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FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLETS OF NITROGLYCERIN BY USING FLAX SEED POWDER AS SUPERDISINTEGRANT

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ABSTRACT
The aim of the present research work were to formulate and evaluate the fast disintegrating tablets (sublingual) of Nitroglycerin by using the Flax seed mucilage extract powder. Now a days, the drug delivery system are becoming more difficult day by day, as pharmaceutical researchers dealing with new techniques for the better understanding of biochemical and physico-chemical properties to make their performance better. In the last 10 years, the fast disintegrating tablet (sublingual) demand has been increased, because of the pediatric patients and geriatric patients due to the problem of swallowing, and due to the properties of fastdisintegrating for the effective emergency treatment. The superdisintegrant used in this studywas flax seed mucilage extract powder and croscarmellose. The tablets of Nitroglycerin were evaluated for hardness, friability, disintegration time study.

KEYWORDS: Fast disintegrating tablets, Nitroglycerin, Flax seed mucilage extract powder, Croscormellose, superdisintegrant.

INTRODUCTION
The recent advancement made in novel drug delivery system, having the main objective to increase the effects and protection of the drug molecules by the preparation of a suitable dosage form used for the administration. The patients like disabled and mentally sick, pediatric, bedridden, geriatric including unexpected incidents of allergic attack and motion sickness thus, consequentially in more episodes of ineffective treatment and non-conformity.[1]

The fast disintegrating sublingual tablet is capable of directly absorption into systemic circulation to avoid first pass metabolism in the gut and liver, this is the main advantage of Fast disintegrating sublingual tablet. The fast disintegrating sublingual tablets have and excellent drugpenetration (absorption) to acquire high plasma drug concentration with a rapid onset of action, due to an additional merit, that is availability of sufficient amount of blood supply at the sublingual region and thin sublingual mucosa (about 190 µm compared to 500-800 µm of the buccal mucosa). The Nitroglycerin drug is the best example, which is used in the acute angina treatment.[2]

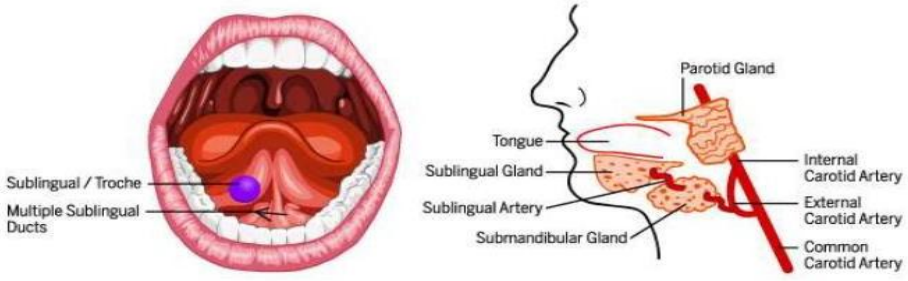


Figure 1: Sublingual Glands.[3]

The patients suffering from ischemic heart disease uses the Nitroglycerin and long time action producing nitrates are used from the oldest times. The Murrell, in 1879 was the first person, who administered the Nitroglycerin to a patient suffered from Angina Pectoris.[4]

The mitochondrial aldehyde dehydrogenase (mt ALDH) is responsible for the conversion of Nitroglycerin into nitric oxide (NO) and this nitric oxide act as an active substance which is responsible for activating the guanylate cyclase enzyme.[5] The guanylate cyclase enzyme is responsible for the synthesis of Cgmp (cyclic guancosine 3, 5- monophosphate) activating a flow of protein kinase dependent phosphorylation actions in smooth muscles. The dephosphorylation of the myosin light chain of smooth muscles is due the activation of flow of protein kinase – dependent phosphorylation responsible for increased and relaxed blood flow in veins, cardiac tissue and arteries.[6,7] These all above mentioned work is responsible for reduced blood pressure and reduced work of heart, liberation from angina sign and symptoms and the enhanced blood flow to myocardium.[8]

