RESEARCH ARTICLE

Formulation and the Study of Finished Products used for Anginal Disease

Charanjeet Singh[1], Yashwant[1], Anil K. Gupta[2]

[1]*Biyani Institute of Pharmaceutical Sciences, Jaipur, Rajasthan, India*
[2]*Jaipur College of Pharmacy, Jaipur, Rajasthan, India*

Received: 20th October, 2022; Revised: 18th November, 2022; Accepted: 10th December, 2022; Available Online: 25th December, 2022

ABSTRACT

Congestive heart failure is a type of disease which is mainly observed due to the improper supply of blood to the heart. In this disease patient feels severe pain in the chest and may cause serious illness. Sudden treatment is needed in this disease to prevent any fatality. Nitroglycerin is the choice of drug for this disease. This study prepares a dosage form that can deliver the drug at a fast rate like a sublingual tablet of nitroglycerin. Sublingual dosage form was manufactured by direct compression method. For the formulation, multiple excipients like super disintegrants, sweeteners and lubricants were used. The finished dosage form was evaluated for different quality parameters. Optimum formulation was compared with the marketed product and kept on the accelerated stability study. Results were observed as satisfactory and comparable with the marketed product.

Keywords: Nitroglycerin, Sublingual dosage form, Superdisintegrant.

International Journal of Pharmaceutical Quality Assurance (2022); DOI: 10.25258/ijpqa.13.4.07

How to cite this article: Singh C, Yashwant, Gupta AK. Formulation and the Study of Finished Products Used for Anginal Disease. International Journal of Pharmaceutical Quality Assurance. 2022;13(4):385-388.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Nitroglycerin (glyceryl trinitrate) is a Nitrate derivative which is primarily used in the anginal diseases. Glyceryl trinitrates act by dilating the blood vessels (Figure 1). Due to vasodilatation capacity of vascular muscles increases and the venous return or preload decreases. This decreases the work of cardiac muscles and therefore reduces the requirement of oxygen. Glyceryl trinitrate is highly volatile and explosive in nature. Therefore, glyceryl trinitrate is supplied in diluted form for the pharmaceutical industries. In is provided in the form of powder, where glyceryl trinitrate is adsorbed on the inert carrier excipient like lactose, mannitol or dextrose. Generally, 10% diluted form of glyceryl trinitrate is used for the formulation of dosage form. Sublingual tablet of nitroglycerin is official in the different pharmacopeia. Sublingual tablets are the preferred dosage form among patient who are suffering from angina and congestive heart failure due to its quick action. Sublingual tablets shows the effect within a few minutes which is a primary need for a patient. For the development of dosage form, multiple superdisintegrants like kollidon CL and vivasol, lycatab were used. Each superdisintegrant has own mechanism of disintegration.

MATERIALS AND METHODS

Materials

A sample quantity of diluted nitroglycerin provided by M/s Bharat Pharma. Sample quantities of superdisintegrants were received from Signet Pharma.

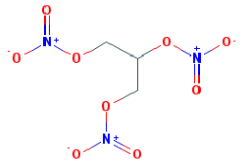

Figure 1: Structure of Nitroglycerin

Methods

As per the pharmacopeia and other literature sources, the therapeutic dose of nitroglycerin sublingual tablet is 0.6 mg. Therefore, in all formulations API strength of the tablet was kept 0.6 mg. in the manufacturing process API and other excipients were mixed in a geometrical manner using the mesh of #40. Lubricants were added at the final stage and mixed properly. Tablets were compressed at the target weight of 100 mg using the 6.0 mm biconvex punch (Table 1).

Study of Powdered Blend Before Compression[9,10]

Angle of Repose

This is the method used to estimate powder flow ability from hopper. In this technique, a heap is formed on the surface after pouring the powder blend thru the glass funnel. Different dimensions of the heap are measured like its base diameter and heap height from the surface. Then powder flowability is measured using the following formula (Table 2).

$$\tan \theta = h/r$$

Where, the Theta value shows the angle of repose.

