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FORMULATION AND INVITRO EVALUATION OF SUMATRIPTAN SUCCINATE FAST DISSOLVING TABLETS

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ABSTRACT

Fast Dissolving Tablets are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. FDTs or orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. The present dissertation work is an attempt to select the best possible diluents- disintegrant combination to formulate rapidly disintegrating tablets of Sumatriptan Succinate, which disintegrates in matter of seconds in the oral cavity, thereby reducing the first-pass metabolism and the time of onset of pharmacological action. The percentage drug content of all the tablets was found to be between 97.12±0.280% and 99.25±0.670% of Sumatriptan Succinate, which was within the acceptable limits.

KEYWORDS: Disintegrants, conventional tablets, first pass metabolism.

INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance.

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, ease of administration lead to high levels of patient compliance.

It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in NDDS aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Mouth Dissolving Tablet (MDT) is one among such approaches.

Ideal properties of a mouth dissolving tablet

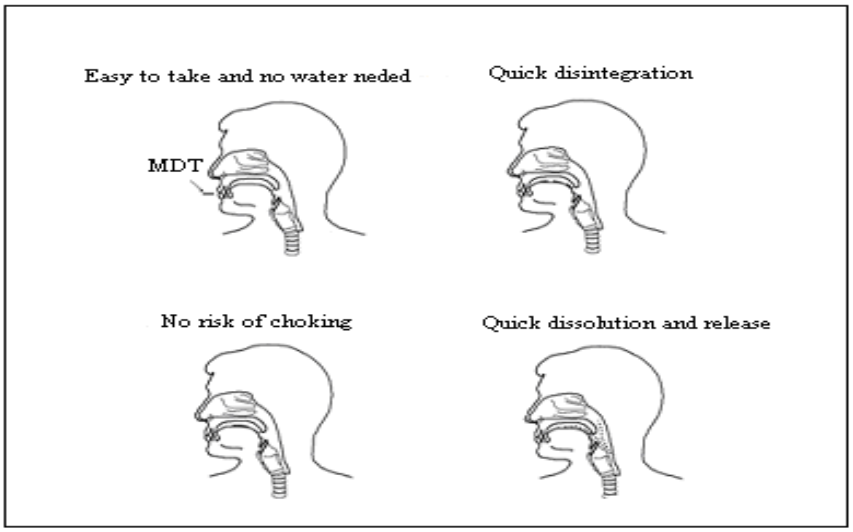
Though nothing or nobody is ideal or perfect in this world, yet there are certain limits or characteristics that judge the nearness to perfection. A mouth dissolving tablet should:

1. Not require water or other liquid to swallow.
2. Easily dissolve or disintegrate in saliva within a few seconds.
3. Have a pleasing taste.
4. Leave negligible or no residue in the mouth when administered.
5. Be portable and able to tolerate the transportation stress.
6. Be able to be manufactured in a simple conventional manner within low cost.
7. Be less sensitive to environmental conditions like temperature, humidity etc.

Advantages of Mouth dissolving tablet

1. No need of water to swallow the tablet.
2. Can be easily administered to pediatric, elderly and mentally disabled patients.

3. Accurate dosing as compared to liquids.
4. Dissolution and absorption of drug is fast, offering rapid onset of action.
5. Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva, passing down into the stomach.
6. Advantageous over liquid medication in terms of administration as well as transportation.
7. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
8. Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
9. Suitable for sustained/controlled release actives.



Figures showing Advantages of Mouth dissolving tablet

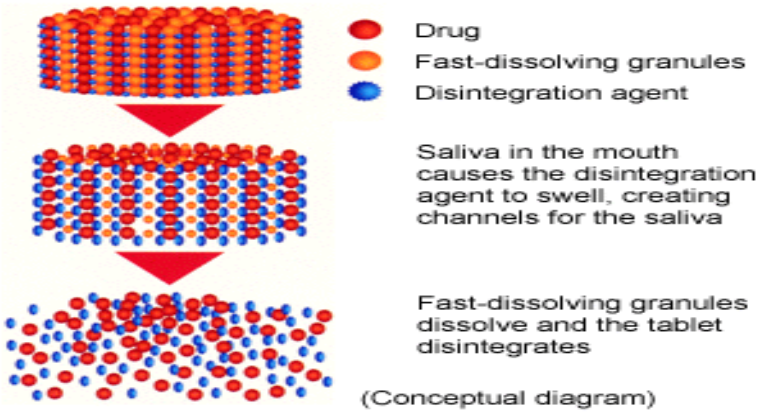
Important ingredients that are used in the formulation of Fast dissolving tablet should allow quick release of the drug, resulting in faster dissolution. This includes both the actives and the excipients.

