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FORMULATION AND EVALUATION OF FAST DISSOLVING UNCOATED TABLETS OF DROTAVERINE HCL

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ABSTRACT

In the present work, fast dissolving tablets of drotaverine HCl were prepared by direct compression method with a view to enhance patient compliance The aim of the present research work was to formulate drotaverine HCl tablets using Ac-Di-Sol Superdisintigrant, which is already used as antispasmodic drug. It was selected to enhance solubility and consequently bioavailability of Drotaverine HCl, by determining the Quality assurance parameters during manufacturing, which influence the dissolution behavior of the drug hence its bioavailability.

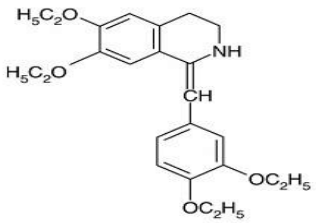
KEYWORDS: Fast dissolving tablets, drotaverine HCl & Ac-Di-Sol Superdisintigrant.

INTRODUCTION

Numerous patients express complexity in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. Current advances in novel drug delivery systems endeavor to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach led to development of fast dissolving tablets.[1] The main aim of design fast dissolving tablets is to increase the bioavailability of the poorly soluble drugs. These are conveniently administrable to the pediatric and geriatric patients who are suffering from swallowing of solid dosage forms orally.[2-3]

Benefits of Fast Dissolving Drug Delivery System[4-5]	Limitations of Fast Dissolving Drug Delivery System[6]
Administered without water, anywhere and anytime. Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated. Beneficial in cases such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.	The tablets usually have insufficient mechanical strength. Hence careful handling is required. The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Drotaverine hydrochloride, 1-[(3, 4-diethoxy phenyl) methylene]-6, 7-diethoxy-1, 2, 3, 4-tetra hydroisoquinolene is an analogue of papaverine.[4] It is phosphodiesterase IV enzyme inhibitor and acts as an antispasmodic agent, specific for smooth muscle spasm and pain, used to reduce excessive labor pain.[5] Drotaverine hydrochloride is official in Polish Pharmacopoeia.[7]

Drug (Drotaverine hydrochloride) description[8]	
IUPAC Name	(*Z*)-1-(3,4-diethoxybenzylidene)-6,7-diethoxy-1,2,3,4-Tetrahydroisoquinoline
Structure	
Molecular formula	$C_{24}H_{31}NO_4$. HCl
Molecular Weight	433.97
Description	Light yellow or slightly greenish yellow crystalline powder, almost odourless
Solubility	Sparingly soluble in water, soluble in ethanol(96%), freely soluble in chloroform, slightly soluble in acetone, practically insoluble in petroleum ether.
Therapeutic category	Antispasmodic

In the present works an attempt was made to study preformulation parameters of Drotaverine HCl which helps to generate information useful in developing stable and Bioavailable dosage forms.

MATERIAL AND METHODOLOGY

Procurement of Drug: Drug (Drotaverine hydrochloride) was obtained as a gift sample from Provizer Pharmaceutical, Surat.

Formulation of Drotaverine HCL tablets

Preparation of Granules

The Granules was prepared by wet granulation method. Sifted Drotaverine HCl with starch through 40# and mixed well. Binder solution was prepared by dissolving Gelatin and PVP-30, and after that dissolves Sodium starch Glycolate in the above binder solution. The granules were kept for drying in FBD. Passed the dried granules through 20# and check the LOD. For lubrication, filter Magnesium stearate through 40# and mixed with dried granules.

Formulation of core tablets

Table 1: Core Tablets Were Formulated as Per Formula.

S.no	Ingredient	Quantity (mg/tablet)
1	Drotaverine HCl	83.3
2	Lactose monohydrate	34.1
3	Ac-Di-Sol	5.6
4	Cross Povidone (CP)	2.8
5	PVP K 30	6.6
6	Sodium starch glycolate	6.6
7	Magnesium stearate	4.4
8	Methylene Chloride	q.s.
Total		143.6

Preparation of Tablets

Drotaverine HCL tablets were formulated as per the formula given in the table 1. Each tablet was of 145 mg containing 80mg of the drug and rest excipients. The granules were kept for drying in FBD. The granule was mixed in appropriate quantities of talc (as glidant) and magnesium stearate (as an lubricant and antiadherent). The above dried granules were subjected to compression. Compression was done on 27 station B tooling single rotary machine, using Standard concave 8.0 mm punch plain on both sides.

