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FORMULATION, TASTE MASKING AND EVALUATION OF ALMOTRIPTAN ORAL DISINTEGRATING TABLETS

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ABSTRACT

The aim of the present study is to formulate and evaluate taste masked Almotriptan orally disintegrating tablet by using different taste masking agents and different superdisintegrants in different ratios, Almotriptan is a triptan class anti-migraine drug with rapid action, highest bioavailability and low side effects compared to other triptan class of drugs used in the treatment of migraine, Thus formulating Almotriptan as an orally disintegrating tablet is extremely advantageous. However due to its bitter taste formulating Almotriptan into an orally disintegrating tablet is a challenge. Two taste masking agents namely Eudragit EPO and Precirol A To5 are used to taste mask the drug. The oral disintegrating tablets of Almotriptan were prepared using different superdisintegrants and the effect of different superdisintegrants at different concentration on *in-vitro* release was studied. Almotriptan release from ODT was directly proportional to the concentration of the superdisintegrant used. The optimized formulation was found to release the drug in minimum time and is found to be stable.

INTRODUCTION [1]**:** Orally disintegrating tablets are similar to melts and are designed to disperse in the mouth and to be washed down with saliva. United States Food and Drug administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue**"** [3]. Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient compliance. Oral route of drug administration have wide acceptance up to 50-60% of total people experience inconvenience in swallowing conventional dosage forms such as tablets when water is not available, difficulty in swallowing the tablet (Dysphagia) which is a common phenomenon in all the age groups most commonly in pediatric, geriatric patients [4, 5], in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic conditions and bronchitis. For these reasons, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted great deal of attention [6]**.** Orally disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. The disintegration time for ODTs generally ranges from several seconds to about a minute. As will sub-lingual, buccal and melts, orally disintegrating tablets require an adequate amount of saliva production [7, 8].

Almotriptan is an extremely potent member of triptan class drugs which is widely used in in the treatment of migraine. It shows high bioavailability, rapid action with fewer side effects when compared to other drugs

of the same class, but due to its bitter taste formulating it into an ODT is a challenge.

The present study is aimed to develop an oral disintegrating solid dosage form of Almotriptan which disintegrates rapidly without the need of water or chewing and release its drug instantaneously showing rapid action for sudden attacks of migraine with good patient compliance for all age groups.

MATERIALS AND METHODS:

Chemicals: Almotriptan was obtained as a gift sample from Optimus Pharma Pvt. Ltd. All the other chemicals were purchased from A to Z pharmaceuticals, Chennai.

Compatibility studies: The compatibility of Almotriptan with different excipients was tested using FT-IR Spectrophotometer.

Preparation of Taste masked granules using Eudragit EPO and Precirol A to 5: The taste masking of Almotriptan was done by melt granulation technique. Similar technique was followed for the taste masking the drug with both the taste masking agents which is as follows:

The taste masking agent i.e. Eudragit EPO or Precirol A to 5 was maintained at about 50-55^{o}C for 3 minutes. When the taste masking agent slightly started melting the drug was added and mixed. The drug: taste masking agent ratio was maintained at 1:0.5. The melt was then dried and passed through sieve # 40.

Preparation of Orodispersible Tablets by Direct Compression Method: Orodispersible tablets are prepared by direct compression. The various disintegrants like crosspovidone, crosscarmellose and sodium starch glycolate were used. All the ingredients are passed through sieve no. 40. Required quantity of each ingredient is taken for each specified formulation and all ingredients were mixed. Aerosil and magnesium stearate were then passed through mesh no.60 mixed and blended with initial mixture. The resulting mixture is compressed into tablet using 16 station rotatory press (**table 1 and 2**).

