Journal of Drug Discovery and Health Sciences

journal home page : https://jddhs.com/index.php/jddhs/index

Research Article

Study on Synergistic Effect of Dioctyl Sodium Sulfosuccinate, Sodium Starch Glycolate and Crospovidone on Drug Release Profile of Orodispersible Tablets of Rizatriptan Benzoate

Diwas Adhikari[1*], Sharada Pokhrel[1], Meenakshi Kandwal[2], Arti Kori[2], Shivanand Patil[3]

[1]*M. Pharm-Veer Madho Singh Bhandari Uttarakhand Technical University, Dehradun, India.*

[2]*Associate Professor, Shree Dev Bhoomi Institute of Education, Science and Technology (Affiliated with Veer Madho Singh Bhandari Uttarakhand Technical University), Dehradun, India.*

[3]*Director, Shree Dev Bhoomi Institute of Education, Science and Technology (Affiliated with Veer Madho Singh Bhandari Uttarakhand Technical University), Dehradun, India.*

ARTICLE INFO

Article history:

Received: 03, October, 2024

Revised: 02 November, 2024

Accepted: 04 December, 2024

Published: 30 December, 2024

Keywords:

Orodispersible, Superdisintegrants, DOSS, Synergistic, Wet granulation

DOI:

10.21590/jddhs.01.04.08

ABSTRACT

Orodispersible tablets are expected to have disintegration rapidly within the mouth cavity. To overcome the problems of solid dosage forms and to facilitate the patients with easy swallowing, tablets pharmaceutical companies have formulated oral disintegrating tablets, which disintegrate in saliva, within few seconds. Rizatriptan Benzoate can be formulated as orodispersible tablet successfully by using the wet granulation process. Crospovidone, SSG and DOSS were used in the varying concentrations during the formulation. Other excipients like microcrystalline cellulose, sodium stearyl fumarate, colloidal silicon dioxide (aerosil) and aspartame were also used and IPA was used as the solvent in the wet granulation technique. Nine different formulations were prepared. Formulation containing SSG in the intermediate concentration and crospovidone in the higher concentration in presence of DOSS showed the least time for disintegration and highest amount of in-vitro drug release. DOSS helps to facilitate the dissolution rate of the dosage forms. Thus the formulations containing DOSS along with the other Superdisintegrants help to increase the dissolution rate of the dosage forms. Formulation containing highest concentration of SSG, lowest concentration of crospovidone and without the use of DOSS showed the maximum disintegration time and lowest dissolution rate. SSG in concentration greater than 8% shows gelling and viscosity producing effects which results increase in DT and decreased dissolution rate.

Background

To overcome the problems of solid dosage forms and to facilitate the patients with easy swallowing tablets pharmaceutical companies have formulated oral disintegrating tablets, which disintegrate in saliva, within few seconds. Drug dissolution, absorption, bioavailability and onset of action are found significantly greater in this novel oral dosage form compared to the conventional dosage forms (Roy, 2015).

Oral mucosa is utilized as a mean for the drug delivery. It has both advantages and disadvantages. Easily accessible, self-administrable, faster repairing capacity, higher amount blood that is supplied in oral mucosa, first pass metabolism & GI interaction of the drugs are avoided.

***Corresponding Author:** Diwas Adhikari

Address: M. Pharm-Veer Madho Singh Bhandari Uttarakhand Technical University, Dehradun, India

Email ✉**:** adhikaridiwas51@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Minimization of the systemic side effects etc. are some advantages associated with this. In contrast, washing of the drug by the saliva, permeability barrier of the oral mucosa, requirement of the delivery device, risk of chocking on swallowing, relatively smaller surface area etc. are some of the disadvantages of using the oral mucosa as means for the drug delivery.(Nagar, et al., 2011)

Orodispersible tablets are expected to have disintegration rapidly within the mouth cavity. Ideal ODTS should have shorter time for disintegration and the drug must be release in the large quantity within the defined time. Wet granulation method is commonly popular in these days. (Ghosh, Ghosh, & Prasad, 2011)

