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Study depicting impact of variation of compression speed on Tablet dosage forms formulated with Ibuprofen, Loperamide hydrochloride and Cetirizine dihydrochloride as active ingredients

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Abstract

During manufacturing of tablet dosage forms, monitoring of processing parameters of machines/equipments play an important role in inherent qualities of manufactured tablets. If these processing parameters are not controlled as per defined specifications mentioned in batch manufacturing record of said batch, then it will impact its ideal characteristics/physical properties as well as its performance and effectiveness in biological system. Therefore it is very important to monitor processing parameter like speed of compression machine during compression stage of tablet manufacturing. In this study, an attempt has been made to demonstrate impact of variation of processing parameter (compression machine speed) on ideal properties like weight variation, hardness, disintegration time and friability of tablet dosage form manufactured by using active materials of Ibuprofen, Loperamide Hydrochloride and Cetirizine Dihydrochloride.

In this study individual tablet dosage forms have been formulated by using mentioned active drugs along with similar excipients. Individual tablets samples were collected after subjecting compression machine to slow, optimum and fast compression speed for carrying out respective in-process tests of weight variation, hardness, disintegration time and friability test. Thereafter an comparative analysis have been made through this study to demonstrate impact of compressing machine speed on ideal characteristics of tablet dosage forms.

Keywords: Tablet Dosage Form, Weight variation, Hardness, Disintegration time, Friability

Introduction

Tablets may be defined as solid unit dosage form which contains one or more drugs with or without excipients[7]. Tablets and capsules are used worldwide on a large scale and can be considered as largest used dosage form. According to Indian Pharmacopoeia, pharmaceutical tablet are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs with or without diluent. The excipient can be a diluent, binder, granulating agent, glidant, lubricants, etc. and are needed in tablet formulation to ensure properflow property to the powdered blend and to provide strength to withstand mechanical shocks during the course of its production, packing and transportation.[8,9,10,11,12]

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A tablet property varies with the type of excipients like disintegrants used in tablet formulation[1]. During manufacturing of tablet, monitoring of processing parameters of machines/equipments plays an important role in inherent qualities of produced tablets. The compression speed and the tablet dimensions, can affect the mechanical strength of the resulting tablet[4]. A change in the compression speed significantly affects the deformation of the material[5,6]. If these processing parameters are not controlled as per defined specifications mentioned in batch manufacturing record of said batch then it will impact its ideal characteristics/physical properties as well as its performance and effectiveness in biological system. For example if hardness of tablet increases then it will also increase disintegration time of respective tablet, which will result into slow dissolution and consequently slow absorption of drug in the biological system. This will finally impact pharmacokinetic profile of drug in the biological system. The properties of tablet are affected by both the ingredients as well as the processing parameters. In recent years many new research works have been conducted with respect to nanoparticles and nano-crystals so as to increase drug solubility, dissolution and absorption by use of nanoparticle or Nano-crystals to increase bioavailability of poorly water soluble drugs[2]. Many research work have been done to characterizes and compared various physico-chemical properties like hardness, weight variation, friability, and disintegration time, in vitro dissolution profile of drugs.

In the proposed study an attempt has been made to demonstrate impact of variation in processing parameter (Compression machine speed) on ideal properties of tablet like weight variation, hardness, disintegration time and friability.

Material and Methods

A. Materials:

Following materials were used in the manufacturing of tablet dosage form by processing them through processes of shifting (for segregation of powdered material into mass of uniform particle sizes) and blending (for uniform distribution of drug material in the resulted blend) before subjecting them into the compression machine for compression process which produces tablets dosage form. Individual tablet dosage forms have been manufactured by using below mentioned excipients as well as active drug molecules (API) of Ibuprofen, Loperamide Hydrochloride, and Cetirizine Dihydrochloride by subjecting them to variable compression speeds (low, optimum and maximum speed) which were individually subjected for evaluation of physicochemical properties of tablet dosage form,

