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Original Review Article

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF HYOSCINE BUTYLBROMIDE

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Abstract

In present scenario, the drug delivery system has become highly competitive and rapidly most evolving with ever increasing demand. Fast dissolving tablet (FDT) is such type of a novel and unique drug delivery system which is intensely gaining much attention in the research field of rapid dissolving technology.

In the present projected study, the effect of natural Super disintegrants in the of fast dissolving tablet formulation of Hyoscine Butylbromide is carried out Butylscopolamine**,** also known as HBB is a peripherally acting antimuscarinic, anticholinergic agent. It is used in treatment of pain and discomfort caused by abdominal cramps, menstrual cramps, or any other spasmodic activity in the digestive system. In the present work 9 formulations of FDT (Fast dissolving tablet) of Hyoscine Butylbromide were prepared by using Super disintegrants was evaluated and compiles with the official parameters and specifications. Various formulations were prepared using different super disintegrants with three concentrations (2%, 4%, 6%) by direct compression method. The mixed blend was evaluated for pre-compression parameters like Angle of repose, bulk density, tapped density, and then tablet evaluated with various post-compression parameters like thickness, drug content, hardness, weight variation, wetting time, friability, disintegration time, dissolution time, drug release study. Formulation F5 showed 98.50% drug release at the end of 3 minutes. The best formulations among these were also found to be stable and optimized formulations were subjected to the stability studies as per ICH guideline.

KEYWORDS: Fast dissolving tablets (FDT), Super disintegrants, Hyoscine Butylbromide (HBB), sodium starch glycolate, Dysphagia, Bioavailability, direct compression, dissolution time, Evaluation.

INTRODUCTION

The tablet is most widely used dosage form because of its convenience in term of self-administration, compactness, accurate drug dose and ease in manufacturing. Over this preference, these have one drawback of conventional tablet is difficulty in swallowing by pediatric and geriatric (old age) patients.[1-2]

Hence, to overcome these problems, fast disintegration tablets have started which gaining popularity and acceptance as new drug delivery systems aim for providing the safety of a drug molecule because they are easy to administer and lead to better patient compliance. The fast dissolving defined as the tablets that dissolve in few seconds in the mouth when they come with contact saliva without requirement of additional water. The major advantage of FDT is onset of action, higher patient acceptance, and increased bioavailability.[3-4]

Hyoscine butylbromide, also known as scopolamine butylbromide[5] and sold under the brandname Buscopan. Hyoscine Butylbromide among others, is an antispasmodic and anticholinergic agent used for the symptomatic treatment of abdominal cramping and pain. Particularly, it helps to ease bloating and the spasm-type pain that can be associated with irritable bowel syndrome. It works by relaxing some of the muscles in your gastrointestinal tract and urinary systems.[6-7]

Butylscopolamine is a peripherally acting antimuscarinic, anticholinergic agent. It is used in treatment of pain and discomfort caused by abdominal cramps, menstrual cramps, or any other spasmodic activity in the digestive system. It is not a pain medication in the normal sense, since it does not directly affect pain, but rather works to prevent painful cramps and spasms from occurring.[8-9]

Scopolamine butylbromide binds to muscarinic M3 receptors in the gastrointestinal tract. This prevents acetycholine from binding to and activating the receptors which would result in contraction of the smooth muscle. The inhibition of contraction of the smooth muscle reduces spasms and their related pain during abdominal cramping.[10]

Scopolamine butylbromide has extremely low oral bioavailability with only 0.25-0.82% reaching systemic circulation. Peak plasma concentration is reached 0.25-2 hours. Scopolamine butylbromide does not cross the blood brain barrier. However, because of its high tissue affinity for muscarinic receptors, hyoscine butylbromide remains available at the site of action in the intestine and exerts local spasmolytic effect.[11-13]

MATERIALS AND METHOD

Materials

Hyoscine Butylbromide was received as gift sample by Cipla Limited, Mumbai; Magnesium stearate used were procured from S.D. Fine Chemie., Mumbai; Lactose used was procured from Central Drug House (P) Ltd., Mumbai; Kyron T-314 was procured by Corel Pharma Chem, Gujrat, Aspartame used was procured from Sweetener India, Delhi, and other reagents and chemicals used were of analytical grade.

