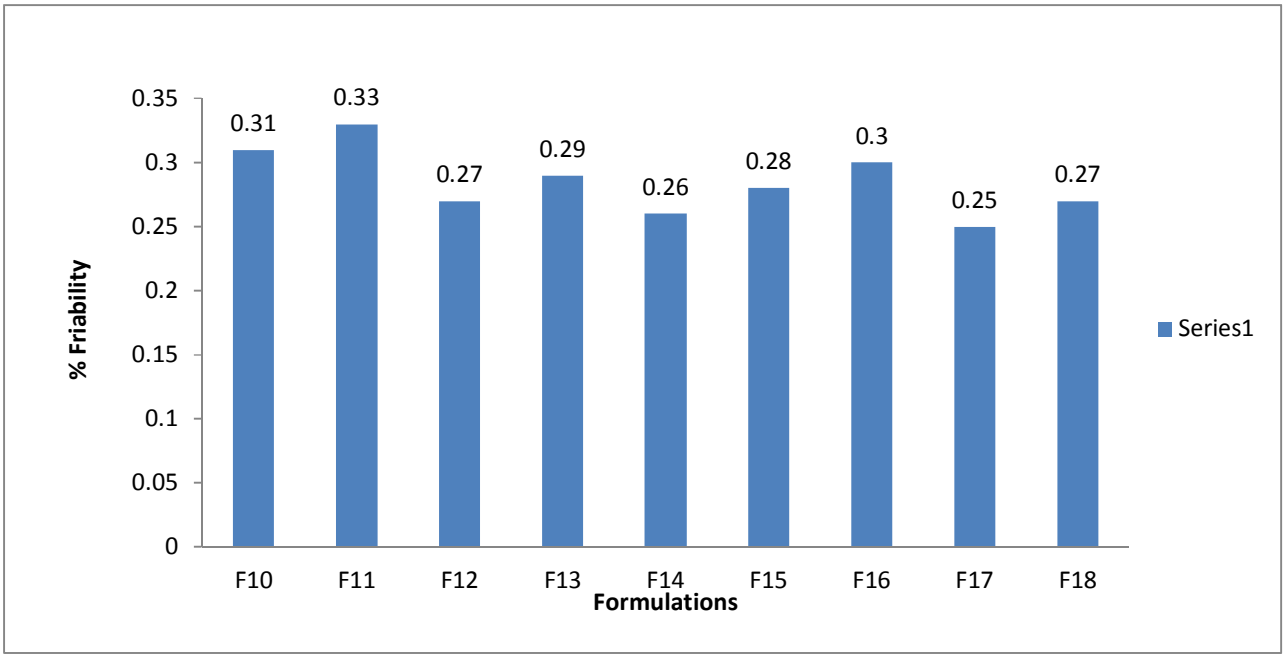


Figure 13: Bar graph comparison between friability for formulations (F10- F18)

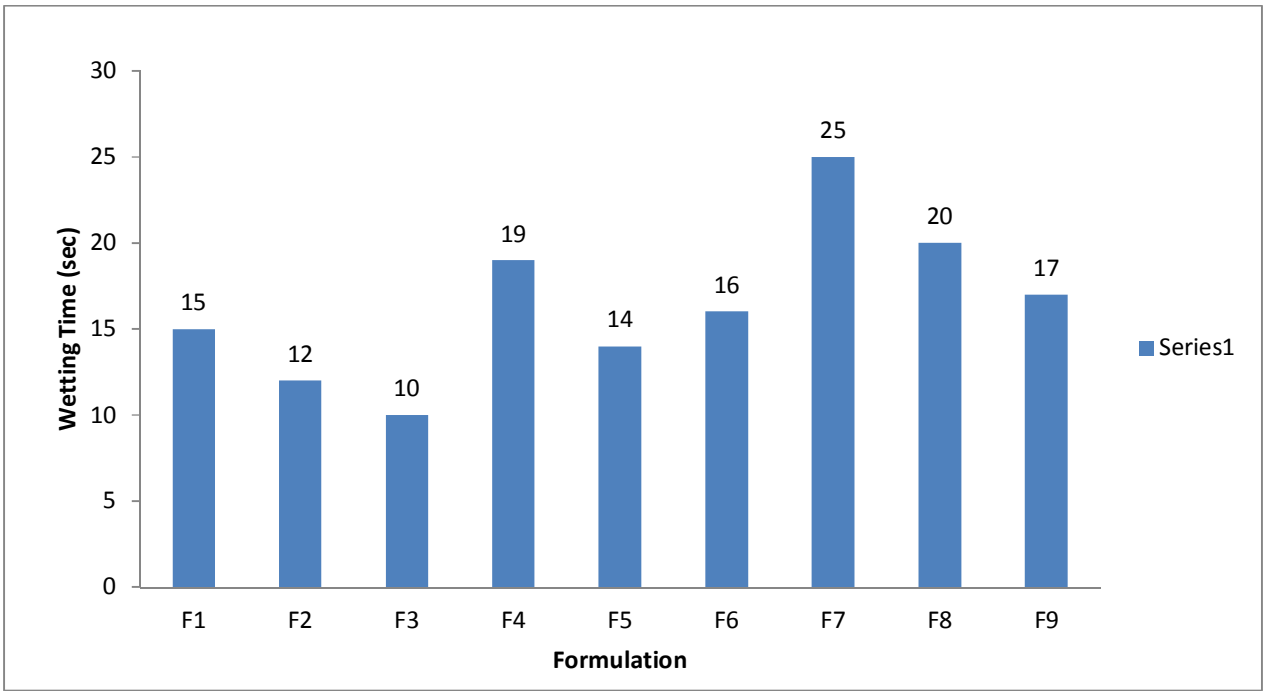


Figure 14: Bar graph comparison between wetting time for formulations (F1- F9)