1. Loperamide Hydrochloride
2. Ibuprofen
3. Cetirizine Dihydrochloride
4. Potato Starch
5. Microcrystalline Cellulose
6. Alginic Acid
7. Povidone K90
8. Magnesium Stearate
9. Colloidal Anhydrous silica
10. Sodium Starch Glycolate
11. Croscarmellose Sodium
12. Sodium Lauryl Sulphate

Separate tablet formulations containing Ibuprofen, Loperamide hydrochloride and Cetirizine Dihydrochloride as active material (API) have been manufactured by using above mentioned materials(Individual drug and excipients). During compression process for production of tablets, compression machine was subjected to three different speeds ie, slow, optimum and maximum. Tablets were collected from each speed range and individual samples were taken from each speed range for carrying out analysis of these tablets to evaluate impact of variation of speed of compression machine on physicochemical properties (ie. Hardness, weight variation, friability, disintegration time etc.)of resulted tablets.

B. Equipments Used:

Equipments like hardness tester, disintegration test apparatus, friabilator, vernier caliper, sifter, Rapid Mixer Granulator, Blender and Compression machine were used in this research work.

C. Method:

Separate powdered mass of above materials containing individual drug as active material, was processed through following steps to produce tablets containing

Ibuprofen, Loperamide Hydrochloride and Cetirizine Dihydrochloride drug molecule.

- Sifting
- Pre-mixing
- Blending
- Compression

Following process was followed for manufacturing of individual tablet dosage forms containing Ibuprofen, Loperamide hydrochloride and Cetirizine Dihydrochloride as active materials.

Sifting of materials:

Shifting of powdered mass through 20# sieve size have been carried out to get powdered mass of uniform particle size.

Sifting of active drug, Microcrystalline cellulose, potato starch, povidone K-90, colloidal anhydrous silica, alginic acid, magnesium stearate, sodium lauryl sulphate, sodium starch glycolate, crosscarmellose sodium through 20# sieve was performed to get sifted material of uniform particle size.

Pre- mixing:

Above shifted mass containing individual active drug was then subjected to premixing stage for uniform mixing of powder material for proper distribution of drug molecule throughout the powdered mass.

Sifted material of active drug, microcrystalline cellulose, potato starch, povidone K-90 were loaded in the rapid mixer granulator (RMG) and mixed for 15 min at slow speed with chopper in off mode.

Blending:

Premixing stage is followed by blending process wherein pre-mixed powdered mass was subjected to blending process to get the blend of uniform drug distribution and to lubricate the powdered mass with lubricating materials so as to enable smooth compression process.

Sifted colloidal anhydrous silica, alginic acid, magnesium stearate, sodium lauryl sulphate, sodium starch glycolate, croscarmellose sodium were loaded into the blender and mixed for 3 minutes at 24 RPM to get powdered blend of uniform drug distribution.

Compression:

Above powdered blend was then subjected to compression process which was carried out in compression machine. Above powdered mass was loaded in the hopper of compression machine and compression machine was set with upper punch set and lower punch set along with the die in turret assembly. Compression machine was subjected to variable machine speed to evaluate the impact of processing parameter(speed) on resulted compressed tablets. Powdered. For this powdered mass was allowed to fill in die cavity for compression of powdered mass with the help of upper and lower punch set.

At control parameters compression of powdered blend was carried out by using compression machine. Compression process was carried out at below mentioned compression speed(RPM)

- Slow speed (20RPM)
- Optimum speed (30 RPM)
- Fast speed(40 RPM)

Tablets were collected from each speed range and individual samples were taken from each speed range for carrying out analysis of these tablets to evaluate impact of variation of speed of compression machine on physicochemical properties (ie. Hardness, weight variation, friability, disintegration time etc.) of resulted tablets.

Results and Discussion

Individual tablet dosage forms have been manufactured by using excipients as well as active drug molecules (API) of Ibuprofen, Loperamide Hydrochloride, and Cetirizine Dihydrochloride by subjecting them to variable compression speeds (low, optimum and fast speed) which were individually subjected for evaluation of physicochemical properties of tablet dosage form.Based on conducted research work wherein tablets dosage forms of Ibuprofen, Loperamide Hydrochloride and Cetirizine Dihydrochloride were manufactured by compression process by subjecting the compression machine to variable compression speed of slow, optimum, and fast RPM of compression machine, following results of physicochemical properties of all three tablet dosage forms were obtained.