Characterization of Blends[9-13]

The quality of tablet, once formulated by rule, is generally utter by the quality of physiochemical properties of blends. There are many formulations and process variables involved in mixing step and all these can affect the characteristics of blend produced. The characterization of blend done for the flow property of powder that are:

Bulk Density

Apparent bulk density (ρ_b) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula.

$$\rho_b = \frac{M}{V_b}$$

Tapped Density

The measuring cylinder containing a known mass of blend was tapped 100 times using density apparatus. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using the formula.

$$\rho_t = \frac{M}{V_t}$$

Compressibility Index

The simplest way for measurement of flow of powder is its compressibility, an indication of the ease with which a material can be induced to flow is given by Compressibility (Carr's) index (I) which is calculated as follows

$$I = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

Where, ρt = Tapped density;

ρb = Bulk density

Hausner Ratio

Hausner ratio (HR) is an indirect index of ease of powder flow. It is calculated by the following formula.

$$H_r = \frac{\rho_t}{\rho_b}$$

Where, ρ_t is tapped density and ρ_b is bulk density.

Lower Hausner ratio (< 1.25) indicates better flow properties than higher ones (> 1.25).

Angle of Repose

Angle of Repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a specified cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the formula.

$$\tan\theta = \frac{h}{r};$$

Therefore, $\theta = tan^{-1}\left(\frac{h}{r}\right)$

Evaluation of Tablets

General Appearance

The tablet were examined for their general appearance like tablet shape, colour, presence or absence of odour, taste.

Weight Variation Test

The variation of weight of individual tablet is a valid indication of the corresponding variation in the drug content. Twenty tablets were selected at random and their average weight was determined using an electronic balance. The tablets were weighed individually and compared with average weight. It is done in order to ensure uniformity in the weight of tablet in a batch.

Weight variation tolerance for uncoated tablets (IP1996)[14]

Average weight of tablet(mg)	Maximum % difference allowed
130 or less	10
130-324	7.5
More then 324	5

Hardness determination

The hardness of three tablets from each batch was measured by using hardness tester of Monsanto hardness tester.

Friability test

Friability was determined taking 20 tablets. Tablets samples were weighed accurately and placed in Roche's Friabilator. After the rotations at given specifications (100 revolutions at 25 rpm), loose dust was removed from the tablets. Finally tablets were weighed and determine the friability. Friability is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport.

$$\%Friability = \frac{W1 - W2}{W1} \times 100$$

Where, **W1**= Weight of tablet before test

W2= Weight of tablet after test

Disintegration test

Disintegration was evaluated to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. In disintegration test, measured using USP tablet disintegration test apparatus using 900 ml of distilled water without disk at room temperature (37±20C).

RESULT AND DISCUSSION

Granules were prepared by the wet granulation method. Drotaverine HCl granules were prepared successfully. Pre-compression study of powder was studied. The powder blend was evaluated for the blend property like bulk density, tapped density, Carr's index, Angle of repose and Hausner's ratio. The results obtained are tabulated in table(2-6). Angle of repose is characterized to the flow rate. In general, when angle of repose $\theta \geq 40^{\circ}$ indicates a powder with poor flowability. It is a parameter that is dependent on interparticulate friction and cohesion. Bulk density depends on the density of powder particle and the spatial arrangement of particles in the powder bed. The tapped density is an increased bulk density attained after mechanically tapping a container containing the powder sample. The tapped density values were greater than bulk density in accordance with the principle. No major difference in bulk and tapped density was observed for all the formulations. Carr's employs angle of repose and compressibility value measuring together with angle of internal friction to arrive a flow for a particular material. This property of powder is also known as compressibility index. It is indirectly related to the relative flow rate, cohesiveness and particle size. The value between 13-20% indicates a powder with usually good flow characteristics above 21% indicates poor flow ability. The Hausner ratio was found to be in range of 1.10-1.24. The hausner ratio measures the flow properties of powders. A hausner ratio of <1.25 indicates a powder that is free flowing whereas >1.25 indicate poor flow ability. Thus the result obtained is within limits and the granules will not posses any problem during tableting. On the basis of obtained result of Angle of repose, Bulk density, Tapped density, Carr's compressibility index and Hausner's ratio represents the data within limit. The tablet were characterized for their physical characteristic like general appearance, thickness, friability, hardness, weight variation, disintegration time. The result was tabulated in table 7-10. The result showed that

