Section A-Research paper
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USE OF SODIUM STARCH GLYCOLATE, CROSPOVIDONE AND DIOCTYL SODIUM SULPHOSUCCINATE (DOSS) FOR FORMULATION & EVALUATION OF ORODISPERSIBLE TABLET OF RIZATRIPTAN BENZOATE.

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ABSTRACT:
Rizatriptan benzoate is the potent drug molecule for the treatment of the migraine. Wet Granulation Technique was used for development of Orodispersible tablets of Rizatriptan Benzoate to enhance the flow properties of the granules during compression. For granulation, IPA was selected and two different types of the superdisintegrants were used for the formulation such as SSG and Crospovidone. Apart from these, Dioctyl Sodium Sulphosuccinate was also used in the formulation. Diluents used were MCC pH 101 and MCC pH 102. Aspartame was used as sweetening agent, Colloidal Silicon dioxide was used as Glidiant and Sodium Stearyl Fumarate was used as Lubricating agent. Total Nine formulations from F1 to F9 were designed and concentration of two Superdisintegrants was varied keeping the concentration of other excipients constant. Three different concentration of SSG i.e. 26 mg per tab, 10 mg per tab and 18 mg per tab were used. Also three different concentration of Crospovidone i.e. 9 mg per tab, 15 mg per tab and 12 mg per tab were used. DOSS was used as 0.1 mg per tab in formulations from F5 to F9 and DOSS was not used in remaining formulations. Prepared Orodispersible tablets were analyzed for different In-Vitro parameters such as Physical Description, Average weight, Tablet's Hardness, Tablet's thickness, Moisture content, Friability, Time of Disintegration, Assay%, Dissolution% and Uniformity of content. Formulation number F5 was

determined as best formulation with disintegration time of 12 seconds and Dissolution value of 99.53% whereas formulation number F3 was comparatively less beneficial with disintegration time of 56 seconds and Dissolution of 86.17%.Concentration of the Superdisintegrants mainly showed its effect in dissolution and Disintegration value where as others parameters were not subjected for significant changes. For the formulation of Orodispersible tablet of Rizatriptan benzoate, DOSS can be used in lower concentration for decreasing the disintegration time and for having higher dissolution %. Similarly SSG should be used at intermediate concentration and Crospovidone at higher concentration. Synergistic combination of them plays crucial role for having the optimum value of disintegration and dissolution value

Keywords*: Orodispersible, Migraine, Superdisintegrants, Wet granulation, Formulation*

INTRODUCTION

Due to the various reasons like accuracy in dosing, comparatively lower cost, ease of administration, avoidance of pain, ease of self-medication and more patient compliance solid dosage form are gaining more popularity. Tablets, capsules are the most common solid dosage form. First pass metabolism, GI irritation and GI interaction of drugs with the content in the gastric region etc are the frequently encountered problem associated with the many dosage form. In order to avoid such problems, development of Orodispersible tablets of different drug is gaining more popularity. These Orodispersible formulations are subjected for designing so as to disintegrate within the Buccal/Oral cavity at rapid rate so that the drug is not adversely affected as a result of GI disturbance and does not suffer from the hepatic first pass metabolism. Drug incorporated as Orodispersible tablets disintegrate faster and thus enhancing the bioavailability of the formulation. (Satyanarayana, et al. 2011) Many people are suffering from problem of swallowing. Especially the people suffering from Dysphagia are having trouble in swallowing of the oral tablets or capsules. Pediatric and geriatric patients are also facing the same issues in taking the tablets. Thus development of the Orodispersible tablets is overcoming such issue as a part of modern drug delivery. (Roy 2016)

Orodispersible tablets can be prepared using the different techniques. Especially the Techniques like Direct Compression, Sublimation, Freeze drying or Lyophilization, Tablet moulding, Spray drying and wet granulation are used for the preparation of tablet (Ghosh, Ghosh and Prasad 2011). Direct compression technique is the commonly used technique. For using this technique, the powder must have the good flow properties. Milling the Active Pharmaceutical Ingredient and Excipients, Mixing and finally compression of the mixed powder is the general sequence for direct compression. Use of subliming agent is required for the formulation of orodispersible tablets using the sublimation method. Subliming agents such as camphor can be used and upon vaporization of the subliming agents, pores are created in the tablets thus enhancing the faster disintegration. For the heat sensitive drugs another technique such as freeze drying or Lyophilization is used .in the lyophilization technique drug is dissolved in the aqueous solvent

which is Lyophilized and the water content is removed after it is frozen. This technique is a bit costly and expensive. Moulding technique is also used for the formation of Orodispersible tablet. Both solvent method and heat method are used for this. In the solvent method, drug is suitably made wet using the hydroalcoholic solvent and is allowed for the evaporation by using the air where as in the heat methods suspension is formed by using drug, agar and sugar. Thus formed jellies are then poured in the mould and dried using the vacuum at 30^{o}c. Spray drying technique helps to produce the porous fine powders by removing the solvents. Hydrolized and Non Hydrolized gelatins are used as supporting agents and Different superdisintegrants are also used for this technique. (Gupta, Maurya and Varshney 2020) (Dey and Maiti 2010)