Super disintegrants

Use of disintegrants is the basic approach in development of mouth dissolving tablets. Disintegrants play a major role in the disintegration and dissolution of MDT. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates.

Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of

the carrier increases, which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.



Various Approaches for Fast Dissolving Tablets

The fast-dissolving property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration. Hence, the basic approaches to developing fast dissolving tablets include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent, and using highly water-soluble excipients in the formulation.

Various technologies used in the manufacture of Fast dissolving tablets include:

- Freeze –drying or lyophilization
- Spray drying
- Direct compresion
- Moulding
- Mass extrusion
- Direct compression

Direct compression

This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the compression of blend into tablet. Removal of volatile material by direct compresion creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.

Disintegration and solubilzation of a directly compressed tablet depend on single or combined effects of disintegrants, water-soluble excipients and effervescent agents. Tablet size and hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates. Above the critical concentration level, however, disintegration time remains approximately constant or even increases.

Some commercially available mouth dissolving tablets

Trade name	Active drug	Manufacturer
Nimulid-MD	Nimesulide	Panacea Biotech, New Delhi, India
Feldene Fast Melt	Piroxicam	Pfizer Inc., NY, U.S.A
Zyrof Meltab	Rofecoxib	Zydus, Cadila, India
Pepcid RPD	Famotidine	Merck and Co., NJ, U.S.A
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex Instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, Ahmedabad, India
Febrectol	Paracetamol	Prographarm, Chateauneuf, France

METHODOLOGY

Determination OF UV Absorption maxima

Sumatriptan Succinate solution was prepared in 0.1 N HCL and diluted suitably. The UV spectrum of the solution was taken on Shimadzu 1700 UV/Vis double beam Spectrophotometer (Japan). The Solution exhibited UV maxima at 230.0 nm.

Preparation of Standard Calibration Curve of Sumatriptan Succinate

100 mg of Sumatriptan Succinate was accurately weighed and dissolved in the final volume up to 100 ml with 0.1 N HCl to prepare stock solution. The 1 ml of stock solution was further diluted with 0.1 N HCl in 100ml to get 10 µg/ml (working standard). Then 2,4,6,8,and10ml of working standard was taken in 10 ml standard volumetric flask and made up the volume with 0.1N HCl to prepare 2µg,4µg,6µg,8µg,10µg, drug per ml solution. Then the absorbance was measured in a UV spectrophotometer at 230 nm against 0.1 N HCl as blank. .The method was validated for linearity, accuracy and precision.

TABLET FORMULATION

Formulation of Sumatriptan Succinate Dispersible Tablet by Direct- Compression

Composition of preliminary trials for Sumatriptan Succinate Dispersible Tablet by direct compression is shown in Table 2.1. All the ingredients were weighed.

Required quantity of drug and Excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-12 station with 8mm flat punch, B tooling. Each tablet contains 25 mg Sumatriptan Succinate and other pharmaceutical ingredients.

Table 2.1 Formulation using Direct compression technique.

Ingredient	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Sumatriptan Succinate	25	25	25	25	25	25	25	25	25
Croscarmellose sodium	25	_	_	12.5	12.5	_	08	17	_
Sodium starch glycolate	_	25	_	12.5	_	12.5	17	08	08
Crospovidone	_	_	25	_	12.5	12.5	_	_	17
Talc	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mannitol	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Magnesium Stearate	7	7	7	7	7	7	7	7	7
Dicalcium phosphate	173	173	173	173	173	173	173	173	173
TOTAL	250	250	250	250	250	250	250	250	250

All ingredients are expressed in mg only

EVALUATION

Precompression parameters

1. Bulk Density (D_b)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

2. Tapped Density (D_t)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is

continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where,

M is the mass of powder

V_t is the tapped volume of the powder.