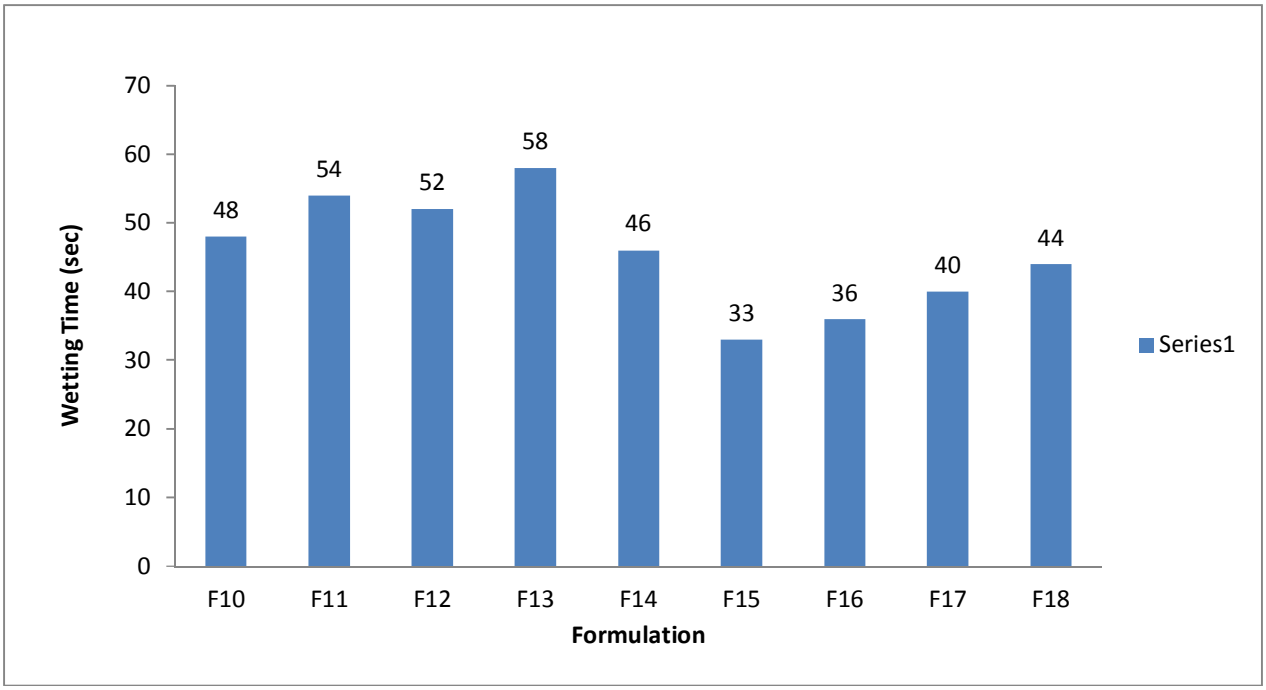


Figure 15: Bar graph comparison between wetting time for formulations (F10- F18)

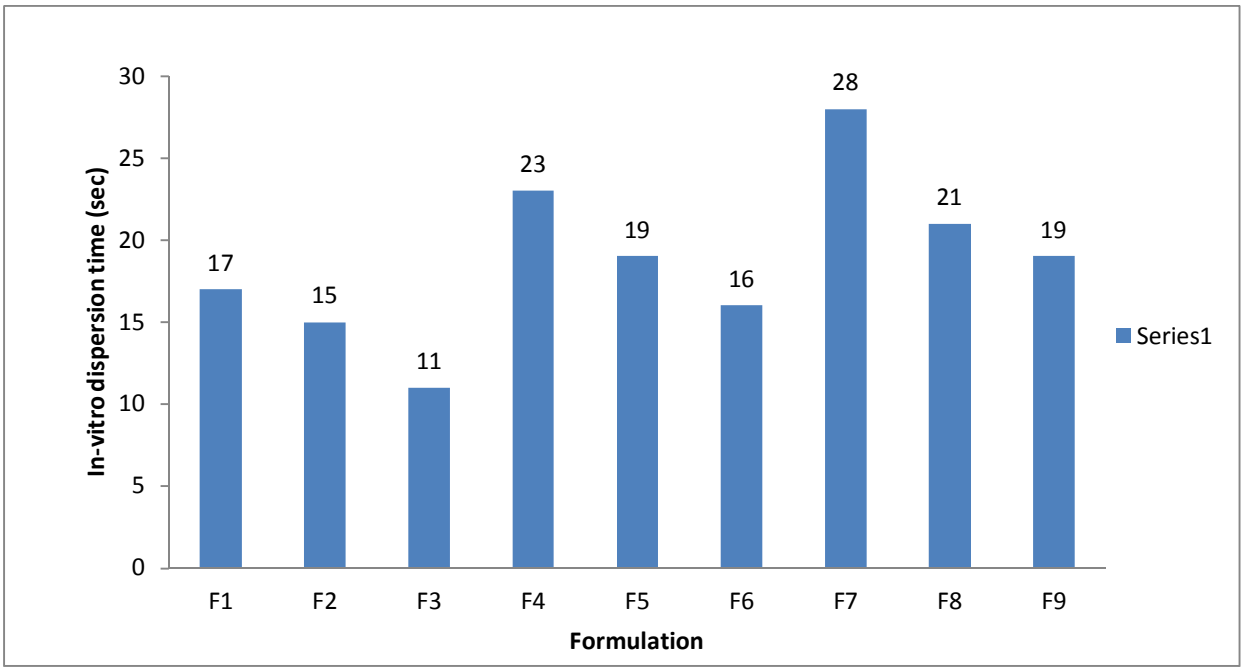


Figure 16: Bar graph comparison between In-vitro dispersion time for formulations (F1- F9)