**Author for Correspondence: anilpharma2001@gmail.com*

Table 1: Formulations of tablets employing Multiple Superdisintegrants

Constituents	*Batch No.*								
	F-01	*F-02*	*F-03*	*F-04*	*F-05*	*F-06*	*F-07*	*F-08*	*F-09*
Drug	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Kollidon CL	5	10	15	-	-	-	-	-	-
Vivasol	-	-	-	5	10	15	-	-	-
Lycatab	-	-	-	-	-	-	5	10	15
Pearlitol	63.4	58.4	53.4	63.4	58.4	53.4	63.4	58.4	53.4
Aerosil 200	2	2	2	2	2	2	2	2	2
Cal. Stearate	5	5	5	5	5	5	5	5	5
Purified Talc	4	4	4	4	4	4	4	4	4
Total wt. (mg)	80	80	80	80	80	80	80	80	80

Powdered Blend Before Compression

Table 2: Physical parameters of powdered formulations

Batch No.	*Angle of Repose*	*Bulk Density (gm/mL)*	*Tapped Density (gm/mL)*	*Compressibility*	*Hausner Ratio*
F-01	24.2	0.556	0.968	42.593	1.742
F-02	23.8	0.545	0.968	43.636	1.774
F-03	24.0	0.556	0.968	42.593	1.742
F-04	26.4	0.508	0.968	47.458	1.903
F-05	26.1	0.508	0.968	47.458	1.903
F-06	25.7	0.508	0.968	47.458	1.903
F-07	28.1	0.492	0.968	49.180	1.968
F-08	28.4	0.500	0.968	48.333	1.935
F-09	26.3	0.492	0.968	49.180	1.968

Tablet After Compression

Table 3: Physical parameters of formulations after compression

Batch No.	*Avg. weight(mg)*	*Tablet Strength (Kp)*	*Thickness (mm)*	*Friability (%)*	*DT (Sec)*	*Assay (%)*
F-01	82.4	3.2	3.18	0.26	32	99.8
F-02	83.1	2.7	3.27	0.21	15	99.7
F-03	84.2	3.4	3.13	0.38	16	99.4
F-04	83.8	2.9	3.28	0.25	53	99.0
F-05	82.7	3.1	3.18	0.27	48	98.8
F-06	81.8	3.0	3.07	0.29	20	99.8
F-07	80.7	2.9	3.11	0.27	125	99.6
F-08	81.0	3.1	3.13	0.19	114	99.8
F-09	82.1	3.4	3.21	0.24	105	99.7

Initial and Tapped Density (Table 2)

This parameter measures the volume occupancy by the powder during filling in the blender and in the tablet die.

Both densities are measured by dividing the bulk volume or tapped volume from the powder mass value.

Study of Tablet After Compression[11,12]

Variability in the Tablet Weight

This parameter indicates the obtained rang of tablet weight during compression. As per the Pharmacopoeial requirement for 80 mg tablet weight all tablets must fall within the range of + 7.5% of tablet avg. weight (Table 3).

Thickness

Tablet thickness should remain in the controlled range because this parameter has directly impact on the packaging. Tablet thickness is calculated by using the instrument Pharma Test PTB 330 (Table 3).

Strength of Tablet

A tablet should have sufficient strength to maintain its shape during handling by the patient and during tablet packaging and transport. Tablet strength was measured using the instrument Pharma Test PTB 500. This is an automated Hardness tester.

Table 4: % Drug release of different formulations

Batch No.	*Percent Release*			
	1minutes	*3 minutes*	*5 minutes*	*10 minutes*
F-01	58	79	91	100
F-02	63	86	97	100
F-03	74	91	99	100
F-04	48	62	76	97
F-05	55	76	89	99
F-06	64	87	98	100
F-07	46	58	69	93
F-08	49	57	73	95
F-09	51	57	74	94
Commercial product	65	85	98	100

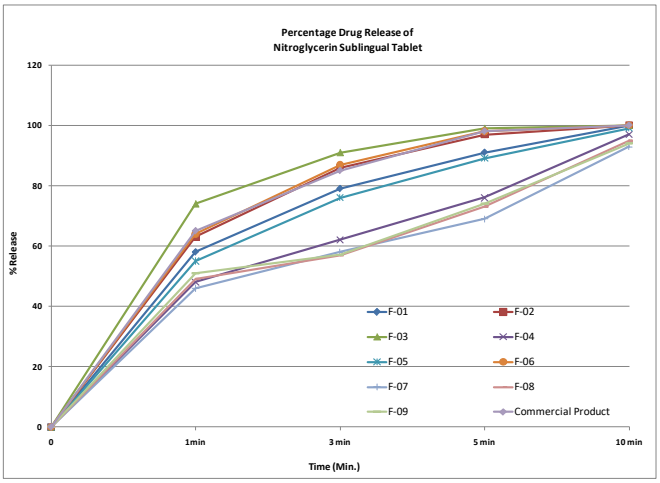

Figure 2: % Drug release of different formulations

Friability

This is the measure of tablet powder loss during tablet coating, packaging, or transport. It was determined by using the instrument Pharma Test PTF 100. The percent loss of powder was calculated after tumbling the tablet in the instrument for 4 minutes (Table 3).