3. Angle of Repose (Θ)

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane

$$\tan(\Theta) = h / r$$

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

Where,

Θ is the angle of repose.

h is the height in cm

r is the radius in cm

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particles slip and roll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property.

Angle of Repose as an Indication of Powder Flow Properties

Sr. No.	Angle of Repose(^{0})	Type of Flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very Poor

4. Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is give by,

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where,

Dt is the tapped density of the powder and

Db is the bulk density of the powder.

Relationship between % compressibility and flow ability.

Sr no.	% Compressibility	Flow ability
1	5-12	Excellent
2	12-16	Good
3	18-21	Fair Passable
4	23-35	Poor
5	33-38	Very Poor
6	<40	Very Very Poor

5. Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following Formula.

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, D_t is the tapped density, D_b is the bulk density.

Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Post compression parameters

1. Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P.

Weight Variation Specification as per IP

Average Weight of Tablets	%Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

2. Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

3. Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper.

4. Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at the height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

5. Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$dl/dt = r¡cos\Theta/(4hl)$$

Where,-

l is the length of penetration,

r is the capillary radius,

¡ is the surface tension,

h is the liquid viscosity,

t is the time, and

Θ is the contact angle.

It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place. A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified

by maintaining water at 37^{o}C.Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

6. In-Vitro drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile.

DISSOLUTION TEST

USP II Paddle apparatus was used and paddle was allowed to rotate at 50 rpm, acid buffer 0.1N HCL (900 ml) was used as a dissolution medium.

7. Assay

10 tablets were weighed and triturated. The tablet triturate equivalent to 10 mg of the drug was weighed accurately, diluted to 100 ml with the same. Further dilutions were done suitably to get a concentration of 10 µg/ ml. Absorbance was read at 230 nm against the reagent blank, and the concentrations of Sumatriptan Succinate in µg/ ml was determined by using the regression equation.

$$Y = 0.122x - 0.007$$

Drug content in mg / tablet = conc. µg/ml * dilution factor

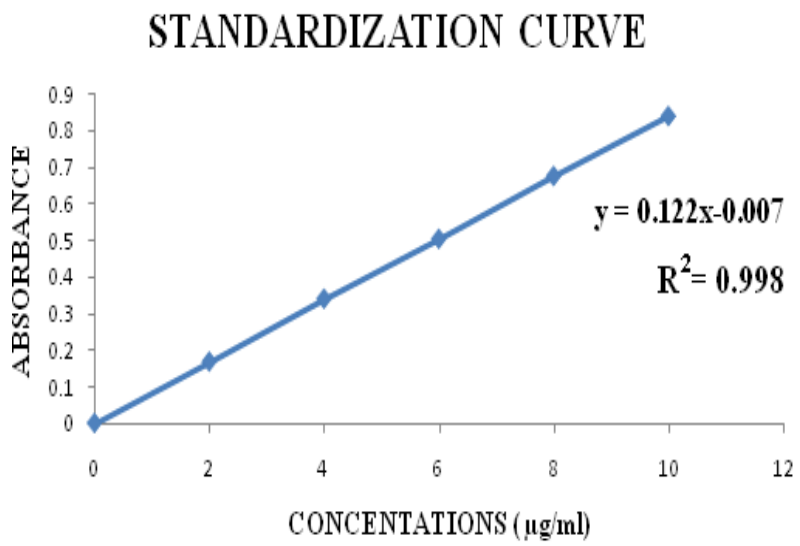
% Drug content = drug content in mg * 100 / label claim.

RESULTS

Standard Calibration curve of Sumatriptan Succinate

Concentration and absorbance obtained for calibration curve of Sumatriptan Succinate in 0.1 N hydrochloric acid

S. No.	Concentration (µg/ml)	Absorbance* (at 230 nm)
0	0	0
1	2	0.168
2	4	0.34
3	6	0.504
4	8	0.676
5	10	0.84
Correlation Coefficient = 0.998 Absorbance = y = 0.122x - 0.007		



Standard Calibration Curve of Sumatriptan Succinate.

