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Original Research Article

DESIGN, DEVELOPMENT AND EVALUATION OF FAST DISSOLVING TABLET OF TIZANIDINE USING FENUGREEK SEED MUCILAGE

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Abstract

The demands for fast dissolving tablets have received ever increasing day by day during the last decade. In the present projected study, the effect of natural superdisintegrant was compared with synthetic super disintegrants and conventional super disintegrants in the of fast dissolving tablet formulation of tizanidine Hcl. Tizanidine Hcl is a potent muscle relaxant which management of increased muscle tone associated with spasticity. In the present work 12 formulations of FDT (Fast dissolving tablet) of tizanidine were prepared by using isolated mucilage of fenugreek seed was evaluated and compiles with the official parameters and specifications. Various formulations were prepared using four different superdisintegrsnts namely- fenugreek seed mucilage, kyron T-104, sodium starch glycolate, cross carmelose sodium with three concentrations (5%, 10%, 15%) by direct compression method.

The blend was evaluated for pre-compression parameters like Angle of repose, bulk density, tapped density, and then tablet evaluated post-compression parameters like thickness, drug content, hardness, weight variation, wetting time, friability, disintegration time, dissolution time, drug release study. The best formulations were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline.

Keywords: Muscle relaxant, Tizanidine Hcl, fenugreek seed Mucilage, dissolution time

INTRODUCTION

The tablet is most widely used dosage for because of its convenience in term of self-administration, compactness, accurate dosage and ease in manufacturing. Over this one drawback of conventional tablet is difficulty in swallowing by pediatric and geriatric patients.[1-4]

Tizanidine Hcl is an imidazole derivative acting as agonist on centrally located alpha 2 receptor has myotonolytic effects on skeletal muscles. TizanidineHcl may also be used adjunct to NSAIDS in the treatment of analgesic rebound headache.TizanidineHCl (tizanidine) is off-white, fine crystalline, odorless powder in nature.[5-10]

MATERIAL AND METHOD:

MATERIAL:

Tizanidine Hcl was received as gift sample by IPCA labs, Mumbai, and other reagents and chemicals used were of analytical grade.

METHOD:

Fast dissolving tablet of Tizanidine HCL were prepared by direct compression method. Pure drug and excipients were passed through # 60 No. mesh, Required amount of drug and excipients were taken for every formulation (Table No. 1). The powdered drug, Mannitol and Lactose were mixed uniformly with continuous trituration using mortar and pestle. Then required quantity of super disintegrates and aspartame taken for each formulation and mixed, finally magnesium stearate and talc powder were added and mixed well. The mixed blend of drug and excipients were compressed using 10 station tablet punching machine. A Batch of 50 tablets of each formulation was prepared for all the designed formulation. Before the tablet preparation /punch the mixture blend of all designed formulations were subjected to compatibility studies (IR) and pre-compression parameters like- Angle of repose, Bulk density, Tapped density, compressibility index, Hauser's ratio.[11]

Pre-formulation studies:

Angle of Repose (θ):

Angle of repose is defined as, the maximum possible angle between the surface of the pile of the powder and the horizontal plane of the powder. When more quantity powder is added to the pile, it slides down, until the mutual friction of the particles producing a surface angle θ, is equilibrium with the gravitational force.[12]

Bulk Density:

Density defined as weight per unit volume. Bulk density is defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/ cm3.

Low bulk density

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

High bulk density:

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density

Tapped Density (Dt):

It was the ratio indexof total mass of the powder to tapped volume of the powder. Volume was reported by tapping the powder for 500 times and the tapped volume was recorded, if the difference between these two volumes was less than 2%. If it more than 2%, then tapping was continued for 750 times and tapped volume was noted.[13]

Carr's index (or) % compressibility:

Carr's index indicates powder flow properties. It is expressed by percentage and is given by:

$I=Dt-Db/Dt\times100$ Where, Dt denotes the tapped density of the powder

And Db is the bulk density of the powder. [14]

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

Hausner ratio=Dt/Db, Where, Dt show the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)[15]

EVALUATATION OF TABLET:

All prepared tablets of Tizanidine HCL were evaluated for the following parameters as per IP guideline; all the calculations are represented in the table No.3

WEIGHT VARIATION:

Twenty tablets of Tizanidine HCL formulation were selected randomly from each of the formulation and weighted individually using Citizen Digital Balance for their weight data. The average weight of the tablets as well as percentage deviation was calculated.[16]

HARDNESS:

Hardness of the Tizanidine HCL tablet was measured with the tablet hardness testing apparatus known as Monsanto tablet harness tester.