TABLE 1: FORMULATION DESIGN OF AN ORAL DISINTEGRATING TABLET USING EUDRAGIT EPO AS TASTE MASKING AGENT:

Ingredients	EF1 (mg)	EF2 (mg)	EF3 (mg)	EF4 (mg)	EF5 (mg)	EF6 (mg)	EF7 (mg)	EF8 (mg)	EF9 (mg)
Almotriptan	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Eudragit EPO	3.125	3.125	3.125	3.125	3.125	3.125	3.125	3.125	3.125
Mannitol	74.425	71.925	69.425	74.425	71.925	69.425	74.425	71.925	69.425
L HPC	10	10	10	10	10	10	10	10	10
Crosspovidone	2.5	5	7.5	-	-	-	-	-	-
Crosscarmellose sodium	-	-	-	2.5	5	7.5	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	2.5	5	7.5
Aerosil	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Aspartame	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Peppermint Flavour	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total Wt in mg	100	100	100	100	100	100	100	100	100

TABLE 2: FORMULATION DESIGN OF AN ORAL DISINTEGRATING TABLET USING PRECIROL A TO 5 AS TASTE MASKING AGENT:

Ingredients	PF1 (mg)	PF2 (mg)	PF3 (mg)	PF4 (mg)	PF5 (mg)	PF6 (mg)	PF7 (mg)	PF8 (mg)	PF9 (mg)
Almotriptan	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Precirol A TO 5	3.125	3.125	3.125	3.125	3.125	3.125	3.125	3.125	3.125
Mannitol	74.425	71.925	69.425	74.425	71.925	69.425	74.425	71.925	69.425
L HPC	10	10	10	10	10	10	10	10	10
Crosspovidone	2.5	5	7.5	-	-	-	-	-	-
Crosscarmellose sodium	-	-	-	2.5	5	7.5	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	2.5	5	7.5
Aerosil	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Aspartame	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Peppermint Flavour	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total Wt in mg	100	100	100	100	100	100	100	100	100

Evaluation of Almotriptan Oral Disintegrating Tablets: The Formulated ODT's were evaluated for weight variation, Hardness, Friability, Thickness, Content uniformity, Disintegration time, Water absorption ratio, and *in-vitro* drug release.

Weight variation: 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. The weight variation test was performed and the weights of the tablets were between 99 to 101 mg, as the weight of the tablet is 100mg, the weight variation limit is ±7.5%.

Hardness, Friability (F) and Thickness: Hardness or tablet crushing strength is the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester and the friability was tested using a Roche Friabilator. The thicknesses of the tablets were measured using Vernier callipers.

Content Uniformity: Ten tablets were randomly selected and tested for their drug content. Each tablet was powdered and to it 10 ml of 0.1 N HCl was added and the resulting solution was measured for its absorbance at 283nm using a UV-Visible spectrophotometer.

Disintegration Time: Tablet was placed in the disintegrating apparatus or a disintegrator having pH 6.8 phosphate buffer solution at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

Wetting time or Water Absorption Ratio: The water uptake characteristic of the loose disintegrant powder allows and evaluation of both the intrinsic swelling and the wettability of the superdisintegrants water uptake were performed at room temperature. Water absorption ratio, R, was determined.

Palatability Test: The palatability test was carried out with 10 volunteers for each taste masking agent and the unmasked drug was taken as the control which was compared with the taste masked drug. A scale of three variations i.e. 0, 1, 2 were given which was interpreted as average, good, better

***In-vitro* Release Studies:** The *in-vitro* drug release studies were carried out in an USP Type II (Paddle) dissolution apparatus to simulate the physiological conditions of the GIT. The medium used for dissolution is 0.1N HCl with a pH of 1.2. The volume of the medium in the dissolution apparatus was maintained at 900ml. The stirring rate was 50 rpm and the temperature was maintained at 37±0.5°C. Aliquots of dissolution medium were withdrawn at predetermined time intervals and the same volume of medium was replaced to maintain the constant volume.

RESULTS AND DISCUSSIONS:

Compatibility Study: From the FT-IR study the drug was found to be compatible with all the excipients.

Micromeritic Properties: Almotriptan powder blends were free flowing as indicated by the values of bulk density (0.45 to 0.56 gm/cc), Tapped density (0.55 to 0.69 gm/cc), Hausner's ratio (1.057 to 1.25), Compressibility index (11.2 to 20 %) and the Angle of repose ranged from 18.17° to 22.26°. The values are given in **table 3.**

Post Compression Evaluation parameters of formulated ODT's: Almotriptan tablets were uniform in weight (99.9 to 100.2 mg), the thickness (0.210 to 0.218 mm) of all tablets were uniform. The hardness of all the tablets was found to be between 3.00 to 3.04kg/cm^2, while the friability of the ODT'S ranged from 0.082 to 0.32% the tablets had enough hardness and friability to withstand stress and were mechanically stable during handling and transportation.