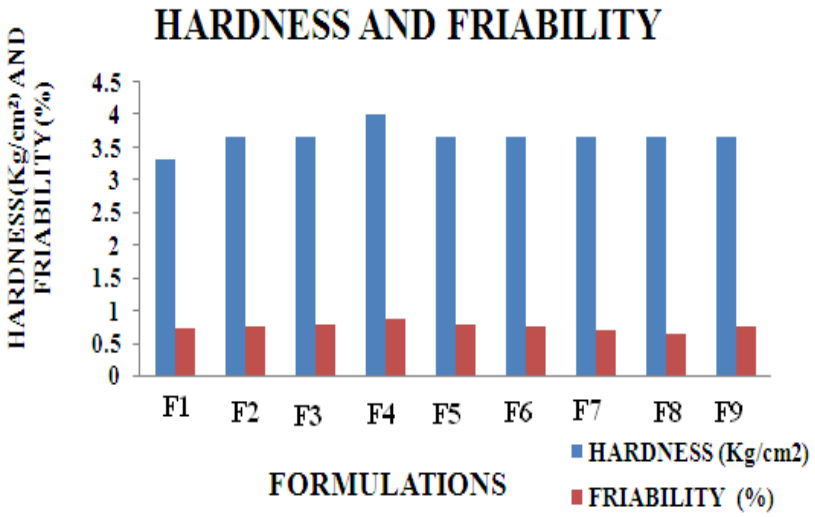
Result of Evaluation of Sumatriptan Succinate Dispersible Tablet Using.

Pre-compression parameters :					
Formulations	**Bulk Density (gm/cm^2)**	**Tap Density (gm/cm^2)**	**Carr's Index (%)**	**Hausner ratio**	**Angle Of Repose(Θ)**
F_1	0.45	0.55	13.54	1.16	27.91
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	13.79	1.16	29.34
F_4	0.46	0.55	16.36	1.19	26.71
F_5	0.50	0.58	13.79	1.16	29.34
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.41	0.50	18	1.21	26.78
F_9	0.41	0.50	18	1.21	26.78

Physical parameter of Sumatriptan Succinate dispersible tablet.

Post-Compression parameters:							
FD	**Weight variation (mg)**	**Hardness (kg/cm^2)**	**Thickness (mm)**	**Disintegration Time (sec)**	**Friability (%)**	**Wetting time (sec)**	**Assay (%)**
F_1	251	3.33	3.59	12	0.73	14	97.25
F_2	247	3.66	3.64	17	0.74	18	99.12
F_3	248.5	3.33	3.59	19	0.73	14	98.52
F_4	249	4.00	3.58	19	0.87	14	99.10
F_5	248.5	3.66	3.59	30	0.79	24	98.45
F_6	247	3.66	3.64	22	0.74	18	98.75
F_7	248.5	3.66	3.59	30	0.69	24	98.57
F_8	252.5	3.66	3.56	17	0.64	15	98.50
F_9	252.5	3.66	3.56	17	0.74	15	98.65

Physical parameter of Sumatriptan Succinate dispersible tablet



Effect of differnet super-disintegrants on Hardness and Friability

Table 2.4: Dissolution profile and percentage of drug release of all formulations.

Time (mints)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
2mints	64.15	65.36	50.21	43.56	48.98	61.36	39.23	48.68	68.24
4mints	72.32	70.16	55.36	48.93	50.56	69.47	42.85	60.59	73.62
6mints	79.42	75.37	59.25	54.86	56.36	74.95	49.31	65.58	78.32
8mints	89.36	79.08	64.23	59.11	61.72	77.31	52.04	70.32	84.64
10mints	**100.9**	85.27	66.62	63.77	68.78	84.65	56.68	75.54	90.64
15mints	95.01	94.42	70.7	68.88	75.85	88.19	62.34	81.14	94.32
20mints	87.37	**101.48**	72.59	71.06	79.37	**100.32**	67.27	85.85	**100.54**
30mints	85.14	96.16	**74.95**	**74.06**	**81.73**	70.12	**70.52**	**92.06**	79.04