Orodispersible tablets offers different advantages such as: they are beneficial for the patient who feel problem/ difficulty in swallowing, lower age group patient (pediatric), higher age group patients (geriatric) and the people suffering from the disease called dysphagia are benefitted, dissolution and absorption is faster. It helps in increasing the bioavailability of the intended drug. In comparison to other liquid medications, it is advantageous in terms of accurate dosing, administration, transportation, cost effective. High drug loading is possible. It avoids first pass metabolism, offers acceptable taste and pleasant mouth feeling. It should not create any traces/residue in the mouth cavity after delivery of drug and offers improved safety.(Ramessa & Drisya, 2015)

Superdisintegrants are to facilitate break down or dissociation/breakage of tablets into smaller particles (Satyanarayana, Krishna, Kumar, Krishna, & Shaji, 2011). They bring rapid disintegration of the solid dosage forms. Use of superdisintegrants decrease DT which enhances dissolution of solid dosage forms and it make the drug available for the action in a shorter time and helps the patient to get immediate relief.

Superdisintegrants works by different mechanisms such as wicking or porosity and capillary action, enlargement/ product swelling, by releasing the gases, repelling force within the particles, heat produced in wetting, by reaction of enzymes.(Bishal, Ali, Bandyopadhyay, Bandyopadhyay, & Debnath, 2022) (J & S, 2020)

Superdisintegrants should have different characteristics such as good mouth feel, poor gel formation, poor solubility and good disintegrating properties. They should not form complexes with the drugs and should have good flow and moulding properties.(Rada & Kumari, 2019)

Migraine, a neurovascular disorder in which there is severe autonomic system dysfunction and headache and in some cases it also involves neurological symptoms. Migraine is a disorder of brain which is caused by the recurrent attacks of headache and other several problems related to the autonomic nervous system. Oral disintegrating tablets can be a boon for the victims of migraine attacks. Recent advancement in the neurological science has led to the development of triptans, which has been of great help to the patients of migraine. These are the selective serotonin receptor agonist that activates 5-HT1B and 5-HT1D receptors.(Singh, Jaiswal, Gupta, & Singh, 2017) (Goadsby, Lipton, & Ferrari, 2002)

Drug Profile- Rizatriptan Benzoate (Ch & Triveni, 2021)

Molecular formula of Rizatriptan Benzoate is $C_{22}H_{25}N_5O_2$ **[Figure 1].** Its molecular weight is 391.475. In water it is found soluble, in 96% ethanol it is found soluble sparingly where as in the methylene chloride it is found slightly soluble. It is powdery or crystalline and is sometimes white and sometimes almost white in color.

Mechanism of Action

There is dilation of the blood vessels i.e. extra cerebral within the cranial cavity which supplies the blood to Dura mater in brain.

Migraine is also associated with nausea and vomiting which is caused when there is imbalance in the serotonin level in the brain. When its level is disrupted then the pathophysiology associated with it also gets disrupted, pain causing neurons also gets activated. Due to the activation of the pain enhancing nerves headache occurs.

Excipients Profile-Superdisintegrating Agents

Dioctyl sodium sulfosuccinate:

This molecule appears like a waxy solid and it has a molecular weight of 444.56. Solubility study shows that DOSS is easily soluble in both organic solvents and water. Its molecular formula is $C_{20}H_{37}NaO_7S$ **[Figure 2].**

Dioctyl sodium sulfosuccinate is the anionic surfactant. This excipient is widely used for increasing the dissolution rate or to increase the drug release rate. It has different functional properties such as it helps in the appropriate reduction of surface/interfacial tension. It helps in increasing the capacity of wetting/wettability and for increasing the capacity of dispersion.It increases the capacity for emulsification/penetration and solubilization.