Wet granulation technique is used for those drugs which have comparatively poor flow rate of the powder and both aqueous and non-aqueous solvents may be used for the wet granulation. In this technique, Mixture of the drug and excipients is suitably granulated which are dried using suitable drying method and upon drying Lubrication shall be performed so as to increase the flow rate of the powder. These powders are then compressed using the tableting machine. Various excipients such as Superdisintegrating agent, Lubricating agent may be used for the formulation. (Singh, et al. 2022) (Agrawal and Naven 2011) (Bhanu 2016)

Migraine is a common chronic neurovascular disorder which is characterized by the severe autonomic system dysfunction, headache and some neurological symptoms. Recurrent and throbbing headache is common in the migraine patient. Pain differs from person to person. Migraine Headache can be with or without aura. (Goadsby, Lipton and Ferrari 2002) Nausea, Visual disturbance, sensitivity to the light are the problems associated with autonomic nervous system and often encountered in the migraine disease. Migraines attach lasts for4-72 hours if it is untreated. Rapid action of the drug is required for the patients suffering from the migraine. (Singh, et al. 2017)

Drug Rizatriptan Benzoate is s selective agonist on 5- Hydroxy tryptamine $_{1B/1D}$ Receptor which acts on the trigeminal system's sensory nerves and intracranial blood vessels. It causes the constriction of blood vessels of intracranial extracerebral blood vessels. It inhibits the nociceptive neurotransmission in the trigeminal pathways. Rizatriptan is available in crystalline or powder form which is almost white or white in colour. It is water soluble, sparingly soluble in 96% ethanol and slightly soluble with methylene chloride. Its molecular weight is 391.475. Rizatriptan reaches the peak plasma concentration rapidly and has a faster onset of action that has shorter elimination half-life as compared to other triptans. Rizatriptan benzoate has about 45% of the bioavailability. This low bioavailability is because of hepatic metabolism and incomplete drug absorption. Tmax of the drug is found to be 1 to 2.5 hours depending upon the formulation of the drug. Rizatriptan is usually given in the daily dose of 5-10 mg**.** (Goadsby, Lipton and Ferrari 2002) (Singh, et al. 2017) (Mothilal, et al. 2012) Formulation of Orodispersible tablet requires combination of various materials that includes both Active

Pharmaceutical Ingredient and Excipients. In addition to the API, various materials like superdisintegrants such as Crospovidone, Sodium Starch Glycollate, Diluents such as Microcrystalline cellulose, Lactose Monohydrate, Sweetening agents such as Aspartame, Mannitol Glidiants such as Colloidal Sillicon Dioxide, Lubricating agents such as Colloidal Silicon Dioxide Granulating Fluids such as water , Isopropyl Alcohol etc are used during the formulation of Orodispersible tablets. Wetting agents, Flavouring agents and Colouring agents may be added optionally. (Kushare 2015)

Orodispersible Tablets offers the various advantages such as; Ease of administration to pediatric, geriatric and mentally ill patients, faster disintegration rate and enhanced dissolution thus enhances bioavailability of intended drug. (Joshi, Garud and Akram 2020) It leaves no residue in the mouth after administration, it removes the fear of chocking associated with administration of tablets/capsules through the GI route, It bypasses the hepatic metabolism and GI interaction that may occur with the GI content, It removes the possibility of the suffocation that may occur while swallowing the drugs. (Rameesa and Drisya 2015) In contrast it has several disadvantages also such as requirement of the taste masking agents in case of some bitter taste and noxious drugs, special packaging is required for preventing the product from various environmental factors such as moisture, heat etc., Light sensitive drugs cannot be formulated in these dosage form as there is no option for film coating in the tablets. (Ozyilmaz, et al. 2018) (Rewar, et al. 2014) Rizatriptan Benzoate is not suitable for the patients who are suffering from ischemic heart disease. (Tripathi 2013)

MATERIALS AND METHODS:

Materials:

Rizatriptan Benzoate, an API was purchased from Glenmark Life Science. Sodium Starch Glycol late was purchased from Roswell Industry. Similarly another disintegrant Crospovidone was purchased from Znongwei New Materials Technology (Tiaozuo) Co.Ltd. Others excipients such as Dioctyl Sodium Sulphosuccinate, Isopropyl alcohol, Sodium Stearyl Fumarate, Colloidal Sillicon Dioxide , Aspartame and Microcrystalline Cellulose pH 101 and 102 were purchased from Laxachem Organics P. Ltd, Deepak Fertilizers and Petrochemicals P. Ltd., Nitika Pharmaceutical Specialities P. Ltd., Evonik Industries, Nantong Changhai Food Additive Co. Ltd & Ankit Pulps and Boards P. Ltd respectively. All the chemicals were purchased with the good quality.

Methods:

***Drug Solubility Study*:** Solubility of the material Rizatriptan Benzoate was studied in different solvent such as Water, Ethanol (96%) and Methylene Chloride.

Compatibility between Drug and Excipients: It was performed with the FTIR Spectrophotometer. Spectra of pure drug and drug with other excipients were compared to find out the level of compatibleness between Excipients and the intended drug. (Singh, et al. 2022)

Determination Calibration Curve: Samples of different concentration ranging from 4 to 12 mcg/ml were prepared and prepared samples were analyzed using UV Visible Spectrophotometer. Absorbance was determined for each concentration and Calibration graph was plotted with Absorbance against the concentration.