Method

Fast dissolving tablet of Hyoscine Butylbromide were prepared by direct compression method. Pure drug (api) 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 pestle and mortor. Then weighed quantity of super disintegrates and aspartame taken for each formulation and properly mixed, finally magnesium stearate and talc powder were added and mixed well. The mixure blend of drug and excipients were compressed using 10 station tablet punching machine. (Shakti pharmaceuticals**)**. A Batch consisting of 50 tablets of each formulation was prepared for all the designed tablet formulations. 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.[11-13]

Pre-formulation studies: -

Angle of Repose (θ):

The angle of repose is determined by the funnel method suggested by scientist Newman. Angle of repose is determined by the following formula[14]

Tan θ = h/r

θ = Tan-1 h/r

Where θ = Angle of repose, r = Radius of the cone, h = height of the cone

Bulk Density:

Density defined as weight per unit volume. Bulk density can be defined as the mass of the powder is divided by the bulk volume of powder and is expressed as gm/ cm3.[15]

Tapped Density (Dt): 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%. It was expressed in g/ml and was given as following,[16]

Dt= M/Vt

Where, M = mass of powder, Vt = tapped volume of the powder.

Carr's index (or) % compressibility:

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

I=Dt−Db/Dt×100

Where, Dt = tapped density of the powder, And Db = bulk density of the powder.[17]

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 = tapped density, Db = bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).[18-20]

Evaluation of Tablets:

All prepared tablets of Hyoscine Butylbromide 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 Hyoscine Butylbromide 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 calculated was found in standard range.[21]

Hardness

Hardness of the Hyoscine Butylbromide tablet was measured with the tablet hardness testing apparatus known as Monsanto tablet harness tester.[22]

Thickness

The thickness of the tablet was measured in mm by the Vernier Calipers for all the designed formulation batches.[23]

Friability

The friability of the Hyoscine Butylbromide tablet, a sample of twenty tablets was measured using USP type Roche fraibilator. The tablets reweighed and percentage weight-loss was calculated, was found in standard range.[24]

% 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 of every batch was placed on the paper and time for complete wetting of the tablet was measured in seconds. Three random 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} × 100

Where, Wa and Wb were weights of the tablets after and before study.[25]

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 then the average wetting time was noted.[26]

Disintegration Study

Disintegration time study was carried out by selecting 6 tablets of Hyoscine Butylbromide and performed disintegration test using 900 ml distilled water at temperature (370C±20C)[27]

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 as per standard guidelines. The speed of the dissolution apparatus paddle was set at RPM 50, then 5 ml dissolution medium was withdrawn and the same amount (5ml) of fresh medium was replenished to the dissolution medium. The calculations of the Concentration were calculated by absorbance base. The release of the drug formulation was performed in replicates of three .[28]

Table 1: Hyoscine butylbromide Fast Dissolving Tablets by direct compression method

Ingredients(mg)	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8	FL9
Hyoscine Butylbromide	8	8	8	8	8	8	8	8	8
Crosscarmellose Sodium	3	6	9	-	-	-	-	-	-
Kyron T-314	-	-	-	3	6	9	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	3	6	9
Aspartame	3	3	3	3	3	3	3	3	3
Flavour	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Mannitol	40	40	40	40	40	40	40	40	40
Lactose	45	45	45	45	45	45	45	45	45
MCC	42	39	36	42	39	36	42	39	36
TOTAL	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Result and Discussion

Table 2: Pre-compression parameters of Hyoscine Butylbromide FDTs

Parameters / Formulation	Bulk Density (mg/ml)	Tapped Density (mg/ml)	Hausners Ratio	Compressibilty Index (%)	Angle of Repose 0
FL_1	0.461±0.011	0.511±0.015	1.108±0.090	09.78±0.15	24.11±1.38
FL_2	0.463±0.031	0.523±0.011	1.129±0.089	11.47±0.03	25.22±1.35
FL_3	0.455±0.017	0.516±0.013	1.134±0.019	11.82±0.18	24.25±1.40
FL_4	0.471±0.014	0.539±0.011	1.144±0.015	12.61±0.05	24.47±0.55
FL_5	0.482±0.011	0.551.±0.012	1.143±0.021	12.52±0.03	28.01±1.25
FL_6	0.481±0.021	0.561±0.016	1.166±0.025	14.26±0.19	24.29±1.17
FL_7	0.468±0.19	0.525±0.015	1.121±0.019	10.85±0.15	25.39±0.15
FL_8	0.465±0.018	0.535±0.013	1.150±0.0.29	13.08±0.05	26.25±0.29
FL_9	0.485±0.011	0.574±0.012	1.183±0.025	15.50±0.16	24.42±1.10

