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Research article

Formulation and Evaluation of Trihexyphenidyl HCl Fast Dissolving Tablets

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Abstract

The main objective of the present study was aimed to formulate and evaluate fast dissolving tablets by direct compression method using Trihexyphenidyl hydrochloride as a model drug. Fast dissolving tablets of Trihexyphenidyl hydrochloride formulated using different concentration of super-disintegrants like sodium starch glycolate and crospovidone. All the prepared tablets were evaluated for pre & post compression and in vitro dissolution studies. Drug-excipients interactions of optimized were evaluated by FT-IR study. The formulation prepared with sodium starch glycolate as super disintegrants in the concentration of 6%w/w (F8) shows rapid disintegration and 99.9% of drug released within 35 min when compared with other disintegrants used in. All the formulations were subjected to kinetics study and fitted to Higuchi model explaining the diffusion controlled release mechanism.

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Key Words
Trihexyphenidyl HCl
Pre-gelatinized starch
Fast dissolving tablet
Superdisintegrants

INTRODUCTION

Fast dissolving technology is one of the best opportunities to improve bioavailability, immediate relief and patient compliance in comparison to conventional tablets. Fast dissolving drug delivery can be achieved by various conventional methods like direct compression, wet granulation, spray drying, freeze drying and sublimation. In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable or brittle, which are difficult to handle, often requiring specialized peel off blister packaging. Fast dissolving tablets disintegrate or dissolve rapidly in the saliva without the need for water[1-2]. They contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. When put on the tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach[3-4].

Trihexyphenidyl HCl was used as an anti-Parkinson's agent and indicated for the management of all forms of Parkinsonism. It is also often used as an adjuvant therapy, when treating the Parkinsonism with Levodopa. It is white, crystalline powder and slightly soluble in water, sparingly soluble in alcohol and in methylene chloride and oral administration is well absorbed from gastrointestinal tract. Peak plasma concentration was reached[5] 3-5 h following oral dosing and it has got elimination half life[6] of 6-12 h. On the basis of these considerations, in the present study, it was proposed to formulate an oral delivery device, in the form of rapidly dissolving tablets by using direct compression technology, with the aim of reaching a high serum concentration in a short period of time using different super-disintegrants.

MATERIALS AND METHODS

Materials

Trihexyphenidyl hydrochloride was procured gift sample from NATCO Pharma Ltd. Hyderabad (AP). Pharmatose, Cross povidone, pregelatinised starch, microcrystalline cellulose, Magnesium sterate, Sodium starch glycolate, was purchased from S.D. Fine Chem. Ltd., Mumbai.

Methods

Preparation of fast dissolving tablets by direct compression technique [7]

All the formulation compositions as given in table 1 were passed through 40 mesh sieve individually. The drug and microcrystalline cellulose was mixed by small portion of both each time and blending it to get a uniform mixture kept aside. Then other ingredients were weighed and mixed in geometrical order and tablets were compressed of 11mm sizes flat round punch to get tablet by using REMEC compression Machine.

Tab 1. Formulation composition of Trihexyphenidyl HCl FDTablets

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8
Ingredients								
THP HCl (mg)	5	5	5	5	5	5	5	5
MCC (mg)	339.95	329.95	342.75	225	223.75	345.62	343.20	343.75
PGS (mg)	-	-	-	18.75	13.54	-	-	-
Aerosil (mg)	-	-	1.0	1.875	2.09	-	-	-
Pharmatose (mg)	-	-	-	107.5	97.5	-	-	-
CP (mg)	6.3	6.3	6.3	-	-	-	-	-
Mg St (mg)	3.75	3.75	3.75	1.875	3.12	1.875	4.3	3.75
SSG (mg)	20	30.0	22.5	15.0	30.0	22.5	22.5	22.5
Total (mg)	375	375	375	375	375	375	375	375

THP HCL=Trihexyphenidyl hydrochloride, MCC=Microcrystalline cellulose, PGS=Pregelatinised starch, CP=Crospovidone, SSG=Sodium starch glycolate, Mg St= Magnesium sterate

COMPATIBILITY STUDY

FTIR Studies

IR spectra of Trihexyphenidyl hydrochloride and its formulation were obtained by KBr pellet method using Perkin Elmer spectrum RX1 FT-IR Spectrophotometer model.

PRECOMPRESSION PARAMETERS

The prepared powder blend was evaluated for various parameters[8-14] like bulk density, tapped density, angle of repose, compressibility index and Hausner's ratio. The results are presented on table 2.

POSTCOMPRESSION PARAMETERS

The prepared tablets were evaluated for[14- 17] weight variation, hardness, friability, Disintegration time, wetting time, water absorption ratio and drug content studies.