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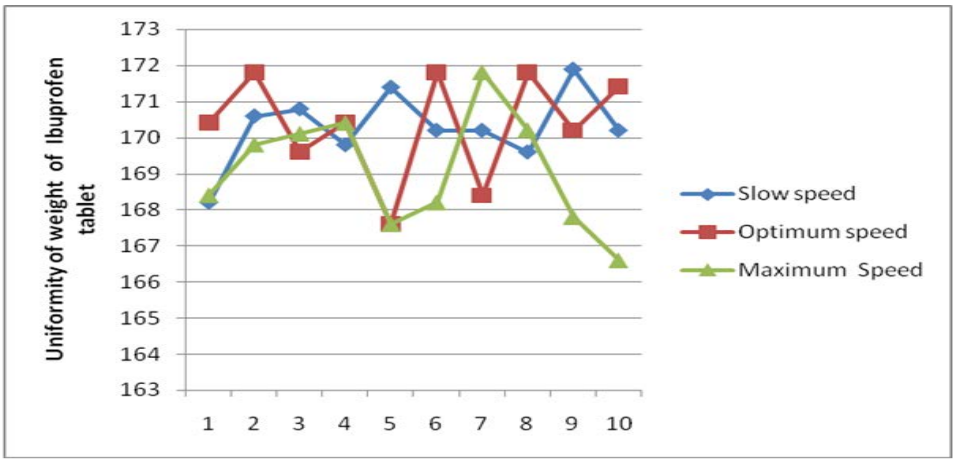
Properties	Ibuprofen tablets			Loperamide Hydrochloride Tablets			Cetirizine Dihydrochloride tablets		
	Slow (20RPM)	Optimum 30RPM	Fast 40RPM	Slow 20RPM	Optimum 30RPM	Fast 40RPM	Slow 20RPM	Optimum 30RPM	Fast 40RPM
AvgWt	170.29mg	170.34 mg	169.09 mg	171.53 mg	170.7 mg	170.16 mg	171.89 mg	171.04 mg	171.19 mg
% Maximum Weight	0.95%	0.85%	1.60%	0.74%	1.23%	0.25%	0.76%	0.44%	0.35%
% Minimum Weight	1.22%	1.6%	1.47%	1.18%	1.34%	0.79%	0.98%	0.49%	0.22%
Thick(3.0 mm to 3.3 mm)	3.15 mm	3.13 mm	2.9 mm	3.13 mm	3.14 mm	2.97 mm	3.13 mm	3.08 mm	3.01 mm
Mean hardness (Not less than 4 Kp)	5.46 Kp	5.49 Kp	4.72 Kp	6.63 Kp	7.07 Kp	5.88 Kp	7.19 Kp	7.24 Kp	6.28 Kp
Friability: (NMT 1% w/w in 4 minutes)	0.88 %	0.65%	1.18%	0.52 %	0.35 %	0.76%	0.15%	0.12%	0.35%
Disintegration Time:	1 min 15 seconds	1 min 45second	52 seconds	2 min 10 seconds	2 min 02seconds	1 min 40 seconds	3 min 48 second	3 min 58seconds	2 min 32seconds

A. Trend Analysis of Uniformity of weight of Ibuprofen tablet (Limits- 166.6 to 173.4 mg)

To determine the trend of uniformity of weights of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in uniformity of weight of Ibuprofen tablets produced at slow, optimum and fast speed of compression machine.