Formulation of Orodispersible Tablet of Rizatriptan Benzoate: Mixture of Microcrystalline Cellulose pH 101, Sodium Starch Glycolate and Crospovidone was subjected for granulation with the granulating fluid, prepared by dissolving DOSS and Rizatriptan Benzoate in IPA. Wet mass was formed which was sieved through mesh size #20 and dried using the FBD. Dried granules were then lubricated and compressed to obtain the tablets of 300 mg.

Formulation of Orodispersible tablet of Rizatriptan Benzoate

Table1: Design of different formulations

		Mg/Tablet								
S.N	Component	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Rizatriptan Benzoate	14.54	14.54	14.54	14.54	14.54	14.54	14.54	14.54	14.54
2	Sodium Starch Glycolate	10	26	26	26	18	18	18	10	10
3	MCC pH 101	206.46	187.46	190.46	184.46	192.36	198.36	195.36	203.36	200.36
4	DOSS	-	-	-	-	0.1	0.1	0.1	0.1	0.1
5	Crospovidone	9	12	9	15	15	9	12	12	15
6	Colloidal Silicon Dioxide	2	2	2	2	2	2	2	2	2
7	MCC pH 102	47	47	47	47	47	47	47	47	47
8	Aspartame	8	8	8	8	8	8	8	8	8
9	Sodium Stearyl Fumarate	3	3	3	3	3	3	3	3	1.5
10	Iso-Propyl Alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total (mg)		300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0

Methods for Evaluation

***General Appearance*:** Developed formulations were analyzed physically to find color and shape of the formulated tablet.

Average Weight: From every formulation, twenty different tablets were weighed with the calibrated analytical balance and finally average weight of tablets was calculated including the standard deviation.

Hardness: Formulated Tablets of each formulation from F1 to F9 were tested for Hardness using the calibrated hardness tester.

Diameter and Thickness: Diameter and thickness of the tablet were measured by using calibrated vernier caliper. An average value for diameter and thickness was calculated.
Friability: Friability of tablets were evaluated using Roche Friabilator.

Time of Disintegration: Time for Disintegration was evaluated using Disintegration test apparatus.

Moisture content: Moisture content was analyzed using Moisture Balance.

Assay: Standard and Sample were prepared and analyzed using the High performance Liquid Chromatography using the UV detector at 226 nm.
Dissolution: Standard and samples of the formulations were prepared and analyzed using the UV visible spectrophotometer having 1 cm path length at the wavelength of 278 nm.

Content Uniformity: Content uniformity was performed by using HPLC Technique and taking 10 tablets from every formulation. The chromatographic conditions and standard preparation was same of that of Assay.

RESULT

Solubility of Rizatriptan: Rizatriptan Benzoate was found soluble in water, in 96% Ethanol it was sparingly soluble and in Methylene Chloride it is slightly soluble.

Determination of Calibration Curve:

a) For UV Visible spectrophotometer

Table 2: Concentration Vs. Absorbance of UV

S.N.	Concentration (mcg/ml)	Absorbance
1	4	0.0569
2	6	0.0839
3	8	0.1118
4	10	0.1396
5	12	0.1679

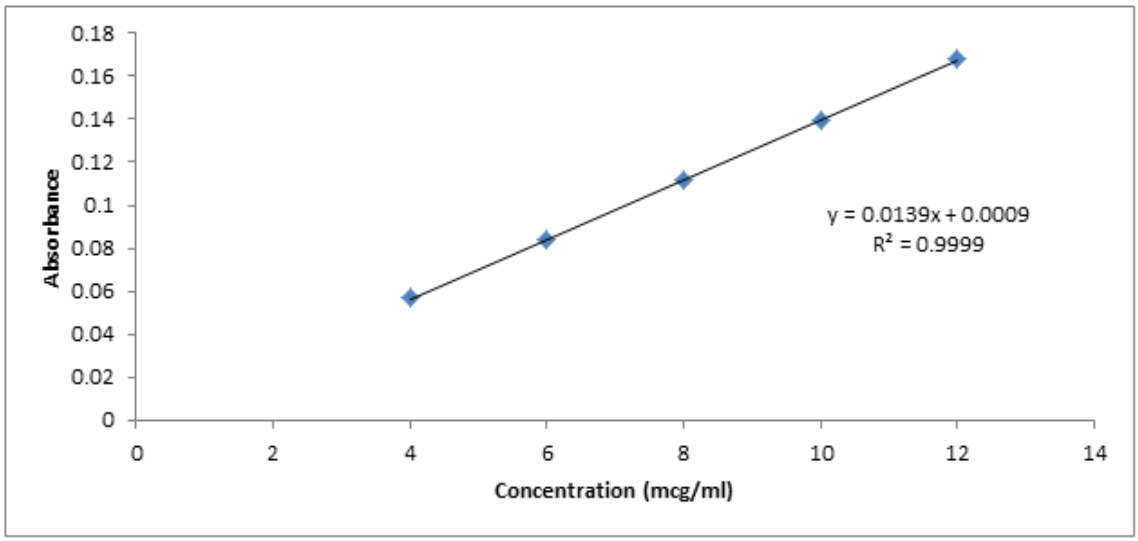

Figure 1: Calibration Curve

Drug Excipients Compatibility: It was studied using FTIR. There were no any interactions between excipients and drug.