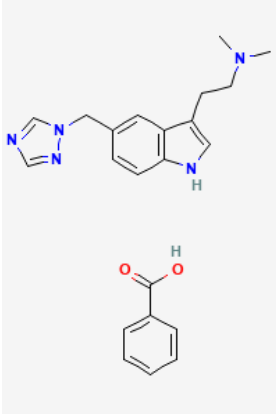

Figure 1: Chemical structure of Rizatriptan Benzoate

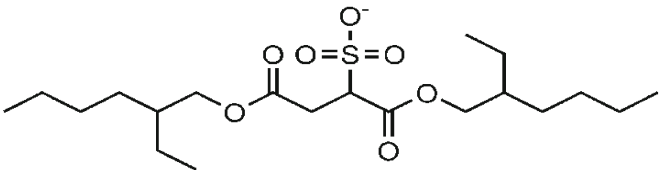

Figure 2: Chemical Structure of dioctyl sodium sulfosuccinate (DOSS)

Commonly 0-10% w/w concentration can be incorporated for formulation. (Buwade, Jadiya, Shukla, & Upmanyu, 2015) (Willis, 1988)

Crospovidone

This is an excipient used in the formulation of tablets and capsules for the purpose of causing the disintegrating effect. This synthetic superdisintegrants helps to increase and extend the rate of tablet disintegration enhancing dissolution for orodispersible formulations. It is insoluble form of polyvinyl pyrrolidone. Crospovidone is produced by the proliferous polymerization of vinylpyrrolidone monomer. Molecular weight is 111.141 and molecular formula of crospovidone is C_6H_9NO (Figure 3).

Crospovidone disintegrates the tablet by swelling and wicking mechanism. It has a high cross link density. Other superdisintegrants have a lower crosslink density so they have gelling tendency when they are fully hydrated. They wick up the saliva quickly in the tablet and facilitate the disintegration of tablets by wicking and swelling action. Crospovidone can be used as superdisintegrant even in the higher concentration unlike other superdisintegrants which have the tendency to form gel when used in higher concentration. (P.S, G, & Kiran, 2011)

Sodium starch glycolate (SSG):

It is a superdisintegrant whose molecular weight is 98.03 and molecular formula is $C_{10}H_{19}NaO_8$ (Figure 4). It can be derived with chemical modifications involving substitution and cross linking. Substitution helps to increase the hydrophilicity and cross linking helps to reduce the gel formation and increases the solubility when material comes in contact with water. Use of superdisintegrants like SSG helps to facilitate the breakdown of tablets, reduces the time for the disintegration and improves the dissolution rate. (Rani, Dev, & Prasad, 2022)

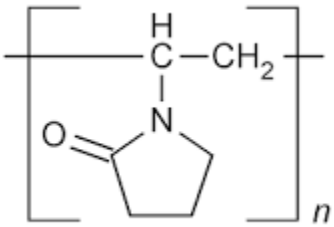

Figure 3: Chemical structure of Crospovidone

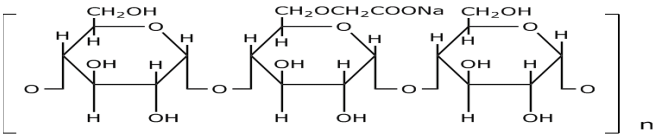

Figure 4: Chemical structure of SSG

SSG works by extensive swelling with minimal gelling. The optimum concentration of SSG is 4-6%.They is the starch which is obtained by modification & cross linking of starches obtained from potato. This superdisintegrant absorbs water and swells rapidly from 200-300%.Its optimum concentration are 4-6% as above concentration of 8%. It increases the time of disintegration as there occurs the gelling and viscosity producing effects. (Manzoor, 2021) (Sharma, 2013)

Rationale of using the DOSS along with superdisintegrants

Dioctyl sodium sulfosuccinate is extensively used as surfactant and wetting agents in the pharmaceutical formulation in the very small amount. It sufficiently increases the dissolution pattern/profile of the drug. It can be synergistically used along with the superdisintegrants, so that faster disintegration can be achieved for the ODT.

METHODOLOGY

Formulation Design

Different Nine formulations were designed altering the concentration of Crospovidone, Sodium Starch Glycolate and DOSS **[Table 1]** and formulated as below:

Premixing

Crospovidone, sodium starch glycolate and microcrystalline cellulose PH-101 was mixed in the double Polybag.

Granulation

Dioctyl sodium sulfosuccinate was dissolved in isopropyl alcohol. Rizatriptan benzoate was dispersed in it. Thus prepared granulating solution was poured into the above blend. It was subjected for proper mixing and wet mass was passed through mesh size #20. It was subjected to drying in FBD initially with heater off until the smell of the IPA escapes and later finally at 45-50ºc until the moisture was +- 0.5% of initial moisture.