there were variations in the weight of the tablets and all tablets were found to be within the limit for weight variation. Thicknesses of tablets were found to be 2.60-2.67mm and the hardness of the tablets were found to be 4.75-5.10kg/cm^2 which are in the limit. The tablets showed % friability in the range of 0.46-0.55% which was within the limit. The disintegration time was determined by disintegration apparatus and found to be within the range 4.01-5.45 minute. This study represents that Disintegration time of Drotaverine HCl can be improve with the help of superdisintegrant Ac-Di-Sol, which is best superdisintegrant crosslinked Sodium Carboxymethylcellulose. It is effective at very low concentration has enhanced long term stability and facilitates quick disintegration and dissolution in drotaverine HCl tablet granules and other dosage form.

Table 2: Tabular representation of Angle of repose of powder.

Batch code	Angle of repose	Inference
F1	26º51’	Satisfactory
F2	25º04’	Satisfactory
F3	27°12’	Satisfactory
F4	25°69’	Satisfactory
F5	28°40’	Satisfactory

Table 3: Tabular Representation of Bulk and Tapped Density.

Batch code	Bulk Density gm/cm^3	Tapped density gm/cm^3
F1	0.76	0.87
F2	0.73	0.83
F3	0.72	0.80
F4	0.68	0.82
F5	0.69	0.78

Table 4: Tabular representation of Carr’s index.

Batch code	Carr’s Index	Inference
F1	16.20	Excellent flow
F2	18.24	Excellent flow
F3	15.26	Excellent flow
F4	19.70	Excellent flow
F5	19.90	Excellent flow

Table 5: Tabular Representation of Hausner’s Ratio.

Batch code	Hausner’s ratio	Inference
F1	1.16	Good
F2	1.10	Good
F3	1.24	Good
F4	1.21	Good
F5	1.19	Good

Table 6: Tabular presentation of flow ability parameters of powder system.

Batch code	Angle of repose (º)	Bulk density(gm/cm$^{2)}$	Tapped density(gm/cm$^{2)}$	%Compressibility Index	Hausner ratio
F1	26º51’	0.76	0.87	16.20	1.16
F2	25º04’	0.73	0.83	18.24	1.10
F3	27°12’	0.72	0.80	15.26	1.24
F4	25°69’	0.68	0.82	19.70	1.21
F5	28°40’	0.69	0.78	19.90	1.19

Table 7: Tabular representation of thickness of formulated tablets.

S.No	Batch code	Thickness(mm)	Mean
1	F1	2.65 2.58 2.57	2.60
2	F2	2.66 2.62 2.59	2.62
3	F3	2.63 2.62 2.58	2.61
4	F4	2.68 2.64 2.65	2.65
5	F5	2.70 2.65 2.68	2.67

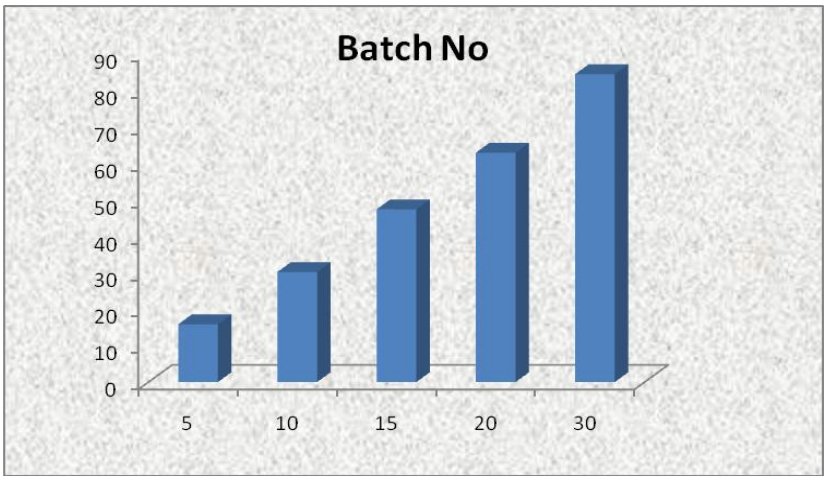


Fig. 1: Histogram representing the thickness of various formulations.

Table 8: Tabular representation of Hardness of formulated tablets.