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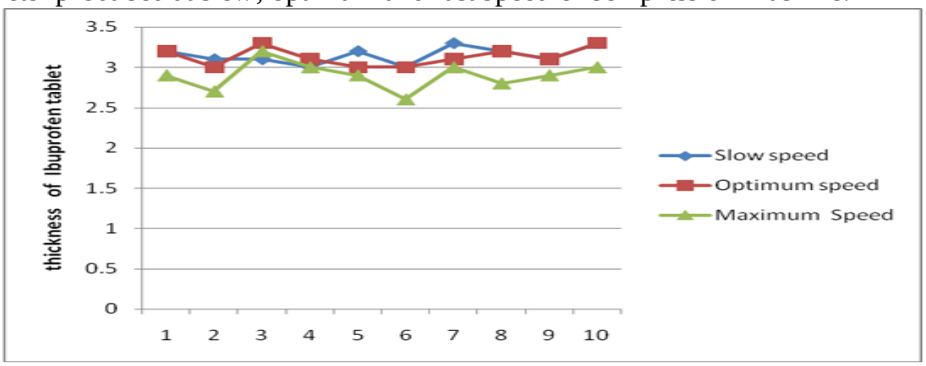
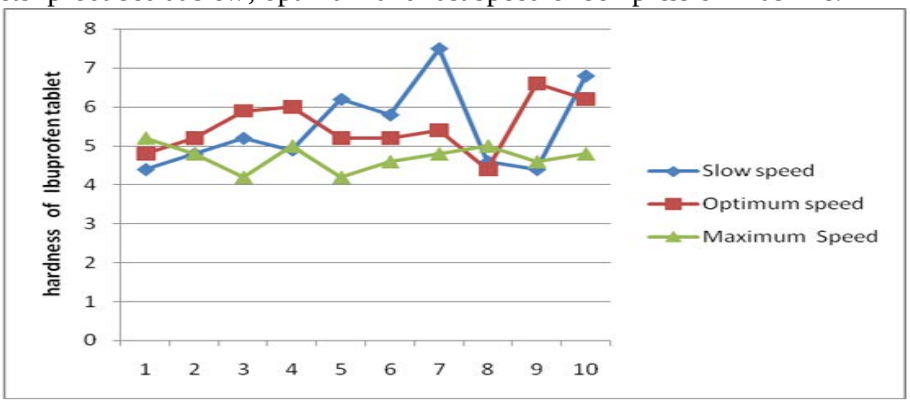
B. Trend Analysis of thickness of tablet of Ibuprofen tablet (Limit-3.0 mm to 3.3 mm)

To determine the trend of thickness of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in thickness of Ibuprofen tablets produced at slow, optimum and fast speed of compression machine.



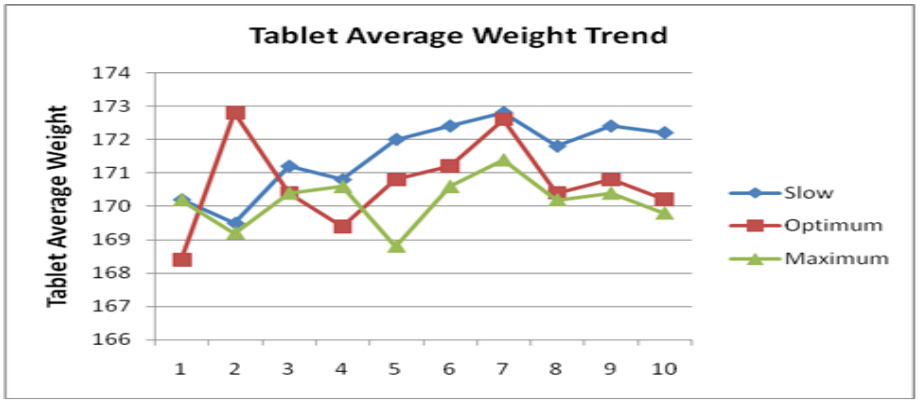
C. Trend Analysis of hardness of tablet of Ibuprofen tablet (Limit-Not less than 4 Kp)

To determine the trend of hardness of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in hardness of Ibuprofen tablets produced at slow, optimum and fast speed of compression machine.