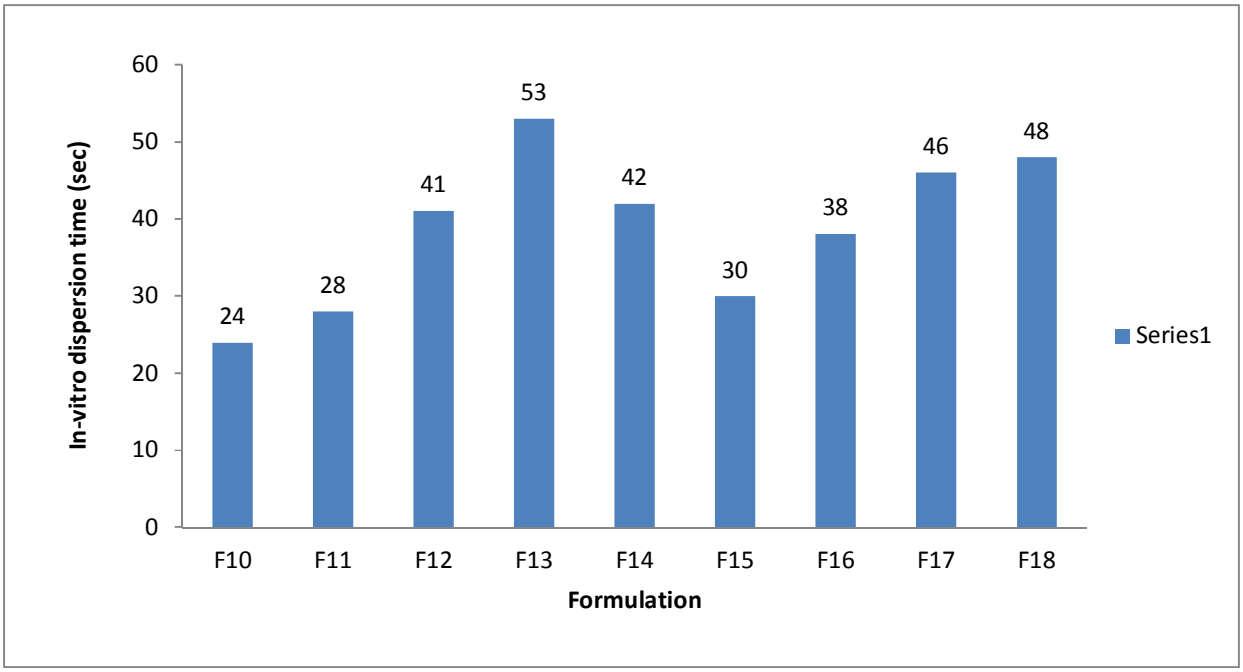


Figure 17: Bar graph comparison between In-vitro dispersion time for formulations (F10- F18)

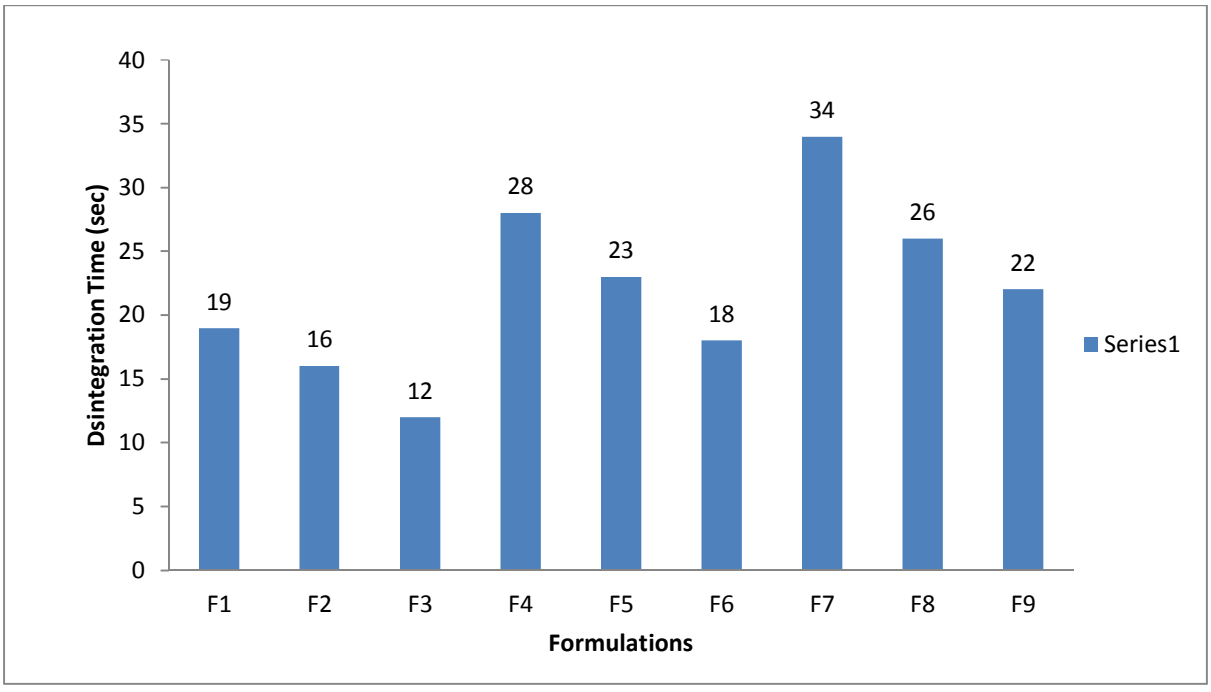


Figure 18: Bar graph comparison between Disintegration time for formulations (F1- F9)