THICKNESS:

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.[17]

FRIABILITY:

The friability of the Tizanidine HCL tablet, a sample of twenty tablets was measured using USP type Roche Friabilator. The tablets were dusted reweighed and percentage weight-loss was calculated. (25-26)

%Friability= Initial Weight−Final Weight * 100/ Initial Weight

Water absorption ratio:

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in small Petri-plate (ID = 6.5 cm) containing 10 ml of water. A tablet was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three trials for each batch were performed and the standard deviation was also determined. The wetted tablet was weighed and water absorption ratio R, was determined by following equation

$R = \{(Wa – Wb) / Wa\} \times 100$

Where, Wa and Wb were weights of the tablets after and before study.[18]

Wetting Time

A piece of tissue paper (12cmX10.75cm) folded twice was placed in a small Petri dish (ID = 9 cm) containing 6ml pH 6.8 phosphate buffer, A tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted.[19]

DISINTEGRATION STUDY:-

Disintegration time study was carried out by selecting 6 tablets of Tizanidine HCL and performed disintegration test (Lab India) using 900 ml distilled water at temperature (370C±20C)[20]

DISSOLUTION STUDY:

The In-vitro for the dissolution study was carried out in the USP (United states pharmacopeia) dissolution test apparatus type 2 known as Paddle dissolution apparatus, used phosphate buffer as dissolution medium as 900 ml containing PH 6.8 was taken in vessel and the temperature maintained at 37±0.50C.[21]

RESULTS AND DISCUSSION:

Bulk density and tapped density of powder blend has been evaluated. The angle of repose for the entire formulations blend was found to be in the range 24.19 to 26.53°. Formulations with Crosscarmelose Sodium (FCCS1-FCCS3) as a disintegrant showed angle of repose values ≤ 25.32o. Other the formulation Sodium Starch Glycolate containing (FSSG4-FSSG6) was showed angle of repose values <25.11o, Fenugreek seed mucilage (FF7-FF9) was showed angle of repose values ≤25.32o and last one formulation with Kyron T-104 showed Angle of repose values 26.53 indicating only fair flow property of the powder blend. Compressibility index was found to be in the range 14.20 % to 16.89 %. All formulations showed good flow properties. Hausner‟s ratio was found to be in the range 1.10 to 1.18 and that indicated that all formulation has good flow properties. The batches FF8, showed low hardness and FF9 higher (3.20±0.28kg/cm2). Higher friability FSSG6 and low friability FF9 (0.38%). From all the above observations it was concluded that the formulation FF8 containg Fenugreek seed mucilage 10% found to be better formulation in terms of rapid dissolution (85%) and but maximum percentage drug release was found 98.64 of formulation FF8, with fenugreek 10%.

CONCLUSION:

It can be concluded from the whole study that fast dissolving tablets of Tizanidine drug. Natural Superdisintegrants can be used as pharmaceutical excipients for oral drug delivery. It was concluded formulation FF8 maximum percentage drug release was found 98.64, with fenugreek 10%.

From the study, it was concluded that Natural Super disintegrate like Fenugreek seed mucilage showed better disintegrating property over the synthetic super disintegrate like, SSG(Sodium starch glycolate) CCS (Crosscarmelose Sodium) and Kyron T-104. Hence the fenugreek mucilage can be used at higher concentration at it has advantage of being non-toxic, low cost, biodegradable and biocompatible with no side effect.