Table 3: Post-Compression parameters of Hyoscine Butylbromide FDTs

Formulation	Weight (mg)	Hardness (Kg/cm^2)	Friability(%)	Disintegration Time(Sec)	Swelling Time(Sec)
FL_1	155.05±0.51	4.15±0.15	0.51±0.24	58±1.24	15±1
FL_2	145.57±0.71	3.11±0.01	0.55±0.21	42±1.14	14±2
FL_3	148.01±0.15	3.31±0.09	0.56±0.17	55±1.26	16±1
FL_4	153.02±0.21	3.55±0.12	0.51±0.15	53±1.25	21±1
FL_5	149.19±0.19	3.51±0.01	0.62±0.12	40±1.22	13±2
FL_6	154.05±0.35	3.29±0.10	0.71±0.32	49±1.31	17±2
FL_7	146.01±0.15	3.35±0.05	0.63±0.13	65±1.01	13±2
FL_8	155.50±0.04	3.50±0.09	0.62±0.20	42±1.19	22±2
FL_9	152.02±0.21	3.40±0.18	0.68±0.11	41±1.18	13±1

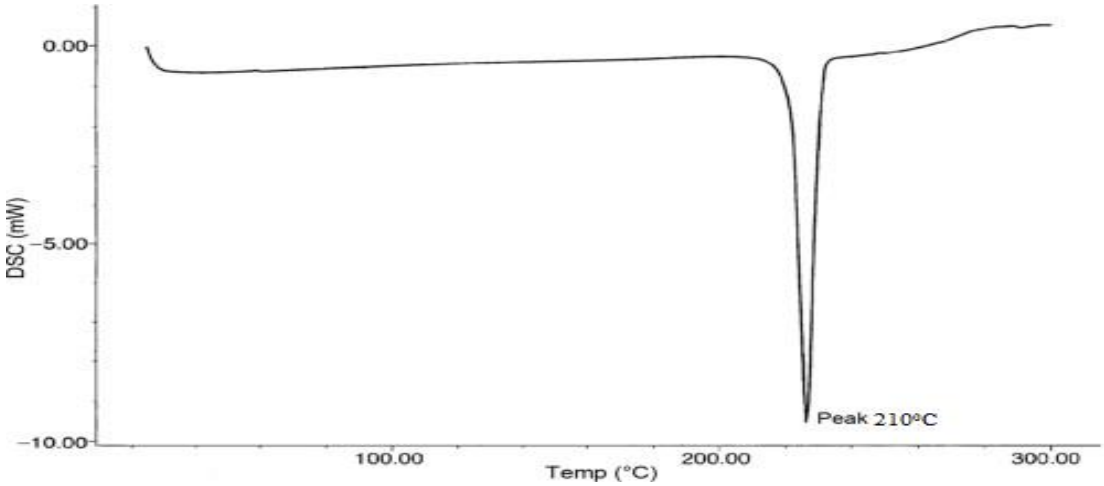

Figure 1: DSC Thermogram of Hyoscine Butylbromide

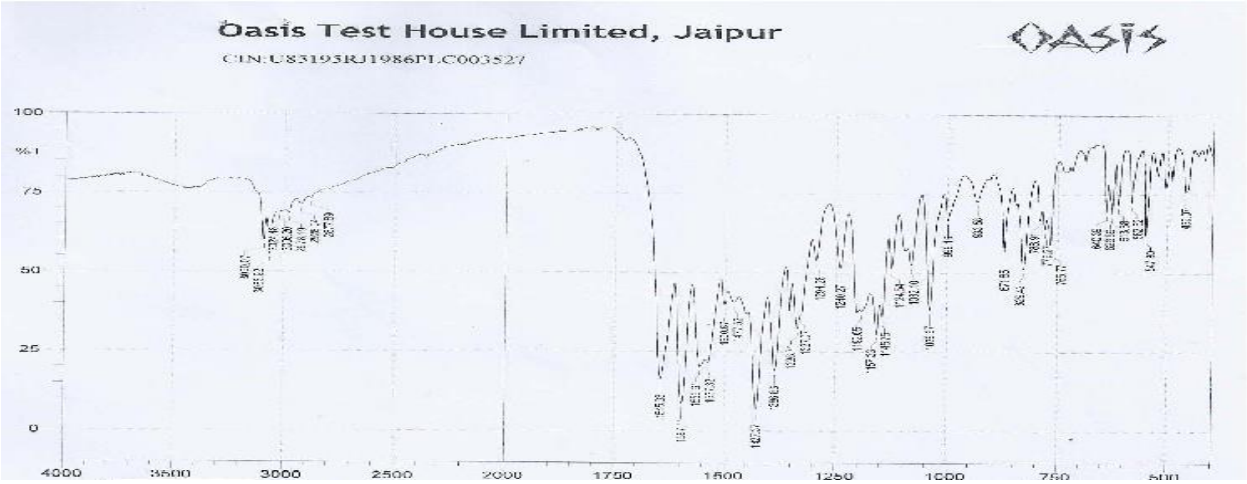

Figure 2: IR spectra of Hyoscine Butylbromide

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 $28.11^{0.}$ Formulations with Super disintegrants (Kyron T 314) (F4-F6) as a disintegrate showed angle of repose values below then 30^0 showed good to excellent flow properties of powder. Other the formulation Sodium Starch Glycolate containing (F7-F9) was showed angle of repose values <35.12o and last Cross carmelose sodium (F1-F3) was showed angle of repose values ≤30.20o indicating only fair flow property of the powder blend. Compressibility index was found to be in the range between 09.07% to 15.23%. Hausner's ratio was found to be 1.177 or less indicating the good flowability. The batches showed low hardness 3.09 and higher 3.50. F6 shows Higher friability and F3 show low friability (0.45%).