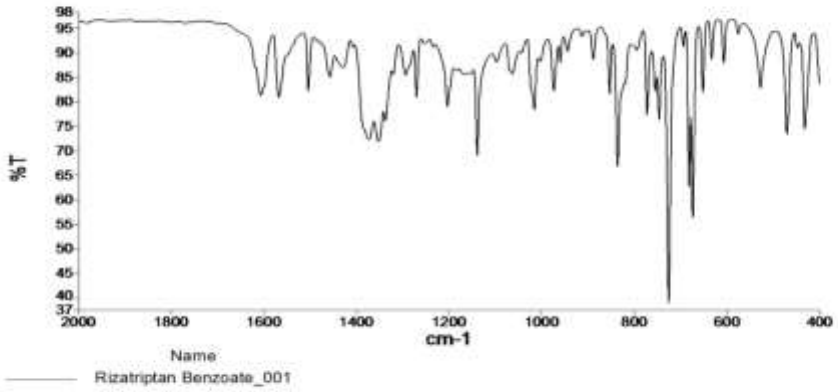

Figure 2: FTIR Spectra of Rizatriptan Benzoate

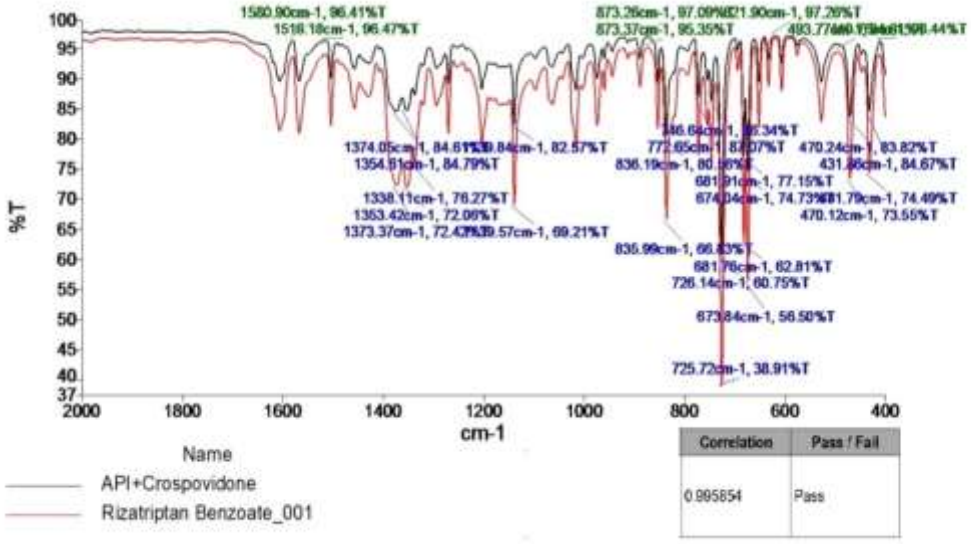

Figure 3: FTIR Spectra showing compatibility between Rizatriptan Benzoate and Mixture of API and Crospovidone

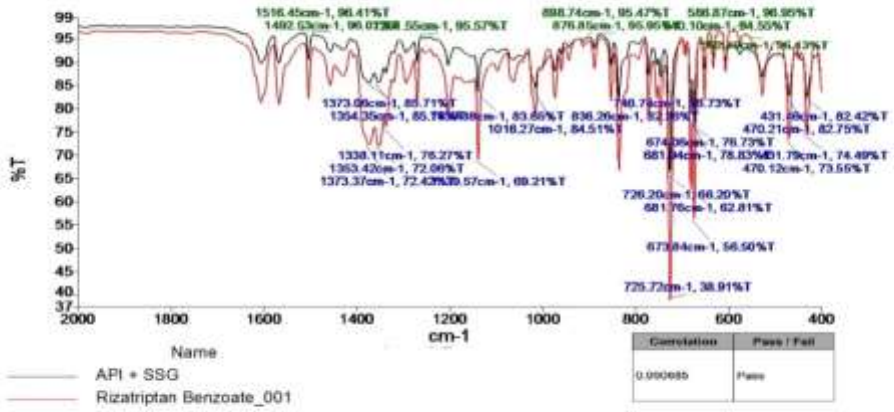

Figure 4: FTIR Spectra showing compatibility between Rizatriptan Benzoate and Mixture of API and SSG.

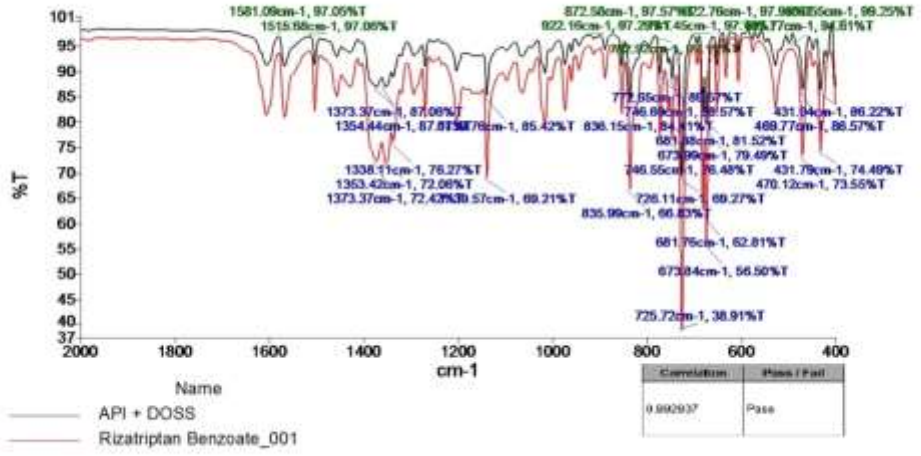

Figure 5: FTIR Spectra showing compatibility between Rizatriptan Benzoate and mixture of API and DOSS