S.No	Batch code	Hardness(Kg/cm^2)	Mean
1	**F1**	4.72 5.30 4.78	4.93
2	**F2**	4.90 5.32 4.76	4.99
3	**F3**	5.22 4.98 5.12	5.10
4	**F4**	4.79 5.04 4.82	4.88
5	**F5**	4.90 4.67 4.70	4.75

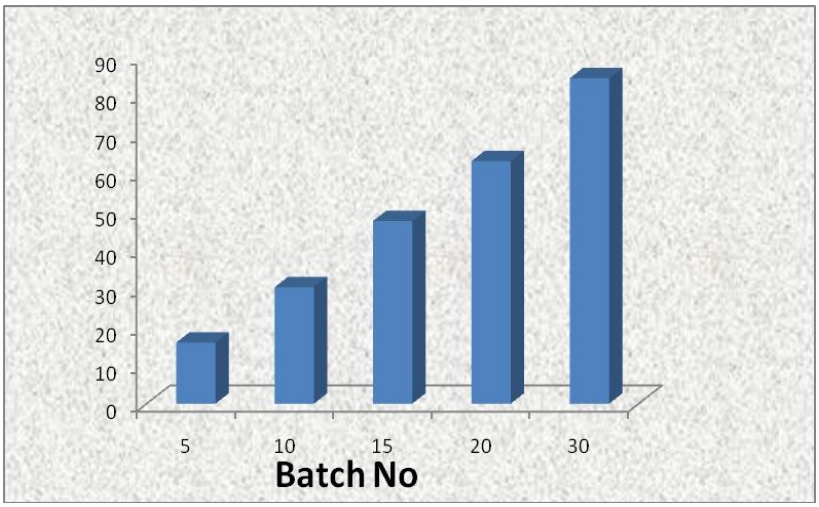


Fig. 2: Histogram representing the hardness of various formulations.

Table 9: Friability of Various formulated batches.

S.No	Batch code	Friability (%)	Mean
1	F1	0.69 0.52 0.46	0.55
2	F2	0.53 0.70 0.65	0.62
3	F3	0.60 0.45 0.57	0.54
4	F4	0.60 0.56 0.30	0.48

5	F5	0.49 0.43 0.46	0.46

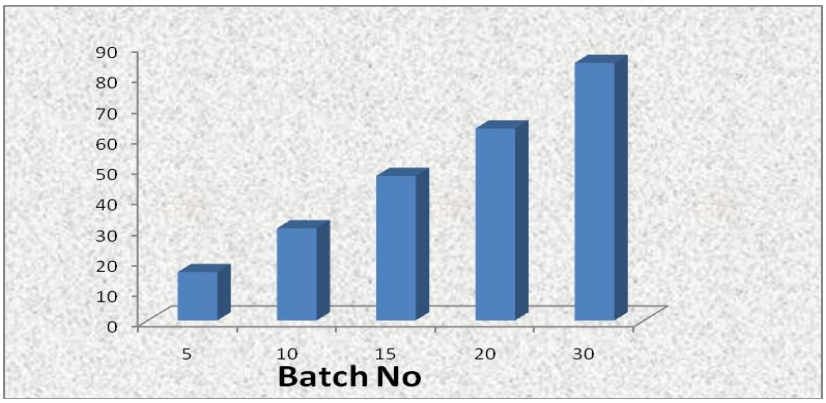


Fig. 3: Histogram representing the Friability of various formulation batches.

Table 10: Disintegration results of various formulated batches.

S.No	Batch code	D.T(min)	Mean
1	**F1**	4.42 4.49 4.60	4.50
2	**F2**	5.22 5.70 5.44	5.45
3	**F3**	4.55 4.72 4.56	4.61
4	**F4**	3.96 3.88 4.20	4.01
5	**F5**	4.65 3.91 4.11	4.22