Table 1: Formulation of fast-dissolving tablet of Tizanidine HCL

Ingredients (mg)	FCCS1	FCCS2	FCCS3	FSSG4	FSSG5	FSSG6	FF7	FF8	FF9	FK10	FK11	FK12
Tizanidine HCL	8	8	8	8	8	8	8	8	8	8	8	8
Cross carmellose Sodium	7.5	15	22.5	-	-	-	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	7.5	15	22.5	-	-	-	-	-	-
Fenugreek seed mucilage	-	-	-	-	-	-	7.5	15	22.5	-	-	-
Kyron T-104	-	-	-	-	-	-	-	-	-	7.5	15	22.5
Aspartame	2	2	2	2	2	2	2	2	2	2	2	2
Flavour	2	2	2	2	2	2	2	2	2	2	2	2
Talc	6	6	6	6	6	6	6	6	6	6	6	6
Magnesium Stearate	6	6	6	6	6	6	6	6	6	6	6	6
Mannitol	30	30	30	30	30	30	30	30	30	30	30	30
Lactose	35	30	25	35	30	25	35	30	25	35	30	25
MCC	30	35	40	30	35	40	30	35	40	30	35	40
Sorbitol	23.5	16	9	23.5	16	9	23.5	16	9	23.5	16	9
TOTAL	150	150	150	150	150	150	150	150	150	150	150	150

Table 2: Pre-compression parameters of Tizanidine HCL FDTs

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose 0
$FCCS_1$	0.591±0.12	0.621±0.11	1.180±0.05	14.25±0.15	24.19±1.38
$FCCS_2$	0.521±0.11	0.616±0.69	1.100±0.09	15.89±0.23	25.32±1.35
$FCCS_3$	0.531±0.18	0.495±0.54	1.101±0.19	16.28±0.28	24.45±1.40
$FSSG_4$	0.551±0.17	0.642±0.22	1.171±0.15	14.87±0.55	24.52±0.55
$FSSG_5$	0.540±0.05	0.592±0.29	1.161±0.19	15.98±0.63	25.11±1.25
$FSSG_6$	0.551±0.11	0.692±0.27	1.175±0.58	16.89±0.89	24.19±1.89
FF_7	0.501±0.15	0.551±0.10	1.170±1.01	15.05±0.25	25.29±0.15
FF_8	0.500±0.01	0.561±0.19	1.171±1.12	15.10±0.55	25.20±0.29
FF_9	0.502±0.12	0.591±0.11	1.161±1.14	14.20±0.56	25.32±1.11
FK_{10}	0.531±0.15	0.621±0.18	1.181±0.15	15.82±0.59	25.54±1.65
FK_{11}	0.551±0.19	0.511±0.11	1.161±1.13	15.25±0.98	26.53±1.57
FK_{12}	0.541±0.17	0.519±0.99	1.171±1.18	15.25±0.67	25.11±1.97

Table 3: Post-Compression parameters of Tizanidine HCL FDTs:

Parameters Formulation	Diameter (mm)	Thickness (mm)	Weight (mg)	Hardness (Kg/cm^2)	Friability (%)	Disintegration Time (Sec)	Swelling Time (Sec)
$FCCS_1$	4	3	154.05±0.55	3.05±0.15	0.48±0.84	44±1.44	15±1
$FCCS_2$	4	3	145.07±0.78	3.09±0.01	0.59±0.25	39±1.14	14±2
$FCCS_3$	4	3	147.01±0.11	3.14±0.99	0.57±0.17	45±1.46	16±1
$FSSG_4$	4	3	152.02±0.25	3.10±0.12	0.51±0.16	63±1.25	21±1
$FSSG_5$	4	3	154.01±0.11	3.08±0.01	0.69±0.12	69±1.52	22±2
$FSSG_6$	4	3	152.05±0.15	3.20±0.10	0.75±0.32	49±1.36	17±2
FF_7	4	3	150.01±0.15	3.15±0.05	0.65±0.13	31±1.01	13±2
FF_8	4	3	150.00±0.04	3.01±0.09	0.62±0.23	30±1.59	12±2
FF_9	4	3	147.02±0.22	3.20±0.28	0.38±0.19	33±1.58	13±8
FK_{10}	4	3	146.09±0.19	3.16±0.29	0.60±0.15	57±1.54	20±3
FK_{11}	4	3	151.02±0.23	3.15±0.25	0.52±0.16	49±1.22	17±2
FK_{12}	4	3	147.08±0.82	3.10±0.29	0.71±0.11	50±1.36	18±1

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