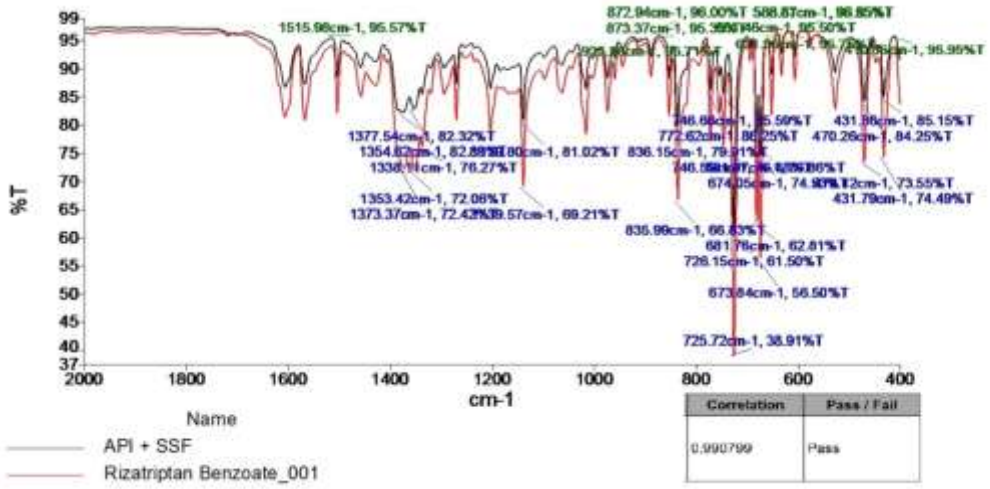

Figure 6: FTIR Spectrum showing compatibility between Rizatriptan Benzoate and Mixture of API and SSF

Pre compression Parameters: Tapped Density, Bulk Density, Angle of Repose, Carr's Index, Hausner's ratio were evaluated. Result shows the flow property of the lubricated granules as good to excellent.

Table 3: Pre Compression Evaluation

Formulation Code	Bulk Density(g/cm^3)	Tapped Density(g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (θ)
F1	0.504 ± 0.01	0.566 ± 0.01	10.87 ± 0.89	1.122 ± 0.01	29.50 ± 0.07
F2	0.502 ± 0.01	0.568 ± 0.01	11.62 ± 0.32	1.132 ± 0.004	29.90 ± 0.06
F3	0.495 ± 0.01	0.555 ± 0.01	10.73 ± 0.34	1.120 ± 0.004	29.04 ± 0.11
F4	0.506 ± 0.01	0.570 ± 0.01	11.22 ± 0.77	1.126 ± 0.01	30.05 ± 0.10
F5	0.518 ± 0.01	0.571 ± 0.01	9.20 ± 0.07	1.101 ± 0.001	28.7 ± 0.06
F6	0.510 ± 0.02	0.573 ± 0.01	11.01 ± 1.01	1.124 ± 0.01	29.41 ± 0.06
F7	0.507 ± 0.01	0.561 ± 0.004	9.63 ± 0.58	1.107 ± 0.01	28.70 ± 0.07
F8	0.519 ± 0.01	0.584 ±0.01	11.14 ± 0.36	1.125 ± 0.005	29.22 ± 0.14
F9	0.511 ± 0.01	0.570 ±0.02	10.43 ± 0.56	1.117 ± 0.01	28.70 ± 0.09

General Appearance: All the Tablets of each formulation were found white coloured, smooth and round in nature. None of the tablets were found with any defects

Post Compression Parameters

Average Weight: Average weight of the tablets ranged from 300.5mg to 303.6mg.

Table 4: Average weight

Formulations	Average Weight (mg) (Mean±SD)
F1	303.5±2.01
F2	302.0±2.87
F3	302.3±2.62
F4	303.6±2.06
F5	300.5±1.67
F6	301.2±1.82
F7	300.5±1.85
F8	300.8±2.46
F9	301.5±2.50

Hardness: Hardness of the tablets from different formulation ranging from 3.95 kg/cm^2 to 4.23 kg/cm^2 was obtained.

Table 5: Hardness

Formulations	Hardness (kg/cm^2) (Mean±SD)
F1	4.23 ± 0.27
F2	4.16 ± 0.11
F3	3.98 ± 0.23
F4	4.17 ± 0.11
F5	3.95 ± 0.15
F6	3.96 ± 0.28
F7	3.96 ± 0.25
F8	3.95 ± 0.37
F9	4.00± 0.48

Diameter and Thickness of the film: Diameter of the tablets was determined as 9.02 mm to 9.11 mm and Thickness of the tablets was determined as 4.77 mm to 4.85 mm respectively

Table 6: Thickness/Diameter

Formulations	Diameter (mm) (Mean±SD)	Thickness (mm) (Mean±SD)
F1	9.07±0.11	4.81±0.11
F2	9.11±0.11	4.84±0.11
F3	9.04±0.12	4.85±0.08
F4	9.06±0.09	4.81±0.03
F5	9.04±0.06	4.81±0.03
F6	9.04±0.15	4.78±0.07
F7	9.10±0.07	4.77±0.05
F8	9.06±0.12	4.82±0.07
F9	9.02±0.11	4.83±0.08

Friability, Disintegration time and moisture: Friability of the tablets ranging from 0.16% to 0.31% was obtained. Similarly Disintegration time was determined as 12 seconds to 56 seconds. Likewise moisture content was obtained ranging from 2.10 % to 3.12 %.