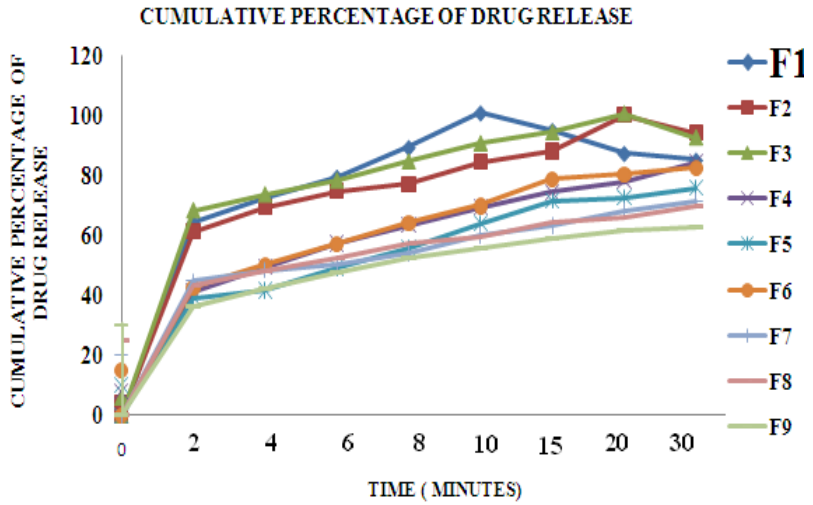
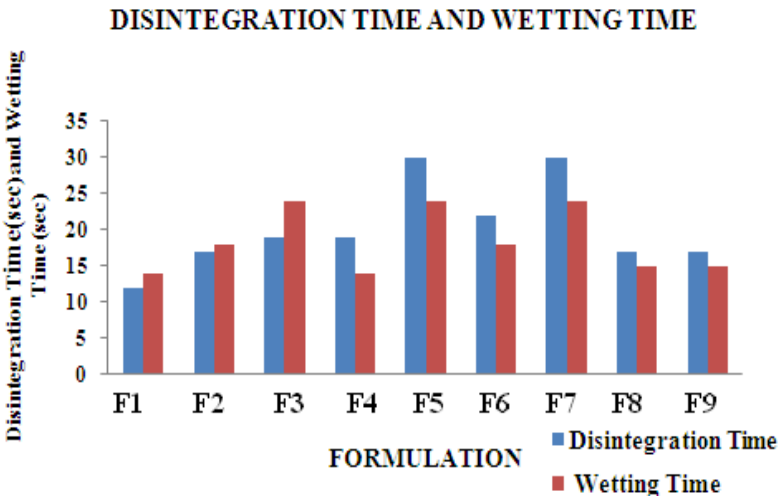


Figure 2.10: Effect of Each super-disintegrants on dissolution profile.



Effect of differnet super-disintegrants on Disintegration Time and Wetting Time in all formulations

CONCLUSION

The present dissertation work is an attempt to select the best possible diluents- disintegrant combination to formulate rapidly disintegrating tablets of Sumatriptan Succinate, which disintegrates in matter of seconds in the oral cavity, thereby reducing the first-pass metabolism and the time of onset of pharmacological action.

Crospovidone, Croscarmellose sodium and Sodium starch glycolate were used as super-disintegrants. In all the formulations aqueous granulating agent was used as a binding agent to attain adequate hardness. Dicalcium phosphate was used as diluents. Aspartame was used as a sweetening agent. Magnesium stearate and Talc were used as lubricant and gliding respectively.

The results of the drug–excipients compatibility FT-IR studies revealed that there was no chemical interaction between the pure drug and excipients.

The pre-compression parameters like bulk density, tapped density, Carr's index and angle of repose were determined. All the 9 formulations showed acceptable flow properties.

The post compression parameters of the tablet like the hardness, thickness, friability and weight variation, disintegration time, wetting time, and *Invitro* release were carried out and the values were found to be within IP limits.

The percentage drug content of all the tablets was found to be between 97.12±0.280% and 99.25±0.670% of Sumatriptan Succinate, which was within the acceptable limits.

From the data obtained, it is observed that Amongst the various combinations of diluents and disintegrants used in the study, tablets that were formulated (Direct compression) using Crosscaremellose sodium 10% exhibited quicker disintegration of tablets than compared to those other combination of disintegrants in different concentration. The effectiveness of super-disintegrants was in order of CCS>SSG>CP.