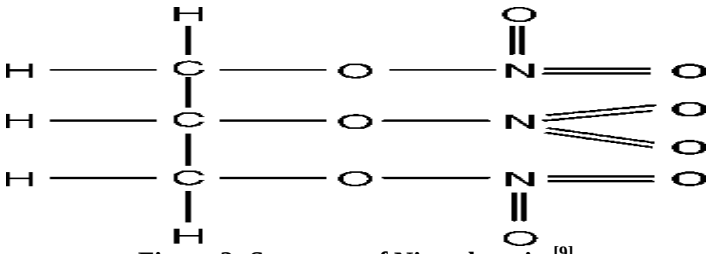


Figure 2: Structure of Nitroglycerin.[9]

Superdisintegrants

In the preparation of tablet, the disintegrating agents are the necessary thing to be added in the tablets, to enhances the breakdown of the compact mass to make easy release of primary content of the active pharmaceutical ingredients, when it is kept in a solvent or fluid. The disintegrating agent ratify the dispersion and penetration of moisture of the tablet.[10] To make the disintegration mechanism more better, new substance is introduced, which is known as "Superdisintegrant". Superdisintegrant are the new definition of the super-absorbing substances with modified swelling properties. The superdisintegrants does not have the nature to absorb large quantity of aqueous fluids or water but it is having fast and strong swelling property. They are substantially sinked within the medium of the tablet and will spread when the tablet is come in contact of wet environment.[11] The components of the superdisintegrants are generally porous and small, due to which the tablet will disintegrate rapidly in the mouth feeling. The friability and hardness of the tablet increased by the compressible particles of the superdisintegrant.[12] The 10-40 gram of water or any other aqueous can be absorbed by the 1 gram of superdisintegrant. After the absorption process, the stress concentrated area were developed by the particles of superdisintegrants due to the swelling pressure and isotropic swelling, where the mechanical properties inclined due to which the whole tablet will break down.

Classification of Superdisintegrants-

On the basis of availability, the superdisintegrants can be divided into two categories-

1-Synthetic Superdisintegrants.

2-Natural Superdisintegrants.

MATERIALS AND METHODS

Nitroglycerin IP (As a gift sample from Samarth Life Sciences Pvt. Ltd., Solan, Himanchal Pradesh and Bharat Pharma, Chandigarh), Flax seed (In pure form obtained from fields of Azamgarh, Uttar Pradesh), Crospovidone, Croscarmellose, Lactose IP, Naphthalene, Polyvinyl pyrrolidone, Magnesium Stearate, Talc of pure grade (obtained from SHEAT College of Pharmacy), Ethanol, Distilled Water were used. All ingredients were weighed as per requirement.

Preparation and Extraction of Flaxseed mucilage powder-Extraction

- For extracting the mucilage of flax seed, it was weighed in accurate amount.
- 250 gram of flax seed and 900 ml of distilled water were transferred in the 1000 ml of beaker.
- By continuous stirring, the above mixture was boiled for 7 hours and 50-60 ℃ of temperature were maintained due to which in distilled water, enough amount of mucilage were released.
- Until, the half quantity were obtained from the initial quantity the mixture were allowed to boil to get concentrated.
- The concentrated mixture were filtered and the marc were separated from filtrate with the help of muslin cloth and the filterate of flax seed were allowed to cool at 25℃.[13]

Isolation of Flaxseed Mucilage

- The ethanol were added in equal quantity for obtaining the precipitated mucilage of theextract.
- For the rapid precipitation of flax seed mucilage, the continuous stirring were performedat the time of addition of ethanol.
- The precipitated mucilage of flax seed mucilage were again treated against ethanol andcollected by

filtering through the muslin cloth.

- The obtained mucilage of flax seed were dried in hot air oven at 45℃, and hard mucilagecake of flax seed were obtained.
- The hard cake was then grinded and passed through sieve no. # 22.[14,15]

Fig. 3: Flax seed (Natural Superdisintegrant).

Fig. 4: The final mucilage of flaxseed.

Fig. 5: Powdered isolated mucilage of flaxseed.

Preparation of Nitroglycerine Fast Disintegrating Tablets

- All the ingredients were weighed and passed through sieve no. # 66 prior mixing to get uniformity.
- By using glass mortar and pestle, the flax seed mucilage extract powder, napthlene,crospovidone, croscarmellose were mixed with Nitroglycerin.
- Now, magnesium stearate and talc were added to the powder mixture.
- The mixture were compressed by using punching press and convex faced tablets ofnitroglycerin were formed.