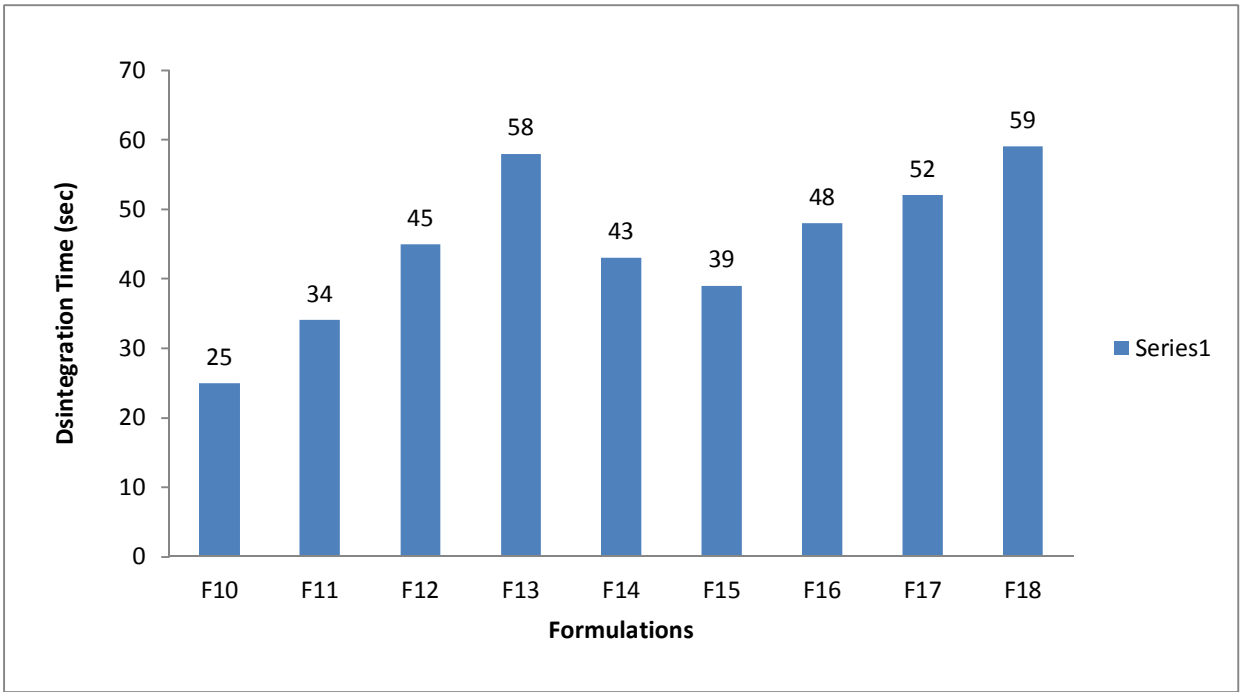


Figure 19: Bar graph comparison between Disintegration time for formulations (F10- F18)

Table 12: Cumulative % drug release for formulations (F1 – F9)

Cumulative % drug release									
Time	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
2 Min	55.81±0.89	58.11±0.98	63.69±0.52	48.4±0.53	51.59±0.55	62.71±0.65	45.93±0.88	50.86±0.61	56.58±0.65
4 Min	68.4±0.32	72.01±0.27	74.65±0.58	57.28±1.0	62.12±0.54	71.97±0.56	55.74±0.49	61.23±0.34	64.72±0.53
6 Min	71.73±0.46	80.75±0.65	82.38±0.46	72.58±0.54	76.74±0.63	81.92±0.77	71.89±0.74	73.5±0.44	77.51±0.50
8 Min	82.13±0.72	85.06±0.98	88.82±0.58	79.06±0.67	85.33±0.89	86.45±0.83	76.83±0.89	82.15±0.87	84.23±0.55
10 Min	91.7±0.93	94.58±0.57	96.96±0.54	88.51±0.75	92.54±0.84	93.12±0.63	85.74±0.40	87.11±0.33	89.02±0.74

n=6

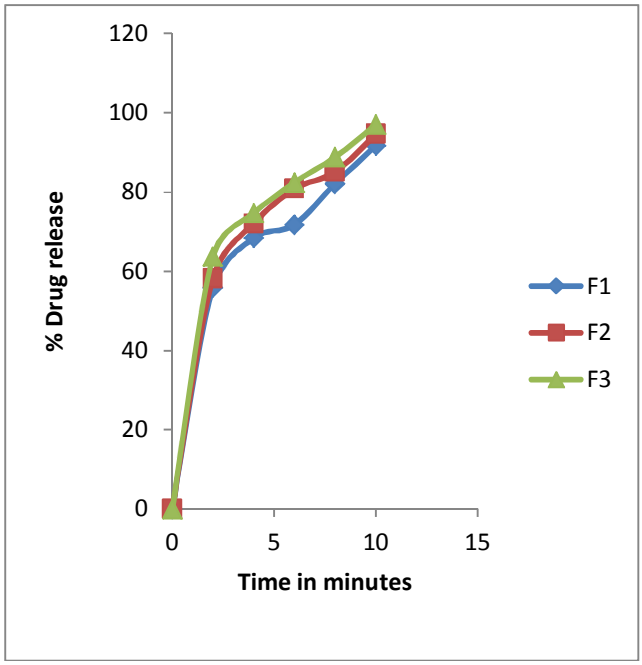


Figure 20: Linear graph comparison between cumulative % drug release for formulations (F1- F3)