Disintegration time [18]

The in-vitro disintegration time of a

tablet was determined using disintegration test apparatus as per I.P. specifications. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at 37±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37±2°C. The time in sec taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

Wetting time [18]

In wetting time a piece of tissue paper folded twice was placed in a small Petri dish (i.d = 6.5cm) containing 10mL of water, a tablet was placed on the paper, and the time for complete wetting was measured. The wetted tablet was then weighed and water AR was determined according to Equation:

$AR = (W_a - W_b)/W_b$

where W_a and W_b are the tablet weights after and before wetting.

In-vitro release studies [19-20]

In vitro release study was conducted by using USP type-II apparatus. Paddle speed was maintained at 50rpm and 900mL of pH 4.5 acetate buffer was used as the dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C; aliquot of dissolution medium was withdrawn at predetermined time intervals and filtered. The absorbance of filterate was measured by UV spectrophotometrically at 250nm. Further, various kinetic models such as Zero order, First-order, Higuchi, and Korsemeyer-Peppas were analyzed with obtained release data's.

Stability studies [21-22]

The stability study of the selected formulations was carried out according to ICH guidelines at 40±2°C/75 ±5% RH for three months by storing the samples in stability chamber.

RESULTS AND DISCUSSION

FTIR spectroscopic analysis was carried out to ascertain whether there is any interaction between drug and excipients used (Fig1).

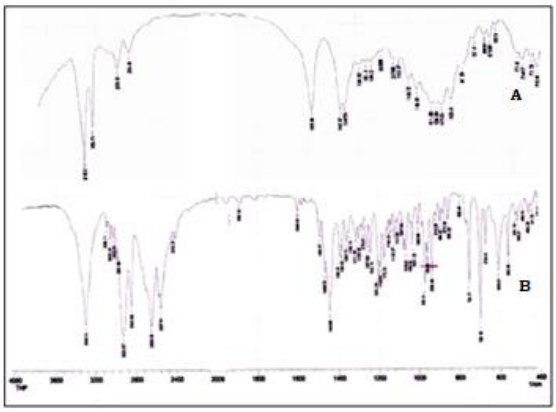

Fig 1. FTIR Spectrum of a) pure Trihexyphenidyl HCl; b) FDT of containing Trihexyphenidyl HCl (F8)

The IR spectra of pure drug shows characteristic functional peaks[23] were at 3303 cm^{-1} (for OH stretching), 3023 cm^{-1} (for Aromatic C-H stretch), 936cm^{-1} (for C-N) and 700 cm^{-1} (for C-H bending) and peaks were observed in the formulation FTIR spectra as well. This confirms the absence of any interaction between the drug and excipients used in the preparation.

Tab 2. Illustrates Pre-Compression parameters of powder blends

Formulations	Angle of Repose (θ) ± SD	Bulk Density (g/ml) ± SD	Tapped Density (g/m) ±SD	Carr's Index (%)±SD	Hausner's Ratio ±SD
F1	27.97±0.04	0.44±0.062	0.64±0.028	14.87±0.62	1.52±0.002
F2	28.64±0.05	0.41±0.022	0.61±0.040	13.72±0.28	1.51±0.006
F3	27.65±0.07	0.42±0.064	0.68±0.034	10.71±0.72	1.12±0.009
F4	26.32±0.08	0.38±0.030	0.67±0.055	15.46±0.99	1.18±0.012
F5	25.71±0.09	0.43±0.055	0.71±0.086	13.81±0.75	1.56±0.011
F6	26.93±0.06	0.41±0.014	0.70±0.022	14.96±0.49	1.54±0.007
F7	27.65±0.05	0.36±0.028	0.62±0.036	10.24±0.63	1.51±0.006
F8	26.99±0.05	0.44±0.052	0.60±0.026	12.60±0.88	1.44±0.001