Fig. 6: Granules with Croscarmellose.

Fig. 7: Granules with Flaxseed mucilage powder.

Fig. 8: Granules with Croscarmellose and flaxseed mucilage powder.

Fig. 9: FDT containing Croscarmellose.

Fig. 10: FDT containing Flaxseed extract.

Fig. 11: FDT containing Flaxseed extract and Croscarmellose.

Evaluation of Tablet

Hardness

By using Monsanto Hardness tester, the hardness of tablet were evaluated between the jaws ofthe tester, the tablet was placed vertically. With the help of screw gauge and spring the two jaws placed under the jaws. The pressure which is applied is measure in kg/cm, from the spring, by turning on the screw, the load were enhanced and collapsed.[16]

Friability

For testing the property of tablets to withstand abrasion

in packing, transporting and handling the friability test were used. The average friability percentage for all the formulations were found within the limits as per the standard.[17]

In vitro disintegration time

Due to the penetration of the saliva into the pores of tablets, the fast disintegrating sublingual tablet disintegrate rapidly, due to this penetration the particles of the superdisintegrant swells, and leads to enough hydrodynamic pressure for fast, quick and complete disintegration of the tablet. Flax seed mucilage extract powder when interact with water, the water will quickly wicks into tablet through the capillary action due to which internal pressure develops due to which tablet will disintegrates.[18]

In vitro dissolution Studies

By using USP dissolution apparatus-II, the in vitro drug release of the formulated batches were evaluated. The 900 ml of alkaline borate buffer (pH 8.4) at 37±0.5℃ were used for performing the dissolution test. The 100 rpm were the speed set for the rotation of paddle. At a decided time interval, 5 ml sample solution were withdrawn and Whatman filter paper were used to filter the sample solution.

RESULT AND DISCUSSION

By using wet granulation technique nine formulation of Nitroglycerine were formulated. The Flax seed mucilage extract powder were used as a natural superdisintegrant. Polyvinyl pyrrolidone were used as a binder. All the tablet from each preparation is gone through with various test, such as hardness test, friability, in vitro disintegration time, and in vitro dissolution test. The Lactose were selected as a soluble diluents and Naphthalene is used as a sublimating agents due to its porosity increasing property, Thus, all properties proves that, flax seed mucilage extract powder is a good superdisintegrant.

Table 1-Formulation composition of Nitroglycerin FDT Tablet

Table 1.1- Formulation composition of Nitroglycerin FDT Tablet containing Flaxseed.

Ingredients	T1	T2	T3
Nitroglycerin	0.3 mg	0.4 mg	0.6 mg
Flax seed mucilage extract powder	3 mg	3 mg	3 mg
PVP	2 mg	2 mg	2 mg
Lactose	5 mg	10 mg	15 mg
Magnesium stearate	5 mg	5 mg	5 mg
Naphthalene	2 mg	2 mg	2 mg
Talc	2 mg	2 mg	2 mg

Table1.2-Formulation composition of Nitroglycerin FDT Tablet containing Croscarmellose.

Ingredients	T4	T5	T6
Nitroglycerin	0.3 mg	0.4 mg	0.6 mg
Croscarmellose	3 mg	3 mg	3 mg
PVP	2 mg	2 mg	2 mg
Lactose	5 mg	10 mg	15 mg
Magnesium stearate	5 mg	5 mg	5 mg
Naphthalene	2 mg	2 mg	2 mg
Talc	2 mg	2 mg	2 mg

Table 1.3: Formulation composition of Nitroglycerin FDT Tablet containing Flaxseed powder and Croscarmellose.

Ingredients	T7	T8	T9
Nitroglycerin	0.3 mg	0.4 mg	0.6 mg
Croscarmellose	3 mg	3 mg	3 mg
PVP	2 mg	2 mg	2 mg
Lactose	5 mg	10 mg	15 mg
Magnesium stearate	5 mg	5 mg	5 mg
Naphthalene	2 mg	2 mg	2 mg
Talc	2 mg	2 mg	2 mg
Flax seed mucilage extract powder	3 mg	3 mg	3 mg

Table 2: Hardness of Nitroglycerin FDT Tablet.