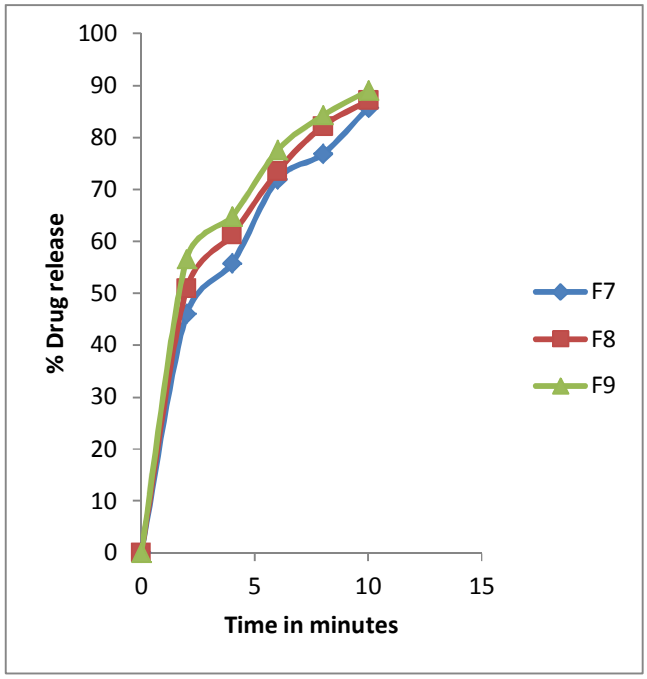


Figure 22: Linear graph comparison between cumulative % drug release for formulations (F7- F9)

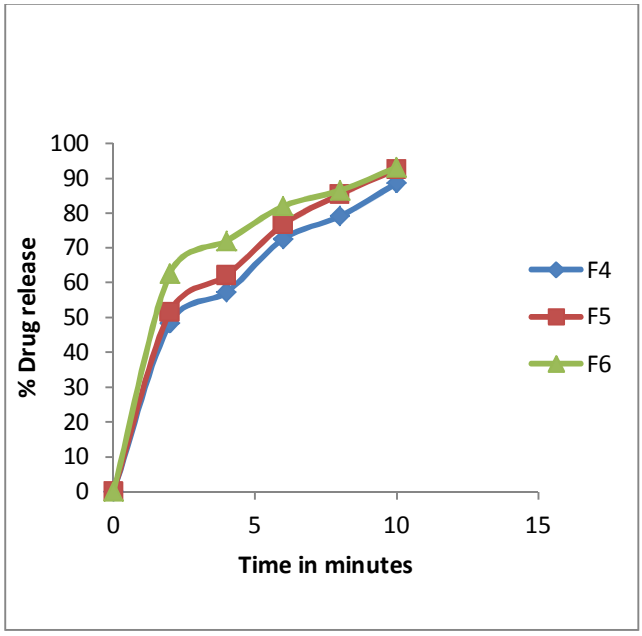


Figure 21: Linear graph comparison between cumulative % drug release for formulations (F4 - F6)

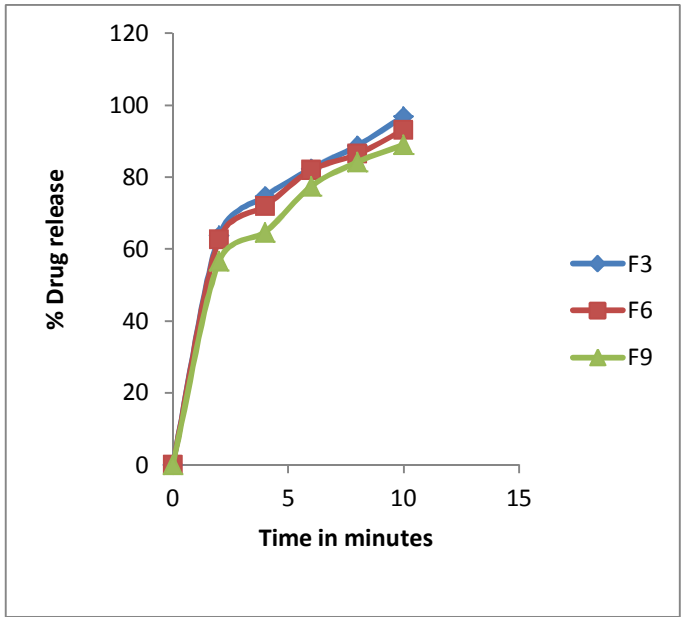


Figure 23: Linear graph comparison between cumulative % drug release for formulations (F3, F6 and F9)

Table 13: Cumulative % drug release for formulations (F10 – F18)