All parameters show weight variation, thickness, Disintegration time (sec) within standard limit. All formulation was subjected to dissolution. From all the above observations it was concluded that the formulation F5 contain Kyron T 4% found to be better formulation in terms of rapid dissolution and but maximum

percentage drug release was found 98.50% of formulation F5, with Kyron T (4%).

Conclusion

It can be concluded from the whole study that fast dissolving tablets of Hyoscine Butylbromide drug. Superdisintegrants like Kyron T exhibited faster drug dissolution which leads to improve bioavailability, effective therapy (Therapeutic ratio), improve patient compliance, and satisfies all the standards as fast dissolving tablet. It was concluded formulation F5 maximum percentage drug release was found 98.50%, with Kyron T.

From the study, it was concluded that Superdisintegrants Kyron T showed better disintegrating property over the other super disintegrate like, SSG (Sodium starch glycolate) and CCS (Cross Carmellose Sodium). Hence the Kyron T can be used at higher concentration at it has advantage of being non-toxic, low cost, biodegradable and biocompatible with no side effect.

Table 4: Drug Content in the Fast-Dissolving Tablet of Hyoscine Butylbromide

Parameters Formulation	Drug Content (mg per tablet)	% Drug Content
FL_1	140.51±0.02	93.67
FL_2	142.83±0.04	95.22
FL_3	141.65±0.12	94.43
FL_4	145.25±0.13	96.83
FL_5	147.75±0.15	98.50
FL_6	146.27±0.21	97.51
FL_7	143.23±0.18	95.48
FL_8	145.14±0.14	96.76
FL_9	144.85±0.20	96.38

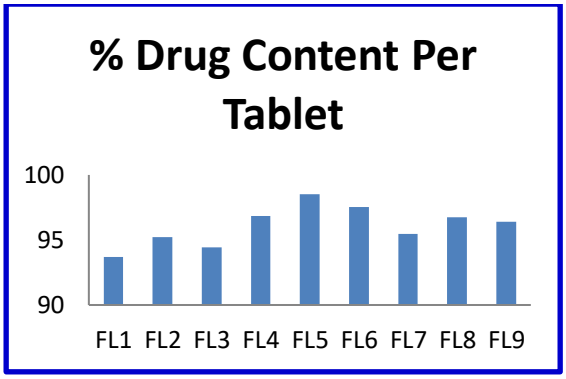

Figure 3: Drug Content in the Fast-Dissolving Tablet of Hyoscine Butylbromide

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