Dry Mixing

Dried granules were mixed with colloidal silicon dioxide and MCC PH-102 was presieved through mesh size #40.

Lubrication

Dry mixed granules were mixed with sodium sterayl fumarate which was presieved with mesh size #60 and lubrication was done for about 2 minutes.

Table 1: Formulation design (Formulation were designed after performing different trials)

S. No.	*Component*	*Mg/Tablet*								
		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	3
10	IPA	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Tablet weight (mg)		300	300	300	300	300	300	300	300	300

Compression

Compression was performed by taking the bulk blend of the lubrication step at 300 mg.

Results And Discussion

Disintegration Time

Disintegration was performed using water at 25ºC±1º*C. A tablet was taken and it was introduced into each tube. The assembly was kept suspended in the water containing beaker and operated for specified time. This procedure was repeated for each* formulation and the result was noted [Table 2]. Bar graph was prepared taking the formulation code and disintegration time of each formulation [Figure 5].

Inferences

The disintegration time with minimum of 12 seconds to maximum of 56 seconds was obtained as seen in the Table 2 and Figure 5. Formulation (F5) disintegrated in the least time. All the tablets disintegrated within the acceptable limit that is not more than 3 minutes.

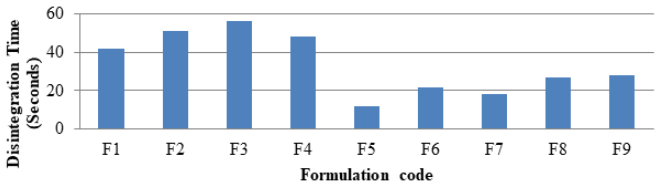

Figure 5: Graphical representation of DT Vs Formulation Code

Dissolution

Dissolution test was carried out using the dissolution test apparatus at 37ºC±0.5ºC. Dissolution % value of each formulation were calculated and tabulated [Table 3]. Bar graph was prepared taking the different formulations and dissolution % of each formulation [Figure 6].

Inferences

The dissolution value from 86.17% to 99.53% was obtained as seen in the Table 3 and Figure 6. F3 formulation showed the least rate of dissolution whereas F5 showed the highest rate of dissolution in specified time. Formulation F5 contains 15mg of crospovidone, 18mg SSG and 0.1mg DOSS. This shows that the optimum concentration of sodium

Table 2: Disintegration time observed in different formulations

Formulation code	*Disintegration time*
F1	42 seconds
F2	51 seconds
F3	56 seconds
F4	48 seconds
F5	12 seconds
F6	22 seconds
F7	18 seconds
F8	27 seconds
F9	28 seconds

Table 3: Dissolution profile of different formulations

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

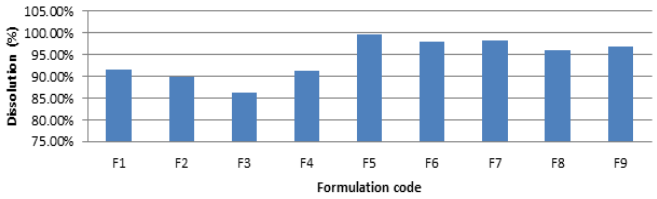

Figure 6: Graphical representation of Dissolution (%) Vs Formulation Code

starch glycolate is required to produce good disintegrating effects. This may be because SSG in concentration greater than 8% shows gelling and viscosity producing effects. All the tablets showed dissolution within the acceptable limits that is not less than 80 % (Q) of the stated amount of Rizatriptan.

Conclusion

Superdisintegrants like crospovidone and SSG were used in the varying concentrations for the formulation of the dosage form. Other excipients like MCC, sodium stearyl fumarate, colloidal silicon dioxide and aspartame were used. IPA was used as the solvent in the wet granulation technique. DOSS was used in five formulations whereas in four formulations, DOSS was not used. Formulation was done using the wet granulation method as from evaluation we found the poor flow property of the drug.