Cumulative % drug release									
Time	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**	**F16**	**F17**	**F18**
2 Min	71.69±0.62	61.82±0.69	57.76±0.86	35.69±0.48	36.35±0.65	38.58±0.63	52.36±0.56	46.87±0.74	41.18±0.63
4 Min	82.01±0.56	78.17±0.81	75.31±0.54	47.54±0.77	48.52±0.58	52.9±0.57	63.57±0.51	61.45±0.80	53.84±0.65
6 Min	93.61±0.64	87.57±0.47	86.35±0.64	58.55±0.70	61.04±0.70	63.4±0.61	68.71±0.73	66.61±0.68	64.75±0.50
8 Min	94.47±0.48	91.75±0.36	88.59±0.80	69.42±0.84	71.73±0.54	74.52±0.77	78.6±0.48	75.9 ±0.68	74.36±0.73
10 Min	94.83±0.52	92.59±0.73	89.62±0.79	81.43±0.56	83.56±0.98	85.67±0.85	87.84±0.5	85.64±0.52	82.63±0.83

n=6

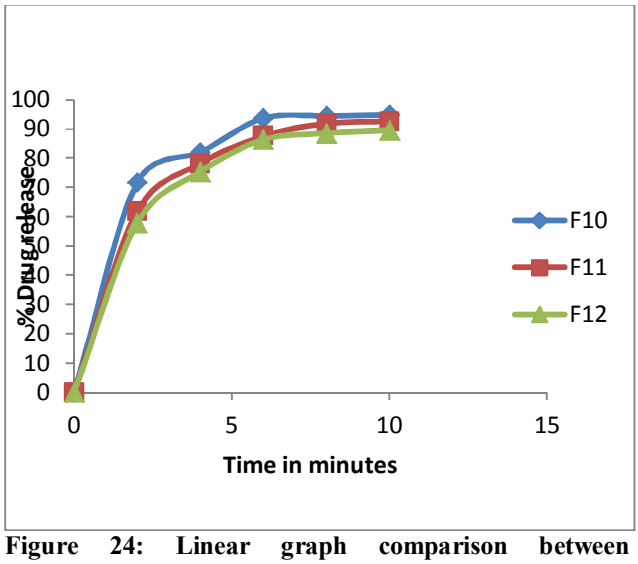


Figure 24: Linear graph comparison between cumulative % drug release for formulations (F10- F12)

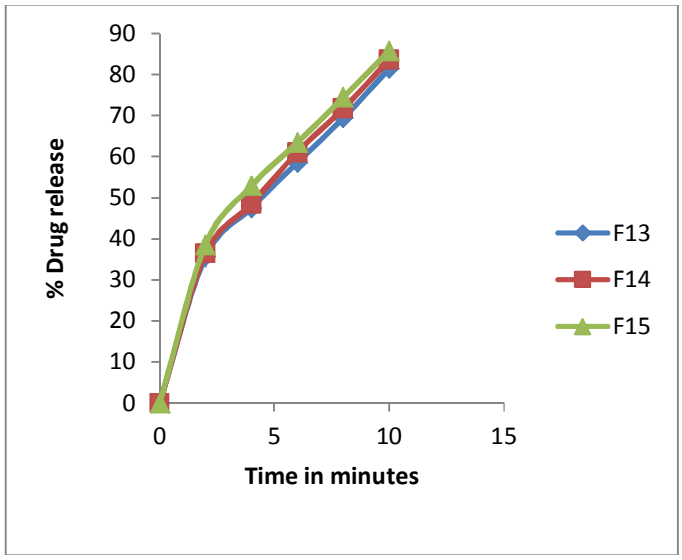


Figure 25: Linear graph comparison between cumulative % drug release for formulations (F13- F15)

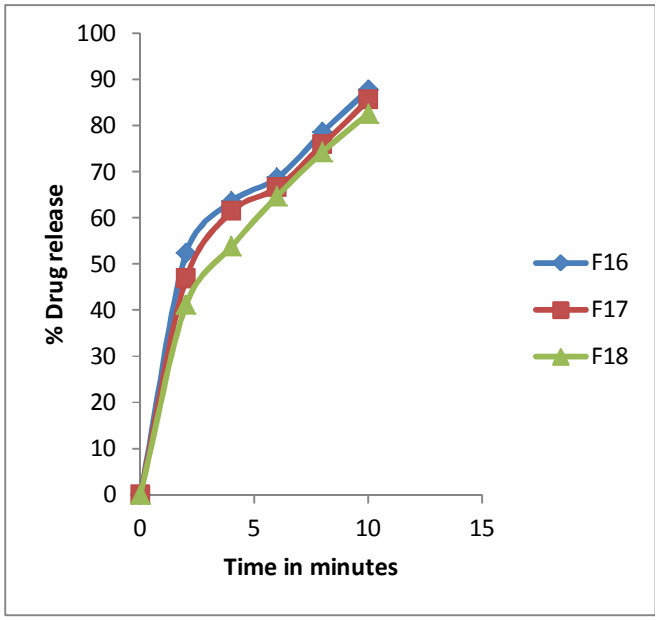


Figure 26: Linear graph comparison between cumulative % drug release for formulations (F16- F18)

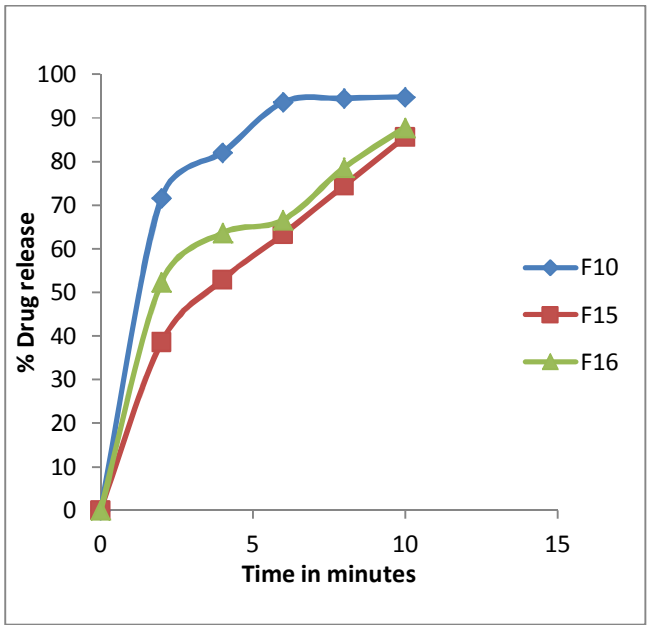


Figure 27: Linear graph comparison between cumulative % drug release for formulations (F10, F15 and F16)