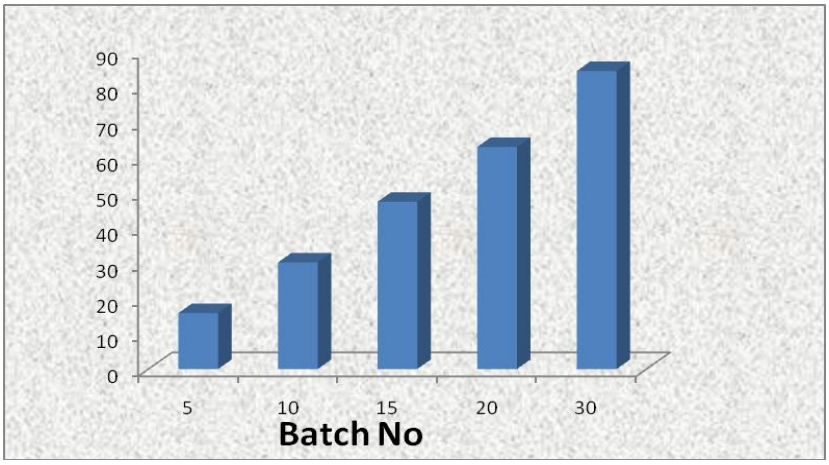


Fig. 4: Histogram the D.T. of various formulated tablets.

CONCLUSION

In the present work it was conclude that we are able to achieve our objective of preparing fast dissolving tablets of Drotaverine HCL with natural excipients and simple method of manufacture and enhance the dissolution of the drug. Drotaverine HCl is an antispasmodic drug, structurally related to papaverine prescribed for pain and dysfunction caused by smooth muscle spasm. One of the major problems with this drug is high variability in the bioavailability and solubility. The formulated fast dissolving tablet formulation was selected to enhance solubility and consequently bioavailability of Drotaverine HCl, by determining the Quality assurance parameters during manufacturing, which influence the dissolution behavior of the drug hence its bioavailability.

REFERENCES

1. S.B. Shisand, Sarasija Suresh, P.V. Swamy, D. Nagendra Kumar & M.V. Rampura. Design and Evaluation of Fast Dissolving Tablets of Clonazepam. Indian Journal of Pharmaceutical Sciences, 2008; 1: 792.
2. Chirravuri S Phani Kumar, J Vijaya Ratna, Pvvsn Aditya, SK Raakhiya, SV Sunitha, S Revathi. Formulation and Evaluation of Fast Dissolving Tablets of Paracetamol Using Oats Powder. International Journal of Pharmaceutical Science Invention, 2016; 5: 3,7.
3. Himesh Soni & A.K. Singhai. Formulation and Development of Hydrogel Based System for Effective Delivery of Rutin. IJAP, 2013; 5(1): 5-13.
4. Agrawal, P., Rajput, S., Pathak, A., A Magical Novel Drug Delivery System. World Journal of Pharmacy And Pharmaceutical Sciences", 2012; 1(1): 439-455.
5. Alderman D.A., A review of cellulose ethers in hydrophilic matrices for oral controlled-release dosage forms. International Journal of Pharmaceutical Technologyproduction, 1984; 5: 1-9.
6. Kandharkar Kaustubh Review on Industrial Process Validation of Tablet Dosage Form International Journal of Interdisciplinary and Multidisciplinary Studies (IJIMS), 2014; 1(4): 112-124.
7. Dahivelkar PP, Bari SB. Simultaneous derivative and multi-component spectrophotometric determination of Drotaverine hydrochloride and Mefenamic acid in tablets. Indian J. Pharm. Sci., 2007; 69: 812-4.
8. National Center for Biotechnology Information. PubChem Database. Drotaverine, CID=1712095, https://pubchem.ncbi.nlm.nih.gov/compound/Drotaverine (accessed on Nov. 12, 2019).

9. Indian Pharmacopoeia, "Government of India Ministry of health & family welfare", The Indian Pharmacopoeia commission, Ghaziabad, 2010; 2: 1331-1333.
10. Indian Pharmacopoeia, Ministry Of Health And Family Welfare, Indian Pharmacopoeia commission, 2010; 2: 104.
11. Jagdale S.C., Kuchekar B.S., Preparation &in vitro evaluation of Alluprenol Gelucire 43/01 50/13 Solid dispersion, International Journal of Pharmaceutical Sciences, 2010; 6: 60-67.
12. Jatav R.K., Gandhi Yogesh K., Jatav Rakesh K., "Formulation development and evaluation of controlled release tablets of Famotidine", 2012; 3(4): 858-866.
13. Jayswal BD, Yadav VT, Patel KN, Patel BA, Patel PA, Formulation and Evaluation of floating insitu gel based Gastro retentive drug delivery of cimetidine, International Journal for Pharmaceutical Research Scholars, 2012; 1: 327-337.
14. Raymond C. Rowe. Paul J Sheskey, Marian E Quinn. Handbook of pharmaceutical excipient, sixth edition. Pharmaceutical Press, 2009; 345-348.