In the Formulations, where DOSS is not used along with other Superdisintegrants, it is seen that there is high disintegration time and ultimately the lower dissolution rate. In contrast, presence of DOSS in the formulation significantly lower the disintegration time (DT) and improves the dissolution (release) rate of the drug.

Formulation containing optimum concentration of SSG, highest concentration of crospovidone and including DOSS in small amount in its formulation disintegrated in the lowest time providing highest amount of in vitro drug release whereas the formulation containing highest concentration of SSG, lowest concentration of crospovidone, without the use of DOSS disintegrated in maximum time compared to other formulations and showed the lowest dissolution rate. SSG in concentration greater than 8% shows gelling and viscosity producing effects which results increase in DT and decreased dissolution rate. DOSS helps to facilitate the dissolution rate of the dosage forms. Formulations containing DOSS were found to show higher release pattern among others. Superdisintegrants in optimum concentration and use of DOSS helps to increase the dissolution rate of the dosage forms.

Authors Contribution

All authors have contributed for gathering the information, research and preparation of the research article and finalization for the publication.

Conflict Of Interest

None

References

Bishal, A., Ali, K. A., Bandyopadhyay, B., Bandyopadhyay, R., & Debnath, B. (2022). Study of different superdisintegrants and their use as a magic ingredients for different immediate release tablets. *Journal of Pharmaceutical Negative Results, 13*(5), 1222-1232.

Buwade, P., Jadiya, S., Shukla, T., & Upmanyu, D. N. (2015). Advantages of Immediate Release Tablets Over The Other Tablet Forms. World Journal of Pharmaceutical Research, 4(11), 757-780.

Ch, S., & Triveni, P. (2021). Formulation Development and Evaluation of Orally Disintegrating Tablets Rizatriptan Benzoate. International Journal of Pharmacognosy and Chemistry, 2(4), 79-87.

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.

Goadsby, P. J., Lipton, R. B., & Ferrari, M. D. (2002). Migraine: Current Understanding and Treatment. New England Journal of Medicine, 346(4), 257-270.

J, R. K., & S, S. (2020). Superdisintegrants and Their Inevitable Role in Orodispersible Tablet. International Journal of Research and Review, 7(10), 462-471.

Manzoor, A. (2021). Review Article: Sodium Starch Glycollate as a Superdisintegrant. Journal of Contemporary Pharmacy, 5(1), 33-39.

Nagar, P., Singh, K., Chauhan, I., Verma, M., Yasir, M., Khan, A., et al. (2011). Orally disintegrating tablets: formulation,preparation techniques and evaluation. Journal of Applied Pharmaceutical Science, 1(4), 35-35.

P.S, M., G, S. P., & Kiran, T. (2011). Siperdisintegrants: An Overview. Inetrnational Journal of Pharmaceutical Sciences Review and Research, 6(1).

Rada, S. K., & Kumari, A. (2019). Fast Dissolving Tablets: Waterless Patient Compliance Dosage Forms. Journal of Drug Delivery and Therapeutics, 9(1), 303-317.

Ramessa, 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.

Rani, N., Dev, D., & Prasad, D. (2022). Recent trends in development of superdisintegrants: An Overview. Journal of Drug Delivery and Therapeutics, 163-169.

Roy, A. (2015). Orodispersible Tablets: A Review. Asian Journal of Pharmaceutical and Clinical Research, 9(1), 19-26.

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

Sharma, D. (2013). Formulation Development and Evaluation of Fast Disintegrating Tablets of Salbutamol Sulphate for Respiratory Disorders. Hindawi Publishing Corporation, 1-8.

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.

Willis, L. (1988). Amended Final Report on the Safety Assessment of Dioctyl Sodium Sulfosuccinate. International Journal of Toxicology, 17(4), 1-20.

HOW TO CITE THIS ARTICLE: Adhikar, D., Pokhrel, S., Kandwal, M., Kori, A., Patil, S. Study on Synergistic Effect of Dioctyl Sodium Sulfosuccinate, Sodium Starch Glycolate and Crospovidone on Drug Release Profile of Orodispersible Tablets of Rizatriptan Benzoate. J. of Drug Disc. and Health Sci. 2024;1(4):244-248. **DOI:** 10.21590/jddhs.01.04.08