Table 7: Friability, Disintegration time and moisture content

Formulation Code	Friability (%)	Disintegration Time	Moisture Content (%)
F1	0.23%	42 seconds	2.23%
F2	0.26%	51 seconds	3.12%
F3	0.31%	56 seconds	2.64%
F4	0.21%	48 seconds	2.10%
F5	0.18%	12 seconds	2.62%
F6	0.20%	22 seconds	3.06%
F7	0.16%	18 seconds	2.72%
F8	0.24%	27 seconds	2.21%
F9	0.27%	28 seconds	3.03%

Assay %: All the formulations showed the assay percentage within the specification limit i.e from 93.4 % to 105.0 % of the label claim. Minimum assay percentage was obtained as 97.05% and maximum was obtained as 99.79%.

Table 8: Assay percentage

Formulations	Mean (mg) ±SD	Assay Percentage (%)
F1	9.7305±0.04	97.31%
F2	9.7565±0.04	97.57%
F3	9.7266±0.01	97.27%
F4	9.7047±0.02	97.05%
F5	9.9794±0.01	99.79%
F6	9.8113±0.03	98.11%
F7	9.8985±0.01	98.98%
F8	9.7855±0.01	97.85%
F9	9.7192±0.02	97.19%

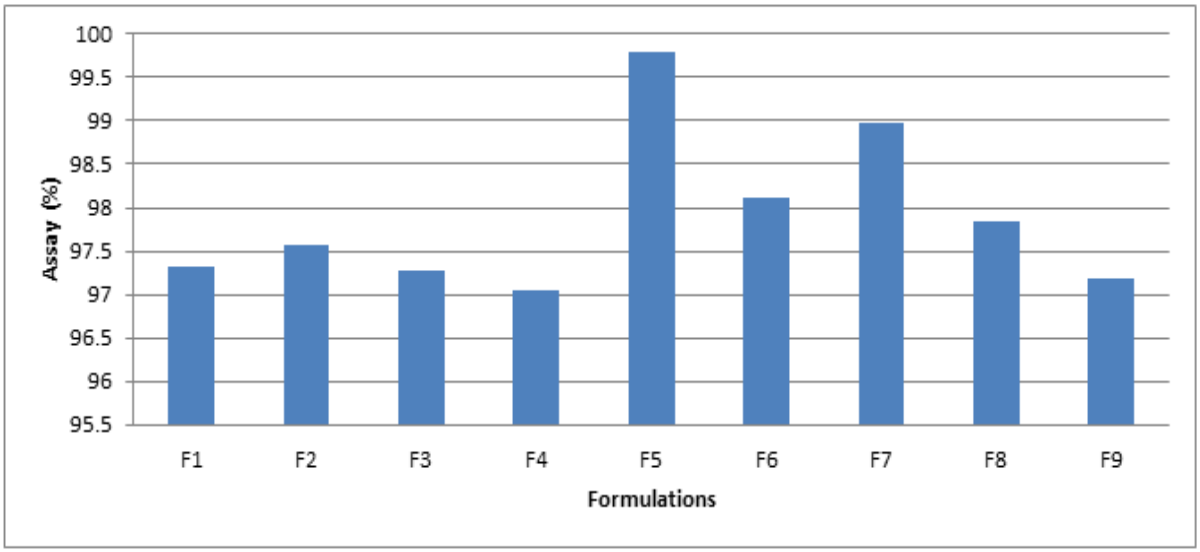

Figure 7: Bar Graph for Assay percentage of the different formulations

Dissolution: All the formulations were found to have good dissolution. Minimum value of 86.17 % to maximum of 99.53% was obtained. Formulation number F5 showed the highest dissolution value whereas the formulation number F3 showed the least dissolution value.

Table 9: Dissolution %

Formulations	Dissolution %(Mean±SD)
F1	91.60% ± 2.46
F2	89.95% ± 3.72
F3	86.17% ± 0.69
F4	91.29% ± 5.01
F5	99.53% ± 0.79
F6	97.97% ± 2.61
F7	98.35% ± 4.12
F8	96.09% ± 3.25
F9	96.85% ± 3.77