The content uniformity of all the formulations were ranged from 98.1% to 100.02% w/w The disintegration time of all the formulations ranged from 38 to 15 seconds, the wetting time values ranged from 40 to 18 seconds The values are given in **table 4**. The palatability results of optimised batch with both the taste masking agents were evaluated and the result was observed to be good, thus indicating good taste masking of the drug with both the taste masking agents. The results are tabulated in **table 5 and 6**.

TABLE 3: MICROMERITIC PROPERTIES OF THE POWDER BLEND

Drug and Formulation blend	Bulk Density gm/cc	Tapped Density gm/cc	Hausner's ratio	%Compressibility/Carr's index (%)	Angle of Repose (Θ)
Drug	0.52	0.58	1.115	10.3	20.21
EF1	0.5	0.625	1.25	20	18.17
EF2	0.52	0.55	1.057	15.45	19.24
EF3	0.45	0.55	1.22	18.18	20.42
EF4	0.5	0.62	1.24	19.35	22.34
EF5	0.46	0.55	1.195	16.36	19.17
EF6	0.56	0.69	1.23	18.84	20.24
EF7	0.53	0.59	1.113	12.01	19.17
EF8	0.52	0.62	1.192	16.12	18.24
EF9	0.5	0.62	1.25	19.35	22.26
PF1	0.45	0.56	1.24	19.64	21.24
PF2	0.52	0.59	1.134	11.86	20.17
PF3	0.52	0.59	1.134	11.86	18.24
PF4	0.50	0.62	1.124	19.35	19.24
PF5	0.46	0.55	1.195	16.36	18.17
PF6	0.55	0.62	1.127	11.290	20.34
PF7	0.45	0.56	1.124	19.642	18.36
PF8	0.50	0.60	1.20	16.66	20.36
PF9	0.52	0.62	1.192	16.1290	19.24

TABLE 4: POST-COMPRESSIONAL CHARACTERISTICS OF THE FORMULATED ODT

Formulation	Weight variation	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Content uniformity (%)	Disintegration time (Sec)	Wetting time (sec)
EF1	passes	3.02	0.210	0.12	99.5	32	35
EF2	passes	3.01	0.214	0.15	100.01	17	19
EF3	passes	3.03	0.212	0.24	98.3	15	18
EF4	passes	3.04	0.224	0.19	98.5	33	37
EF5	passes	3.00	0.226	0.09	98.9	20	22
EF6	passes	3.02	0.220	0.10	99.2	16	19
EF7	passes	3.01	0.218	0.31	98.6	38	40
EF8	passes	3.03	0.216	0.24	98.9	32	35
EF9	passes	3.01	0.218	0.082	99.2	26	29
PF1	passes	3.02	0.214	0.3	98.6	32	38
PF2	passes	3.00	0.210	0.12	98.1	24	27
PF3	passes	3.04	0.211	0.129	99.2	22	25
PF4	passes	3.01	0.214	0.31	98.6	34	37
PF5	passes	3.02	0.212	0.11	100.02	28	30
PF6	passes	3.03	0.213	0.32	98.2	26	29
PF7	passes	3.04	0.216	0.19	98.7	38	42
PF8	passes	3.02	0.212	0.26	99.3	31	35
PF9	passes	3.01	0.218	0.105	99.5	24	27

TABLE 5: PALATABILITY EVALUATION OF OPTIMISED BATCH OF ODT USING EUDRAGIT EPO AS TASTE MASKING AGENT

S. No.	Volunteers	Age	Sex	Taste Evaluation		
				Good	Better	Average
1.	Volunteer 1	21	M	✓		
2.	Volunteer 2	23	M	✓		
3.	Volunteer 3	25	M		✓	
4.	Volunteer 4	26	M	✓		
5.	Volunteer 5	21	M	✓		
6.	Volunteer 6	28	M			✓
7.	Volunteer 7	25	M		✓	
8.	Volunteer 8	24	M	✓		
9.	Volunteer 9	32	M	✓		
10.	Volunteer 10	30	M			✓