Disintegration Time

This parameter measure the time of tablet needed to completely disintegrate. It was determined by using the instrument Pharma Test PTZ 100. Before releasing of the drug from the tablet it needs to complete disintegration of the tablet (Table 3).

Drug Content in the Tablet

This is the parameter which measures the amount of drug available in the tablet. This is measured by converting the tablets first in the powder form. Then this powder is diluted with suitable media. After proper dilution and filtration drug content was measured by the UV spectrophotometer at the λ_{max} 220.0 nm (Table 3).

In-vitro Drug Dissolution[13]

This parameter measures the amount of drug releases from the dosage form at different time period. Study was carried out as per the USFDA dissolution method. Study was done in 500 mL, 6.5 pH buffer at 50 rpm. Samples were collected at 1, 3, 5 and, 10 minutes using the apparatus USP type 2 - Pharma Test PT-DT70 (Table 4 and Figure 2).

RESULT AND DISCUSSION

As per observed results flowability of powder for all formulations were found to be satisfactory and suitable for the direct compression process. The angle of repose for all formulations was below 300, a characteristic of a powder having good flowability.

The average targeted weight of the compressed tablets was found to be within the pharmacopoeial range. Additionally, tablet thickness and strength were also satisfactory for all the formulations. For the formulations F-02, F-03 and F-06, disintegration time was found to be 15, 16 and 20 seconds, respectively; for all other formulations, it was observed to be more than 30 seconds. The drug content of all formulations were within the Pharmacopoeial limit.

In dissolution, more than 90% drug release was observed for almost all formulations. But when we compared the drug release with the commercial product it was found that only the formulations F-02 and F-06 qualify the criteria needed for a sublingual tablet.

CONCLUSION

As per the dissolution data and the graphical representation of different formulations, F-02 and F06 formulations were observed to be equivalent to the commercial drug product. These formulations qualify all the criteria which are a prime need in the manufacturing of sublingual tablet. Therefore, these formulations can be scaled up to confirm reproducibility and manufacture commercial batches.

REFERENCES

1. Aulton`s Pharmaceutics. The design and manufacture of medicines, Biopharmaceutics and pharmacokinetics, A Treatise, Valabh Prakashan. 2021; 315-384.
2. Ansel´s Pharmaceutical dosage forms & drug delivery systems. 2021; 227-260.
3. The Indian Pharmacopoeia. Ministry of Health and Family Welfare. India: Govt. of India. 2021; 134 (1).
4. Lachmann L, Liberman HA, Kaing JL. The theory and practice of Industrial Pharmacy. 2020; 293-303.
5. Rowe RC, Sheskey PJ, Owen SC. Handbook of Pharmaceutical Excipients. Pharmaceutical Press. 2020; 10.
6. Kulkarni AS, Ghadge DM, Kokate PB. Formulation and in vitro evaluation of orally disintegrating tablets of olanzapine-2-hydroxypropyl-β-cyclodextrin inclusion complex. Iran. J. Pharma. Res. 2019; 9:335-347.
7. Maheswarappa MK, Desai PD. Design and in-vitro evaluation of mouth dissolving tablets of olanzapine. Asian J. Pharm. 2019; 5:107-13.
8. Bhowmik D, Chiranjib B, Krishnakanth P, Chandira RM. Fast Dissolving Tablet: An Overview. Journal of Chemical and

Pharmaceutical Research. 2019; 1(1): 163-177.
9. Harding L, Qi S, Hill G, Reaing M, Craig DM. The development of micro thermal analysis and photothermal microspectroscopy as novel approaches to drug-excipients compatibility studies. Int. J. Pharm.2018; 354:149-157.
10. Manisha T, Garima C, Arvind KB. Quantification of olanzapine polymorphs using powder X-ray diffraction technique. J. Pharm. Biomed. Anal. 2007; 43:865-872.
11. Singhal R, Thakkar V, Srivastava A. Evaluation of Bioequivalence of Two Oral Formulations of Olanzapine. Indian J. Pharm. Sci. 2011; 73(6): 678–682.
12. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Stability Testing of New Drug Substances and Products. QIA (R2). 2003.
13. Mazzo DJ, Crowley PJ. International stability testing. Buffalo Grove: Inter pharm. Press Inc. 1999.