Tab 3. Shows the post-Compression parameters of Trihexyphenidyl HCl tablets

Formulations	Thickness (mm) ± SD	Hardness (kg/cm2) ± SD	Weight Variation (mg) ± SD	Friability ± SD	Disintegration time (Sec) ± SD	Wetting time (Sec) ± SD	Water absorption ratio ± SD	Content uniformity (%)±SD
F1	4.51± 0.040	3.23 ± 0.12	372.54 ± 0.33	0.52± 0.18	40.16± 0.61	42.22± 0.25	91.68± 0.16	98.27± 0.63
F2	4.75± 0.039	3.11 ± 0.31	374.15 ±0.32	0.60± 0.14	33.11± 0.42	28.90± 0.11	89.27± 0.22	96.99± 0.55
F3	4.58± 0.055	3.62 ± 0.25	371.48 ±0.64	0.52± 0.19	24.51± 0.23	44.45± 0.20	107.42± 0.48	99.81± 0.32
F4	4.27± 0.045	3.26 ± 0.13	369.41 ±0.23	0.58± 0.11	14.20± 0.55	26.15± 0.24	90.65± 0.55	98.85± 0.24
F5	5.02± 0.049	3.59 ± 0.23	372.60 ±0.21	0.59± 0.16	17.86± 0.82	34.75± 0.35	82.36± 0.77	97.81± 0.24
F6	4.83± 0.048	3.22 ± 0.37	369.41 ±0.33	0.49± 0.14	56.52± 0.41	32.65± 0.53	95.28± 0.94	98.92± 0.85
F7	4.77± 0.052	3.31 ± 0.34	370.30 ±0.12	0.54± 0.10	18.52± 0.84	28.90± 0.47	90.91± 0.68	96.96± 0.34
F8	4.56± 0.050	3.40 ± 0.06	374.55 ±0.28	0.61± 0.20	10.69± 0.76	32.98± 0.58	92.69± 0.74	99.84± 0.49

For each designed formulation, blend of drug and excipients was evaluated for precompression properties shown in table 2. The values for angle of repose were found in the range of 25.71 ± 0.09θ to 28.64 ± 0.05θ. This indicates good flow property of the powder blends. Bulk densities and tapped densities of various formulations were found to be in the range of 0.36±0.028 to 0.44±0.052 (g/ml) and 0.60±0.026 to 0.71±0.086

(g/ml) respectively. Compressibility index and Hausner's ratio of the prepared blends/granules fall in the range of 10.24 ± 0.63 to 15.46 ± 0.99 % and 1.12 ± 0.009 to 1.56 ± 0.011 respectively which indicates that the blends have the excellent flow property and strength for compression. The prepared tablet was in round without any surface imperfections. No tablet defects were observed during direct compression.

The physical parameters for the prepared tablets such as weight uniformity, hardness, friability and drug content were found to be as per the standards of official compendium.

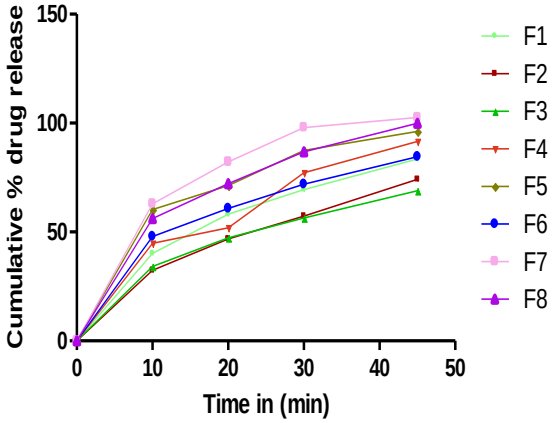

Fig 2: Shows *in vitro* drug release of F1 to F8 tablet formulations

Tablets from each batch show immediate disintegration ranges from 10.69 ± 0.76 to 56.52 ± 0.41 seconds. F8 formulation showed least disintegration time, which composition of merely sodium starch glycolate, which acts by swelling on contact with aqueous medium. SSG containing FDTs which showed the next highest water AR value and the longest WT to F3 prepared crospovidone.

Crospovidone containing FDTs which showed the highest water AR value of 107.42±0.48 and longest WT 44.45±0.20 seconds, possibly due to its porous particle morphology might draw water into the tablets through capillary action. However disintegration time was at 24.51±0.23 which may caused due to swelling of SSG be accompanied by gelling this could possibly occlude the pores in the tablet preventing further penetration of water into the tablet matrix hence the delay observed in the DT^{24} of these tablets which were prepared with combination of crospovidone and SSG. The results from disintegration test; it was observed that contribution of excipients such as MCC, PGS, and Aerosol shown no differences in DT and dissolution profile either.

Dissolution profile of the formulations is as shown in Figure 2. Formulation F7 and F8 shows 100% drug were released in 30 & 35 minutes respectively. From drug release it was observed that formulations containing merely SSG show higher dissolution rate relatively than combination of SSG and CP. The results of kinetics study shows best fitted to Higuchi model which explains the diffusion controlled release mechanism.

CONCLUSION

Overall result indicates that formulation (F8) contains composition merely SSG as superdisintegrants (6%) was better one and satisfies all the criteria as fast dissolving tablet rather than combination with crospovidone. Stability study shows that that there was no significant change in hardness, friability, drug content, and dissolution profile of the selected formulation. Thus SSG alone can be successfully used in the

formulation of fast disintegrating tablets.

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