TABLE 6: PALATABILITY EVALUATION OF OPTIMISED BATCH OF ODT USING PRECIROL A TO 5 AS TASTE MASKING AGENT

S. No.	Volunteers	Age	Sex	Taste Evaluation		
				Good	Better	Average
1.	Volunteer 1	23	M	✓		
2.	Volunteer 2	23	M			✓
3.	Volunteer 3	22	M		✓	
4.	Volunteer 4	26	M	✓		
5.	Volunteer 5	31	M	✓		
6.	Volunteer 6	26	M	✓		
7.	Volunteer 7	25	M		✓	
8.	Volunteer 8	28	M	✓		
9.	Volunteer 9	35	M	✓		
10.	Volunteer 10	30	M			✓

***In-vitro* release study of the Tablets:**

***In-vitro* Dissolution Study of formulations using Eudragit EPO as Taste Masking Agent:** EF1 to EF9 formulations were prepared using Eudragit EPO as taste masking agent. EF1 to EF3 formulations were prepared using crosspovidone as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 57.02-87.71%, 64.43 - 100.3% and 71.10 – 101.2% respectively shown in **figure 1**. EF4 to EF6 formulations were prepared using crosscarmellose sodium as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 56.59 -92.75%, 61.76-99.34%,65.21-101.5% respectively shown in **figure 2.** EF7 to EF9 formulations were prepared using Sodium starch glycolate as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 49.20-91.29%,51.16-95.12%,60.02-98.76% respectively shown in **figure 3**. It was observed that all the formulations showed a gradient and proportional increase in the drug release. The results were tabulated in **table 7**.

TABLE 7: *IN-VITRO* DISSOLUTION STUDIES OF FORMULATED ODT'S USING EUDRAGIT EPO AS TASTE MASKING AGENT:

Time (min)	Cumulative Percentage Drug Release (%)								
	EF1	EF2	EF3	EF4	EF5	EF6	EF7	EF8	EF9
5	57.02	64.43	73.10	56.59	61.76	65.21	49.20	51.16	60.02
10	62.30	94.42	98.14	69.96	69.98	86.21	65.48	69.92	75.93
15	82.49	100.0	100.02	86.22	90.25	92.42	81.37	85.62	87.59
30	87.71	100.3	101.2	92.75	99.34	101.5	91.29	95.12	98.76