D. Trend Analysis of Uniformity of weight of Loperamide Hydrochloride tablet (Limits- 166.6 to 173.4 mg)

To determine the trend of uniformity of weights of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in uniformity of weight of Loperamide Hydrochloride tablets produced at slow, optimum and fast speed of compression machine.



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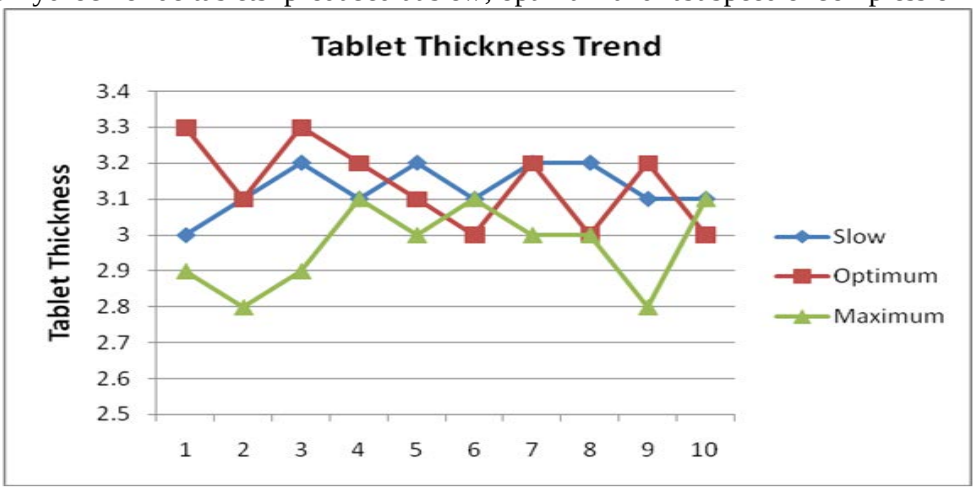
E. Trend Analysis of thickness of Loperamide Hydrochloride tablet (Limit-3.0 mm to 3.3 mm)

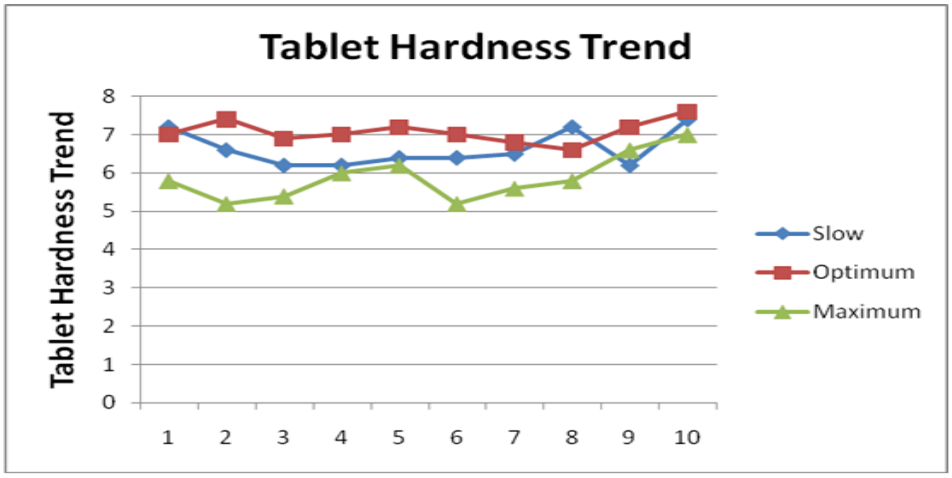
To determine the trend of thickness of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in thickness of Loperamide Hydrochloride tablets produced at slow, optimum and fast speed of compression machine.



F. Trend Analysis of hardness of Loperamide Hydrochloride tablet (Limit-Not less than 4 Kp)

To determine the trend of hardness of tablets produced at slow, optimum and fast speed of compression machine following

figure has been drawn which reflects variation of pattern observed in hardness of Loperamide Hydrochloride tablets produced at slow, optimum and fast speed of compression machine.