S. No.	Tablet (T)	Hardness (kg/cm^2)
1	T1	3.05 kg/cm^2
2	T2	3.2 kg/cm^2
3	T3	4.2 kg/cm^2
4	T4	3.51 kg/cm^2
5	T5	3.7 kg/cm^2
6	T6	4.2 kg/cm^2
7	T7	4.1 kg/cm^2
8	T8	3.08 kg/cm^2
9	T9	4.52 kg/cm^2

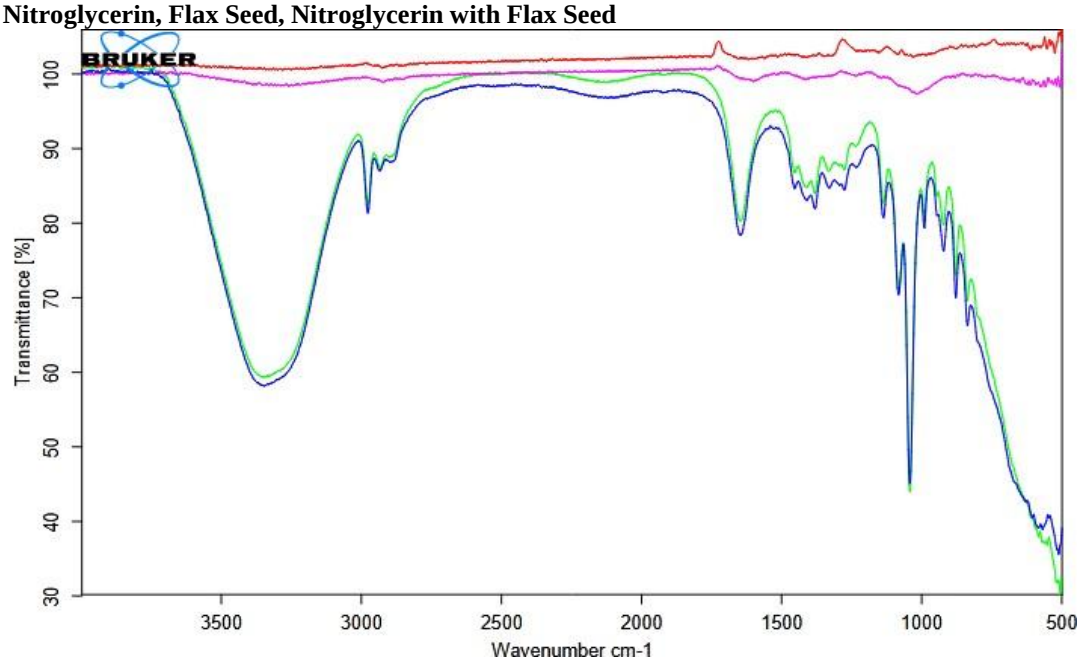
Table 3: Friability Test of Nitroglycerin FDT Tablet.

S. No	Tablet (T)	Friability (%)
1	T1	0.85
2	T2	0.60
3	T3	0.88
4	T4	0.15
5	T5	0.52
6	T6	0.20
7	T7	0.90
8	T8	0.75
9	T9	0.80

Table 4- In-vitro Disintegration TimeNitroglycerin FDT Tablet.

S No.	Tablet (T)	Time (seconds) Mean ± SD, where n=3
1	T1	10 ± 0.55
2	T2	12 ± 0.55
3	T3	10 ± 0.58
4	T4	8 ± 0.52
5	T5	14 ± 0.56
6	T6	11 ± 0.58
7	T7	12 ± 0.50
8	T8	7 ± 0.57
9	T9	11 ± 0.32

FTIR of Nitroglycerin, Flax Seed, Nitroglycerin with Flax Seed



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CONCLUSION

From this present research work we had concluded that, the flax seed mucilage extract powder is a better superdisintegrant and can be used in Fast disintegrating sublingual tablets to reduce the disintegration time such as Nitroglycerin sublingual FDT tablets. The natural superdisintegrant is effective and affordable and having less adverse effects in comparison of synthetic one.

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