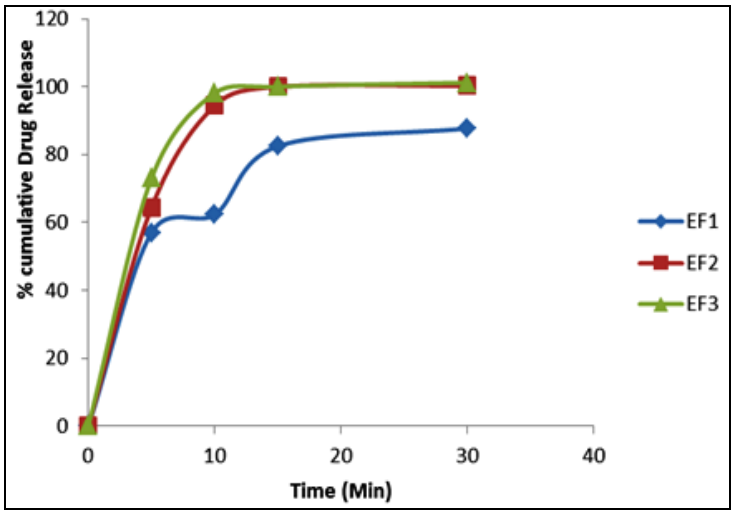

FIGURE 1: DRUG RELEASE PROFILE OF FORMULATIONS WITH CROSPOVIDONE USING EUDRAGIT EPO AS TASTE MASKING AGENT

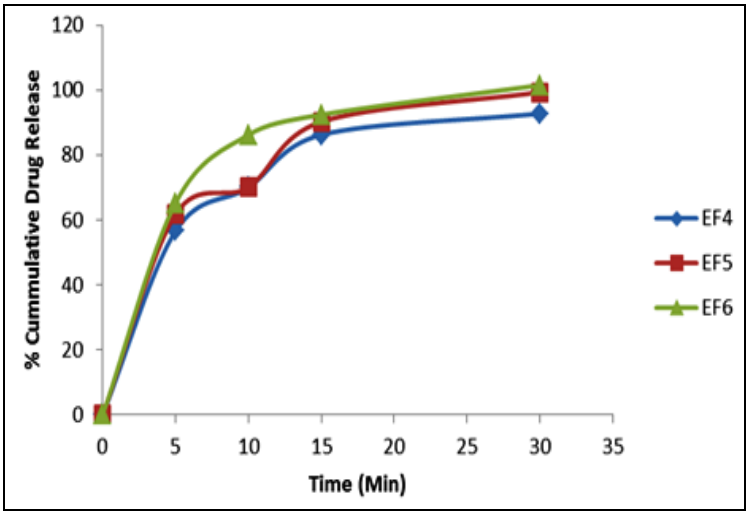

FIGURE 2: DRUG RELEASE PROFILE OF FORMULATIONS WITH CROSSCARMELLOSE SODIUM USING EUDRAGIT EPO AS TASTE MASKING AGENT

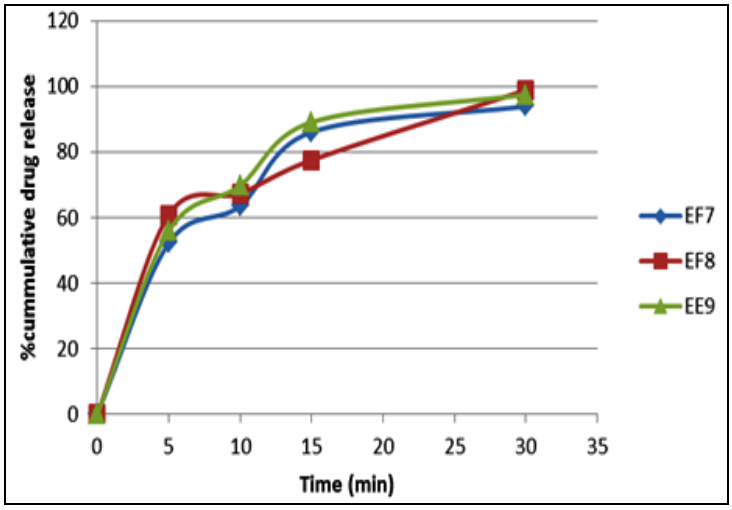

FIGURE 3: DRUG RELEASE PROFILE OF FORMULATIONS WITH SODIUM STARCH GLYCOLATE USING EUDRAGIT EPO AS TASTE MASKING AGENT

***In-vitro* dissolution study of formulations using Precirol A to 5 as Taste Masking Agent:** PF1 to PF9 formulations were prepared using Precirol A To5 as taste masking agent. PF1 to PF3 formulations were prepared using crosspovidone as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 52.15-92.75%, 60.78-100.0%, 63.24-101.5% respectively shown in **figure 4**. PF4 to PF6 formulations were prepared using Sodium starch glycolate as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 48.46-93.92%, 52.15-98.95%, 58.19-101.48% respectively shown in **figure 5**.

PF7 to PF9 formulations were prepared using crosscarmellose sodium as the superdisintegrant at a concentration of 2.5, 5 and 7.5% and the *in-vitro* dissolution values ranged from 52.16-93.92%, 60.78-98.87%, 55.85-97.48% respectively shown in **figure 6**. It was observed that all the formulations showed a gradient and proportional increase in the drug release. The results were tabulated in **table 8.**

TABLE 8: *IN-VITRO* DISSOLUTION STUDIES OF FORMULATED ODT'S USING PRECIROL A TO 5 AS TASTE MASKING AGENT

Time (min)	Cumulative Percentage Drug Release (%)								
	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9
5	52.15	60.78	63.24	48.46	52.15	58.19	52.16	60.78	55.85
10	76.89	79.85	81.96	64.63	72.16	77.11	63.53	67.28	69.72
15	86.36	97.28	99.6	88.51	93.28	97.50	86.06	77.50	89.08
30	92.75	100.0	101.5	93.92	98.95	101.48	93.92	98.87	97.48