G. Trend Analysis of Uniformity of weight of Cetirizine Dihydrochloride tablet (Limits- 166.6 to 173.4 mg)

To determine the trend of uniformity of weights of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in uniformity of weight of Cetirizine Dihydrochloride produced at slow, optimum and fast speed of compression machine.

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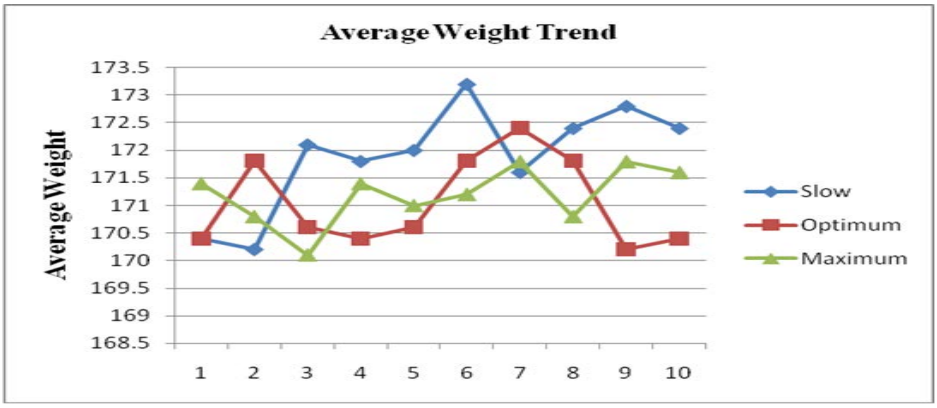
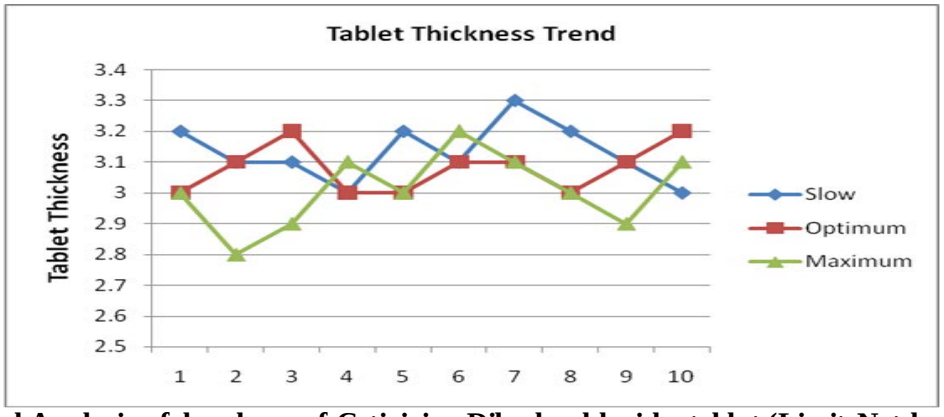


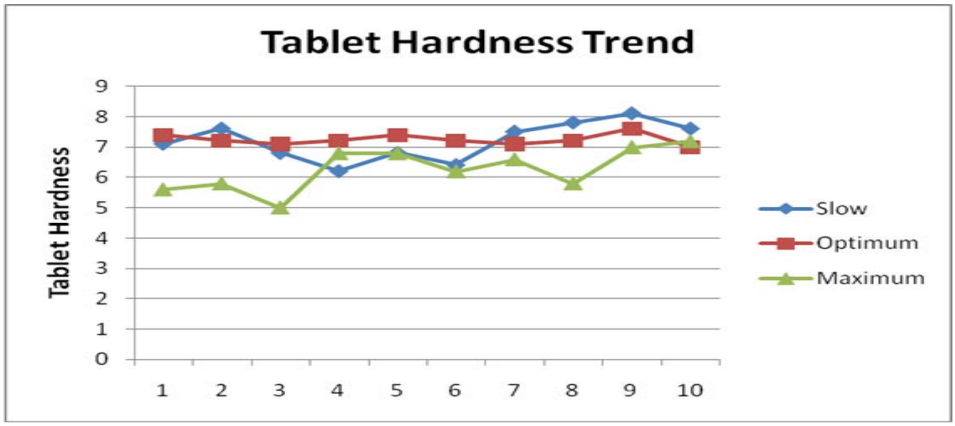
H. Trend Analysis of thickness of Cetirizine Dihydrochloride tablet (Limit-3.0 mm to 3.3 mm)

To determine the trend of thickness of tablets produced at slow, optimum and fast speed of compression machine following figure has been drawn which reflects variation of pattern observed in thickness of Cetirizine Dihydrochloride tablets produced at slow, optimum and fast speed of compression machine.