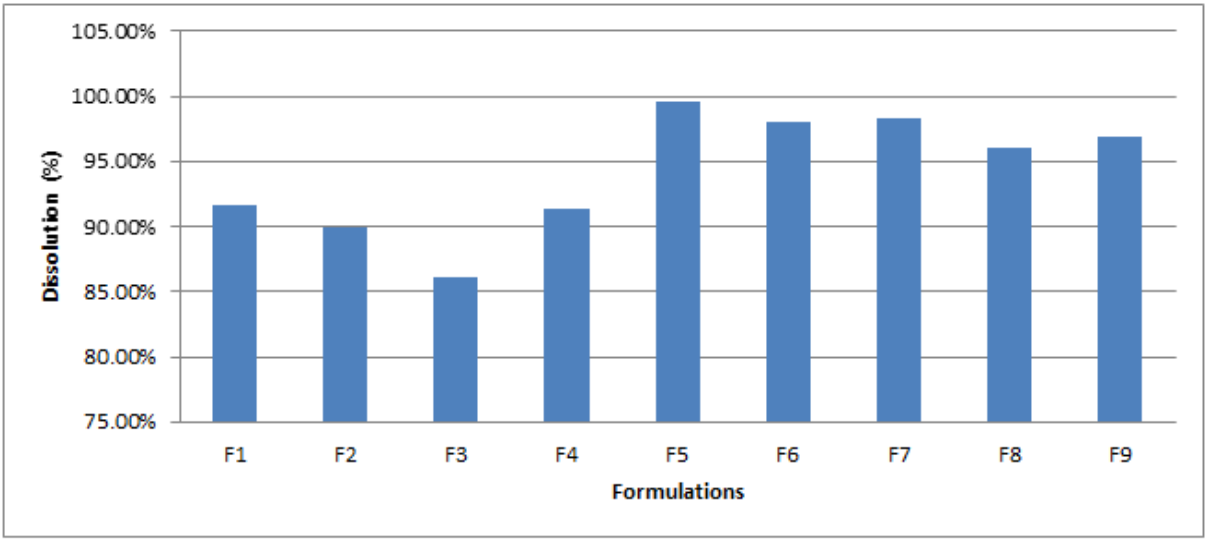

Figure 8: Bar Graph for Dissolution percentage of different formulations

Content Uniformity: All the formulations from F1 to F9 were found to have good uniformity of content. Minimum content of 9.6062 mg and maximum content of 10.0938 mg was obtained.

Table 10: Uniformity of content

Formulations	Mean(mg)±SD
F1	9.7084±0.16
F2	9.6146±0.13
F3	9.7701±2.95
F4	9.6062±0.18
F5	10.0938±0.14
F6	9.8514±0.25
F7	9.9006±0.20
F8	9.9041±0.16
F9	9.8859±0.18

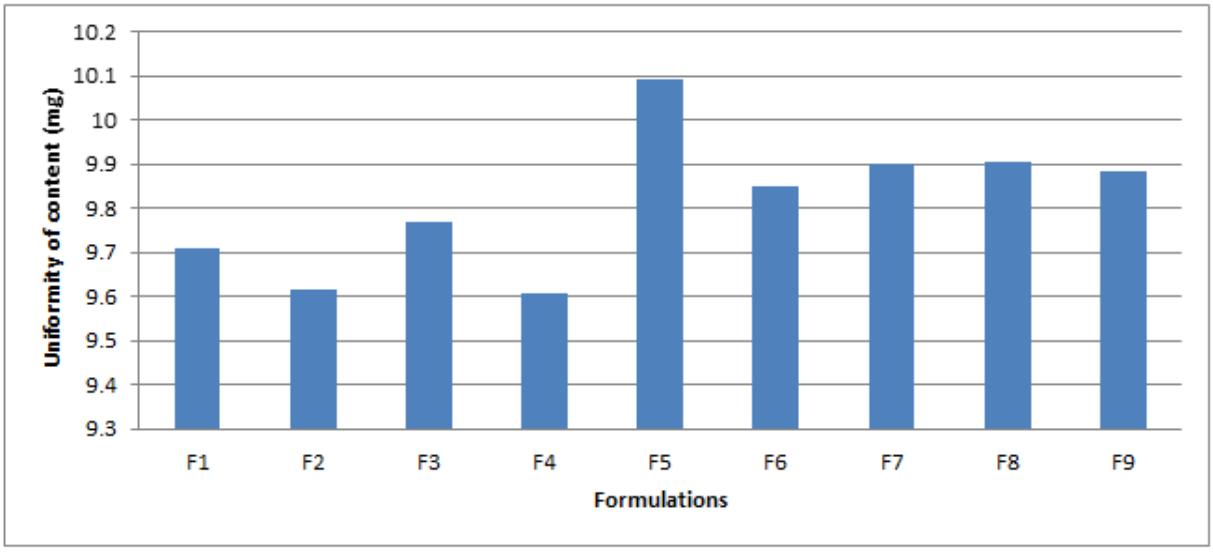

Figure 9: Bar Graph showing the Content Uniformity of the different formulations

CONCLUSION

It can be stated that choice of the super disintegrating agent and its concentration is the major concern that must be assured before formulation of the Orodispersible tablets. Not all the superdisintegrants are suitable for the formulation of ODT. They must be compatible enough with the drug under study. Concentration selection of the excipients plays major role. Dioctyl Sodium Sulphosuccinate must be used in minimal concentration and it minimizes the time for disintegration of ODT & thus enhances the rate of dissolution of the drug. Formulations with DOSS are found disintegrated faster and have high dissolution percentage than the formulation without DOSS. Concentration of the Sodium Starch Glycolate should be optimum. It should not be too high and not too low. Higher concentration of the SSG decreases the Disintegration time and retards the dissolution rate. It is due to the formation of gellies at higher concentration of Sodium Starch Glycolate. Lower concentration of SSG does not sufficiently decrease the disintegration time and Dissolution rate may not be enhanced. Crospovidone used as higher concentration at permissible range offers greater advantage for reduction of the disintegration time and for enhancing the dissolution rate. Among the Nine Formulation, Formulation F5 shows the better results where Intermediate concentration of Sodium Starch Glycolate, Higher Concentration of Crospovidone was used along with the DOSS. Similarly the formulation number F3 shows the poor result as compared to others, in which high concentration of Sodium Starch Glycolate, Low concentration of Crospovidone was used and Dioctyl Sodium Sulphosuccinate was not used during the formulation.