REFERENCES

1. Chein YW. Oral Drug Delivery and Delivery Systems. 2nd ed. New York: Marcel Dekker; 1992.
2. Kaur T, Bhawandeep G, Sandeep K, Gupta GD. Mouth dissolving tablets: a novel approach to drug delivery. Int J Curr Pharm Res., 2011; 3(1): 1-7.
3. Augsburger LL, Stephen WH. Orally disintegrating tablets. Pharmaceutical dosage forms: tablets. Infroma Healthcare Publication, 3rd ed., 2: 293-312.
4. Schwartz BJ, Connor RE. Optimization technique in pharmaceutical formulations and processing. Modern Pharmaceutics. 3rd ed. Marcel Dekker Inc. New York, 1996; 607-24.
5. Bolton S. Pharmaceutical statistics- Practical and clinical applications. 3rd ed. Marcel Dekker Inc. New York, 1997.
6. Two level full factorial tutorials. Design expert Software, Version 8.0.4.1, users guide. Inc., New York.
7. Meyer SB, Jacques LF, Donald E. Canadian guidelines for the management of acute exacerbation of chronic bronchitis. Can Repir J., 2008 Aug; 10(5): 248-58.
8. Simone S, Peter CS. Fast dispersible ibuprofen tablets. Eur J Pharmaceut Sci., 2002 Feb 1; 15: 295–305.
9. Nishant V, Vikas R. Preparation and optimization of mouth/orally dissolving tablets using a combination of glycine, carboxymethyl cellulose and sodium alginate, a comparison with superdisintegrants. Pharmaceut Dev Tech., 2008; 13: 233–43.
10. Bruno CH, Joshua TC, Matthew PM, Andrey VZ. The relative densities of harmaceutical powders, blends, dry granulations and immediate-release tablets. Pharmaceut Tech., 2003 Apr; 64-80.

11. Mohanachandran PS, Krishnamohan PR, Fels S, Bini KB, Beenu B, Shalina KK. Formulation and evaluation of mouth dispersible tablets of amlodipine besylate. Int J App Pharm., 2010 Apr; 2(3): 1-6.
12. Deshika R, Viness P, Yahya EC, Lisa CT. Rapidly disintegrating oramucosal drug delivery technologies. Pharm Dev Tech., 2009; 14(6): 588-601.
13. Nitin S, Sanjula B, Alka A, Javed A. Fast-dissolving intra-oral drug delivery systems. Expert Opin Ther Patents., 2008; 18(7): 769-81.
14. Bipin P, Patel JK, Ganesh R, Rashmin T. Formulation and evaluation of mouth dissolving tablets of cinnarizine. J Pharm Res., 2009 Mar; 3(2): 510-13.
15. Mutasem MR, Estelle RS, Keith JS. Fast-disintegrating sublingual epinephrine tablets: effect of tablet dimensions on tablet characteristics. Drug Dev Ind Pharm., 2007; 33: 523-30.
16. Tansel C, Aysegul D, Selcuk C, Nursabah B. Formulation and evaluation of diclofenac potassium disintegrating tablets and their clinical application migraine patients. Drug Dev Ind Pharm., 2010: 1-9.
17. Francesco C, Irma EC, Paola M, Francesca S, Luisa M. Fast dissolving films made of maltodextrins. Eur J Pharm Biopharm, 2008; 70: 895-900.
18. Sameer GL, Yi-ying Y, Ajay KB. Effects of disintegration-promoting agent, lubricants and moisture treatment on optimized fast disintegrating tablets. Int J Pharm, 2009; 365: 4-11.
19. Jinichi F, Etsue Y, Yasuo Y, Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. Int J Pharm, 2006; 310: 101-09.
20. Rahul C, Zahra H, Farhan A, Alan MS, Afzal RM. The role of formulation excipients in the development of lyophilized fast-disintegrating tablets. Eur J Pharm Biopharm, 2009; 72: 119-29.
21. Shery J, Arun S, Anroop N. Preparation and evaluation of fast-disintegrating effervescent tablets of glibenclamide. Drug Dev Ind Pharm, 2009; 35: 321-28.