I. Trend Analysis of hardness of Cetirizine Dihydrochloride tablet (Limit-Not less than 4 Kp)

To determine the trend of hardness of tablets produced at slow, optimum and fast speed of compression machine following figure has been
drawn which reflects
variation of pattern observed in hardness of Cetirizine Dihydrochloride tablets produced at slow, optimum and fast speed of compression machine.



At same speed of compression machine, hardness of Cetirizine Dihydrochloride tablets is comparatively higher than the Loperamide Hydrochloride Tablets and Ibuprofen tablets. The observed trend of hardness was cetirizine dihydrochloride>Loperamide Hydrochloride> Ibuprofen tablets. This is attributed due to variation in physicochemical properties of these drugs.

At same speed of compression machine friability of Cetirizine Dihydrochloride tablets is comparatively lower than the Loperamide Hydrochloride Tablets and Ibuprofen tablets. The observed trend of friability was Ibuprofen tablets>Loperamide Hydrochloride Tablets> Cetirizine Dihydrochloride tablets. This is attributed due to variation in physicochemical properties of these drugs.

At same speed of compression machine disintegration time of Cetirizine Dihydrochloride tablets is comparatively higher than the Loperamide Hydrochloride Tablets and Ibuprofen tablets. The observed trend of disintegration time was cetirizine dihydrochloride>LoperamideHydrochloride> Ibuprofen tablets. This is attributed due to variation in physicochemical properties of these drugs.

This variation in hardness, disintegration time and friability among these three selected drugs can be explained based on the variation of physicochemical properties of these drug molecules.

Since Cetirizine Dihydrochloride has comparatively higher hygroscopicity followed by LoperamideHydrochloride and Ibuprofen drug molecule, therefore Cetirizine Dihydrochloridehas higher tendency to absorb moisture from surrounding environment followed by Loperamide Hydrochloride and Ibuprofen drug molecules.

This attribute of Cetirizine Dihydrochloride drug molecules added in subsequent higher binding of tablet formulation which resulted into better compaction under die cavity of compression machine when respective machine was subjected to similar conditions of machine speed (RPM).

Based on above discussion of results it can be said the ideal properties of tablets formulation like hardness, disintegration time, friability, weight variation , thickness varies as per the speed of compression machine. Whenever there is change in the speed of machine, respective parameters will show variation in its value. It has also been proved through this research work that, variation in processing parameters of machine, like speed of machine(RPM) consequently have its impact on pharmacokinetic behavior of drug molecule.

Conclusion

It can be said through this research work that physico-chemical properties of active drug molecule have major influences on the ideal characteristics of tablet formulation which in turn will affect performance of tablet formulation.

It has been proved through this research work that physical properties of tablet formulation like hardness, disintegration time, thickness, weight variation, friability etc. varies as per the variation in speed of machine. It has been proved through this research work that as the speed of compression machine increases there is drastic change in the physicochemical properties of tablet formulations like hardness, disintegration time, weight variation, friability. Hence from this it can be concluded that to get desired physicochemical properties of tablet, speed of compression machine should be monitored properly.

At higher compression speed hardness of tablet was found to be on lower side as comparison to that of at lower speed.Similarly at lower compression speed disintegration time was found to be higher than that of at high compression speed.

It can also be concluded through this study that physicochemical properties of active material also impacted the properties of tablet formulation. The variation in hardness, disintegration time and friability among these three selected drugs can be explained based on the variation of physicochemical properties of these drug molecules.

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