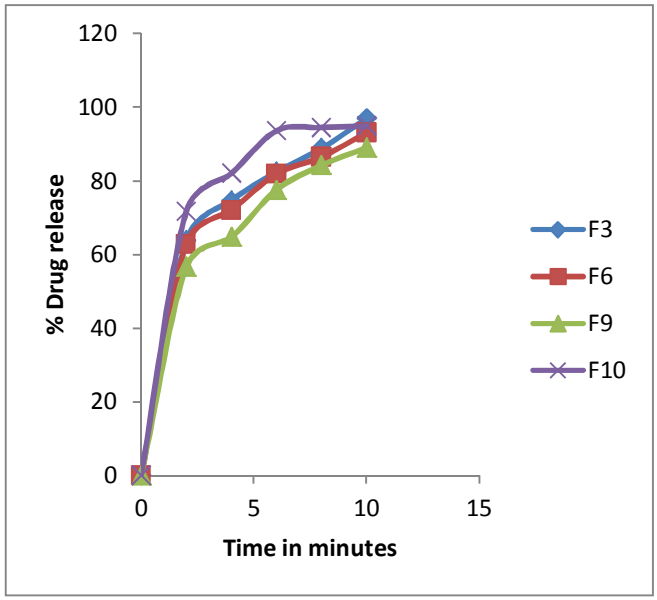


Figure 28: Linear graph comparison between cumulative % drug release for formulations (F3, F6, F9 and F10)

DISCUSSIONS

The FT-IR represents the peaks of the sumatriptan succinate functional groups. These peaks were not affected, they were prominently observed in IR-spectra of sumatriptan succinate along with superdisintegrants, simpledisintegrants and other excipients. The spectral details of the drug and the excipients shown in (Table.7) and (Figure.2 - 11). There was no difference in the position of the absorption bands, hence providing evidence for the absence of any chemical incompatibility between pure drug with the excipients.

Determination of λ_{max}

UV scanning of the model drug sample (sumatriptan succinate) was carried out using UV-2450 shimadzu spectrophotometer and the wavelength maximum was found to be at 226nm.It is coinciding with standard values, so confirmed it as sumatriptan succinate.

Development of calibration curve with 6.8pH phosphate buffer

The scanning of the solution in UV range showed maximum absorbance at 226nm and hence, the calibration curve was developed at this wave length. The calibration curve was linear between 2 - 10µg/ml concentration ranges. The calibration curve is shown in (Table.3) and the (Figure.1).

EVALUATION OF TABLETS:

1. Hardness test

By using the superdisintegrants, the hardness values ranged from 3.0±0.15 kg/cm^2 - 3.2±0.24 kg/cm^2 for formulations (F1-F9) and were given in (Table.8). By using simple disintegrants, the hardness values ranged from 3.0±0.16 - 3.3±0.15 kg/cm^2 for formulation (F10 - F18) and were almost same (Table.9).

There is no variation between superdisintegrants tablets and simple Disintegrant tablets in hardness. They are within the acceptable range.

2. Weight variation test

The entire tablet passes weight variation test, as the average % weight variation was within the Pharmacopeial limit - 7.5%. It was found to be 198±0.63 mg - 203±0.90 mg. The weight of all the tablets was found to be uniform with less deviation (Table.8, 9).

3. Friability test

The friability values were found to be within the limit (0.5 - 1%). The above evaluation parameter showed no significant difference between F1-F18 formulations, details were given in (Table.8, 9) and comparative profile in (Figure.12, 13).

4. Drug content uniformity

The concentration of the drug in all the formulations with superdisintegants was found to be 97±0.56 – 100.8±0.27%. It was within the IP limits. The results of drug content of all batches are shown in (Table.8).

The concentration of the drug in all the formulations with simple disintegrants was found to be 96.76±0.38 - 101.92±0.27 %. The results of drug content of all batch are shown in (Table.9).

5. Wetting time

The experiment mimics the action of saliva in contact with the tablet to illustrate the water uptake and subsequent wetting of tablet. This shows the wetting process was very rapid in almost all formulations. This may be due to the ability of swelling followed by breaking and also capacity of water absorption and causes swelling.

By using superdisintegrants wetting time was found to be in the range of 10±0.35 - 25±0.16 sec. It shows crospovidone formulations take less wetting time comparing with that of crosscaramellose, sodium starch glycollate formulations, details were given in (Table.10) and comparative profile in (Figure.14).

With simple disintegrants wetting was found to be in the range of 33±0.32 - 58±0.43 sec. It shows carbomer (carbopol 940) formulations take less wetting time comparing with that of sodium CMC, sodium alginate, details were given in (Table.11) Comparative profile shown in (Figure.15).

By using the superdisintegrants the wetting time was shorter when compared to the formulation with simple disintegrants. As the name represents due to presence of superdisintegrants it is disintegrating fastly due to wicking and swelling properties of superdisintegrants.