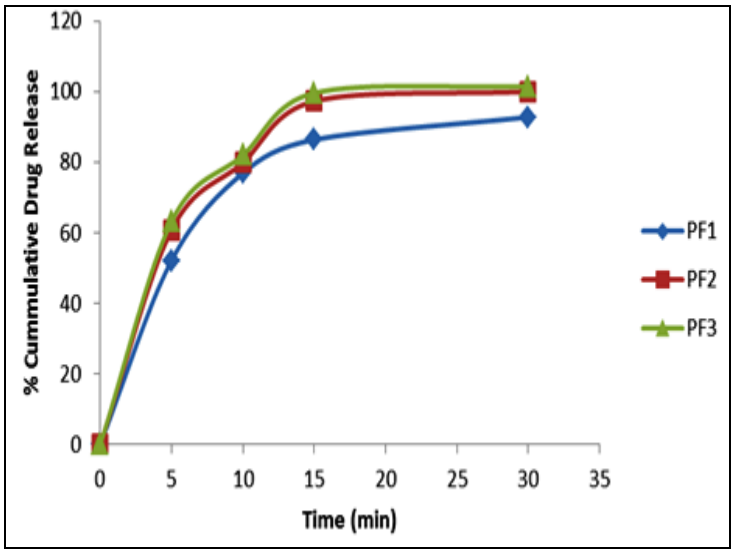

FIGURE 4: RELEASE PROFILE OF FORMULATIONS WITH CROSPOVIDONE USING PRECIROL A TO 5 AS TASTE MASKING AGENT

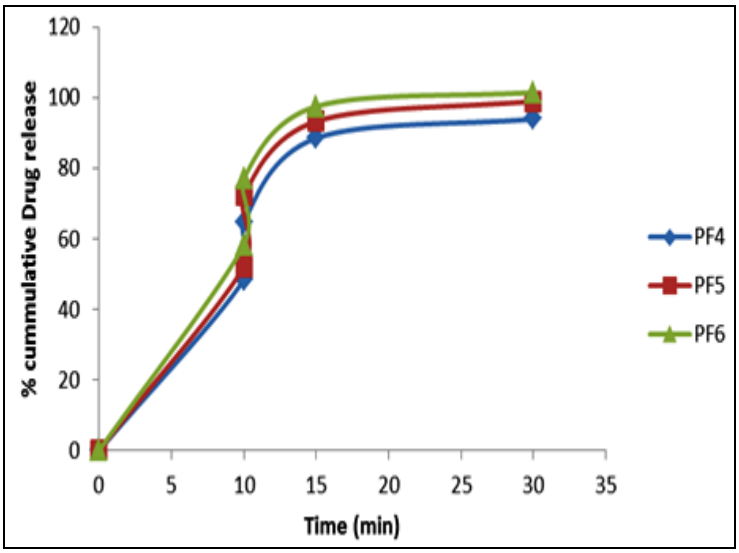

FIGURE 5: RELEASE PROFILE OF FORMULATIONS WITH CROSCARMELLOSE SODIUM USING PRECIROL A TO 5 AS TASTE MASKING AGENT

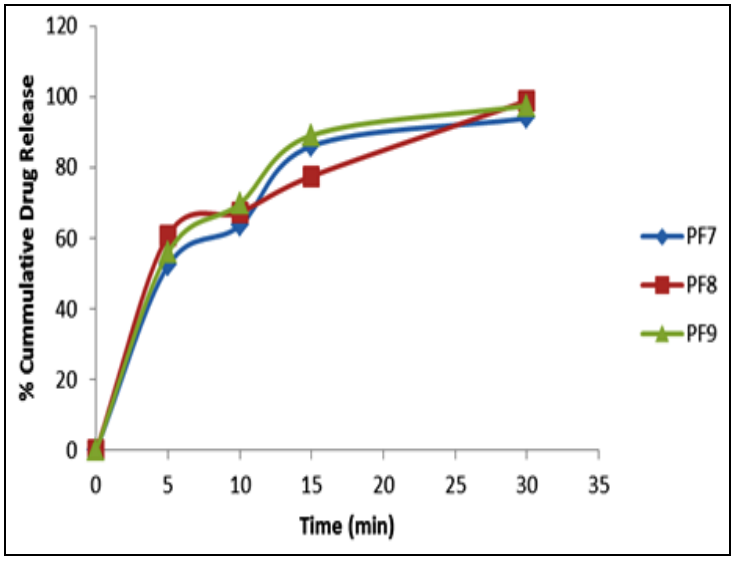

FIGURE 6: RELEASE PROFILE OF FORMULATIONS WITH SODIUM STARCH GLYCOLATE USING PRECIROL A TO 5 AS TASTE MASKING AGENT

CONCLUSION: EF1 to EF3 batches were formulated using crosspovidone as superdisintegrant at different concentrations of 2.5%, 5% and 7.5% respectively. EF2 batch with 5% crosspovidone showed better results. Though the results indicate that crosspovidone showed concentration dependent disintegration and dissolution in which higher concentration of crosspovidone is responsible for faster water uptake, it facilitates wiking action and brings about faster disintegration and dissolution, EF3 with a concentration of 7.5% crosspovidone showed faster disintegration and dissolution than EF2, The difference was almost negligible so EF2 formulation was found to be the best as it was economical and showed optimum disintegration and dissolution values and it's the same in the case of all formulations.

It must also be observed that the *in-vitro* drug release of the tablets prepared using Eudragit EPO as taste masking agent and Precirol A to 5 as taste masking agent differed. It was found that Eudragit EPO being hydrophilic facilitated the increase in the uptake of the saliva thus showing a complimentary action with that of the superdisintegrants. This was not observed in case of Precirol A to 5 which was hydrophobic in nature. Thus the release profiles using different superdisintegrants are different though the concentration of superdisintegrants remains the same.

REFERENCES:

1. Aulton M.E: Pharmaceutics-The sciences of dosage form design, third ed. International student edition, Churchill Living Stone 2007.
2. Benette P.N, Brown M.J: Clinical pharmacology, 2003.
3. Brahmankar D.M, Jaiswal S.B: Biopharmaceutics and Pharmacokinetics. New Delhi, 2003.
4. Seager H: Drug delivery products and the Zydis fast dissolving dosage form. International Journal of Pharmaceutical Technology 2005; 50:375-382.
5. Shirwalkar A.A, Ramesh A: Fast Disintegrating Tablets of Atenolol by Dry Granulation Method. Indian J. pharmaceutical Sciences 2004; 66: 422 – 426.
6. Fu T, Yang S, Jeong S.H., Kimura S, Park K:Orally fast disintegrating tablets: Developments, Technologies, Taste-masking and clinical studies. The Drug carrier ststems2002; 21:433-476.
7. Brown D: Orally Disintegrating Tablets-taste over speed & Taste masking techniques.
8. Chien Y.W and Lin S: Drug Delivery- Controlled Release In Encyclopaedia of Pharmaceutical technology, 2nd edition, Vol-I.
9. Sastry S.V, Nyshadham Jr., Fix J.A., 2002: Recent technological advances in oral drug delivery. Pharmacy Science Technology Today; 3:138-45.
10. Shargel L, Andrew BC: Applied Biopharmaceutics and Pharmacokinetics. IV edition. Prentice-Hall International: 139-143.
11. Chein Y.W: Novel Drug Delivery Systems. 2nd edition.
12. Chatap V.K, Gupta R.D, Jaiswal N.R, Patidkar V.S: Recent advances in mouth disintegrating tablet technology. Asian Journal of Pharmacy 2009; 1: 191-195.
13. Dandagi P.M, Mastiholimath V.S, Srinivas A.P, Gadad, Godbole S.P, and S.T. Bhagawati: Orodispersible Tablets: New-fangled Drug Delivery System. Indian. J. of Pharmacy Education and Research 2002; 39:177-181.
14. Reddy L.H, Ghosh B, Rajneesh: Fast Dissolving Drug Delivery Systems. Indian Journal Pharmaceutical Sciences 2004; 64: 33-36.

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