Wet granulation techniques was successful in increasing the flow properties, Angle of repose, Haussner's ratio and Carr's index evaluated after lubrication shows the flow properties from

good to excellent level. Thus wet granulation technique can be used for increasing the flow properties in case of the materials having poor flow.

For the formulation of Orodispersible tablet of Rizatriptan benzoate, DOSS can be used in lower concentration for decreasing the disintegration time and for having the higher dissolution %. Similarly Sodium Starch Glycolate should be used at intermediate concentration and Crospovidone at higher concentration. Synergistic combination of them plays crucial role for having the optimum value of disintegration and dissolution value.

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CONFLICT OF INTEREST:
There is no any financial and intellectual conflict in this work.

REFERENCES:

1. Agrawal, R., & Naven, Y. (2011). Pharmaceutical Processing- A Review on Wet Granulation Technology. *International Journal of Pharmaceutical Frontier Research, 1*(1), 65-83.
2. Bhanu, N. (2016). A Review: High Shear Granulators for Tablet Dosage Form Development. *Reasearch and Reviews: Journal of Pharmacy and Pharmaceutical Sciences, 5*(4), 43-51.
3. Dey, P., & Maiti, S. (2010). Orodispersible Tablets: A new trend in drug delivery. *Journal of Natural Science, Biology and Medicine, 1*(1), 2-5.
4. Ghosh, T., Ghosh, A., & Prasad, D. (2011). A Review on New Generation Orodispersible Tablets and its Future Prospective. *International Journal of Pharmacy and Pharmaceutical Sciences, 3*(1), 1-7.
5. Goadsby, P. J., Lipton, R. B., & Ferrari, M. D. (2002). Migraine: Current Understanding and Treatment. *New England Journal of Medicine, 346*(4), 257-270.
6. Gupta, D. K., Maurya, A., & Varshney, M. M. (2020). Orodispersible Tablets: An Overview of Formulation and Technology. *World Journal of Pharmacy and Pharmaceutical Sciences, 9*(10), 1406-1418.
7. Joshi, R., Garud, N., & Akram, W. (2020). Fast Dissolving Tablets:A Review. *International Journal of Pharmaceutical Sciences and Research, 11*(4), 1562-1570.
8. Kushare, A. A. (2015). Formulation and Evaluation of Orodispersible Tablets of Rizatriptan Benzoate. *World Journal of Pharmaceutical Research, 4*(8), 685-717.

9. Mothilal, M., Kota, S., Babu, S. G., Kumar, G., Manimaran, V., & Damodharan, N. (2012). Formulation and Evaluation of Rizatriptan Benzoate Orally Disintegrating Tablets. *International Journal of Drug Development and Research, 4*(2), 117-123.

10. Ozyilmaz, D. E., Pozharani, L. B., Alhadi, M., & Ochanya, A. E. (2018). Oral Disintegrating Tablets: A Short Review. *EMU Journal of Pharmaceutical Sciences, 1*(1), 76-81.

11. Rameesa, C. K., & Drisya, M. K. (2015). Orodispersible Tablet:A Patient Friendly Dosage Form (A Review). *Bali Medical Journal (Bali Med J), 4*(1), 17-20.

12. Rewar, S., Singh, C. J., Bansal, B. K., Pareek, R., & Sharma, A. K. (2014). Oral Dispersible Tablets: An Overview; Development, Technologies and Evaluation. *International Journal of Research and Development in Pharmacy and Life Sciences, 3*(6), 1223-1235.

13. Roy, A. (2016). Orodispersible Tablets: A Review. *Asian Journal of Pharmaceutical and Clinical Research, 9*(1), 19-26.

14. Satyanarayana, T., Krishna, J. M., Kumar, P. S., Krishnan, S. N., & Shaji, G. (2011). Formulation and Evaluation of Rizatriptan Benzoate Orodispersible Tablets. *Scholars Research Library, 3*(6), 125-130.

15. Singh, H., Jaiswal, P., Gupta, S., & Singh, S. (2017). Formulation of Rizatriptan Benzoate Sublingual Tablets Prepared by Direct Compression with Different Bioadhesives Polymer: In Vitro and Ex Vivo Evaluation. *Asian Journal of Pharmaceutical and Clinical Research, 10*(16), 36-42.

16. Singh, M. K., Mazumder, R., Padhi, S., & Singh, D. K. (2022). Formulation Development and Optimization of Bioenhanced Sublingual Tablets of Rizatriptan Benzoate to Combat Migraine. *Indian Journal of Pharmaceutical Education and Research, 56*(2), S200-S215.

17. Tripathi, K. (2013). 5-Hydroxytryptamine, its Antagonists and Drug Therapy of Migraine . In *Essentials of Medical Pharmacology* (7 ed., p. 179). New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.