6. Water absorption ratio

Water absorption ratio is important criteria for understanding the capacity of disintegrants. Tablet absorbs the water and loses its integrity. By using superdisintegrants water absorption ratio was found to be in the range of 47±0.32 - 59±0.78 (Table.10). By simple disintegrants water absortion ratio was found to be in the range of 36±0.35 - 45±0.21 (Table.11). This shows that all the formulations have good water absorption capacity and can easily disintegrate in the oral cavity within a short period, for better bio-availability.

By using the superdisintegrants the water absorption ratio was more compared to the formulation with simple disintegrants.

7. *In-vitro* dispersion time

The in vitro dispersion time is measured by time taken to uniform dispersion. By

superdisintegrants in vitro dispersion time was found to be in the range of 11±0.64 - 28±0.87 sec. The result showed that the in vitro dispersion time of F1, F2 and F3 formulations was almost better than F4, F5, F6, F7, F8 and F9 formulations (Table.10), and comparative profile (Figure.16).

By simple disintegrants in vitro dispersion time was found to be in the range of 24±0.40 - 53±0.52 sec. The result showed that the in vitro dispersion time of F10, F11, F12 are better than F13, F14, F15, F16, F17, F18 formulations (Table.11), and comparative profile in (Figure.17).

By using the superdisintegrants the dispersion time was shorter when compared to the formulation with simple disintegrants.

8. *In-vitro* Disintegration test

Disintegration test carried out in modified dissolution apparatus, Results shows the formulations with 1.5%, 3%, 6% of SSG having high disintegrating time as 34, 26, 22 sec. The disintegration time of F1, F2, F3 with 1.5%, 3%, 6% CP formulations is 19, 16, 12 sec respectively and is almost better than F4, F5, F6, F7, F8, F9 formulations (Table.10), and comparative profile (Figure.18).

Disintegration test for formulations with 2%, 4%, 6% sodim alginate showed high value for disintegrating time as 48, 52, 59 secs. The results showed that the disintegration time of F10, F11, F12 with 2%, 4%, 6% carbomer (carboplo 940) formulations to be as 25, 34, 45 secs respectively and is almost better than F13, F14, F15, F16, F17, F18 formulations (Table.11), and comparative profile (Figure.19).

By using superdisintegrants the disintegration time was shorter when compared to the formulation with simple disintegrants

9. *In-vitro* Dissolution studies

Dissolution is carried out in USP apparatus type-2 apparatus at 50rpm in 900ml dissolution media (phosphate buffer pH 6.8) for 10 minutes. At the end of 10 minutes almost total amount of the drug is released (i.e. 96.96±0.54%), from the formulation prepared by the direct compression method with 6% crospovidone and 94.83±0.52% of drug release with 2% carbomer (carbopol 940). The % drug release of all the formulation is given in (Table.12, 13) and comparative release profile is shown in (Figure.20 - 28).

By using superdisintegrants the drug release was higher when compared to the formulation with simple disintegrants

The drug release is more with crospovidone and carbopol 940 among all formulations of superdisintegrants and simple disintegrants respectively. When compared with other superdisintegrants carbopol at 2% concentration is showing the similar release profile, but at higher concentrations once again it decreasing release profiles of the drug due to its gelling property.

CONCLUSION

The above results suggest that the formulated oral disintegrating tablets of sumatriptan succinate exhibited good physical parameters and rapidly disintegrating without affecting the release profile and is very effective in case of elderly and pediatric patients. The overall results indicated that formulation with crospovidone (12%) had a higher edge compared to other formulations containing superdisintegrants and Carbopol (2%) had higher edge compared to other formulations made of simple disintegrants like cabomer (4%, 6%), Sod. CMC, Sod. Alginate. They satisfy all the criteria for oral disintegrating tablets. This direct compression process is simple, reproducible and robust to prepare orally disintegrating tablets of sumatriptan succinate and other anti-migraine drugs. Carbopol can be used as a superdisintegrant at lower concentration (2%), but at higher concentrations once again it decreasing release profiles of the drug due to its gelling property.

SUMMARY

The aim of the present study was to develop and optimize oral disintegrating tablets of model drug (sumatriptan succinate) to give quick onset of action by rapidly disintegrating in a few seconds without the need of water with better patient compliance. In such cases, bioavailability of drug

is significantly greater and adverse event is reduced than those observed from conventional tablet dosage form. By performing compatibility studies by IR spectrophotometry, no interaction was confirmed. Oral disintegrating tablets were formulated by direct compression method and evaluated by UV-Visibile spectrophotometer. Standard calibration curve prepared to determine the drug content in the prepared tablets. Prior to compression, the blend of drug and excipients were evaluated for flow properties such as Angle of repose, Bulk density, Tapped density, % Compressibility, and Hausner ratio. All the formulation showed good flow properties. Oral disintegrating tablets were prepared by direct compression technique using CADMACH 16 station tablet punching machine, equipped with round flat punches of 8.7 mm diameter. Post compression evaluation of prepared oral disintegrating tablets were carried out with the help of different pharmacopoeial and non-pharmacopoeial (industry specified) tests. The shape and color of all the formulations were found to be circular and white in color. The thickness was found to be uniform in specific formulations. The hardness and friability are also within the permitted limits. Dissolution of tablets was carried out. The crospovidone used formulation gave the more dissolution profile compared to other superdisintegrants and other simple disintegrants. But the carbopol 2% contain formulation gave almost nearer to similar dissolution as that of formulation containing superdisintegrants. But by increasing the carbopol concentration the release of the drug was decreased due to its gelling property. So carbopol at 2% acting as superdisintegrants, but at higher concentrations once again it decreases release profiles of the drug due to its gelling property.

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